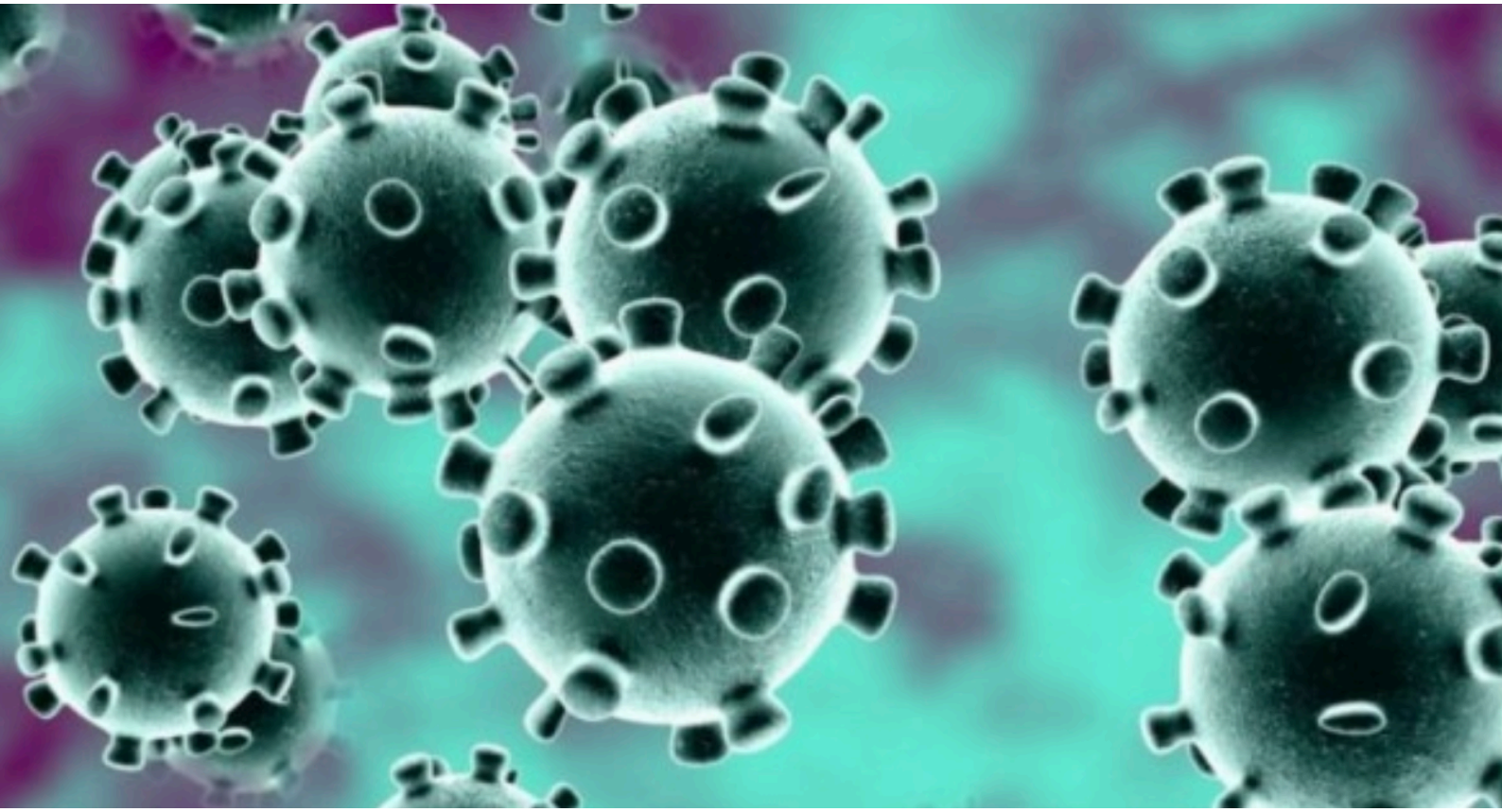
ISSN 2622-7258 (Online)

Asian Institute of Research

Journal of Health and Medical Sciences

Vol. 3, No.2 June 2020



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Asian Institute of Research
Journal of Health and Medical Sciences
Vol.3 No.2 June 2020

Journal of Health and Medical Sciences
ISSN 2622-7258 (Online)

ASIAN INSTITUTE OF RESEARCH
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The Asian Institute of Research
Journal of Health and Medical Sciences
Vol.3, No.2, 2020:150-156
ISSN 2622-7258

DOI: 10.31014/aior.1994.03.02.108

Emblica Officinalis (Amloki) – Could Be the Remedy for Side Effects of Iron Supplementation in Pregnancy

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Abstract
Background: Iron deficiency anemia (IDA) is the most common nutritional disorder in pregnancy in developing countries. Different iron preparations are supplemented to treat IDA in pregnancy, which can lead to different side effects like nausea, vomiting, decreased appetite, constipation or diarrohea, hyperacidity. Emblica officinalis is a well known traditional fruit to reduce these side effects. Aim: To determine the side effects of iron supplementation and beneficial role of amloki in pregnancy to reduce these side effects.Methods and materials: This interventional study was done in the Department of Physiology, Dhaka Medical College, Dhaka from July 2016 to June 2017. From the Outpatient Department of Obstetrics and Gynaecology, Dhaka Medical College and Hospital, 46 pregnant women were selected purposively on the basis of inclusion and exclusion criteria. Anaemic pregnant women supplemented with oral iron and amloki were considered as study groups (Group A) and pregnant women supplemented with only iron for 45 days were considered as control group (Group B). A previously formed structured questionnaire was used to evaluate the subjective complaints. Chi-square test was performed to compare between the groups. The test of significance was calculated & p value < 0.05 was accepted as level of significance. Results: Significant improvement in different subjective parameters nausea, vomiting, decreased appetite, constipation, hyperacidity ($p<0.001$), were seen in iron and amloki supplemented group. Conclusions: It can be concluded that, amloki supplementation along with iron can reduce the side effects of iron and improve the subjective complains of the iron deficient anemic pregnant women.

Keywords: Iron Deficiency Anaemia, Pregnancy, Amloki, Constipation, Acidity

Introduction

Anemia is a worldwide public health problem. Among different types of anaemia iron deficiency anemia is the most common type (Layeeq & Thakar, 2015). In developing countries, multi-parity, prolonged lactation, dietary deficiency and worm infestation are the causes of development of IDA in women of reproductive age (Khot, Patil & Kakad, 2013). Again, during pregnancy maternal blood volume increases and there is increased demand of iron for the growth of the fetus. Pregnancy also reduces the erythropoietic function of bone marrow. All these factors make a pregnant women iron deficient, though she was previously healthy (Roy & Dwivedi, 2014; Sharma, Jain, Rani, Jaitawat & Kantawa, 2015).

The common clinical presentations are pallor of the skin, pale nail, pale tongue, glossitis, stomatitis, lassitude, fatigue, anorexia, indigestion, palpitation, weakness, tiredness, shortness of breath (dysnoea), giddiness, oedema and pica in pregnancy with IDA (Nirali & Shankar, 2015).

Several studies have done about iron deficiency anemia in pregnancy in Bangladesh and worldwide. Iron and folic acid supplementation are the WHO recommended standard treatment for IDA in pregnancy (Klemn et al., 2011). But, it has several side effects, like heartburn, nausea, upper gastric discomfort, constipation and diarrhea. Recently it has been shown to generate free radicles, which cause damage to the intestine (Khot, Patil & Kakad, 2013). About, 20-30% of total iron is absorbed in subjects with IDA, when it is administered orally. The remainder travels through the gut lumen and causes free radical-mediated damage to the gut mucosa (Evans and Halliwell, 2001; Idoate Gastearena, Gil, Azqueta, Coronel & Gimeno, 2003;Hutchinson, Al-Ashgar, Liu, Hider, Powell & Geissler, 2004; Erichsen, Ulvik, Grimstad, Berstad, Berge & Hausken, 2005). It also causes destruction of beneficial colonic microflora (Zimmermann et al., 2010; Werner et al., 2011; Dostal et al., 2012). But if the Amloki is added with iron pills it raises its absoption and decreases the side effects (Sharma et al., 2015).

General wellbeing of individuals depends on Gastrointestinal symptoms (Schultink, van der Ree, Matulessi & Gross, 1993; Jeong et al., 2008; Lutsey, Dawe, Villate, Valencia & Lopez, 2008).So, it can affect compliance with oral iron therapy and, therefore, treatment efficacy (Lutsey, Dawe, Villate, Valencia & Lopez, 2008; Seck & Jackson, 2008).

To evaluate gastrointestinal symptoms before and after iron supplementation self-reporting questionnaires may be used (Talley, Boyce, Owen, Newman & Paterson, 1995; Quan et al., 2003; Brunner et al., 2005; Foster JM & van der Molen, 2008; Varma et al., 2008).

Methods and materials

This interventional study was done in the Department of Physiology, Dhaka Medical College, Dhaka from July 2016 to June 2017. This study conformed to the Helsinki Declaration and was approved by the concerned departments, Research Review Committee and Ethical Review Committee of Dhaka Medical College, Dhaka. From the outpatient department of Obstetrics and Gynaecology, DMCH, 46 pregnant women in between 18 to 36 years of age having 13^{th} to 20^{th} weeks of gestation were recruited with the clinical signs and symptoms of Anaemia along with blood Hb level 8≥ to <11 gm/dl. After recruitment, the benefit, purpose and procedures of the study were explained to each subject in detail. Their voluntary participations were encouraged. They were free to withdraw themselves whenever they wanted from the study. Informed written consent was taken from the participants. Their socio economic condition, food habit, parity, menstrual history was taken along with subjective complaints and clinical examination. All the informations were recorded in a prefixed questionnaire. Amloki capsules and iron tablets were given in boxes for 45 days and participants were encouraged to continue the supplied medicine daily. Compliance to the supplementation was monitored by regular telephonic communications. After 45 days, again clinical examination was done and subjective complaints were taken from the subjects. Subjective complaints were graded in the previously formed structured questionnaire (table I) at the beginning of the study (baseline) and after 45 days of study period. Participants were divided into two groups, 25 pregnant women with IDA, were supplemented with oral amloki capsules (1.072 gm) thrice daily and iron tablet [ferrous fumarate (200mg) + folic acid (0.02 mg)] once daily for 45 days, were considered as study group

(Group A). Again, 21 pregnant women with IDA, supplemented with only iron tablet once daily for 45 days were considered as control group (Group B). After 2 weeks of study period one subject was excluded from study group due to reluctance. After 4 weeks of study, 2 subjects from control group left Dhaka. So, finally 24 subjects of study and 19 subjects of control groups completed the study.

The amloki capsule (Amlahills) used in this study was manufactured by Isha Agro Developers PVT.LTD, India and authentified by the Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Dhaka.
For statistical analysis, Chi-square test was performed to compare between the groups using SPSS Version 22.0. Data were expressed as n (%). The p-value < 0.05 was taken as the level of significance.

Table I: Preformed Grading pattern for subjective complaint

Sl. No.	Presenting Clinical Features	Grade Before & After Treatment		Severity
1.	Nausea and vomitting	0	0	Absence of nausea.
		1	1	Occasional feeling of nausea.
		2	2	Regular feeling of nausea without vomiting.
		3	3	Regular feeling of nausea with occational vomiting.
		4	4	Regular feeling of nausea with regular vomiting.
2.	Loss of appetite	0	0	Very good appetite.
		1	1	Irregular appetite.
		2	2	Persistent poor appetite.
		3	3	Persistent very poor appetite.
		4	4	Complete loss of appetite.
3.	Constipation /diarrhoea	0	0	No constipation/diarrhea.
		1	1	Passes hard & soft stool regularly.
		2	2	Pass hard stool all the time/soft stool ≤ thrice a day
		3	3	Need of laxative to pass stool /pass soft stool > thrice a day.
		4	4	have to stop iron intake
4.	Hyperacidity	0	0	No heart burn
		1	1	Occasional heart burn on spicy food intake
		2	2	Regular heart burn but no need of antiulcerant
		3	3	Irregular use of antiulcerant
		4	4	Regular use of antiulcerant

Result and Discussion

Results are showing (table II, table III) significant improvements in different side effects nausea and vomiting, loss of appetite, constipation/diarrhoea, and hyperacidity (p < 0.001). At the beginning of the study about 50% patients had the symptoms of nausea in both groups. After supplementation, in group A only 20% patients had the symptoms of nausea with or without vomiting, while 68% patient developed nausea with or without vomiting in group B. Most of them (>95%) had poor appetite in both groups before supplementation. But after supplementation about 88% patients had developed good appetite in group A, while in group B about 85% patients were suffering from persistent poor appetite. Before supplementation all patients had regular or irregular bowel habits in both groups. But after supplementation, no one developed diarrhea or constipation in group A, while about 90% patients developed constipation and 10% developed diarrhea in group B. Before supplementation none of them had the history of taking antiulcerant in both groups. After supplementation, only about 9% patients had hyperacidity in group A, while about 85% patients in group B were suffering from hyperacidity.

Table II: Subjective complaints of the study subjects at baseline in both groups (n=43)

Parameters	Group		p value
	Group A (n=24) [n(%)]	Group B (n=19) [n(%)]	
Nausea and vomitting			
Absence of Nausea	2 (8.3)	2 (10.5)	0.936 ns
Occasional feeling of nausea	10 (41.7)	7 (36.8)	
Regular feeling of nausea without vomiting	12 (50.0)	10 (52.6)	
Appetite			
Irregular appetite	1 (4.2)	0 (0.0)	0.638ns
Persistent poor appetite	7 (29.2)	5 (26.3)	
Persistent very poor appetite	16 (66.7)	14 (73.7)	
Constipation/diarrhoea			
No constipation/diarrhoea	2 (8.4)	1 (5.3)	0.094ns
Passes hard & soft stool regularly	17 (70.8)	8 (42.1)	
Pass hard stool all the time /soft stool ≤ thrice a day	12/3 (62.5)	8/2 (52.6)	
Hyperacidity			
No heart burn	2 (8.4)	1 (5.3)	0.094ns
Occational heart burn on spicy food intake	17 (70.8)	8 (42.1)	
Regular heart burn but no need of antiulcerant	5 (20.8)	10 (52.6)	

Results are expressed as n (%). Chi-square test was performed to compare between groups. The test of significance was calculated & p value < 0.05 was accepted as level of significance.
n = number of subjects; ns = non significant.

Table III: subjective complaints of the study subjects after intervention in both groups (n=43)

Parameters	Group		p value
	Group A (n=24) [n(%)]	Group B (n=19) [n(%)]	
Nausea and vomiting			
Absence of Nausea	6 (25.0)	0 (0.0)	<0.001***
Occasional feeling of nausea	13 (54.2)	6 (31.6)	
Regular feeling of nausea without vomiting	3 (12.5)	9 (47.4)	
Regular feeling of nausea with occasional vomiting	2(8.3)	4(21.0)	
Appetite			
Very good appetite	10 (41.7)	1 (5.3)	<0.001***
Irregular appetite	11 (45.8)	2 (10.5)	
Persistent poor appetite	3 (12.5)	12 (63.2)	
Persistent very poor appetite	0 (0.0)	4 (21.0)	
Constipation/diarrhoea			
No constipation/diarrhoea	24 (100.0)	0 (0.0)	<0.001***
Need of laxative to pass stool/pass soft stool>thrice a day	0 (0.0)	17+2 (100.0)	
Hyperacidity			
No heart burn	7 (29.2)	0 (0.0)	<0.001***
Occational heart burn on spicy food intake	15 (62.5)	3 (15.9)	
Regular heart burn but no need of antiulcerant	1 (4.2)	7 (36.8)	
Irregular use of antiulcerant	1 (4.2)	9 (47.4)	

Results are expressed as n (%). Chi-square test was performed to compare between groups. The test of significance was calculated & p value < 0.05 was accepted as level of significance.
n = number of subjects; *** = significant
Group A: Study group (treated with Amloki powder and Iron tablet)
Group B: Control group (treated with Iron table)

Significant percentage of women are suffering from nausea and vomiting during pregnancy, which is known as morning sickness. Increased Human chorionic gonadotrophin hormone may be the cause of these symptoms (Verberg, Gillott, Al-Fardan & Grudzinskas, 2005; Festin, 2009; Garshasbi, Ghazanfari, Zayeri & Kamali).Different studies shows that iron deficiency anaemia causes increased oxidative stress (Sevgi, Gönenç & Ciðdem 1986; Ferreira, Machado & Matsubara, 1999; Isler et al., 2002; Binkoski, Kris-Etherton & Beard, 2004; Olivares, Araya, Pizarro & Letelier, 2006). On the other hand iron is a known agent to increase oxidative stress by lipid peroxidation of cell membrane. As a result it causes erosion and damage of the intestinal mucosa leading to gastrointestinal symptoms like nausea, vomiting, constipation, diarrhea, hyperacidity in experimental animal as well as in human being (Jansson, Perkkiö, Willis, Refino & Dallman, 1985; Acharya, Punchard & Taylor, 1991; Srigiridhar & Nair, 1998; Srigiridhar & Nair, 2000; William et al., 2000; Srigiridhar, Nair, Subramanian & Singotamu, 2001; Lund, Wharf, Fairweather-Tait & Johnson, 2003; Gambling et al., 2004; Chen, Le, Shi, Zhang, Jin, 2007; Saha, Pandhi, Gopalan, Malhotra & Saha, 2007). So IDA itself, as well as its treatment with iron, may cause gastrointestinal symptoms, which can be worst in pregnancy for both mother and fetus.

