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# Immunohistochemical Expression of Cyclin D1 in Oral Lichen Planus

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**Abstract**
Background: Many studies have reported that a condition initially classified as oral lichen planus (OLP) has a variable chance of developing cancer progression over time, although these results are still questionable. Cyclin D1 controls the mitotic cell cycle's transition from G1 to S. Cyclin D1 has a significant function in carcinogenesis due to its critical involvement in cell cycle control. Cyclin D1 deregulation or overexpression may result in shortened G1 phase, enhanced cell replication, and decreased reliance on growth regulators, causing disruption in conventional cell cycle progression and the progression of cancer. The aim of the current study was to evaluate the expression of Cyclin D1 in histopathologically confirmed OLP samples and to predict the rate of malignant transformation in these lesions by comparing the level of expression with some clinical parameters. Materials and Methods: The immunohistochemical procedure was used to examine the expression of cyclin D1 on paraffin-embedded sections of (40) OLP lesions and (10) specimens of normal oral mucosa. We used the SPSS software version (18.0) to do the statistical analysis in this work. Results: There is a very significant difference between the people investigated (P = 0.01), which is statistically significant. CyclinD1 was found in all of the oral lichen planus cases in the research (100%), but it was also found (80%) in the normal oral mucosa. There was also no statistically significant difference between the clinical types of OLP and the Cyclin D1 scoring (P = 0.942), which revealed that the reticular type was the most frequent (7) in mild scoring, whereas the erosive type was the most frequent in severe scoring, which accounted for the majority of the cases. Conclusion: This research found that higher cyclinD1 expression increases the risk of cancer and many of the markers should be tested. Furthermore, larger sample numbers, improved designs, and gene-reduction studies should be performed. OLP patients should be continuously monitored for OSCC progression.

**Keywords:** Immunohistochemistry, CyclinD1, Malignancy, Oral Lichen Planus

## 1. Introduction

Oral lichen planus (OLP) is a mucocutaneous chronic autoimmune condition that impacts the oral mucosal surface and is widely encountered. This condition affects approximately 0.5–2.2 percent of the population (Kurago, 2016; Georgescu et al., 2017; Giannetti et al., 2018). Various antigen-specific and nonspecific processes are considered

to be involved in the development of OLP, which is categorized as a premalignant condition (Roopashree et al., 2010; Sagari et al., 2016). Despite the fact that the normal age of patients is 50 to 60 years, it is commonly seen in middle-aged women and younger-aged men, and it affects women more often than men. OLP is relatively uncommon in children and frequently occurs in combination with cutaneous disorders (Bardellini et al., 2013; Kurago, 2016; Giannetti et al., 2018). OLP appears clinically in three types: reticular, atrophic, and erosive. They are classified as either erosive (erosive abnormalities) or non-erosive (reticular and atrophic abnormalities) (Zhou et al., 2012; Lorenzini et al., 2013; Giannetti et al., 2018). It may manifest as asymptomatic reticular white streaks or as symptomatic ulcers with burning, irritability, and discomfort. OLP is now thought to be a T-cell-mediated disorder, although the specific pathophysiology remains unknown (Sugerman et al., 2002; Van der Meij et al., 2003; Lavanya et al., 2011). It's been shown in the past that immunologic pathways can play a big part in the development or spread of oral lichen planus (Van Der Meij and colleagues 2007; Agha-Hosseini et al., 2009; Lavanya et al., 2011). OLP is classified as a precancerous disease by the World Health Organization (WHO), and its most serious consequence is the development of cancer (Shen et al., 2011; Peng et al., 2017). In contrast to carcinoma, which may be anticipated by precancerous lesions that do not always lead to cancer, malignancy is a complex mechanism in which carcinoma can develop (Siar et al., 2011; Dragomir et al., 2012). The ability to multiply more cells is one of the processes required for malignancy to progress and grow (De Sousa et al., 2009). The limited range of apoptotic events in OLP epithelial cells indicates that it may provide a suitable substrate for cancer development (Bascones et al., 2005). For several years, the potential of OLP malignancy has been considered and described (Fitzpatrick et al., 2014; Giuliani et al., 2019). A meta-analysis was carried out to look at the risk variables for OLP carcinogenic transition to squamous cell carcinoma (Aghbari et al., 2017). Information sources such as PubMed and Scopus were systematically analyzed to establish the cancerous transformation rate of OLP and associated risk factors (Giuliani et al., 2019). The link between OLP and squamous cell carcinoma has aroused people's importance, and researches on this issue have been conducted (Fitzpatrick et al., 2014; Giuliani et al., 2019). While OLP is already recognized as a condition with malignant potential, its precancerous potential and how it progresses to malignancy are not entirely understood (Fitzpatrick et al., 2014). The primary impediment to examining the cancer progression of OLP is indeed the lack of broadly agreed diagnostic criteria for OLP (Gandolfo et al., 2004). Mortazavi et al. found that if OPMDs are found and treated early, they have a much lower chance of becoming cancerous (Mortazavi et al., 2014). Several studies have been conducted in an effort to establish OLP's malignant alteration risk. These investigations demonstrate that a disease initially identified as OLP may undergo malignant change over time. Nevertheless, these conclusions continue to be challenged (Mignogna et al., 2001; Tizeira et al., 2003). The evidence suggests that the most likely proportion of malignant transformation of OLP is between 0.1-3 percent (Irani et al., 2016; Hadzi-Mihailovic et al., 2017).

Furthermore, there are certain prognostic indicators that may be used to determine which chronic OLP lesions are most likely to progress. Hence, it is critical to understand the molecular pathways leading to OLP's oncogenesis in order to facilitate accurate diagnosis and the development of novel treatment options (Lavanya et al., 2011; Zuo et al., 2015). Molecular biomarkers may target individuals with possibly malignant tumors before malignant cells are detected histologically at the main location (Partridge et al., 2005). Several molecular methods have been reported to identify the transformation from healthy epithelium to precancerous lesions to cancer (Pitiyage et al., 2009). The cell cycle is controlled by cyclin-dependent kinases (CDKs) and their primary blockers, p16, p21, and p27, all of which are tumor suppressors (Poomsawat et al., 2011).

Cyclin D1 is a proto-oncogene that is encoded by the CCND1 gene and is located on chromosome 11q13. It is a part of the molecular system that observes and controls the cell cycle during the transition from the G1 to the S phase of the cell cycle (Basnaker et al., 2014; Batool et al., 2019). Cyclin D1 is the first cyclin to accumulate throughout the cell cycle; it rises during the G1 phase but is not detected during the S phase. It stimulates CDK4 and the cyclin D–CDK4 complex in the G1 phase, phosphorylates the Rb protein, and stimulates cell proliferation upon E2F liberation. Cyclin D1 overexpression is associated with a shortened G phase and aberrant cell growth. From healthy oral tissues to dysplastic abnormalities and OSCCs, cyclin D1 levels increase sequentially (Pitiyage et al., 2009; Ramakrishna et al., 2013). Previous research has suggested that CCND1 may play a significant role in the etiology of OLP (Zhang et al., 2010; Abid and Merza, 2014). Additionally, further studies have shown changes in the expression of some cell regulatory proteins in premalignant and malignant lesions of the oral cavity (Poomsawat et al., 2010). The goal of this research was to determine whether or not OLP had malignant potential

based on Cyclin D1 expression. In addition, the relationship between Cyclin D1 and clinical and histological characteristics in OLP was investigated.

## 2. Materials and methods

Forty specimens of oral lichen planus (OLP) and ten cases of normal oral mucosa were obtained from the documents of the oral pathology laboratory/oral diagnosis department/Baghdad University. Formalin-fixed, paraffin-embedded tissue blocks from each case were collected, as well as clinical information on the patient's health (age, gender, and type) as described in the oral and maxillofacial reports. Two professional pathologists independently verified the diagnosis by examining hematoxylin and eosin (H&E) stained tissue segments from each patient. Tonsil tissue was selected and used as a positive tissue control in each immunohistochemistry run in accordance with the Cyclin D1 manufacturer's data sheets. Pathnsitu/USA produced and employed primary monoclonal antibodies throughout the experiment. The PolyExcel detection system was developed for use with primary antibodies generated against mouse and rabbit to qualitatively identify proteins in paraffin-embedded normal and pathological tissues, cryostat tissues, or cellular preparations using light microscopy. PathnSitu is unequaled in terms of specificity and sensitivity. PolyExcel's two-step detection method is a non-biotin-based micropolymer-based recognition system that significantly decreases or removes background avidin or biotin levels. It is based on a polymer that is HRP-labeled and conjugated to secondary antibodies.

### *2.1. Immunohistochemical technique*

The paraffin block technique was used to obtain the control and study tissue samples. Tissue samples were sliced into two pieces following formalin fixation. In order to increase tissue adhesion during immunohistochemical staining, one 5 mm segment was put on a positively charged microscope slide, while another 5 mm section was mounted on a pre-cleaned microscope slide. As positive controls, 5 mm thick tissue sections were placed on positively charged slides. The antibody was diluted (1:50) and applied to the tissue samples for 30–60 minutes at room temperature in humid environments. The segments were thoroughly cleaned with PBS, dried, and rinsed three times with PBS (5 min. for each). As a negative control, each slide received a second tissue section stained with PBS. A drop of soluble rabbit anti-mouse antibody was incubated at 37 °C for 15 minutes before being washed twice with PBS and dehydrated. A HRP-labeled polymer was incubated at 37oC for 15 minutes with secondary antibodies before being rinsed multiple times with PBS and left to dry. This mixture was applied to the tissue slice (15–20l) and incubated at 37 °C for 5–10 minutes before being cleaned with ordinary water and dried. The slides were gently rinsed with distilled water after being immersed in Mayer's Haematoxylin for 1-2 minutes. An optical microscope was used to examine the presentations after serial dipping in alcohol and xylene, then fixing with 1-2 drops of DPX fixing medium and immediately covering with cover slips.

### *2.2. Immunohistochemical evaluation*

According to the product's datasheet, the appearance of a brown granular DAB pigment pattern within the cellular or tissue compartment targeted by primary antibodies on positive control tissue slides and the lack of darkening on negative control tissue samples indicated immunohistochemical signal specificity. The expression of CyclinD1 was assessed in a semiquantitative manner. All study presentations were evaluated independently, with no prior knowledge of any other features. Subsequently, the slides were reviewed by an expert pathologist.

### *2.3. Interpretation of immunohistochemical expression*

The severity of nuclear cyclin D1 immunoreactivity expression was assessed through the intensity scale criterion given by Sharada et al. The level score criteria were as follows: 0 indicates no definite cells, 1 indicates a mild score, 2 indicate a moderate score, and 3 indicate a strong score. For quantitative immunohistochemical analysis, The H score was computed and tallied for each sample using the formula as given below (Sharada et al., 2018).

***1× (% cells 1+) +2 × (% of cells 2+) +3× (% of cells 3+)***

The micrographs collected were organized and saved on the computer in appropriately designated files. The Imagej® program, a freely available image processing tool built in Java that operates on a computer's operating system, has been used to assess photomicrographs.

*2.4. Statistical Analysis*

In order to evaluate and appraise the results, this research used the statistical program (SPSS) version (18.0) for descriptive analysis (mean and standard deviation) and graphs (bar and pie charts, histograms) to display the information. In order to examine and evaluate the results of the research, the data analysis approaches listed below were used. The Spearman rank correlation and the Pearson correlation coefficient are both employed in inferential data analysis, in addition to chi square tests and they are utilized in the same way. The presence of a p-value of less than 0.05 was considered statistically significant.

## 3. Results

As indicated in Table 1, the general clinical characteristics of the 40 patients who participated in the current investigation are summarized. It appears that there are no distinct changes in the age group distribution of the study subjects, denoting that the chance of confirmed disease doesn't really differ according the dispersion of age categories, and also the age shifted the focus at the sixth decade of life with mean and standard deviation (52.75±12.588), (Table 1).

In regards to gender, there are no statistically significant differences between the analyzed cases, and it can be inferred that the chance of the reported analyzed disorder does not alter depending on the sex of the patients (Fig.1).

According to the results of the study, there is a highly significant difference at P=0.01 among the participants examined, and in conformance with this finding, it is reasonable to state that the statistical likelihood of documented explored disturbed patients has represented important variations according to dissemination of clinical type, as it has been clearly indicated by the wide range of patients with "Reticular" type (Table 1).

Immunohistochemical analysis showed that brown nuclear positivity of CyclinD1 was expressed in all oral lichen planus cases of the study (100%) and 8 (80%) in normal oral mucosa (Fig.3).

The analyzed results showed no significant correlation between the expression Cyclin D1 and the age groups of the studied patients, P = 0.965, but these results revealed that the highest score was in seventh decade (Fig.2). Furthermore, there was no statistically significant difference between the clinical types of the OLP and the Cyclin D1 scoring, P = 0.942, which revealed that the reticular type was the most frequent (7) in mild scoring, whereas the erosive type was in severe scoring, which accounts for the majority of the cases (5) (Table 2).

Table 1: Frequencies of age groups, gender and clinical types for the patients with OLP lesions

| **Parameters** | Age groups | Frequencies | ( % ) | P- Value |
|---|---|---|---|---|
| Age groups | ( < 40 ) | 8 | 20 | P= 0.070 Non Sig. |
| | (40-50) | 4 | 10 | |
| | (50-60) | 12 | 30 | |
| | (60-70) | 14 | 35 | |
| | ( > 70) | 2 | 5 | |
| | Total | 40 | 100 | |
| | **Mean ± SD** | 52.75±12.588 | | |
| | Male | 16 | 40 | P = 0.268 |

| | | | | |
|---|---|---|---|---|
| Gender | Female | 24 | 60 | Non Sig. |
| Clinical types | | Frequency | ( % ) | P = 0.000 Sig. |
| | Reticular | 17 | 42.5 | |
| | Erosive | 15 | 37.5 | |
| | Atrophic | 3 | 7.5 | |
| | Plaque | 3 | 7.5 | |
| | Bullous | 2 | 5.0 | |
| | Total | 40 | 100.0 | |

NS: Non Sig. at P>0.05; S: Sig. at P<0.05; Testing are based on One Sample Chi Square Test.

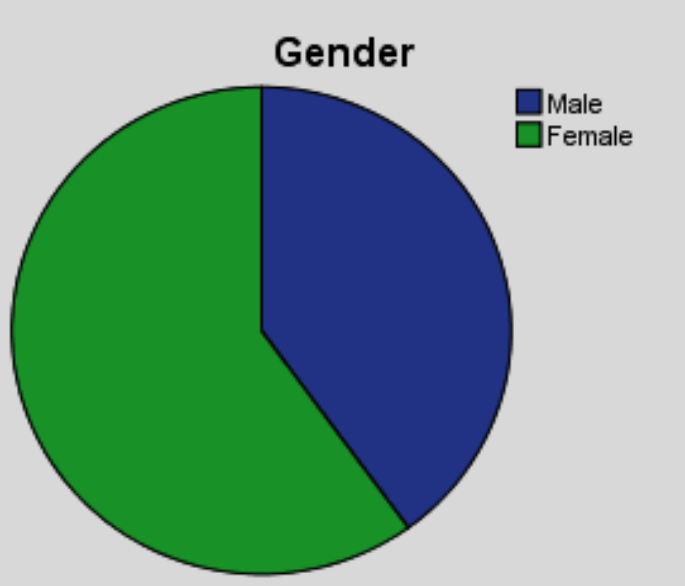


Figure 1: Pie chart shows the distribution of studied patients with OLP lesions according to gender factor.

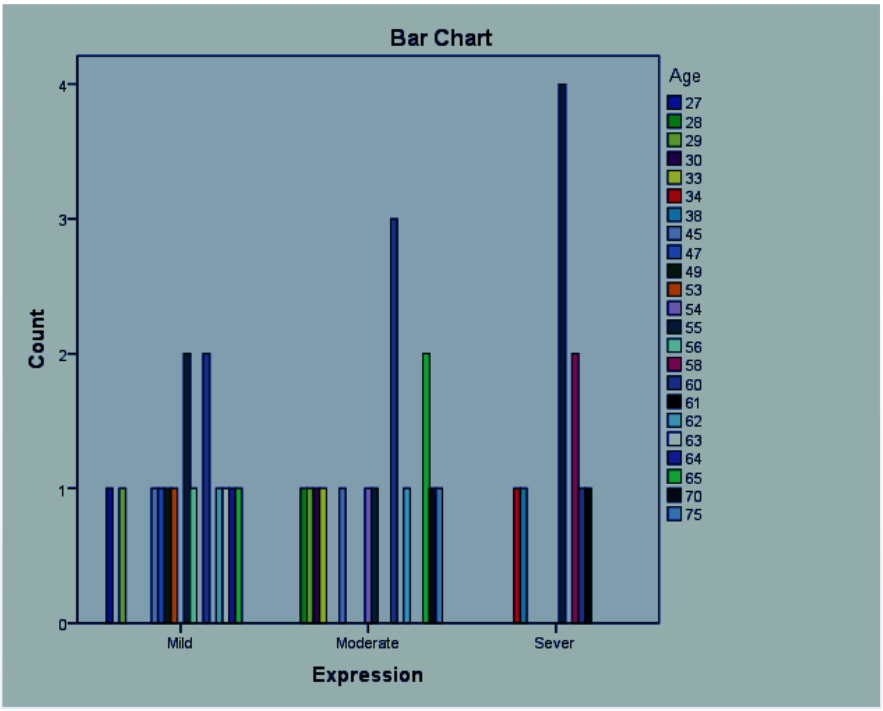


Figure 2: Bar chart shows the distribution of Cyclin D1 expression in regarding to the age groups of the patients with OLP lesions.

Table 2: Shows the frequencies of the CyclinD1 expression according to the clinical types of OLP and comparison's significant.

| Clinical types * Expression Crosstabulation | | | | | |
|---|---|---|---|---|---|
| | | Expression of Cyclin D1 | | | Total |
| | | Mild | Moderate | Sever | |
| Clinical types | Reticular | 7 | 6 | 4 | 17 |
| | Erosive | 5 | 5 | 5 | 15 |
| | Atrophic | 1 | 2 | 0 | 3 |
| | Plaque | 1 | 1 | 1 | 3 |
| | Bullous | 1 | 1 | 0 | 2 |
| Total | | 15 | 15 | 10 | 40 |

Pearson Chi-Square Test (Asymp. Sig. (2-sided), P = 0.942, Likelihood Ratio = 0.863

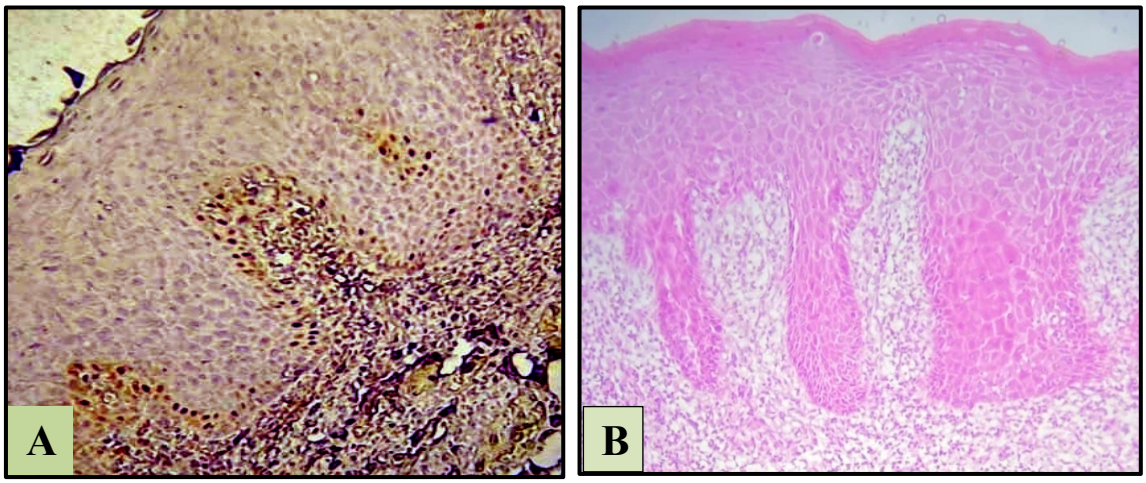


Figure 3: A- Immunohistochemical expression of Cyclin D1 in oral lichen planus, (magnification 20X), B- High power field of basal layer and subepithelial tissue of oral lichen planus (OLP) (Hematoxylin and Eosin staining, x20).

## 4. Discussion

Understanding the processes that lead to cancer development is critical in explaining how cancer develops. Oncologists may use this information to assess the likelihood of precancerous lesions progressing to malignancy and can use it to apply preventative interventions. So, in this study, we wanted to find out if Cyclin D1 was found in OLP, which is thought to be a condition that can lead to oral cancer.

Carcinogenesis, on the other hand, may arise as a consequence of unregulated cellular proliferation caused by numerous genetic changes coupled with abnormal cell signaling (Carlos et al., 2002; Martin-Ezquerra et al., 2010). Cellular proliferation is regulated by CDKs that interact with cyclin components. CDK4 and CDK6 interact with cyclin D and contribute to G1 phase advancement. By phosphorylating retinoblastoma proteins (pRb), Cyclin D, CDK4, and CDK6 create a complex that promotes cell progression from S to G1 (Poomsawat et al., 2011). Moreover, Bascones et al. proposed that translocates linked to cell cycle regulation may result in an epithelial substrate that promotes the progression of malignancy in OLP (Bascones et al., 2005).

For decades, many studies that estimated the rate of malignant transformation in the OLP lesions were performed by using different techniques (Fitzpatrick et al., 2014; Laniosz et al., 2019; Hwang et al., 2020). Because different types of OLP have the same chance of becoming cancerous, unique clinical criteria can't be used to describe the malignant transformation of OLP conditions (Mattsson et al., 2002; Agha-Hosseini et al., 2011).

In the present study, the most frequent age group was in their sixth decade of life, and women had more incidence than men, with no significant difference in each of them. These findings are in accordance with other studies

reporting that the high-risk groups are older age groups and female patients (Sugerman and Savage, 2002; Hwang et al., 2020), although much lower mean ages have also been documented (Mahboobi et al., 2010), and it appears that the risk is higher in women than in men (Shen et al., 2011; Bombeccari et al., 2011). But other researchers said that men were more likely to get sick in their fourth and fifth decades of life than women. This may be because different studies used different sample sizes when they did their research (Van der Meij et al., 2003; Raju et al., 2005; Tripathi et al., 2018).

In terms of Cyclin D1 expression, our findings showed that there were no significant differences among various clinical categories of OLP. Such findings were similar to earlier studies that found increased Cyclin D1 overexpression in the erosive subtype and deemed the erosive group of OLP to be at a greater risk of malignant alterations, although this variation did not reach statistical significance (Kurago, 2016; Hwang et al., 2020). Furthermore, Rezaee et al. observed that the erosive and atrophic OLP epithelium seems to be more prone to cancer development and is more vulnerable to cancerous exposures than the usual oral mucosa (Rezaee et al., 2013). On the other hand, Gandolfo et al. indicated that the hypothesis of a greater link between atrophic-erosive or plaque forms to cancer progression had been based on isolated case reports as well as no controlled investigations (Gandolfo et al., 2004).

The findings of this investigation revealed that cyclin D1 levels were substantially higher in OLP than in normal mucosa. According to earlier authors who reported that cyclin D1 upregulation is correlated with cellular proliferation of oral epithelial tissues, a large rise in the cyclin D1 index might promote generative conditions in OLP epithelium (Gambichler et al., 2011; Ghallab et al., 2017; Sharada et al., 2018). The overexpression of Cyclin D1 distinguished in OLP caused increased cell proliferation due to shortening in the cell cycle G1 phase (Rezaee et al., 2013; Tripathi et al., 2018).

The present study found that OLP patients had positive Cyclin D1 expression in all OLP samples, which is consistent with prior research (Ghallab et al., 2017), whereas other researchers suggest that not all OLP cases have positive expression. This discrepancy is determined by the kind and conditions of their study (Zhang et al., 2010; Gambichler et al., 2011).

The proliferative capacity of epithelial cells of OLP is associated with changes in the cell cycle regulatory system, suggesting that this highly proliferative state in OLP is a protective technique of the epithelium to preserve its architecture in the presence of vigorous lymphocyte attack(González-Moles et al., 2006).

The increased cell proliferation in OLP promotes the accumulation of cell cycle genetic alterations, which may be regarded as a significant signal of malignant potential in OLP (Rezaee et al., 2013; Ghallab et al., 2017).

Oncogenic effects acting on proliferating cells may induce a malignant cell pattern in OLP individuals. This result supports recent findings that imply amplification of CCND1 at both the protein and gene expression levels in OLP may impair normal cell cycle control, allowing cancer cells to develop (Yao et al., 2007; Abid and Merza, 2014).

The current data indicates that Cyclin D1 inactivation is a recognizable early event in oral carcinogenesis and precancerous oral conditions. Therefore people who had oral lichen planus (OLP) had more CyclinD1 staining than people who had normal oral mucosa.

## 5. Conclusions

The findings of this study revealed that greater cyclinD1 expression is related to an increased risk of cancer. Due to the absence of an appropriate biomarker that might predict OLP malignancy, various markers should be performed. In the future, more research on Cyclin D1 should have bigger sample sizes and better designs, as well as gene-reduction tests. OLP patients should be closely watched for predictive factors of malignant progression into OSCC. It is very important to know what causes OLP, what causes it to become malignant, and how to properly treat it.

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Not applicable.

*Consent for publication*
Not applicable.

*Availability of data and material*
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MM contributed to writing and grammar correction of the manuscript. FD contributed in spelling and punctuation correction of the manuscript. All authors have read and approved the manuscript.

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# "Hyperfeedback" as a Tool to Assess and Induce Interpersonal Synchrony: The Role of Applied Social Neurosciences for Research, Training, and Clinical Practice

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**Abstract**
In the last 25 years, the field of neuroscience has seen exponential growth due to technological advances, which have not only allowed for collecting more accurate data, but also for addressing a variety of innovative studies for human development understanding. Neurofeedback (NF), and particularly Brain–Computer Interfaces (BCI) applications, are among the most promising methods, since they enable individuals to interact with a computer by using their brain activity to learn implicitly and train some specific cognitive and affective functions. These applications proved to be suitable for many different fields, from research to clinical practice. However, NF was used only in individual settings, with participants interacting with a computer, while more ecological and complex phenomena could be better explored in interactive contexts. In the present work, we propose that the future of BCI provided NF may lie in the development of interactive settings where two or more participants can be informed about their inter-brain synchrony to train and reinforce them towards enhanced joint interactions and promote learning and empowerment. We propose that BCI methods should move to brain-X-brain-computer interfaces ($B^2CI$). In this new protocol, that we called "hyperfeedback," brain signals coming from two people involved in a joint setting are processed so to provide a compound feedback. The possible applications of such a paradigm are discussed.

**Keywords:** BCI, $B^2CI$, Interpersonal Coordination, Hyperscanning, Neurofeedback, Hyperfeedback, Dyadic Interactions

## 1. Introduction: Applied Neuroscience and wellbeing

In the last 25 years we have witnessed a huge progress in the field of neurosciences, with the development and improvement of sophisticated techniques, such as neuroimaging and non-invasive electrical brain stimulation, that can support the research and the understanding of human development. One of the most promising techniques is

neurofeedback, a non-invasive procedure that aims to modulate learning, cognition and behaviors at a neurocognitive level making use of low-density electroencephalography (EEG), generally implemented by a normal device with a targeted montage or by brain-computer interfaces (BCI) tools, which use algorithms to process in real-time brain signals, so allowing a direct interaction with a machine (e.g., launching commands, operating on a keyboard or moving a robotic arm). Thanks to focused training sessions, individuals can learn to modulate their own brain activity eliciting purposed functional patterns. This learning process occurs at an implicit level: Trainees are rewarded with visual or auditory stimulation when the brain pattern falls within the chosen range. For example, if they can maintain brain rhythms within a range associated to states of calm (if the goal is relaxation), or concentration (focal attention), they receive a reinforcement in the form of a sound, volume change, a visual sign (e.g., a positive emoji) or a successful performance in a videogame (e.g., hitting a target with an arrow). On the other hand, undesirable patterns of activity are ignored or disincentivized (Coben & Evans, 2010), for example by producing a noise. NF was proven to be effective in different protocols and for a number of purposes, yet it presents some limitations. Indeed, the training is often perceived as too demanding and a consistent amount of participants prove to be, *de facto*, non-responders (Kadosh & Staunton, 2019). Indeed, previous research underlined that mood, motivation, but especially attention resources may affect NF success. Also, the majority of available software is rather tricky and not always simple to adjust to different experimental and clinical settings.

Generally speaking, neurofeedback studies were initially referred specifically to clinical contexts, where traditional rehabilitation programs were impossible or scarcely successful. Now, the field is expanding, following the general trend of Neuroscience research that went beyond the study of classic cognitive studies to investigate new fields. The new frontiers concern abilities, talents and contexts, including creativity, social dynamics, and interpersonal relationships, previously considered addressable only by a more qualitative approach. Applied neurosciences investigate these fields extensively, trying to translating the most recent advances about the brain functions into real-life applications and ecological settings, also with the aim of investigating the human mind/brain in its broadest expression and promoting people's wellbeing and growth. Thus, the research process does not necessary occur in the lab, but also in schools, companies, shops, clinics, and social groups, obviously opting for research methods usable in these contexts. The basic idea that supports these studies, that may be considered examples of Applied Social Neuroscience (ASN), is that human beings can be seen as energy systems in continuous interaction with each other and with instruments around them (Dennett, 2013). ASN leads to thee need of a paradigm shift, from a "one-person" to a "two-person" (Balconi et al., 2017; Balconi & Vanutelli, 2017; García & Ibáñez, 2014; Konvalinka & Roepstorff, 2012; Schilbach, 2010), or even "multi-person" settings (Hildt, 2019; Jiang et al., 2019).

In this paper, we propose a research and intervention model that, based on these principles and thanks to technological tools, could be applied in many different contexts related to the theme of cognitive empowerment, rehabilitation, education, and well-being. In the following paragraphs the theoretical rationale, the technical structure, and the possible applications will be described in detail.

## 2. Why an interpersonal perspective?

Have you ever tried to spend a lot of time with a mate from another city, or region? Did you notice how, after a very few moments, you began modifying your own accent, prosody, even non-verbal behavior? Have you ever heard the joke for which, over time, spouses get more and more similar? These stories from everyday life are just examples of how people, when interacting with peers, automatically mimic their behaviors and feelings due to the activation of what can be described as a sort of unconscious mirroring mechanism. It has been defined with terms like alignment, behavioral matching, interpersonal or interactional coordination, behavioral resonance, which all include the idea of a spatial and temporal synchrony (Cornejo et al., 2017; Dumas et al., 2010). This mechanism can be thought as a tool devoted to facilitate emotional contagion to pursue shared goals (Hari et al., 2013) and, more generally, the construction and reinforcement of a collective cognition (Cornejo et al., 2017), a sort of social-cognitive space for mutual understanding. Actually, examples of dyadic synchrony have been observed in the very early stages, e.g. the mother-infant interactions (Feldman, 2007, 2012; Kinreich et al., 2017; Ramseyer, 2011), that will be the basis of a sound attachment (Barber et al., 2001; Ham & Tronick, 2009). From a phylogenetic point of view, interpersonal synchrony has been conceptualized as a fundamental evolutionary mechanism to promote group cohesion and collaboration, with significant effects on group dynamics (Levy et al., 2016; Vanutelli et al.,

2016). Moreover, it has been suggested that the closer we perceive others, the better we can understand their behaviors, intentions, and emotions, with improved empathy and ability to make inferences and predictions (Preston & de Waal, 2002; Vanutelli & Balconi, 2015).

These synchronization patterns can take the form of a behavioral synchrony, for example at the level of facial or body movements (Gordon et al., 2020; Mayo & Gordon, 2020), but also at the level of autonomic signals such as breathing, electrodermal activity, heartbeat, and so on (Feldman et al., 2011; Levenson & Gottman, 1983; McAssey et al., 2013; Vanutelli et al., 2017, 2018). Working, learning, or even making simple actions is modulated by the mere presence of others. This fact is particularly important if we think that we are social beings but generally scientific evidence is collected within individual settings. Furthermore, since humans' brain developed essentially in social contexts, we may consider it a "social device." Thus, it is plausible that it works better in social rather than in individual settings. The former contexts are then exploitable to increase cognitive performance, foster learning, and promoting healthy lifestyle. Instead, psychological and neuroscientific setting generally use individual setting even when trying to promote or change behaviors that are social in nature.

## 3. Hyperscanning + Neurofeedback = Hyperfeedback

It has been proven that interpersonal synchrony can be observed also at the level of neural processes coordination of multiple social partners. A neuroscientific approach called hyperscanning (Montague, 2002) emerged in this context twenty years ago to provide a more ecological setting for real-time psycho-social processes to be measured in the lab. The idea comes from the ability of the brain to mirror others' actions, feelings or emotions, by predisposing a similar activation in the perceiver (Hasson et al., 2012) and reflects embodied cognitive processes (Szymanski et al., 2017).

We believe that advanced Brain-Computer Interface (BCI) systems could be developed starting from hyperscanning recordings as input information and using the coherence of such signals to provide a visual/auditory feedback. Indeed, neurofeedback may be used to help people experiencing neurophysiological states in real-time so to implicitly learn how to manage them. However, we claim that it could be easily applied to multiple users into a "hyperfeedback" paradigm (HF). This way, it is possible to assess and train inter-brain synchrony as a whole within a new frame: $B^2CI$, brain-X-brain-computer interfaces. The use of a $B^2CI$ protocol will offer the unique possibility to give rise to a complex interaction, where two human beings (or even more in future applications) can interact with a computer in a purposed way. The role of the computer here is not simply to collect and combine data coming from the two brains. Instead, a specific software will process this information and a dedicated algorithm will be chosen and adapted to the dual task run and the goals to be reached. Thus, starting from the general idea of brains coherence (a classic index of synchronization), other computations can be performed and other indices can be used to provide a specific feedback. Furthermore, we propose that HF protocols should involve a synergy of both neural and autonomic signals, in order to monitor excessive cognitive load, stress levels and fatigue, to design calibrated interventions, and to increase the success rate.

In this frame, we believe that HF as many other ASN tools and protocols, will benefit from the use of coupled BCI tools ($B^2CI$), since they are conceived and implemented to process real-time brain(s) signals using them in purposed and flexible ways. BCIs are generally easier to adapt to different settings than traditional EEG systems, that are designed for clinical and research purposes and generally use proprietary software and expensive hardware. Commercial BCIs, instead, are cheaper, wearable, and often open source. These characteristics offer the opportunity to easily translate basic research into applications in educational, professional, and real-life contexts.

The hyperfeedback protocol takes advantage of the benefits of the well-known and validated neurofeedback technique, adding the expected benefits of a social context, that can improve achievement both at a dyadic, and at the individual level. In fact, within the HF protocol the collaboration between trainees (co-activity) is totally implicit and does not necessarily lead to a joint outcome. Consequently, the expected advantage is for each individual involved. In this way, the paradigm of hyperfeedback aims to exploit the potential of implicit learning on the double side of neuro-cognitive modulation (i.e. the neurofeedback-related learning) and on that of social facilitation. It is possible to define the combination of these protocols as "connected cognition", as if the two

cognitions were connected at a deep, implicit level. Connected cognition, more generally, can be thought as the consequence of the innate tendency of the human brain to resonate with the brains of others. From an evolutionary point of view this phenomenon represents a process which is capable of enhancing some fundamental cognitive processes, such as mind-reading, empathy and linguistic comprehension. In addition, synchronization phenomena may also be linked to some predictive coding processes. In few words, connected cognition allows us to "see" the brains functioning as a dance, in which one dancer leads the other towards a certain goal or, more simply, within a shared experience without any explicit instructions, but letting one carrying the other.

From a cognitive point of view, the study of connected cognition can be linked to the classical work of Zajonc (1966), who showed that performing a cognitive task in an individual context or with the presence of others substantially changes cognitive performance. This is referred to as the Social-Facilitation-and-Impairment Effect, since the presence of others can both increase and decrease performance. In fact, the social facilitation effect, from a neuro-cognitive point of view, is based on the automatic and therefore implicit activation of an attentional gradient, able to increase the general cortical excitability of the individual, and channeling cognitive resources towards the task at hand (Belletier et al., 2019). In particular, as suggested by Baron's model (Baron et al., 1996), the presence of others would allow a greater attentional focus and an increase in the performance of simple and repetitive tasks, while an opposite effect (worsening of performance) would occur in the case of complex tasks, requiring the development of new cognitive algorithms or a deep adaptation of those previously developed.

From this theoretical overview, it appears evident that the HF paradigm, and more generally ASN, may serve not only for research purposes in the lab, providing new insights into shared cognitive and emotional experience in a social-cognitive setting. Indeed, it has a significant application potential. We believe that HF may be developed and applied in different fields and that applications related to the clinical contexts are particularly interesting. In the present paper, we propose two hypotheses of intervention in relation to clinical practice (I), and to education and training (II).

### *3.1. Hyperfeedback and B²CI in clinical practice*

In clinical practice, HF may be applied to enhance the quality of parent-child relationships especially dealing with developmental disorders associated with social or emotional impairment. Let’s consider, for example, the possible positive effects in the case of Autism Spectrum Disorders (ASD), characterized by difficulties in social interaction, communication, and empathic mechanisms (Baron-Cohen et al., 1994). Previous research (Koehne et al., 2016) underlined that the degree of behavioural synchrony can be associated with higher cognitive empathy performance in ASD children. In this framework, HF could reinforce mirroring mechanisms and help the acquisition of competencies such as the capacity to share others’ feelings and to understand intentions and emotions at an implicit level. In fact, for people with ASD the explicit learning of such competences is particularly impaired or even impossible. The same principles could be applied to other meaningful dyadic problem interactions, with the aim to improve emotional engagement, tuning, and connectedness.

Another important clinical application may be linked to learning disorders. In this case, traditional NF programs have been implemented to improve reading abilities, including innovative methods to restore inter-hemispheric balance (Cancer et al., 2021). However, NF trainings are usually rather demanding. In this context, a HF paradigm may be more effective, since it could facilitate the implicit learning typical of NF, but with the boost of social facilitation, thus decreasing attentional and cognitive resources needed to obtain a good outcome. Furthermore, HF could be used coupling typical readers with people with dyslexia. The starting hypothesis here is that the typical and atypical readers may achieve implicitly a brain synchronization such that the “typical” inter-hemispheric balance is reached with much less effort and time than required by a traditional NF protocol.

Another possible application refers to the treatment of social anxiety, as recently proposed by an interesting paper by Saul and colleagues (2022). Indeed, studying and treating the psychological and behavioral reactions of people suffering from social anxiety in a social setting might be beneficial, since a straightforward and focused intervention might be easily implemented. This dual approach would show a high ecological validity, and the achievements obtained during the training could be easily extended to real-life contexts. Our HF approach could be used in a similar setting as well, incorporating both a social context and an algorithm able to foster

improvements in emotional management when cooperating with others. Furthermore, our approach is based on mutual learning, so it is possible to set an HF protocol to include couples made by individuals with different levels of social anxiety to develop focused expectations and coherently guide the therapeutic journey. For example, at the beginning of the training it is unlikely to expect that a person with a high level of social anxiety may find benefits in a dual neurofeedback training with a low anxiety person. Instead, better results are expected when little differences are present. Also, the integration in our protocol of autonomic measures such as electrodermal activity thought to prevent excessive treatment-related stress, but also to be a measure of anxiety level in social contexts.

### *3.2. Hyperfeedback and B²CI for group dynamics and training*

A study by Dikker and colleagues (Dikker et al., 2017), thanks to the simultaneous acquisition of EEG activity from 12 students, showed that brain-to-brain group synchrony was associated with classroom social dynamics. Accordingly, a hyperfeedback training could be proposed in schools to promote group engagement and empathy, to enhance mutual understanding and to discourage social exclusion, bullying, and discrimination. Similarly, hyperfeedback may be applied at the workplace, including both horizontal (colleague-colleague), and vertical dynamics (leaders-employees) to enhance perceived closeness and symmetry, as well as to identify the best practices for groups formation, so to increase collective intelligence and facilitate teamwork. B²CI could also be used for training purposes. For instance, in negotiation training it's important to learn how to regulate emotions and to be empathetic with the counterpart to accomplish a timely settle achievement. We propose that the use of a B²CI might accelerate the training also improving emotional and relational skills (Cominelli et al., 2017, 2020). Indeed, HF protocol's benefits are generally expected in contexts where social learning is required.

A similar situation may be described when a physician meets a patient to discuss a diagnosis and set a treatment. We believe that the doctor/patient encounter is a kind of implicit negotiation. In the era of patient empowerment (Tomes, 2007), patients and doctors must be considered at the same level. They must collaborate to set and share goals, since the doctor's interest is to treat the disease, and the person's interest is to reach a good quality of life. Most of the work needed to achieve this settlement is implicit since overt communication is generally hindered by technical, emotional, social, and personal issues that are not commonly discussed and often are simply unmanageable in a clinical setting (Ranjan et al., 2015). As in the case of negotiators training, it is not possible to use HF protocols in a real situation; However, we believe that HF may be beneficial during doctors' education, especially in the area of communication. Using HF training, doctors could test their ability to communicate with a person about significant health-related issues, or evaluate how the emotional reactions of others influence the communication process and the achievement of a proper therapeutic relationship. This aim can be pursued in an educational setting by the use of B²CI protocol. It is enough to set the synchronization parameters and the hyperfeedback to tune the communicator 1 (doctor role) and communicator 2 (patient role) so to achieve implicitly a proper cognitive and emotional empathy, a skill considered playing a key role in clinical contexts (Dehning et al., 2013). This way, a doctor learns how to resonate with a patient and communicate properly without any explicit instruction or intention.

A last significant application in this context could be the use of HF using simulated agents. This is an extension of the B²CI HF protocol that we have designed, and we are going to test in different applications. Using an agent-based simulated model, doctors may be trained to improve communication skills and empathy with the use of simulated patients with different emotional, social, and personal characteristics (e.g., values, preferences, expectations, and so on). Doctors would learn how to regulate communication and emotions within these different conditions and develop a focused emotional intelligence skill that would be fundamental in any doctor's psychological toolbox, beyond technical skills and scientific knowledge. This training might be completed in a few weeks and could be repeated during the doctors' education even during her professional career when needed or desired. In this protocol, hyperfeedback is provided combining the real data coming from the trainee's brain and a simulated dataset, designed to associate brain patterns with personal characteristics, such as emotional stability and personality traits.

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**Declaration of interest**

None

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# The Effect of Tooth Carving Technique on Dental Technician Student Perception and Performance in Tooth Morphology and Manipulation Course

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**Abstract**
Tooth carving is done to develop the psychomotor skills necessary for dental technician practice and teach tooth morphology. This study aimed to determine the effect of tooth carving as a teaching method for tooth morphology and assessment. 116 students trained in teeth carving at Istanbul Aydın University Dental Technician Department were subjected to 2 different teeth carving exams with soap and wax. Instructors evaluated tooth carvings according to a standard checklist. At the end of this study, a student satisfaction survey was carried out to get feedback on tooth carving as a teaching methodology. The scores given by the instructors did not differ by material and gender ($p > 0.05$). Overall, student feedback on teeth carving was equally positive. The vast majority found the tooth they carved to be confirmed (75.86%). They believed that carving exercises would help develop laboratory skills (76.03%). They found the training method and materials applied sufficient. Dental carving applications develop dexterity and psychomotor skills for dental prosthesis technician applications. Before laboratory applications, it should be an integral component of the dental prosthesis technician curriculum to develop cognitive and psychomotor skills related to clinical applications. Based on this study, live representation of teeth carving skills and different educational materials (plaster models, videos, slides, etc.) should be the preferred teaching method.

**Keywords:** Prosthodontics, Dental Technician, Dental Education, Dental Models, Psychomotor Performance, Dental Laboratories

## 1. Introduction

The dentist needs to have comprehensive knowledge of morphology and function of teeth in the construction of aesthetic restorations (Nance et al., 2009; Obrez et al., 2011). Along with theoretical knowledge of tooth structure and function, it is essential to have technical skills, dexterity, and more for proper restoration. It makes purely artistic sense (Rubinstein & Nidetz, 2007). A clinician can only reproduce anatomical details to make a dental restoration look natural (Capote et al., 2018).

Dental students' psychomotor skills in carving need to be developed early to acquire the dexterity to reconstruct fine-tooth forms for restorative clinical procedures and functional purposes (Giuliani et al., 2007). In the preclinical years, dental anatomy and dental morphology is the first course that introduces dental students to the structure and function of human teeth (Schroeter, 1959). Knowledge of tooth morphology, alignment, and occlusion is critical for identifying teeth and relating morphology. It is vital to develop psychomotor skills as it helps students later identify the details of the tooth surface and the changes that may occur (A. Kilistoff, 2011). Oral anatomy and dental morphology are traditionally taught through didactic lectures, books, manuals, artificial tooth models, and extracted teeth. Wheeler's first introduced tooth carving in wax blocks. 10 In many dental schools worldwide, dental carving is an integral part of the curriculum. Students carry out carving teeth from wax or soap molds (Capote et al., 2018).

The purpose of tooth carving is to reconstruct different positive and negative anatomical features, such as tubercles, cingulum, ridges, fossae, and grooves, close to the dimensions of natural teeth. Each tooth has six surfaces, and each surface of the tooth has its characteristics. Dental wax carving is an exercise for learning the contours, convexities, and concavities specific to tooth type and location. Dental wax carving skills introduce dental students to hand tool techniques. Provides improvements in-hand manipulation.

Today, many experts think that the examination of tooth morphology is an age-old exercise that serves no purpose, even though it has been practiced for many years (Baskar, 2009; Rao, 2010; Sivapathasundharam, 2008). Teaching dental morphology is exhausting as it requires expertise and manual dexterity. Although it is an education that is also applied in the education of dental students, several reasons can be given that dental morphology education is not necessary. First, learning dental morphology can prepare a student to be a good technician rather than a clinician (Baskar, 2009). Second, since most restorative work is done by dental technicians, they may not need dental morphology and carving training to perform surgery and learn anatomy (Sivapathasundharam, 2008).

These assumptions are a precious argument against not including dental morphology in education for dental students (undergraduate and graduate students). Dental technicians can benefit from pre-carved dental materials and earn this title without school. (Some of the current technicians have never been enrolled in dental schools or colleges in Turkey). In addition, dental technicians do not need more information about tooth morphology other than the exact determination of the tooth to be replaced. Dental students or technicians do not necessarily need to learn dental morphology at the curriculum level, which takes a lot of time and effort. Even if they learn all the tricks of tooth morphology, there is no guarantee that they will pass the exam successfully (Ponniah, 2010).