Different components present in amloki have been proven beneficial against oxidative damage of the gastrointestinal mucosa. Phenolic compounds like gallic and tannic acid have strong antioxidant activity. So phenolic compounds present in amloki may reduce oxidative stress produced by iron supplementation by free radical scavenging activity (Muthuraman, Sood & Singla, 2011). Another compound present in amloki known as Tannins also has antioxidant action which promotes tissue repair. Tannin may be the cause of antiulcer property of many natural products (de Jesus et al., 2012). Again, flavonoid substances present in amloki have the property of increasing microcirculation of gastric mucosa. Increased gastric mucosal blood supply is probably related to enhanced neuropeptide expression like, CGRP (calcitonin gene-related peptide) released from sensory afferent nerves (Zayachkivska, Konturek, Brzozowski & Ghegotsky, 2005).So, in this study all these factors may act combindly to reduce gastrointestinal side effects of iron supplementation.

Conclusions

From the results of the study, it can be concluded that oral amloki (Emblica officinalis) can effectively improve different subjective complains like nausea, vomiting, diarrhea/ constipation and hyperacidity in pregnant women with iron deficiency anemia. Therefore oral supplementation of amloki along with iron may be helpful to increase iron tolerability and physical well being in pregnancy.

Acknowledgement
The authors acknowledge Department of Obstetrics and Gynaecology, Dhaka Medical College and Hospital, Dhaka and Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Dhaka for their kind cooperation.

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The Asian Institute of Research
Journal of Health and Medical Sciences
Vol.3, No.2, 2020: 157-162
ISSN 2622-7258

DOI: 10.31014/aior.1994.03.02.109

Emerging Mental Health Issues from the Novel Coronavirus (COVID-19) Pandemic

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Abstract
The unprecedented widespread pandemic of the novel coronavirus (COVID-19) has continued to have a tremendous impact on nations around the world. Government controls and restrictions were put in place and are currently being updated to increase social isolation and social (physical) distancing to slow the spread of the virus. As a result, it is expected that there will be unparalleled psychological distress impacting individuals at a global level. Given that the COVID-19 pandemic is expected to continue for the coming months with the possibility of multiple waves, it is imperative to understand the magnitude of mental health issues that will arise during and after this public health crisis. A review of existing literature was assessed to understand the mental health issues that emerge during a pandemic. MEDLINE, Pubmed, APA PsycInfo & CINAHL Plus were reviewed to identify articles published from 2000 to 2020. Of the 203 unique articles reviewed, 16 articles were included in this study. From these articles, important mental health themes identified were related to social isolation, social (physical) distancing, quarantine, caregiver stress, unemployment, and death/illness. The impact on frontline workers and those suffering from mental health disorders are also important factors during this pandemic. These themes provide important areas for mental health strategies and policies which will ultimately impact the burden of mental health in the months to come.

Keywords: Coronavirus, COVID-19, Mental Health, Pandemic, Psychological Distress

1. Introduction

Throughout history there have been major influenza outbreaks that have resulted in high morbidity and high mortality. It has been repeatedly predicted that another disease pandemic will emerge and spread throughout the global population, primarily due to increased air travel and globalization (P. Douglas, D. Douglas, Harrigan & K. Douglas, 2009; Kessler & Wittchen, 2008; Perrin, McCabe, Everly & Links, 2009). As predicted, an unprecedented pandemic began in late 2019, affecting hundreds of thousands of people worldwide. The novel coronavirus, known as COVID-19, is an infectious disease, primarily spread through droplets of saliva or discharge from an infected person (World Health Organization, 2020). COVID-19, unlike previous pandemics of this century, spread rapidly due to the increased socialization of individuals and the nature of the virus.

As countries aggressively push to get ahead of the pandemic and protect their inhabitants, there is widespread uncertainty, confusion, and anxiety (Pfefferbaum, Schonfeld, Flynn & Dodgen, 2012). As a result of this public health crisis, there will be unparalleled mental health issues or psychological distress that arise with substantial impact at a global level (Pfefferbaum et al., 2012). Mental health issues during pandemics are related to acute stress and fear associated to the outbreak, adverse effects from prolonged social distancing, social isolation, and quarantine, and the loss of loved ones or caring for the ill (Douglas et al, 2009). It is expected that there will be a severe strain on mental health resources during and following the pandemic, putting extreme pressure on existing resources and potentially leading to untreated mental health concerns across populations worldwide.

To move forward with mental health considerations during and after the pandemic, there needs to be better understanding of the magnitude of psychological distress experienced by individuals. Currently, there is little published information available on the actual mental health impact directly related to pandemics. This is mainly because few pandemics have actually occurred in the past century (Hughes, 2010). In the case of COVID-19, the highest impacted groups in terms of morbidity and mortality are those 65 years and older and those with underlaying medical conditions (Centres for Disease Control and Prevention, 2020). New cases are increasingly diagnosed in younger age groups, however less common (Centres for Disease Control and Prevention, 2020). Given the rising number of cases and deaths around the world, there will be a significant toll on mental health across all age groups and populations. There is an urgent need to maintain mental health in these large populations as the COVID-19 pandemic continues to progress at a large scale. This paper will review the available published literature on mental health issues resulting from pandemics. Based on the reviewed literature, important mental health themes will be addressed, mainly in the context of North America.

2. Method

To better understand the mental health impact from pandemics, a number of online search tools were assessed to identify existing literature. MEDLINE, Pubmed, APA PsycInfo & CINAHL Plus were reviewed to identify articles published in the past 20 years (2000-2020). Studies included were those published on pandemics and mental health in the English language. Key words used were ‘pandemic’, ‘outbreak’, ‘mental health’, ‘mental illness’ and ‘psychological distress’. Information was extracted from these articles to determine mental health themes that emerge during a widespread pandemic.

3. Results

The literature search resulted in 203 unique studies published in English. A majority of the studies were excluded (92%) because they did not include the topic of widespread pandemics or mental health, were based on specific chronic health conditions only (ex. HIV/AIDS, cancer, heart disease) or natural/man-made disasters, were editorial or commentary articles, and were duplicates of what was already included. Studies that primarily focused on the Ebola epidemic in Western Africa were also excluded. A total of 16 articles were included in this study.

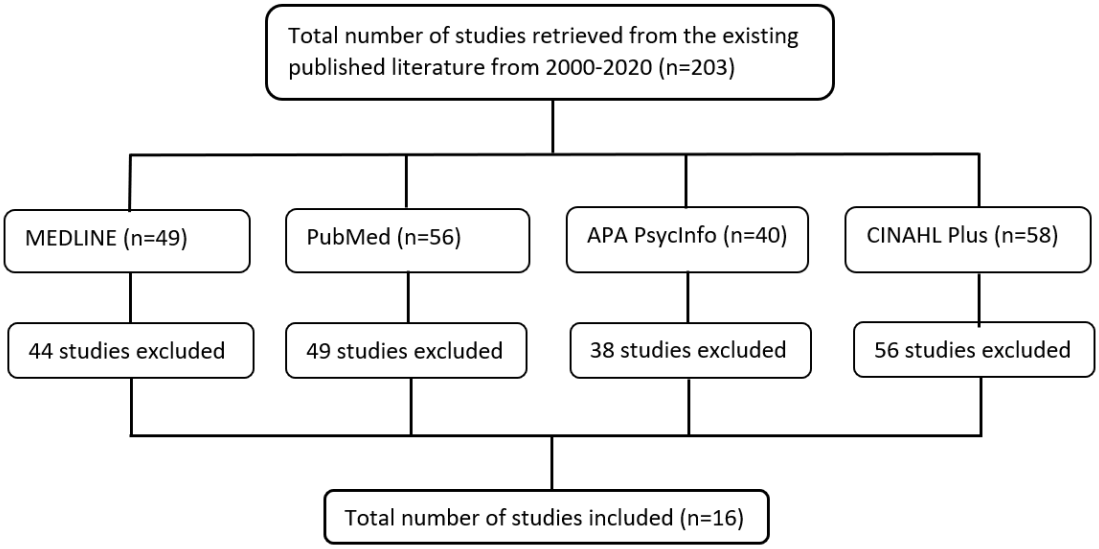

Figure 1. A flow diagram representing the 203 studies retrieved from the existing published literature from 2000 to 2020. A total of 16 studies were included in this study for further discussion.

4. Discussion

COVID-19 differs from previous outbreaks, such as SARS, which affected specific countries and had a lower number of infected individuals and deaths than COVID-19. During the SARs outbreak, the mental health services were considered a low priority as resources were immediately directed to urgent health services and research (Chan, Lam & Chiu, 2009). As the magnitude of COVID-19 on health resources is far greater, it is expected that current mental health services will decline in terms of emergency, community outreach, rehabilitation, prevention, and early intervention services (Chan et al., 2009). Similar to the SARS outbreak, there will be increased mass fear, limited social networking, and significant limitations with access to the health care system which will trigger physical, social, behavioural, and mental health problems (Chan et al., 2009). The increased uncertainty can lead to the uptake of high-risk behaviours such as smoking or alcohol consumption, absenteeism in the workforce, recklessness, panic buying, and unsafe work practices (Pfefferbaum et al., 2012). Health care professionals may not be able to meet the excess needs for mental health following the COVID-19 pandemic. Given the uncertainty of how long the COVID-19 outbreak and subsequent waves will last and given that lengthy process of vaccine development, there is a crucial need to prepare for the mental health impact.

Factors Negatively Impacting Mental Health During a Pandemic	Factors Positively Impacting Mental Health During a Pandemic
Social Isolation	Technology Advances
Quarantine	Availability of Support Systems
Social (Physical) Distancing	Access to Health Resources
Unemployment	Media Messaging
Caregiver Stress	Government Support
Death/Illness	Sense of Global Community

Figure 2. Key factors that can negatively or positively impact mental health during a widespread pandemic.

4.1 Social isolation, social (or physical) distancing, and quarantine

During the COVID-19 crisis, many countries enforced the closure of public settings, encouraging individuals to self-isolate if infected, quarantine if in contact with others who contracted the infection, and to socially distance themselves to keep a two-meter distance from others. To reduce the spread of COVID-19, these are effective defense strategies prior to the development of a vaccine (Douglas et al., 2009). As pandemics can occur in waves over a long period of time, there is a correlation between the degradation of mental health and social isolation (Douglas et al., 2009). Measures of social isolation, social distancing, and quarantine can have significant social,

psychological, and economic implications on the public (Perrin et al., 2009). There is an expected emotional strain related to social isolation and quarantine, and increased anxiety and confusion related to the uncertainty of what is to come. Increased psychological distress is also expected in regions where there are tighter levels of disease control which are put in place when the incidence of the disease is increasing (Taylor, Agho, Stevens & Raphael, 2008; Lee, Chi, Chung & Chou, 2006). The longer the duration of quarantine or social isolation, the more likely there will be higher distress symptoms in individuals (Lee et al., 2006). As social distancing continues during this pandemic, there will be a lack of social interaction especially related to social milestones such as birthdays, graduations, and weddings. A decline in mental health is expected given the lack of common social interactions.

4.2 Caregiver stress

Psychological distress is also an important factor among caregivers who are parents to young children, those with elderly parents or looking after elderly family members, and those looking after the ill. As COVID-19 appears to have the most impact on elderly populations, there may be increased fear and anxiety among caregivers responsible for elderly individuals. The fear and anxiety are related to possibility of infecting susceptible individuals like the elderly, or other illnesses resulting in the need for health resources for these individuals. There is also fear and anxiety when looking after young children or dependents. A previous study assessing psychological distress during a disease epidemic in Australia identified that families with one child had a 1.2 times higher risk of psychological distress than those with no children (Taylor et al, 2008). These families were likely to be younger families with younger parents. However, they also found that families with three or more children appeared slightly protective for psychological distress (Taylor et al, 2008). School and child care closures and government restrictions on social interactions impact caregivers of young children, which may result in decreased mental health in caregivers and children. In the United States, public schools are the largest provider of mental health services to children (Stevenson et al., 2009). The closing of schools and mandatory social distancing will disrupt children's routines and potentially increase stress levels within the family. If a parent contracts the virus, there may likely be parent-child separation which can lead to further anxiety and stress (Stevenson et al., 2009). Children may experience the illness themselves or the loss of loved ones and may find difficulty in coping with the grief if rituals such as funerals are prohibited due to social distancing (Stevenson et al., 2009). Mental health preparedness should include considerations for children, who are significantly impacted during and after pandemic.

4.3 Impact of death/illness

Individuals who tested positively for COVID-19 or are suspected to be ill will likely experience social stigmatization, loss of anonymity through the media, fear of transmitting the virus to loved ones, death or illness among those in close proximity, and the inability to be present for those who are affected due to social isolation or quarantine (Douglas et al., 2009; Perrin et al., 2009; Tansey et al., 2007). In dense populations were there are high numbers of cases and deaths, residing individuals may suffer from increased anxiety, hyper-alert state, and intrusive memories based on their experiences (Lee et al., 2006). As seen during the SARS outbreak, older adults living in high SARS prevalent regions had a higher incidence of post traumatic stress disorder (PTSD) compared to older adults living in low SARS prevalent regions even if they did not contract the virus (Taylor et al., 2008; Lee et al., 2006). Although these individuals were not ill, they perceived that they were at a higher risk due to age and being in a high incidence rate population, especially if the death toll increased drastically. Family members of individuals with severe illness or hospitalized in the ICU reported higher levels of stress and depression, indicating a need for psychological support for families of patients (Elizarraras-Rivas et al., 2010). This is especially important, given the restrictions in hospital and home care institutions during the pandemic, where families have limited or no contact with the ill member of the family. The isolation of the ill individual may increase levels of fear, anxiety, stress, grief, and depression among loved ones. Coping mechanisms are absolutely necessary to guide individuals and families dealing with death or illness, as there will be lasting impacts on families.

4.4 Unemployment

With the economy recessing during the pandemic, this will significantly affect the population's overall health. The increase in unemployment due to the pandemic will result in financial strain, debt, and job-seeking challenges impacting individual mental health. Studies have shown that a recession period resulting in

unemployment is associated to deterioration of a population's self-reported health and a lower life satisfaction level (Frasquilho et al., 2016). This in return increases population psychological distress and prevalence of depression and anxiety disorders. Studies have also shown associations between unemployment and suicidal behaviour (Frasquilho et al., 2016). Economic stress not only impacts individual mental health but can decrease the overall mental health of families and communities collectively. As a result, there may be a decline in parenting quality and children's mental health (Frasquilho et al., 2016). The impact from unemployment can be long term if there is no financial support or economic improvement.