Since dental anatomy is one of the first lessons directly related to teeth and mouth function, it presents particular challenges for students and teachers (Mitov et al., 2010). In most schools, the didactic part of dental morphology is usually taught in the traditional course format, and written exams test students' knowledge (Maggio et al., 2012). These conventional teaching methods have revealed some weak points that cause frustration for both students and faculty (Nayak et al., 2014). The student's perception of the education received is valuable information for curriculum planners and should include advice from dental carving students and educators (Nayak et al., 2014). Therefore, the study evaluates dental technician students' knowledge, perception, and attitudes about tooth carving.

## 2. Method

The research was conducted on 116 students studying in the first year of dental prosthesis technology (man=58, woman=58) at Istanbul Aydın University. The study was carried out with the permission of the ethics committee of Istanbul Aydın University, numbered 2022/44. All participants signed consent forms.

Tooth morphology was taught to both groups (woman and man) with handouts, plaster models, slides, videos, and demonstrations. The demonstrations included a step-by-step application of the notes given in the laboratory environment. The demonstrations were recorded as videos and regularly watched during the training. Carving training was given for the same tooth from the wax and soap block in equal time (6 hours), and carving operations were carried out in the laboratory studies. The maxillary first molar was selected for this study. A soap and wax block (50x25x25mm) were given to the students. The teeth were collected anonymously without disturbing the group's integrity. Both groups were asked to carve a right maxillary molar tooth from wax and soap blocks. Ninety

minutes were given for carving from each block. 2 prosthodontists and two dental technicians evaluated carved teeth.

The examiners evaluated the teeth against the same grading chart. A grading chart was formulated based on work by Kilistoff et al. (Table 1) to standardize the grading of the teeth (A. J. Kilistoff et al., 2013). This standardized chart scored different morphological features of the maxillary first molar. (2 marks for each completed feature, 1 mark for a full feature, and 0 points for a missing feature.)

Table 1: Scoring criteria

| Tooth Characteristics | Score: 0= No feature, 1 = feature exists but weak not as desired, 2= feature is evident as requested |
|---|---|
| The geometric form of surfaces | Labial |
| | Palatal |
| | Approximal |
| | Occlusal |
| | Roots |
| Tooth dimensions | Cervico-occlusal |
| | Mesio-distal ve Labio-palatal |
| | Roots |
| Anatomical features | Developmental grooves |
| | Tubercles |
| | Fossas (central, mesial, distal) |
| | Edge ridges (Mesial-Distal) |
| | Cusp ridges (triangular, oblique, transversal) |
| | Roots |

A survey created by Abu Eid et al. was modified to collect students' feedback on tooth carving (Table 2) (Eid et al., 2013). Descriptive tests were applied for the gender and exam results of the students. An independent sample t-test was used to compare the average results of scores given by students and examiners. A P value less than 0.005 was retained as significant. The frequency of the answers to the questionnaire was calculated by applying descriptive tests (Table 2).

## 3. Results

The answers to the survey questions are shown in Table 2. The scores obtained from the answers given in the questions graded according to the Likert scale were converted into percentages. The percentages of the responses given give information about the perceptions and thoughts of the students. The majority state that they are successful while they think that the training provided helps to improve their laboratory skills. The usefulness and accuracy of the materials used during the training are confirmed by the results obtained. It was found that the material and gender did not affect success in the teeth carving process. The difficulty of carving specified for materials affects time but not success. Although 72% of participants stated that they liked tooth carving, 53.62% viewed carving as an unnecessary waste of time. It was found that 3D plaster models were more useful in the materials used during training.

Table 2: Surveys questions and evaluation results

| **1- Do you like teeth carving? (72%)*** | | | | | **11- How long does it take to carve a big molar out of wax?** | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **(1)** | **(2)** | **(3)** | **(4)** | **(5)** | 15 m | 30 m | 45m | 1 h | 1.5h | 2 h | 2 h |
| 8<br>6,9% | 7<br>6,0% | *33*<br>28,4<br>% | 30<br>25,9<br>% | 38<br>32,8<br>% | 1<br>0,9% | 3<br>2,6% | 5<br>4,3% | 1<br>14,7% | 45<br>38,8<br>% | 35<br>30,2<br>% | 10<br>8,6<br>% |

**2- Did carving help recognize the morphological features of the teeth? (79%)***

| (1) | (2) | (3) | (4) | (5) |
|---|---|---|---|---|
| 7<br>6,0% | 5<br>4,3% | 20<br>17,2 % | 36<br>31,0 % | 48<br>41,4 % |

**3- Were plaster tooth models helpful? (88,79%)***

| (1) | (2) | (3) | (4) | (5) |
|---|---|---|---|---|
| 1<br>0,9% | 5<br>4,3% | 9<br>7,8% | 28<br>24,1 % | 73<br>62,9 % |

**4- Did the tooth carving practice help you get to know some lab equipment? (79,31%)***

| (1) | (2) | (3) | (4) | (5) |
|---|---|---|---|---|
| 9<br>7.8% | 9<br>7.8% | 19<br>16.4 % | 29<br>25% | 50<br>43,1 % |

**5- Will tooth carving help improve your lab skills? (76,03%)***

| (1) | (2) | (3) | (4) | (5) |
|---|---|---|---|---|
| 8<br>6,9% | 11<br>9,5% | 22<br>19,0 % | 30<br>25,9 % | 45<br>38,8 % |

**6- Is it easy to work on wax blocks? (47,24%)***

| (1) | (2) | (3) | (4) | (5) |
|---|---|---|---|---|
| 45<br>38,8% | 22<br>19,0 % | 22<br>19,0 % | 16,<br>13,8 % | 11<br>9,5% |

**7- Do you think the anatomical structures in the carved tooth are realistic? (75,86%)***

| (1) | (2) | (3) | (4) | (5) |
|---|---|---|---|---|
| 3<br>2,6% | 9<br>7,8% | 32<br>27,6 % | 37<br>31,9 % | 35<br>30,2 % |

**8- Did you find tooth carving a waste of time? (53,62%)***

| (1) | (2) | (3) | (4) | (5) |
|---|---|---|---|---|
| 35<br>30,2% | 21<br>18,1 % | 30<br>25,9 % | 14<br>12,1 % | 16<br>13,8 % |

**9- Do you think the applied teaching method improved your skills? (78,62%)***

| (1) | (2) | (3) | (4) | (5) |
|---|---|---|---|---|
| 6<br>5,2% | 9<br>6,9% | 20 | 38 | 44 |

**12- How long does it take to carve a big molar out of soap?**

| 15 m | 30 m | 45 m | 1 h | 1.5 h | 2 h | 2 h |
|---|---|---|---|---|---|---|
| 2<br>1,7% | 16<br>13,8% | 31<br>26,7% | 40<br>34,5% | 24<br>20,7 % | 3<br>2,6% | - |

**13- Which material is easy to work with?**

| soap | wax | both easy | both hard |
|---|---|---|---|
| 86<br>74,1% | 7<br>6,0% | 15<br>12,9% | 8<br>6,9% |

**14- Which part of the tooth is difficult for carving?**

| root | crown | both |
|---|---|---|
| 9<br>7,8% | 93<br>80,2% | 14<br>12,1% |

**15- Is the time allotted for tooth carving training sufficient?**

| no | yes |
|---|---|
| 28<br>24,1% | 88<br>75,9% |

**16- Which of the following do you think would be useful in education?**

| | | |
|---|---|---|
| Slides | 51 | 12,4% |
| Models | 90 | 21,8% |
| Animations | 31 | 7,5% |
| Videos | 61 | 14,8% |
| Plastic theeth | 35 | 8,5% |
| Extraxted teeth | 37 | 9,0% |
| Atlas | 5 | 1,2% |
| Drawing | 38 | 9,2% |
| Carving exercise | 60 | 14,6% |

| Exam material | Gender | *n* | Exam grade Mean ± SD | *p* |
|---|---|---|---|---|
| Wax | Man | 58 | 61,20±17,72 | 0.692 |
| | Woman | 58 | 59,91±17,35 | |
| Soap | Man | 58 | 62,03±19,60 | 0.302 |
| | Woman | 58 | 58,27±19,43 | |

**(1),(2),(3),(4),(5) =** Likert scale values, m= minute, h= hour, n= respond, P= 0.05 significantly degree, *****= Average preference rate = [ 380 (maximum score (maximum likert value (5) x total number of participants)) / score obtained

| | | | | | |
|---|---|---|---|---|---|
| | | 17,2 % | 32,8 % | 37,9 % | (preferred likert value x number of participant preferences)] x 100<br><br>**Exam grade** = (Total score obtained according to Table 1 x 100) / 28 (maximum score according to Table 1) |
| **10- Should carving be taught in Grade 1? (88,96%)*** | | | | | |
| **(1)** | **(2)** | **(3)** | **(4)** | **(5)** | |
| 7 6,0% | 4 3,4% | 11 9,5% | 17 14,7 % | 77 66,4 % | |

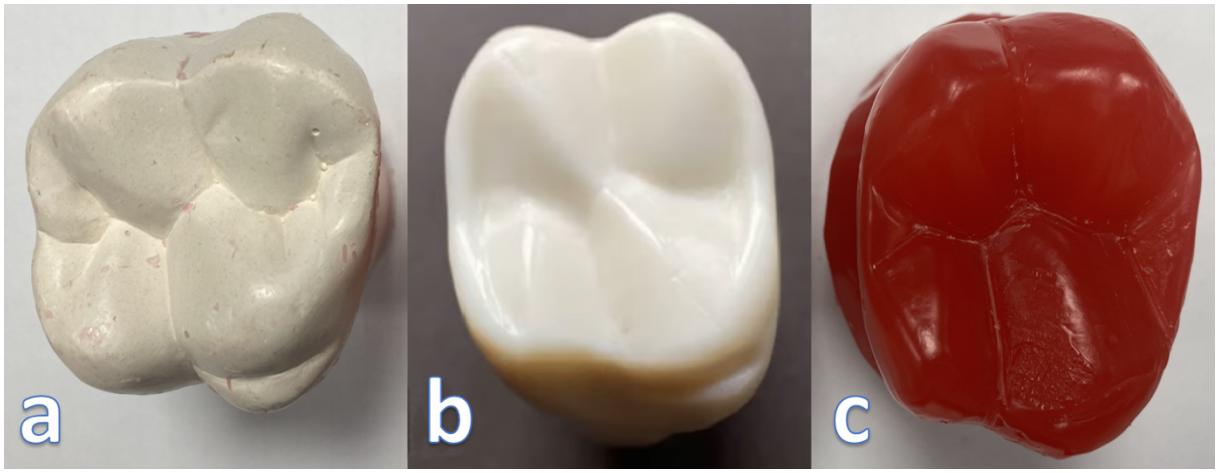

Figure 1: a: plaster model; b: soap tooth; c: wax tooth

## 4. Discussion

The demographic information of the students and grades given by faculty members are shown in Table 2. The morphological features on the plaster model teeth given to the students during the scoring were taken as a basis. Therefore, plaster models can also help reproduce the same features on the surface of the carved tooth. 88.79% of the students responded positively to whether plaster models were good teeth. This demonstrates that magnified dental plaster models provide a three-dimensional teaching method for tooth morphology that surpasses videos and other resources. So it can be used as a reference for tooth carving practice.

When students were asked if they found the crown or root part difficult when carving, 80.2% of the participants stated that the crown part was more complex than the root. This contrasts with the results of the study by Azevedo RA et al., who reported that the root is thinner than the crown and, therefore more difficult to carve and manage because it can easily break during the carving (de Azevedo et al., 2018).

The majority of students in this study agreed that tooth carving should be taught in the first year of education (88.96%). Regarding the usefulness of the teaching methodology used, 78.62% of the group's students agreed that it helped improve their skills. 76.86% of students of both groups agreed that the marking criteria for dental carving were realistic, robust, and comprehensive. The marking criteria included a detailed analysis of all the anatomical features of a maxillary right upper molar. Similar surveys previously conducted on dental students reported similar results. They also emphasized that dental carving is important to clinical skills and should be an integral part (Eid et al., 2013; Nayak et al., 2014). They find it challenging to carve from wax while they need about 1.5-2 hours. This difficulty and duration can be attributed to the material's physical properties being harder than soap.

The teaching of dental morphology begins with two-dimensional (2D) drawing and proceeds toward making the wax and tooth model in 3D. Carving wax teeth different from actual tooth size and morphology is a controversial teaching practice, as it significantly impairs the development of visual ability as does not give the student an idea of the deviations that actually exist. Newer technologies such as videos, computerized 3D models, and mobile

applications such as 3D tooth anatomy have been and should be implemented by authors (Chowdhry & Sircar, 2020). Since the morphology of restoration is determined by the morphology and location of neighboring and opposing teeth, meticulous carving exercises can be helpful to some extent in crown carving. However, the logic behind root carving remains unclear. Although the knowledge of the shape, the number of roots, and several canals within the root are significant in endodontic and exodontic applications, this is not needed in laboratory applications, and it makes root carving exercises in dental techniques unnecessary.

A systematic review of PRISMA guidelines suggested that practical demonstration of dental wax carving with an instructor is one of the most effective ways to learn about dental anatomy (de Azevedo et al., 2018). The limitations of this study are that it was based on a single institution. It is necessary to include more central studies to generalize and confirm the findings of this study. Based on the recommendations from the results of this study, dental carving should be an integral component of the dental technician curriculum in Turkey.

Based on the results of this study, dental wax carving was found to be an effective strategy for improving lab psychomotor skills of dental prosthesis technician students by recreating dental morphological features in wax and soap. Students' progress will be traced to their laboratory skills and then their laboratory work. Therefore, it is imperative that dental carving be included in the national prosthesis technician curriculum for longitudinal or spiral integration to be possible.

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# Prevalence, Risk Factors, Awareness, and Control of Hypertension: A Cross-Sectional Study in an Urban Slum Area of Bangladesh

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**Abstract**
Background: Although hypertension was formerly thought to be a disease in affluent countries, recent data suggest that low- and middle-income countries account for three-quarters of the worldwide hypertension burden. Several studies have shown a high prevalence of HTN in Bangladesh, while data on urban slum areas are scarce. Objective: The purpose of this study was to assess the prevalence, risk factors, awareness, treatment, and control of hypertension in an urban slum area of Bangladesh. Methods: This cross-sectional study included 602 adults aged 18 years and above living in slum areas of Donia union at Kodomtali Thana, Dhaka, from September to October 2018 by simple random sampling. Multivariate logistic regression analysis was performed to predict the risk factors for hypertension. Results: A quarter of the urban slum dwellers were suffering from hypertension. Higher aged groups, 31 to 45 years [adjusted odds ratio (AOR): 2.56; 95% confidence interval (CI): 1.54-4.27] and 46 and above years [AOR: 5.13; 95% CI: 2.68-9.82], family history of hypertension [AOR: 1.93; 95% CI: 1.24-2.99], and obesity [AOR: 2.86; 95% CI: 1.34-6.12] were found to be the significant risk factors of hypertension. Middle socio-economic status [AOR: 0.56; 95% CI: 0.34-0.93] and underweight [AOR: 0.36; 95% CI: 0.15-0.83] showed negative association with hypertension. Among the hypertensive participants, 20.6% were aware of their hypertension, 16.8% were on antihypertensive treatment, and 7.7% had their blood pressure controlled. Conclusion: A high prevalence of hypertension associated with poor awareness and control in an urban slum community needs government initiatives for prevention.

**Keywords:** Bangladesh, BMI, Hypertension, Urban Dwellers, WH Ratio

## 1. Introduction

Cardiovascular disease (CVD) accounts for one-third of total global death annually (Schutte, 2021). According to the Global Burden of Disease (GBD) Study, roughly 18.6 million people died of CVD in 2019, representing a 17.1% increase over the previous decade (Roth et al., 2020). This increased prevalence ranks hypertension (HTN) as the top modifiable risk factor for global CVD burden (Roth et al., 2020).

HTN directly contributes to the pathogenesis of most of the CVDs, such as stroke, coronary artery disease, heart failure, etc., and eventually causes premature mortality and disability (Mills et al., 2016). Being undiagnosed due to incomprehensive symptoms of early-stage HTN and non-compliance to the treatment, many people have their blood pressure (BP) uncontrolled over a long period which causes further complications like kidney failure, dementia, and cognitive decline (Mills et al., 2016; Tzourio, 2007).

HTN was once stereotyped as the problem of affluent society due to its high prevalence in developed countries. However, contrariety in improving awareness, treatment, and control over the past few decades has shifted the scenario where three-quarters of the global HTN cases belonged to low- and middle-income countries (LMICs) (Mills et al., 2016). In addition to established risk factors such as unhealthy diet, physical inactivity, tobacco and alcohol use, and obesity, emerging risk factors such as environmental pollution, rapid urbanization, and a loss of green space boost the rising prevalence of HTN (Schutte, 2021).

Because of demographic transition, aging, and urbanization, together with an unhealthy lifestyle, LMICs had a greater prevalence of HTN, estimated at 32.3% in 2015, compared to a global prevalence of 22% (Sarki, 2015; Zhou et al., 2017). CVD-related mortality is rapidly increasing in these underprivileged areas due to a lack of HTN awareness, medication, and control among the affected population (Mills et al., 2016). In the South Asian setting, the pooled prevalence of HTN in India, Pakistan, Bangladesh, and Nepal was reported 31.5%, with a higher incidence in urban (30-56%) than in rural areas (11-43%) (Gupta et al., 2017).

Bangladesh is highly vulnerable to HTN-related disease burden due to socio-demographic factors. Several studies based on diverse socio-demographic contexts in Bangladesh have found varying HTN prevalence ranging from 1.1% to 75%, with a weighted pooled prevalence of 20% and a higher trend in urban areas (M. Z. I. Chowdhury et al., 2020).

Approximately 14 million people live in Dhaka, where more than four million live in about 5000 slum areas (United Nations Children's Fund, 2015). Slum inhabitants are vulnerable to unhealthy lifestyles and related diseases due to poor socio-environmental conditions and poverty, while access to basic healthcare services is also limited.

The few studies so far conducted in Bangladesh only highlighted the prevalence and risk factors of HTN. Thus, this study aimed to evaluate the prevalence, risk factors, awareness, treatment, and control of HTN in urban slum areas of Bangladesh.

## 2. Methods

### *2.1. Study settings*

This cross-sectional study was conducted in the slum areas of Dania Union (the smallest administrative unit) under Kadamtali Thana (sub-district) of Dhaka, the capital of Bangladesh, from September to October 2018. The land area of this union is 3.32 sq. km and has approximately 261,000 populations (Banglapedia. Kadamtali Thana, 2021). Adults aged 18 years and above living in this area were the targeted population.

*2.2. Sampling technique and sample*

Sampled households were chosen from a list of pre-prepared slum households using simple random sampling. A lottery method was used to select an adult from each household. The sample size was determined considering the prevalence of HTN as 26.4% (Chowdhury, 2016), 3.5% error, and 10% non-response rate. A total of 602 were enrolled, with a drop-out rate of 10%.

*2.3. Data collection methods*

Respondent's age, sex (male/female), educational attainment, socio-economic status (SES) (based on wealth index [WI]), smoking habit (non-smoker, ever smoker), extra salt intake history (every day, sometimes, never), smokeless tobacco consumption (no, yes), fruit consumption (low consumption: <four servings or two cups per day, adequate consumption), vegetable consumption (low consumption: < five servings or two and a half cups per day, adequate consumption), waist-hip ratio (WHR), body mass index (BMI), and HTN (no, yes) were collected in a semi-structured questionnaire. In addition, history of smoking and smokeless tobacco consumption (tobacco leaf, gul, noshi, snuff, and zarda) were taken and categorized as tobacco user (current and ever smoker) and non-tobacco user. Household assets data such as a table, chair, watch, computer, energy supply, refrigerator, television, radio, mobile phone, bicycle, and air conditioner were collected to construct WI.

Weight, height, waist, and hip circumference measurements; BMI and WHR calculation; and BP recording and HTN diagnosis were performed using standardized methods and guidelines (Olack et al., 2015). Each participant's weight was measured in kilograms by setting a digital weighing machine on a flat surface, and their height was measured in centimeters using a measuring tape while they were barefooted and heavy clothing, if any, was removed. BMI was calculated as weight in kilograms divided by height in meters squared. Overweight and obesity were defined as BMI $\geq$ 25.0 – 29.9 kg/m2 and BMI $\geq$ 30 kg/m2, respectively. The waist circumference was measured to the nearest 0.1 cm by putting a measuring tape at the midpoint between the lower margin of the last rib and the tip of the iliac crest at the end of expiration. The hip circumference was measured at the widest part of the buttock with a tape parallel to the floor. WHR was calculated, and WHR $\geq$0.90 in males and $\geq$0.80 in females were considered as abdominal obesity.

BP was recorded three times at 5 minutes intervals in an upright sitting position in the right arm, using a digital BP measuring machine (OMRON, Model HEM-7120). The average of the last two readings was used for analysis. Hypertensive participants were defined as those with systolic blood pressure (SBP) equal to or more than 140 mm of Hg and/or diastolic blood pressure (DBP) equal to or more than 90 mm of Hg or those who were on antihypertensive medication.

*2.4. Statistical analysis*

Descriptive analysis was performed for the socio-demographic and other predictive factors. For continuous variables, mean and standard deviation (SD) were calculated. WI was generated using household assets. In this regard, the first factor of the principal component analysis, as described by Filmer and Pritchett, was used to determine SES (Filmer & Pritchett, 2001). Chi-square statistics were used to compare categorical variables, where multivariate logistic regression analysis was performed to examine the risk factors (expressed in adjusted odd ratio, [AOR] with 95% confidence interval, [CI]) of HTN. Participant's occupation was not included in the adjusted analysis due to collinearity. Analyses were performed using the Statistical Package for Social Sciences (SPSS) version 25.0. A P-value less than .05 was considered statistically significant.

*2.5. Ethical consideration*

Ethical permission was obtained from the Institutional Review Board of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka (Memo no. 2017/7389) and followed the ethical code of the Declaration of Helsinki.

## 3. Results

### *3.1. Participants*

Among the participants, three-fourths were female. The participants' mean (SD) age was 34.07 (12.43) years, ranging from 18 to 81 years. Approximately half of the participants were young adults (up to 30 years old), while 17% were aged above 45 years. About 60% of participants had normal BMI. Most of the participants consumed raw salt every day (74.4%), had adequate daily vegetable consumption (64%), and did not use tobacco products (74.8%). One-third of the participants had a family history of HTN, while abdominal obesity was 63.4%.

Table 1: Prevalence of hypertension in several categories, along with risk factors

| Characteristics | Percentage of the total sample (N=602) | Hypertension n (%) | AOR [95% CI] [a] |
|---|---|---|---|
| **Gender** | | | |
| Male | 22.9 | 40 (29.0) | 1 (Ref.) |
| Female | 77.1 | 115 (24.8) | 0.87 (0.41 – 1.82) |
| **Age group** | | | |
| Up to 30 | 48.3 | 45 (15.5) | 1 (Ref.) |
| 31 – 45 | 34.2 | 64 (31.1) | 2.48 (1.49 – 4.14) *** |
| 46 and above | 17.4 | 46 (43.8) | 5.24 (2.55 – 10.77) *** |
| **Educational attainment** | | | |
| Non-formal education | 42.7 | 76 (29.6) | 1 (Ref.) |
| Up to Grade V | 31.2 | 48 (25.5) | 1.24 (0.73 – 2.10) |
| Grade VI to X | 23.4 | 26 (18.4) | 0.68 (0.36 – 1.26) |
| Grade XI and above | 2.7 | 5 (31.2) | 1.12 (0.30 - 4.17) |
| **Occupation** | | | |
| Service holder | 2.3 | 1 (7.1) | - |
| Business | 7.6 | 17 (37.0) | - |
| Labor | 20.8 | 27 (21.6) | - |
| Housewives | 53.3 | 85 (26.5) | - |
| Unemployed | 6.5 | 12 (30.8) | - |
| Others | 9.5 | 13 (22.8) | - |
| **Socio-economic status** | | | |
| Lower | 33.4 | 58 (28.9) | 1 (Ref.) |
| Middle | 36.7 | 43 (19.5) | 0.53 (0.32 – 0.86) * |
| Upper | 29.9 | 54 (30.0) | 0.95 (0.58 – 1.57) |
| **Salt intake history** | | | |
| Never | 11.6 | 17 (24.3) | 1 (Ref.) |
| Everyday | 74.4 | 113 (25.2) | 1.10 (0.57 – 2.14) |
| Sometimes | 14.0 | 25 (29.8) | 1.28 (0.56 – 2.90) |
| **Use of tobacco products** | | | |
| No | 74.8 | 109 (24.2) | 1 (Ref.) |
| Yes | 25.2 | 46 (30.3) | 0.94 (0.59 – 1.49) |
| **Fruit consumption** | | | |
| Proper consumption | 11.0 | 18 (27.3) | 1 (Ref.) |
| Less consumption | 89.0 | 137 (25.6) | 0.82 (0.44 – 1.54) |
| **Vegetable consumption** | | | |
| Proper consumption | 64.1 | 100 (25.9) | 1 (Ref.) |
| Less consumption | 35.9 | 55 (25.5) | 0.90 (0.59 – 1.36) |
| **Smoking history** | | | |
| Non-smoker | 83.9 | 129 (25.5) | 1 (Ref.) |
| Ever smoker | 16.1 | 26 (26.8) | 1.11 (0.46 – 2.65) |

| | | | |
|---|---|---|---|
| **Family history of hypertension** | | | |
| No | 67.9 | 93 (22.7) | 1 (Ref.) |
| Yes | 32.1 | 62 (32.1) | 1.84 (1.21 – 2.82) ** |
| **BMI** | | | |
| Underweight | 13.6 | 10 (12.2) | 0.40 (0.18 – 0.85) * |
| Normal | 58.8 | 86 (24.3) | 1 (Ref.) |
| Overweight and obese | 27.6 | 41 (32.0) | 1.62 (1.05 – 2.53) * |
| **WH ratio** | | | |
| Normal (<.90 M, <.80 F) | 36.4 | 43 (19.6) | 1 (Ref.) |
| Abdominally obese (≥.90 M, ≥.80 F) | 63.6 | 112 (29.2) | 1.40 (0.87 – 2.27) |

* *P* value< .05
** *P* value< .01
*** *P* value < .001
[a] AOR [95% CI] = adjusted odds ratio [95% confidence interval]
Nagelkerke R-square =0.22

*3.2. Prevalence and risk factors of HTN*

The overall prevalence of HTN in the study population was 25.7%. In bivariate analysis, the prevalence of HTN was significantly higher in older adults, people with a family history of HTN, high BMI, and people with abdominal obesity. After adjusting potential confounders, age, body weight, family history of HTN, and SES were significantly associated with HTN in the logistic regression model. Compared to those under 30 years of age, the risk of HTN was about 2.5 times higher in the age group 31 to 45 years (AOR= 2.48, 95% CI: 1.49–4.14) and 5 times higher in the age group >45 years (AOR = 5.24, 95% CI: 2.55–10.77). The risk of HTN was about double in people with a family history of HTN (AOR = 1.84, 95% CI: 1.21–2.82) and people with overweight and obesity (AOR = 1.62, 95% CI: 1.05–2.53). People of middle SES (AOR: 0.53; 95% CI: 0.32 – 0.86) and underweight (AOR: 0.40; 95% CI; 0.18 – 0.85) showed negative association with HTN.

*3.3. Awareness, treatment, and control of HTN*

Overall, 71.3% of the study participants mentioned that their BP was measured at least once in their lifetime. Females had their BP measured more (75.2%) compared to males (58.0%). Of the total 155 hypertensive participants, 20.6% were previously aware of their hypertensive condition, and the remaining 79.4% were unaware before the survey. Around 17% of hypertensive participants were on antihypertensive medication prescribed by a registered physician, and 7.7% had their BP controlled.

Table 2: Prevalence, awareness, treatment, and control of hypertension

| | Sample (N) | Number (%) | 95% CI |
|---|---|---|---|
| Prevalence | 602 | 155 (25.7) | 22.3-29.4 |
| Awareness | 155 | 32 (20.6) | 14.6-27.9 |
| Treatment | 155 | 26 (16.8) | 11.3-23.6 |
| Control | 155 | 12 (7.7) | 4.1-13.1 |

## 4. Discussion

According to our findings, approximately one out of every four persons aged 18 years and above is hypertensive. The overall prevalence of HTN in this study (25.7%) is higher than that of similar populations in Maharashtra (15.15%) and Bangalore city (21.5%) in India (Bendhari et al., 2016; Ramani & Suresh, 2020). However, the prevalence is considerably lower than that of the population from Kolkata, India (42%), Lagos, Nigeria (38.2%), and Cairo, Egypt (31.2%) (Banerjee et al., 2016; Daniel et al., 2013; Gadallah et al., 2018). These differences can

be ascribed to methodological variations, such as participant selection, age group, sex distribution, and geographical differences.

Nearly a third of the population had never had their BP checked, and 80% of the hypertensive population had gone unnoticed until this study, indicating a low level of HTN awareness. In a study of the rural Bangladeshi population, Islam et al. found a similar finding, estimating 82% of undiagnosed HTN (Islam et al., 2016). Furthermore, undiagnosed HTN was prevalent in 60% of the population in Bangladesh, according to a nationwide survey (Ahmed et al., 2019), with a higher incidence among persons with poor SES and low education levels. These findings are relevant to ours since slum residents generally have low education and SES.

The overall treatment and control status among hypertensive participants in our study was poor, with estimates of 16.8% and 7.7%. However, according to a study of nationally representative data of 1.1 million adults from 44 LMICs, among hypertensive participants, 29.9% (28.6–31.3%) received treatment, and 10.3% (9.6–11.0%) achieved HTN control, estimated using sampling weights (Geldsetzer et al., 2019).

The low level of awareness of HTN, its treatment, and control among the hypertensive participants of our study can be related to some factors reported in previous studies, which are more prevalent among the urban poor than the general population. These include poor socio-economic status, illiteracy, unemployment, lack of understanding and acceptance of the disease, poor health-seeking behavior, less affordability and inaccessibility to healthcare services, transportation time to a medical facility, long waiting time, and monetary costs (Daniel et al., 2013; Uddin et al., 2014; Khan et al., 2016).

We found that age was the most important risk factor for HTN, consistent with other studies in similar conditions (Bendhari et al., 2016; Ramani & Suresh, 2020; Banerjee et al., 2016; Daniel et al., 2013; Gadallah et al., 2018). The prevalence of HTN increased with age by nearly two and three times, from 15.5% in the 30-year group to 31% in the 31-45-year group and 43.8% in the above 45-year group. Age is a major non-modifiable risk factor for HTN that is present in every community worldwide. Aging causes vascular resistance, which prolongs inflammation, increases cellular oxidative stress and causes endothelial dysfunction (Buford, 2016). The proportion of elderly people in Bangladesh is rapidly increasing due to the ongoing demographic transition (M. Islam, 2016). In this flow, approximately 45 million elderly people will reside in Bangladesh by 2050 (M. Islam, 2016)(25), resulting in many hypertensive and other chronic disease-prone populations. It emphasizes the critical importance of effective intervention measures that anticipate other modifiable risk factors.

In this study, a family history of HTN was identified as one of the major risk factors widely regarded as a traditional non-modifiable risk factor for HTN. According to family-based studies, 30–50% of the variance in BP readings may be heritable, which is supported by studies showing a link between HTN and the renin-angiotensin-aldosterone system-related genes (Patel et al., 2017; Civeira et al., 2008).

Obesity is a well-known modifiable risk factor for HTN-related adverse cardiovascular conditions (Roth et al., 2020). In our study, participants who were overweight or obese were about 1.6 times more hypertensive than those who had a normal BMI. This finding is comparable with studies from India, Nigeria, and Egypt in similar conditions (Ramani & Suresh, 2020; Daniel et al., 2013; Gadallah et al., 2018). Obesity and HTN are more common in those over 35 years among slum dwellers in Nigeria and Uganda due to a poor diet, sedentary lifestyle, and lack of physical activity (Daniel et al., 2013; Mayega et al., 2012). Obesity causes HTN by increasing sodium reabsorption in the kidneys, activating the renin-angiotensin system and the sympathetic nervous system, altering intrarenal physical forces, and impairing pressure natriuresis (Aronow, 2017).

In our study, the prevalence of HTN was nearly halved in the middle SES group compared to the high and low SES groups. In both developed and developing countries, socioeconomic status is associated with hypertension. However, the associations are not linear which may reflect broad adoption of unhealthy lifestyles like sedentarism and high-fat diets across various SES groups (Mendez et al., 2003). There are also alternative risk factors like early malnutrition or psychosocial stress that potentially increase HTN prevalence among low SES groups in LMICs (Schutte, 2021). Therefore, identifying behavioral and environmental factors contributing to HTN in various SES groups in developing countries is critical for strengthening preventive strategies.

Underweight participants had a four times lower trend of HTN than those who were overweight and obese. A nearly similar trend was reported in a study based on South Asian BMI cut-off points, which estimated four times and three times lower HTN in underweight people than in obese and overweight people in the Bangladeshi population, respectively (Hossain et al., 2019). Underweight people may have improved insulin sensitivity and reduced sympathetic nervous system activity due to decreased renin-angiotensin-aldosterone system activation, natriuresis, and lower plasma volume, explaining why they have a lower prevalence of HTN (Aronow, 2017).

### *4.1. Strengths and limitations of the study*

The survey method used in this study was a strength as it allows cross-study and cross-regional comparison. The selection of one adult from each home reduced the likelihood of over-representation bias. The study, however, had several limitations. First, data were collected from a single area, so the result cannot be generalized. Second, as this study was cross-sectional in design, the temporal association between variables could not be established. Third, data on self-reported harmful habits like tobacco, alcohol, and drug could not reflect the true picture due to the societal norm of not disclosing these habits. Fourth, we interviewed adults only and who were available at the selected households during the daytime. During the day, males are out at the workplace, and females remain at home, resulting in more female participation in this study. Finally, assessing HTN in a single day, BP measurement may cause some cases with white-coat HTN and result in overestimation.

## 5. Conclusions

HTN in urban slums is a public health concern that affects at least one in every four adults aged 18 and older. Participants' age, family history of HTN, overweight and obesity are significant risk factors for HTN. Unfortunately, most hypertensive participants are undiagnosed, which is a challenge for HTN control among underprivileged communities in slum areas. This emphasizes the need for promoting HTN awareness and encouraging health-seeking behavior.

### *Authors' Contributions*

IJ contributed to the conception and design of the study, acquired the data, and carried out the data analysis; SMS contributed to the conception, carried out the data analysis, and drafted the manuscript; AIA helped in data analysis and interpretation; MS, SM, MIIT, MTI, WWM, and MMHK were major contributors in writing the manuscript and revised the manuscript for important intellectual content; MAH contributed to the conception and supervision of the study, was a major contributor in writing the manuscript, and edited for submission. All the authors read, approved the manuscript, and consented to publish.

### *Availability of data and material*

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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### *Competing interest*

The authors declare that they have no competing interests.

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# Evaluation of Discoloration After Thermocycling in CAD/CAM Blocks of Different Thicknesses

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**Abstract**
The study aims to evaluate the color of CAD/CAM blocks of different thicknesses after thermocycling as in-vitro. A total of 180 samples (n=10) were prepared in 2 thicknesses (0.5mm, and 1.0 mm) from various CAD/CAM blocks of different structures (Katana UTML, Prettau® 4 Anterior® Dispersive, IPS e-max Cad, Vita YZ-XT, Vita YZ-T, Vita Suprinity PC, Vita Enamic, Shofu HC, G-Ceram). The color values of the samples (L*, a*, b*) were measured before and after thermocycling. The discoloration (ΔE) data obtained were statistically compared with two way-ANOVA, Tukey HSD posthoc tests, and Paired Sample T-Test ($p<0.05$). The highest average discoloration was found in the Katana group (ΔE=3.07) with a thickness of 1 mm, while the lowest was found in the Shofu HC group (ΔE=0.49) with a thickness of 0.5 mm. In contrast, the ΔE value was significantly different in samples with a thickness of 1 mm and 0.5 mm ($p<0.05$), there was no difference in the ΔE values in the groups in themselves. Discoloration values of test materials depending on thickness varied, but the difference of thickness in the same material did not affect the color change. All the color changes were clinically accepted.

**Keywords:** Computer-Aided Design, Prosthesis Coloring, Dental Materials

## 1. Introduction

The undesirable features of metal-ceramic restorations and the increasing aesthetic demands of dentists and patients have led to all-ceramic systems as an alternative. A wide range of ceramic products was introduced in terms of content, starting with John Mclean's introduction of aluminous core porcelain materials in 1965 and then with improvements in the aesthetic, durability properties, and production methods of all ceramic materials (Conrad et al., 2007; McLean & Hughes, 1965; Ueda et al., 2015). When current all-ceramic materials were examined, it was observed that the mechanical properties of ceramics, which usually have excellent aesthetic properties, were inadequate, and the aesthetic properties of ceramics with good mechanical properties were insufficient (Zarone et al., 2011). Feldspathic porcelain and glass ceramics exhibit excellent optical properties. Although aesthetic restorations close to the surface features of the natural tooth can be obtained, its mechanical properties are inadequate in posterior region restorations (Matsuzaki et al., 2015; Sen & Us, 2018). Hence high durability

zirconium oxide ceramics were developed in the early 1990s, and full ceramic restorations were allowed in posterior regions with high chewing forces (Harianawala et al., 2014). Since zirconium ceramics have an opaque structure, they need to be coated (veneering) with feldspathic porcelain to achieve natural-looking restorations. However, fractures in veneer porcelain (chipping) have been a severe problem (Guess et al., 2008). Thanks to the developing computer-aided design and computer-aided production (CAD/CAM) technologies, monolithic zirconium restorations have been achieved in a more light-passing (translucent) and color-layered (polychromatic) structure with improvements in production processes and sinterization temperatures. Thus, an important alternative has been created to solve the problem of fracture seen in traditional zirconium cor infrastructure restorations (Jiang et al., 2011; Zhang et al., 2013). Studies aimed at increasing the translucent properties of zirconia ceramics and monolithic zirconium blocks with polychromatic properties similar to the color transitions of the tooth between enamel dentin look very promising for restoration production brings mechanical and aesthetic properties together. The thickness of the restorative material, surface properties, color of the tooth structure, the cement used, the final color of the ceramic materials of the translucent feature can affect the result, as well as the long-term exposure of restoration to the oral environment (Dede et al., 2013).

CAD/CAM technology has become frequently used in dentistry today. With the advances in technology and materials, CAD/CAM technology will play an essential role in producing dental restorations in the future. This technology makes it possible to make high-quality and error-accurate restorations. It also requires less laboratory work than other techniques used (Douglas, 1997). The biggest challenge encountered in aesthetic restorations is achieving color harmony with natural teeth. Obtaining the final color of a ceramic restoration as planned is a highly complex phenomenon. It depends on many factors such as the color, light source, ceramic variety, ceramic thickness, coping color, adhesive cement color, and opacity perceived in ceramic restorations. These factors can change the final restoration color (Terzioğlu et al., 2009). Another factor that affects the final color of restorations is the color of the infrastructure. The color and thickness of the infrastructure material, the number and thickness of the porcelain used in the superstructure, glazing processes, and the selected cementation agent affect the color in all-ceramic systems (Chu et al., 2007).

Studies have shown that material thickness affects the optical properties of its material (Kim et al., 2016). As the thickness of the material increases, the path of light in the material increases. As a result, the light is further absorbed and emitted, reducing the amount of light passing through the material (O'Keefe et al., 1991). This causes the material to have different optical properties of different thicknesses. The fact that the optical properties of restoration remain stable after aging is also one of the main factors determining the success of the material used. This study aims to evaluate the effect of thermocycling on the color of samples of two different thicknesses prepared with different types of CAD/CAM ceramic blocks.

## 2. Method

This study evaluated color changes after thermocycler of 0.5 and 1-mm thick samples obtained from different types of CAD/CAM blocks (Table 1). Partially sintered zirconia blocks were sintered, and blocks of the green stage of lithium disilicate glass-ceramics were heated according to the manufacturer's specifications. Test specimens (n=10) each were prepared with 10 mm (length) x 10 mm (width) x 0.5 or 1.0 mm (thicknesses). The color chosen for the samples was A2. These sample thicknesses were chosen based on the recommended 0.5 mm margin and 1.0 mm occlusal thickness for monolithic zirconia restorations. Samples were cut with a diamond disc from each block, ground with a surface grinding plate (#100, #600) on a grinding machine (MINITEC-333 ;Presi Eybens; France), and polished with water-resistant sandpapers #1000 and #2000 (Figure 1a). For producing 0.5mm and 1.0mm thicknesses. The thickness of the samples was measured and verified with a digital caliper.

### *2.1 Aging in Thermal Cycle (Cycle)*

Universal-Testing Machine MTE-100 (Mod Dental; Turkey) is a thermal cycle device used for thermal cycle testing (Figure 1b). A thermal cycle was applied to all groups at 5°- 55° C de 10000 times.

*2.2 Making Color Measurements before and after Aging of Samples*

The color measurements of the samples, which are produced from 9 different materials and aged in 2 different thicknesses, were re-calibrated with the Lovibond RT Series Reflectance Tintometer UK spectrophotometer (Lovibond; Germany) before each measurement and made before and after aging.

*2.3 Calculation of Color Changes of Samples*

Measurements were recorded before and after aging, ΔE color differences were made to the 3D International Commission on Illumination International Lighting Bordu CIE Lab specifications by detecting the L* a* b* coordinates of 3 locations in the CIE Lab color space. ΔE value, change in L* a* b* coordinates before and after aging $\Delta E = [(\Delta L^*)^2 + (\Delta a^*)^2 + (\Delta b^*)^2]^{1/2}$ formula. ΔE value, mean and standard deviations were calculated from L* a* b* values for ten samples in each group tested.

*2.4. Statistical Analysis*

Bi-directional variance analysis was used for repeated measurements in comparison of ΔE color change values. In contrast, ANOVA analysis, a parametric test, was performed in the IBM SPSS 20.0 package program. The Tukey multi-comparison test and paired sample T-Test were applied to compare groups. The results for $p<0.05$ were considered statistically significant. ΔE values below 3.0 are clinically undetectable, ΔE values between 3.0 and 5.0 are clinically acceptable, and ΔE values above 5.0 are clinically unacceptable. These ΔE values are based on previous studies' mean acceptability and detectability thresholds (Nogueira & Della Bona, 2013).

Table 1: Used test materials

| | | | |
|---|---|---|---|
| Yttrium stabilized Zirconia | Katana UTML | Noritake Dental Co, Nagoya, Japon | ($ZrO_2$ + $HfO_2$ + $Y_2O_3$)> 99.0%, Y2 O3 > 4.5-≤6.0%, $HfO_2$ ≤5.0%, other oxits ≤1.0% |
| Yttrium stabilized Zirconia | Prettau® 4 Anterior® Dispersive | Zirkonzahn GmbH, Bruneck,Italy | <12% $Y_2O_3$, <1% $Al_2O_3$, max. 0.02% SiO2, max. 0.01% $Fe_2O_3$, max. 0.04% $Na_2O$ |
| Lithium distilled glass ceramic | IPS e-max Cad | İvoclar Vivadent, Schaan, Liechtenstein | $SiO_2$ 57-80%, $Li_2O$ 11-19%, $K_2O$ 0-13%, $P_2O_5$ 0,-11%, $ZrO_2$ 0–8%, ZnO 0–8% with other oxides and ceramic pigments 0≤10% |
| Extra translucent zirconia | Vita YZ-XT | Vita Zahnfabrik H. Rauter GmbH, Bad Sackingen, Germany | $Zro_2$ 86-91%, $Y_2O_3$ 8-10%, $HfO_2$ 1-3%, $Al_2O_3$ 0-1%, Pigments 0-1% |
| Translucent zirconia | Vita YZ-T | Vita Zahnfabrik H. Rauter GmbH, Bad Sackingen, Germany | $ZrO_2$ 90-95%, $Y_2O_3$ 4-6%, $HfO_2$ 1-3%, $Al_2O_3$ 0-1%, Pigments 0-1% |
| Lithium silicate reinforced with zirconia | Vita Suprinity PC | Vita Zahnfabrik H. Rauter GmbH, Bad Sackingen, Germany | $SiO_2$ 56–64 % ,$Li_2O$ 15–21%, $K_2O$ 1 – 4%, $P_2O_5$ 3–8%, $Al_2O_3$ 1–4%, $ZrO_2$ 8–12%, $CeO_2$ 0–4%, $La_2O_3$ %0.1, Pigments 0 – 6% |
| Feldspar ceramic enriched with aluminum oxide | Vita Enamic | Vita Zahnfabrik H. Rauter GmbH, Bad Sackingen,Germany | UDMA, TEGDMA 86.0 (75.0) |
| Hybrid ceramic | Shofu HC | Shofu Inc., Kyoto, Japan | UDMA, TEGDMA Silica powder, micro fumed silica, zirconium silicate 61.0 |
| Feldspathic monochromatic glass ceramic | G-Ceram | Atlas-Enta Dental A.Ş., İzmir, Turkey | $SiO_2$ 56-58%, $Al_2O_3$ 18-25%, $Na_2O$ 8-12%, $K_2O$ 8-14%, CaO 0,2-1%, $TiO_2$ 0,1-0,2% |
| Bis-GMA, bisphenol A di glycidyl ether methacrylate; UDMA, urethane dimethacrylate; TEGDMA, triethylene glycol dimethacrylate; Bis-EMA, ethoxylated bisphenol-A dimethacrylate | | | |

Table 2: Overall discoloration values

**Descriptive Statistics**
Dependent Variable: Discoloration

| Thickness | Groups | Mean | Std. Deviation | N |
|---|---|---|---|---|
| 0.5-mm | VİTA YZ-T | 1.24 | 0.20 | 10.00 |
| | SUPRİNTY | 0.90 | 0.29 | 10.00 |
| | VİTA YZ-XT | 1.34 | 0.33 | 10.00 |
| | G-CERAM | 1.97 | 0.79 | 10.00 |
| | KATANA | 1.92 | 0.15 | 10.00 |
| | PRETTAU | 1.11 | 0.09 | 10.00 |
| | E-MAX | 2.81 | 0.40 | 10.00 |
| | SHOFU | 0.49 | 0.09 | 10.00 |
| | VITA ENAMIC | 1.05 | 0.31 | 10.00 |
| 1-mm | VİTA YZ T | 1.25 | 0.14 | 10.00 |
| | SUPRİNTY | 0.98 | 0.26 | 10.00 |
| | VİTA YZ XT | 1.44 | 0.24 | 10.00 |
| | G-CERAM | 1.76 | 0.58 | 10.00 |
| | KATANA | 3.07 | 0.61 | 10.00 |
| | PRETAU | 1.27 | 0.08 | 10.00 |
| | E-MAX | 2.93 | 0.71 | 10.00 |
| | SHOFU | 0.56 | 0.12 | 10.00 |
| | VITA ENAMIC | 0.96 | 0.29 | 10.00 |
| | Total | 1.50 | 0.83 | 180.00 |

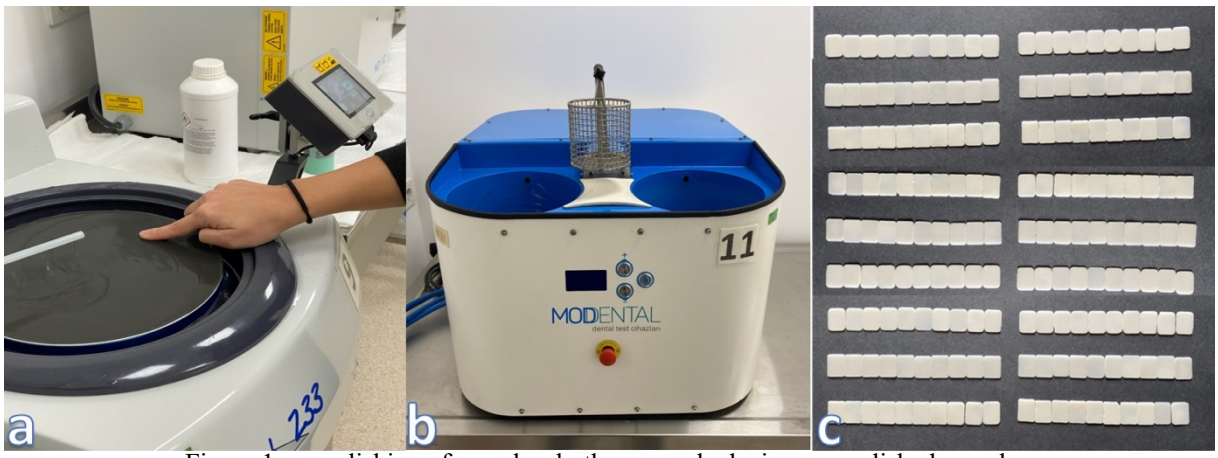

Figure 1: a: polishing of samples; b: thermocycle device, ; c: polished samples

## 3. Results

There was a difference in the values of discoloration between the groups. It was found that the highest color changes were in the Katana group (3.07) (Table 2) and that the different material thicknesses did not make a statistical difference in the color change of the materials (Table 3 and 4). All values were clinically accepted (2.1< ΔE < 3.5) (Figure 2).