4.5 Impact on frontline workers

Health care workers, such as physicians and nurses, are at the core of the pandemic. Given the widespread impact of COVID-19, there is increased psychological stress in health care workers who are expected to perform their duty at the highest capacity possible while being at risk themselves and are essentially putting their loved ones at risk (Perrin et al., 2009). As with the SARS outbreak, 20% of those affected were health care workers (Perrin et al., 2009), and with COVID-19, reports are already showing high rates of health care workers infected. During the SARS outbreak, healthcare workers in Taiwan, Singapore, and Saudi Arabia reported increased anxiety, depression, hostility, fear, nervousness, and psychiatric symptoms (J. Park, Lee, N. Park & Choi, 2018). Frequent concerns among health care workers during the SARS outbreak were the possibility of becoming infected themselves and transmitting the virus to family and friends, which in turn increased social isolation, intentional absenteeism, stigma, insomnia, and psychological distress (Park et al., 2018; Goulia, Mantas, Dimitroula, Mantis & Hyphantis, 2010; Lia et al, 2020). Health care workers directly involved with diagnosing, treating, and providing care of COVID-19 patients in China experienced a higher risk of depression, anxiety, insomnia, and distress (Lai et al, 2020). As health care workers continue to make life and death decisions, it is expected that the mental health toll on these workers will be tremendous during and after the pandemic. Other frontline workers, such as paramedics, police officers, firefighters, active military personnel, hospital staff, care home staff, pharmacists, and grocery store staff are also impacted psychologically. These essential workers interact with the public more frequently than other workers and are at a higher risk of contracting the virus. Protecting essential workers, especially health care workers, through public health measures is imperative during the pandemic (Lai et al, 2020). There is a need to promote mental health well-being among frontline workers during and following the pandemic.

4.6 Impact on individuals with mental health disorders

Individuals with mental health disorders are often overlooked during large widespread outbreaks as the focus is shifted towards other priority health needs, infected persons, and frontline workers (Yao, Chen & Xu, 2020). Individuals with mental health disorders are less likely to be able to access their regular health resources given the stringent restrictions in place during a pandemic. They may also be at higher risk for infection or contraction of the virus due to decreased cognitive function, awareness of risk, and personal protection (Yao et al., 2020). They may be more susceptible to emotional responses or stress brought on by the pandemic (Yao et al., 2020). There is very limited understanding of how a pandemic affects individuals with mental health disorders, and this is an important gap to address in future studies.

4.7 Mitigating Factors

Although there are multiple mental health issues that arise from pandemics, there are mitigating factors that can reduce psychological distress. Increased technology development and social media interaction allows for individuals to remain somewhat intact with a support system or with others around the world (Tansey et al., 2007). Increased access to media also provides individuals with access to up to date information and a sense of connection to others (Tansey et al., 2007). Consistent government public messaging and support can also provide a sense of comfort and security for individuals. Also, there is comfort in knowing that collectively the global population is impacted similarly, which can provide some level of unity.

Mental health preparedness for widespread pandemics should be developed with effective action plans worldwide, especially in countries where resources are abundant. When health resources are tremendously strained during a widespread pandemic, it is expected that mental health services will not be the principal priority during the pandemic (Chan, Lam & Chiu, 2009). However, there will be significant challenges to the

depth of the mental health impact following the pandemic, which will strain the health services even further. Psychological longitudinal surveillance may be necessary during this pandemic to identify important determinants of psychological distress and to improve understanding for future pandemics (Perrin et al., 2009).

5. Conclusion

As the course of the COVID-19 pandemic continues to unfold and is expected to affect global populations in multiple waves, there is an urgent need for mental health resource preparation. This will be especially apparent as the virus is contained or begins to slow down. Mental health issues need to be considered in order for appropriate programs and strategies to be developed. Direction and policies need to be put into place to effectively facilitate the burden of mental health in the months to come.

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The Asian Institute of Research
Journal of Health and Medical Sciences
Vol.3, No.2, 2020: 163-169
ISSN 2622-7258

DOI: 10.31014/aior.1994.03.02.110

Needlestick and Sharp Injuries Among Workers in Primary Health Care

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Abstract
Introduction: Needlestick injuries (NSIs) are one of the most frequent routes of the transmission of bloodborne pathogens in health care settings and the substantial source of occupationally acquired bloodborne infections. They remain a significant problem for developing countries that lack the ability to implement more reliable technologies and available guidance because of the economic situation. The objectives of the study were to determine the frequency of NSIs among healthcare workers (HCWs) and supporting staff in primary health care, to investigate the factors that caused these injuries and to evaluate a set of implemented guides. Methods: A retrospective study of the Department of infection control records of NSIs between January 2003 and January 2016 was conducted. Incidence proportion (rate of injury risk) was calculated for each profession with reported NSIs. Results: A total of 156 NSIs and sharp injuries were reported to the Department of infection control during the 12-year period. Among the group of HCWs, medical nurses/technicians (54.49%) were the most common injured workers, and the lowest numbers were reported by a physical therapist and dental technicians (0.64%). In a total number of cases, support staff accounted for 16.67%. The most incidents occurred during the use of needles, in 146 (90.6%) cases. Calculated incidence proportion for medical doctors is 0.24%, 5.33% for dentists, and 13.8% for medical and dental nurses/technicians and laboratory technicians. For support staff, the calculated rate is 6.04%. Conclusions: At the primary health care level, the NSIs frequency among all employee profiles is lower and it is suggesting the possibility of underreporting cases. Healthcare facility management should consider introducing new and more reliable technologies to reduce the number of NSIs especially among nurses/technicians, laboratory technicians, and cleaning staff. Additional training and preventive measures should be directed towards the proper disposal of medical waste. Management of the Institution presented engagement to prevent the occurrence of NSIs, and it is a positive example for all countries in transition.

Keywords: Needlestick and Sharp Injuries, Healthcare Workers, Support Staff, Primary Health Care

1. Introduction

Needlestick injury (NSI) is recognized as an important hazard for healthcare workers (HCWs) (Canadian Centre for Occupational Health & Safety [CCOHS], 2018). It is defined as an accidental percutaneous piercing wound caused by a contaminated sharp instrument (Phillips, 2012). These injuries can occur at any time when people use, disassemble, or dispose of sharp instruments. If the sharp instruments are undisposed of properly, they can cause injury to other workers who encounter them unexpectedly. NSIs are one of the most frequent routes of transmission in occupationally acquired bloodborne infections (CCOHS, 2018). Injuries have transmitted many diseases to HCWs, but the most significant infections are hepatitis B, hepatitis C and Human Immunodeficiency Virus (HIV). According to the World Health Organization, 1 in 10 HCWs worldwide sustains it each year (Prüss-Üstün, 2005). The average number of HCWs injuries annually for the Europe B region, where Bosnia and Herzegovina belong, is 0.93 (Rapiti, 2005). Every injury will not result with infection, but significant factors contributing to their development are infectivity of contaminated biological material, depth of the wound, length of exposure, degree of viremia of the patient, and health status of the HCW (Vasic, 2011). It is estimated that after an injury in workplace situations from a needle contaminated with hepatitis B virus, there is a 6 to 30% chance that an exposed person will be infected, 1.8% remains a chance of infection for hepatitis C, and 0.3% chance for HIV infection (Ontario Hospital Association & Ontario Medical Association, 2018). Of the three million accidental injuries among HCWs annually, 40-65% of hepatitis B viral infections develop in developing countries, while in developed countries the percentage is less than 10% (Elseviers, 2014; Singhal, 2011; Tandir, 2005).

The previously mentioned differences are due to the developed precautionary awareness, availability of immunization, improved sharp waste disposal practices, and post-exposure prophylaxis, which is consistent with the recommendations of the Centers for Disease Control and Prevention (CDC) continuously available since 1987 (Centers for Disease Control and Prevention [CDC], 2001). The implementation of adequate preventive measures can preserve the health capacity of employees, but at the same time significantly reduce the cost of testing and treatment, since annual costs are estimated at €7 million in Italy and $118 million to $591 million in the United States (Saia, 2010).

The incidence of HCWs exposures and occupational infections in Bosnia and Herzegovina is unknown. In our country there is no surveillance program for occupational exposures to bloodborne viruses, even though there are published rules for reporting (Official Gazette Federation B&H, 2010). Over the last decade in Bosnia and Herzegovina, the infection morbidity rates for hepatitis B, hepatitis C, and HIV infection have increased. Currently, the country is experiencing a migrant crisis, and most migrants coming from endemic areas towards above mentioned viruses. Therefore, the objectives of the retrospective study were to determine the frequency of NSIs among HCWs and supporting staff in primary health care, to investigate the factors that caused these injuries and to evaluate a set of implemented guides. Our results will provide practical information for improving the effectiveness of prevention strategies.

2. Method

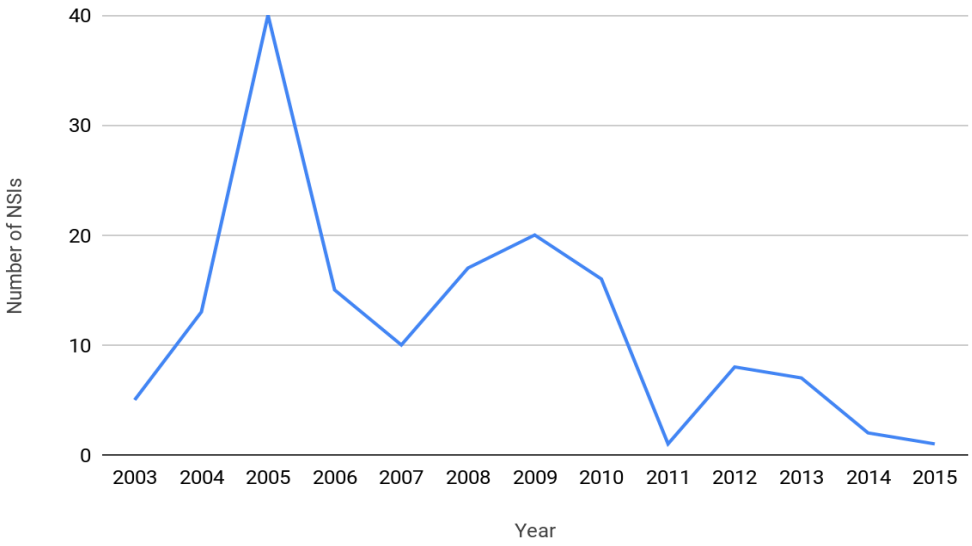
The Public Institution Health Centre of Sarajevo Canton is the largest institution in Bosnia and Herzegovina with 2031 employees. They are providing primary health care medical services to the general population. During 2017, they had 13.816,187 visits and services. A retrospective study of the Department of Infection Control records of needlestick injuries between January 2003 and January 2016 was conducted. Ethical approval was obtained from the Ethics committee of the Institution. Incidence Proportion (rate of injury risk) was calculated for each profession with reported NSIs according to available instructions (CDC, 2012). Collected data were analyzed in the statistical package SPSS 10.0 for Windows, and results are shown in charts and tables.

3. Results

A total of 156 NSI and sharp injuries were reported to the Department of Infection Control during the 12-year period. Of the 156 employees, 127 (81.41%) were females and 29 (18.59%) males. The mean age of individuals

was 40.5 ± 8.1 years. In total, 7.68% of employees had NSIs. The majority were reported during 2005, in total 40 (25.64%). The numbers of reported NCIs through the years are shown in Figure 1.

Figure 1. Reported NSIs of Public Institution Health Centre of Sarajevo Canton through years



Among the group of HCWs, medical nurses/technicians (85) were the most common injured workers, which constituted 54.49% of all reported NSIs. Twenty-one (13.46%) of the incidents were reported by laboratory technicians and eleven (7.05%) by dental nurses. Eight dentists (5.13%) and three physicians (1.92%) reported various causes of injuries. The lowest number of injuries among this group of workers was reported by a physical therapist and dental technicians (0.64%). In a total number of cases, support staff accounted for 26 (16.67%). Among them, the majority (13.46%) were reported by the cleaning staff. All results are presented in Table 1.

Table 1. Job category of workers with reported NSIs (2003.-2015.)

Group of workers	Job category	Number (n)	Percentage (%)
Healthcare workers	Medical nurses/technicians	85	54.49
	Laboratory technicians	21	13.46
	Dental nurses	11	7.05
	Dentists	8	5.13
	Physicians	3	1.92
	Dental technicians	1	0.64
	Physical therapist	1	0.64
Support staff	Cleaning staff	21	13.46
	Housekeeper	3	1.92
	Labware cleaners	1	0.64
	Security officer	1	0.64
	Total	156	100

The most reported incidents among all profiles occurred during the use of needles in 146 (90.6%) cases. Except for needles, laboratory technicians reported lancets in three (1.86%) and recapping in one case (0.64%). Among dental professionals, other sharp objects (dental explorer and elevator) were causes in individual cases (0.64%). Furthermore, the contact of blood (splash event) with mucous membranes of eyes was recorded by one dentist (0.64%), and it occurred during the extraction of teeth. During an intervention, the dentist didn't use personal protective equipment. There were, moreover, two attacks on staff by patients.

Calculated Incidence Proportion (rate of Risk) of NSIs for medical doctors is 0.24%, 5.33% for dentists, and 13.8% for medical and dental nurses/technicians and laboratory technicians. For support staff (cleaning staff, housekeepers, labware cleaners, security officers) the calculated rate of injury risk is 6.04%.

4. Discussion

The NSIs potentially represent one of the most significant dangers to HCWs. Although the world's umbrella authorities have been continuously issuing guides for over 30 years, undeveloped countries often do not have the ability to implement them, primarily for economic reasons. For healthcare providers, prevention programs that have a legal foothold and compliance with guidelines are more cost-effective than treating occupational infections. These infections serve as high occupational risks and threats to healthcare workers, especially where basic rules of occupational safety and health are unimplemented (Sagoe-Moses, 2001).

Changes in the organization of the work process, the investments in protective equipment and innovative technologies, the availability of immunization, the introduction of prevention programs and education of the HCWs provide benefits to all stakeholders. This was recognized as a priority by the management of the Public Institution Health Centre of Sarajevo Canton and resulted in the adoption of a series of internal regulations in 2005. Among them, the most significant places are taking Guides on preventing and controlling home infections and measures to spread the infection within a healthcare organization. They contain the methodology for the organization of the processes, implementation of hygienic-prophylactic and anti-epidemic measures and their control. Implementation of these measures, the introduction of immunization with the engagement of employees has significantly reduced the number of NSIs, as it can be seen in Figure 1. This type of approach is typical in highly developed countries, but for Bosnia and Herzegovina as an undeveloped country with still visible war consequences, has been a significant step forward. According to our results, over the twelve-year period, 156 (7.68%) primary health care employees reported NSIs. A higher prevalence of injuries was registered in a study by Musa et al. (63.3%), conducted at a secondary level hospital in Sarajevo (Musa, 2015). A significant difference can be related to the complexity of medical interventions or possible cases of underreporting. However, the problem of underreporting is also encountered in highly developed countries like Sweden (Voide, 2012). In the region, 85 injuries were registered in Serbia over a nine-year period, and at a clinical hospital in Zagreb 1.881 in two years, placing health care in fourth place in the total number of occupational injuries (Janićević, 2011; Ministry of Health of the Republic of Croatia [MHRC], 2015). According to the results presented by Cooke & Stephens, studies from various countries reported a broad range from 14.9% to 69.4% of HCWs who have experienced an NSI (Cooke & Stephens, 2017). Based on the study by Rapiti Elisabetta et al., the most modest number of HCWs injuries per year was registered in Saudi Arabia (Rapiti, 2005).