Table 3: Tests of Between-Subjects Effects

Dependent Variable: Discoloration

| Source | Type III Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|
| Corrected Model | 101.208[a] | 17 | 5.953 | 40.907 | 0.000 |
| Intercept | 406.231 | 1 | 406.231 | 2791.298 | 0.000 |
| thickness | 1.100 | 1 | 1.100 | 7.557 | 0.007 |
| groups | 93.960 | 8 | 11.745 | 80.702 | 0.000 |
| thickness * groups | 6.148 | 8 | 0.768 | 5.280 | 0.000 |
| Error | 23.577 | 162 | 0.146 | | |
| Total | 531.015 | 180 | | | |
| Corrected Total | 124.784 | 179 | | | |

a. R Squared = .0811 (Adjusted R Squared = 0.791)

Table 4: Levene's Test of Equality of Error Variances[a]

Dependent Variable: Discoloration

| F | df1 | df2 | Sig. |
|---|---|---|---|
| 6.969 | 17 | 162 | 0.000 |

Tests the null hypothesis that the error variance of the dependent variable is equal across groups.

a. Design: Intercept + thickness + group+ thickness * groups

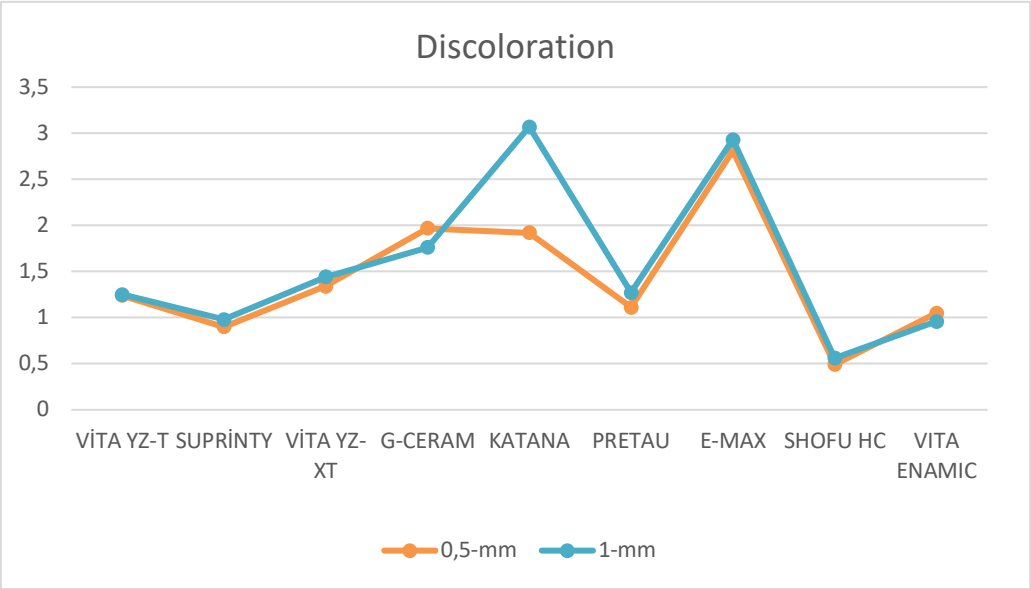


Figure 2 : Discoloration values of samples

## 4. Discussion

As the ceramic thickness increases, the opacity of the material increases. Furthermore, the effects of light reflection from the bottom tooth decrease. (Turgut, Bagis, & Ayaz, 2014) This increases the masking feature of the material. Material thicknesses affect the final color (Terzioğlu et al., 2009). ΔE values of sample groups with a thickness of 1mm are higher than 0.5 mm thickness groups. We think this result results from decreased light permeability and increased opacity of the material as the material thickens, as mentioned in the studies. Restorations are requested to maintain their physical, mechanical, and optical properties throughout their lifespan. However, the oral environment is dynamic, and restorations are subject to wear, heat differences, and dyeing agents. These factors affect the color change of the restoration and, accordingly, the duration of use (Bagis & Turgut, 2013). Accelerated aging methods are also used in studies to evaluate the color change of materials. These methods mimic clinical

and living conditions by exposing materials to ultraviolet light (UV), heat, continuous humidity, and variations (De Oliveira et al., 2014).

H.-Y.Jeong and his colleagues examined the mechanical properties of CAD/CAM materials after aging procedures (Jeong et al., 2018). Lava Ultimate, Vita Enamic, Cerasmart, IPS E.max CAD, IPS E.max Zir CAD materials were applied to 22,000 thermocycling procedures and aging procedures in the autoclave bending resistance, surface roughness, and SEM image. The Lava Ultimate group reported that silica and zircon particles of various sizes, visible in the resin matrix before aging decreased after aging. Compared to Lava Ultimate and Cerasmart, ceramic fillers, evenly distributed in all groups, reported no significant change even after aging. The IPS e.max CAD group reported that rectangular lithium dioxide particles were well observed, but some irregular shapes were observed after aging, especially in the group aging with autoclave, and there was much fragmentation. On the other hand, they reported that small-sized particles exhibit changes in distribution due to the decrease of particles after aging, which may be related to changes in the surface. The IPS E.max values (2.93 and 2.81) in this study may depend on this change in the surface.

Gürdal et al. evaluated the color differences by cementing CAD/CAM (Lava Ultimate, Cerasmart, Cerec Bloc, IPS e.max CAD, VITA Suprinity, Brilliant Crios, IPS Empress CAD) block material samples with two different thicknesses and three different types of resin types of cement (Gürdal et al., 2018). They applied it after 5000 thermal cycles and examined color changes. They stated that aging has a significant effect on color values. They noted that the lowest ΔE values were observed in Vita Suprinity and Cerasmart, followed by Lava Ultimate, IPS e.max CAD, and Brilliant Crios, due to the material contents.

Acar et al. evaluated color differences between materials that applied coffee and aging to hybrid dental ceramics (Vita Enamik), resin nano ceramic (Lava Ultimate), lithium disilicate glass-ceramic (IPS e.max CAD), and nanocomposite resin (Filtek Supreme Ultra Universal) materials of different thicknesses (Acar et al., 2016). ΔE values for IPS e.max CAD material have been reported below the perceptible threshold regardless of thickness. They said that ΔE values for Vita Enamic material were above the detectable threshold and below the threshold for clinical acceptability. Filtek Supreme Ultra Universal and Lava Ultimate reported that ΔE values are above the point of clinical acceptability and are declining as their thickness increases. They attributed this result to the colorability of materials associated with monomer hydrophobicity and water absorption properties. They reported that Vita Enamik's pores contain a porous ceramic matrix filled with polymer materials, while Lava Ultimate has nano-ceramic particles embedded in the cross-linked resin matrix, which should be considered composite resins. They stated that the materials contain both hydrophobic UDMA and hydrophilic TEGDMA that TEGDMA has much water absorption so that the materials can be sensitive to discoloration. The results of this study are consistent with previous results for similar materials.

Alp et al. investigated the effects of different surface treatments (polishing and glazing) and coffee and aging (5000 thermocyclers) on the color and translucence of monolithic (zircon glass-ceramic and lithium disilicate glass-ceramic) CAD/CAM blocks (Alp et al., 2018). They stated that only the color change of polished lithium disilicate glass-ceramic samples is detectable but clinically acceptable, and color changes in all other groups are not detected. They reported that the surface of glass-ceramic material with zircon content has a homogeneous, thin, bar-like crystal structure with a crystal size of approximately 0.5 μm and that the surface of the lithium disilicate glass-ceramic material has a needle-shaped crystal size of approximately 1.5 μm. Hence, the glass-ceramic material with zircon content is less colored than the glass-ceramic material with lithium disilicate (Belli et al., 2017). Consistent with the findings of this study.

Quek et al. investigated the effects of beverages containing dyes (cola, tea, coffee, red wine, distilled water) on various composite materials (direct composite (Filtek Z350), indirect composite (Shofu Ceramage), and CAD/CAM composite blocks (Shofu HC, Lava Ultimate, Vita Enamic) color and translucency. They stated that there were differences in color changing and translucence between direct, indirect, and CAD/CAM composites and that CAD/CAM composites showed more color changes in red wine than direct and indirect composites. They noted that most materials show a detectable discoloration (ΔE>3.3) when exposed to red wine, tea, and coffee. They reported that this was due to Bis-GMA, UDMA, TEGDMA content, and water absorption in the material contents.

In another study, Eğmez et al. examined surface roughness, topography, and SEM images by applying different aging methods to Cerasmart, Lava Ultimate, and Vita Enamic CAD/CAM materials (Turgut & Bagis, 2011). When SEM images of the materials tested in each aging group were examined, Cerasmart showed smoother surface textures with small particles distributed properly, while lava ultimate showed larger clustering filler particles protruding from the surface. When the surface topography of the aging groups was examined, Cerasmart aged groups and control groups had similar surface patterns. They stated that lava ultimate has different surface characteristics and irregularities from the control group in some aged groups; micropores and pits are seen in these groups. Cerasmart and Lava Ultimate reported that surface roughness values were in the clinically recommended range after aging methods.

The optical properties of resin-containing materials may vary due to aging (Egilmez et al., 2018). The color changes resulting from aging are often associated with deterioration of the polymer matrix, unrestrained monomers of polymerization agents, and outer painting agents (Albuquerque et al., 2013). The resin-containing materials include monomers such as Bis-GMA, Bis-EMA, TEGDMA, UDMA. Bis-GMA increases the viscosity of materials and disadvantages color stability. TEGDMA and UDMA are added to the material to reduce viscosity. These monomers reduce the viscosity of Bis-GMA while enhancing cross-linking and mechanical properties. However, the color stability of the material is still controversial (Karaokutan et al., 2016). The water absorption properties of bis-GMA, TEGDMA, and UDMA monomers can cause differences in the degree of color stability of the material (Turgut, Bagis, Turkaslan, et al., 2014). The addition of TEGDMA to the material increases water absorption and prevents color stability. TEGDMA-based materials release monomers in larger quantities than Bis-GMA and UDMA-based materials into aqueous environments. Water absorption of bis-GMA-containing materials increases due to TEGDMA concentration and increases proportionately but decreases with the displacement of TEGDMA with UDMA. UDMA is less susceptible to painting than Bis-GMA (Turgut, Bagis, Turkaslan, et al., 2014). Gajewski et al. reported that Bis-GMA causes the highest, TEGDMA and Bis-EMA lowest, and UDMA causes water absorption similar to other monomers. Their resolutions were observed in UDMA, Bis-GMA, and Bis-EMA after the highest TEGDMA. They reported that these contents could be hydrolyzed by filtering out their unrestrained monomers or low molecular weight oligomers when exposed to oral fluids (Gajewski et al., 2012). In our study, UDMA, TEGDMA, Vita Enamic material with content, UDMA, TEGDMA, Shofu HC material with content showed more ΔE changes in the resin structure of approximately 86% after aging thermally. We believe that the ΔE change in Vita Enamic and Shofu HC hybrid materials is due to their content and structural differences. The contents of CAD/CAM materials may cause them to be resistant to long-term aging procedures. Exposing materials of this solid structure for longer-term aging processes and measuring them by adding dyeing agents can make color change differences clinically noticeable. When we look at the contents of CAD/CAM materials used in our study, after aging without dyeing agents in as little as one year (aging process with 10,000 cycle thermals), color changes are not expected to reach the clinically "acceptable" threshold value and exceed this threshold value. ΔE values are below the clinically acceptable threshold in our study as in previous studies compared to before the aging process with thermal cycles (Alp et al., 2018; Lauvahutanon et al., 2017; Turgut & Bagis, 2011).In the new studies, color changes of materials can be examined by increasing aging time with dyeing agents and functional adhesion processes. In addition, the addition of detailed color parameters and SEM reviews can contribute to the new studies.

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# Optimizing Fetal Outcomes in Twin-Twin-Transfusion Syndrome using Serial Amnioreduction in Resource-Constrained Unit: A Case Report

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**Abstract**
Background: Twin-twin transfusion syndrome is an important complication of monochorionic placentation in twin pregnancy. The management of this condition in Nigeria and many other developing countries has always been "watchful expectancy" with attendant high perinatal morbidity and mortality. Amnioreduction is a less demanding treatment option compared with fetoscopic laser coagulation management option in terms of cost and expertise, but has not been reported from any unit in Nigeria. Case Presentation: A 28-year-old gravid 2 para $1^{+0}$, 1 alive, carrying twin pregnancy was referred at 22 weeks gestation with complaint of mild discomfort due to sudden rapid enlargement of the abdomen. Physical examination and ultrasound scan assessment confirm Quintero stage II Twin-twin transfusion syndrome and she underwent serial amnioreduction at 24, 28 and 31 weeks of gestation with satisfactory outcomes. She had caesarean section at 33 weeks due to an acute episode of severe maternal discomfort and was delivered of 2 live female babies. There were no adverse perinatal events. Conclusion: This case presented demonstrates the role of amnioreduction in the management of carefully selected cases of twin-twin transfusion syndrome and further encouraged its utilization. in resource-constrained units instead of 'watchful expectancy' and in the absence of fetoscopic laser photocoagulation

**Keywords:** Twin-to-Twin Transfusion Syndrome, Serial Amnioreduction, Fetoscopic Laser Photocoagulation, Quintero Staging, Resource-Constrained Unit

## 1. Introduction

Nigeria has the highest global rate of multiple pregnancies (Osaghae and Unuigbe, 2016). The management of Twin-twin transfusion syndrome (TTTS), which is one of the important complications and a significant contributor to the associated high perinatal morbidity and mortality has not been reported in literature. It is however reported that there is dearth of skill and expertise, equipment and other logistic requirements in Nigeria and other developing

countries that are required for the optimum management of cases (Osaghae and Unuigbe, 2016). Hence units practice conservative approach of 'watchful expectancy.'

Twin-twin transfusion syndrome was first described in 1975, and affects 8-15% of monochorionic diamniotic (MCDA) twin pregnancies, most of which present between 16-26 weeks of pregnancy (Simpson 2012, Xueju et al., 2015). In TTTS, the imbalance in the intertwin blood transfusion from donor fetus to the recipient fetus is characterized by unidirectional deep arteriovenous flow that dominates the protective bidirectional superficial anastomoses (Durbin 2011, Bansal et al., 2020). The overall perinatal mortality in untreated TTTS rises from 60-70% to 90-100% in pregnancies delivered before 26 weeks, while long term neurodevelopmental deficit occurs in 20-40% of surviving fetuses (Durbin 2011, Simpson 2012, Salomon and Ville 2018 Bansal et al., 2020). The Quintero staging system is mostly used in clinical management. It defines early stages (I and II) by ultrasound finding of discordance in bladder and amniotic fluid (AF) volumes, intermediate stage III by abnormal Doppler findings, and late stages (IV and V) as hydrops and fetal death. In addition however, the gestational age, and the available skill and facilities are the core determinants of treatment modality. The treatment modalities available for the management of TTTS range from conservative approach to the more advanced fetoscopic laser coagulation. Amnioreduction procedure provides opportunity to prolong the pregnancy and improving the fetal outcomes through iatrogenic withdrawal of amniotic fluid and lowering of intrauterine pressure (Osaghae and Unuigbe, 2016).

We report the successful management of stage II TTTS with serial amnioreduction in the unit, in order to encourage feto-maternal medicine centres and specialists in Nigeria and other developing countries to utilize this procedure in appropriate cases instead of the current practice of 'watchful expectancy.'

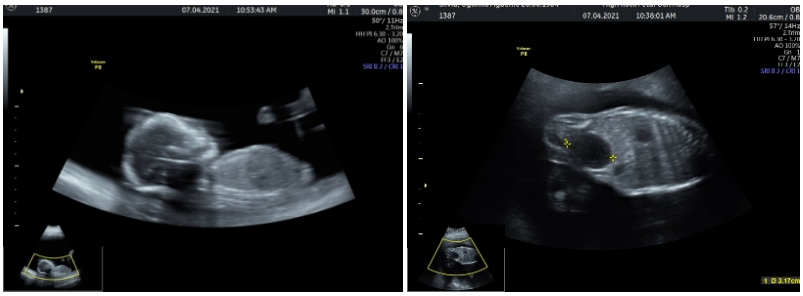
## 2. Case Report

A 27-year-old gravida 2 para $1^{+0}$, 1 alive, with twin pregnancy was referred at 22 weeks with ultrasound scan diagnosis of increased AF in one fetus and reduced AF in the other fetus of a twin pregnancy. She also complained of an acute experience of rapidly enlarging abdomen, which was mildly discomforting. The initial mild abdominal discomfort however worsened progressively over 24 hours prior to admission at 24 weeks gestation. Physical examination reveals an apparently healthy pregnant woman, with no obvious signs of palor, anicteric, but has moderate to severe pretibial pedal edema. She was dyspnoeic in supine position and respiratory rate was 24 cycles per minute. The pulse rate and blood pressures were 78bpm and 136/78 mmHg respectively. The abdominal examination shows grossly enlarged and shinny abdomen, with symphysio-fundal height of 44cm. Multiple fetal parts were palpated and the fetal heart rates were faintly audible. Ultrasound scan assessment was carried out which demonstrated the main findings as poly-/oligohydramnios sequence and enlarged/collapsed bladder in fetuses I and II respectively (table 1 and figure 1).

Table 1: Ultrasound Scan Findings at Presentation based on Quintero Parameters

| | **Fetus I** | **Fetus II** |
|---|---|---|
| AF (DVP) | Increased | Reduced |
| Fetal Bladder | Enlarged | Collapsed |
| UA PI | 1.4 (Normal) | 1.2 (Normal) |
| DV a-wave | Normal FVW | Normal FVW |
| EFW | 543g | 411g |
| Cervical Length: 27.8mm | | |

A: Increased/Reduced Amniotic Fluid



B: Collapsed Bladder Enlarged Bladder

Figure 1: Ultrasound Scans Diagnosis of Stage II TTTS

The ultrasound scan and clinical findings were discussed with her, and she consented to amnio-reduction which was carried out at 24, and repeated at 28 and 31 weeks due to recurrence of unbearable abdominal enlargement and maternal discomfort. Between 2500-3800mls of AF was aspirated under standard protocol during each procedure and follow up clinical monitoring and weekly ultrasound scan were done. Post-procedure, she continued on bed rest, oral indomethacin and salbutamol twice daily for 5 days, phenobarbitone for 3 days, and intravenous cefuroxime for 5 days. There was noticeable increased fetal activity, gradual increase in bladder, and amniotic fluid filling in twin II from the ultrasound scan report after the procedure. At 33 weeks of gestational, she had caesarean section due to acute and severe maternal discomfort and was delivered of two female babies with APGAR scores at 1 and 5 minutes respectively of 8 and 9 in baby I, and 7 and 9 in baby II. The babies weighed 2.1kg (baby I), and 1.6kg (baby II) (fig 2). There was no other remarkable post-operative event.

Baby I: 2.1Kg Baby II: 1.6Kg

Figure 2: Babies at delivery

**3. Discussion**

The fetal outcomes in TTTS can be substantially improved by early diagnosis and timely commencement of appropriate management modality (Sebir et al., 2010, Osaghae and Unuigbe, 2016). The possibility of early diagnosis through screening with markers such as the nuchal translucency (NT) scan, folding of the intertwin membrane and crown-rump length (CRL) is low in Nigeria and most developing countries, thus contributing to late diagnosis and poorer outcomes (Osaghae and Unuigbe, 2016). The diagnosis, in this case, was based on the Quintero staging which defines the severity and prognosis of the pathology, but reported to be a poor predictor of disease progression and weakly correlates stage with treatment outcomes (Mylrea-Foley et al., 2019, Couck et al.,

2021). The classification as stage II was based on the significant disparity in the AFV between fetus I and II, and the bladder volume measurements. The ultrasound diagnosis of stage II, gestational age of 24 weeks and rapidly worsening maternal discomfort were the basis for intervention, as recommended in pregnancies above 18 weeks (Prefumo and Jauniaux 2018, Mylrea-Foley et al., 2019). The choice of amnioreduction was based on the above considerations and the availability of expertise and equipment in the unit. The goal of the procedure was to reduce the intrauterine pressure (IUP), risk of preterm labour and improve the intraplacental blood circulation, through iatrogenic reduction in the amniotic fluid volume. The procedure was discontinued when deepest vertical pool of amniotic fluid (DVP AF) in the recipient twin was < 8cm. This skill for amnioreduction can be easily acquired through appropriate training, while the minimal equipment required is relatively cheap compared to other management modality especially FLP. The independent or adjunctive use of septostomy to equilibrate amniotic fluid volume, has not been shown to have better survival advantage over amnioreduction alone (Osaghae and Unuigbe, 2016). Moreover, it requires additional expertise for successful use. Fetoscopic laser coagulation which is the gold standard for all stages of TTTS, because it has better fetal survival and long-term neurological outcomes, was not used because of non-availability and expertise (Roberts et al., 2014, Prefumo and Jauniaux, 2018, Mylrea-Foley et al., 2019). Overall survival rate with serial amnioreduction is about 50% for at least one twin delivered at around 28 weeks, and the risk of sequelae is reduced to about 20% among survivors following amnioreduction.[6] She was delivered at 33 weeks, which is within previously reported 30-34 weeks when most pregnancies are delivered, usually due to severe maternal discomfort (Mylrea-Foley et al., 2019). There was no adverse perinatal event in both babies, and long-term follow up strategy is on-going.

## 4. Conclusion

The perinatal outcomes of TTTS presenting in resource-constrained units in Nigeria and other developing countries could be improved using serial amnioreduction in appropriate cases as demonstrated in this case. The acquisition of proficiency in procedure can be obtained through collaborations with fetal medicine centres experienced in the procedure.

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None to declare

**Ethical Approval:**
Obtained from the institutional ethics committee

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# An Evaluation of the Reflective Constructs Influencing Community Pharmacists' Decision-to-Procure from Pharmaceutical Suppliers: A Structural Equation Modeling Study

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**Abstract**
In low-and middle-income countries, patients' access to affordable medicines is a perennial challenge at all levels of healthcare delivery. Community pharmacists are expected to bridge the supply and demand gap. Unlike the plethora of studies done at the hospital and government institutions level, there is a paucity of empirical evidence on the factors influencing medicine procurement decisions from supply channels at the community pharmacy level. The study aimed to investigate the influence of community pharmacists' professional and entrepreneurial considerations on their decision-to-procure from medicine suppliers. A cross-sectional survey which adopted a self-administered questionnaire approach to obtain primary data from randomly sampled respondents (**N**=398) from three purposively selected states in southwestern, Nigeria. Structural equation modeling (SEM) methodology was used to test the hypothesized model at $p<0.05$. The study revealed acceptable model fit and validity measures for measurement and structural models. Cost and profitability factors were significant predictors of decision-to-procure compared to service and product quality factors among respondents [$\beta=0.343$, $p=0.001$ *vs.* $\beta=0.044$, $p=0.606$]. Product selection had a positive moderating effect on cost and profitability factors [$t=1.980$, $p=0.048$] and a negative directional effect on service and product quality factors in the hypothesized model [$t=-2.960$, $p=0.003$]. Community pharmacists should balance financial considerations with a professional focus to ensure patients' access to quality and affordable medicines. Study outcomes suggest the development and implementation of universally acceptable guidelines on medicine procurement in community pharmacy settings in low-and middle-income countries. The study validated the SEM model for evaluating priorities influencing community pharmacists' buying decisions. To the best of the authors' knowledge, this is the first study to use the SEM framework to explore factors informing drug procurement decisions from the community pharmacists' perspective in low-and middle-income countries.

**Keywords:** Community Pharmacy, Cost Management, Low and Middle-Income Countries, Medicines, Pharmacoeconomics, Pharmaceutical Marketing, Procurement, Structural Equation Modelling

## 1. Introduction

The ultimate objective of any procurement process in medicine supply is to ensure unrestricted availability and seamless access to medicines by end-users or patients. This is of paramount value in all spheres of medicine supply chain management [WHO, 2018]. According to the World Health Organization (WHO), there are at least six important criteria that characterize a good procurement process namely; cost-effectiveness of drugs, expected quality, properly estimated quantities, supplier reliability, timely supply, and manageable costs [WHO, 1999; 2002; 2018]. The focus of studies in academic literature has been placed on studying procurement in hospital and institutional settings, with less attention to community pharmacy settings [Njoki & Kimiti, 2018: Vogler *et al.*, 2013: Lima-Dellamora *et al.*, 2014; Muhia *et al.*, 2017]. In low and middle-income countries (LMICs) where expenditure on medicine is essentially out of pocket at the individual level, medicine affordability is still a challenge. [Ekmann, 2007; Adebiyi and Adeniji, 2021: Oamen and Osemene, 2021] In Nigeria, the government developed the National Health Insurance Scheme to minimize costs and improve access to healthcare. [NHIS, 2012; Adesokun *et al.*, 2020] However, this strategy has not sufficiently covered the vast majority of people as well as limited coverage of medicines under the scheme [Adesokun *et al.*, 2020; Adeniji, 2017]. Other challenges inherent in the scheme include operational problems [Adesokun *et al.*, 2020], limited funding [Adesokun *et al.*, 2020; Ekmann, 2007], corruption, and misappropriation of resources [Adesokun et *al.*, 2020], and underrepresentation of the population due to low coverage [Adeniji, 2017]. Hence, the majority of patients have no option but to access or procure prescribed medicines from community pharmacies [Oamen, 2021]. Unlike the case in institutions or hospital-based environments where procurement follows laid down processes and procedures, community-level pharmacies take a more direct-from-supplier, individual approach. Despite the speed and flexibility associated with this process at the community level; there is the need to unpack the factors influencing the decision to buy from supply channels. Evidence in this regard from LMICs has been mostly anecdotal, suggesting a gap exists in the literature. Community pharmacists are expected to maintain a practical balance between their commercial interests and the welfare of the patient [Hepler & Strand, 1990; Oamen *et al.*, 2021]. Therefore, procurement decisions should be guided by considerations such as cost, affordability, and business profitability [Mathews *et al.*, 2020: Lee *et al.*, 2021: Suh, 2011], service quality from suppliers [Njoki & Kimiti, 2018], and product quality [Njoki & Kimiti, 2018: Giralt *et al.*, 2020], the type of product selected whether generic or substitutes or branded medicines [Seeley & Singh, 2021: Dedrick and Eckel, 1984: You *et al.*, 2019: Perumal—Pillay and Suleman, 2020: Desai *et al.*, 2019] and quantity of products requested.[Dubois *et al*., 2019]. However, the absence of procurement guidelines for community pharmacy practice strengthens the need for further studies to validate the key elements. To the best of the authors' knowledge, the influence of the aforementioned factors on community pharmacists' decision-to-procure medicines from supply channels has not been fully explored in a low- and middle-income environment like Nigeria.

### *1.1 The novelty of the study*

The uniqueness of this study stems from the fact that it evaluated the factors influencing the buying decisions of community pharmacists from supply channels in an LMIC setting using a structural equation modeling (SEM) framework. Furthermore, the study proposed a validated checklist to provide a foundation for the development of a universally agreed guideline or protocol on procurement by community pharmacists in developing countries. The perspective of analysis was the healthcare provider or community pharmacists' perspective and the prototype of the supply channel evaluated was pharmaceutical sales and marketing companies.

### *1.2 Conceptual Framework*

Generally, the interaction between supply channels and community pharmacy practice has proven to have beneficial effects such as; ensuring drug supply, distribution, drug information, updates on drug development, and support services [Khan *et al.*, 2016: Oamen and Omorenuwa, 2021]. However, several pertinent concerns exist such as quality assurance of products supplied [WHO, 2018], price stability and affordability [Matthew *et al.*, 2020: Kho *et al.,* 2017; Dubois *et al.*, 2019], logistics and delivery [WHO, 2008], unethical drug promotion activities [Hall *et al.*, 2006; Lexchin, 1993; Brett *et al.*, 2003: Zaki, 2014: Khan *et al.*, 2016]. Although there is a plethora of studies focused on access to medicines in LMICs from the point of view of institutions and primary healthcare centers managed by governments [Njoki and Kimiti, 2018: Vogler *et al.*, 2013]. This is not the case in

community pharmacy practice. However, the reality is that lack of transparency and resources in government or publicly owned health institutions have shifted the burden of access and affordability of medicines to the private sector inclusive of community pharmacies. [Njoki & Kimiti, 2018: Adesokun *et al.*, 2020: Seeley & Singh, 2021] Supply channels to community pharmacists include wholesale, distributors, and pharmaceutical companies but for this study, a focus is placed on pharmaceutical companies due to their impact on prescribing and dispensing actions of community pharmacists [Khan *et al.*, 2016: Mukherjee, 2012: Bader, *et al.,* 2017)]. In the study, the structural equation modeling (SEM) technique was used to evaluate the relationships between variables as well as test the validity of the theoretical and empirical models. [Henseler *et al.,* 2015; Oamen, 2021]. The key constructs examined were cost & profitability factors, service and product quality factors, and their influence on the decision to procure medicines from suppliers. Each construct was elucidated by reflective indicator items to provide clarity about the possible causal relationships. The study unpacked the influence of these critical factors on community pharmacists' procurement decision-making behavior in an LMIC setting.

### *1.3 Study Hypotheses*

***H1*:** There are dominant reflective indicators of the factors influencing the decision behavior of community pharmacists
***H2***: Cost and Profitability factors **(CP)** significantly influence the decision-to-procure of community pharmacists from supply channels
***H3*:** Service and product quality factors **(SP)** significantly influence the decision-to-procure of community pharmacists from supply channels
***H4***: The influence of **CP** and **SP** factors on decision-to-procure of community pharmacists is moderated by product selection **(PT)** and quantity demanded **(PQ)** from supply channels

## 2. Methods

### *2.1 Study Design*

A cross-sectional study with structured questionnaires administered to randomly selected community pharmacists situated in three purposively selected states in southwest Nigeria. The study was conducted between the months of April to May 2021. The study applied structural equation modeling (SEM) techniques to evaluate the factors influencing medicine procurement decisions of community pharmacists. The study adopted a community pharmacist's perspective in the analysis.

### *2.2 Study Population and setting*

The study population consisted of all registered community pharmacists in Ogun, Oyo, and Lagos states situated in South Western, Nigeria. Based on statistics from the apex regulatory body in Nigeria, the Pharmacists' Council of Nigeria (PCN) there are about 2000 registered community pharmacists in Southwest, Nigeria. [PCN, 2020: Ihekoronye *et al*., 2020]. The study purposively selected Lagos, Ogun, and Oyo states respectively because they represent approximately 70% of the population of community pharmacies (1400) in the geographical zone [Ihekoronye *et al.*, 2021; PCN, 2020]

### *2.3 Selection Criteria*

Community pharmacists with a minimum of one-year post-graduation practice experience and with procurement roles were selected. They could be pharmacist-owners or employed as pharmacist managers. Respondents could be in retail, wholesale, and/or a combination of retail and wholesale business models.

### *2.4 Ethical Approval and Consent to Participate*

Ethical approval was obtained from the Department of Health Planning, Research and Statistics, Ministry of Health, Ogun State, Nigeria; with approval ID Number- HPRS/381/371/2021. Informed consent was obtained from respondents.

*2.5 Questionnaire design and data collection*

The 25-item research instrument was developed based on information obtained from extant literature and industry experts and was administered using a random sampling method to 500 community pharmacists distributed across the three states in southwest, Nigeria. Responses used to rate perception were based on a 5-point scale which ranged from strongly agree (5) to strongly disagree (1). For ease and focus of the questions, they were divided into 2 main parts; Part 1 contained the demographic details of respondents while Part 2 had 5 subdivisions representing the proposed constructs namely- 1) 9 questions on cost and profitability criteria, 2) 11 questions on service and product quality criteria, 3) 2 questions on product type purchased, 4) 2 questions on product quantity criteria, and 5) purchase decision was determined by a single item (mean response score)

*2.6 Reliability and Validity of Research Instrument*

The internal reliability of the 25-item questionnaire was evaluated using the Cronbach alpha statistic. The overall alpha score was 0.865, hence establishing the reliability of the instrument. Face validity of the instrument was confirmed for relevance and applicability. by a focal group of experienced community pharmacists.

*2.7 Sample size determination and sampling*

Since the study is essentially a structural equation modeling study (SEM), the inverse square root method as advocated by Knock & Hadaya (2018) was used to determine the sample size. It is based on the probability that the ratio of the path coefficient and standard error is greater than the critical value of a test statistic for a given significance level [Kock and Hadaya, 2018; Hair *et al.*, 2021]. Therefore, assuming a statistical power of 0.8 [80%], a p-value of 0.05, and a minimum path coefficient of 0.2 denoted by Pmin, the sample size [S] is given by;

$$\mathbf{S} > \left[\frac{\mathbf{2.486}}{\mathbf{Pmin}}\right]^2$$

The computed sample size was approximately 155 as the minimum requirement to obtain statistically valid and reliable SEM results. However, a definite final sample size of 398 spread across three states [Lagos-117, Ogun-193, and Oyo-88] was obtained using a simple random sampling method.

*2.8 Common Method Bias (CMB)*

Common Method Bias (CMB) was adequately addressed by varying the phrasing of questions and ordering of questions sequence. This was done to avoid bias from respondents [Peter and Troth, 2020: Chin *et al.*, 2012]. Harman's single factor method was used to determine the absence or presence of CMB in the dataset. It showed that the variance due to a single factor was 20.835% which is less than the benchmark value of 60% [Peter and Troth, 2020: Chin *et al.*, 2012].

*2.9 Data analysis*

Data analysis was done using the statistical package for social sciences (SPSS version 25) and open-source online software JAMOVI [The Jamovi Project, 2021]. Analysis was in four unique stages- 1) dataset was assessed for collinearity, reliability, convergent and divergent validity. 2) Exploratory factor analysis (EFA) was used to identify the factor structure of the dataset, to determine if it fits with the theoretical framework of the study. Indicators or items which failed to load above 0.4 cutoffs were eliminated from the dataset. Constructs or factors which did not fit with the theoretical base of the study were also excluded. 3) Confirmatory factor analysis (CFA) was used to confirm or validate the constructs obtained from EFA as well as model fit characteristics. 4) Structural equation modeling (SEM) analysis was used to examine the hypothesized structural relationship between the identified factors or constructs. 5) Moderation analysis using Product selection (PT) and Product quantity (PQ) variables as moderators

2.9.1 Model specification

The hypothesized structural model was based on the contribution of three constructs; two exogenous or independent variables- cost & profitability factors [**CP]** with 7 indicators, service & product quality factors **[SP]** with 10 indicators, and the endogenous or dependent variable Decision-to-procure **[D]** with a single item indicator **[P9].** The perspective of the analysis was that of the healthcare professional (community pharmacist). Product-type selection **(PT)** and Product quantity **(PQ)** (with two indicator items each) were not included in the initial structural model but were included as moderators in the path model. The exploratory factor analysis was performed using parallel analysis with oblimin (oblique) rotation) and the baseline for factors included in the model was set at 0.4 and above. CFA was executed using the factor structure obtained from the exploratory factor analysis. The maximum likelihood method was adopted for the computation of the structural model parameters.

## 3. Results

### *3.1 Response rate and Demographic characteristics of Sample*

A total of 398 out of 500 administered questionnaires were valid representing a response rate of 79.6%. A significant number of respondents 218 (55%) were male and 181 (45%) were female. The average age of respondents was 35 (SD=1.50) and the mean years of practice experience was 11 (SD=2.04). Respondents who practiced in wholesale settings were 60 (14.8%), 238 (60%) who practiced in the retail setting, and 100 (25.2%) who practiced in a mix of retail and wholesale settings. Respondents were distributed in three major states in the southwest, Nigeria as follows: Lagos (117, 29%), Ogun (193, 49%), and Oyo (88, 22%).

Table 1: Factor Loadings, collinearity, and reliability measures of study constructs

| Constructs | Indicators | Description | [a] Factor loading | [b]Cronbach | [c]VIF |
|---|---|---|---|---|---|
| **Service & Product focus (SP)** | **s16** | product quality | 0.766 | | 1.975 |
| | **s3** | reduced cost of logistics | 0.730 | | 1.667 |
| | **s13** | saves administrative time | 0.702 | | 1.945 |
| | **s7** | provide product information | 0.689 | | 1.898 |
| | **s11** | replace defective products | 0.653 | | 1.805 |
| | **s12** | give trade discounts/promos | 0.583 | | 1.661 |
| | **s20** | high supplier accessibility | 0.533 | | 1.765 |
| | **s1** | ease/convenience of business | 0.490 | | 1.386 |
| | **s19** | provide credit facility | 0.469 | | 1.462 |
| | **s22** | satisfactory customer service | 0.469 | 0.885 | 1.507 |
| **Cost & Profitability system (CP)** | **s2** | give favorable supply prices | 0.587 | | 1.389 |
| | **s24** | give contractual business | 0.532 | | 1.207 |
| | **s23** | high profitability | 0.504 | | 1.522 |
| | **s4** | provide variety/range | 0.490 | | 1.278 |
| | **s10** | negotiable pricing | 0.455 | | 1.32 |
| | **s15** | provide price updates | 0.443 | | 1.393 |
| | **s25** | increase business during COVID | 0.427 | 0.753 | 1.242 |
| **Product type selection (PT)** | **s9** | buy brand products | 0.598 | | 1.115 |
| | **s8** | buy generic products | 0.509 | 0.686 | 1.115 |
| **Product Quantity (PQ)** | **s18** | buy small quantities per order | -0.644 | | 1.137 |
| | **s17** | buy large quantities per order | 0.601 | 0.614 | 1.137 |

Note: s5, s14, and s21 were excluded due to low factor loadings <0.4, VIF=Variance Inflation Factor

Threshold values for; **a=**Factor loading> 0.4; **b**=Cronbach alpha set at> 0.6 to 0.7; VIF=Variance Inflation Factor set at <5.0. [Hu and Bentler, 1999: Henseler *et al.*, 2012; Taber, 2018]

Table 1 shows the output of the exploratory factor analysis with factor loadings of the indicators of each reflective construct. The VIF of the indicators showed acceptable values; hence multicollinearity concerns have been eliminated.

Table 2: Divergent Validity Measure of Constructs (Heterotrait Monotrait)

| Constructs | PQ | CP | PT | D | SP |
|---|---|---|---|---|---|
| **Product quantity (PQ)** | | | | | |
| **Cost and Profitability focus (CP)** | 0.521 | | | | |
| **Product selection (PT)** | 0.434 | 0.539 | | | |
| **Purchase Decision (D)** | 0.176 | 0.360 | 0.254 | | |
| **Service and Product quality (SP)** | 0.399 | 0.676 | 0.572 | 0.302 | |

Table 2 showed that the key constructs of the proposed structural model are different from each other as they fall below the 0.85 cutoff values. [Henseler *et al.*,2015]. This validates the constructs

Table 3: Measurement Model showing relations between CP, SP, and DECISION Constructs

| | | | 95% C. I | | | |
|---|---|---|---|---|---|---|
| **Construct** | **Indicators** | **β** | **Lower** | **Upper** | **t-value** | **p-value** |
| **DECISION** | **P9** | 1.000 | 1.000 | 1.000 | | |
| **SP** | **s16** | 0.725** | 1.000 | 1.000 | | |
| | **s3** | 0.646 | 0.759 | 1.046 | 12.32 | 0 .001 |
| | **s13** | 0.722 | 0.858 | 1.143 | 13.78 | 0 .001 |
| | **s7** | 0.700 | 0.854 | 1.148 | 13.35 | 0 .001 |
| | **s11** | 0.702 | 0.882 | 1.184 | 13.40 | 0 .001 |
| | **s12** | 0.664 | 0.766 | 1.047 | 12.66 | 0 .001 |
| | **s20** | 0.693 | 0.873 | 1.177 | 13.23 | 0 .001 |
| | **s1** | 0.552 | 0.580 | 0.847 | 10.50 | 0 .001 |
| | **s19** | 0.582 | 0.718 | 1.027 | 11.09 | 0 .001 |
| | **s22** | 0.614 | 0.630 | 0.883 | 11.70 | 0 .001 |
| **CP** | **s2** | 0.569 | 1.000 | 1.000 | | |
| | **s24** | 0.369 | 0.554 | 1.074 | 6.14 | 0 .001 |
| | **s23** | 0.695** | 1.018 | 1.527 | 9.79 | 0 .001 |
| | **s4** | 0.492 | 0.702 | 1.177 | 7.75 | 0 .001 |
| | **s10** | 0.576 | 0.862 | 1.363 | 8.69 | 0 .001 |
| | **s15** | 0.683 | 1.037 | 1.563 | 9.69 | 0 .001 |
| | **s25** | 0.443 | 0.677 | 1.189 | 7.14 | 0 .001 |

Note: β=standard regression coefficient, p<0.05 (significant at t-value >1.96), **highest beta values

In table 3, the measurement model reveals significant values of all the indicators/ items, hence validating the model. The results revealed that items **s16**- 'product quality' with *β= 0.725* and **s23**- 'high profitability' with *β=0.695* were the dominant items under **CP** and **SP** constructs respectively at p<0.01, in the measurement model.

*3.2 Model fit Measures*

The dataset was assessed using the following parameters: Kaiser Meyer Olkin (KMO) =0.907; Bartlett's test $\chi 2$ [*DF=300, p<0.001] =3320.801*. Chi square test $\chi 2$ *[DF=206, p<0.001*] *=357.468*. Furthermore, the structural model showed acceptable measures of fit for the model; comparative fit index *CFI-0.914*, Tucker Lewis Index *TLI=0.901*, non-normed fit index *NNFI=0.901*, and Goodness of fit index *GFI=0.967*. [Hu and Bentler, 1998; 1999]. The effect size as measured by the coefficient of determination R2 of the endogenous variable-Buying decision was 14.1% (0.141). This implies that 14.1% of the variance in the dependent variable is explained by the independent or predictor variables-CP and SP [Hair *et al*., 2014] *SRMR was 0.057 and RMSEA was 0.062* (*Lower limit=0.053, Upper limit=0.07*). [Hu and Bentler,1998; 1999].

Table 4: Parameter estimates of structural equation model

| Dependent | Predictors | Estimate | SE | 95% C. I | | β | t-value | p-value |
|---|---|---|---|---|---|---|---|---|
| | | | | Lower | Upper | | | |
| **Buying Decision** | **SP** | 0.0575 | 0.111 | -0.161 | 0.276 | 0.0438 | 0.516 | 0.606 |
| **Buying Decision** | **CP** | 0.5855 | 0.159 | 0.273 | 0.898 | 0.3427 | 3.676 | 0 .001 |

The structural model showed the relationship between the independent (predictor) variables- service and product quality factors (**SP**) & cost and profitability factors (**CP**) and the dependent (outcome) variable, Buying decision **(D)**. Table 4 showed that **CP** *[β=0.343, p=0.001]* significantly predicts **D** compared to **SP** which did not *[β=0.044, p=0.606].*

Table 5: The Moderating effect of Product selection (PT) and Product Quantity (PQ) on Hypothesized Model

| Variables | Estimate | SE | 95% C. I | | t-value | p-value |
|---|---|---|---|---|---|---|
| | | | Lower | Upper | | |
| **PT** | 0.0989 | 0.0519 | -0.0029 | 0.201 | 1.900 | 0.057 |
| **CP * PT** | 0.1315 | 0.0664 | 0.00133 | 0.262 | 1.980 | 0.048 |
| **PT** | 0.0645 | 0.0521 | -0.0376 | 0.1666 | 1.240 | 0.216 |
| **SP *PT** | -0.2003 | 0.0677 | -0.3329 | -0.0676 | - 2.960 | 0.003 |

Note: * =interaction, PQ has no moderating effect on the relationship

Table 5 showed that product selection factors **(PT)** positively improved *[t=1.980, p=0.048]* the impact of cost and profitability **(CP)** factor of respondents in decision making **(D)** compared to an inverse moderating effect on service and product quality factor **(SP)** ***[****t=-2.960, p=0.003].*

## 4. Discussion

This structural equating modeling study investigated the factors influencing the buying decisions of community pharmacists from pharmaceutical supply channels in selected states in southwest, Nigeria. The objective of the study was to empirically evaluate the influence of community pharmacists' considerations on medicine procurement decisions. Figure 1 showed the structural relationships between independent (SP and CP) and dependent (decision-to-procure) variables used to test study hypotheses. The implications on pharmaceutical service delivery by community pharmacists and pharmaceutical suppliers were discussed. The validity of the measurement and structural models showing the hypothesized relationship exhibited acceptable model fit. The initial measurement model revealed that 'product quality [*β=0.725, p<0.01*] and 'high profitability' [*β=0.695, p<0.01*] were the dominant items under cost & profitability factors (**CP)** and service & product quality factors (**SP)** constructs respectively, in the model. Hence, the hypothesis ***(H1)*** was supported by the study results. This feedback from respondents theoretically aligns with the premise that obtaining a product of the best quality as well as overall business profitability should be the focus of any procurement entity [WHO, 2018; Cavicchi and Vagnoni, 2020].

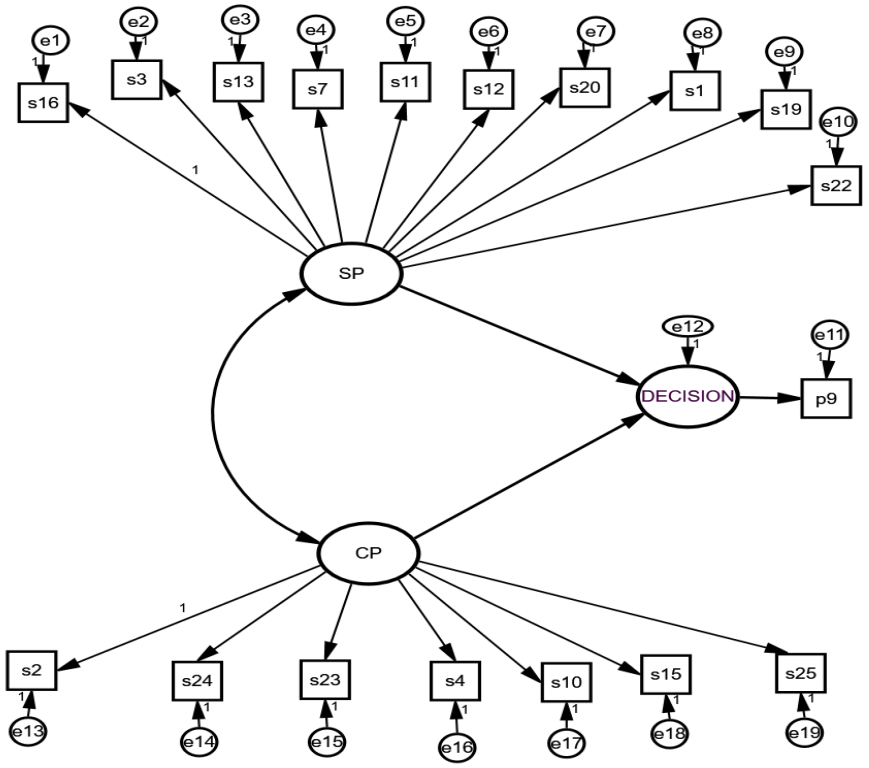


Figure 1: Structural diagram showing the relationship between **CP** and **SP** constructs on decision-to-procure [observed reflective indicators and error terms indicated]

The findings from the study model revealed that respondents showed more propensity to cost and profitability considerations compared to service and quality considerations. [*β=0.343, p=0.001 vs. β=0.044, p=0.606*] as shown in Table 4. Hence, hypothesis ***H2*** is supported and ***H3*** rejected. The issue of cost management is even more pertinent as an essential entrepreneurial trait for community pharmacists considering the competitiveness of the community pharmacy landscape at the level of price. This has necessitated the focus on the cost of procuring medication as revealed by the significant influence of cost and profitability factors on procurement decisions in the study. [Seeley and Singh, 2021: Cavicchi and Vagnoni, 2020]. Cost savings achieved as a result of better pricing as a consequence of adequate cost control measures in direct purchases from pharmaceutical companies should translate to cost reduction for the consumer. This assertion aligns with the pharmaceutical care model advanced by Hepler and Strand (1990) [Hepler and Strand, 1990]. On the other hand, the non-significant impact of the construct- service and quality factors (**SP**), on the decision behavior of community pharmacists suggests low prioritization on issues of quality and service delivery of suppliers compared to disproportionately higher emphasis on cost-based considerations. Therefore, the study suggests that community pharmacists go beyond just cost management and apply pharmacoeconomic tools such as cost-minimization analysis, cost-benefit analysis, and cost-effectiveness analysis in their practice. Therefore, at the community pharmacy practice level, community pharmacists must play the role of both the health professional and business decision-maker [Cavicchi and Vagnoni, 2020: Chappell and Barnes, 1984: Bader *et al.*, 2017: Kho *et al.*, 2017]. They should blend both cost and patient outcomes optimally; hence training and deliberate application of these tools in community pharmacy practice is advocated [Oamen *et al.*, 2021]. Moreover, from the consumer or end-user perspective, due to the high out-of-pocket cost of obtaining medicines, patients or consumers have become more price-sensitive and comparative in attitude. Hence, availability and competitive pricing are key expectations by the general public when visiting a community pharmacy [Iffat *et al.*, 2015: Suh, 2011]. Some studies suggest that increased competition among community pharmacies and the price sensitivity of customers also account for the focus on the issues of price [Mathews *et al.*, 2020: Cavicchi and Vagnoni, 2020]. This may be partly or wholly responsible for high levels of price competition among pharmacies which may have stimulated a paradigm shift preferentially to cost and profit

maximization strategies [Mathews *et al.*, 2020: Hassali *et al.*, 2010; Cavicchi and Vagnoni, 2020]. As a guiding principle, pricing systems or mark-up mechanisms should be such that the final cost should not be inhibitive to the end-user who is paying essentially out of pocket [Lee *et al.*, 2021]. The balancing act between service provision as pharmaceutical care providers and profitability should be targeted at the ultimate welfare of the patient. This finding is in support of the assertion of Giralt *et al.* (2020) which revealed a low emphasis on quality-assured medications from the supply channel in low and medium-income countries [Giralt *et al.*, 2020]

*4.1 Moderation effect of Product-type selection and Product quantity on the relationship between CP and SP on buying Decision (D)*

The study further investigated the impact of two constructs- product-type selection (PT) and product quantity (PQ) on the hypothesized relationship between cost & profitability factors (CP), and service & product factors (SP) on the dependent variable- buying Decision (D). The study revealed that PT significantly enhanced or improved the capability of community pharmacists to make better procurement decisions. On the other hand, PQ did not affect the relationship. (Table 5) These moderation effects are shown in Figures 2a & 2b. Therefore, hypothesis ***H4*** was supported for only the PT moderator for both factors-CP and SP respectively (*t=1.980, p=0.048 & t=-2.960, p=0.003)*. This perception of respondents is probably because generic medicines or substitutes tend to cost less than branded or more established brands. [Seeley and Singh, 2021: You *et al.*, 2019: Oamen and Osemene, 2021] However, it is expected that before the brand switch, consultation with the prescriber, patient awareness of the reason for the switch, and quality assurance of generic are holistically considered [Seeley & Singh, 2021]. Therefore, applying basic pharmacoeconomic tools such as cost-minimization and cost-effectiveness tools would enable the pharmacist manager to make more optimal buying decisions [Oamen *et al.*, 2021].

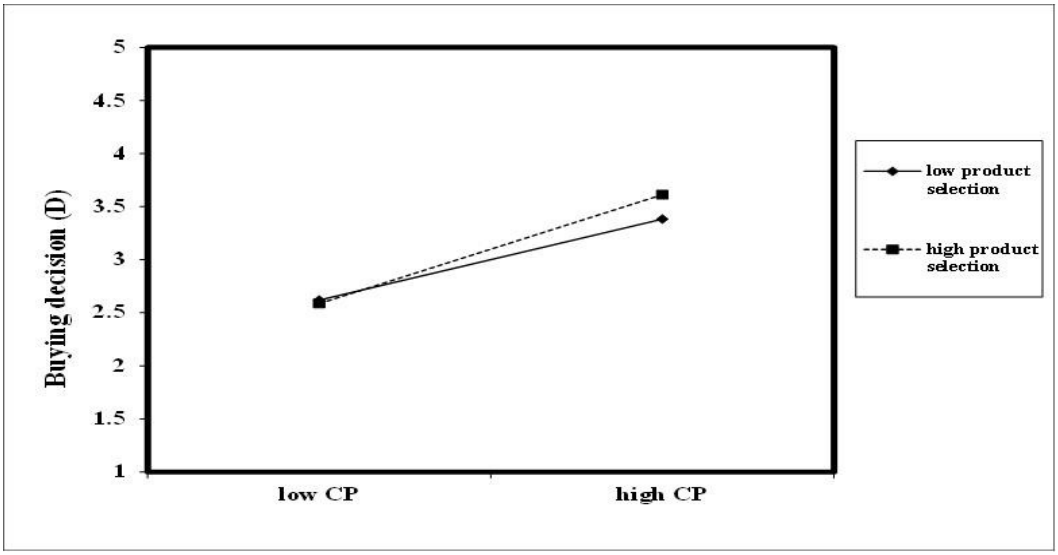


Figure 2a: The Moderating Effect of Product type (PT) on the influence of CP on Procurement decision (D)

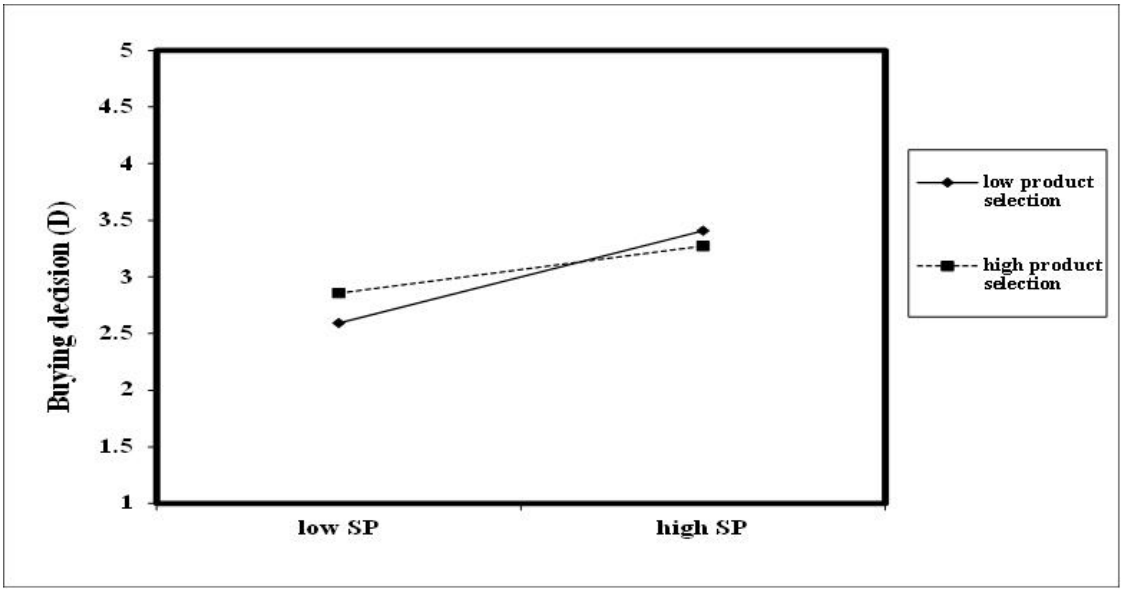


Figure 2b: The Moderating effect of Product type (PT) on the influence of SP on Procurement decision (D)

*4.2 Interpretation of moderating effect of Product type (PT) on Model*

In figures IIa and IIb, the study revealed that at low CP, when community pharmacists do not primarily consider cost and profitability factors in their decision-making, there is a lower influence of product selection on their buying decisions. Conversely, at high CP, product selection is a priority consideration in procurement decision-making. This finding aligns with the basic principle underlying cost-minimization analysis, in which case the lowest-priced generic is preferred, provided therapeutic equivalence is established [Oamen and Osemene, 2021] However when service and product quality are not primary considerations (low SP), community pharmacists tend to make their decisions based on product selection. This is supported by the focus on purchasing low priced generic products without a necessary focus on the quality of the product or integrity of the supplier [Khan *et al.*, 2016: Giralt *et al.*, 2020: Seeley & Singh, 2021] In contrast, at high levels of SP consideration (high SP) their buying decisions are not primarily defined by product selection. This means when service and product quality is a priority, the choice to procure medicines whether generic or branded drugs, is not a major concern or consideration compared to low SP considerations. This finding may be due to increased awareness about the comparable efficacy of generic and branded medicines [Desai *et al.*, 2019] However, there is a need for a medicine quality assurance system to support the decisions of the community pharmacist. [Ozawa *et al.*, 2020]. Therefore, study outcomes showed that product type had a significant effect on the relationship between key constructs (CP & SP) thereby supporting the hypothesis of moderation effect (***H4)***

*4.3 Implications of study to community pharmacy practice and pharmaceutical marketing companies in LMICs*

From the study outcomes, it is pertinent for community pharmacists in LMICs to improve their focus on holistic quality and cost factors from supply channels. Thus, it is necessary for a paradigm shift from basing procurement decisions primarily on obtaining low-cost medicines to a more balanced evaluation of medicines purchased from suppliers. To safeguard the quality assurance of drugs purchased, it is recommended that regulatory bodies supervising community pharmacists should enforce and monitor the adherence of community pharmacists to good procurement practices. The development and implementation of guidelines is a necessary step to actualizing the goal of standardizing procurement practices among community pharmacists in LMIC settings like Nigeria. The pooling purchasing strategy adopted in public procurement should also be applied in community pharmacy practice to facilitate or achieve a reduction in the costs of medicines purchased from suppliers [Dubois *et al.*, 2019; Nguyen *et al.*, 2013]. However, a policy framework to ensure that the price discounts enjoyed through the pooling system percolate or are cascaded down the supply chain to enhance affordability by the end-user. Thus, enforcement of some form of price uniformity may be enhanced by this approach compared to the negative effects of price wars due to inappropriate competitive behaviors among community pharmacies [Hassali *et al.*, 2010; Matthews *et al.,* 2020; Cavicchi & Vagnoni, 2020]. Therefore, to achieve this, a focus by healthcare professionals

on the quality of products and services (offered by suppliers) at price-friendly rates is advocated. There is a need for investments in capacity building of community pharmacists to embrace an overall focus on delivering cost-effective healthcare services to patients. This assertion is in sync with study outcomes, which support a paradigm shift from an uneven focus on cost and supply factors to health-centered activities. Pharmaceutical companies should adapt their marketing and sales strategies to the needs of community pharmacists, and not merely on achieving sales target and/or sales volume. Furthermore, there is a need for clear communications between representatives of pharmaceutical companies/suppliers and community pharmacists to ensure that issues of quality assurance and cost-minimization are common grounds for transactional relationships [Mukherjee, 2015]

*4.4 Limitations of the study*

The study adopted a cross-sectional study design and therefore there is a need for a longitudinal study design to examine if the constructs studied vary over time. Also, more constructs should be included in future studies to improve the robustness of findings.

*4.5 Conclusion*

The study adopted a structural equation modeling (SEM) framework to investigate the influence of community pharmacists' entrepreneurial and professional considerations on procurement decision-making from supply channels. The study validated a model for evaluating priorities influencing community pharmacists' buying decisions. Community pharmacists should adopt a balance between entrepreneurship considerations and patients' cost of accessing medicines. Pharmaceutical companies should adapt sales strategies to the patient-centered considerations of community pharmacists. The development and implementation of community pharmacy specific guidelines is a necessary step to actualizing the goal of standardizing procurement practices among community pharmacists in LMIC settings

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# COVID-19 Pandemic vs. Pre-Pandemic Period: Changes in Hospital Admission Rates, Length of Stay, and In-Hospital Mortality of Common Neurologic Conditions

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**Abstract**
Background and Objective: COVID-19 pandemic caused massive adjustments to healthcare systems in the country. This study determined the change in hospital admission rates, length of hospital stay and in-hospital mortality of common (non-COVID related) neurologic conditions during the COVID-19 pandemic and pre-pandemic period. Methods: The study utilized a retrospective cross-sectional study of patients admitted under the Department of Neurology at Jose R. Reyes Memorial Medical Center from the period of March 2019 to March 2020 (pre-pandemic group), and April 2020 to April 2021 (COVID-19 pandemic). Admission rates, length of stay and in-hospital mortality were calculated for cerebrovascular diseases, CNS infections, CNS neoplasms and Seizure disorders. Results: There were 1090 admissions from April 2019 to March 2020 and 393 admissions from April 2020 to March 2021 with an over-all decline of 63%. During the pandemic, the duration of hospital stay was longer for CNS neoplasms. Duration of hospital stay for cerebrovascular disease, CNS infection, and seizure disorders were not significantly different. There was an increase in over-all in hospital mortality from 22.75% to 26.46% with significant increase in the case fatality rate of cerebrovascular diseases. Conclusion: We observed a large decline in the over-all admission rate and longer hospital stays. The over-all in-hospital mortality rate also increased during the pandemic period.

**Keywords:** COVID-19, Admission Rate, Length of Stay, Mortality Rate, Cerebrovascular Diseases, CNS Infection, CNS Neoplasm, Seizure Disorders

## 1. Introduction

Coronavirus Disease 2019 (COVID-19) is caused by a novel strain of coronavirus (SARS-CoV 2) and first emerged in Wuhan, China in December 2019. Since then, it has affected millions of people worldwide and on

March 11, 2020, the World Health Organization declared the disease outbreak as a pandemic (WHO announces COVID-19 outbreak a pandemic, 2020). COVID-19 has been associated with various clinical manifestations with a wide spectrum of severity. SARS-CoV-2 primary attacks the lower respiratory system causing viral pneumonia, but it may also affect the heart, gastrointestinal system, liver, kidney, and central nervous system (Zhang, et al., 2020).

The first case of COVID-19 in the Philippines was reported on January 30, 2020 and as of March 7, 2020, there were already reports on local transmission of the disease. Luzon was placed under a state of enhanced community quarantine on March 16, 2020 and travel was restricted for most people except for healthcare workers, security services, and those involved in essential goods and services (COVID-19 in the Philippines, 2021). By then end of January 2021, the total number of confirmed cases in the country reached 525,618 where approximately 40% of these cases came from the National Capital Region (NCR) (COVID-19 pandemic: Latest situation in the Philippines – June 2021, 2021).

The imposition of lockdown and quarantine measures throughout the country not only has economic and political implications but also greatly affected the healthcare delivery systems. This unprecedented situation has led to immense pressure to re-organize and adapt quickly to the growing pandemic. Hospitals constructed isolation rooms, rolled out safety measures for healthcare workers and patients - including but not limited to social distancing and the use of personal protective equipment. However, the risk of health systems being overwhelmed poses a great concern to low and middle income countries with limited capacities.

Predicting hospital bed demand and understanding how long each patient may require hospitalization, may provide evidence for decision-making, contingency planning and allocation of resources. This requires an estimate of the number of patients requiring hospitalization and an estimate of how long each person will require hospital care in order to use and manage the limited resources our health systems have (Rivera-Rodriguez & Urdinola, 2020). Therefore, this study aims to determine if there is a significant change between the rates of admission, length of hospital stay and in-hospital mortality of common neurologic conditions (non-COVID related) requiring immediate care such as CNS infections, cerebrovascular diseases, seizures, and CNS neoplastic diseases.

## 2. Methods

### *2.1 Study design and data collection*

The study utilized a retrospective cross-sectional study of patients admitted under the Department of Neurology of Jose R. Reyes Memorial Medical Center from the period of March 2019 to March 2020 to represent the pre-COVID pandemic group, and patients admitted from April 2020 to April 2021 to represent the COVID pandemic group. Jose R. Reyes Memorial Medical Center is a DOH-retained tertiary hospital that has been one of the country's brain center, catering to thousands of patients with neurologic diseases annually.

The subjects were composed of non-COVID patients admitted and diagnosed with CNS infections, cerebrovascular diseases, seizures and CNS neoplasm from the period of April 2019 to March 2020 to represent the pre-pandemic group, and patients admitted from April 2020 to March 2021 to represent the COVID group. The total number of cases included in the study is based on the total number of admissions under the Neurology Department for the covered time period.

### *2.2 Statistical analyses and outcomes*

Descriptive statistics were used to summarize the general and clinical characteristics of the participants. Frequency and proportion were used for categorical variables. Shapiro-Wilk test was used to determine the normality distribution of continuous variables. Continuous quantitative data that met the normality assumption was summarized using mean and standard deviation (SD), while those that do not were described using median and range. Continuous variables were compared using the Mann-Whitney U test was used. For categorical variables, chi-square test was used to compare the outcomes. All valid data were included in the analysis. Null hypothesis

was rejected at 0.05α-level of significance. STATA 15.0 (StataCorp SE, College Station, TX, USA) was used for data analysis.

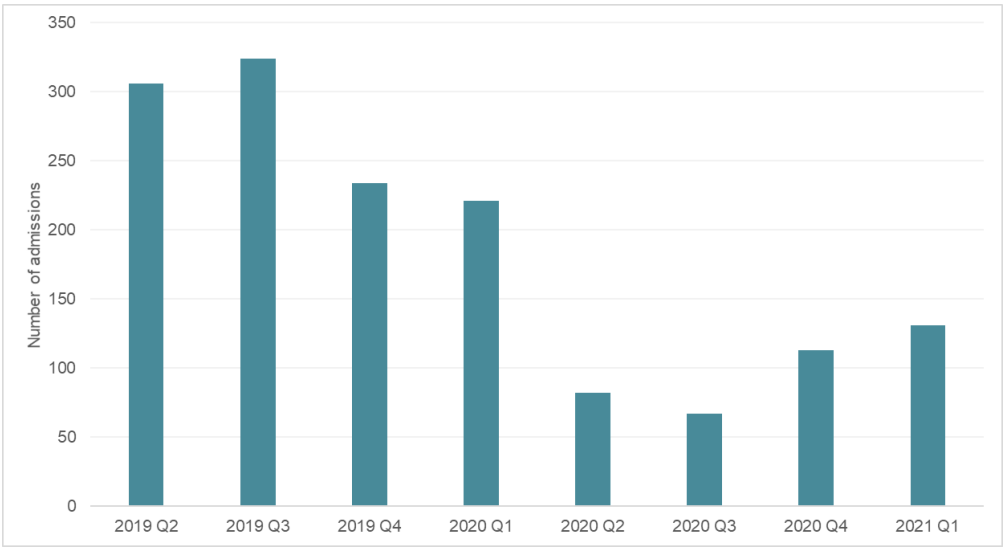
*2.3 Ethical Approval*

This study was reviewed and approved by the Institutional Review Board at Jose R. Reyes Memorial Medical Center (IRB No. 2021-084).

## 3. Results

There were 1090 admissions from April 2019 to March 2020 (pre-pandemic period) and 393 admissions from April 2020 to March 2021 (pandemic period) with an over-all decline of 63%. The census of patient admissions was lower during the four quarters of the COVID-19 pandemic period compared to corresponding quarters of the pre-pandemic period. The greatest differences were with the corresponding 2nd and 3rd quarters of the two durations (Figure 1).

A)




b)

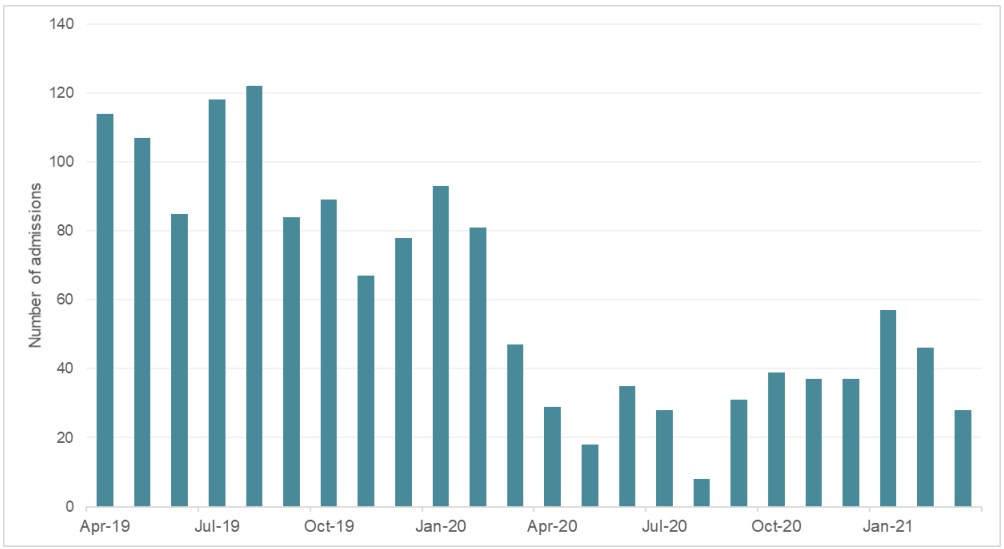



Figure 1: Census of neurology department admissions: a) quarterly; b) monthly.

Patients' characteristics of age (median [range]: 54 [20-97] years vs. 54 [19-91] years), male composition (61% vs. 58%), prevalence of cerebrovascular disease (87% vs. 88%) or CNS infection (4% vs. 5%) as primary

diagnosis, and total length of stay (median [range]: 6 [0-165] days vs. 6 [0-110] days) were not found to significantly differ between the two considered durations (Table 1). On the other hand, there were significantly less CNS neoplasms (3% vs. 6%) and more seizure disorders (5% vs. 3%) diagnosed after the onset of COVID-19 pandemic.

Table 1: Demographic and clinical profile of patients

| | **All (n=1483)** | **Pre-COVID-19 (n=1090)** | **COVID-19 Period (n=393)** | ***P*** |
|---|---|---|---|---|
| | **Median (Range); Frequency (%)** | | | |
| Age, years | 54 (19-97) | 54 (20-97) | 54 (19-91) | .243* |
| Sex | | | | .346† |
| Male | 890 (60.01) | 662 (60.73) | 228 (58.02) | |
| Female | 593 (39.99) | 428 (39.27) | 165 (41.98) | |
| Primary neurologic diagnosis | | | | |
| Cerebrovascular disease | 1297 (87.46) | 953 (87.43) | 344 (87.53) | .959† |
| CNS infection | 65 (4.38) | 46 (4.22) | 19 (4.83) | .610† |
| CNS neoplasm | 74 (4.99) | 63 (5.78) | 11 (2.80) | **.020**† |
| Seizure disorder | 47 (3.17) | 28 (2.57) | 19 (4.83) | **.028**† |
| Hospital stay, days | 6 (0-165) | 6 (0-165) | 6 (0-110) | .501* |

The pre COVID-19 period includes April 2019 to March 2020, while the COVID-19 period covers April 2020 to March 2021.
Statistical tests used: * - Mann-Whitney U test; † - Chi-square test.

Lengths of hospital stay of patients admitted primarily for cerebrovascular disease, CNS infection, or seizure disorder were comparable during the pre-COVID-19 and COVID-19 pandemic times (Figure 2, Table 1.1). Hospital stay among cases with CNS neoplasm appeared to be longer during the pandemic period than prior to it.

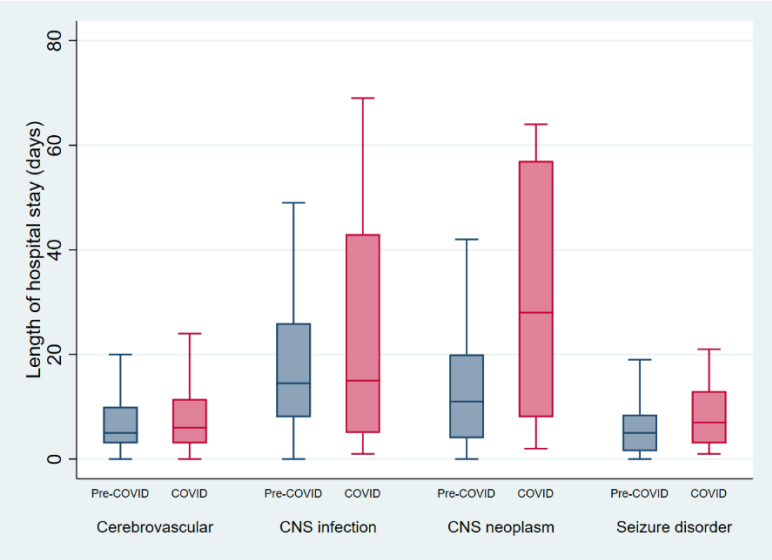



Figure 2: Lengths of hospital stay before and during COVID-19 pandemic, by primary neurologic diagnosis.

The median length of hospital stay per neurologic disease class is in Table 1.1. During the pandemic, the median duration of hospital stay was longer for CNS neoplasms (28 versus 11 days, p = 0.028). The duration of hospital stay for cerebrovascular disease, CNS infection, and seizure disorder were not significantly different for the two periods (Table 1.1).

Table 1.1: Length of hospital stay per neurologic disease

| | Pre-COVID-19 | COVID-19 Period | *P* |
|---|---|---|---|
| | Median (Range) | | |
| Length of hospital stay, days | | | |
| Cerebrovascular disease | 5 (0-165) | 6 (0-75) | .626 |
| CNS infection | 14.5 (0-94) | 15 (1-110) | .863 |
| CNS neoplasm | 11 (0-92) | 28 (2-64) | **.028** |
| Seizure disorder | 5 (0-20) | 7 (1-21) | .333 |

Statistical test used: Mann-Whitney U test

In-patient mortality rate was higher among neurologic admissions after onset of COVID-19 pandemic (26.46%) than before it (22.75%), although this was not significantly different between the two groups (Table 2). This increase in mortality was driven by the rise in case fatality rate for cerebrovascular diseases (from 20.88% to 27.62%), even though death rates for CNS infections (from 39.13% to 31.58%), CNS neoplasms (42.86% to 18.18%), and seizure disorders (from 14.29% to 5.26%) were lower during the COVID-19 pandemic than at pre-pandemic. The case fatality rate for cerebrovascular disease was markedly higher during the pandemic, at 27.62% (95% CI 22.96 to 32.67%, p = 0.013).

Table 2: Case fatality rate, by primary neurologic disease

| | All | Pre-COVID-19 | COVID-19 Period | *P* |
|---|---|---|---|---|
| | Frequency; Case fatality in % [95% CI] | | | |
| Total (n=1483) | 352; 23.74 [21.59–25.99] | 248; 22.75 [20.29–25.36] | 104; 26.46 [22.17–31.12] | .147 |
| Cerebrovascular disease (n=1297) | 294; 22.67 [20.41–25.05] | 199; 20.88 [18.34–23.60] | 95; 27.62 [22.96–32.67] | **.013** |
| CNS infection (n=65) | 24; 36.92 [25.28–49.80] | 18; 39.13 [25.09–54.63] | 6; 31.58 [12.58–56.55] | .778 |
| CNS neoplasm (n=74) | 29; 39.19 [28.04–51.23] | 27; 42.86 [30.46–55.95] | 2; 18.18 [2.28–51.78] | .183 |
| Seizure disorder (n=47) | 5; 10.64 [3.55–23.10] | 4; 14.29 [4.03–32.67] | 1; 5.26 [0.13–26.03] | .635 |

## 4. Discussion

The pandemic has caused a serious strain on the healthcare system not only in the Philippines but also worldwide. Since the detection of the first case of COVID-19 in the Philippines, the healthcare system adjusted its resources to cater to both COVID-19 patients and other diseases. However, this resulted to postponement of elective procedures, out-patient department closure, shift from face-to-face out-patient clinic to teleconsultation and reducing the over-all bed capacity to follow the imposed health protocols.

A large decline in admissions was noted during pandemic period and one reason could be the reduced bed capacity. As hospitals dedicate certain wards as isolation wards and to ensure adequate spacing between beds, the number of beds was markedly reduced. This was similar to other medical conditions and hospitals as reported in other countries. In one study done in Qatar, there was a decline of 5% to 75% drop in their over-all admissions, together with a drop in the number of elective and non-elective cases. Also, about 9%–58% decline was observed in admissions for acute appendicitis, acute coronary syndrome, stroke, bone fractures, cancer, and live births (Baum & Schwartz, 2020). In the United States, a significant decline of 42% in over-all admissions were noted in the Department of Veterans affairs hospitals (Butt et al., 2020).

Other possible reasons could be the imposition of lockdowns and limited transportation options, and fear of going to hospitals due to fear of contracting the virus.

The decrease in the number of over-all admissions were accompanied by longer hospital stay duration. Possible reason could be the imposition of lockdowns on certain wards or extension of quarantine period when exposed to COVID-19 patients. A significant decrease in the number of CNS neoplasm admissions was seen, but the length of hospital stay was markedly increased for admitted patients during the pandemic period compared to pre-pandemic period. This is primarily because of the postponement of elective surgeries in the hospital during the pandemic period, and limiting the use of operating rooms for emergency cases. However, despite longer hospital stay for CNS neoplasms, the over-all case fatality rate for the disease remained non-significant both pre-pandemic and during the pandemic period.

Over-all in-hospital mortality rate for all 4 neurologic conditions increased significantly from 22.75% to 26.46% during the pandemic period. This was brought about by the higher case fatality rate of cerebrovascular illnesses, however, reasons for the higher case fatality rate were not explored and one of the limitations of the scope of this study.

These findings must be taken into consideration for future pandemic planning and response but no causal relationship must be inferred from these results. Follow-up studies must be performed in order to see and infer causality and to explore other factors that might have contributed to the findings discussed.

## 5. Conclusion

In summary, as the pandemic unfolded, we observed a decline in the number of over-all admissions in the hospital and longer hospital stays. The over-all in-hospital mortality rate also increased during the pandemic period with significant increase in the case fatality of cerebrovascular diseases.

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# Trend of Antenatal Bookings in a Teaching Hospital in South Western Nigeria

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**Abstract**
Introduction: The age-long practice of late booking is gradually changing towards early pregnancy booking because of the benefits. Implementation of new medical guidelines is however often delayed in developing countries. Aim: The study proposes to observe the trend in antenatal booking in respect of booking gestational age, and the relationship with maternal socio-demographic and obstetric characteristics. Methodology: A retrospective study of antenatal bookings between 2016 and 2020 in Olabisi Onabanjo University Teaching Hospital, Sagamu Ogun State, Nigeria was carried out. Data were collected from pregnant women that had a minimum of 4 clinic attendances and delivered in the hospital. Data analysis was by descriptive statistics and presented in simple frequency tables. Results: Six thousand, eight hundred and ninety-nine pregnancies were booked, with early bookings (< 13 weeks) in 23.9% and late bookings in 64.6% (14-26 weeks) and 11.5% (27-36 weeks). The proportion of early bookings (23.9%) was higher compared with 18.8% reported in 2014 in same centre. Every year, the number of early bookings was initially stable at 20.4%, but rose to 26.7 - 30.8 in the last 2 years of study. Maternal age < 30 years, secondary or tertiary educational level and previous caesarean delivery were the predominant variables among women that booked in early pregnancy. Previous or on-going medical disorders and/or delivery complications were not strongly associated with early booking. Conclusions: The practice of late pregnancy booking is still a major issue, though the proportion of early bookings has continued to increase compared with previous study. Improvement in education, economic empowerment and health education that emphasizes preventive rather than curative role of ANC is advised.

**Keywords:** Antenatal, Booking, Early and Late Booking, Gestational Age, Developing Countries

## 1. Introduction

The gestational age at booking have effect on the fetal and maternal outcomes of pregnancy and also determines the number andfrequencies of antenatal visit for clinic-laboratory evaluations of pregnancy and allocation into risk groups**.** The term booking is sometimes used interchangeably with registration and it is regarded as the entry point visit for ANC in an index pregnancy (Aduloju et al., 2016). Longer interval between booking and delivery

GA is believed to be associated with better quality of obstetric performance (Ifenne and Utoo, 2012, Zaman et al., 2019, Okunlola, 2006). Consequently, booking early in pregnancy is advocated in order to allow for more weeks of pregnancy evaluation, and care. Early pregnancy booking has the advantage of establishing the most accurate GA in women with unsure last menstrual period, early diagnosis of fetal structural and chromosomal abnormalities, and ascertainment of baseline health parameters of the woman through urinalysis, packed cell volume, genotype test, retroviral and hepatitis screening and blood group determination (Adegbola and Kuku, 2015, Tolefac et al., 2017, Jice et al., 2018). In addition, common but important medical disorders that contribute to adverse pregnancy outcomes can be predicted through screening tests in early pregnancy, especially in the first trimester (Adegbola and Kuku 2015, Nicolaides 2011). These medical disorders can be prevented and/or the severity significantly reduced by early commencement of preventive measures such as low dose aspirin, thus impacting positively on maternal and perinatal morbidity and mortality (Nicolaides 2011). The World Health Organization (WHO) recommendation on ANC is that first antenatal contact in pregnancy should be within 12 weeks, while other researchers proposed a model in which the first contact should be within13 weeks because of its demonstrated superior advantages in the overall obstetric performance and reduced perinatal and maternal morbidity and mortality (WHO, 2016, Nicolaides, 2011, Ndidi and Oseremen, 2010, Mohammed at al., 2011). This practice should be promoted in developing countries because of resource limitations to manage disorders in pregnancy and prevent morbidity and mortality.

The pattern of antenatal booking is also related to other maternal socio-demographic and obstetric characteristics. Few studies from Nigeria have concurrently focused on the trend in ANC booking and their relationship with maternal socio-demographic and obstetric factors (Ifenne and Utoo, 2012, Zaman et al, 2019, Lamina, 2004). The only study available from Sagamu was published over a decade (Lamina, 2004). The aim of this retrospective study is to observe the trend of antenatal booking in terms of booking GA, using GA < 13 weeks as cut-off between early and late booking and to express booking GA in relationship with maternal socio-demographic and obstetric factors in Olabisi Onabanjo University Teaching Hospital, Sagamu, Ogun State, Nigeria.

## 2. Methodology

It is a descriptive retrospective study that was conducted in the Department of Obstetrics and Gynaecology, Olabisi Onabanjo University Teaching Hospital, Sagamu, Ogun State. The case notes of all the pregnant women that were booked between 1st January, 2016 and 31st December, 2020, were retrieved from the Health Information System Department and those with complete records that shows minimum of 4 antenatal clinic attendances and delivery notes were selected for data extraction and analysis, while excluding women who booked after 36 weeks and/or did not attend minimum of 4 antenatal clinics before delivery. The number and frequency distribution of booked antenatal women every year, according to gestational age groups of < 13 weeks, 14-26 weeks and 27-36 weeks were obtained. Additional data about maternal socio-demographic characteristics (maternal age, educational level attained) and obstetric characteristics (parity, previous medical conditions, mode of previous delivery, and complications in previous delivery) were collated. Previous medical conditions involving any systems and complications during delivery were also recorded.

In this study, a booked pregnancy is one that has attended at least four antenatal visits and has had tetanus toxoid (Villar et al., 2001).The booking is considered early, if registration is done before 13 completed weeks of pregnancy and late, if it occurs from the 14th week.

The extracted information was entered and analyzed using the Statistical Package for Social Sciences (SPSS) version 20.0 (SPSS Inc, Chicago, IL). The mean, and range values were determined for gestational ages and other variables and documented in both absolute figures and percentages. Study results are presented as simple frequency tables. Ethical approval for the study was obtained from the Health Research Ethics Committee (OOUTH/HREC/483/2022AP)

## 3. Results

Six thousand, eight hundred and ninety-nine pregnant women were booked for antenatal during the study period of 5 years, with an average of 1,379.8 booked pregnancies per year.

### *3.1. Trend of Antenatal Booking*

Table 1: Pattern of antenatal booking at different gestational ages

| Year | Antenatal Bookings | | Booking Gestational Age in Weeks (%) | | |
|---|---|---|---|---|---|
| | Total (%) | Mean Booking GA | < 13 | 14-26 | 27-36 |
| 2016 | 1298 (18.8) | 26.5 ± 3.4 | 312 (20.4) | 837 (64.5) | 149 (11.5) |
| 2017 | 1514 (21.9) | 19.3 ± 2.5 | 309 (20.4) | 982 (64.8) | 223(14.7) |
| 2018 | 1795 (26.0) | 17.4 ± 4.1 | 361 (20.1) | 1213 (67.6) | 221 (12.3) |
| 2019 | 1275 (18.5) | 16.6 ± 5.3 | 393 (30.8) | 720 (56.5) | 162 (13.7) |
| 2020 | 1017 (14.7) | 17.1 ± 5.5 | 272 (26.7) | 703 (67.2) | 42 (4.1) |
| **Total** | **6899 (100.0)** | **17.0 + 4.1** | **1647 (23.9%)** | **4455 (64.6%)** | **797 (11.5%)** |

The trend of antenatal bookings shows a rise from 1298 (18.8%) in 2016 to its peak of 1795 (26.0%) in 2018 and then declines to its lowest of 1017 (14.7%) in 2020. The majority of pregnancies were booked between 14 and 26 weeks during the study period, with the highest mean booking GA of 26.5 weeks in 2016, the lowest of 16.6 weeks in 2019 which then increased to 17.1 weeks in 2020. The study however also shows that proportionally in each succeeding year, increasing number of pregnancies were booked at GA less than 13 weeks (20.4% in 2016, 20.4% in 2017, 20.1% in 2018, 30.8% in 2019 and 26.7% in 2020), while less numbers were booked at GA of 27-36 weeks (11.5% in 2016, 14.4% in 2017, 12.3% in 2018, 13.7% in 2019 and 4.1% in 2020)

### *3.2. Maternal Socio-demographic and Obstetric Variables among booked Pregnancies*

Table 2: Frequency Distributions of Socio-demographic and Obstetric variables among Booked Pregnancies

| Characteristics | Antenatal Bookings (N=6899) | Frequency Distribution (Weeks) < 13 (n=1647) | 14-26 (n=4455) | 27-36 (n=797) |
|---|---|---|---|---|
| **Maternal Age (years)** | | | | |
| < 20 | 519 (8.2) | 311 (18.8) | 180 (4.0) | 28 (3.5) |
| 21 – 30 | 3170 (54.9) | 1002 (60.8) | 1885 (42.3) | 283 (35.5) |
| 31 – 40 | 2692 (29.1) | 240 (14.6) | 2063 (46.3) | 389 (48.8) |
| 41 – 50 | 451 (7.1) | 73 (4.4) | 283 (6.4) | 95 (11.9) |
| >51 | 68 (0.8) | 21 (1.3) | 44 (0.9) | 3 (0.4) |
| **Education** | | | | |
| No Formal Education | 445 (8.0) | 8 (0.5) | 404 (9.1) | 33 (4.1) |
| Primary | 1155 (12.0) | 165 (10.0) | 749 (16.8) | 241 (30.2) |
| Secondary | 3372 (53.1) | 667 (40.5) | 2267 (50.8) | 438 (54.9) |
| Tertiary | 1927 (29.9) | 807 (48.9) | 1035 (23.2) | 85 (10.7) |
| **Parity** | | | | |
| 0 | 2337 (33.9) | 378 (22.9) | 1698 (38.1) | 261 (32.7) |
| 1-2 | 2352 (34.1) | 1167 (70.9) | 903 (20.3) | 282 (35.3) |
| 3-4 | 1908 (27.6) | 81 (4.9) | 1636 (36.7) | 191 (23.9) |
| ≥ 5 | 302 (4.4) | 21 (1.3) | 218 (4.9) | 63 (7.9) |
| **Pre-Existing Medical Disorder** | | | | |
| Present | 847 (12.3) | 199 (12.1) | 623 (13.9) | 25 (3.1) |
| None | 6052 (87.7) | 1448 (87.9) | 3832 (86.1) | 772 (96.9) |
| **Mode of Previous Delivery** | | | | |
| Vaginal | 5773 (83.7) | 1054 (63.9) | 3977 (89.3) | 742 (93.1) |
| Cesarean Section | 1126 (16.3) | 593 (36.1) | 478 (10.7) | 55 (6.9) |
| **Complications in Previous Delivery** | | | | |
| Present | 1041 (15.1) | 271 (16.5) | 674 (15.1) | 96 (12.1) |
| Absent | 5858 (84.9) | 1376 (83.5) | 3781 (84.9) | 701 (87.9) |

Table 2 presents the analysis of frequency distribution of some maternal socio-demographic and obstetric variables at different gestational age intervals in the study population.

Generally in all gestational age groups, more pregnancies (63.1%) were booked in women below 30 years compared with women above 30 years (37.0%). The majority of bookings at GA below 13 weeks were in women below 30 years (77.6%), compared with bookings in women above 30 years (20.3%). The maternal age range with the highest number of bookings below 13 weeks is 21-30 years (60.8%). Most of the antenatal bookings between 14 and 26 weeks and after 27 weeks were in women above 30 years of age (53.6% and 61.1% respectively). The maternal age range with highest number of bookings was 31-40 years (46.3%) at 14-26 weeks and 31-40 years (48.8%) at GA between 27 and 36 weeks. Only eight percent of the booked women had no formal education and twelve percent had primary education. Most of the women received either secondary (53.1%) or tertiary (29.9%) education. Women with secondary and tertiary levels of education constituted the majority of bookings in all trimesters.

The bulk (68.0%) of booked women had low parity ($\leq$ 2), while para 3-4 constituted 27.6% and grand multiparity was only 4.4%. Low parity constituted the majority of pregnancies booked in all trimesters. It is however most prominent (93.8%) in those booked at < 13 weeks of pregnancy, compared with 58.4% in 14-26 weeks and 68.0% in > 27 weeks. The majority (87.7%) of booked women did not have any pre-existing medical disorder. The numbers of booked pregnancies without pre-existing medical disorders are similar at < 13 weeks (12.1%) and at 14-26 weeks (13.9%), but lower in those booked at 27-36 weeks (3.1%). Previous caesarean section was the mode of previous delivery in 16.3% of pregnancies. Proportionally, there were more women that had previous caesarean section among bookings at <13 weeks (36.1%), than among women that booked at 14-26 weeks (10.7%) and at 27-36 weeks (6.9%). Previously complicated deliveries occurred in 84.9% of pregnancies booked. The proportion of deliveries that were complicated was similar in all the gestational age groups (83.5% in < 13 weeks, 84.9% in 14-26 weeks and 87.9% in 27-36 weeks).