Among the HCWs group, the most significant number of NSIs was reported by medical nurses/technicians 85 (54.49%). The result of our study correlates with the studies conducted in the world (Cooke, 2017; Khraisat, 2014). Matsubara presented that 12.8% nurses had NSI and that their low risk rate is connected to adequate equipment and educational classes (Matsubara, 2017). This result supports our opinion that decreasing of NSIs is possible, but it requires a great deal of engagement. According to Cho, 92 nurses consider it is important to report all body fluid exposure, but 58% perform that properly (Cho, 2013). Raising of awareness should be one of the primary goals together with the provision of safe work equipment. Studies conducted worldwide reported different results for laboratory technicians. A lower representation was registered in India (1.1%), Croatia (8%), and Mauritius (11.9%) (Goel, 2017; MHRC, 2015; Subratty & Moussa, 2007). Our result (13.46) correlates with a study conducted in the Lao People's Democratic Republic (12.5%) (Matsubara, 2017). Mentioned results are significantly lower than in Africa (46.6%) (Auta, 2017). In total, 7.05% of dental nurses reported NSI and it is similar with the study conducted in Taiwan (7.55%) (Lee,2014).

Current results for medical doctors and dentists (1.92 and 5.13%) deviate from the results of studies conducted worldwide. The prevalence of NSIs among physicians ranges from 7.7% to 73.7% and dentists from 15.8% to 78.57% (MHRC, 2015; Matsubara, 2017; Goel, 2017; Lee, 2014; Khader, 2008). Reported differences in results and estimated risk for these HCWs profiles can be linked to the providing of simpler healthcare services at a primary health care level.

According to results of our study, notable attention should be directed to the group of support staff, since they significantly participate in the total number of NSIs (16.67%). Our results for the representation of NSIs in cleaning staff are correlated with the Khraisat and Musa studies in studies conducted in Malaysia and Bosnia and Herzegovina (12.8% and 15%, respectively) (Musa, 2014; Khraisat, 2014). The results imply the need for intensive training and control of staff work, especially in the segment of proper disposal of medical waste. We believe that future studies on NSIs should target the support staff group since the focus is solely on HCWs as a high-risk group.

The most frequent cause of NSIs in all employee profiles was a stab on a contaminated needle during the use and disposal of sharp waste (93.59%). Zhang and Cho reported significantly lower percentages (59% and 70.4%, respectively) (Cho, 2013; Zhang, 2015). This indicates that to reduce NSIs in the healthcare industry, it is necessary to introduce more reliable technologies into work, in line with the recommendations of the world authorities.

Our findings on the cause of NSIs in the dental service are correlated with Lee and Al Qahtani research conducted in China and Saudi Arabia (Lee, 2014; Qahtani, 2017). Although the representation of NSIs among dental staff is lower, excessive caution during manual work is important since they use a wide range of sharp instruments. The rate of injury risk based on our results varies from 0.24 to 13.8%. According to Elsevier et al. the risk rate based on different methodologies varied from 1.4 to 9.5 per 100 HCWs (Elseviers, 2014). Regarding the mentioned above, the possible impact on worker's well-being after NSI can be serious, and in most cases includes high level of stress.

5. Conclusions

At the primary health care level, the NSIs frequency among all employee profiles is lower and it is suggesting the possibility of underreporting cases. Healthcare facility management should consider introducing new and more reliable technologies to reduce the number of NSIs especially among nurses/technicians, laboratory technicians, and cleaning staff. Additional training and preventive measures should be directed towards the proper disposal of medical waste. Management of the Institution presented engagement to prevent the occurrence of NSIs, and it is a positive example for all countries in transition.

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The Asian Institute of Research
Journal of Health and Medical Sciences
Vol.3, No.2, 2020: 170-176
ISSN 2622-7258

DOI: 10.31014/aior.1994.03.02.111

Patient Satisfaction on Pain Management Post Open Cardiac Surgery at the First 24 Hours after Extubation in Hasan Sadikin Hospital Bandung, Indonesia

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Abstract
Assessment of postoperative cardiac pain management needs to be conducted to evaluate success in pain management after cardiac surgeries. Up to the present time, assessment of postoperative cardiac pain management has not been done in Indonesia. This study aims to determine the level of patient's satisfaction on pain management after having an open cardiac surgery at the first 24 hours post-extubation at Hasan Sadikin Hospital Bandung. A cross sectional study was conducted by using a questionnaire in the ICU of Hasan Sadikin Hospital Bandung from 18th June 2019 until 10th January 2020. The examination of patient satisfaction was carried out through the Indonesian-version of American Pain Society Patient Outcome Questionnaire Revised (APS-POQ-R). All 51 patients in that period agreed to participate in the study. The results showed that patients were satisfied (90.2%) and very satisfied (9,8%) with pain management in the first 24 hours after open cardiac surgery extubation at Hasan Sadikin Hospital. In summary, all patients were highly satisfied with pain management in the ICU of Dr. Hasan Sadikin General Hospital Bandung

Keywords: APS-POQ-R, Pain Management, Patient Satisfaction

1. Introduction

The number of open heart surgeries in the world reaches 800.000 cases each year. One third of open heart postoperative patients experience moderate to severe pain. Chronic pain after open heart surgery occurs around 21% to 51% of patients. The pain experienced is an unpleasant thing due to tissue damage (Lahtinen, Kokki, &Hynynen, 2006; Sattari, Baghdadchi, Kheyri, Khakzadi, & Ozar, 2013; Akhtar, Hamid, & Gangwani, 2015). The intensity of pain is higher in younger subjects. Inadequate postoperative analgesics cause several negative

effects, including chronic pain, tachycardia, increased of oxygen demand, hypercoagulation, pulmonary complications, psychological consequences, and decreased patient satisfaction. Pain at the site of the surgical incision and intubation results in prolonged immobility (Akhtar et al., 2015; Karabulut, Gurcayir, Yaman, Yilmaz, & Gokmen, 2015). Various methods have been used to control postoperative pain by using opioid and non-opioid drugs in bolus doses or intravenously. In addition, non-pharmacological techniques have been implemented to relieve pain, such as cold or hot compresses, meditation, and massage (Katz, & Seltzer Ze, 2009; Choiniere, Watt-Watson, & Victor, 2014).

The American Pain Society Patient Outcome Questionnaire Revised Questionnaire (APS-POQ-R) is the most commonly used instrument in several countries that were designed to assess the quality of pain management in hospitals during the first 24 hours after surgery in adult patients by measuring six aspects of quality, including (1) severity and pain reduction; (2) the impact of pain on activity, sleep, and negative emotions; (3) side effects of treatment; (4) the benefits of information about pain treatment; (5) ability to participate in pain treatment decisions; and (6) the use of non-pharmacological strategies (Akhtar et al., 2015; Gordon et al, 2010). Adequate postoperative pain management is important because it can reduce the risk of patient's morbidity (Karabulut et al., 2015; King, Parry, & Southern, 2008). Monitoring the quality of postoperative pain management needs to be done to minimize the possibility of inadequate pain management. The aim of this study is to determine the level of patient's satisfaction on pain management after having an open cardiac surgery in the first 24 hours post-extubation at Hasan Sadikin Hospital Bandung.

2. Methods

This cross sectional study was conducted from 18th June 2019 until 10th January 2020 in the cardiac intensive care unit (CICU) of Hasan Sadikin Hospital Bandung. Ethical approval has been obtained from Health Research Ethics Committee Universitas Padjadjaran Indonesia with number LB.02.01/X.6.5/191/2019. All post open cardiac surgery patients were between the age of 18 and 65 and agreed to join the study. Informed consent was taken preoperatively. Subject with chronic pain, on antipsychotic drugs, RASS score < 0 or > 0, and on emergency cases were excluded.

APS-POQ-R questionnaire in Bahasa was explained by the researcher and the patients answered the questions. All data were recorded on a questionnaire form. Data collected including socio-demographics, questions related to pain intensity, the effect on activity, side effects, patient's experience and satisfaction. Patient's satisfaction result was classified into poor (score 0-3), satisfactory (score 4-6), good (score 7-8), and excellent (score 9-10). The results of descriptive analysis were displayed in frequency and percentage. Data recording and statistical analysis were performed by using Statistical Packages for Social Science version 16 (SPSS Inc., Chicago, IL).

3. Results

Total 51 subjects participated in the study, among whom 12 (23.5.0%) were males and while 39 (76.5%) were females. Their mean of age was 50.98 ± 13.26 years. Almost 33.4 % of them were obese. Pain medications were varied among participants. There were 16 subjects (31.4%) who received morphine sulfate and 35 subjects (68.6%) who received combination of morphin and paracetamol. 36 subjects (70.6%) or most of the subjects underwent coronary artery bypass graft surgery while 15 subjects (29.4%) had valvular surgery. Other subjects' characteristics are enlisted in Table 1.

Table 1. Baseline characteristics

Characteristics	Value
Age (year)	
Mean±Std	50.98±13.26
Range	18–69
Gender (n, %)	
Male	39 (76.5)

Female	12 (23.5)
Weight (kg)	
Mean±Std	62.43±12.26
Range	42–115
Height (cm)	
Mean±Std	160.8±5.75
Range	150–175
Body Mass Index (BMI)	
Underweight	1 (2)
Normal	22 (43.1)
At risk	11 (21.6)
Obese 1	14 (27.5)
Obese 2	3 (5.9)
Education (n, %)	
Elementary - junior high school	10 (19.6)
High school	19 (37.3)
University	22 (43.1)
Canadian Cardiovascular Society (CCS) grading of Angina (n, %)	
CCS 1	23 (45.1)
CCS 2	28 (54.9)
ASA Classification (n, %)	
ASA II	32 (62.7)
ASA III	19 (37.3)
Smoker (n, %)	
Yes	17 (33.3)
No	34 (66.7)
Type 2 Diabetes (n, %)	
Yes	19 (37.3)
No	32 (62.7)
Hipertension (n, %)	
Yes	35 (68.6)
No	16 (31.4)
Surgery Operation Type (n, %)	
CABG	36 (70.6)
Valve	15 (29.4)
Extubation Period (n, %)	
First 24 hour	44 (86.3)
More than 24 hour	7 (13.7)
Medication Type (n, %)	
Morphin	16 (31.4)
Morphin dan Paracetamol	35 (68.6)

*CABG = Coronary Artery Bypass Grafting; BMI cut off score based on Asian classifiation

Most of participants stated that pain management was good (46 participants or 90.2%), while 5 participants (9.8%) stated excellent. In severity and pain reduction aspect, data analysis showed that the mean score of mild and moderate pain intensity in subject were 1.14±0.722 and 5.94±1.1 consecutively. The mean score of pain intensity relieved by taking pain medications was 8.84±0.758. There were several impacts of pain on activity and

negative emotions in patients. The mean score of movement and activity disturbance on the bed due to the pain from a scale of 0 to 10 was 2.47 ± 1.405. The mean score of anxiety was 2.73 ± 0.568, while the mean score of stress, fear, and helplessness was 0.73 ± 0.568, 1.55 ± 0.577, and 2.53 ± 0.542 respectively.

The mean score of nausea as a pain medication side effect in this study was 2.9 ± 1.025, while itching was 0.12 ± 0.588, dizziness was 0.2 ± 0.601, and drowsiness was 5.78 ± 1.119. Total 47 subjects (92.2%) received some information about pain treatment options before surgery. The mean score of subject's ability to participate in pain management decisions was 7.84±0.758. Majority of subjects stated that holding a pillow or scratching the side of pain (72.5%), and praying (80.4%) could minimize the postoperative pain, followed by immobility (51%), and deep breathing (33.3%) as methods of non-pharmacological strategy. The most common pain type was described as sharp by 21 subjects (41.2%). Pain mostly felt at the site of incision found in 24 subjects (47.1%). The most aggravating factor for pain was cough/deep breathing as experienced by 41 subjects (80.4%). Table 2 shows other pain responses of participants. Responses related to side effects of management were enlisted in Table 3.

Table 2. Pain intensity

Pain related interview	Value
Pain intensity (mean score ± std.dev)	
Mild	1.14±0.722
Moderate	5.94±1.1
Percentage of time that was in severe pain during ICU stay (n,%)	
≤30%	46(90.2%)
30% to 50%	4(7.8%)
>50%	1(2%)
Alleviating factors	
Pain medications (mean score ±std.dev)	8.84±0.758
Rest/staying immobile (n,%)	51(100%)
Breathing superficially (n,%)	17(33.3%)
Rubbing the pain site or holding a pillow on the chest (n,%)	37(72.5%)
Praying (n,%)	41(80.4%)
Factors associated with pain during ICU stay after extubation (n,%)	
Deep breathing	41(80.4%)
Ambulation	18(35.3%)
Turning or change of position	14(27.5%)
Back pain	2(3.9%)
Deep breathing + Ambulation	0
Type of pain (n,%)	
Sharp/cutting	21(41.2%)
Burning	14(27.5%)
Throbbing	16(31.4%)
Pressure	9(17.6%)
Area that patient feel the pain mostly (n,%)	
Incision site	24(47.1%)
Chest tube site	20(39.2%)
Back pain	11(21.6%)
Throat	4(7.8%)

Table 3. Patients satisfaction and responses regarding pain and medication services

Questions	Responses	Value
Receive information about pain management options before surgery (n,%)	Yes	47(92.2%)
Pain was interfering with mobility or movement (mean score ±std.dev)	2.47±1.405	

Side effects (mean score ±std.dev)	Nausea	2.9±1.025
	Itching	0.12±0.588
	Dizziness	0.2±0.601
	Drowsiness	5.78±1.119
Pain causing patient to feel (mean score ±std.dev)	Anxious	2.73±0.568
	Depressed	0.73±0.568
	Frightened	1.55±0.577
	Helpless	2.53±0.542
Patient satisfaction on pain treatment during ICU stay (n,%)	Excellent	5 (9.8)
	Good	46 (90.2)
	Satisfactory	0
	Poor	0

4. Discussion

Majority of participants were very satisfied with postoperative pain management in Hasan Sadikin Hospital (Table 3). This result was in line with several studies in Pakistan, Turkey and Bangkok that showed high levels of satisfaction in patients after open heart surgery. This may occur due to the quality of service that is already good, in accordance with pain management procedures (Akhtar et al., 2015; Karabulut et al., 2015; Al-Abri, & Al-Balushi, 2014; Mello, Rosatti, & Hortense, 2014). In this study, the type of medication used in most subjects was a combination of morphine and paracetamol (Table 1). Multimodal administration can reduce side effects of using just one drug. A study in Pakistan used combination tramadol and paracetamol in open heart postoperative patients (Akhtar et al., 2015). Most subjects stated that they felt pain for ≤30% within 24 hours. Only a few subjects reported to have experienced pain for a range of 30% to 50% and >50% within 24 hours (Table 2). A similar result was also found in another study (Akhtar et al., 2015). The results of this study also showed that pain was successfully alleviated by therapies. That was in line with the results of studies in countries mentioned above. It shows the effectiveness of pain reduction with therapy (Akhtar et al., 2015; Karabulut et al., 2015). Data in this study showed that the most aggravating factor for pain was cough/deep breathing, followed by moving, changing positions, and back pain. This result was in line with several other studies in Pakistan, Brazil, and Canada (Akhtar et al., 2015; Mello et al., 2014; Gelinas, 2007). A research conducted in Turkey showed that the most aggravating factor for pain was moving (Karabulut et al., 2015). Another study in Finland showed that pain is especially felt when coughing and moving (Lahtinen et al., 2006).

Majority of subjects in this study stated that the most common type of pain was sharp, followed by throbbing, burning and pressure (Table 2). Another study in Pakistan showed a similar result (Akhtar et al., 2015). On the other hand, a study showed different results in which most of subjects felt throbbing pain with a small number felt sharp pain. Pain expression is very subjective and can be influenced by several factors including social, environmental, psychological, and cultural factors (Aslan, Badir, Arli, & Cakmakci, 2009). The most common site of pain in this study was in the incision area, followed by chest tube area, back area, throat area, and in all areas (Table 2). The findings of this study were in accordance with other studies regarding the location, distribution and intensity of postoperative cardiac pain, with the highest level of pain is in the sternum area, epigastric region, and chest tube placement area (McNeill, Sherwood, Starck, & Thompson, 1998).

Most of subjects in this study claimed that immobility, holding a pillow or scratching the side of pain, and praying could minimize the pain (Table 2). A research in Pakistan showed a similar result and stated that the intensity of pain decreased further after the removal of the chest tube in several subjects (Akhtar et al., 2015). A study in Turkey showed that several subjects mentioned about the use of non-pharmacological interventions for pain management. The most commonly used non-pharmacological method was breathing exercises (Karabulut et al., 2015). A research conducted in the United States showed that more than half of the subjects used praying method, and less than a third of subjects used relaxation techniques, diversion of concentration, warm

compresses, cold compresses, and massage therapy as non-pharmacological methods in pain management (Mueller, Tinguely, Tevaearai, Revelly, & Chiolero, 2000).

In this study, almost all patients received information about pain management options (Table 3). Another study in Pakistan explained that pain control was discussed in only one third of subjects during the preoperative visit. Patients who were given information had a higher level of satisfaction than subjects who were not informed before surgery. Preoperative counseling about the use of analgesics to control pain can reduce the amount of pain killers after surgery (Akhtar et al., 2015). Several studies showed that the use of preoperative counseling in the first 48 hours after surgery decreases the amount of prescription painkillers (Kol, Alpar, & Erdogan, 2014; Silva, Pimenta, & Cruz, 2013).

The side effects that appear due to pain in this study based of mean score from highest to lowest were drowsiness, nausea, dizziness, and itching. It was in line with another study in Pakistan (Akhtar et al., 2015). In contrast to the results of this study, another research showed that the side effect experienced by most of the participants were nausea and vomiting. The higher incidence of nausea in that study population may be due to the fact that intravenous tramadol is the main narcotics given to patients (Karabulut et al., 2015). In this study, it is known that the most common pshychological side effect based on mean score was feeling helpless, followed by afraid, and depressed. A study in Pakistan stated that anxiety was associated with pain in some subjects (Akhtar et al., 2015). Another study study showed that patients with high levels of depression tend to complain of higher pain levels (Morone et al., 2010).

5. Conclusion

Patients in Hasan Sadikin Hospital from 18th June 2019 until 10th January 2020 were highly satisfied about pain management after open cardiac surgery.

Acknowledgments
We would like to express appreciation to Doddy Tavianto as the head of the Department of Anesthesiology and Intensive Care Hasan Sadikin Hospital, the study's participants, and to Dwi Monik Purnamasari who helped in data analysis.

Conflict of Interest
There is no conflict of interest to declare in this study.

Authorship
R.W.S wrote the manuscript with input from all authors. A.F.H, S, and R.W.S did a survey, analyse and interpret the results. The following participated in the analyses and interpretation of the data, R.H, A.P, R.A, and N.D. All the authors reviewed and approved the final manuscript.

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The Asian Institute of Research
Journal of Health and Medical Sciences
Vol.3, No.2, 2020: 177-183
ISSN 2622-7258

DOI: 10.31014/aior.1994.03.02.112

Management of Septic Shock According to SSC 2016 in Post Laparotomy Exploration due to Gastric Perforation

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Abstract
According to International Guidelines for Management of Sepsis and Septic Shock 2016, sepsis was defined as life threatening organ dysfunction caused by a dysregulated host response to infection. Sepsis and septic shock are major healthcare problems and the incidence increased by year. Septic Shock was defined as subset of sepsis in which underlying circulatory and cellular metabolism abnormalities are profound enough to substantially increase mortality and can be identified with persisting hypotension requiring vasopressors to maintain MAP>65mmHg and having serum lactate level > 2 mmo/L despite adequate volume resuscitation. Intraabdominal infection was reported as contributor to a high mortality rate for infection case in intensive care units. We reported a case of a patient with sepsis and septic shock caused by intraabdominal infection post laparotomy exploration ec gastric perforation. The patient was monitored prospectively, received antibiotics, hemodynamic support and mechanical ventilation support while being treated in the ICU. On the sixth day, the patient was transferred to ward.

Keywords: Sepsis, Shock, Septic, Intraabdominal, Infection

Introduction

Sepsis was defined as life threatening organ dysfunction due to dysregulation or disproportion of immune response to infection, a major health problem and reported incidence continue to increase.[1] Several studies reported sepsis as the leading cause of death in critically ill patients throughout the world, in spite of its uncertain incidence. Septic shock is defined as subset of sepsis in which underlying failure in notably circulatory and cellular metabolism which may significantly increase mortality. Septic shock is characterized by persisting hypotension requiring vasopressors to maintain MAP≥65mmHg and having serum lactate level > 2 mmo/L despite adequate volume resuscitation with mortality reaching 40%.[1]

Sepsis is the main cause of death in the Intensive Care Unit (ICU), with almost 15% diagnosed sepsis and two-thirds of these fall in septic shock. Sometimes patients treated in the ICU also have accompanying diseases which aggravate their condition and organ failure which increases mortality. A study stated 60% of 305 patients with severe sepsis experienced lung infection followed by 39% due to abdominal infection. In an observation

conducted by the Complicated IAI Observational World (CIAOW) in 2014 stated that the source of infection were intraabdominal infection, as much as 14.3%, ranks third, after appendix 34.6% and cholecystitis 14.8%, as for mortality due to Intraabdominal Infection (IAI) reached 10.7%. Etiology of IAI mostly includes gram-negative *Escheria coli* bacteria and gram-positive *Enterococus faecalis*.[2]

Management of sepsis based on International Guideline for Management of Surviving Sepsis Campaign (SSC) 2016 includes crystalloid fluid resuscitation for at least 30 mL/kg iv in the first three hours to overcome hypoperfusion caused by sepsis. Additional fluid can be administered after reevaluation of hemodynamic status, whether pulse, blood pressure, arterial oxygen saturation, breathing frequency, temperature, urine output, etc., with invasive or non-invasive devices as available. Assess cardiac function, predict fluid responsiveness, maintain MAP 65 mm Hg with vasopressors, normalize lactate, take microbiological culture samples, and give antibiotics immediately after diagnosis of sepsis within the first 1 hour.[3]

Patients who experienced sepsis after intraabdominal infection should get their source of infection controlled, treated in the ICU and get correct antibiotics to avoid complication towards better improvement.

Case Report

A 68 year old woman from a private hospital presented to the emergency department of Hasan Sadikin General Hospital Bandung with generalized abdominal tenderness and difficulties to defecate since two days prior admission, it was accompanied with epigastric pain two weeks prior admission aggravated by pressure but without vomiting. She admitted taking medicine and herbs for back pains and a year history of uncontrolled hypertension, with highest systolic blood pressure 160 mmHg but unknown diastolic pressure.

In the emergency department, the patient was conscious but with severe general condition; blood pressure was measured 115/70 mmHg, heart rate 118x/min, respiratory rate 34x/min, no additional lung sound was found in physical examination, body temperature of 37.7^{o}C, *Numeric Rating Scale* (NRS) 4-5, oxygen saturation (SpO_2) 99% with O_2 in *non-rebreathing simple mask* (NRM) 10 lpm. Laboratory investigation shown hemoglobin (Hb) 13.1 g/dL, leukocyte count 11.820/µL, hematocrit (Ht) 39.5%, thrombocyte 261.000/µL, prothrombin time (PT) 15.5, INR 1.42, *activated partial tromboplastin time* (aPTT) 34.4, free blood glucose (FBG) 111 mg/dL, SGOT 26, SGPT 17, albumin 2.05, ureum (Ur) 108.1 mg/dL, creatinine (Cr) 1.65 mg/dL, lactate 3.0 mmol/L, pH 7.451, pCO_2 32.5 mmHg, pO_2 145.7 mmHg, HCO3 22.9 mmol/L, BE 0.1 mmol/L, SaO2 99.11%, blood gas analysis (BGA) mixed vein SaO2 68.2%. Chest radiology result from previous hospital was bilateral pneumoperitoneum, cardiomegaly with aorta atherosclerosis without pneumonia. Electrocardiogram showed infrequent unifocal VES (Figure 1).

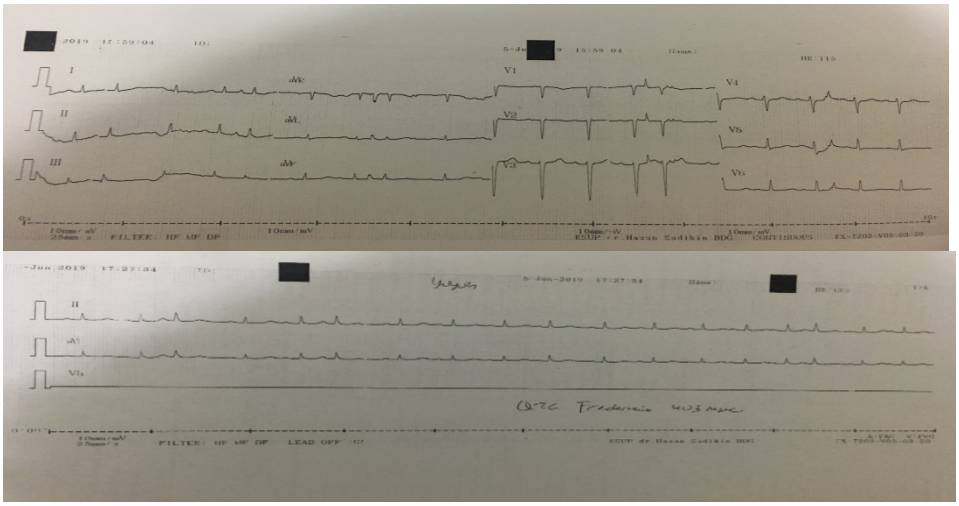

Figure 1 Electrocardiogram in emergency department
Source: private documentation

Patient was priorly diagnosed as diffuse peritonitis due to Suspected Hollow Viscus Perforation; Suspected Gastric Perforation; Hypertensive Heart Disease; Stage I Acute Kidney Injury, was given 1800 cc NaCl 0.9% intravenous fluid in the first 6 hours and continued by 1800 cc for 18 hours; combination of intravenous antibiotics including ceftriaxone two grams every 24 hours and metronidazole 500 mg every eight hours, also planned to have laparotomy exploration.

After being consulted to Anesthesiology Department, consciousness was decreased to 14, blood pressure 90/72 mmHg, heart rate 120x/min, respiratory rate 24x/min, temperature 37.8^{o}C, NRS 5-6, SpO2 99% with NRM 10 lpm. Crystalloid Ringer Lactate solution was given for 2000 cc and started norepinephrine from 0.05µg/kg/m. Central Venous Catheterization (CVC) was done in right subclavian vein before laparotomy. Pneumoperitoneum and 70 cc intraabdominal greenish fluid were identified during laparotomy.

Surgery was done with general anesthesia. Perforation in pre-pyloric area with diameter of 1 cm was fixed by primary suture, omental patch and done biopsy. During operation, patient received 900 cc of crystalloid solution with average blood loss of 150 cc and urine output 200cc. Hemodynamic status during the two hour surgery using norepinephrine 0,05-0,2µg/kg/m had an average systolic pressure 90-140 mmHg, diastolic 60-78 mmHg and heart rate 78-130x/min. After surgery, patient was transferred to *Intensive Care Unit* (ICU).

In the ICU, patient was under sedation with blood pressure 95/54 mmHg, heart rate 67x/min using norepinephrine 0,05µ/kg/m , SpO2 97-99%, ET no. 7.0 connected to SIMV mode ventilator with PS 16, PEEP 5, fiO2 70%, peak pressure 26-28 TV 320-370 cc. Hemodynamic monitoring, signs of blood loss, urine production, fluid balance was monitored, sample was taken for bulyon culture. Antibiotics were changed to combination of meropenem 1 gram and metronidazole 500 mg every eight hours intravenously, with morphine 10µ/kg/hr iv and paracetamol 1 gram every 6 hours.

On the first day in ICU, patient was stable with E2M2Vt under sedation. Systolic blood pressure (SBP) shown 95-127 mmHg, diastolic blood pressure (DBP) 54-72 mmHg, heart rate (HR) 67-84x/min with norepinephrine 0,05 µ/kg/hour and temperature 36-36.5^{o}C; respiratory rate (RR) 16x/min with SIMV ventilator mode PS 12 PEEP 5 fiO2 70% and tidal volume 320-360 cc; urine production 0,4-0,5 cc/kg/hour, cumulative of 670 cc/4 hours with balance +1566 cc. NGT showed dark production with positive bowel sound, abdomen was not found distended. Meropenem and metronidazole antibiotics were continued. Post-operative laboratory result shown Hb 11.5 g/dl, Ht 35.2%, Leucocyte count 12240/mm^3, trombocyte 206000/mm^3, Ur 101.6, Cr 1.22, PT 16,8, INR 1.55, APTT 39.80, FBG 103, Na 140, K 4.3, Cl 114, Ca 4.29, Mg 1.6 and Albumin 1.68.

On the second day, consciousness was E4M6Vt, with SBP 105-152 mmHg, DBP 54-72 mmHg and MAP 71-98 mmHg, HR 70-84x/min with norepinephrine 0.05µg/kg/min, temperature 36-36.5^{o}C, RR of 16x/min, SpO2 96-98% with SIMV ventilator mode PS 16 PEEP 5 FiO2 70% and tidal volume 360-540 cc. NGT production was still dark without abdominal distention and positive bowel sound. Patient was given TPN Triofusin 500cc/24 hours and aminofluid 1000 cc/24 hour. Ventilator was set to PSIMV PEEP 5 FiO2 70% then weaning was done with PS to 9 and FiO2 to 50%. The patient received Ringer Lactate intravenous (iv) fluid 1000 cc/24 hour, meropenem iv, metronidazole iv, norepinephrine 0.05µg/kg/hour, 2 gr of magnesium iv, 2 gr of calcium gloconas iv, extra Digoxin 500 µg iv. Second day laboratory results showed SGOT 46, SGPT 23, total bilirubin (BT) 0.632, direct bilirubin (BD) 0.301, indirect bilirubin (BI) 0.331, lactate 2.1, mixed vein pH 7.278, pCO2 65.0, pO2 65.0, HCO3 21.2, BE -4.9, SaO2 88.0. Chest xray shown minimal right pleural effusion, cardiomegaly without lung edema, aorta atherosclerosis with no signs of pneumonia as in Figure 2.

On the third day, patient was stable with consciousness E4M6Vt, vital signs shown SBP 138-161 mmHg, DBP 56-72 mmHg, MAP 83-101, HR 60-102 x/min with norepihephrine 0.05µg/kg/hour. Ventilator weaning was done by changing mode to CPAP PS 15 PEEp 5 FiO2 50% and tidal volume 500-710 cc. Diuresis was found 0.8-1.2 cc/kg/hour with balance +256 cc and a cummulative of 1985 cc/24 hour. Nutrition and antibiotics were still as previous days, intravenous dexmedetomidine 0.2µg/kg/min and omeprazole 40 mg every 12 hours were added. NGT production was still dark without abdominal distention and positive bowel sound. Third day laboratory results showed Hb 9.5, Ht 29.9, leucocyte count 15170, thrombocyte count 185000, FBG 174, lactate 1.3, Ur 136, Cr 1.7, Na 139, K 4.9, Cl 117, Mg 2.7. Echohemodynamic examination was done and shown CO

5.2 L/min, CI 3.05 L/min/m^2 SV 42 cc/beat SVR 1046 dynes.sec.cm^{-5} LVOT Umax 1.17 m/s , LVOT Umin : 0.79 ml/s, Dist. Index 32 %, IVCmax 2.24 cm, IVCmin 1.94 cm, Dist. Index : 13%; fluid responsive, fine CO with support and suggestive additional fluid administration was seen.