**4. Discussions**

Using an upper limit of 13 completed weeks as cut-off for classification into early and late booking, as previously used in the same institution and reportedly used in several other studies allows for more scientifically acceptable data comparison (Lamina 2004, Ndidi and Oseremen 2010). Additional reason for the this choice of cut-off GA is the fact that recommended upper limit for screening and invasive fetal procedures is $13^{+6}$ weeks, while early ultrasound scan diagnosis of major congenital abnormalities and safe terminations of affected fetuses, are best performed before the $14^{th}$ week (Nicolaides 2011).Majority of spontaneous miscarriages are expected to have occurred before 13 weeks, leaving behind the apparently healthy fetuses. The other group of studies is those that used 17 weeks as cut-off based on an earlier WHO model of focused antenatal care recommendation (Ifenne and Utoo 2012, Ndidi and Oseremen, 2010).

Although most pregnancies were booked during 14-26 weeks, there was an observable increase in the proportion of pregnancies booked early (23.9%) in this study, compared with the 18.8% reported by Lamina in 2014. Another important finding is that the relative yearly proportion of pregnancies booked in first trimester witnessed a dramatic rise in the last 2 years of the study from its stable frequency in the first 3 years of study. The study therefore confirms the persistence of the tradition of late antenatal booking within the study population, which was also reported in Awka, Nigeria (65%), and Malaysia (56.2%) (Namani et al., 2022, Aung et al., 2016). Our study mean booking GA is 17.0 + 4.1 weeks, while in Lagos, South western Nigeria, it was 19.1 +/- 7.8 (Ifenne and Utoo. 2012), and in Nnewi, Eastern Nigeria, it was 17.58 ± 7.91 weeks (Namani et al., 2022).

This trend of pregnancy booking demonstrates the relationship of maternal age and educational level with booking as previously reported (Ifenne and Utoo, 2012, Adegbola and Kuku, 2015). Specifically, younger women and those who have attained secondary and/or tertiary education are more likely book their pregnancies earlier. The older women tend to book late because they rely on ‘experience’, and ‘would book only when an obvious or potentially catastrophic complication is anticipated’ (Adegbola and Kuku, 2015). The study finding that most women who booked in early pregnancy attained secondary and tertiary educational level agrees with

previously reported research conclusions, and also emphasizes the importance of the girl education towards improving better reproductive outcomes (Ifenne and Utoo, 2012).

Our study findings demonstrate the predominance of low parity (para 0-2) among women that booked early. This pattern could be attributed to the 'fear of the unknown' and lack of experience among this group of women, as previously explained in a study (Okunlola et al., 2006). Those who are of higher parity are believed not to be 'enthusiastic to visit the hospital early to book, probably because of past experience as long as there was nothing unusual with their current pregnancy' (Namani et al., 2022).

Previous or on-going medical disorder and/or delivery complications was not a strong indicator of early booking, as evidenced in this study where only small proportions of women affected by these factors book in early pregnancy, while the majority booked after 14 weeks. A similar observation was made by Ndidi and Oseremen, who reported that majority (73%) of the women booked late because they did not have any serious problem (Ndidi and Oseremen, 2010). Traditionally, women who considered themselves sick constituted the bulk of late bookers (Ifenne and Utoo, 2012). The above practice can be easily reversed through health education emphasis on the preventive rather than curative role of antenatal care, as currently believed by most women (Ndidi and Oseremen, 2010).

## 5. Conclusion

The practice of late pregnancy booking is still predominant. Concurrently however, the proportion of women that book in early pregnancy is higher than reported in 2004 and increased further in the last 2 years of study. This trend of early pregnancy booking can be sustained through improvement in education, economic empowerment and health education that emphasizes preventive rather than curative role of ANC.

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**Ethical approval**
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**Competing interests**
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# DNA Cell Cycle Analysis with Propidium Iodide (PI) in Liver Cancer Patients

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**Abstract**
Hepatocellular Carcinoma (HCC) ranks as the fifth most common cancer and, with over 600,000 deaths per annum, it constitutes a major global health problem. The main aetiologies of chronic liver injury are chronic hepatitis C virus (HCV) and hepatitis B virus (HBV) infections, alcohol abuse and, as a result of metabolic syndrome reaching epidemic proportions, an increasing prevalence of non-alcoholic steatohepatitis (NASH). Biomarkers are being developed as alternatives to liver biopsy for predicting liver fibrosis in patients with chronic hepatitis C. The aim of this study was to investigate DNA Cell cycle in HCC, Fibrosis patients and compare with healthy control group. They were classified into three different groups 51 individuals diagnosed Fibrosis patients, 30 Hepatocellular Carcinoma patients and 40 healthy Control individuals with no liver diseases. Tumor Markers including CEA and AFP were estimated using ELISA method, DNA cell cycle was assessed using Flow Cytometry. Results showing sub G1 was increased significantly in both HCC and Fibrosis patients with values 9.55 ± 4.72 and 17.7 ± 5.9; respectively comparing with Healthy control group 5.7 ± 3.36 ($p<0.005$). On the other hand, G0/G1 was decreased significantly in both HCC and Fibrosis patients with values 62.2 ± 10.02 and 53.4 ± 11.1, respectively while in Healthy control. In addition, AFP and CEA were increased in both HCC and Fibrosis patients comparing with Control. Conclusion based on this study DNA cell cycle could help in assessment of Liver damage especially HCC.

**Keywords:** Hepatocellular Carcinoma, HCV, NASH

## 1. Introduction

Liver diseases affect the normal functions of the liver causing decrease in its performance. Abnormalities in the liver functions, however, are usually not apparent in most individuals with chronic liver disease until the disease is rather advanced. Liver diseases could be classified into infectious (e.g., viral hepatitis), toxic (e.g., alcohol-related diseases), genetic (e.g., hemochromatosis), immune (e.g., autoimmune hepatitis primary biliary cirrhosis), and neoplastic (e.g., hepatocellular carcinoma) Dufour et al. (2000). Hepatitis is inflammation of the liver. Viral infection is responsible for around half of all cases of acute hepatitis. The term is generally used to refer to the diseases caused by viruses including the diseases hepatitis A–E, and disease due to cytomegalovirus, Epstein-Barr virus, adenovirus, rarely herpes simplex virus and others Akiba et al. (2005). Only hepatitis B virus and hepatitis

C virus are able to persist in the host and cause chronic hepatitis Herzer et al. (2007). Hepatitis C virus is also a major public health problem Michielsen et al. (2005). Chronic hepatitis is defined as ongoing hepatic necrosis and inflammation of the liver, often accompanied by fibrosis. Chronic hepatic injury may progress to cirrhosis (15-20 % in the case of chronic hepatitis C virus) and predisposes to hepatocellular carcinoma. Most commonly, it is the result of chronic viral infection. Chronic hepatic injury is a relatively common disorder with minimal symptoms but long-term risk of significant morbidity and mortality Michalopoulos et al. (2010). Hepatocellular carcinoma (HCC) is a primary malignancy of the liver and occurs predominantly in patients with underlying chronic liver disease and cirrhosis. The cell(s) of origin are believed to be the hepatic stem cells, although this remains the subject of investigation. Tumors progress with local expansion, intrahepatic spread, and distant metastases Hashimoto et al. (2004).

The cell cycle itself consists of an ordered set of events, ultimately resulting in cell growth and division to produce daughter cells. The eukaryotic cell cycle can generally be divided into four stages known as G1, S, G2 and M. G1 also known, as gap-phase 1 is the period during which cells prepare for the process of DNA replication. S-phase is defined as the stage in which DNA synthesis occurs. G2 is the second gap-phase during which the cell prepares for the process of division and M stands for mitosis, the phase in which the replicated chromosomes are segregated into separate nuclei and cytokinesis occurs to form two daughter cells. In addition to G1, S, G2, and M, the term G0 is used to describe cells that have exited the cell cycle and become quiescent (Johnson and Walker 1999). The liver is exposed to insults from external factors that can induce hepatocyte cell death and liver mass loss, triggering liver regeneration. During this process, which depends on reactivation of transcriptional program leading to exit from quiescence and to enter into the cell cycle of (mostly) hepatocytes, the liver maintains all its metabolic functions Sumpter et al. (2005)

## 2. Subjects and Methods

This study Carried on 121 individuals they were classified into three different groups: Group (I): 51 individuals diagnosed Fibrosis patients they were, 42 males and 9 females, their age ranged from 43-87 year with a mean of 59.9±10.1 year. Group (II): 30 Hepatocellular Carcinoma patients, 23 males and 7 females, and their age ranged from 43-74 year with a mean of 57±8.81 year. Group (III): 40 healthy Control individuals with no liver diseases 28 males and 12 females, and their age ranged from 20-51 year with a mean of 30.8±7.57 year. Patients with clinically and laboratory confirmed chronic hepatitis C (CHC) were included in the present study; other causes of chronic liver disease were ruled out. They were recruited from Gastroenterology Surgical Center, Mansoura University, Egypt, that approved the present study. An informed consent was obtained from each individual participated in the present study and all were fully informed concerning the nature of the disease and the diagnostic procedures involved. No patient had received interferon treatment before liver biopsy and blood collection. Patients with reduced production of platelets other than hepatic infection with HCV such as infection of typhoid, deficiency of vitamin B12 and leukemia were excluded from the study.

The HCV infection classification of the three groups was diagnosed based on biochemical, serologic, and histological criteria. None of the patients had history of habitual alcohol consumption or hepatocellular carcinoma. Moreover, all individuals were positive for anti-HCV antibody and were negative for hepatitis A and B viruses testing. All patients were negative test for anti-HIV antibodies. In addition to 40 samples were obtained from healthy individuals. Blood samples were collected from all patients by vein-puncture within 2 weeks of liver biopsy and a part of the blood was treated immediately with EDTA-K2. Routine blood pictures including platelet counting were determined by KX-21 Sysmex automated hematology analyzer (Sysmex Corporation, Japan). Sera were separated from the rest of blood samples and tested fresh for liver function indexes.

Sera were processed for the biochemical analysis of Albumin, Bilirubin, Aspartate aminotransferase (AST) and Alanine aminotransferase (ALT) according to the manufacture instructions. All serum samples were obtained with informed consent. The AST-ALT ratio was calculated as [AST/ ALT].

Aspartate Platelet Ratio Index (APRI): was calculated according to Wai et al. (2003) as the following equation: (AST [IU/L] / upper limit of normal AST [IU/L]) × 100 / platelet count [109/L].

Fibrosis-4 index (FIB-4): was calculated according to Sterling et al. (2006) as the following equation: AST [IU/L] × age [years]/ platelet count [109/L] × ALT [IU/L] 1/2

Estimation of Alpha Fetoprotein (AFP): AFP was estimated according to method of Silver et al. (1973). Based on the principle of a solid phase enzyme-linked immunosorbent assay. The assay system utilizes a rabbit anti-AFP antibody directed against intact AFP for solid phase immobilization (on the microtiter wells).

Quantitative Determination of Carcinoembryonic Antigen (CEA): CEA was estimated according to method of Hansen et al. (1989). The CEA Quantitative Test Kit is based on a solid phase enzyme-linked immunosorbent assay. The assay system utilizes one monoclonal anti-CEA antibody for solid phase (microtiter wells) immobilization and another mouse monoclonal anti-CEA antibody in the antibody-enzyme (horseradish peroxidase) conjugate solution.

Flow Cytometry Technique for Evaluation of DNA Cell Cycle. Peripheral Blood Mononuclear Cell (PBMC) Isolation and Red Cell Lysis Procedures: PBMC isolation: Human PBMC are isolated using a density gradient technique. The two most commonly used density gradient solutions are Ficoll-Paque PLUS (Sigma-Aldrich, St. Louis, MO, United States). DNA Cell Cycle Analysis with Propidium Iodide (PI): Propidium Iodide: The most commonly used dye for DNA content/cell cycle analysis is (PI). It can be used to stain whole cells or isolated nuclei. The flow cytometer must be equipped with an argon laser with an optimal emission of 488 nm. Primary emission of propidium iodide is between 580 and 650 nm Vindelov et al. (1983). key phases of the cell cycle may be defined: G0/G1 = Phase in which the cell is resting or preparing for mitosis. S-Phase = Phase between G0/G1 and G2/M when the cell is in the process of DNA synthesis. G2/M = Phase in which the DNA content of the cell is twice the amount of the DNA content of the cell in the resting phase.

*Statistics*

A computer software package SPSS was used in the analysis. For quantitative variables, mean and median, standard deviation. Frequency. ANOVA test was used for comparing between different groups.

## 3. Results

Table 1: Clinical Parameters in all groups

| Clinical Parameters Mean ± Sd | Fibrosis | HCC | Healthy Control | P-value |
|---|---|---|---|---|
| ALT (U/ml) | 59.9 ± 36.7 | 56.3 ± 35.7 | 12.15 ± 2.6 | P< 0.005 |
| AST (U/ml) | 73.2 ± 35.6 | 70.1 ± 28.3 | 12.4 ± 2.7 | P<0.005 |
| Bilirubin (mg/dl) | 4.1 ± 6.3 | 7.4 ± 11.0 | 0.3 ± 0.18 | P<0.005 |
| Platelets ($\times 10^9$) | 200.8 ± 47.9 | 153.8 ± 54.5 | 289.3 ± 16.6 | P= 0.000 |
| AST/ALT Score | 1.4 ± 0.7 | 1.5 ± 0.58 | 1.07 ± 0.37 | P<0.005 |
| APRI Score | 1.3 ± 1.3 | 0.98 ± 0.61 | 0.1 ± 0.2 | P<0.005 |
| FIB-4 Score | 4.2 ± 3.6 | 3.7 ± 2.3 | 0.38 ± 0.13 | P<0.005 |
| Albumin (g/dl) | 3.2 ± 0.15 | 2.91 ± 0.25 | 4.3 ± 0.43 | P<0.005 |

P > 0.05 is considered not significant. P < 0.05 considered significant < 0.001 considered very significant. P < 0.0001 is considered extremely significant

Table 2: Tumor Markers Parameters in all groups

| Tumor Markers Parameters | Fibrosis | HCC | Healthy Control | P-value |
|---|---|---|---|---|
| Alpha FetoProtein (ng/ml) Mean ± SD | 25.08 ± 22.2 | 423.3 ± 4.7 | 1.68±0.74 | P < 0.001 |
| Carcinoembryonic Antigen (µg/l) Mean ± SD | 2.64 ± 0.66 | 3.61 ± 0.6 | 1.26±0.13 | P < 0.005 |

P > 0.05 is considered not significant. P < 0.05 considered significant < 0.001 considered very significant. P < 0.0001 is considered extremely significant

Table 3: DNA Cell Cycle in all groups

| DNA Cell Cycle | Fibrosis | HCC | Healthy Control | P-value |
|---|---|---|---|---|
| Sub G1 phase | 17.7 ± 5.9 | 9.55 ± 4.72 | 5.7 ± 3.36 | P = 0.000 |
| G0/G1 phase | 53.4 ± 11.1 | 62.2 ± 10.02 | 88.8 ± 3.32 | P < 0.001 |
| S – phase | 9.75 ± 3.34 | 15.8 ± 7.6 | 3.0 ± 0.27 | P < 0.005 |
| G2/M phase | 18.3 ± 11.3 | 10.2 ± 7.23 | 2.4 ± 0.81 | P <0.005 |

P > 0.05 is considered not significant. P < 0.05 considered significant < 0.001 considered very significant. P < 0.0001 is considered extremely significant

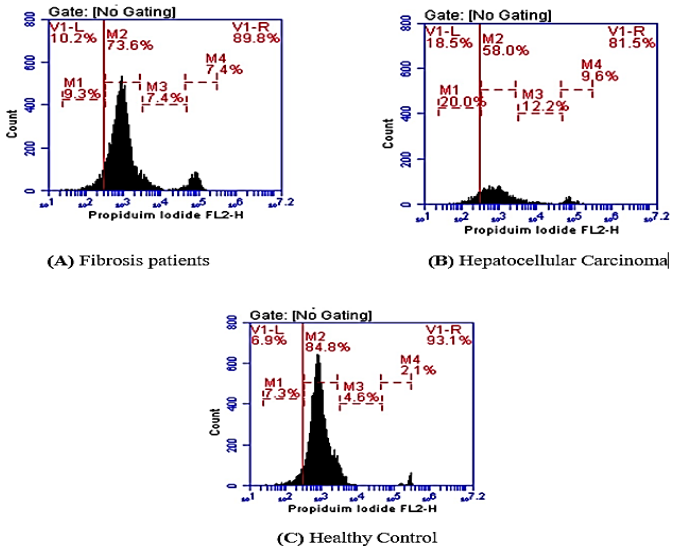


Figure 1: Flow Cytometry of DNA cell cycle using PI

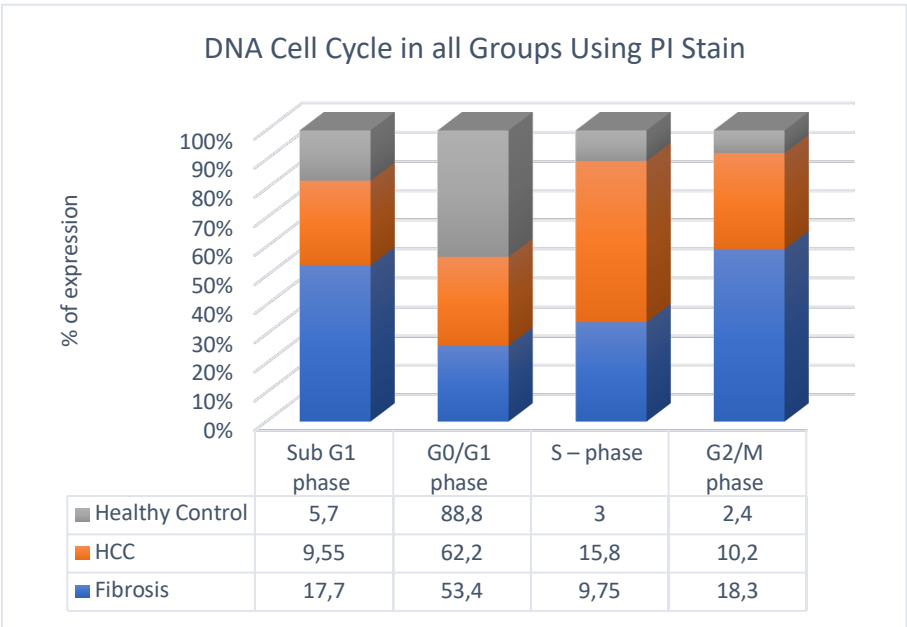


Figure 2: DNA Cell cycle in all groups

## 4. Discussion

Egypt is the highest HCV prevalence country in the world; in 2008, the Egyptian Demographic Health Survey (EDHS), which was conducted on a large nationally representative sample, estimated the prevalence of HCV antibodies and HCV RNA, among the 15–59-year age group, to be 14.7 and 9.8% respectively. Based on the population census and the EDHS done in 2008, it was estimated that more than 6.8 million persons aged 15–59 years had HCV antibodies, of which more than 4.5 million individuals had active HCV infection (El-Zanaty and Way 2009). Hepatocytes in the liver are the predominant targets of HCV infection, and the entry of HCV into hepatocytes is a stringently coordinated process that relies on successive and concerted interactions between the envelope glycoproteins E1 and E2 and host cellular factors that are present on the cell surface, i.e., the so called "entry (co)receptors" The known (co)receptors, including the tetraspanin CD81 (Pileri et al. 1998; Zhang et al. 2004). In the present study ALT was increased in Fibrosis and HCC patients significantly compared with Healthy control group Mean ± SD. were 59.9± 36.7, 56.3± 35.7 and 12.15± 2.6; respectively (P<0.005). Also, AST was increased in both Fibrosis and HCC patients comparing with Healthy control group Mean ± SD. were 73.2 ± 35.6, 70.1 ± 28.3 and 12.4 ± 2.7; respectively (p<0.005). Serum bilirubin was increased significantly in both HCC and Fibrosis patients comparing with Health control group with values 7.4 ± 11.0, 4.1 ± 6.3 and 0.3 ± 0.18; respectively (p< 0.005). In our study albumin was decreased significantly in both HCC and Fibrosis patients comparing with Healthy control group with values 2.91 ± 0.25, 3.2 ± 0.15 and 4.3 ± 0.43; respectively (p<0.005). The elevated aminotransferase value in HCC reflects damage to adjacent hepatocytes as a direct result of tumor growth or damage to more remote liver cells caused by interference with their blood supply or venous drainage. It may also be due to continuing liver cell necrosis in those with concomitant active cirrhosis or chronic active hepatitis Domingo et al. (2013).

Out of 30 patients 13 HCC patients showed AFP level below 200 ng/ml. In our study, AFP was significantly higher in HCC patients compared to Fibrosis group. An elevated AFP (> 400 ng/mL) level was associated with advanced disease stage in HCC patients. Some previous studies showed that AFP has a low specificity for diagnosing HCC to the extent that the American Association for the Study of Liver Diseases-Practice Guidelines Committee has recently recommended ultrasound examination alone (without AFP) to be used for HCC surveillance Massoud et al. (2006). However, the interpretation of ultrasound is operator dependent and can be difficult in persons who are obese or have underlying cirrhosis. Therefore, other reliable biomarkers are required to complement ultrasound and AFP for proper diagnosis and early detection of HCC Lok et al. (2011). In the present study AFP was estimated in Fibrosis, Hepatocellular Carcinoma and Healthy Control using ELISA, the Mean values of AFP were in Fibrosis, HCC patients and control were 25.08 ± 22.2 and 423.3 ± 4.7 and 1.68±0.74; respectively (p<0.001). Carcinoembryonic antigen (CEA) is a high-molecular-weight glycoprotein (180–200 kDa) consisting of a 60% carbohydrate composition. Normally, serum CEA concentrations are below 5 ng/mL. In contrast to healthy conditions, elevated serum CEA levels have been found in other types of cancers aside from colorectal cancer, to include gastric, pancreatic, breast, and genitourinary cancers Tangkijvanich et al. (2000). Cell cycle begins from the completion of one division to the end of the next, leading to the generation of two daughter cells. Mammalian cell cycle is tightly regulated and can be artificially divided into four distinct phases (G1, S, G2, and M) according to their specific characteristics (Martínez-Alonso et al. 2019; Martínez-Alonso and Malumbres 2020) G1 phase is the gap phase, which is characterized by cell growth in size and the synthesis of RNAs and proteins required for DNA duplication. S phase is the synthesis phase during which DNA is synthesized. G2 phase is another gap phase, in which stage cells are characterized by rapid growth in cell size, more protein synthesis and preparation for division. M phase is the mitosis phase, during which the replicated chromosomes are segregated into separate nuclei and cytokinesis promoting the formation of two daughter cells. At the end of the M phase, 1 cell divides into two daughter cells, each of which contains one copy genomic DNA of the mother cell, and a cell cycle is accomplished.

Sub G1 was increased significantly in both HCC and Fibrosis patients with values 9.55 ± 4.72 and 17.7 ± 5.9; respectively comparing with Healthy control group 5.7 ± 3.36 (p<0.005). On the other hand, G0/G1 was decreased significantly in both HCC and Fibrosis patients with values 62.2 ± 10.02 and 53.4 ± 11.1; respectively while in Healthy control group G0/G1 was 88.8 ± 3.32 (p<0.005). Our data revealed that S-phase was increased significantly in both HCC and Fibrotic patients with Mean ± SD. values 15.8 ± 7.6 and 9.75 ± 3.34; respectively while in Healthy control group S-phase was 3.0 ± 0.27 (p<0.005). In our study G2/M phase DNA Cell cycle was

increased significantly in both HCC and Fibrosis patients with values 10.2 ± 7.23 and 18.3 ± 11.3; respectively while in Healthy control group G2/M phase was 2.4 ± 0.81 ($p<0.005$).

## 5. Conclusion

Based on this study, liver exposed to insults from external factors can induce hepatocyte cell death and liver mass loss, triggering liver regeneration. HCC causing increasing in S-Phase in DNA cell cycle comparing with fibrosis and healthy control which could help in assessment of Liver damage.

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# Comparison of Intravenous Fentanyl and Intravenous Remifentanil on Emergence Time and Discharge Time in Patients Undergoing Odontectomy: An Observational Analytical Review

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**Abstract**
Background: Recovery time and fast patient discharge after surgery are goals of fast-track surgery that uses the concept of ERAS (Enhanced Recovery After Surgery) to minimize pain, speed up recovery, and reduce pain and complications. Fast-track surgeries such as odontectomy require drugs with a fast onset of action and short duration hence the patient can recover from the drugs as soon as possible. The use and types of opioids have been developed for optimal fast-track surgery. One of the most widely used opioids is remifentanil. Purpose: This study aims to compare the administration of fentanyl and remifentanil to the emergence and discharge time of post-odontectomy patients with general anesthesia. Methods: Patients were divided into two groups, the fentanyl group (group F, n=21) and the remifentanil group (group R, n=21). This study used a retrospective cohort analysis of the medical records of 42 patients with elective odontectomy surgery for the period December 2020 to June 2021 at RSUP dr. Hasan Sadikin Bandung. Emergence time was assessed using the OAA/S score and discharge time was considered using the modified Aldrete score. Results: This study showed a significant difference between the emergence time in group R (168+47.98 seconds) and group F (368+58.16 seconds) with a p-value = 0.0001. There was a significant difference between the discharge time in group R (20.00+7.24 minutes) and group F (58.57+12.46 minutes) with a p-value = 0.001. Conclusion: Recovery time and discharge time for patients receiving remifentanil were faster than for patients receiving fentanyl for odontectomy.

**Keywords:** Discharge Time, Fentanyl, Odontectomy, Recovery Time, Remifentanil

## 1. Introduction

Emergence from general anesthesia can be defined as a condition where neuromuscular conduction, protective reflexes, airway, and consciousness have returned after discontinuation of anesthetic drugs and completion of surgery (Permatasari et al., 2017).

Emergence from anesthesia is a process that can cause high physiological stress levels. Emergence from anesthesia should be smooth and controlled. The time required can vary depending on the patient's condition, types of anesthesia given, and duration of the surgery. In waking up from anesthesia, one can face airway obstruction, chills, agitation, delirium, pain, nausea, and vomiting. After general anesthesia, the patient should be able to regain consciousness within 30–60 minutes. The leading cause of delayed emergence is the effects of the anesthetic drugs still present. Impaired healing of consciousness can occur because of the potentiation of the effects of anesthetics with preoperative medications (Permatasari et al., 2017).

A study in India in 2016 reported factors that affect emergence time into 4 groups, namely the patient, drug, procedure, and metabolic factors. Patient factors were age, gender, genetic variation, Body Mass Index (BMI), comorbid smoking history, and duration of fasting before surgery. Drug factors are influenced by drug pharmacokinetics in absorption, distribution, metabolism and excretion, dose, duration of use, previous drug use, drug interactions, and selection of anesthetic drugs. Surgical factors that affect emergence time are duration of surgery, type of surgery, and use of instruments such as nasogastric tubes and catheters. Meanwhile, metabolic factors influence blood glucose status, electrolyte balance disorders, and temperature (Misal et al., 2016).

Discharge time for odontectomy patient is determined by several factors, namely pre-existing medical conditions and the location of the infection that can prolong up to 1-1.8 days (Katznelson & Fisher, 2015). The concept of fast-track surgery, which aligns with the idea of ERAS (enhanced recovery after surgery), has been mentioned in the surgical literature for the last two decades. The ERAS protocol provides a transformative plan to minimize pain, reduce opioid administration, accelerate patient recovery, and reduce perioperative complications and length of hospital stay (McLean House et al., 2016).

Anesthesia with rapid onset, minimal post-operative pain, good patient satisfaction, and low cost without complications such as nausea, vomiting, and delirium is the main goal in outpatient or fast-track surgery, one of which is performed on patients undergoing odontectomy. Since most dental surgeries are performed on One Day Surgery (ODS) patients, an anesthetic technique that allows for rapid recovery is preferred. Low lipid-solubility volatile with short-acting opioids such as Remifentanil, sufentanil, and fentanyl, or a targeted propofol infusion remifentanil are preferred for anesthesia maintenance in order to ensure rapid recovery (Permatasari et al., 2017; Twersky et al., 2001)

Currently, fentanyl is the opioid of choice for induction and analgesia in surgery. Fentanyl is the first generation of the fentanyl group, with its derivative opioids such as fentanyl, alfentanil, and Remifentanil. Fentanyl is a synthetic opioid in the form of a solution that binds to citrate and has good analgesic properties. Fentanyl has rapid onset, short duration, and slight effect on depressing the cardiovascular, and do not cause histamine release (Gül et al., 2013). Analgesia effect occurs 1-2 minutes after intravenous (IV) administration. The duration of action lasts for 2–4 hours after IV administration. The plasma concentration of fentanyl required is about 1–2 ng/ml to achieve an analgesic effect, which can achieve by administering 2–8 µg/kg. Maximum plasma concentration is reached within the first 5 minutes. Therefore, fentanyl is the agent of choice in general anesthesia. Fentanyl is a mu (µ) receptor agonist, and its analgesic properties are 100 times more potent than morphine. Fentanyl is generally given intravenously, although it can also be given intramuscularly, intrathecally, and epidurally (Awad & Chung, 2006; Twersky et al., 2001).

In addition, other opioid drugs are currently being developed; namely, Remifentanil which is an opioid that acts on mu (µ) receptor agonists, has an ester group chemical structure, has a concise action with a fast onset, a very short half-life of 3-10 minutes, while the peak effect of the drug is around 3-5 minutes. Remifentanil is rapidly metabolized by the blood by non-specific esterification in blood plasma to produce inactive carboxylic acids. The clinical effect wears off in 2 to 5 minutes. Therefore, Remifentanil can provide controlled levels of sedation and analgesia with minimal or unsustainable side effects (DG et al., 2021; Pavlin et al., 1998). This study aims to compare the administration of fentanyl and remifentanil to the recovery time and discharge time of post-odontectomy patients with general anesthesia.

## 2. Materials and Methods

This research is an analytic observational study with a retrospective cohort design. The research subjects were medical records of patients who underwent odontectomy surgery under general anesthesia at the Central Operating Theater (COT) at Hasan Sadikin General Hospital until June 2021 who met the inclusion and exclusion criteria. The research sample was taken by consecutive sampling. The study was conducted after obtaining approval from the Research Ethics Committee with the number LB.02.01/X.6.5/274/2021 and authorized by the Director of Hasan Sadikin Hospital Bandung with the number LB.02.01/X.2.2.1/22170/2021.

The inclusion criteria in this study were: 1. Patients aged 18 to 64 years who underwent elective odontectomy surgery; 2. Patients with normal BMI range; 3. Patients with physical status in categories I-II (WHO) according to the American Society of Anesthesiologists (ASA); 4. Patients who received remifentanil 1 µg/kgBW bolus for induction followed by maintenance remifentanil at a dose of 0.1µg/kg BW/min, without any additional opioid drugs; 5. Patients who received induction drug fentanyl 2 µg/kgBW for induction without additional opioid medications; and 6. Odontectomy patients who received propofol 2 mg/kgBW and atracurium 0.5 mg/kgBW as induction agents; 7. Patients who received maintenance anesthesia with sevoflurane with O2:N2O, FiO2 50%; 8. Patients who received analgesic paracetamol 20 mg/kgBW intravenously during the surgery; and 9. Patients with complete data regarding emergence time and discharge time in the PACU. While the exclusion criteria in this study were: 1. Patients who received additional opioids before emergence time could be assessed; 2. Odontectomy patients surgery duration more than two hours; 3. Patients who received opioids other than remifentanil and fentanyl; 4. Patients who were induced with drugs other than propofol and atracurium, and 5. Patients who received premedications of sedative and tranquilizers drugs in the ward.

Numerical scale data such as patient age are presented with mean, standard deviation, median, and range. Characteristic data in the form of categorical data such as the gender of the patient, coding is given and presented as a distribution of frequency and percentage. Normality test using Shapiro-Wilk test. The significance test to compare the characteristics of the two research groups used an unpaired t-test. The Chi-square test was used for categorical data. The data obtained were recorded in a particular form and then processed through the SPSS version 24.0 for the Windows program.

## 3. Results

### *3.1. Characteristics of patients*

The study was conducted to 42 patients who had undergone odontectomy surgery. The research subjects were divided into two groups: the group that received fentanyl 2 µg/kgBW as a single bolus and the group remifentanil 1 µg/kg BW given during induction followed by maintenance at 0.1 µg/kg BW/min during intraoperatively with 21 samples in each group.

The data on the characteristics of the research subjects can be seen in Table 1 based on age, gender, Body Mass Index (BMI), ASA physical status, and duration of surgery. The fentanyl group had a mean patient age of 24.95 ± 5,861 years and consisted of 10 (47.6%) male patients and 11 (52.4%) female patients. BMI has an average of 21.59±1,836 kg/m$^2$. Most of the patients were ASA 1 (90.5%). The length of operation has an average of 96.19±12,339 minutes.

Table 1: Comparison of Research Subject Characteristics in the two groups

| Variable | Groups | | p-value |
|---|---|---|---|
| | Fentanyl N=21 | Remifentanil N=21 | |
| **Age (year)** | | | **0.112** |
| Mean±Std | 24.95±5.861 | 27.10±5.674 | |
| Median | 24.00 | 27.00 | |

| | | | |
|---|---|---|---|
| Range (min-max) | 18.0-40.00 | 19.00-40.00 | |
| **Gender** | | | **0.758** |
| Male | 10(47.6%) | 11(52.4%) | |
| Female | 11(52.4%) | 10(47.6%) | |
| **IMT (kg/m$^2$)** | | | **0.918** |
| Mean±Std | 21.59±1.836 | 21.54±1.345 | |
| Median | 21.63 | 21.91 | |
| Range (min-max) | 18.67-24.24 | 19.15-24.49 | |
| **ASA** | | | **1.000** |
| 1 | 19(90.5%) | 20(95.2%) | |
| 2 | 2(9.5%) | 1(4.8%) | |
| **Duration of surgery (minutes)** | | | **0.230** |
| Mean±Std | 96.19±12.339 | 100.00±12.145 | |
| Median | 95.00 | 100.00 | |
| Range (min-max) | 80.00-120.00 | 80.00-120.00 | |

The * sign indicates the $p < 0.05$ and the ** sign indicates the $p < 0.01$ value, which means that it is statistically significant or significant.

The remifentanil group had an average patient age of 27.10 ± 5,674 years and consisted of 11 (52.4%) male patients and 10 (47.6%) female patients. The mean BMI was 21.54±1.345 kg/m$^2$. Most of the patients were ASA 1 (95.2%). The duration of operation has an average of 100.00±12.145 minutes. From the comparative analysis of the characteristics of the two groups above, it can be concluded that there were no differences in characteristics at the beginning of the examination. This shows that the two groups are the same or homogeneous.

*3.2. Comparison of Emergence Time and OAA/S Score in Fentanyl and Remifentanil groups*

Comparison of emergence time and OAA/S scores in the two groups can be seen in Table 2. The fentanyl group had an average emergence time of 368.57±58.162 seconds and an average OAA/S score of 2.86±0.478. The remifentanil group had an average emergence time of 168.57±47.988 seconds and an average OAA/S score of 3.33±0.577.

Table 2: Comparison between Emergence Time and OAA/S Score in Both Groups

| **Variable** | **Groups** | | **p-value** |
|---|---|---|---|
| | **Fentanyl N=21** | **Remifentanil N=21** | |
| **Emergence time (seconds)** | | | **0.0001**** |
| Mean±Std | 368.57±58.162 | 168.57±47.988 | |
| Median | 360.00 | 160.00 | |
| Range (min-max) | 260.00-460.00 | 80.00-300.00 | |
| **OAA/S** | | | **0.007*** |
| Mean±Std | 2.86±0.478 | 3.33±0.577 | |
| Median | 3.00 | 3.00 | |
| Range (min-max) | 2.00-4.00 | 2.00-4.00 | |

OAA/S = Observer Assessment of Alertness/ Sedation.. The * sign indicates the p value <0.05 and the ** sign indicates the p value < 0.01 which means statistically significant or significant.

The results of statistical tests in both research groups obtained information on the P-value of the emergence time of 0.0001 and OAA/S score of 0.007, which is smaller than 0.05 ($p < 0.05$). Therefore, it can be concluded that there is a statistically significant difference in the average emergence time and OAA/S score between the fentanyl and remifentanil groups.

*3.3. Comparison of discharge time in the Fentanyl and Remifentanil groups*

Table 3 compares discharge time in the fentanyl and remifentanil groups. In the fentanyl group, the average discharge time was 58.57±12,464 minutes, while in the remifentanil group, the average discharge time was 20.00±7,246 minutes. Based on the Mann-Whitney test's analysis results, the p-value was less than 0.05. Therefore, there was a statistically significant difference in discharge time between the fentanyl and remifentanil groups.

Table 3: Comparison of discharge time in the Fentanyl and Remifentanil groups

| Variable | Groups | | p-value |
|---|---|---|---|
| | Fentanyl N=21 | Remifentanil N=21 | |
| **Discharge time (second)** | | | **0.0001**** |
| Mean±Std | 58.57±12.464 | 20.00±7.246 | |
| Median | 60.00 | 15.00 | |
| Range (min-max) | 45.00-75.00 | 15.00-30.00 | |

The * sign indicates the $p < 0.05$ and the ** sign indicates the $p < 0.01$ value, which means that it is statistically significant or significant.

## 4. Discussion

Characteristics of study subjects are based on gender, age, BMI, ASA status, and duration of surgery, as described in Table 1. Previous study has shown that women recover more quickly from anesthesia than men. This is due to the high concentrations of the hormones estrogen and progesterone in women, which affect the excitability of the central nervous system so that it affects the receptor modulation of sedative drugs and makes women less sensitive to the hypnotic effects of anesthetics than men (Buchanan et al., 2011).

Body Mass Index can affect recovery time and discharge time in patients undergoing general anesthesia. This is because patients with higher BMI tend to have more adipose tissues. Anesthetic agents are mostly lipophilic, so they are distributed to adipose tissue. This causes changes in the volume of distribution and lengthens drug clearance time. As a result, the duration of action of anesthetic drugs is longer and can affect emergence and discharge time of the patient (Katznelson & Fisher, 2015).

ASA physical status is based on patient's morbidity and its effect on functional limitations, thereby helping anesthesiologists to predict perioperative risk. High ASA physical status indicates the presence of morbidities, including diabetes mellitus, morbid obesity, alcohol dependence, kidney failure, and others that may alter the effect of anesthetic drugs on the patient's emergence and discharge time. The duration of surgery is related to the patient's exposure to anesthetic agents. The longer the surgery, the longer it will take for the patient to regain consciousness. Previous studies have shown that surgery duration of more than 2 hours increases recovery time by 1.2 times (McLean House et al., 2016).

This study found that the emergence time in the remifentanil group was faster than in the fentanyl group. These results are consistent with a previous study in Japan which stated that patients receiving remifentanil showed faster emergence time characterized by faster time to follow orders, extubation, and adequate ventilation compared to other opioids, including fentanyl. This may be caused by the pharmacokinetics of remifentanil with

smaller distribution volume (30 L) compared to fentanyl (335 L). The systemic clearance of remifentanil is 4,000 ml/minute, which is faster than fentanyl which is 1,530 ml/minute. This causes the effect of remifentanil to wear off more quickly and predictable (Twersky et al., 2001).

Previous study in Turkey showed similar result which stated that the average emergence time in the remifentanil group was 10.78 + 3.32 minutes compared to the fentanyl group of 13.87 + 3.0 minutes. These results show a statistically significant difference. This may be due to the slow clearance of fentanyl, resulting in a longer duration of anesthesia. This study recommended using low-dose remifentanil for induction of anesthesia in outpatient procedures because it produces the same anesthetic qualities as fentanyl without increasing the risk of complications, especially in children (Gül et al., 2013).

This study is also supported by previous study, which stated that remifentanil showed a faster emergence time than fentanyl which is characterized by a quicker response to verbal commands and faster time to leave the operating room. Rapid clearance of remifentanil by esterase results in faster recovery however it also shows higher postoperative pain, so postoperative pain management with other strategies or agents is recommended. A survey on anesthesiologists showed that 54% anesthesiologists rated “complete” emergence in remifentanil group compared to only 19% in the fentanyl group (Twersky et al., 2001).

This study showed that remifentanil group had faster discharge time than fentanyl group, with statistically significant effects. Discharge time is influenced by various factors, both in nursing and anesthesia. In terms of anesthesia, the prevention of pain, nausea, and dizziness (drowsiness) are the most crucial factors. The selection of appropriate anesthetic techniques and drugs can reduce recovery duration and discharge time (Awad & Chung, 2006; Pavlin et al., 1998).

In this study, the remifentanil group had an average discharge time of 20.00±7,246 minutes. This is in accordance with a previous study of dental surgery patients receiving propofol and remifentanil, which showed a discharge time of about 20 minutes after surgery (DG et al., 2021). The results of this study are also in line with previous studies on short urological surgery, which stated that patients receiving remifentanil had lower Aldrete scores better than fentanyl with less sedative effects. This is because remifentanil has a short half-life of about 9 minutes. The prolonged continuous infusion did not result in tissue accumulation of remifentanil nor changes in the half-life and elimination of the drug. With many surgeries with short duration and minimum postoperative pain, remifentanil can be an alternative opioid of choice to achieve faster discharge times or fast-track surgery (Kovac & Summers, 2009; Min et al., 2008).

Another study in one day surgery patients undergoing urological surgery showed that remifentanil is an ideal short-acting opioid in achieving the balance of anesthesia in ODS surgery, especially in procedures with short duration and minimal postoperative pain where discharge time from PACU is the main focus in cost efficiency. This study showed that the group receiving remifentanil achieved an Aldrete score of 10 faster than the fentanyl group, with a significant difference. This difference might be caused by the short elimination half-time and less sedative effect of remifentanil which is shown by lower end-tidal concentration of isoflurane compared to fentanyl. The group receiving remifentanil was discharged from the PACU within 60 minutes (Kovac & Summers, 2009).

In contrast, the study on various types of surgery showed different where patients who received fentanyl and remifentanil had similar discharge time. The difference in the results of this study was because remifentanil did not provide analgesia postoperatively when the infusion was stopped. This is due to the pharmacology of remifentanil that has rapid half-life and elimination. Therefore, in surgery with moderate to severe postoperative pain, patients who received remifentanil without additional analgesia might feel disturbing pain that prolongs the patient's discharge time. In this study, all patients underwent odontectomy with mild postoperative pain therefore the remifentanil group did not feel disturbing pain that might prolonged discharge time (Syroid et al., 2010).

## 5. Conclusion

This study showed that patients' emergence time and discharge time on remifentanil 1 μg/kgBW at induction followed by maintenance at 0.1 μg /kgBW/min were faster than fentanyl 2 μg/kg BW single bolus undergoing odontectomy surgery.

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# Diffused Multifocal High Grade Glioma

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**Abstract**
Multiple glioma represent approximately 2 to 5% of all high grade gliomas which are categorized as multifocal or multicentric which depends on its timing, location and pattern of spread. Most of the clinical manifestation of patient with High Grade Glioma are headache and seizures, however, some may present with cognitive symptoms like memory loss, personality changes, focal weakness or numbness related to the site of the mass. There are several ways on treating high grade glioma these include surgery, radiation and/or chemotherapy. This report is a case of 54-year-old male, without no known comorbidities who presented two months history of right hemi cranial headache, accompanied with left sided weakness. Cranial MRI revealed uni-hemispheric, non-contiguous high-grade gliomas. This case underwent surgical excision and concurrent chemo-radiotherapy.

**Keywords:** Multiple Multifocal Glioma High-Grade

## 1. Introduction

Glial tumors account for 42 percent of all primary adult CNS neoplasms, with malignant high-grade gliomas accounting for over 75 percent.[4] GBMs most commonly occur as solitary lesions with multiple GBMs occurring rarely (with reported incidence of 2–20%). Multiple GBMs are further categorized into multifocal and multicentric depending whether dissemination or growth by an established route, spread via commissural or other pathways, (i.e. corpus callosum, fornix, internal capsule, or massa intermedia), or spread via cerebrospinal fluid channels exists or not.[4]

To rule out any conceivable relationship between the neoplastic foci, multicentric tumors require comprehensive macro- and microscopic examination. Gliomatous tumors having many foci are known as multifocal gliomas. With or without evidence of cerebral spinal fluid spread, with microscopic continuity.[10] While multicentric gliomas are tumors arising independently in more than one site of the brain with absence of seeding along easily accessible routes.[4]

Despite the fact that the incidence of multicentric and multifocal glioblastomas is unknown, A series of 209 cases were studied by Batzdorf last 1963 and discovered a 2-4 percent and 25 percent for multicentric and multifocal gliomatous tumours, respectively.[8] Furthermore another 2 case study of multifocal glioblastoma was noted by Zhang et al., last 2021 at China. [10]

Currently, there is no noted literature regarding multiple multifocal high-grade glioma in Philippines. In this study we report a case of multiple multifocal high-grade glioma, we consider its course of illness, diagnostics, management and treatment and their outcome.

## 2. Case Report

This is the case of a 54 year old, male, who sought consult due to 2 months history of progressive right hemicranial headache, accompanied with left sided numbness and weakness. He had no comorbidities with no familial history of hereditary diseases.

### *2.1. Assessment*

Upon consult patient was seen to be coherent, oriented with appropriate response. Vital signs and general physical examinations were unremarkable. On neuro examination, patient was awake, with, homonymous hemianopsia on the left, left hemiparesis and left hemisensory loss. The rest of the neurologic examination were normal.

### *2.2. Laboratory workup*

Basic laboratory examinations such as CBC, electrolytes and coagulation studies all revealed unremarkable. Other ancillaries like random blood sugar, lipid profile, PSA, CEA and AFP were normal. A cranial CT scan was without contrast done showing a heterogenous predominantly hyperdensity focus in right parieto-occipital lobe measuring 4.9x 4.2x 4.9cm with surrounding hypodensity, which is considered as an intracranial mass. Furthermore, a cranial MRI with contrast was done showing a fairly defined nodule and mass in the right high parietal lobe and right temporo-parietal-occipital lobes exhibiting T1 hypo to isointense signal, interspersed with hyperintense signals and T2/ FLAIR heterogenous hyperintense signal abnormalities with respective measurement of 2.0x 1.4x2.1cm and 5.2x 4.5x 5.0cm. Surrounding vasogenic edema involving the right temporo-parieto-occipital lobes is observed, suggesting of a hemorrhagic metastatic process.