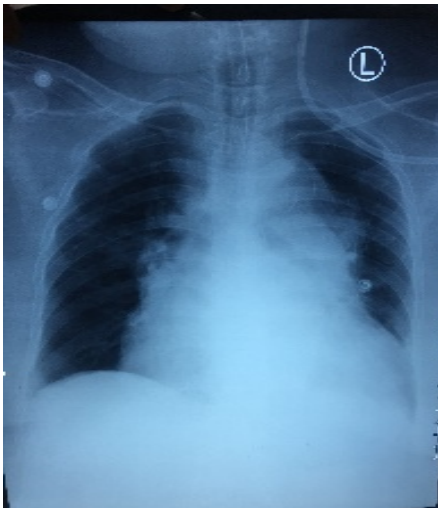

Figure 2 Chest x-ray result in the ICU
Source: private documentation

On the fourth day, patient was stable with E4M6Vt, vital signs were SBP 120-154 mmHg, DBP 60-70 mmHg, MAP 80-98 mmHg, HR 54-68x/min, RR 16-20x/min, SpO2 98-99%, Ventilator mode CPAP PS 1-15 PEEP 5 FiO2 50%, temperature 36.4-37.1 ^{o}C, diuresis 1-1.7 cc/kg/hour, balance -492 cc with a cumulative of 2476 cc/24 hour. Antibiotics and medications were still as previous days. Ventilator weaning was done with removing ventilator and connecting ETT to T-piece at 14.00 and extubation was done at 18.00. NGT had no retension, laboratory results showed FBG 143, Na 139, K 4.1, CL 111, Mg 2.4, Ca 4.99, pH 7.454, pCO2 39, pO2 129.7, HCO3 27.8, BE 4.1, SaO2 97.2. Sputum examination was done.

On the fifth day of treatment, amlodipine 10 mg, captopril 12.5 mg and perdipine iv 0.5µg/kg/min were given for the increasing blood pressure.

On the sixth day, laboratory results showed FBG 159, Na 139, K 4.0, Cl 105, Mg 1.9, Ca 4.83, patient was moved to *High Care Unit* (HCU). Patient was given RL solution 500 cc/24 hours, liquid diet with calory needs of 1500 to 2400 kkal. Urine production shown >0.5-1 cc/kg/hour with cumulative balance of -2778 cc.

Discussion

The word sepsis derives from the Greek word “sepo” which means “I rot” and was first mentioned in the poems of Homer (18th century BC). In 1914, Hugo Schottmuller formally defined “*septicaemia*” as a disease caused by microbial blood stream invasion. Despite its definition, terms such as septicaemia, sepsis, toxemia and bacteremia were often overlapped.

Sepsis is now known as a condition involving early activation of pro-inflammatory and anti-inflammatory response in the body. Along with this condition, circulatory abnormalities such as decreased intravascular volume, peripheral vascular vasodilation, myocardial depression, and increased metabolism generate an imbalance between systemic oxygen delivery and oxygen demand which will lead to systemic tissue hypoxia. The pathophysiology of this condition starts with reactions to infection which will trigger neurohumoral response in the presence of pro-inflammatory and anti-inflammatory responses, starting with cellular activation of monocytes, macrophages and neutrophils that interact with endothelial cells. Subsequent bodily responses include mobilization of plasma contents as a result of cellular activation and endothelial disruption. Plasma contents include cytokines such as tumor necrosis factor, interleukin, caspase, protease, leukotriene, kinin, reactive oxygen species, nitric oxide, arachidonic acid, platelet activating factor, and eicosanoids.

Proinflammatory cytokines such as tumor necrosis factor α, interleukin-1β, and interleukin-6 will activate the coagulation chain and inhibit fibrinolysis. Activated Protein C (APC) is an important modulator of the coagulation and inflammatory chains that enhances the process of fibrinolysis and inhibits the process of thrombosis and inflammation. Activation of the complement and the coagulation chain help strengthen the process. The interaction dominantly occurs in vascular endothelium and as a result microvascular injury, thrombosis and capillary leakage will follow and leads to tissue ischemia. This endothelial disorder plays a role in the occurrence of organ dysfunction and global tissue hypoxia.

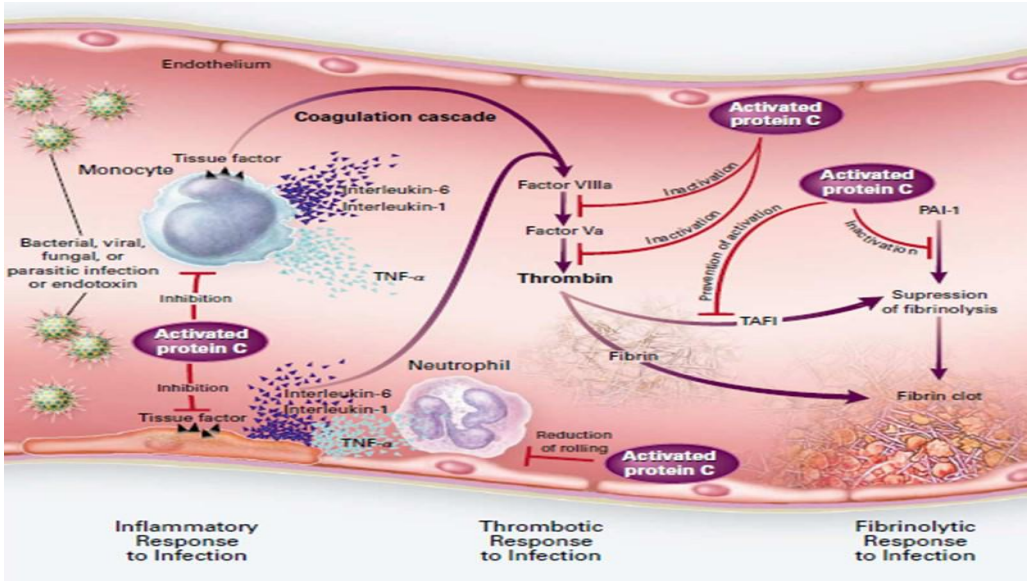

Figure 3 Coagulation Chain started with inflammatory response, thrombosis and fibrinolysis as response to infection.

Source: Bernard GR, Vincent JL, et al.[9]

According to a study in 2014 that explains the wide pathophysiology of sepsis, identification of sepsis with SIRS criteria is no longer appropriate because SIRS indirectly stated dysregulation of body response to infection.[4] An amount of patients were admitted to the hospital with SIRS criteria but ultimately without evidence of infection. Pathological condition in the state of sepsis affects almost every component of micro-circulating cells including endothelial, smooth muscle cells, leucocyte, erythrocyte and tissues. Microcirculation determine oxygen availability for each cell and tissues which ensures organ functions properly and if not corrected properly may cause respiratory distress in tissues and cells and leads to macro circulation dysfunction and finally results in one and multiple organ failure.

Management of sepsis based on *Surviving Sepsis Campaign* (SSC) guideline were implemented to sepsis bundles with revised consensus that issued *hour 1 bundle* with the aim of providing resuscitation and sepsis management as soon as possible, to prevent subsequent organ dysfunction, in the first hour after patient was identified as having organ dysfunction with Quick SOFA (qSOFA) criteria that includes 2 out of three following criterias: Respiratory rate ≥22 x/min, loss of consciousness and systolic blood pressure of ≤ 100 mmHg, make sure hour 1 bundle is carried out as the main priority that is to measure of lactate levels, re-measuring if previous lactate levels >2 mmol/L, blood culture examination before administration of antibiotics, administration of broad-spectrum antibiotics, administration of crystalloid fluids 30 cc/kg if there is hypotension or lactate levels ≥ 4 mmol/L, administer vasopressors if hypotension occurs either during or after fluid resuscitation, to maintain the MAP value ≥ 65 mmHg.[3] In this patient, before surgery was planned, qSOFA score was found ≥3 including loss of consciousness with glassglow coma scale from 15 to 14, respiratory rate 24x/min and decreasing SBP 90 mmHg. In accordance with one hour bundle, lactate levels were examined and showed 3.0 mmol/L, but in the next 2 hours no lactate examination was done, a study stated that using lactate levels as a guide in resuscitation, decreased mortality rates. She was then given 2000 cc intravenous Ringer Lactate crystalloid fluid for resuscitation, broad spectrum intravenous antibiotic Ceftriaxone 2 gram every 24 hours and Metronidazole 500

mg every eight hours, vasopressor norepinephrine was used starting 0.05μg/kg/min. Blood culture was obtained after surgery in the ICU.

Next management focused on controlling the source of infection where most sepsis diagnosis may need emergency operation for diagnostic and infection source control. Laparotomy exploration was done for suspected gastric perforation in this patient. Empirical antibiotics with adequate concentration in the first hour after diagnosis were given. Administration of antibiotic must be evaluated everyday to prevent antibiotic de-escalation. Use combination of antibiotics for septic shock patients, neutropeni patients and patients with multi drug resistant pathogen microbial infection. Duration of therapy may range from 7-10 days, longer usage may be given to delayed clinical response patients, *S. aureus* bacteremia, fungal infection, viral infection or immunological deficiency. Low procalcitonin levels may be used for guidance to stop antibiotic therapy in patients earlier with sepsis.

Abdominal sepsis is sepsis due to in intra-abdominal infections with or without peritoneal involvement, intra-abdominal infection is divided into Community Acquired IAI (CCA-IAI) and Health Care Acquired IAI (HC-IAI). Based on the extent of the infection, it is divided into Uncomplicated IAI, which is a one organ infection without damage of intra-abdominal organs and Complicated IAI, which is an infection that extends from the source of the infectious organ into the peritoneum through the perforated viscus.[6]

Guidelines issued by IDSA regarding diagnosis and management of intra-abdominal infections in 2010 recommend the administration of broad-spectrum empirical antibiotics to overcome the activity of gram-negative bacteria including meropenem, imipenem-cilastatin, doripenem, piperacillin-tazobactam, ciprofloxacin or levofloxacin in combination with metronidazole, or administration of ceftazidime, or cefepime in combination with metronidazole for high-risk community acquired IAI patients (late intervention> 24 hours, APACHE II score ≥15, extreme age, comorbid organ dysfunction, and low albumin).[7] In this patient, intravenous empirical antibiotic meropenem was given 1 gram every 8 hours and metronidazole 500 mg every 8 hours. Blood culture and sputum examination were also obtained but resulted no growth of microorganism.

Patient was treated in the ICU post operatively and given mechanical ventilation support with consideration of having major surgery, geriatrics with unstable cardiovascular condition, as previously seen VES unifocal infrequent + AF RVR on echocardiogram and received Digoxin during operation and on the first day of ICU hospitalization, as seen clinically, no lung problems was found but chest X-ray revealed minimal pleural effusion. Ventilator weaning gradually went well every day until patient was extubated. In accordance with the 2016 SSC recommendations, the use low tidal volume is reecommended in adult patients with respiratory failure induced by sepsis without ARDS, by giving tidal volume 4-6 cc/kg may offer good results, reduce the duration of mechanical ventilation usage, reduce the incidence of subsequent ARDS, and, in sepsis patients with abdominal surgery, the use of low tidal volume may reduce the incidence of respiratory failure and decrease the length of stay in the ICU.[1]

Enteral nutrition in the first 24-48 hours of treatments in the ICU was recommended as nutritional management in sepsis and septic shock patients.[1] Administration of only parenteral nutrition or combination of parenteral and enteral nutrition is not recommended in patients that are able to be given enteral nutrition. Parenteral nutrition is more invasive, increases the risk of infection, does not reduce mortality, and is high cost. [8] In this patient, on the first day of ICU treatment, parenteral nutrition is given directly without combination with enteral, because patient fasted until the 5th postoperative day.

During treatment at the ICU, hemodynamic monitoring, hemodynamic support, urine production and fluid balance monitoring, empirical antibiotics, mechanical ventilation, sedation, analgesia, with the aim of giving better tissue perfusion. On the fifth day of treatment at the ICU, the patient was transferred to the ward in a stable condition.

Conclusion

Septic shock is a part of sepsis based on circulatory and cellular metabolic failure that may increase mortality significantly. Early and adequate diagnosis of sepsis since patient was admitted to emergency department, accompanied by appropriate management of sepsis such as fluid resuscitation, hemodynamic support, source control surgery, specific antibiotic administration will improve patient's outcome and reduce morbidity as well as mortality.

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The Asian Institute of Research
Journal of Health and Medical Sciences
Vol.3, No.2, 2020: 184-184
ISSN 2622-7258

DOI: 10.31014/aior.1994.03.02.113

Current Research Status of SARS-CoV-2 as a Pathogen of COVID-19

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Abstract
COVID-19 was first identified in an outbreak in Wuhan, China, in December 2019. COVID-19 is defined as Corona Virus Infectious Disease 2019, and it's caused by SARS (severe acute respiratory syndrome)-CoV (coronavirus)-2. This article shows the current research status on SARS-CoV-2.

Keywords: SARS-CoV-2, Vaccine

SARS-CoV-2 is a positive-sense single-stranded RNA virus, and its sequence was analyzed and compared to SARS-CoV (outbreak in 2002.11.16～2003.7.5), and another Bat-RaTG13, Pangolin, Bat-SARS-CoV-related (Andersen, 2020).

First of all, the characteristic feature of this virus has a receptor-binding domain of ACE2 (Angiotensin-converting enzyme) which bind host cell receptor. ACE is one of the Renin-Angiotensin-Aldosterone System (RAAS) which raises blood pressure.

The second feature of this virus has a cleavage site of surface Spike protein which newly acquired 4 amino acids compared to other coronaviruses. It is a unique amino acid that binds tightly and cleavage the host surface. This site is contributed to be one of the vaccine candidates. Actually, 5 candidates of Vaccine are now estimated in humans (Le, 2020). Making of vaccine after animal experiment needs 1 or 2 years.

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The Asian Institute of Research
Journal of Health and Medical Sciences
Vol.3, No.2, 2020: 185-195
ISSN 2622-7258

DOI: 10.31014/aior.1994.03.02.114

Perceived Service Quality, a Key to Improved Patient Satisfaction and Loyalty in Healthcare Delivery: The Servqual Dimension Approach

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Abstract
Hospital's perceived service quality is a degree of discrepancy between patients' perceptions and their expectations about hospitals services. The quality of services which is provided by healthcare providers emphasizes the actual hospital service process. In the hospital, patients' satisfaction and hence loyalty could be widely used to determine hospital service quality. The study adopted a regression and path analysis utilizing SmartPLS V3.2.8; a second-generation multivariate data analysis method (PLS-SEM) approach to analyze the influence of perceived quality of services of hospitals on patient's satisfaction and loyalty based on the SERVQUAL dimensions. The study used data from (562) out-patients who had received services from (4) four major private hospitals in Ghana using purposive census sampling technique. Based on the analysis results, all five dimensions of the health services quality predictor of patients' level of satisfaction and loyalty to the hospital's services, explained that patients' satisfaction and loyalty was affected by all dimensions of health service quality (RATER) simultaneously. Nonetheless, different impacts will be obtained if all dimensions were measured separately. The study incited that patients' satisfaction and loyalty are influenced by the quality of medical/hospital services through its five components: reliability, assurance, tangibility, empathy and responsiveness.

Keywords: Private Health/Clinic, Service Quality, Patient Loyalty, Satisfaction, PLS-SEM

Introduction

Competition within the provision of well-being services triggers enhancements in effectiveness, productivity and quality of care (Ferrand et al., 2016). Increasing competition among health administrations drives patients to select a hospital/clinic with a trusted track record as clinics compete for patients by making strides in its quality of services which is a vital element to realize patients' fulfillment and loyalty towards the hospital/clinic (Brown et al., 2016; Erickson, Rockwern, Koltov, & McLean, 2017). Clinic/hospital service quality is a degree of

disparity between patients' discernment's and their desires of hospitals/clinic services(Fatima, Malik, & Shabbir, 2018). Service quality which is given by medical staff of hospitals emphasizes the actual hospital/clinic service process (Namana & Al-Dori, 2018). Within the hospital, patients' fulfillment might be broadly utilized to decide hospital/clinic service quality (Budiwan, 2016) as past studies investigated that patient loyalty and service quality were influenced by understanding satisfaction creation (Setyawan, Supriyanto, Tunjungsari, Hanifaty, & Lestari, 2019). Quality of healthcare services has been a contention centered around three components: quality of structure (tangibles), quality of process (services given by therapeutic staff) and results (impacts of care arrangement on patients' contentment) (Ferreira & Marques, 2019), as these strike as critical factors which can be useful for distinguishing and improving organization's performance in the era of intense competition (Farooq et al., 2018; Jamaluddin & Ruswanti, 2017). In principle, making improvements as an extension of more better access to healthcare provision from organizational boundaries is additionally imperative to realize the foremost hoisted benchmarks for quality care (Setyawan et al., 2019). Per work in literature healthcare providers can by leeway achieve high quality of healthcare administrations if they can tune into their patients' needs and count such inside the well-being services provision as healthcare organizations are subsequently, obliged to be more inventive and innovative in engaging clients, by endorsing products, services and administrations that best addresses needs and command patronage by its clients (Asnawi, Awang, Afthanorhan, Mohamad, & Karim, 2019; Kalaja, Myshketa, & Scalera, 2016).

Patients are the determinants of the healthcare framework, and this often than not quest healthcare service providers a vital notch to supply the most noteworthy service needed for a better, effective and viable quality of care (Rosha & Kaur, 2018) this comes off as rapid advancements in competitive business environment, customer expectations and demands keep increasing on the daily, leading to a situation where most companies find it difficult to retain their customers (Bentum-Micah et al., 2019; Farooq et al., 2018; Fatima et al., 2018). Progressing health services into a friendly clinic and understanding both therapeutic staff and patient's fulfillment strengthen and reinforce the management of well-being care institutions and guarantee the patients' satisfaction towards the hospital and its services as a whole, which transcendently draws positive consumer behavioral intent or general demeanor (Janicijevic, Seke, Djokovic, & Filipovic, 2013; Mankar, Velankar, Joshi, & Nalgundwar, 2013).

Underling our understanding of quality of service may well be the foremost broadly utilized instrument of SERVQUAL, which was developed by Parasuraman of the *Marketing Science Institute* (Alex & Ondiek, 2014; Parasuraman, Zeithaml, & Berry, 1988) with five measurements of service quality. SERVQUAL/RATER instrument comprises of: Reliability, Assurance, Tangibles, Empathy, Responsiveness, which is used as a measure of consumers expectations (before) and perception (post usage) of a service (Ahrholdt, Gudergan, & Ringle, 2017). Per evidence in literature, service quality determinants can be divided into two primary categories: the tangible and intangible components of a service. Tangible measurements allude to physical facilities, restorative staff, communication and any others of the service components that can be seen and readily felt. Intangible dimensions comprise of four sub-sectors which then is categorized into reliability, responsiveness, assurance and empathy. Earlier studies have illustrated that all the service dimensions had to a certain degree a positive connection with patients' satisfaction, with tangibility, reliability and assurance been the foremost indicators of patient's satisfaction and loyalty of the patients to the service (Setyawan et al., 2019). SERVQUAL measurements give a positive understanding to the health teach where they ought to center to provide better service to the patients (Aliman & Mohamad, 2016).

Although measurement of service quality has gotten an extraordinary bargain of attention in driving satisfaction and loyalty amongst patrons and providers of the healthcare service, quality of service of the clinic industry in developing nations like Ghana still remains one with an exhaustive examination still required (Boadi, Wenxin, Bentum-Micah, & Jerry, 2019; Paul & Sahadev, 2018; Tenkorang, 2016). With globalization fueling fierce competition in the service sector of the global economy, the hospital's principal goal in building patient satisfaction and driving loyalty is perhaps one embedded in understanding the link between specific dimensions of quality healthcare service delivery, patient satisfaction, and patient loyalty. Linking the conceptual and empirical measurement of the relationship between these dimensions of quality of service, satisfaction of the patients and hence their loyalty to the hospital is key into turning concepts into a core marketing instrument (Farooq et al., 2018). With the over-reliance of densely populated patients on the services of public hospitals

with few healthcare specialist in developing countries like Ghana, due to the governments subsides on healthcare costs of patients in public hospitals and a few approved private hospitals in a quest to reducing financial burden for the general populace and ensuring access to primary healthcare for all with little or no financial shocks, there only leads to a healthcare trap with patients experiencing low to no forms of customer service satisfaction at all in such conditional settings. Nonetheless, with their daily unmet needs, these patients have little to no option than to return to the same hospitals and it services that leave them dissatisfied on the regular (Anabila, 2019; Bucher, Jäger, & Prado, 2016).

Irrespective of the many undocumented report of outcries of patients by the media, most of these investigates into the service delivery by healthcare providers have only to a larger extent been led in public clinics. There isn't much extant work in literature to fully address this connection in the context of private hospitals in developing countries as Ghana as described in the foregoing lines of assertions, meaning work in this sector is still understudied. This study, therefore, seeks to fill this gap in literature. Again, there is no well-designed study examining the exact effects of each of the SERVQUAL dimensions on patient's satisfaction and loyalty to private healthcare delivery in a developing country like Ghana. Essentially, the use of variance based structural equation model (PLS- SEM), has been under-utilized in this setting. And so, our investigation will also determine the most vital quality dimensions and their predictive estimation and significance on the patient's satisfaction and loyalty creation in the delivery of private healthcare.

Given the past empirical findings, it would be only reasonable to hypothesize the positive impacts of the service quality on the patients' satisfaction and loyalty via enhancing the SERVQUAL dimensions. Thus, this study aimed at examining the hypothesized effects of the impact of the quality of service on patients' satisfaction and loyalty through the SERVQUAL dimensions in the private healthcare delivery sector of Ghana. The study finding will inform health care system-level changes for enhancing the patient's attitudes and perceptions e.g., patient's perceptions about service quality and loyalty in the context of private healthcare delivery.

Rooted on these queries we formulate the following hypothesis:

Hypothesis 1: All the SERVQUAL dimensions impact the patient's satisfaction in private health delivery.
Hypothesis 2: All the SERVQUAL dimensions impact patient's loyalty in private health delivery.

Figure: 1

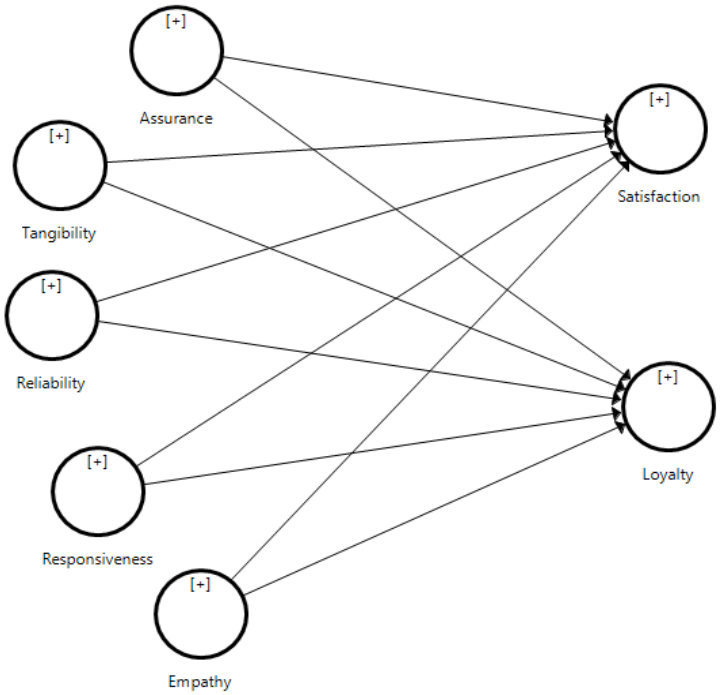

Figure 1: Conceptual Framework of The Study.

Research Method

Data Source and Collection

This study used a survey design with a cross-sectional approach. There were (562) respondents taken from outpatients' hospital admission from four major private hospitals in Ghana using purposive census sampling technique. The target population for this study was identified as all outpatients who have used services of the selected hospitals between March and June of 2019. To minimize the perplexing factors, the researchers restricted respondents into several inclusion criteria: [1] have received treatment from the hospital, [2] mentally healthy, [3] willing to be a respondent [4] Between the ages 18-60 years and [5] Proficient in English language, with identifiable personal information not recorded to maintain confidentiality of the respondents.

Study Variables

Quality of service was examined using a previously tested perceived service quality index; SERVQUAL dimensions. (Parasuraman et al., 1988), SERVQUAL is composed of 22 items with 5 Likert-type response categories: strongly agree, agree, neutral, disagree, and strongly disagree, used as a reflective post-usage measure of a product or service. However, this study's final questionnaire included a total of 17 items of the 5 quality service dimensions modified for this study, out of which three items belonged to each of the dimensions. based on the RATER (Reliability, Assurance, Tangible, Empathy and Responsiveness), with sub-variables as clarified as follows:

- Reliability: Is the ability of the service staff to provide services promptly, accurately, reliably and satisfactorily.
- Assurance: Is a guarantee of service of knowledge, politeness, the ability of the service staff to build patient's trust in the medical services provided.
- Tangibles: This dimension measures the physical environment of the hospital in relation to the out-patient department. The nature of the equipment used at the hospital. (Physical facilities, equipment, and appearance of personnel).
- Empathy: This dimension deals with the caring nature of the staff, meaning how helpful the staff are (caring and personalized attention provided to customers).
- Responsiveness: Is the ability of the service staff to provide prompt and appropriate services to patients by responding to patient complaints and resolving complaints of patients and their families and conveying clear information to patient complaints.

The constructs internal validity and reliability (measured using the composite reliability (CR) as proposed as more appropriate as it considers the indicators' differential weights, whilst the Cronbach's alpha weights the indicators equally) of the SERVQUAL dimensions among the study population was Reliability: 0.907, Assurance: 0.896, Tangibility: 0.854, Empathy: 0.883, Responsiveness: 0.894.

Patients' level of satisfaction of the service based on patient's satisfaction indicators, which is a measure of the difference in expectations and perceptions of the service received built on the service quality dimensions, were measured utilizing a two single item measure with 5 Likert-type reaction categories: (exceptionally satisfied, satisfied, neutral, unsatisfied, or exceptionally unsatisfied). Which was modified according to particular services in the hospital. Patients were inquired about their satisfaction with the service:(exceptionally satisfied, satisfied, neutral, unsatisfied, or exceptionally unsatisfied), and likewise about the degree of trust they have in the clinic that they gotten healthcare at (very trustworthy, somewhat trustworthy, neither, somewhat untrustworthy, or very untrustworthy). The constructs validity and reliability (measured using the composite reliability (CR) as proposed as more appropriate as it considers the indicators' differential weights, whilst the Cronbach's alpha weights the indicators equally) of the patients' level of satisfaction amongst the study population was 0.831.

Loyalty of the patient to the hospital services as a measure of patients' interpersonal trust in the hospital/clinic and it services, and reflects three overlapping concepts: repurchase, recommendation and positive word-of-mouth, was measured via a two single-item with 5 Likert-type response categories: strongly agree, agree,

neutral, disagree, and strongly disagree, with higher scores indicating greater loyalty to the hospital. The constructs validity and reliability (measured using the composite reliability (CR) as proposed as more appropriate as it considers the indicators' differential weights, whilst the Cronbach's alpha weights the indicators equally) of the patients' loyalty amongst the study population was 0.868.

Results and Analysis

Demography

The analysis began with a brief description of demographic attributes of respondents in terms of their age, gender, education and employment status. Out of a total of (562) respondents, 295 (52.5%) were female, while 267 (47.5%) were male. 204 (36.3%) of the respondents were between the ages 18 and 29years, as 243 (43.2%) accounted for respondents between the ages 30 and 44 years. In count, 88 (15.2%) of the respondents were between 45 and 59 years whilst 27 (4.8%) were 60 years and above. Only, 25 (4.4%) had a master's degree or above, with the remaining respondents of 537 (95.6%) cut across a bachelor degree or equivalent, high school certificate and below secondary education. The self and wage employed accounted for high respondents in the employment category 429 (76.4%), with students and the unemployed following in, at that respective order of 133 (23.7%).

Table 1: Demographic Characteristics

Items	Characteristics	Frequency (N=562)	Valid Percentage (%)
Gender	Male	267	(47.5)
	Female	295	(52.5)
Age	18-29	204	(36.3)
	30-44	243	(43.2)
	45-59	88	(15.2)
	60 above	27	(4.8)
Education	Secondary	238	(42.3)
	Tertiary	99	(17.6)
	Postgraduate	25	(4.4)
	Others	200	(32.6)
Employment	Student	82	(14.6)
	Self employed	187	(33.3)
	Wage employed	242	(43.1)
	Unemployed	51	(9.1)

Source: *Fieldwork, 2019* (N) = Population Size
Note: Percentage breakdowns may not add precisely to 100%

Analysis of Measurement Models

By means of establishing the internal consistency and reliability as well as the discriminant validity of the variables, (J. J. I. M. Henseler, 2016), proposed the composite reliability (CR) approach as more appropriate, as it considers the indicators' differential weights, whilst the traditional Cronbach's alpha, weights the indicators equally. The composite reliability (CR) and average variance extracted (AVE) after running the measurement model via (PLS-SEM) is assumed in Table 2. The composite reliability (CR) of all constructs was above 0.7 and average variance extracted AVE above 0.5. Which by principle, is acceptable, as an average variance extracted (AVE)> 0.50, signify that more than half of the indicator variance is encompassed in the construct score (Hair, Hollingsworth, Randolph, & Chong, 2017). Again, establishing discriminant validity means that each construct captures a unique phenomenon not embodied by any other construct in the model. For the measure of

discriminant validity, we adopted the Fornell-Larcker Criterion (FLC) given in Table 2 as proposed by (J. Henseler, 2018) as it proved better for this study.

Table 2: Validity and Reliability of Constructs

Latent Variables		Loadings	Composite Reliability	Average Variance Extracted (AVE)	Discriminant Validity
		>0.70	0.60~0.90	>0.50	
Assurance	**Ass1**	0.834	0.896	0.742	Yes
	Ass2	0.896			
	Ass3	0.852			
Empathy	**Emp1**	0.854	0.883	0.716	Yes
	Emp2	0.847			
	Emp3	0.837			
Reliability	**Rel1**	0.892	0.907	0.766	Yes
	Rel2	0.871			
	Rel3	0.861			
Responsiveness	**Res1**	0.833	0.894	0.739	Yes
	Res2	0.901			
	Res3	0.843			
Tangibles	**Tan1**	0.832	0.854	0.661	Yes
	Tan2	0.766			
	Tan3	0.839			
Satisfaction	**Sat1**	0.813	0.831	0.712	Yes
	Sat2	0.874			
Loyalty	**Loy1**	0.868	0.868	0.767	Yes
	Loy2	0.884			

Source: Authors contribution; Discriminant Validity (Fornell-Larcker Criterion (FLC)), Note: Yes (square root of AVE > the correlation of the construct).

Evaluation of Structural Model

Table (3) shows the path coefficients of the direct and total effects of: Reliability, Assurance, Tangibility, Empathy, Responsiveness (RATER), and on patient satisfaction and loyalty to the hospital/clinic services with their significance levels. Assurance ($\beta = 0.018$; t-value = 0.509; p= 0.611) was the only construct amongst the (5) Servqual dimensions that evidenced to have no direct effect on the satisfaction of the patient, with Reliability ($\beta = 0.050$; t-value = 0.954; p= 0.340) and Tangibility ($\beta = 0.076$; t-value = 1.238; p= 0.216) also suggesting to have no direct effect on the patients loyalty to the hospital/clinic per this study and it findings. yet confirms the findings of the works of(Meesala, Paul, & Services, 2018).

This study suggested, by affirming previous literature and insight that if the main goal of a research of such kind is to identify the factors that highlight patient satisfaction and patient loyalty, then the SERVQUAL dimensions still proves relevant, since barely two of the five dimensions of SERVQUAL appeared irrelevant in this study setting and context, bearing the reaffirming repetition of the dimension even in this current dispersion and trend. However, caution is incited within the utilization of SERVQUAL in the event that the context is characterized by patients depending intensely on alluding physicians' counsel for choice of service suppliers.