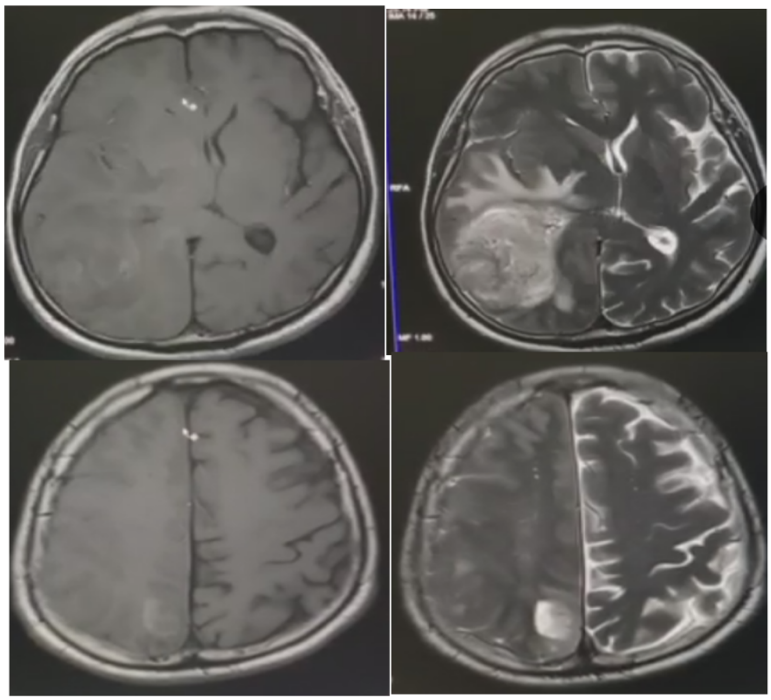

Figure 1 : Cranial MRI with contrast showed a fairly defined nodule and mass in the right high parietal lobe and right temporo-parietal-occipital lobes exhibiting on T1 a hypo to isointense signal, interspersed with hyperintense signals and on T2 showed heterogenous hyperintense signal abnormalities with respective measurement of 2.0x1.4x2.1cm and 5.2x 4.5x 5.0cm.

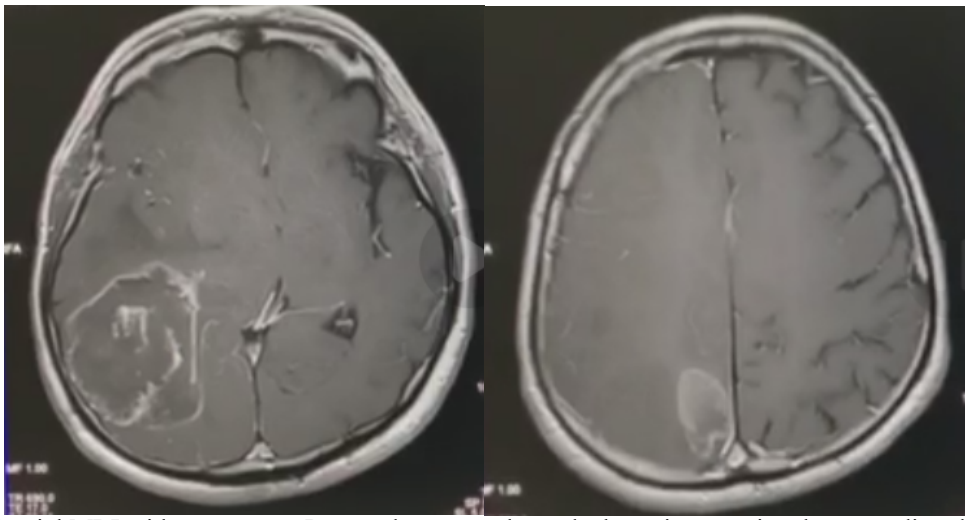

Figure 2: Cranial MRI with contrast on Post-gad contrast showed a hyperintense signal surrounding the fairly defined nodule on both right high parietal lobe and right parieto-temporo-occipital lobe.

Patient was managed with dexamethasone, omeprazole, paracetamol and lactulose. The patient was referred to neurosurgery service and underwent craniotomy, excision of tumor and biopsy was done revealing glioblastoma WHO GRADE IV, most likely wild type furthermore immunohistochemistry were also done revealing positive to GFAP and p53, negative in IDH-1, with retained nuclear stain of ATRX in tumor cells. The patient was then discharged with follow up on radiation-therapy and medical oncology.

*2.3. Outcome*

On follow up after 1 month since discharged, there was persistence of left hemiparesis but with resolution of left hemi sensory loss. Patient completed his chemo-radiation therapy with concurrent adjuvant chemotherapy sessions of Temozolomide. Unfortunately, the patient died after 3 months post treatment.

**3. Discussion**

Glioblastoma (GBM) is the most malignant diffuse glioblastoma of the astrocytic lineage, and according to the WHO classification, it is a grade IV glioma. GBMs account for 54 percent of all gliomas and 16 percent of all primary brain tumors, making them the most prevalent malignant primary brain tumor.[10]

For high-grade gliomas, a different pathway of propagation was seen. Multiple foci high-grade gliomas are considered tumors that spread through several pathways, including commissural fibers or the corpus callosum, and the CSF, and also by local metastasis. Multi focal high grade gliomas are fairly uncommon entities, with a reported incidence from 2–10% to 16% of all reported gliomas. The majority of instances occur supratentorially, whereas lesions in the posterior fossa have a documented prevalence of fewer than 4%.[2]

Multiple gliomas were initially classified by Budka into four categories: Diffuse, multiple, multicentric, and multi-organ. In 1963, Batzdorf and Malamud distinguished two types of multiple gliomas namely multifocal and multicentric gliomas. Multifocal gliomas are those which result from dissemination or growth of tumor cells by a preformed route like commissural fibers, cerebrospinal fluid pathway or by local metastasis. On the other hand, multicentric gliomas are located wide apart in different lobes or hemispheres, and their concurrence cannot be explained by previously mentioned mechanisms. The clinical significance of labeling multiple GBMs as either multifocal or multicentric is fading out. Various studies show that there is no apparent clinical utility in distinction between the two groups. [5]

Gliobastoma Multiforme's clinical manifestations are usually linked to the functional aspect of the brain area involved. Tumors in specific locations might create noticeable symptoms such as prolonged weakness, numbness,

visual loss, or language changes.[1] This is the same as the case presented which was gradual progression of headache accompanied by left hemisensory-motor deficit and left homonymous hemianopia upon examination

Imaging techniques that can be used for patients with intracranial tumors are non-invasive tests such as computed tomography (CT) and magnetic resonance imaging (MRI) scans. On a CT scan, the lesions appear as hypodense patches in comparison to neighboring brain tissue, with a midline shift due to moderate to severe edema. However, due to their higher soft tissue contrast, MRI scans are the gold standard imaging technique employed, allowing the complexity and heterogeneity of the tumor lesion to be better observed than a CT scan. T1–weighted MRI scans reveal hypointense lesions, but proton density weighted and T2-weighted imaging reveals hyperintense lesions. Moreover, a central area of necrosis surrounded by white matter edema can be seen on an MRI scan enhanced with gadolinium in patients with malignant gliomas. Tumors are usually unifocal but can be multifocal too.[3]

The best treatment for multifocal high-grade glioma is still up for debate. This is due to contradicting findings that urge no therapy at all on one hand and aggressive maximal surgical excision followed by chemo-radiotherapy(RT) on the other. Surgical biopsy is however, desirable to establish diagnosis and to decide further adjuvant therapy. Patients with multifocal disease in the modern temozolomide era had 1-year and 2-year survival rates of only 28.5% and 4.3%, respectively.[5]

The prognosis of multiple gliobastoma multiforme has remained unclear until now. There is no definitive study comparing the prognosis of multiple glioblastoma multiforme against a solitary glioblastoma multiforme. In a study by Parsa *et al.*, did not find any survival difference between the two. However, in another study, the authors found that patient with multifocal glioblastoma had a median overall survival of 6 months, compared to a solitary glioblastoma, of which was 11 months. [7]

## 4. Conclusion

We report a rare case of a 54-year-old male who presented with focal neurologic deficit with no known comorbidities and no family history of familial disease. On neuroimaging a multiple intracranial mass on Cranial CT scan was seen, patient underwent surgery and completed his con-current chemo-radiotherapy. Although reports of this condition have been reported in other countries, there is still no known data recorded in the Philippines. Moreover, although multifocal high-grade glioma is rare and has a poor prognosis, one must give all the best treatment to the patient.

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Patient form was secured before submission of manuscript

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# Comparison of Effect of Exercise on Insulin Sensitivity of Overweight Normoglycemic Offspring of T2DM Parents and Non-Diabetic Parents

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**Abstract**
Background: The primary causes of Type 2 Diabetes Mellitus (T2DM) are largely unknown but insulin insensitivity has been reported to be a risk factor for the T2DM through the alteration of insulin sensitivity pattern. There is paucity of studies on the effect of exercise on occurrence of T2DM in offspring of diabetic parents in our population. Objectives: This study was designed to assess the effect of exercise on insulin sensitivity (IS) on offspring of T2DM parents compared with offspring of non-diabetic parents. Design: This study involved 60 offspring of T2DM parents attending University College Hospital, Ibadan and 60 offspring of non-diabetic parents who are undergraduate students of the University of Ibadan, Nigeria. Participants were randomly assigned into two groups. Each participant followed a protocol of graded exercise using ''tummy trimmer'' everyday spending 45 minutes daily for 24 weeks. Blood samples were obtained after an overnight fasting for determination of insulin sensitivity using standard methods at baseline and at 24 weeks. Data were analyzed using descriptive statistic and student t test with significance at $p<0.05$). Results: The most populated aged group was 26 to 35 years of which 47.3% (n=26) were OODP and 52.7% (n=29) were OONDP. However, all subjects were overweight with mean BMI of OODP and OONDP (29.30kg/$m^2$±0.71 versus 26.37kg/$m^2$±0.88) p=.0.035. Significantly, total insulin sensitivity between the two groups increased after 6 months of exercise p=0.045(3.36µ /l±0.24 versus 3.48µ /l±0.24). Conclusions: Male subjects tend to have higher insulin sensitivity than females.

**Keywords:** Diabetes Mellitus, Body Mass Index, Insulin Sensitivity, Offspring of Diabetes

## 1. Introduction

Diabetes mellitus, commonly known as diabetes, is a disorder of intermediary carbohydrate, protein and lipid metabolism. It is characterized by hyperglycemia, glucosuria, polydipsia, polyuria, polyphagia and weight loss. It is usually associated by secondary alterations in glucose, fat and protein metabolism, leading to many biochemical disorders. It is characterized by peripheral insulin resistance, impaired regulation of hepatic glucose production with declining β-cell function and eventually leading to β-cell failure (Bacha, et al, 2010). Type 2 Diabetes Mellitus (Type 2DM) is characterized by a combination of peripheral insulin resistance and inadequate insulin secretion by

pancreatic beta cells. Insulin resistance has been attributed to elevated levels of free fatty acids and pro-inflammatory cytokines in plasma, leading to reduced glucose transport into muscle cells, elevated hepatic glucose production, and pronounced break down of fat. Researchers have found that obesity and diabetes are inter-connected. Individuals who are obese are at high risk of developing T2DM, particular if a close family member is affected with T2DM.

Obesity at younger age, significantly increased lifetime risk of type 2 diabetes mellitus (T2DM) (Bacha et al, 2010). Family history of T2DM is associated with higher body mass index (BMI), dyslipidemia, and impaired glucose tolerance (IGT) in offspring (Narayan et, al 2007, Tan et al,, 2008) There seems to be a vicious cycle, where obesity increases risk for T2DM and a family history of T2DM increasing the risk for obesity (Bacha et al,2010, Jouret et al, 2007). Parental history of T2DM is one of the dominant risk factors for development of T2DM (Chathurvedi et al, 2009). The phenotype varies depending on which parent is affected and if the child was exposed to hyperglycemia in utero ( Chathurvedi et al, 2009, Meigs et al, 2000) β-cell dysfunction has been observed even in non-diabetic offspring of T2DM, more accentuated among those with maternal T2DM compared to paternal inheritance (Shaw et al,1999). Here we report the effect of exercise on insulin sensitivity in normoglycemic subjects.

Maintenance of normal glucose tolerance depends on a finely tuned balance between insulin sensitivity and β-cell function (Bacha et al 2010). The concept that a feedback loop governs the interaction of the insulin-sensitive tissues and the β-cell, as well as the elucidation of the hyperbolic relationship between insulin secretion and insulin sensitivity, explains the elevated insulin response in insulin-resistant subjects and a lower response in insulin-sensitive subjects (Narayan et al, 2007). Consideration of this hyperbolic relationship has helped to recognize the critical role of β-cell dysfunction, in the development of impaired glucose tolerance and type-2 diabetes, (Tan et al, 2008). Assessment of several ethnic groups has shown a progressive reduction in β-cell function from normal to impaired glucose tolerance and subsequently to type-2 diabetes, accompanied by a decline in insulin sensitivity (Bacha et al, 2010). The progressive nature of β-cell dysfunction in type-2 diabetes mellitus (T2DM) was also established in landmark clinical studies, (Natali et al, 2010). The therapeutic or lifestyle interventions should address the underlying pathology and should be started early along the spectrum of glucose tolerance to prevent declining insulin sensitivity and β-cell failure, (Jouret et al, 2007).

Researchers have found that obesity and diabetes are inter-connected. Individuals who are obese are at high risk of developing T2DM, particular if a close family member is affected with T2DM. Researchers have not yet discovered a specific gene that causes obesity although, several genes are considered to play a role. There seems to be a connection between abdominal fat and diabetes, hence anything that will reduce abdominal fat will likely reduce diabetes (Narayan et al, 2007). Exercise has been known to ameliorate the effect of diabetes by improving insulin sensitivity. It is the aim of this to work to compare the effect of exercise on insulin sensitivity of normoglycemic offspring of patients with type 2 DM and non-diabetic parents.

## 2. Methods

The parents of the test group were attending the medical out-patient clinic (MOP) of the University College Hospital (UCH), Ibadan and Catholic Hospital Oluyoro, Oke-Ofa, Ibadan, South Western, Nigeria. The control subjects were normoglycemic offspring of non-diabetic parents who were randomly selected from general population of Ibadan Community, Ibadan, and South-Western, Nigeria and undergraduate students of University of Ibadan.
Experimental interventional study was carried out in which blood sample was collected from offspring of patients with type 2 diabetes mellitus and normoglycemic offspring of non-diabetic parents after an overnight fasting.

10ml of venous blood specimen was obtained from each subject into plain bottles. Separation of serum at centrifugal force of 3,000rpm was carried out at IMRAT (Institute of Medical Research and Training) of the College of Medicine, University of Ibadan. The serum so obtained was stored at temperature not exceeding- 80$^{o}$ C in a refrigerator at IMRAT until used for the determination of insulin sensitivity.

*2.1. Insulin Sensitivity by the Homeostatic Model Assessment*

Insulin was determined using a chemi-lluminescent micro particle immunoassay (Abbort Japan co., ltd). The IR and later IS were calculated using the homeostasis model assessment method according to Matthew formula (Matthew et al, 1985)[8]. IR is Insulin Resistance and IS is Insulin Sensitivity. (Since, IS = 1/IR). The glucose value (in mg/dl) multiplied by insulin level divided by 405 will give us insulin resistance value. The reciprocal of value got will now give us insulin sensitivity value (Jerry Radziuk, 2014 and Matthew et al, 1985)[8].

The measurement of anthropometric variables was done at baseline and after 24 weeks. Heights of participants were taken using standard hospital adult vertical rule with sliding arms which had been recalibrated and certified by a Biomedical Engineering technician prior to use. The height of the subject was imputed into the Omron equipment. The study subject stood erect, upright and bare-footed. Those who had extra clothes such as coats and sweater removed them while Omron equipment measurements of BMI were being taken. Body mass index (BMI) reading values for the subject were read off as displayed on the screen of Omron equipment (reliability and reproducibility index + 0.01%). The readings were then recorded.

The following definitions were utilized: Underweight: BMI <18.5 kg/m$^2$. Normal weight: BMI 18.5-24.9 kg/m$^2$, Overweight: BMI 25.0-29.9 kg/m$^2$, Obesity: BMI ≥30 kg/m$^2$.

Tummy trimmer, a portable, aerobic exercise, lightweight equipment (European Home Choice Company, Lagos, Nigeria) was selected for the study. It is in-door aerobic equipment. It is compact and can fit right in the subject's hand-bag. During each phase of exercise the Tummy trimmer, a portable lightweight equipment, is held at the two handles and the sole of the two feet are put inside the pedal rest while the subject assumes different positions. The subject will then pull the tummy trimmer's spring towards himself or herself either while lying flat or sitting up on the floor or carpeted hard surface. Subject sits up with leg straight, leans his or her body backwards until completely lying back with head on floor. He/she returns to sitting position in harmonic fashion. The subject was advised to start slowly and work up to repetition as she/he feels comfortable with harmoniously. The subject was advised to lie flat on floor, extend his/her legs straight up in the air. He will be keeping his/her back on the floor and raise lower legs without bending them. The subject was later advised to sit erect with legs straight horizontally, he/she raises handle to tummy height using arms only. Then finally, subject was advised to lie flat on the floor while he/she bends knees up to his/her chest. He/she makes a circular motion push feet up and then round towards the floor again. The different positions were observed for exercise period of 45 minutes (a video clip of the exercise procedure was shown to the subject before the commencement of the exercise). Each subject was advised as follows: (1) He/she to undergo the 4 phases of exercise for 45minutes daily (in the evenings). (2) He/she to contact the researcher on cell phone anytime when he/she has any problems with the unit. (3) There were regular weekly cell phone calls made to each of the subjects by the research assistant to ensure compliance with exercise schedule.

*2.2. Sample size estimation*

This was performed using formula $\underline{(Z_{1-\alpha}/2)^2 x SD^2}$ /d$^2$ where Z= normal variant, d= 5.0%, Type 1 error was used with SD of 25mg/dl of fasting blood glucose from previous study. Attrition was 25%. This is equal to $\underline{1.96^2(25)^2}$ = 96

$5.0^2$

If we add 25% attrition (24) making a total of 120 subjects. Cochran's formula (1977).

*2.3. Statistical Analysis*

Statistical analysis was done using SPSS version 15 software (Lead Technologies, Chicago, USA). The data were expressed as mean ± SD for various continuous parameters studied.

The study was approved by the University of Ibadan Teaching Hospital Ethics Committee (UI/UCH joint IRB) and Catholic Hospital Ethics Committee prior to its implementation.

## 3. Results:

A total of 60 subjects with family history of T2DM (OODP) and 60 subjects without family history of T2DM (OONDP) underwent the exercise procedure. There were 60 males and 60 females study subjects, aged 16 to 55 years. The most populated aged group was 26 to 35 years of which 47.3% (n=26) were OODP and 52.7% (n=29) were OONDP. However, all subjects were overweight with mean BMI of OODP and OONDP (29.30kg/$m^2$±0.71 versus 26.37kg/$m^2$±0.88) p= 0.035. Significantly, total mean insulin sensitivity between the two groups increased at 6 months of exercise p=0.045(3.36(µ /l±0.24 versus 3.48(µ/ /l±0.24) In OODP, the mean insulin sensitivity increased from 3.60(µ/l ±0.41to3.80 (µ/l ±0.42 after six months of exercise p=0.122. In OONDP, the mean insulin sensitivity increased from 3.17(µ/l ±0.27 to 3.23µ/l ±0.27) after six months of exercise p=0.198. The increase is higher in OODP than OONDP (-1.620 versus -1.324). The increase is higher in male OODP than female subjects (-2.020 versus 0.048) and similarly for OONDP group (-0.975 versus-0.857). However, all values were not statistically significant but clinically important.

Table 1: Anthropometric Parameters of the Study Groups

| Variable | Category | Total | OODP | OONDP | P |
|---|---|---|---|---|---|
| **Gender** | *Male* | 60 (50.0) | 30 (50.0) | 30 (50.0) | |
| | *Female* | 60 (50.0) | 30 (50.0) | 30 (50.0) | |
| **Age (years)** | *16-25* | 43 (35.8) | 22 (36.7) | 21 (35.0) | |
| | *26-35* | 55 (45.8) | 26 (47.3) | 29 (52.7) | |
| | *36-45* | 19 (15.8) | 9 (15.0) | 10 (16.7) | |
| | *46-55* | 3 (2.5) | 3 (5.0) | 0 (0.0) | |
| **Mean Weight(Kg)** | | 69.80±1.59 | 73.28±2.38 | 67.00±2.01 | 0.185 |
| **Mean BMI(Kg/m2)** | | 27.70±0.61 | 29.30±0.71 | 26.37±0.88 | 0.035* |

P value significant at 0.05.

Table 2: Mean insulin sensitivity before and after Exercise in the study groups.

| Variable | Category | Before Exercise | After Exercise | T | P |
|---|---|---|---|---|---|
| **Mean Insulin Sensitivity(µ/l)** | *Total* | 3.36±0.24 | 3.48±0.24 | -2.014 | 0.045* |
| | *OODP* | 3.60±0.41 | 3.80±0.42 | -1.620 | 0.122 |
| | *OONDP* | 3.17±0.27 | 3.23±0.27 | -1.324 | 0.198 |
| | *OODP-Male* | 4.14±0.88 | 4.57±0.86 | -2.020 | 0.078 |
| | *OODP-Female* | 3.16±0.18 | 3.16±0.18 | -0.048 | 0.963 |
| | *OONDP-Male* | 3.18±0.28 | 3.26±0.28 | -0.975 | 0.355 |
| | *OONDP-Female* | 3.16±0.42 | 3.21±0.41 | -0.857 | 0.406 |

P value significant at 0.05

## 4. Discussion

The present study assessed the insulin sensitivity among normoglycemic offspring of T2DM subjects and controls without family members with T2DM. We observed higher mean insulin sensitivity in the subjects studied after six months of exercise in normo-glycemic offspring of individuals with T2DM compared to controls. It mean that the total insulin sensitivity were significantly higher in the offspring of subjects with diabetes. Pimenta *et al*., 1995 observed similar insulin sensitivity and loss of first-phase insulin secretion in subjects with family history of DM compared to BMI-matched controls (Matthews et al, 1985). Van Haeften *et al*.,1998 observed similar insulin sensitivity but reduced insulin secretion at 90 and 120 minute during OGTT in offspring of individuals with T2DM (Jensen et al, et al,2002). There were three reports where mean age of subjects was less than 16 years. Two of these reports where cases and controls were matched for BMI have reported lower insulin sensitivity in offspring/ first-degree relative using clamp studies (Weyer et al,1999, Warram et al, 1990). The third which did not match

cases and controls for BMI observed higher BMI, fasting insulin levels, and HOMA-IR for cases and the differences were not significant after adjusting for BMI (Meigs et al, 2000) A longitudinal study in Pima Indians reported a twofold greater increase in weight in subjects who progressed to diabetes compared to the non-progressors (Pimenta *et al*., 1995). Our observation of higher BMI in offspring of subjects with T2DM compared to controls is in accordance with these above-mentioned studies. The San Antonio heart (SAH) study has shown that both mean fasting insulin levels and mean insulin sums increased in a stepwise fashion as the family history of diabetes became stronger. The significance of fasting insulin became marginal when adjusted for BMI (Danadian et al, 1999). Mean age of offspring (20 years) in the present study was lower compared to the SAH study which is 42 years. There was significantly higher plasma insulin, C-peptide, HOMA-IR, and BMI when three or more family members were affected (FHD3 group).

In the present study, the mean age of subjects was in their twenties, reducing the confounding effects due to age. Whole-body insulin sensitivity in the present study was measured as WBISI as described by Matsuda and DeFronzo, which was shown to be having an excellent correlation with euglycemic hyperinsulinemic clamp technique by large scale studies (Danadian et al, 1999). The calculated disposition index by OGTT highlighted the inability of β-cell to compensate for declining insulin sensitivity (Taiwo et al, 2017). In their prospective studies, the disposition index declined well before glucose levels rise into the diabetic range, and was mentioned as an early marker for inadequate β-cell compensation or β-cell dysfunction21 (Srinivasan et al, 1998).

Finally, we observed higher BMI, plasma insulin sensitivity in normoglycemic offspring of T2DM subjects compared to controls. In normal glucose-tolerant subjects, insulin sensitivity and insulin secretion varied over a large range. According to a study in obese youth by Yeckel et al., 2005 insulin secretion as measured by the insulinogenic index has a strong impact on postprandial glucose levels even within the normal range, and in all insulin sensitivity tertiles (Chathurvedi et al, 2009).

## 5. The limitations of this study

The limitations of this study were that we did not consider 1° relatives or 2° relatives in particular but only in offspring, however, other family relations were not taken into considerations.

## 6. Conclusion

In conclusion, insulin sensitivity increased after six months of exercise. Male OODP subjects tend to have higher insulin sensitivity than females. Based on the outcome of this research, people with family history of T2DM should reduce their tendency to obesity and engage in exercise

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## Contributions of Authors

## Conflict of interest

No conflict of interest.

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# Adolescents Smokers' Knowledge Level of Dental and Oral Health

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**Abstract**
Smoking is a very popular habit, especially for adolescents, to show self-actualization. This situation also shows the need for guidance on awareness and good knowledge about maintaining a healthy body, not to mention dental and oral health as a whole and continuously, through the prevention of smoking behavior as dental and oral health influence the overall health. The aim of this study is to describe smoking in adolescents based on the knowledge level of dental and oral health in East Boroko Village, Manado, Indonesia. The type of research is descriptive research with a survey method. The sample in this study was a total population of 30 adolescent smokers. The data collection technique used primary data. The data was obtained directly by filling out the questionnaire, sending a google form questionnaire link to each respondent, contacting and cross-checking with respondents. The results show overall respondents' level of knowledge is mostly poor as many as 16 people (53.3%) out of 30 people Meanwhile, the age group of respondents with poor knowledge level is the most in the 15-16 year age group as many as 10 (62.5%) people. Most adolescents do not know the impact of smoking on dental and oral health. In conclusion, the teenage smokers in East Boroko Village are lack of dental and oral health knowledge. Future work should address the causes of adolescents to become a smoker in order to provide precise solutions.

**Keywords:** Adolescent, Dental and Oral Health, Knowledge, Smoking

## 1. Introduction

Smoking is familiar to everyone in general and a very popular habit to show one's self-actualization. Smoking can cause a crucial effect on overall health. Dental and oral parts are interdependent organs in humans. The teeth are one part of the body that serves to chew, speak and maintain the shape of the face. Thus, it is important to maintain dental and oral health early so that dental health can sustain in the oral cavity (Al-qahtani et al., 2020; Gangadi et al., 2021). Maintaining dental and oral health from an early age will be able to improve overall health status.

One of the ways to improve dental and oral health is by taking notice of habits from adolescence. Adolescence is a transition period between children and adults, and the group relationships are very close. They are in a period of developing their identity (Pfeifer & Berkman, 2018). The bad habit that often occurs in adolescents is smoking.

Smoking can cause not only long-term damage to both the health of the body but also the oral cavity (Mubeen et al., 2013). Smokers have less awareness of oral health compared to non – smokers (Puranik et al., 2013). The task of a teenager who should have started to study seriously for their future will be disrupted by the smoking habit, which can undermine the image of students.

The urgency of guidance for adolescents is that the phenomenon of smoking is something very unfortunate and should be watched out for, because half of the active smokers nowadays are adolescents (Hu et al., 2020). Smoking habits must be ceased to improve the degree of dental and oral health so that the life order of adolescents is in positive behavior to develop themselves. The ability to determine needs, concerns, and perspectives increases in the adolescent years (Fuligni, 2019). Adolescents who have a character in an effort to improve their image or get recognition from parents or peers are prone to doing negative things. This situation also shows the need for guidance on awareness and good knowledge about maintaining a healthy body as a whole and continuously through the prevention of smoking behavior which can also affect dental and oral health. Dental and oral health needs to be maintained from an early age to create a younger generation, especially adolescents who are more confident, and able to develop a positive lifestyle.

The WHO (World Health Organization) report on The Global Tobacco Epidemic 2017, that the prevalence of teenage tobacco users in Indonesia currently reaches 12.7%. The prevalence of young smoking currently reaches 11.5% (WHO, 2017). The results of Riset Kesehatan Dasar (Basic Health Research) 2018 also stated that there is an increase in the prevalence of smoking. The prevalence of smoking at the age of 10-18 years has increased from 7.2% in 2013 to 9.1% in 2018 (Kementrian Kesehatan RI, 2018). Therefore, controlling the problem of smoking should target children and adolescents which should be based on data on the causal factors that play the most important role in influencing children to decide on a smoking habit so that the efforts made are in accordance with their needs and carried out effectively and efficiently (Fuligni, 2019).

A study on adolescent knowledge about the influence of smoking on dental and oral health in the community in Lotang Salo village, Panca Rijang district, Sidenreng Rappang district in 2018 shows that the level of knowledge of adolescents is quite good (Supriatna & Angki, 2018). Research at SMK Negeri 3 Tahuna was also conducted, i.e. the knowledge of adolescents about the dangers of smoking shows that the students have good knowledge 91% of the respondents (Vitra A. Pontolawokang, 2012). Meanwhile, the research of adolescents smoking behavior in Jayapura shows that the smoking respondents have the higher knowledge of smoking effect than those non-smoker respodents, although it is not statiscally significant (Herawati et al., 2017). However, the level of knowledge is not described. Survey scale/level is important to help people getting informative results. Studies with item-specific scales provides higher measurement quality (DeCastellarnau, 2018).

The aim of this study is to map the smoking habit of adolescents based on their knowledge level upon dental and oral health in East Boroko Village, Manado. The level is divided into good, fair and poor to show the quality of the knowledge.

## 2. Method

### *2.1 Research Design*

This study was undertaken by a descriptive study with a survey method aimed at describing smoking in adolescents based on the level of dental and oral health knowledge in East Boroko Village, North Bolaang Mongondow Regency, Indonesia.
The variable in this study was the mono variable, i.e. smoking in adolescents based on the dental and oral health knowledge level. The population was 30 teenage smokers and the sample in this study was 30 adolescent smokers in total.

### *2.2 Data Collection*

The data collection technique used primary data, i.e. the data that is obtained directly by filling out questionnaires, collected 30 respondents' phone numbers using a chat media application, contacted 30 respondents online and

explained the purpose of the study as well as sent a google form questionnaire link to each respondent. Subsequently, we contacted and checked back the questionnaire response to ensure that all the respondents filled out the form correctly. This research was carried out after having an ethical clearance. The ethical clearance approval of this research is obtained from Health Research Ethics Committee Poltekkes Kemenkes Manado number KEPK.01/07/184/2021.

## 3. Results

East Boroko Village, North Bolaang Mongondow Regency is one of the regencies in North Sulawesi Province, Indonesia. The area of East Boroko Village is 0.6 km2 with a population of 2,094 people, of which 1,053 are male and 1,041 are female. The boundaries of East Boroko village are North bordering North Boroko village, South bordering Bigo Village, West bordering Boroko Village, and East bordering Kuala Village (Website Desa Kementrian Komunikasi dan Informatika RI, 2020).
The initial survey on 25 to 26 April 2021 on 10 adolescents in East Boroko Village, Bolaang Mongondow Regency conducted by interview shows all the respondents admitted that they smoke because of a friend's invitation and do not know the bad effects of smoking on dental and oral health since the age of 15.

### *3.1 Respondent Based on Age*

Table 1 shows the respondents based on age. Based on the results of respondents by age group, it is noticed that the largest age group is in the 17-18 year age group as many as 16 (53.3%) respondents. While the least in the age group 19 years as many as 2 (6.7%) respondents.

Table 1: Respondent based on age

| Age | Total Respondents | Percentage |
|---|---|---|
| 15 – 16 | 12 | 40 % |
| 17 – 18 | 16 | 53.3 % |
| 19 | 2 | 6.7 % |
| Total | 30 | 100 % |

### *3.2 Respondent Based on Knowledge Level*

Table 2 shows the respondent based on their knowledge level which is grouped into three-level, i.e. good, fair and poor. According to the level of categorization, the most respondents' knowledge level was in the poor level as many as 16 (53.3%) respondents, while the least in the good level was 14 (46.7%) respondents.

Table 2: Respondent based on knowledge level

| Knowledge Level | Total Respondents | Percentage |
|---|---|---|
| Good | 14 | 46.7 % |
| Fair | 0 | 0 % |
| Poor | 16 | 53.3 % |
| Total | 30 | 100 % |

### *3.3 Age of Respondent Based on Knowledge Level*

Table 3 reveals the age group of respondents with the category of poor knowledge level is the most in the 15-16 year age group as many as 10 (62.5%) respondents, and the second is in the 17-18 year age group as many as 6 (37.5%) respondents, while the 19 years old, there are no respondents in the category of poor knowledge level.

Table 3: Age of respondent of knowledge level

| Level \ Age | 15 – 16 | 17 – 18 | 19 |
|---|---|---|---|
| Good | 2 | 10 | 2 |
| Fair | 0 | 0 | 0 |
| Poor | 10 | 6 | 0 |
| Total | 12 | 16 | 2 |

## 4. Discussion

Clean and healthy living behavior is a basic need for public health status. Health is very principal for everyone, including dental and oral health. Poor dental and oral health can disturb the comfort of working activity and decrease study interest (Utami & Prasepti, 2019). Dental and oral health problems most often occur in school-age adolescents. A study found that school-age adolescents suffer from poor oral health more than those who have good oral health and 50 million school hours are lost because of poor oral health (Haque et al., 2016). One of the things that become attention is that smoking behavior. The dangers of smoking to the health of the body have been researched and proven by many people, the World Health Organization has warned that in the 2020-2030 decade tobacco will kill 10 million people per year, 70% of which occur in developing countries (Jha & Peto, 2014).

Regarding the results of this study, the most data are the age group 17-18 years as many as 16 people with a percentage of 53.3% of the total respondents studied, and the most age of having poor dental and oral health knowledge is the age group of 15 – 16 years old. The age of 15-19 years is the age of middle adolescence, in this age group, the adolescents have the characteristics of starting to develop behavioral maturity, learning to control themselves, and setting early decisions according to their goals (Jaworska & MacQueen, 2015). Adolescents are also easily influenced by the surrounding environment, the existence of habits, and assumptions that a smoker is considered strong, steady and even macho. Whereas, the smoking habit can have bad consequences for health, especially dental and oral health. Therefore adolescents must be equipped with good knowledge about their lives for the sake of their health.

The best health is the key to a long, active, and enjoyable life. Even, health is actually a wealth that people can retain (Ali et al., 2017). There is a relationship between mother's knowledge and the habit of children's dental and oral health, where a mother with good knowledge is more aware of the importance of dental and oral health of the children (Moses & Arunachalam, 2018; Shetty et al., 2016). The role of parents in fostering children's character is very much needed, as the parents play a major role in both preventive and treatment of the children. Parents are the closest ones for children to continue to carry out positive behavior, in this case, dental and oral health behavior as general health development. Parents should also pay attention to the consumption of nutritious food as dental pain is associated with the intake of unhealthy food (Nicksic et al., 2018). Because good nutritional status will improve the health and behavior (Kadir, 2019).

Health development includes preventive and promotive efforts to increase the community's ability to carry out health efforts independently (Kumar & Preetha, 2012). Research at SD Negeri Banda Aceh by Liza, et al (2020), on knowledge, attitudes, and actions of parents towards dental and oral health is in a good category (Liza & Diba, 2020). So it is expected that parents need to improve their dental and oral health behavior even better. This shows that parents are the main characters at home who play a role in supporting the maintenance of dental and oral health without neglecting the personal health in terms of this, is the children. There is an influence of dental and oral health maintenance behavior on the OHIS status of Samin Surosentiko residents, Blora Regency (Saptiwi et al., 2019). Health education must always be instilled in the form of health education. Based on the research by Dewi, et al (2021) on dental health education and oral health at Ki Merogan Islamic boarding school Palembang, the education proved that it has a positive influence on increasing knowledge and dental health attitudes of the students in the long-term (Dewi et al., 2021).

An attempt to increase knowledge about dental and oral health, especially positive behavior, can be implemented by performing education about dental health, especially for adolescents. Research on 15 – 16 years old students was conducted in Finland resulting in the conclusion that knowledge influences behavior directly. Good

knowledge about dental and oral health is a principal to act for overall health. Parents can further increase their role in dental and oral health, especially doing supervision (Bozorgmehr et al., 2013).

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# Perioperative Anaesthesia Management for Aorta Dissection Patient Undergo Bentall Procedure

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**Abstract**
Introduction: aortic dissections that involve the ascending aorta (Stanford type A) are considered surgical emergencies. The mortality rate without emergency surgery is about 1% per hour for the first 48 hour, 60% by about one week, 74% by 2 weeks and 91% by 6 month. Open chest surgery with resection of dissected aorta may reduce the expected fatal outcomes to 10% as soon as the treatment provided in the first 24 hour and 20% for next 14 day. Case: A case of 42 years old man, 72 kg weight complained of sharp, tearing, pain from upper abdomen to chest and back of body since a month before admission. The pain endured for 20 minutes, patient had history of hypertension a year ago. Suspected with aortic dissection patient transferred to CVCU got therapy of antihypertension and β-blocker. Laboratory examination showed kidney disorder with enhancement of Ureum and creatinine levels. CT contras showed aortic dissection Stanford A Debakey Type I and patient scheduled for Bentall Procedure with complication Acute Kidney Injury (AKI). Perioperative anaesthesia management from preoperative with β-blocker and ramipril, induction with high dose analgetic, smooth intubation prevent increase in systolic blood pressure and heart rate, also maintain oxygen delivery to brain when DHCA started use SACP monitored with NIRS. after operation patient treated in ICU with ventilator and full sedated. Second day in ICU patient developed high creatinine levels and low urine output per hour. Renal replacement therapy is given and patient transfer to CVCU on the fifth day. Conclusion: it is still challenging to treatment of aortic dissection, started from diagnosis, preoperative management and overcoming the complication. Therefore, careful history taking, early treatment to prevented expansion of dissected aorta, CT angiography for diagnosed, intraoperative management and haemodialysis therapy should be considered to increase patient outcome.

**Keywords:** Perioperative Management, Aorta Dissection, Bentall Procedure, DHCA, AKI

## 1. Introduction

Aortic dissections that involve the ascending aorta (Stanford type A) are considered surgical emergencies. The mortality rate without surgery is about 1% for every first 48 hours, 60% by about 1 week, 74% by 2 weeks and 91% by 6 month (Kaplan,2017). Open chest surgery with resection of the dissected aorta may reduce the expected fatal outcome to 10% in the first 24 hour and 20% for the next 14 days. Therefore, operative management of

ATAAD (Acute type A aortic dissection) it's still accepted as gold standard for the management of this perilous condition (Petrov, 2020).

Aortic dissection results from an intimal tear that exposes the media to the pulsatile force of blood within the aortic lumen. Blood may exit the true aortic lumen and dissect the aortic wall to create a false lumen. The aortic dissection may remain localized at the primary entry site at the original intimal tear, or it may extend proximally, distally, or both (Kaplan,2017). The aetiology is frequently unknown but is related to hypertension (72%), and atherosclerosis (30%). Other predisposing factors are Marfan's syndrome, Ehlers-Danlos syndrome, coarctation, bicuspid aortic valve, Turner syndrome, aortitis, cocaine abuser, pregnancy, and blunt chest trauma (Dewi, 2020). The prevalence of AD has been reported approximately 5200/100.000 in western countries, with a male predominance of 3:1 and in approximately tw0-thirds of case involving the ascending aorta (Claussen, 2008). The incidence of Acute Aortic Syndrome (AAS) ranges from 3,5 to 6.0 per 100.000 patient-years in general population but increases in patients aged 64 to 74 years (27 per 100.000) and older than 75 years (35 per 100.000). acute aortic dissection comprises 85% to 95% of all AAS (Mussa, 2016).

Acute aortic dissection is defined as dissection occurring within 2 weeks of onset of pain. Subacute and chronic dissections occur between 2 and 6 weeks, and more than 6 weeks from the onset of pain respectively. Sudden onset of severe chest and/or back pain is the most typical symptom (Fukui, 2018). Extension of the dissection can lead to involvement of side branch vessels, resulting in cerebral, coronary, mesenteric, renal and limb ischemia (Pawan, 2008). Post-operative acute kidney injury (AKI) is a common complication with a high odds ratio 3.49 for 30-days mortality after operation (Hsiang,2021).

## 2. Case Report

A 42-year-old, 74 kg and height 180 cm complained of sharp, tearing, pain from upper abdomen to chest and back of body since a month before admission. The pain endures for about 20 minutes. Patient also complained shortness of breath especially during strenuous activities. Patient has history of hypertension since a year ago and patient received antihypertension drugs. Other history of disease such as stroke, asthma and Diabetes were declined. Patient treated in Cardiovascular Care Unit (CVCU) and has been given therapy. When examined, the patient appears calm, compos mentis, and don't feel pain. Blood pressure that time 199/57 mmHg with heart rate 56 bpm and respiratory rate 24 times per minute. Oxygen saturation 97% with room air. Chest physical examination revealed a diastolic murmur. The results of laboratory examinations showed that the values of hemoglobin, hematocrit, leukocytes and platelets were within normal limits. Electrolyte results showed hyponatremia (129 mg/dl) and hyperkalemia (5.1 mg/dl). Kidney function is also impaired with the value of urea (108 g/dl) and creatinine (2.24 g/dl). X-ray examination revealed cardiomegaly with interstitial lung edema, ECG examination gave sinus rhythm and LVH results. Another examination is CT Angiography with the conclusion of aortic dissection that extends to the brachiocephalic to the bifurcation common iliac artery along lk. 494 mm Stanford A Debakey I classification. TEE was also performed with the conclusion of mild regurgitation of the mitral, tricuspid, and pulmonary valves with normal right ventricular systolic function, widening of the aortic root and visible aortic dissection.

Table 1: Preoperative Laboratory

| Hemoglobin | Hematokrit | Leukosit | Trombosit | SGOT | SGPT |
|---|---|---|---|---|---|
| 15 g/dL | 44,7 % | 6330/$mm^3$ | 192.000/$mm^3$ | 37 U/L | 42 U/L |
| Ureum | Kreatinin | Natrium | Kalium | Klorida | Magnesium |
| 108 mg/dL | 2,24 mg/dL | 129 mEq/L | 5,1 mEq/L | 105 mEq/L | 2,1 mg/dL |

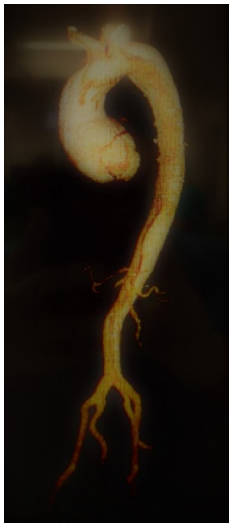

Figure 1: Three-dimensional results of CT Angiography showing Stanford A Debackey Type 1 aortic dissection.

The patient has been admitted to the CVCU for about 1 week and has been given oral therapy with ramipril 7.5 mg once a day, bisoprolol 10 mg once a day, ivabradine 5 mg twice a day, lansoprazole 30 mg once a day, and sucralfate syrup 10 cc three times a day.

**3. Anesthesia Management**

the patient's hypertension was controlled with oral therapy in the form of ramipril, bisoprolol, and ivabradine which were given while in CVCU. The patient is entered into the preparation room for an EKG for monitoring and an EKG for IABP (Intra-Aortic Balloon Pump), external defibrillator, IV line in the right hand, and arterial line in the left radial artery for invasive monitoring. the patient enters the operating room, monitoring equipment is connected including NIRS (Near Infrared Spectroscopy) which is installed in the frontal head of the patient's left and right, at that time the monitor shows blood pressure 110/69 mmHg, pulse rate 50 beats per minute, respiratory rate 18 breaths per minute and saturation 100%. The NIRS value when the patient is awake is the reference value for the patient, which is 64% for the right and left hemispheres.

After all monitoring devices were installed and working properly, induction was started by titrating midazolam 3 mg, fentanyl 225 mcg, propofol 50 mg and rocuronium 80 mg. Intubation was carried out after 3 minutes with a smooth ETT No. 8.0, depth of 21 cm, the anesthetic agent was turned on sevoflurane 1% and the ventilator control volume setting was 475 ml, peep 5 cmH2O, respiratory rate 12 times per minute and O2 fraction at 50%. Hemodynamic post intubation blood pressure 127/49 mmHg, pulse rate 52 beats per minute, respiratory rate 12 x per minute with 100% O2 saturation.

The operation was continued with CVC placement in the right subclavian vein, side port in the right internal jugular vein, and the second line artery in the left femoral artery. Phlebotomy as much as 2 bags of whole blood as much as 250 ml each. Insertion of Transesophageal Echocardiography (TEE) to see the morphology of the patient's heart and nasopharyngeal temperature. Fentanyl 100 mcg is injected five minutes before the incision. The incision was hemodynamically stable, five minutes after the incision heparin 300 mg was injected with an ACT value of 130 s and an ACT after heparinization of 597 s. Cardiopulmonary Bypass (CPB) was initiated 15 minutes post-incision with aortic cannulation of the right femoral artery and venous cannulation of the right atrium leading to the IVC. Deep Hypothermic Circulatory Arrest (DHCA) begins 118 minutes after CPB is working or 105 minutes after AOX, when DHCA is started CPB is stopped, while joining the prosthesis distal and proximal to the aorta at 25$^{O}$C and to avoid injury to the head being covered with ice. Anterograde Selective Cerebral Perfusion (ASCP) is used when DHCA is started to provide O2 supply to the left and right brain so that the NIRS value does not fall to 20% of the reference value. DHCA is finished when suturing is complete and CPB returns to work, the patient is warmed slowly to a temperature of 36$^{O}$C and evaluates the results of the operation.

Post CPB hemodynamically stable with blood pressure 103/68 mmHg to 108/71 mmHg, pulse rate 49 to 52 times per minute, respiratory rate 12 times per minute with cvp 8-12 cmh2O, and PAP 29/22 mmHg. The patient was given an inotropic at that time, dobutamine 10 mcg/kg/min, norepinephrine 0.1 mcg/kg/minute, followed by protamine 400 mg. The bradycardia was treated with the installation of an intracardiac pacemaker with the pulse rate set at 70 beats per minute. Total bleeding during surgery is estimated at 1100 cc. The operation lasted for 6 hours with stable hemodynamics including blood pressure ranging from 105/56 mmHg -135/72 mmHg, pulse rate 48-60 times per minute, CVP 20-22 mmHg, second line arterial 66/32 mmHg to 91/36 mmHg, PAP 50/36 mmHg to 67/37 mmHg, temperature 24$^{O}$ C – 36 C, and right brain NIRS values (51-72%), left brain (57-71%). CPB time was 193 minutes, AOX (148 minutes), ischemic time (20", 27', 21', 11'), ASCP (19 minutes), and DHCA (25 minutes).

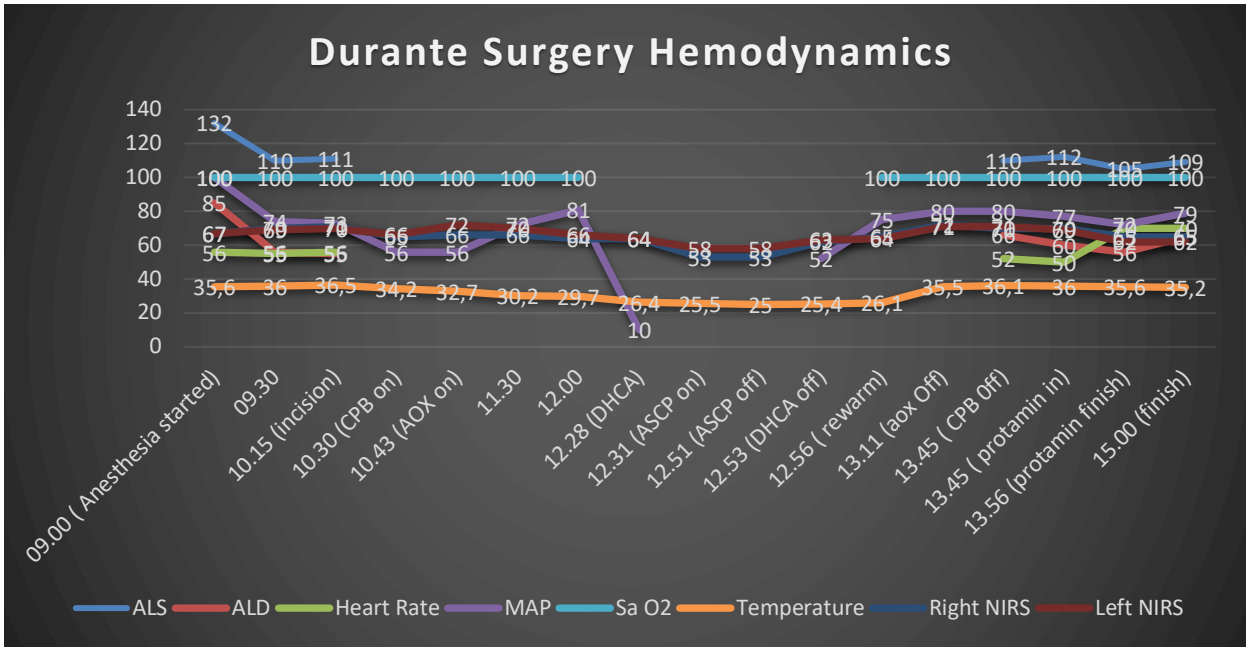

Figure 2: Durante Operation Hemodynamic diagram.

## 4. Postoperative Management

Postoperatively the patient was transferred to the ICU treatment room in an intubated condition and connected to a ventilator, VCV ventilator mode with 500 ml TV, RR 12 times per minute, Peep 5 mmHg, FiO2 50%, I: E = 1:2, MV 7.2 liters per minute. Hemodynamics at that time, blood pressure 128/71 mmHg, pulse rate 70 beats per minute, PAP 19/12 mmHg, CVP 9 cmH2O, temperature 35.4$^{O}$C, and 100% saturation with the help of dobutamine 10 mcg/kg/minute and norepinephrine 0.1 mcg /kg/minute. The patient's consciousness is still under the influence of sedative drugs, dexmedetomidine 0.2 mcg/kg/minute and the analgesic morphine 10 mcg/kg/hour. 2-hour postoperative right and substernal CTT drain about 800 cc. The patient was given transfusion therapy of 7 flasks of PRC, 8 flasks of FFP, and 3 flasks of TC. The patient was also injected with tranexamic acid 500 mg / 8 hours, vitamin K 10 mg / 8 hours, Ca gluconate 2 g and octaplex once given.

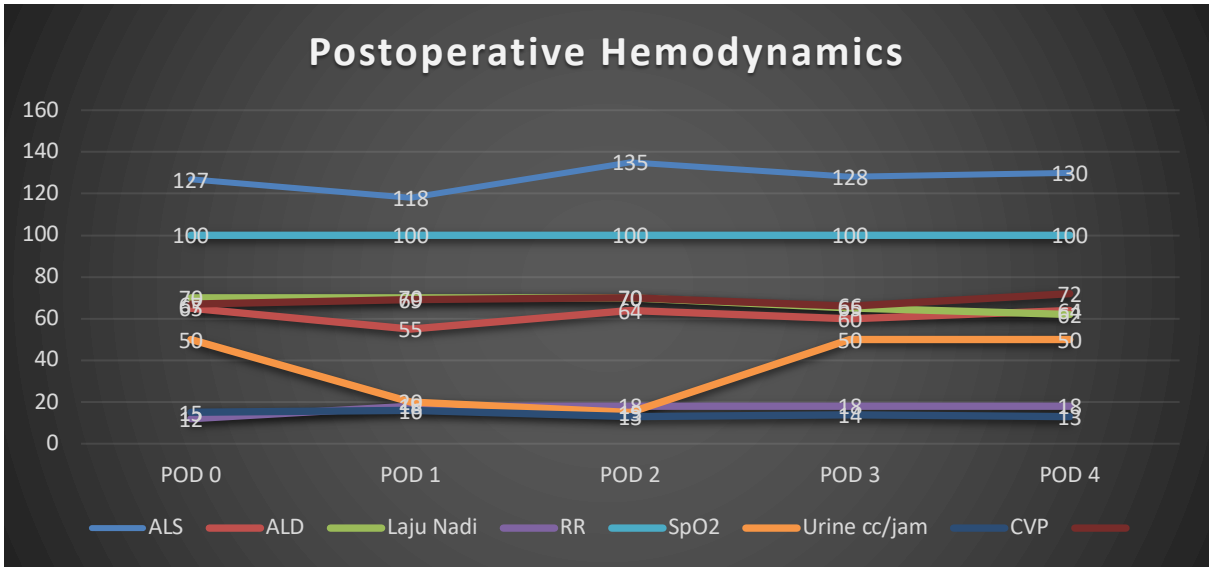


Figure 3: Postoperative Hemodynamic Diagram

The increase in postoperative kidney function was seen from laboratory examinations on the second post-op day with a creatinine value of 3.4 g/dl, an increase in potassium levels of 5.3 mmol/dl and a decrease in the amount of urine to 15-30 cc/hour. Then the patient was consulted for internal medicine to receive renal replacement therapy in the form of hemodialysis. CDL was placed in the left femoral vein followed by hemodialysis for 4 hours, urine output reached 50-100 cc/hour then the patient was extubated, and the patient moved from the ICU to the CVCU room on the fifth day.

**5. Discussion**

Aortic dissection is the separation of the intima and media of the aortic wall. It usually occurs as a result of a small tear in the intima (typically in the ascending aorta) where blood enters under pressure, separates the layers of the aortic wall and creates a false lumen. Propagation of the dissection is dependent on absolute blood pressure, pulse pressure and the rate of systolic arterial pressure rise (δP/δt). Distal propagation is common and, as the dissecting progresses, may occlude branches and compromise organ blood supply. Proximal extension is less common but may result in aortic valve disruption, coronary artery occlusion or rupture into the pericardium (Mackay, 2012).

The pain of aortic dissection typically is severe, abrupt in onset, and has a ripping, tearing, or stabbing quality. Highly suggestive physical findings include a pulse deficit, a systolic blood pressure differential greater than 20 mmHg, focal neurologic deficit, and a new murmur od AR. Electrocardiogram, along with urgent and definitive aortic imaging (TEE, CT, MRI), is strongly recommended in suspected aortic dissection. The most common imaging study is contras-enhanced spiral CT or CTA because it is widely available. Typical finding in acute aortic dissection includes an intimal flap, luminal displacement of intimal calcification, and aortic dilatation. Intra Mural Hematoma appears as a crescent-shaped high-attenuation thickening of aortic wall in noncontrast CT. CT can demonstrate rupture, branch-vessel involvement, and false lumen extent. Although MRI has a near 100% sensitivity and specificity and is widely available, it also takes significantly longer than CT (Kaplan, 2017).

Aortic dissection is classified according to both duration of symptoms and anatomy. Aortic dissection is termed “acute” if the diagnosis is made within 2 weeks of the initial onset of symptoms, otherwise it is termed chronic. The Stanford classification is based on involvement of the ascending aorta (type A dissection involve the ascending aorta; whereas type B does not) and is useful because of the contrasting treatment options. The DeBakey classification further subdivides dissection on an anatomic basis (Mackay, 2012). According to the above description of the signs and symptoms, physical examination of contrast CT imaging and TEE of the patient in this case was diagnosed with Stanford A Debakey Type I Aortic Dissection.

Regardless of whether acute aortic dissection is type A or B, medical therapy to control pain and hypertension is essential in all patients (Fukui, 2018). The European Cardiology Society recommends that patients with acute

aortic dissection should be managed in the intensive care setting. Morphine sulfate is recommended for pain relief. Invasive blood pressure monitoring via arterial line. Treatment is directed toward reducing aortic wall stress by reducing systolic blood pressure and the force of left ventricular ejection (Patel, 2008). Beta blockers have the desired effect of reducing blood pressure and heart rate to the normal range. These medications also protect the myocardium against ischemia. For most patients, systolic blood pressure should be controlled between 100 and 120 mmHg with a heart rate of approximately 60 bpm. Otherwise, vasodilators such as calcium channel blockers (nicardipine or diltiazem) or nitro-glycerine are useful in reducing wall stress with control of heart rate and blood pressure (Fukui, 2018). Esmolol is a particularly useful β-blocker because it has a short pharmacologic half-life and can be rapidly titrated. Esmolol can be administered as an initial bolus of 5 to 25 mg intravenously, followed by a continuous infusion of 25 to 300 μg/kg per minute. In patients with β-blocker contraindications, heart rate control should be gained with titration of nondihydropyridine calcium channel blockers such as verapamil or diltiazem. Metoprolol, a cardio selective β-blocker, may be advantageous in patients with reactive airway disease who are sensitive to β-adrenergic antagonists. Metoprolol is administered at a dose of 5 to 15 mg intravenously every 4 to 6 hours. If the systolic blood pressure remains greater than 120 mm Hg with adequate heart rate control, then vasodilators (e.g., nitroprusside at a dosage of 0.5 to 2.0 μg/kg per minute or nicardipine at a dose of 1 to 15 mg/hour) (Kaplan, 2017). In this case, the patient was given an oral -blocker along with ramipril and ivabradine (Hyperpolarization-activated Cyclic Nucleotide-gated channel blocker) which gave good results.

Table 2: Classification of Acute Aortic Dissection

| DeBakey Classifications | |
|---|---|
| Type I | The entire aorta is involved (ascending, arch, and descending) |
| Type II | Confined to the ascending aorta |
| Type III | Intimal tear originating in the descending aorta with either distal or retrograde extension |
| Type IIIA | Intimal tear originating in the descending aorta with extension distally to the diaphragm or proximally into the aortic arch |
| Type IIIB | Intimal tear originating in the descending aorta with extension below the diaphragm or proximally into the aortic arch. |
| Stanford classifications | |
| Type A | Involvement of the ascending aorta and/or aortic arch regardless of the site of origin or distal extent |
| Type B | Confined to the descending aorta distal to the origin of the left subclavian artery |

In general, the anaesthetic management of type A aortic dissection resembles the management of ascending aortic aneurysms that require DHCA. Large bore intravenous catheters are essential for intravenous medications and rapid volume expansion. A radial arterial catheter for invasive blood pressure monitoring is preferred over a femoral artery catheter to allow for CPB cannulation, depending on surgeon preference. If a pulse deficit is detected, the site for arterial pressure monitoring should be chosen to best represent the central aortic pressure. A central venous or PAC to monitor CVP, pulmonary artery pressure, and cardiac output is useful. TEE insertion is performed after anaesthetic induction, and it can be used to verify the diagnosis. The induction of general anaesthesia in hemodynamically stable patients with aortic dissection should proceed in a cautious manner. The dose of intravenous antihypertensive drugs may need to be reduced at the time of anaesthetic induction to prevent severe hypotension when combined with anaesthetic drugs. The hypertensive response to endotracheal intubation, TEE probe insertion, and sternotomy should be anticipated and attenuated with narcotic analgesics (Kaplan, 2017).

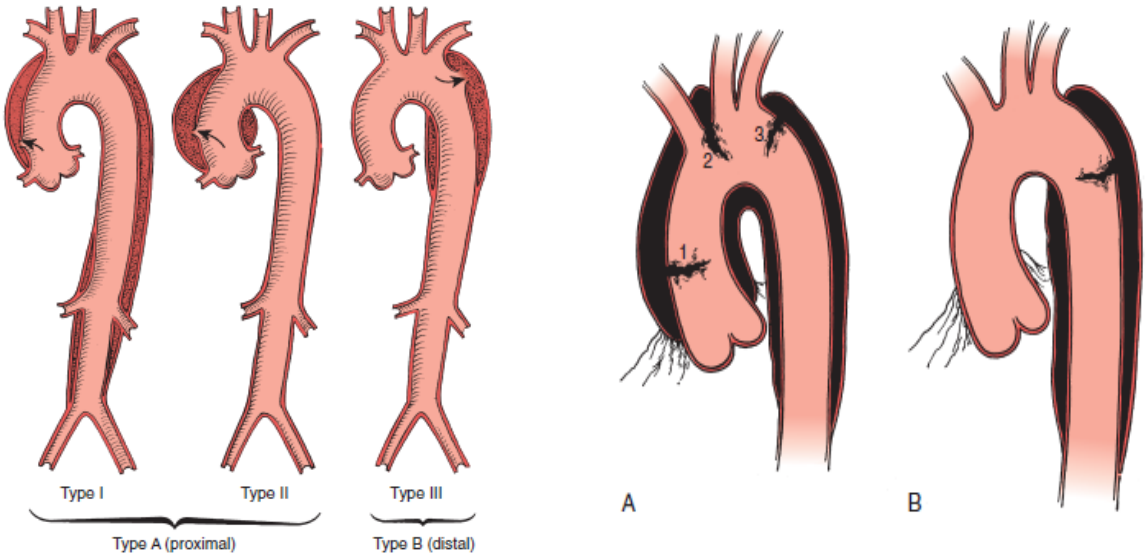


Figure 4: Debakey's classification of aortic dissection (left), Types I, II, and III. Stanford classification for aortic dissection (right) Types A and B. (from Prakash A. Patel MD, John G.T. Augustine, MD, PHASE, FAHA. Et.all, thoracic aorta: Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery. 2017; 23:865)

If disease involves both the aortic valve and the aortic root, the patient requires aortic root replacement and aortic valve intervention. If technically feasible, the aortic valve can be reimplanted with a modified David technique, which includes graft reconstruction of the aortic root with reimplantation of the coronary arteries. If not feasible, aortic root replacement with a composite valve-graft conduit is indicated (Bentall procedure). Repairing aortic aneurysms that extend into or involve the aortic arch requires CPB with DHCA with or without perfusion adjuncts. For ascending aortic aneurysms that involve only the proximal aortic arch. Ascending aorta with hemiarch reconstruction often is performed using DHCA with or without ACP/RCP to make the distal anastomosis feasible without cross-clamping ("open technique"). Although the average nasopharyngeal temperature for DHCA may be about 18°C, the optimal temperature for DHCA has not been established (Kaplan, 2018). The primary method for providing protection against cerebral injury is DHCA. A period of circulatory arrest for up to 30–40 minutes at a body temperature of 15–18_C is tolerated by most patients. More recently two techniques have been developed with the aim of reducing this cerebral morbidity on the basis that some flow is better than no flow. These are retrograde cerebral perfusion (RCP) and selective anterograde cerebral perfusion (SACP). The intention of these techniques is to ensure some oxygen delivery to the brain while normal (anterograde) flow is interrupted (Mackay, 2012). The use of NIRS is a non-invasive brain monitoring to see oxygen flow, detecting the possibility of cerebral injury. After completion of the proximal anastomosis and intercostal artery-to-graft anastomoses under DHCA, the aortic graft is cannulated, and bypass flow is re-established to the upper part of the body. During a period of hypothermic low bypass flow, the distal anastomoses are completed and then rewarming is initiated (Gropper, 2020). The surgical plan for this patient was in accordance with the statement above where in the anastomose connection DHCA was performed and using SACP to deliver oxygen to the brain, NIRS was also installed for monitoring blood oxygenation to the cerebri where the decrease in the NIRS value did not exceed 20% of the basal value.

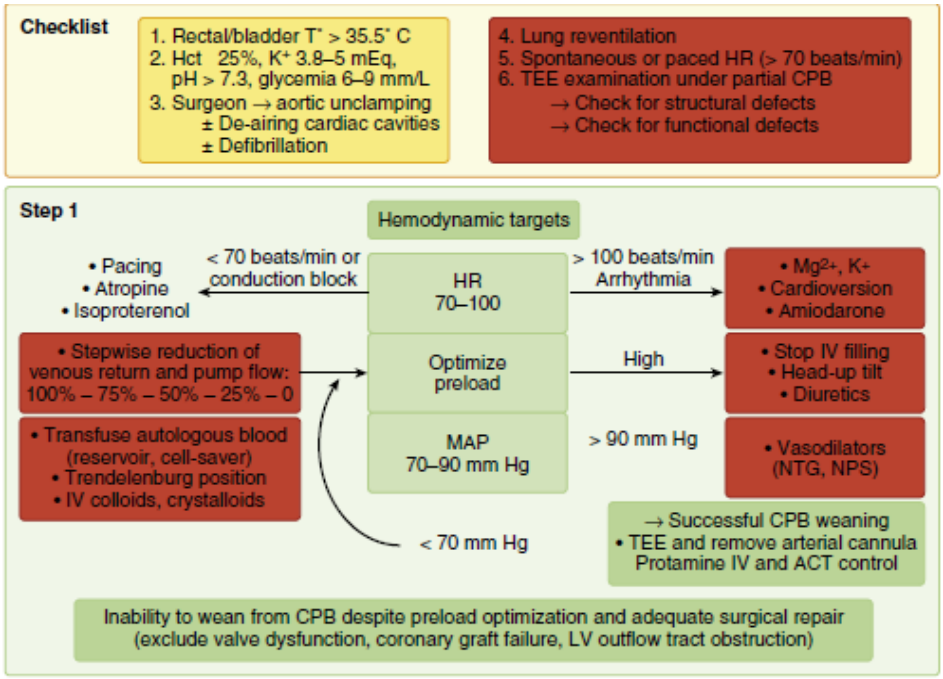


Figure 5: Cardiopulmonary bypass (CPB) release algorithm. From LickerM, Diaper J, et all. Clinical Review: management of weaning from cardiopulmonary bypass. Ann Card Anaesth, 2012; 15:206-223

Causes of death included aortic rupture, cardiac tamponade, myocardial ischemia from dissection, severe AR, stroke due to brachiocephalic dissection and malperfusion disorders including renal failure, bowel ischemia, and limb ischemia (kaplan,2017). In this case the patient had acute renal failure with a urea value of 108 and a creatinine of 2.24. In a study conducted by Hsiang in 2021 which studied the incidence of AKI in type A acute aortic dissection with a total of 696 patients, 376 patients (54%) developed AKI after surgery, from 376 patients 135 (35.9%) developed AKI. In addition, of the 320 patients without AKI, 34(10.6%) patients had worsening renal function and developed AKD. Overall, 169(24.6%) of the 696 patients had AKD after surgery for acute type A aortic dissection. Postoperatively in patients with AKI or AKD, creatinine values increased on the second and third days of treatment and decreased to baseline values on the seventh day of treatment (Hsiang, 2021). In this case, according to the theory above, where on the second day of treatment the creatinine value began to increase (Cr: 3,4 mmol/dl) and there was a decrease in the amount of urine per hour, then hemodialysis therapy was carried out for better results.

The use of an intracardiac pacemaker was carried out because after the process of releasing from the CPB machine the patient's pulse rate was bradycardia, according to the algorithm we applied for the release from the CPB machine (pictured) a pacemaker was installed, and it gave better results for the patient.

## 6. Conclusion

Acute aortic dissection is an emergency condition that requires immediate medical and surgical treatment. Management of pain and hypertension should be prioritized to reduce the extent of the dissection and its complications. To establish the best diagnosis with contrast and non-contrast CT can determine the classification of dissection. Anesthesia management During induction and intubation, adequate analgesia should be avoided to prevent an increase in pulse rate and blood pressure. DHCA is performed to reduce bleeding in the operative field when the anastomosis is connected with the proximal aorta. The use of SACP and NIRS for cerebral oxygenation and monitoring prevents injury to the brain. AKI is one of the complications of acute aortic dissection that often occurs and can worsen after surgery, so hemodialysis is needed to restore kidney function.

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# Perioperative Management of Patient with Coronary Artery Disease 3 Vessels Disease, Chronic Total Occlusion in Left Anterior Descending and Right Coronary Artery, History of Hypertension, Extensive Myocardial Infarction and Low Ejection Fraction: A Case Report

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**Abstract**
Introduction: Achieving a satisfactory hemodynamic performance is the primary objective in the management of cardiac surgery patient. Optimal cardiac function ensures adequate perfusion and oxygenation of other organ systems (in particular vital organs) and improves the chances for an uneventful recovery from surgery. Case: A 46 year old male diagnosed with Coronary Artery Disease 3 Vessel Disease (CAD 3 VD), CTO in LAD and RCA, history of hypertension, extensive myocard infarction with hypertrophy as well as global function impairment of the left ventricle and low ejection fraction, who underwent Coronary Artery Bypass Graft (CABG). Supportive medications, such as dobutamine and nitroglycerin (NTG) were initiated and maintained intraoperatively, especially after anesthetic induction due to hemodynamic alterations. Patient was able to wean from cardiopulmonary bypass (CPB) machine and transferred to the ICU postoperatively.

**Keywords:** CAD 3VD, Low Ejection Fraction, Myocard Infarct, Perioperative Management

## 1. Introduction

Once a patient is considered a candidate for cardiac surgery, a comprehensive evaluation of the patient's overall medical condition and comorbidities is essential. This includes a detailed history and physical examination, which may identify cardiac and noncardiac problems that might need to be addressed perioperatively to minimize postoperative morbidity (Robert M.B, 2011).

Patients undergoing cardiac surgical procedures are extensively monitored. Hemodynamic alterations and myocardial ischemia that occurs during the induction of anesthesia, in the prebypass period, during CPB, and

following resumption of cardiac activity can have significant adverse effects on myocardial function and recovery. It should be noted that even though both hypertension and tachycardia can increase myocardial oxygen demand, an increase in heart rate results in more myocardial ischemia at an equivalent increase in oxygen demand. Standard monitoring in the operating room consists of a five-lead ECG system, central venous catheter (CVC), a radial arterial line, pulse oximetry, an end-tidal $CO_2$ measurement, a Swan-Ganz pulmonary artery (PA) catheter, cerebral oximetry, and a urinary Foley catheter to measure urine output, core body temperature and intraoperative transesophageal echocardiography (TEE) should be obtained (Loeb HS, et al., 1978).

Anesthetic management must be individualized, taking into consideration the patient's age, comorbidities, the nature and extent of coronary or valvular disease, the degree of left ventricular dysfunction, and plans for early extubation. These factors will determine which medications should be selected to avoid myocardial depression, tachycardia, or bradycardia, or to counteract changes in vasomotor tone. Generally, a balanced anesthetic technique using a combination of narcotics and potent inhalational agents is used for all open-heart surgery to minimize myocardial depression (Robert M.B, 2011).

## 2. Case

A 46 years old male diagnosed with CAD 3 VD, was admitted electively to the Hasan Sadikin general hospital and scheduled for coronary artery bypass graft (CABG). The patient experienced shortness of breath and chest discomfort with anginal pain. He had a past history of hypertension for over 10 years. He was diagnosed with CAD since 2021 and was on medical therapies NTG retard 2x2,5 mg, ramipril 1x10 mg, bisoprolol 1x2,5 mg, atorvastatin 1x20 mg, clopidogrel 1x75 mg. He was a former smoker. He weighs 65 kg with the height of 170 cm. Physical examination and evaluation at the time of admission did not reveal any other significant findings. Coronary angiography showed chronic total occlusion (CTO) in mid left anterior descending (LAD), CTO in distal right coronary artery (RCA) and 80-90% stenosis in distal left circumflex artery (LCX). Echocardiography revealed failing left ventricular systolic function with an ejection fraction (EF) of 27% and myocard perfusion scan showed extensive myocard infarction (from apical to basal) with hypertrophy as well as global function impairment of the left ventricle. His preoperative blood examination was unremarkable. His renal and liver functions were normal, and the chest radiograph showed cardiomegaly.

In the preparation room, five-lead ECG was placed and weinserted a 16 G peripheral venous catheter. Arterial line was conducted through the left radial artery to provide invasive blood pressure monitoring. The patient's vital signs upon arrival in the operating room were as follows: BP 170/100 mmHg, HR 78x/min, RR 16x/min and oxygen saturation 100%. Anesthesia induction was commenced with 4mcg/kg fentanyl, 0.05 mg/kg midazolam, propofol 20mg, 1.2 mg/kg rocuronium, 1.5 mg/kg lidocaine. After reaching suitable muscle relaxation, the patient was intubated with endotracheal tube number 8. We inserted a left femoral artery cannulation for intra-aortic ballon pump (IABP) access, central venous catheter (CVC) via the left subclavian vein and Swan-Ganz catheter via the right internal jugular vein. Transesophageal echocardiography (TEE) probe was also established. Anesthesia was maintained with oxygen-air mixture and sevoflurane. Prior to incision, fentanyl 100 mcg and rocuronium 20 mg were administered and dobutamine (3- 5mcg/kg/min) and NTG (0.1mcg/kg/min) were initiated through central venous catheter, due to an episodes of hemodynamic alterations and continued intraoperatively, until the end of surgery.

The patient underwent CABG 3 VD with the aid of cardiopulmonary bypass (CPB) where the left internal thoracic artery was anastomosed to LAD, saphenous venous grafts were anastomosed to OM1, and posterior diagonal artery (PDA). Myocardial protection was achieved using cold cardioplegia. CPB time was 132 minutes and aortic cross clamp time was 92 minutes. The total duration of surgery was about 5 hours 15 minutes, with total blood loss 1200 ml, urine output 870 ml, and 3 packs of packed red cell (PRC) were transfused intraoperatively. He was transferred to the ICU with a continuous infusion of dobutamine (10mcg/kg/min), nor epinephrine (0.05mcg/kg/min) and NTG (0.1mcg/kg/min). Patient was gradually weaned off ventilator and extubated on the 1$^{st}$ post-operative day. He transferred to ward on 2$^{nd}$ post-operative day.

## 3. Discussion

Myocardial ischemia occurs when the oxygen supply to the heart is insufficient to meet metabolic needs. This mismatch can result from a decrease in oxygen supply, a rise in demand, or both. The most common underlying cause of myocardial ischemia is obstruction of coronary arteries by atherosclerosis. In the presence of such obstruction, transient ischemic episodes are usually precipitated by an increase in oxygen demand as a result of physical exertion. Ventricular hypertrophy due to hypertension can predispose the myocardium to ischemia because of impaired penetration of blood flow from epicardial coronary arteries to the endocardium (Thomas HL, 2013).

The achievement of satisfactory hemodynamic performance is the primary objective of postoperative cardiac surgical management. Optimal cardiac function ensures adequate perfusion and oxygenation of other organ systems and improves the chances of an uneventful recovery from surgery. Even brief periods of cardiac dysfunction can lead to impairment of organ system function, leading to potentially life-threatening complications. The important concepts of perioperative cardiac care are those of cardiac output, tissue oxygenation, and the ratio of myocardial oxygen supply and demand (Robert M.B, 2011).

Contractility is the intrinsic strength of myocardial contraction at constant preload and afterload. However, it can be improved by increasing preload or heart rate, decreasing the afterload, or using inotropic medications. Contractility generally reflects systolic function as assessed by the ejection fraction, but is only indirectly related to the cardiac output. Conversely, a low cardiac output does not necessarily imply that ventricular function is impaired. It may be noted with slow heart rates, with hypovolemia, and with a small, hypertrophied ventricle. Nonetheless, the state of contractility is usually inferred from an analysis of the cardiac output and filling pressures, based upon which steps can be taken to optimize hemodynamic performance. In cardiac surgery patients, the cardiac output is usually obtained by thermodilution technology using a Swan-Ganz catheter and bedside computer.

**Myocardial O2 demand (mvO2)** is influenced by factors similar to those that determine the cardiac output (afterload, preload, heart rate, and contractility). Reducing afterload will generally improve cardiac output with a decrease in $mvO_2$, whereas an increase in any of the other three factors will improve cardiac output at the expense of an increase in $mvO_2$. Preoperative management of the patient with ischemic heart disease is primarily directed towards minimizing $O_2$ demand. **Myocardial O2 supply** is determined by coronary blood flow, the duration of diastole, the coronary perfusion pressure, the Hb level, and the arterial oxygen saturation. When complete revascularization has been achieved, postoperative management is directed towards optimizing factors that improve $O_2$ supply and, to a lesser degree, minimize an increase in $O_2$ demand.

A low cardiac output state in patients with a history of CAD may result from abnormal preload, contractility, heart rate, or afterload. It may also be noted in patients with satisfactory systolic function but marked left ventricular hypertrophy and diastolic dysfunction. Management therapy : 1. **Ensure satisfactory oxygenation and ventilation** ; 2. **Treat ischemia or coronary spasm** if suspected to be present. Myocardial ischemia often responds to intravenous nitroglycerin (NTG) but may require further investigation if it persists; 3. **Optimize preload** by raising filling pressure with volume infusion; 4. **Stabilize the Heart rate and Rhythm**; 5. **Improve contractility** with inotropic agents. This should be based on an understanding of the α, β or nonadrenergic hemodynamic effects of vasoactive medications and their anticipated effects on preload, afterload, heart rate, and contractility; 6. **Reduce afterload**; 7. **Maintain blood pressure** (Robert M.B, 2011).

If the cardiac output remains low despite pharmacologic support, physiologic support with an **intra-aortic balloon pump (IABP)** should be strongly considered. If the patient cannot be weaned from bypass or has hemodynamic evidence of severe ventricular dysfunction despite maximal medical therapy and the IABP, use of a circulatory assist device should be considered.

The main perioperative concern in our patient was his past history of hypertension for over 10 years, CAD (CTO in LAD and RCA, 89-90% stenosis in LCX), low EF (27%), extensive myocard infarction (from apical to basal)

with hypertrophy as well as global function impairment of the left ventricle. Providing safe anesthesia to these patient who are posted for CABG has always been challenging. Hemodynamic alterations and myocardial ischemia that occur during the induction of anesthesia, in the prebypass period, during CPB, and following resumption of cardiac activity can have significant adverse effects on myocardial function and recovery. It should be noted that even though both hypertension and tachycardia can increase myocardial oxygen demand, an increase in heart rate results in more myocardial ischemia at an equivalent increase in oxygen demand (Robert M.B, 2011).

We believe that commencement of Dobutamine (3-5mcg/kg/min) and NTG (0.1mcg/kg/min) after anesthesia induction and continued intraoperatively until the end of surgery might have prevented some of the possible adverse outcome in our patient. **Dobutamine is predominantly β-1-adrenergic agent**, making it a potent inotrope useful in stimulating the rate and the force of cardiac contraction with less arrhythmogenic potential. It has been utilized in the treatment of acute myocardial and congestive heart failure as it causes marked improvement in cardiac outuput and stroke volume without increase in heart rate. **Nitroglycerin is a direct vasodilator**, producing greater venous than arterial dilatation, this effect usually reduces Mvo2 and increases diastolic coronary blood flow and relieves coronary spasm. It provides more flow to ischemic myocardium and increases endocardial-to-epicardial flow ratio and improved inotropy of myocardium (Westfall TC & Westfall DP, 2011) (Nirvik & John, 2019).

## 4. Conclusion

Although excellence in pre and postoperative care can often make the difference between an uneventful and a complicated recovery, the care provided in the operating room usually has the most significant impact on patient outcome. Performing a technically proficient, complete, and expeditious operation is only one component of this phase. Refinements in anesthetic techniques and monitoring, cardiopulmonary bypass (CPB), and myocardial protection have enabled surgeons to operate successfully on extremely ill patients with far advanced cardiac disease and multiple comorbidities (Robert M.B, 2011).

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# Mobile Phones as a Source of Nosocomial Infection in the Radiology Department of a Teaching Hospital

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**Abstract**
Background: Mobile phones were first introduced in the United Kingdom and have become an important means of communication among doctors, other healthcare workers, patients and the general public. Objectives: This study was aimed at establishing that mobile phones are sources of nosocomial infections in the radiology department of our teaching hospital and also to determine the pathogens that are responsible for these infections. Methods: This was a prospective study that involved collection of swab samples from radiographers' mobile phones. Three different samples were collected from each mobile phone. Thirty (30) mobile phones were used for this investigation and ninety (90) samples were totally collected. Samples were collected on arrival of the radiographer to the department, after handling patients and after washing hands. Samples collected were sent to the microbiology department for culture analysis. Descriptive data analysis was performed and results presented in frequency tables. Results: On arrival at the department, samples collected revealed that 22 (73.3%) of the phones were contaminated before commencing work for the day while 8 (26.7%) were not contaminated. With direct patient contact, 27 (93.3%) were contaminated and after washing hands it was observed that 16 (53.3%) of the mobile phones were contaminated. The major cause of contamination was staphylococcus aureus especially noted in swabs obtained after direct patient contact. Pseudomonas aeruginosa and Escherichia coli were also identified as contaminants of the phones. Conclusion: Radiographers' mobile phones harbour bacteria and could act as a source of nosocomial infection in the radiology department.

**Keywords:** Mobile, Phone, Nosocomial, Infection, Radiographers, Radiology

## 1. Introduction

Mobile phones also known as global system for telecommunications (GSM) were introduced in Europe in 1982 and have helped to improve the communication network both in Europe and the entire universe. Mobile phones are readily available and affordable that people of all works of life use them for business connections and other purposes. They come in various sizes, can be easily handled, carried around and have helped in improving the

social and economic lives of individuals thereby making them indispensable accessories in modern times (Sowah,2008).
In the hospital, doctors and other health workers use them to effectively communicate among themselves and with their patients. There are infections associated with the hospital which can be contacted by both health workers and patients who visit the hospitals. These hospital infections are prevalent (Brady, et al, 2007), also known as nosocomial infections and can be transmitted from the patient to the health care provider or vice versa. There is a rise in this hospital acquired infections globally and this has been a source of worry (Palmore, et al, 2010; Allegranzi and Pittet, 2009; Razine et al, 2012). Previous study has shown that one third of all nosocomial infections may be preventable and are caused by organisms acquired within the hospital [Hugh, 1998]. Many of these organisms are becoming increasingly resistant to standard antimicrobial agents (Borkow and Monk, 2012). Hands of health care workers may play an important role in transmission of HAI. Mobile phones are repeatedly used by health workers while on duty and may not be cleaned thereby making them act as reservoirs as well as vehicles for transmission of nosocomial infection (Brady et al, 2007; Nyasulu et al, 2012; Datta et al, 2009). Handling of a single mobile phone between HCWs directly facilitates the spread of potential pathogenic bacteria to the community (Trivedi et al, 2011). In the past studies have demonstrated that health care equipment, (Shcabrun and Chip, 2006; Eze et al, 2012) and healthcare environments, (Otter et al, 2011; Tagoe et al, 2011) are a significant source of hospital acquired infections.

There are no existing guidelines or rules for the use and cleaning of mobile phones in the radiology department of our hospital. The radiographers move about with their mobile phones anywhere they go to within the radiology department and even the entire hospital and sometimes make and/or answer calls when attending to patients. With this behaviour, there is every likelihood that such phones may get contaminated. From observation, the use of disinfectant and hand sanitizers is not a common practice within the radiology department of our teaching hospital. It is noteworthy to state that some radiographers do wear gloves, but they have been seen to wear the same pair throughout the day and they answer their mobile phones without removing and replacing them. The potential role of mobile phones as vectors of nosocomial infection has been studied previously (Chawl et al, 2009; Akinyemi et al, 2009; Ulger et al, 2009; Bhatt et al, 2011). However, to the best of our knowledge, no formal study has previously been conducted in our institution. This study is aimed at establishing that mobile phones are sources of nosocomial infection in the radiology department of our teaching hospital and also determining the pathogens that are responsible for this infection.

## 2. Materials and methods

This was a prospective study that involved collection of swab samples from radiographers' mobile phones. Ethical approval to conduct this study was obtained from the faculty of health sciences and technology ethical committee, Nnamdi Azikiwe University, Nnewi campus. Three different samples were collected from each mobile phone. Thirty (30) mobile phones were used for this investigation and ninety (90) samples in - total were collected. The radiographers had no prior information about this study to avoid the bias that may result from such information. On arrival at the department, the radiographers' mobile phones were swabbed and samples collected to check for pathogens on the mobile phones from the radiographers' home. After this, they were allowed to work for three hours. The radiographers were then asked to touch their phones after having direct contact with the patients. Another swab sample was then collected from the phones. After this, the mobile phones were disinfected with alcohol based sanitizer to make sure that there was no pathogen retained on the phones. To further ensure that the phones were not contaminated, swab samples were taken after disinfection. The radiographers were then asked to properly wash their hands and then touch the phones. All collected samples were then sent to the microbiology department of the hospital for culture and isolation of microbes. The culture media (MacConkey and Blood agar) were prepared according to the manufacturer's instructions. The samples were prepared and put into the autoclave and heated for 15 minutes at a temperature of 121ºC to achieve sterilization of the culture medium. The medium was then poured into petri dishes. After allowing the medium to cool to 47 ºC, the culture plates were covered and allowed to set before inoculation of samples. After inoculation, culture plates were placed in an incubator and incubated for 24 hours at a temperature of 37 ºC in order to allow for growth of microorganisms. After incubation the culture plates were examined macroscopically under a bright light in order to identify the isolated microorganisms based on their colonial characteristics.

Data collected was analyzed descriptively and results presented in frequency tables and percentages.

## 3. Results

The result of this study shows that 30 swab samples were collected when the radiographers arrived to the hospital, 30 samples were collected after the radiographer had direct contact with some patients and another 30 samples after washing hands giving a total of 90 samples.

Table 2 depicts the type of bacteria isolated or detected on the mobile phones. Three bacteria were implicated for contaminating radiographers' mobile phones. They are staphylococcus aureus, pseudomonas aeruginosa and Escherichia coli. On arrival to the department, 13 (14.4%) were contaminated by staphylococcus aureus, 4 (4.4%) were contaminated by Pseudomonas aeruginosa, while Escherichia coli was responsible for 5 (5.6%). After direct contact with the patients, 21 (23.3%) of the mobile phones were contaminated with Staphylococcus aureus, Pseudomonas aeruginosa caused 2 (2.2%) of the contamination while 4 (4.4%) were due to Escherichia coli. After washing hands, 13 (14.4%) of the contamination was as a result of staphylococcus aureus, 1 (1.1%) was due to pseudomonas aeruginosa while 2 (2.2%) were due to Escherichia coli. Staphylococcus aureus was the major cause of infection and contributed to a total of 47 (52.2%), followed by Escherichia coli which was responsible for 11 (12.2%) of the infection. Pseudomonas aerginosa contributed to 7 (7.7%) of the infection.

Table 1: Presence of pathogens on the mobile phones of Radiographers in the radiology department

| Samples | On arrival | After direct patient contact | After hand washing | Total |
|---|---|---|---|---|
| With growth | 22 (73.3%) | 27 (93.3%) | 16 (53.3%) | 65 (72.2%) |
| Without growth | 8 (26.7%) | 3 (6.7%) | 14 (46.7%) | 25 (27.8%) |
| Total | 30 | 30 | 30 | 90 (100%) |

Table 1 shows the presence of pathogens on radiographers' mobile phones. A total of 65 (72.2%) of the mobile phones were contaminated while 25 (27.8%) were free of the pathogens.

Table 2: Bacteria detected from the mobile phones

| Bacteria | On arrival | After direct contact with patients | After washing hands | Total |
|---|---|---|---|---|
| Staphylococcus Aureus | 13 (14.4%) | 21 (23.3%) | 13 (14.4%) | 47 (52.2%) |
| Pseudomonas Aeruginosa | 4 (4.4%) | 2 (2.2%) | 1 (1.1%) | 7 (7.7%) |
| Escherichia Coli | 5 (5.6%) | 4 (4.4%) | 2 (2.2%) | 11 (12.2%) |

Table 2 depicts the type of bacteria isolated or detected on the mobile phones. Three bacteria were implicated for contaminating radiographers' mobile phones. Staphylococcus aureus were responsible for most of the contamination (52.2%) while pseudomonas aeruginosa caused the least contamination of the phones (7.7%).

## 4. Discussion

This study investigated mobile phones as a source of nosocomial infection among practicing radiographers. The present study tested for the presence of bacteria on radiographers' mobile phones. Findings revealed that these phones harboured nosocomial pathogens (bacteria). Some of these pathogens were detected on arrival to the department before handling of patients by the radiographers. The implication of this is that radiographers could carry and spread infection in the hospitals from their homes. Majority of the bacteria were detected after direct contact with the patients. This observation may be because the radiographers make and receive calls while working in the department and as the number of patients handled increases there is also the possibility of increased rate of contamination of their phones because some of the patients may also transmit infection to the workers.

This study revealed the presence of bacteria even after hand washing in some of the mobile phones. This indicates that the mobile phones can be contaminated by the hand as reported by Vaibhavi et, al, (2015). It may be because their hands were not properly washed. The department does not regularly provide disinfectants or soap and because of this the radiographers who had not provided such for themselves washed their hands with ordinary water and this may have been the reason for detecting some pathogens even after hand washing.

A total of 72.2% of mobiles phones were contaminated in our study. (Grimma et al, 2014) reported a total of 71.2% in their study and this could be said to be the same with our findings. This finding is also in tandem with other previous studies (Nyasulu et al, 2012; Chawl et al, 2009). Some other studies reported values that are higher than our value (Ulger et al, 2009; Famurewa and David, 2009; Karabay et al, 2009). Lower bacteria contamination was reported by Sepheri et al, (2009) and Arora et al, (2009). This variation noted may be as a result of the participants studied. While most of the studies considered the mobile phones of healthcare workers generally, we considered only radiographers in the radiology department. Conducting this study on radiographers alone in the radiology department may have also affected the types of bacteria detected. The environment and equipment used can also be a contributing factor (Shcabrun and Chip, 2006). A previous study by Grimma et al, (2014) has demonstrated that the adherence to infection prevention, pattern of mobile phone use, mobile phone keeping habits and personal behaviour like nose picking may also affect the number of contaminated mobile phones.

The most predominant bacteria isolate in this study was staphylococcus aureus constituting about 72.3% of the total bacterial isolate. This is in agreement with other studies which also recorded staphylococcus as their most common isolate (Sadat et al, 2010; Raghavendra et, 2014; Tambleka et al, 2008). This finding however does not agree with other previous studies which stated that staphylococcus aureus was their second predominant isolate (Chawl et al, 2009; Grimma et al, 2014; Arora et al, 2009). Staphylococcus aureus can resist dryness and multiply rapidly in warm environments like the mobile phones.

Pseudomonas aeruginosa (11%) and Escherichia coli 11(17%) were also found on these mobile devices in concordance to a similar work done by Nwankwo et al, (2014). Escherichia coli are harmless but most times can cause diarrhea, cramps, vomiting (WHO 2002).

## 5. Conclusion

1. Nosocomial bacteria were found on the mobile phones of radiographers.
2. Radiographers' mobile phones are a source of nosocomial infection. Radiographers should properly wash their hands and their mobile phones should be disinfected regularly.
3. Most of the contamination was recorded after direct contact with patients. Staphylococcus aureus, pseudomonas aeruginosa, and Escherichia coli were the bacteria responsible for the contamination of the mobile phones.

## 6. Recommendations

Based on the results of this study, we recommend the following;

1. Proper hand hygiene should be practiced by scrubbing with soap and water or antiseptics after attending to a patient and before contact with mobile phone.
2. Radiographers should also imbibe the culture of proper hand washing with disinfectants at the close of work.
3. It is also necessary that radiographers should wash their hands after going to the rest room, after shaking hands, after lunch, after using a handrail, after traveling from one location to another, after using the phone etc.
4. There should be a guideline on how to use mobile phones in the department. Such guideline may include restricting the radiographers from handling their phones when they are on duty.
5. Radiographers' mobile phones should be covered. This cover could be such that it can be removed and cleaned after work.

## 7. Limitations of study

1. This study considered only the presence of bacterial pathogens on the mobile phones. The degree of bacterial contamination was not considered in this study.
2. The radiographers were instructed to touch their phones after working for three hours. This may have affected the rate of contamination of the mobile phones.
3. The radiographers were asked to touch their phones to ensure that there was contact with the phone before taking the swab. The number of times contact was made with the phones was not taken into consideration and therefore does not represent daily habits during a regular working day.

**Conflict of interest**.

The authors have no conflict of interest.

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# Depression and Its Associated Factors among Diabetes Mellitus Patients Attending the primary health care centers in United Arab Emirates: A Cross-Sectional Study

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**Abstract**
Diabetes mellitus (DM) and depression are major global public health problems. Depression negatively affects the course of DM through hormonal, neuronal, or immune system changes that directly affect the body's ability to produce or use insulin. The coexistence of depression with DM also results in poor glycemic control by causing poor self-care behaviors such as lack of physical activity. The coexistence of depression with DM also results in poor glycemic control. The study aimed to assessing depression and Its associated Factors among diabetes mellitus patients attending the primary health care centers in United Arab Emirates. This study was conducted on 463 diabetic patients attended the primary health care centers during 8th may to 26th may, 2021. Nine primary health care centers were selected according to the accessibility. The Patient Health Questionnaire-9 (PHQ-9) was selected of the actual 9 criteria upon which the diagnosis of DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition) depressive disorders is based. Our study showed that there was non-significant difference in depression Levels between non-smokers and smokers, there was non-significant difference in depression Levels and education levels, there was significant difference in depression Levels and marital status, non-significant difference in depression Levels and nationality, non-significant difference in depression Levels and type of diabetes. Conclusion based on this study the prevalence of depression among female diabetes mellitus was high. From this study we concluded that depression levels: non-depressed, mild depression, moderate depression, moderately and severe depression are high in married participants comparing with single, divorced and widow participants

**Keywords:** Diabetes Mellitus, Depression, Immune System, Glycemic Control

## 1. Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder caused by the body's inability to utilize insulin.DM Type 1 and DM type 2 diabetes mellitus often start in childhood and adulthood, respectively Beck et al. (2018). Although genetics is thought to be the source of DM type 1, environmental factors such as viruses may have a role in the disease's onset. DM Type 2 is caused by a variety of variables, including lifestyle choices and genetics. Patients who have recently been diagnosed with diabetes face a significant amount of stress in their lives. Many of them go through the grieving process, which includes denial, anger, despair, and acceptance Sridhar and Madhu (2002). Depressive disorder is one of the most common and debilitating psychological disorders in diabetics Waitzfelder et al. (2010) . Depression is a prevalent comorbid illness in diabetic patients, according to studies Ahmad et al. (2018). The prevalence of depression in diabetic patients ranges from 8 to 15%, compared to just 3 to 4% in the general population Marcus at al. (2012). Depression is linked to the burden of complications, financial stress, poor overall health status, diabetes knowledge, and poor glucose control in people with diabetes mellitus. It also affects diabetes prognosis, increases noncompliance with medical therapy, lowers quality of life, delays diabetes recovery, and increases mortality Birhanu et al. (2016). Hospitalizations and diabetes-related comorbidities are both linked to depression Dejene at al. (2014). The study's findings will aid in the development of more effective strategies for the management of comorbid diabetes and depression. The survey's findings will also be utilized as a starting point for other academics who want to perform a large-scale study in United Arab Emirates. This study will also assist anyone who is interested in learning more about the link between depression and diabetes. This study's findings may aid healthcare providers in detecting, diagnosing, and treating depression in diabetic patients at an early stage.

## 2. Method

This study was conducted on 463 diabetic patients attended the primary health care centers during in Dubai, United Arab Emirates. the primary health care centers are fully organized and launched to give service for Patients with DM, the primary health care centers have also given the psychiatric service at the outpatient level.

### *2.1 Study design and period*

This was a cross-sectional study conducted from 8$^{th}$ may to 26$^{th}$ may, 2021.

### *2.2 Inclusion and exclusion criteria*

All diabetic patients aged≥15 years and communicating independently were included. Those who were taking antidepressant drugs for their depressive symptoms were excluded because antidepressant drugs can mask depression signs and symptoms. DM patients who were newly diagnosed at the time of data collection were not part of the study. Finally, DM patients who were seriously ill were excluded from this study.

### *2.3 Study variables*

The dependent variable was depression. Independent variables included sociodemographic factors (age, sex, marital status, ethnicity, educational and occupational status), clinical factors (type of DM, FBG level, duration of DM, type of treatment), and psychosocial factors (social support).

### *2.4 Ethical considerations*

Ethical approval was obtained from the Research Committee, of the research department in Dubai Medical College in Dubai, United Arab Emirates. Consent form was obtained from each study participant, where they were informed about the aim of the study and its nature and their right to interrupt the interview at any time. Patients' confidentiality and privacy were preserved at all levels of the study.

*2.5 Method of data collection and tools*

Data were collected by face-to-face interviews using patient health questionnaire-9 (PHQ-9). The questionnaire of socio-demographic and clinical related information was assessed by using questionnaires adapted from reviewing similar related articles and the patients' medical record. Gelaye et al, (2013)

*2.6 Data Collection*

Before the data collection, the students were trained on how to interview the patients, how to fill the questionnaire and also the translation of English to Arabic was standardized and agreed among the whole group members. A role play was practiced for a whole day duration. A pilot study was done on 30 patients before the actual data collection. The pilot study data collected was revised by the research members and considered to be valuable. The data was collected over a period of 3 weeks (8th May - 26th May) by 19 students from DMC. Each student conducted 25 interview questionnaires which resulted in a sample size of 475. Questionnaire was filled by a one-to-one interview with the patient and some of the information was taken from the patient medical records and the SAM system (such as HbA1c, medications and the BMI).

Table 1: Nine symptoms depression check list

| Over the last two weeks, how often have you been bothered by any of the following? | Not at all | Several days (6/14) | More than half the days (8/14) | Nearly everyday |
|---|---|---|---|---|
| Little interest of pleasure in doing things | 0 | 1 | 2 | 3 |
| Feeling down, depressed, or hopeless | 0 | 1 | 2 | 3 |
| Trouble falling or staying asleep or sleeping too much | 0 | 1 | 2 | 3 |
| Feeling tired or having little energy | 0 | 1 | 2 | 3 |
| Poor appetite or overeating | 0 | 1 | 2 | 3 |
| Feeling bad about your self – or that you are a failure or have let yourself or your family down | 0 | 1 | 2 | 3 |
| Trouble concentration on things, such as reading the newspaper or watching television | 0 | 1 | 2 | 3 |
| Moving or speaking so slowly that other people could have noticed. Or the opposite being so fidgety or restless that you have been moving around a lot more than usual | 0 | 1 | 2 | 3 |
| Thoughts that you be better off dead or of hurting yourself in some way | 0 | 1 | 2 | 3 |
| 1-4 Minimal depression, 5-9 Mild depression, 10-14 Moderate depression, 15-19 Moderately severe depression, 20-27 Severe depression | | | | |

**3. Statistics and Data Analysis**

Data was analyzed using statistical package for social sciences (SPSS) version 20. Descriptive statistics were computed to explain the socio-demographic characteristics. Qualitative data was presented as frequencies and percentages. A chi-square test for independence was used to detect relations between depression and its risk factors. P value $\leq 0.05$ was considered statistically significant.

## 4. Results

Table 2: Socio-Demographic Characteristics of the Participants

| Age | Number | % |
|---|---|---|
| 15-29 years | 17 | 3.7 % |
| 30-39 years | 33 | 7.1 % |
| 40-49 years | 82 | 17.7 % |
| 50-59 years | 165 | 35.6 % |
| 60-69 years | 113 | 24.4 % |
| 70-79 years | 45 | 9.7 % |
| 80-89 years | 8 | 1.7 % |
| Gender | | |
| Male | 195 | 42.1 % |
| Female | 268 | 57.9 % |
| Nationality | | |
| Local | 393 | 84.9 % |
| Nonlocal | 70 | 15.1 % |
| Marital Status | | |
| Single | 27 | 5.8 % |
| Married | 370 | 79.9 % |
| Divorced | 19 | 4.1 % |
| Widow | 45 | 9.7 % |
| Education | | |
| Illiterate | 130 | 28.1 % |
| Read and write | 38 | 8.2 % |
| Primary | 59 | 12.7 % |
| Preparatory | 48 | 10.4 % |
| Secondary | 79 | 17.1 % |
| University and above | 109 | 23.5 % |
| Occupation | | |
| Not Working | 284 | 61.3 % |
| Working | 179 | 38.7 % |

Table 3: Relationship between Depression in Diabetics and Gender

| Depression Levels | Gender | | Total |
|---|---|---|---|
| | Male | Female | |
| Non-Depressed | 172 (88.7%) | 196 (73.1%) | 368 |
| Mild Depression | 12 (6.2%) | 32 (12%) | 44 |
| Moderate Depression | 7 (3.6%) | 20 (7.5%) | 27 |
| Moderately Severe Depression | 3 (1.5%) | 11 (4.1%) | 14 |
| Severe Depression | 0 | 9 (3.4%) | 9 |
| Total | 194 | 268 | 462 |
| $X^2$=19.125, P-value = 0.001 | | | |

Table 4: Relationship between Depression in Diabetics and Type of Diabetes

| Depression | Types of Diabetes | | Total |
|---|---|---|---|
| | Type 1 | Type 2 | |
| Non-Depressed | 30 (68.1%) | 338 (80.9%) | 368 |
| Mild Depression | 7 (15.9%) | 37 (8.9%) | 44 |

| | | | |
|---|---|---|---|
| Moderate Depression | 3 (6.8%) | 24 (5.7%) | 27 |
| Moderately Severe Depression | 4 (9.0%) | 10 (2.4%) | 14 |
| Severe Depression | 0 | 9 (2.2%) | 9 |
| Total | 44 | 418 | 462 |
| $X^2$=9.806, P-value = 0.044 | | | |

Table 5: Relationship between Depression in Diabetics and Level of Education

| Depression | Level of Education | | | | | | Total |
|---|---|---|---|---|---|---|---|
| | Illiterate | read and write | Primary | Prep | Secondary | university and above | |
| Non-Depressed | 98 (75.4%) | 29 (78.4%) | 46 (78%) | 38 (79.2%) | 62 (78.5%) | 95 87.1% | 368 |
| Mild Depression | 17 (13.1%) | 5 (13.5%) | 3 (5.1%) | 4 (8.3%) | 7 (8.9%) | 8 7.3% | 44 |
| Moderate Depression | 4 (3.1%) | 2 (5.4%) | 7 (11.9%) | 5 (10.4%) | 6 (7.6%) | 3 2.8% | 27 |
| Moderately Severe Depression | 5 (3.8%) | 1 (2.7%) | 2 (3.4%) | 0 | 3 (3.8%) | 3 2.8% | 14 |
| Severe Depression | 6 (4.6%) | 0 | 1 (1.7%) | 1 (2.0%) | 1 (1.3%) | 0 | 9 |
| Total | 130 | 37 | 59 | 48 | 79 | 109 | 462 |
| $X^2$: 24.381, P-value = 0.226 | | | | | | | |

Table 6: Relationship between Depression in Diabetics and Smoking

| Depression | Smoking | | | Total |
|---|---|---|---|---|
| | Non-Smoker | Ex-Smoker | Smoker | |
| Non-Depressed | 295 (78.6%) | 42 (87.5%) | 30 (78%) | 367 |
| Mild Depression | 42 (11.2%) | 1 (2%) | 1 (2.6%) | 44 |
| Moderate Depression | 21 (5.6%) | 2 (4.1%) | 4 (10%) | 27 |
| Moderately Severe Depression | 10 (2.6%) | 2 (4.1%) | 2 (5%) | 14 |
| Severe Depression | 7 (1.8%) | 1 (2%) | 1 (2.6%) | 9 |
| Total | 375 | 48 | 38 | 461 |
| $X^2$: 8.989, P-value =0.343 | | | | |

Table 7: Relationship between Depression in Diabetics and Marital Status

| Depression | Marital Status | | | | Total |
|---|---|---|---|---|---|
| | Single | Married | Divorced | Widow | |
| Non-Depressed | 21 (77.8%) | 306 (82.9%) | 12 (63.1%) | 28 (7.6%) | 368 |
| Mild Depression | 3 (11.1%) | 30 (8.1%) | 2 (10.5%) | 9 (20.5%) | 44 |
| Moderate Depression | 2 (7.4%) | 19 (5.1%) | 3 (15.8%) | 3 (11.1%) | 27 |
| Moderately Severe Depression | 1 (3.7%) | 8 (2.2%) | 1 (5.3%) | 3 (21.4%) | 14 |
| Severe Depression | 0 | 6 (1.6%) | 1 (5.3%) | 2 (22.2%) | 9 |
| Total | 27 | 369 | 19 | 45 | 460 |
| $x^2$: 34.173, P value = .005 | | | | | |

Table 8: Relationship between Depression in Diabetics and Nationality

| Depression | Nationality | | Total |
|---|---|---|---|
| | UAE Citizens | Non- UAE Citizens | |
| Non-Depressed | 303 (77.2%) | 65 (92.9%) | 368 |
| Mild Depression | 40 (10.2%) | 4 (5.7%) | 44 |
| Moderate Depression | 27 (6.9%) | 0 | 27 |
| Moderately Severe Depression | 13 (3.3%) | 1 (1.4%) | 14 |
| Severe Depression | 9 (2.3%) | 0 | 9 |
| Total | 392 | 70 | 462 |
| $X^2$=10.190, P-value = 0.037 | | | |

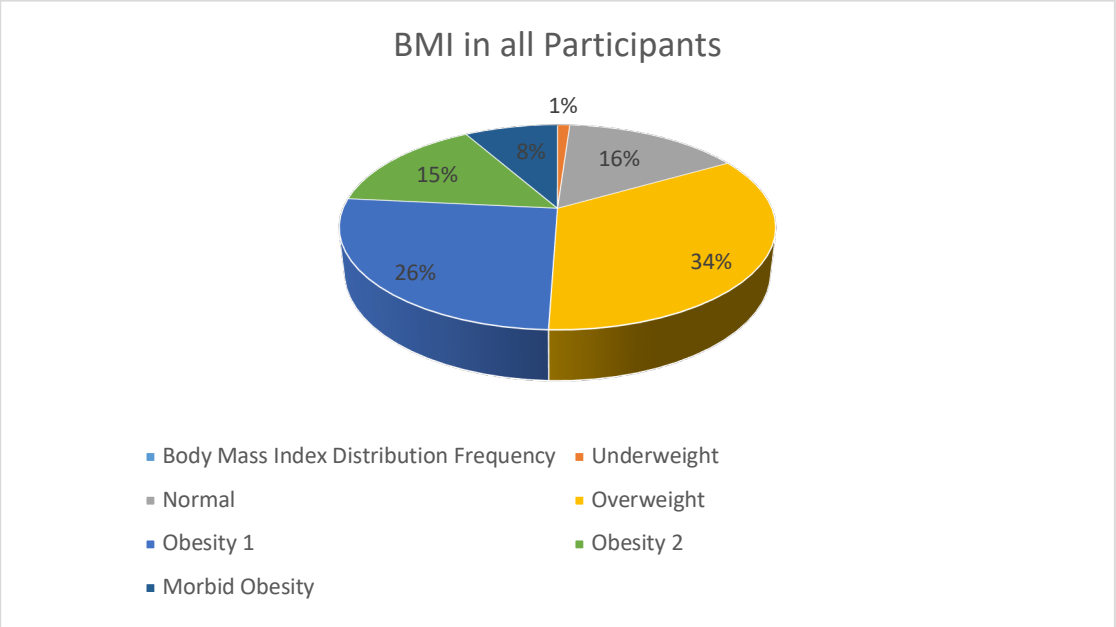


Figure 1: Body Mass Index Distribution

## 5. Discussion

Diabetes mellitus (DM) is a chronic, multifaceted, and progressive disease. According to the International Diabetes Federation (IDF), more than 35.4 million of people in the Middle East and North Africa region have diabetes and it is predicted that the number will rise to 72.1 million by 2040 Ogurtsova et al. (2017). Depression is a common comorbidity in individuals with diabetes, compared to those without diabetes affecting approximately 20% of all patients Ellouze et al. (2017). The study aimed to assessing depression and Its associated Factors among diabetes mellitus patients attending the primary health care centers in United Arab Emirates.

This study was conducted on 463 patients, males 95 (42.1 %) and females 268 (57.9 %), with different ages ranging from 15 to 89 years. 15- 29 years 17 (3.7 %), 30-39 years 33 (7.1), 40-49 years 82 (17.7 %), 50-59 years 165 (35.6 %), 60-69 years 113 (24.4 %), 70-79 years 45 (9.7%) and 80-89 years 8 (1.7%). Table (2). In the present study relationship between depression in diabetics and gender in males' depression Levels: non-depressed, mild depression, moderate depression, moderately and Severe depression values were 172 (88.7%), 12 (6.2%), 7 (3.6%) and 3 (1.5%); respectively. On the other hand, females' depression Levels: non-depressed, mild depression, moderate depression, moderately and severe depression values were 196 (73.1%), 32 (12%), 20 (7.5%), 11 (4.1%), 9 (3.4%); respectively with significant p value< 0.005 Table (3). In the current study, female gender was associated with developing depression. Our results agree with other study showed that female patients with Type 2 DM had a higher incidence of depression Sweileh et al. (2020). Another cross-sectional study in Austria also found that women with Type 2 diabetes were twice as likely to be diagnosed with depression compared with men Deischinger et al. (2020). However, a recent review by Lloyd et al. (2012) concluded that studies from around the world confirm that the prevalence of depression is increased in people with diabetes mellitus although the levels of depression vary between countries, between populations within the same country and between the sexes. Consequently, healthcare providers should manage mental health disorders in patients with diabetes in a culture-centered approach.

In the present study relationship between depression in diabetics and nationality for locals (UAE nationality) depression Levels: non-depressed, mild depression, moderate depression, moderately and Severe depression values were 303 (77.2%), 40 (10.2%), 27 (6.9%), 13 (3.3%), 9 (2.3%); respectively. where Non-UAE depression Levels: non-depressed, mild depression, moderate depression, moderately and severe depression values were 65 (92.9%), 4 (5.7%), 0, 1 (1.4%), 0; respectively with non-significant P value = 0.037 Table (8).

In the present study relationship between depression in diabetics and relationship between depression in diabetics and marital status for single depression Levels: non-depressed, mild depression, moderate depression, moderately and severe depression values were 21 (77.8%), 3 (11.1%), 2 (7.4%), 1 (3.7%), 0; respectively. where married depression Levels: non-depressed, mild depression, moderate depression, moderately and severe depression values were 306 (82.9%), 30 (8.1%), 19 (5.1%), 8 (2.2%), 6 (1.6%); respectively, divorced depression Levels: non-depressed, mild depression, moderate depression, moderately and severe depression values were 12 (63.1%), 2 (10.5%), 3 (15.8%), 1 (5.3%), 1 (5.3%); respectively, widow depression Levels: non-depressed, mild depression, moderate depression, moderately and severe depression values were 28 (7.6%), 9 (20.5%), 3 (11.1%), 3 (21.4%), 2 (22.2%); respectively there was significant difference with P value = 0.005. table (7). Although the current study showed a statistically significant correlation between being married and depression, Previous studies in Sir Lanka and Ethiopia suggested that the marital status of patients with DM plays a role with those being married having less rates of depression in contrast to those who were single/divorced or widowed Asefa et al. (2020).

In the present study relationship between depression in diabetics and level of education for Illiterate depression Levels: non-depressed, mild depression, moderate depression, moderately and severe depression values were 98 (75.4%), 17 (13.1%), 4 (3.1%), 5 (3.8%), 6 (4.6%); respectively, for read and write depression Levels: non-depressed, mild depression, moderate depression, moderately and severe depression values were 29 (78.4%), 5 (13.5%), 2 (5.4%), 1 (2.7%), 0; respectively, for Primary level education depression Levels: non-depressed, mild depression, moderate depression, moderately and severe depression values were 46 (78%), 3 (5.1%), 7 (11.9%), 2 (3.4%), 1 (1.7%); respectively, for Prep level education depression Levels: non-depressed, mild depression, moderate depression, moderately and severe depression values were 38 (79.2%), 4 (8.3%), 5 (10.4%), 0, 1 (2.0%); respectively, for secondary level education depression Levels: non-depressed, mild depression, moderate

depression, moderately and severe depression values were 62 (78.5%), 7 (8.9%), 6 (7.6%), 3 (3.8%), 1 (1.3%); respectively, for secondary level education depression Levels: non-depressed, mild depression, moderate depression, moderately and severe depression values were 95 (87.1%), 8 (7.3%), 3 (2.8%), 3 (2.8%), 0; respectively with non-significant difference p value =0.226. Table (5). Association between depression and low education may be explained by the fact that educated people have better jobs and less likely to be depressed. Our study showed that there was non-significant difference in depression Levels: non-depressed, mild depression, moderate depression, moderately and severe depression between Non-Smoker, Ex-Smoker and Smokers, P-value = 0.343. Our study showed that there was non-significant difference in depression Levels: non-depressed, mild depression, moderate depression, moderately and severe depression between alcohol consumption and non-alcohol consumption, P-value = 0.765. Our study showed that there was non-significant difference in depression Levels: non-depressed, mild depression, moderate depression, moderately and severe depression between not working and working, P-value = 0.087. Our study showed that there was non-significant difference in depression Levels: non-depressed, mild depression, moderate depression, moderately and severe depression between Inadequate, adequate, and adequate and saving socio-economic status, P-value = 0.035. Table (6). The use of a relatively high sample size with a high response rate and using validated tools were the strength of this study. This study was conducted in health facilities; hence the findings might not adequately reflect the depression of the entire diabetic patient in the community.

## 5. Conclusion

The prevalence of depression levels: non-depressed, mild depression, moderate depression, moderately and severe depression are high in UAE-patients comparing to Non-UAE participants, based on this study the prevalence of depression levels: non-depressed, mild depression, moderate depression, moderately and severe depression are high in DM patients type 2 comparing to DM patients type 1. From this study we concluded that depression levels: non-depressed, mild depression, moderate depression, moderately and severe depression are high in married participants comparing with single, divorced and widow participants. Data from our study highlighted those patients with diabetes mellitus are at considerable risk of developing depression. We recommend that public health policymakers in the UAE should utilize more educational tools, in order to increase the awareness of the community on the risk of depression in diabetes patients.

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## Disclosure

The authors have no conflict of interest to declare.

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# Examination of Obesity Awareness Levels of University Students in Terms of Different Variables

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**Abstract**
The purpose of this study is to examine the obesity awareness levels of university students in terms of sport and different variables. The research was carried out on a total of 310 students, 107 male and 203 female, studying at Erzurum Atatürk University Kazım Karabekir Faculty of Education in the 2021/2022 academic year. Research data were collected by the obesity awareness scale developed by Allen (2011) and adapted into Turkish by Kafkas and Özen (2014) and a demographic information form prepared by the researchers. Frequency distribution was used to determine the demographic characteristics of the students. “T-test for Independent Samples” was used to examine the differentiation between two independent variables and obesity awareness scale sub-dimensions, "One-Way Analysis of Variance" was used to examine the differentiation between more than two variables and obesity awareness scale sub-dimensions, Pearson correlation analyzes were applied to determine the relationship between students' ages and obesity awareness scale sub-dimensions. All these tests were analyzed in the SPSS 21 package program and the significance level was taken as $p<.05$. As a result of the analyzes, it was determined that there was a significant difference between the students' personal monthly income and sports activity status and the obesity awareness scale sub-dimensions. It was found that the obesity awareness levels of the students who do sports activities are higher than those who do not.

**Keywords:** Obesity Awareness, University Students and Obesity, Sports and Obesity

## 1. Introduction

Obesity is a chronic disease state characterized by an increase in body fat mass compared to lean body mass, resulting from the fact that the energy taken into the body with food is more than the energy consumed. Obesity is an important health problem that can cause various disorders and even death by affecting all organs and systems of the body, especially cardiovascular and endocrine systems. Obesity, which is accepted as one of the 10 most risky diseases by the World Health Organization (WHO), has also been determined to be closely related to cancer in the latest studies conducted by the same organization (Altunkaynak & Özbek, 2006, WHO, 1997). Obesity,

which has become a global problem, affects not only adults but also children negatively. In addition, the prevalence of obesity in children has reached the level of obesity in adults (Parlak & Çetinkaya, 2007).

Today, the insufficient level of knowledge of the society on physical activity, the insufficient understanding of the importance of physical activity for health, and the adoption of an increasingly sedentary lifestyle have become one of the important reasons that increase the incidence of chronic diseases such as obesity, cardiovascular diseases, hypertension, diabetes, and osteoporosis. Baltacı & Treatment 2008). It is known that due to technological developments, people move less, their physical activity levels decrease, and in parallel, public health is endangered in various ways (Şanlı, 2008). Studies on obesity have generally focused on the physiological aspect of obesity, and psychosocial factors have been ignored (Alçam et al., 2013).

Personal preferences (for example: eating habits, physical activity) that will affect the health of individuals, especially in childhood and adolescence, may affect the state of obesity. It is known that the aims of sports are to improve the physical and mental health of people, to provide self-confidence, socialization and mutual solidarity. This shows that sport is an effective way of physical health (Morgan & Goldstone 1987, Bayraktar, G., Tozoğlu, E. & Acar, K. 2014). The purpose and effort of contributing to the studies carried out on the examination of the data collected in our research and the results of the statistical analysis obtained, especially between the obesity awareness levels of students and among different variables, to bring a perspective to the subject and to provide important contributions to science in terms of information and resources, is the reason for this study.

## 2. Method

### *2.1. Model of the Research*

In this study, the relational survey model, one of the research models, was used. According to Karasar (2007), the relational survey model is defined as "a research model that aims to determine the existence and/or degree of co-variance between two or more variables."

### *2.2. Research Group*

The research group consists of a total of 310 individuals, 107 male and 203 male, studying at Erzurum Atatürk University Kazım Karabekir Education Faculty in the 2021-2022 academic year. In the study, data were collected from the students through face-to-face questionnaires, and the data were collected on a voluntary basis by informing the explanations that the information they provided would not be used outside of the study.

### *2.3. Data Collection Tools*

In this study, demographic information form prepared by the researchers and obesity awareness scale developed by Allen (2011) and adapted into Turkish by Kafkas and Özen (2014) was used for data collection purposes.

### *2.4. Demographic Information Form*

It was developed by the researcher in order to determine the variables and demographic information (gender, age, family structure, personal monthly income, sportive activity status, sportive activity type and duration of sportive activity) to be used in the research.

### *2.5. Obesity Awareness Scale*

The Obesity Awareness Scale used in the study was developed by Allen (2011). It consists of three sub-dimensions and 23 items. Scale; obesity awareness dimension (8 items), nutrition dimension (7 items) and physical activity sub-dimensions (8 items). The scale has a 4-point Likert structure and goes from positive to negative. The internal consistency coefficient of the scale was reported as $\alpha$=.80. The scale was adapted into Turkish by Kafkas and Özen (2014) and has 21 items and 3 sub-dimensions. The item loads range from 0.42 to 0.72 and the total variance is

44.66%. The overall internal consistency Cronbach α value of the scale is 0.87. In our study, Cronbach α internal consistency coefficients were examined and the total value for the obesity awareness scale was found to be 0.797.

*2.6. Analysis of Data*

Before proceeding to the statistical analysis, assumptions such as normality, homogeneity, stationarity, linearity, if any, related to these analyzes should be checked and statistical information should be given about which assumptions are provided. In the light of this information, the researcher should justify which analysis techniques he prefers and which he does not prefer (Tozoğlu & Dursun, 2020).

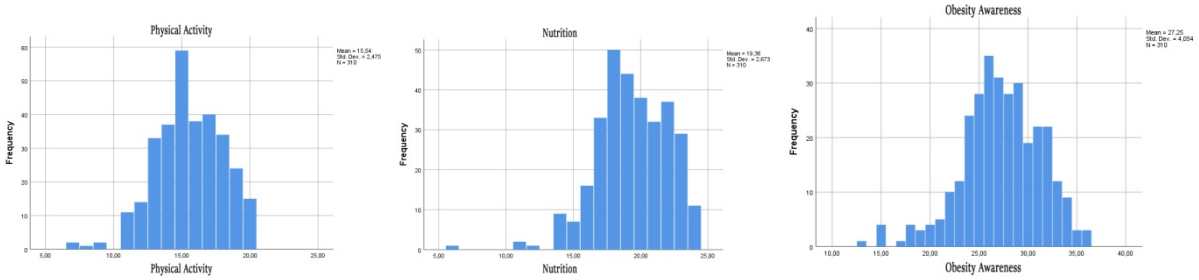
In the research, studies on data processing were carried out before the data obtained through scales could be analyzed. For this, the demographic information form filled by the students and the "Obesity Awareness Scale" was checked in detail. Incomplete or incorrectly filled questionnaires were not taken into consideration. Then, the scales suitable for the research were transferred to the computer and evaluated in the analysis of the data. SPSS 21.00 package program was used in the analysis of the data. While analyzing the data, primarily descriptive analysis (frequency, arithmetic mean, standard deviation, percentile distribution) techniques were used. These are frequency, arithmetic mean, standard deviation, and percentile distribution. "T-test for Independent Samples" was performed to determine the differentiation between two different independent variables and obesity awareness scale sub-dimensions, from parametric tests in normally distributed data. “One-Way Analysis of Variance” test was performed to determine the differentiation between more than two different variables and obesity awareness scale sub-dimensions. Pearson correlation analyzes were conducted to determine the relationship between students' ages and obesity awareness scale sub-dimensions. The results were evaluated according to the p<.05 significance level.

## 3. Findings

In this section, the general purpose of the research and the findings obtained from the analysis of the sub-problems created for this purpose is given.

Table 1: Descriptive Statistics Distribution

| | **Obesity Awareness** | **Nutrition** | **Physical Activity** |
|---|---|---|---|
| N | 310 | 310 | 310 |
| Mean | 27,2516 | 19,3581 | 15,5387 |
| Median | 27,0000 | 19,0000 | 15,0000 |
| Mode | 26,00 | 18,00 | 15,00 |
| Std. Deviation | 4,05399 | 2,67268 | 2,47514 |
| ***Skewness*** | ***-,488*** | ***-,639*** | ***-,344*** |
| Std. Error of Skewness | ,138 | ,138 | ,138 |
| ***Kurtosis*** | ***,592*** | ***1,494*** | ***,204*** |
| Std. Error of Kurtosis | ,276 | ,276 | ,276 |
| Range | 23,00 | 18,00 | 13,00 |
| Minimum | 13,00 | 6,00 | 7,00 |
| Maximum | 36,00 | 24,00 | 20,00 |



Frequency distributions are given for categorical variables in the analysis of the data. n addition, mode, median and arithmetic mean values, skewness and kurtosis coefficients were taken into account in order to look at the condition that the data have a normal distribution. Obesity awareness sub-dimension Skewness -.488 and Kurtosis 592, nutrition sub-dimension Skewness -.639 and Kurtosis 1.494, and physical activity sub-dimension Skewness -.344 and Kurtosis .204, of the obesity awareness scale seen in the table. Mode, median, arithmetic mean, skewness and kurtosis values of obesity awareness scale sub-dimensions are close to each other, within the limits specified by Büyüköztürk (2012), Tabachnik and Fidell (2015), and George and Mallery (2010) (-1 to +1; -1.5 to +1.5; -2.0 to +2.0) data set has a normal distribution. Parametric tests were used because it showed a normal distribution.

Table 1: Average Ages of the Students Participating in the Study

| **Age** | |
|---|---|
| N | 310 |
| Mean | 20,8000 |
| Median | 21,0000 |
| Mode | 21,00 |
| Std. Deviation | 2,07746 |
| Range | 17,00 |
| Minimum | 17,00 |
| Maximum | 34,00 |

It was determined that the average age of the students participating in the study was 20.80±2.07.

Table 2: Gender, Family Structure and Personal Income Levels of the Students Participating in the Research

| **Variable** | | **n** | **%** |
|---|---|---|---|
| **Gender** | Male | 107 | 34,5 |
| | Female | 203 | 65,5 |
| | Total | 310 | 100,0 |
| **Family structure** | Core Family | 252 | 81,3 |
| | Extended family | 51 | 16,5 |
| | Broken Family | 7 | 2,3 |
| **Personal Income** | 750 TL and below | 149 | 48,1 |
| | Between 751-1500 TL | 98 | 31,6 |
| | Between 1501-2000 TL | 23 | 7,4 |
| | 2001 TL and above | 40 | 12,9 |

The research was conducted on a total of 310 students, 107 male and 203 female. Among the students participating in the research, it was seen that 252 students were in core family, 51 students were in extended family, and 7 students were in a broken family structure. In addition, it has been determined that 149 students have an income level of 750 TL or less, 98 students have an income level of 751-1500 TL, 23 students have an income level of 1501-2000 TL and 40 students have an income level of 20001 TL and above.

Table 3: Sportive Activity Status and Type of Sportive Activity and Duration of Sportive Activity of the Students Participating in the Research

| **Variable** | | **n** | **%** |
|---|---|---|---|
| **Sports Activity Status** | Yes | 149 | 48,1 |
| | No | 161 | 51,9 |
| | Total | 310 | 100,0 |
| **Sporting Activity Type** | Not Doing | 161 | 51,9 |
| | Individual Sports | 91 | 29,4 |
| | Team Sport | 38 | 12,3 |

| | | | |
|---|---|---|---|
| | Both of them | 20 | 6,5 |
| **Sports Activity Duration (Weekly Total)** | Not Doing | 161 | 51,9 |
| | 2 hours and less | 62 | 20,0 |
| | 3-5 hours | 62 | 20,0 |
| | 6 hours or more | 25 | 8,1 |

149 of the students participating in the research stated that they do sports activities and 161 of them do not do sports activities. While 91 of the students who do sports activities do individual sports, 38 do team sports, 20 do both sports. When the duration of the sportive activity of the students who do sportive activity is examined, it is observed that 62 of them do sportive activity between 2 hours and 3-5 hours, and 25 of them do sportive activities for 6 hours or more.

Table 4: T-Test Results of the Levels of the Obesity Awareness Scale Sub-Dimensions of the Students Participating in the Study by Gender

| **Obesity Awareness Sub-Dimensions** | **Gender** | **n** | **x** | **s** | **t** | **p** | **x variation** |
|---|---|---|---|---|---|---|---|
| Obesity Awareness | Male | 107 | 26,7196 | 4,48434 | -1,682 | ,094 | -,81239 |
| | Female | 203 | 27,5320 | 3,78934 | | | |
| Nutrition | Male | 107 | 19,0841 | 3,01293 | -1,234 | ,219 | -,41835 |
| | Female | 203 | 19,5025 | 2,47037 | | | |
| Physical Activity | Male | 107 | 15,2523 | 2,74066 | -1,482 | ,139 | -,43732 |
| | Female | 203 | 15,6897 | 2,31595 | | | |

After the t-test analysis between the genders of the students and the sub-dimensions of the obesity awareness scale, it was determined that there was no significant difference between the genders in all sub-dimensions at the $p<.05$ level. In addition, it was found that the awareness level of female students was higher than that of male students in these three dimensions, where there was no significant difference.

Table 5: Results of Correlation Analysis of the Ages of the Students Participating in the Study and the Sub-Dimensions of the Obesity Awareness Scale

| | | **Obesity Awareness** | **Nutrition** | **Physical Activity** |
|---|---|---|---|---|
| **Age** | Pearson Correlation | -,090 | ,046 | ,032 |
| | Sig. (2-tailed) | ,113 | ,418 | ,578 |
| | N | 310 | 310 | 310 |

When the results of the correlation analysis conducted to determine the relationship between the age of the students participating in the study and the obesity awareness scale sub-dimensions were examined, it was determined that there was no significant relationship at the $p<.05$ level between the age of the students and the obesity awareness scale sub-dimensions.

Table 6: Variance Analysis Test Results of the Obesity Awareness Scale Sub-Dimensions of the Students Participating in the Study According to the Family Structure Variable

| **Obesity Awareness Sub-Dimensions** | **Family structure** | **n** | **x** | **s** | **f** | **p** |
|---|---|---|---|---|---|---|
| **Obesity Awareness** | Core Family | 252 | 27,3929 | 4,01893 | 1,472 | ,231 |
| | Extended family | 51 | 26,8627 | 3,99009 | | |
| | Broken Family | 7 | 25,0000 | 5,47723 | | |
| | Total | 310 | 27,2516 | 4,05399 | | |
| **Nutrition** | Core Family | 252 | 19,4563 | 2,68871 | 1,953 | ,144 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | Extended family | 51 | 19,1176 | 2,61264 | | |
| | Broken Family | 7 | 17,5714 | 1,98806 | | |
| | Total | 310 | 19,3581 | 2,67268 | | |
| **Physical Activity** | Core Family | 252 | 15,6468 | 2,37145 | 1,557 | ,212 |
| | Extended family | 51 | 15,1569 | 2,83106 | | |
| | Broken Family | 7 | 14,4286 | 3,20713 | | |
| | Total | 310 | 15,5387 | 2,47514 | | |

After the variance analysis test performed between the family structures of the students and the obesity awareness scale sub-dimensions, it was determined that there was no significant difference at the p<.05 level.
In addition, it is observed that the awareness level of the students in the core family structure is higher than the students in the other family structure in these three dimensions, where there is no significant difference.

Table 7: Variance Analysis Test Results of Obesity Awareness Scale Sub-Dimensions According to Personal Income Variable of Students Participating in the Research

| **Obesity Awareness Sub-Dimensions** | **Personal Income** | **n** | **x** | **s** | **f** | **p** | **difference** |
|---|---|---|---|---|---|---|---|
| Obesity Awareness | Under 750 TL (1) | 149 | 27,0067 | 3,53075 | 2,373 | ,070 | ---- |
| | Between 751-1500 TL (2) | 98 | 27,8061 | 4,06559 | | | |
| | Between 1501-2000 TL (3) | 23 | 25,5652 | 6,04398 | | | |
| | Over 20001 TL (4) | 40 | 27,7750 | 4,26968 | | | |
| | Total | 310 | 27,2516 | 4,05399 | | | |
| Nutrition | Under 750 TL (1) | 149 | 18,8993 | 2,38448 | 2,995 | ***,040*** | ***1<2*** |
| | Between 751-1500 TL (2) | 98 | 19,8163 | 2,76706 | | | |
| | Between 1501-2000 TL (3) | 23 | 19,4783 | 2,87417 | | | |
| | Over 20001 TL (4) | 40 | 19,8750 | 3,11479 | | | |
| | Total | 310 | 19,3581 | 2,67268 | | | |
| Physical Activity | Under 750 TL (1) | 149 | 15,1477 | 2,32604 | 3,121 | ***,013*** | ***1<2*** |
| | Between 751-1500 TL (2) | 98 | 16,1224 | 2,36933 | | | |
| | Between 1501-2000 TL (3) | 23 | 15,5652 | 1,61881 | | | |
| | Over 20001 TL (4) | 40 | 15,5500 | 3,33551 | | | |
| | Total | 310 | 15,5387 | 2,47514 | | | |

After the variance analysis test conducted between students' personal income levels and obesity awareness scale sub-dimensions, it was determined that there was a significant difference in nutrition and physical activity sub-dimensions at p<.05 level. It has been determined that the awareness level of students with a personal income level of 750 TL and below is lower than that of students with a personal income level of 751-1500 TL.

In the obesity awareness sub-dimension, there was no significant difference between personal income levels.

Table 8: The t-Test Results of the Levels Between the Obesity Awareness Scale Sub-Dimensions of the Students Participating in the Study According to the Sub-Dimension of Doing Sports

| Obesity Awareness Sub-Dimensions | Doing Sports Activity | n | x | s | t | p | x difference |
|---|---|---|---|---|---|---|---|
| Doing Sports Activity | Yes | 149 | 27,8255 | 4,06656 | ***2,416*** | ***,016*** | ***1,10501*** |
| | No | 161 | 26,7205 | 3,98154 | | | |
| Nutrition | Yes | 149 | 19,8993 | 2,69821 | ***3,492*** | ***,001*** | ***1,04219*** |
| | No | 161 | 18,8571 | 2,55650 | | | |
| Physical Activity | Yes | 149 | 15,8054 | 2,57503 | 1,832 | ,068 | ,51344 |
| | No | 161 | 15,2919 | 2,36019 | | | |

After the t-test analysis between the students' sports activities and the obesity awareness scale sub-dimensions, it was determined that there was a significant difference at the p<.05 level in the obesity awareness and nutrition sub-dimensions. In the sub-dimensions of obesity awareness and nutrition, it was found that the awareness level of the students who did sports activities was higher than the students who did not do sports.
In the physical sub-dimension, it was determined that there was no significant difference between family structures.

Table 9: Variance Analysis Test Results According to the Variable of Sports Activity Type of Obesity Awareness Scale Sub-Dimensions of the Students Participating in the Research

| Obesity Awareness Sub-Dimensions | Sporting Activity Type | n | x | s | f | p |
|---|---|---|---|---|---|---|
| Obesity Awareness | Individual Sports | 91 | 27,6923 | 4,19177 | ,815 | ,445 |
| | Team Sport | 38 | 27,5789 | 4,24029 | | |
| | Both | 20 | 28,9000 | 3,02446 | | |
| | Total | 149 | 27,8255 | 4,06656 | | |
| Nutrition | Individual Sports | 91 | 19,9341 | 2,77610 | 1,564 | ,213 |
| | Team Sport | 38 | 19,3947 | 2,69674 | | |
| | Both | 20 | 20,7000 | 2,20287 | | |
| | Total | 149 | 19,8993 | 2,69821 | | |
| Physical Activity | Individual Sports | 91 | 16,0000 | 2,42670 | 1,655 | ,195 |
| | Team Sport | 38 | 15,1579 | 3,05381 | | |
| | Both | 20 | 16,1500 | 2,10950 | | |
| | Total | 149 | 15,8054 | 2,57503 | | |

It was determined that there was no significant difference at the p<.05 level after the variance analysis test performed between the type of sportive activity that the students were doing and the obesity awareness scale sub-dimensions.

In addition, it is observed that the awareness levels of the students who do both sports in these three dimensions, where there is no significant difference, are higher than the students who do individual and team sports.

Table 10: Variance Analysis Test Results of the Obesity Awareness Scale Sub-Dimensions of the Students Participating in the Study According to the Variable of Sporting Activity Type and Duration

| Obesity Awareness Sub-Dimensions | Sporting Activity Period (Weekly) | n | x | s | f | p | difference |
|---|---|---|---|---|---|---|---|
| Obesity Awareness | 2 hours and under (1) | 62 | 26,8226 | 4,32501 | 3,409 | ***,033*** | ***1<2*** |
| | 3-5 hours (2) | 62 | 28,6452 | 3,68469 | | | |
| | 6 hours or more (3) | 25 | 28,2800 | 3,92131 | | | |
| | Total | 149 | 27,8255 | 4,06656 | | | |
| Nutrition | 2 hours and under (1) | 62 | 19,4194 | 3,04366 | 1,758 | ,176 | ---- |
| | 3-5 hours (2) | 62 | 20,1774 | 2,35758 | | | |
| | 6 hours or more (3) | 25 | 20,4000 | 2,48328 | | | |
| | Total | 149 | 19,8993 | 2,69821 | | | |
| Physical Activity | 2 hours and under (1) | 62 | 15,5000 | 2,58463 | 1,059 | ,350 | ---- |
| | 3-5 hours (2) | 62 | 16,1613 | 2,69300 | | | |
| | 6 hours or more (3) | 25 | 15,6800 | 2,21209 | | | |
| | Total | 149 | 15,8054 | 2,57503 | | | |

After the variance analysis test performed between the students' duration of doing sportive activities and the obesity awareness scale sub-dimensions, it was determined that there was a significant difference in the obesity awareness sub-dimension at p<.05 level. It has been found that the awareness level of the students who do sportive activities for 2 hours or less is lower than the students who are between 3-5 hours.

No significant difference was found between the duration of doing sports activities in nutrition and physical sub-dimensions.

## 4. Discussion and Conclusion

In our study, no significant difference was found between genders in all sub-dimensions of the students participating in the research. Alasmari et al. (2017) on obesity on university students, no statistically significant relationship was found between gender. In the study of Misiroglu et al. (2007) found no difference between obesity and gender in their study. Pala et al. (2003) found no significant difference in terms of gender in children aged 6-10 years in their study. Results of similar studies support our study.

It was determined that there was no significant difference between the ages of the students and the obesity awareness scale sub-dimensions. Çınar (2013) did not find a statistically significant difference between the age of the students and the incidence of obesity in his master's thesis. In his doctoral thesis, Acaroğlu (2020) concluded that there is no statistical difference between the ages of the participants and obesity. On the other hand In the study conducted by Çayır et al. (2009) when the relationship between obesity and age was evaluated, it was determined that the obesity rate was higher in those aged 61 years and older than those at lower ages. The results of the studies are consistent with the results we found.

It was determined that there was no significant difference between the family structures of the students and the sub-dimensions of the obesity awareness scale. Kaya (2008) reached a conclusion in parallel with our study in his study, and no significant result was reached between family structure and obesity. Aslan et al. (2003) reached the same conclusion as we did in their study. Tezcan et al. (2005) did not find a relationship between gender and family type in the study they conducted on the same field. The results found in other studies examined showed parallelism with our study.

It was found that there was a significant difference between the students' personal income levels and the obesity awareness scale nutrition and physical activity sub-dimensions. t has been concluded that the awareness level of students with a personal income level of 750 TL and below is lower than that of students with a personal income level of 751-1500 TL. Cayir et al. (2009), it was determined that the obesity rate increased as the income level decreased. Özilbey (2013), in his study to determine the obesity frequency of 6-11 age group students and its relationship with their eating habits, found that obesity increases as the income level increases. They prove that there is a significant difference between income level and obesity, as in the result we found in other studies.
It was found that there was a significant difference between students' sports activities and obesity awareness scale awareness and nutrition sub-dimensions. It has been concluded that the awareness level of the students who do sports activities in the obesity awareness and nutrition sub-dimensions is higher than the students who do not do sports activities. A significant difference was found in body mass index according to the sportive activity status of the participants in a study conducted by Sevimli (2008) on 412 people. Karacan et al. (2004) found in their study that regular exercise has a reducing effect on body mass index. Okyay et al. (2002) did not find a significant relationship between obesity and doing sports. The results found in the studies are in line with the results of our study.

It was determined that there was no significant difference between the type of sportive activity that the students were doing and the sub-dimensions of the obesity awareness scale. Spendlove et al. (2012) found that there were no significant differences in nutritional knowledge between those who do team sports and those who do individual sports. In a study by Bozkurt and Nizamlıoğlu (2005), it was found that the level of nutrition knowledge of the athletes who do individual sports is higher than those who do team sports.

It was determined that there was a significant difference in the obesity awareness sub-dimension between the duration of the students' doing sports activities and the obesity awareness scale sub-dimensions. It has been found that the awareness level of the students who do sportive activities for 2 hours or less is lower than the students who have 3-5 hours. No significant difference was found between the duration of doing sports activities in nutrition and physical sub-dimensions. Hassapidou et al. (2013), in a study they conducted in Greece, they found that those who do sports less than four hours a week in women are associated with obesity. Zorba et al. (2000) obtained positive results in the study they conducted on middle-aged sedentary women for 8 weeks, provided that it was 3 days a week. Amano et al. (2001) in their study, they reached a conclusion that was parallel to our study. It has been observed that other studies are in line with our study.

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