Table 3: Path coefficients of the structural model; direct and total effects of constructs

Dimensions	Original Sample (O)	Sample Mean (M)	Standard Deviation (STDEV)	T Statistics (|O/STDEV|)	P Values
Assurance -> Loyalty	0.101	0.099	0.045	2.249	**0.025**
Assurance -> Satisfaction	0.018	0.019	0.036	0.509	**0.611**
Empathy_ -> Loyalty	0.729	0.730	0.062	11.720	**0.000**
Empathy_ -> Satisfaction	0.396	0.398	0.051	7.771	**0.000**
Reliability -> Loyalty	0.050	0.049	0.052	0.954	**0.340**
Reliability -> Satisfaction	0.078	0.078	0.039	1.995	**0.046**
Responsiveness_ -> Loyalty	0.283	0.284	0.055	5.161	**0.000**
Responsiveness_ -> Satisfaction	0.301	0.300	0.061	4.954	**0.000**
Tangibility -> Loyalty	0.076	0.078	0.061	1.238	**0.216**
Tangibility -> Satisfaction	0.166	0.165	0.063	2.643	**0.008**

Source: Authors contribution using Smart-PLS 3.2.8; Regression weights: (ungrouped)

The path diagram (**Figure 2**) shows the graphical regression weights with their significance levels of the servqual dimensions on patient satisfaction and patient loyalty, to the hospital/clinic's services.

Figure: 2

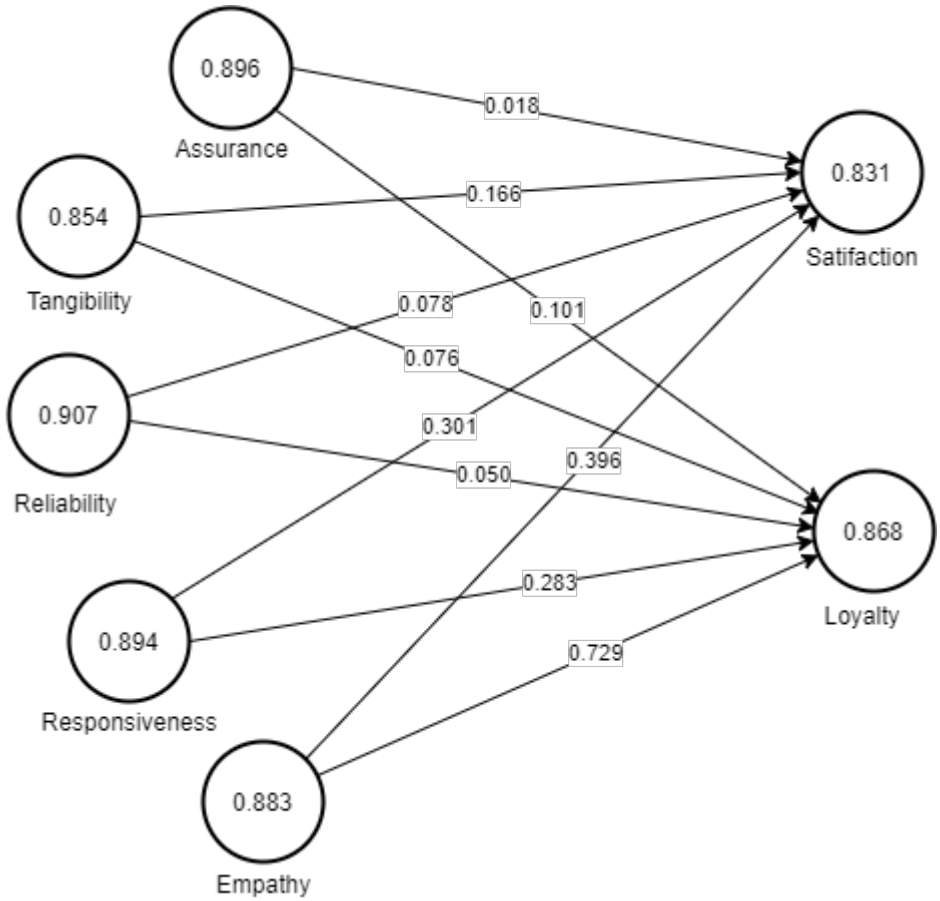

Figure 2: Tested graphical path model depicting the direct effects of the patients' experience with the SERVQUAL dimensions on patient level of satisfaction and patients' loyalty to the hospitals/clinic's services.

All the constructs (SERVQUAL dimensions) to this study had a role to play in driving patient satisfaction and loyalty in the expression of quality healthcare service delivery. However, the most critical factors to consider to drive these effects are when the patients feel satisfied in the light of (1): Timely delivery of services, (2): Caring

employees, (3): The hospital's staff giving patients personal attention. (4): The hospital having patients' best interests at heart, (5): Convenient consultation hours with and the medical services have fulfilled patient's expectation, (6): The hospital has up to date equipment, (7): Hospital's physical facilities are visually appealing and (8): Hospital's staff been well dressed these doesn't just drive satisfaction but has the patient coming back to use the service of the hospital even in the light of intense competitions and other healthcare suppliers promising better service delivery. In essence, these are areas in (Hospital/Clinic) service delivery the hospitals can't afford to fail as they drive higher and critical hospital success. The results of the study showed that overall (RATER) service quality dimension was relatively good in driving satisfaction and loyalty. Assurance, tangible, empathy and responsiveness dimensions were marked very satisfying as it generates the best feeling of patients during their visits to the hospital.

For ease of visual checking, the hypotheses and their status after research are set out in the Table 4 below:

Table 4: Statuses of Hypothesis based on the findings of the study

Hypothesis Number	Hypothesis	Status After Research
Hypothesis 1	All the SERVQUAL dimensions impact the patient satisfaction in private health delivery.	Reliability, Responsiveness, Empathy and Tangibility contribute significantly to patient satisfaction but Assurance does not.
Hypothesis 2	All the SERVQUAL dimensions impact patient loyalty in private health delivery.	Responsiveness, Empathy and Assurance impact patient loyalty but Tangibility and Reliability, does not.

Source: Authors contribution using SmartPLS-SEM.

Discussion

The Servqual dimensions for assessing the quality of services rendered patients in the case of healthcare delivery as posited by (Lee, 2017) is envisioned to reduce or eliminate differences in expectations and perceptions of services that birth either satisfaction or dissatisfaction, and this study suggests the positive impacts of these dimensions on patients' satisfaction creation and loyalty to hospital's/clinics via the level of subjective satisfaction judgement of the patient. Quality of hospital service is determined by patients' satisfaction, loyalty and hospital's productivity and profitability (Kitapci, Akdogan, & Dortyol, 2014). In addition, patients' satisfaction also is a discrepancy about likes and dislikes of the hospital's services (Untachai, 2013). Previous study argued that the primary focus to measure service quality of health care is by analyzing service performance. Yet, current studies suggest that researchers should also explore the gap between patients' expectations and perceptions (Mendes et al., 2018). Hospital competition creates positive effect on better provision of healthcare services (Li et al., 2015). High-quality services could be improved by meeting patients' needs and expectations, through the key factors of improving quality of care by having high quality medical staff to advance the service quality dimensions through education and providing timeless rewards for outstanding medical staff as patients' perceptions of health services could affect the image of the hospital as well as patients' satisfaction and loyalty (Shafiq, Naeem, Munawar, & Fatima, 2017).

As hypothesized, the most imperative facets the hospital managers need to focus on, based on our findings, are (1): Timely delivery of services, (2): Caring employees, (3): The hospital's staff give patients personal attention. (4): The hospital has patients' best interests at heart, (5): Convenient consultation hours with and the medical

services have fulfilled patient's expectation, (6): The hospital has up to date equipment, (7): Hospital's physical facilities are visually appealing and (8): Hospital's staff been well dressed. In its core, these are areas in (Hospital/Clinic) service delivery the hospitals cannot afford to fail as they drive higher and critical hospital success. Assurance and reliability per our study are important but matter little to the patient presumably due to the patient's over-dependence on the treating physician's recommendation characterized in most developing nations like Ghana and many others. Empathy, Tangibility, Reliability and Responsiveness (but not assurance) impact patients' satisfaction and Responsiveness, Empathy and Assurance impact patient loyalty (but not Tangibility and Reliability). In other words, employees' attitude towards patients, their proper communication with patients, and accurate delivery of services are highly critical to the hospital's success. The Attitude, Communication, Delivery (ACD Model) and Tangibles are the key to making patients satisfied and hence return to the same hospital per our findings. This is to also say, that any efforts beyond the basic provision of assurance and reliability to the patient, be directed elsewhere. These conclusions are aligned with the quality dimensions of WHO framework (2006) which recommends that the healthcare systems should be patient-centered and take into account local cultures and preferences of users.

Conclusions

The success of any country depends objectively on its people and their health, and its through a healthy nation that its citizenry can do better for their country by actively participating in their daily activities. Utilizing (PLS-SEM) for healthcare consumer research, which is an emergent path modeling approach, this study in consensus with previous studies on the efforts in bridging the gap between patient's expectations and perceptions about quality of service delivery and patient's satisfaction and loyalty on access to healthcare arrangements, suggests that the quality of service rendered a patient has a potential to enhance the patients' loyalty to the visiting hospital/clinic and increase their level of satisfaction of the service delivery via the evidence of vital quality service dimensions. While this study provides a favorable evidence for the positive role the quality of service plays in creating patient satisfaction and driving loyalty amongst patients in private healthcare delivery through the evidence of the servqual dimensions, this study also is limited from the cross-sectional study design, and further studies are recommended for evaluating its impacts overtime. Further, the dimensions employed in this study did not make use of other dimensional factors e.g. safety matters, culture, technology acceptance, religion, gender etc., which could equally drive satisfaction and loyalty in the conceptual model of this study, hence future research can be directed towards the exploration of these dimensions using latest hospital industry and comparative approaches with other healthcare industries rather than just the private industry.

Acknowledgement
The authorship wishes to express their gratitude to Elder Moses A. Ameyaw and Emmanuel Bosompem Boadi for their immense contributions, to which saw this paper a reality. As well as a big thank you to all respondents for their contribution in this study.

Ethics Statement
The authors affirm that this work is unique and has not been distributed somewhere else, nor is it as of now under consideration for publication elsewhere. All authors participated and contributed to the improvement of this paper. All methods performed in this study were in agreement with the moral guidelines of the morals committee of the School of Management in Jiangsu University and with the (1964) Helsinki declaration and its later amendments or comparable ethical standards.

Conflicts of Interest
The authors affirm that they have no contending conflicts of interests.

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The Asian Institute of Research
Journal of Health and Medical Sciences
Vol.3, No.2, 2020: 196-199
ISSN 2622-7258

DOI: 10.31014/aior.1994.03.02.115

Lung Ultrasound on Critical Ill Patient with Lung Pathology

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Abstract
Differential diagnosis and treatment of critical ill patients with chest X-ray opacifications may be challenging. This particularly includes patients with respiratory failure due to hemodynamic instability. Opacifications in chest x-ray may be due to hemothorax, pleural effusion, atelectasis or consolidations. Physical examination may not always represent the cause of its opacity and thus not always contribute the right therapeutic approach. In that case, bedside ultrasound may be very helpful. We present two cases with similar x-rays but different diagnosis with the aid of bedside ultrasound. There is documented ultrasound accuracy in distinguishing pleural effusion and consolidations.

Keywords: Consolidations, Critical, Lung, Pleural Effusion, Ultrasound

Introduction

Chest X-ray with partial or complete lung field opacifications frequently experienced by critical ill patients. This may introduce some challenges in differential diagnosis and delay management of acute lung pathology in acute respiratory failure patients. Generally, further evaluation must be carried out, such as computed tomography (CT) scan, which is used to guide therapeutic interventions. A large number of criticall ill patients are unstable in such a way so that transportation to CT scanners evokes additional risks. Thoracocentesis when no fluid is present will induce a risk of pneumothorax or losing positive end expiratory pressure during and after the tap which causes alveolar injury and hypoxemia.

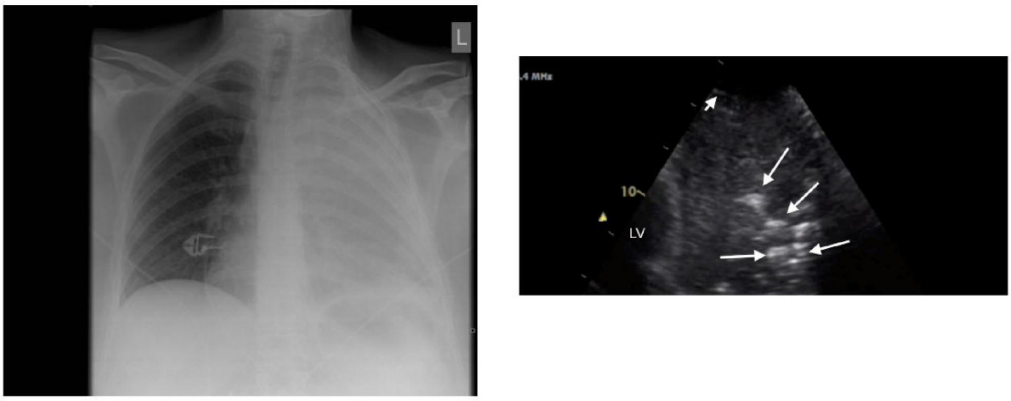
Case Presentation

Case 1
A-45-year-old woman presented in Tangerang General Hospital due to shortness of breath. She had history of allergy, asthma with recurrent bronchitis. A day before hospital admission, she went to a general practitioner who prescribed Augmentin for her respiratory tract infections.

Thoracic X-ray showed opaque shadow on left lung (Figure 1A) with differential diagnosis of pleural effusion, pneumonia or complete left lung atelectasis. Due to its progressive respiratory failure, an intubation was done. Lung ultrasound with 5-MHz probe (ultrasound examination) that is parallel to the upper and lower anterior ribs

was performed (Figure 1B). This examination showed no pleural effusion but an hypoechogenic area with air bronchogram and many hyperogenic spots. CT scan was performed later and resulted in complete lung consolidations compatible with pneumonia.

Figure 1



(A) (B)

Chest x-ray and ultrasound of patient 1. *(A) Chest x-ray showed full opacification of left lung. (B) Chest ultrasound showed pneumonia characterized by irregular hypoechogenic areas with air bronchograms and many hypechogenic regions (long white arrows). The pleural line was hypoechogenic (short white arrow) as often observed.*

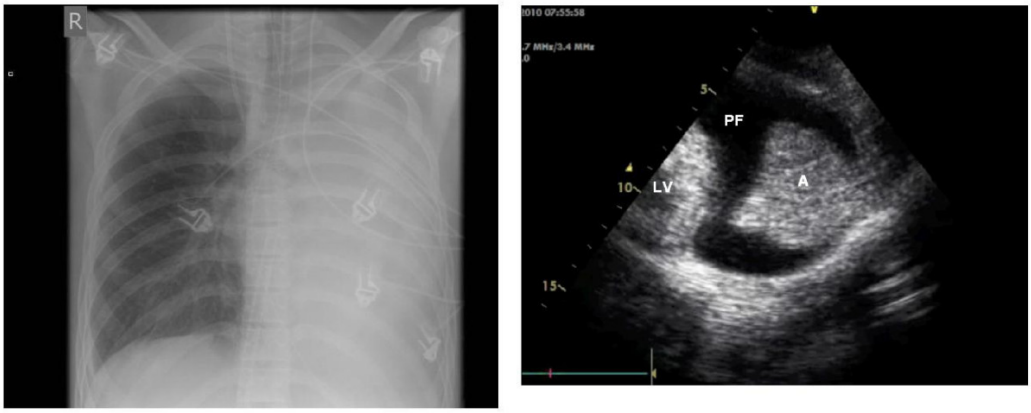
Case 2

A 16-year-old man was admitted to Tangerang General Hospital with cardiogenic shock due to idiopathic dilated cardiomyopathy.

Chest X-ray (Figure 2A) showed complete left lung consolidations with differential diagnosis of pleural effusion and total left lung atelectasis. Bedside ultrasound with 5-MHz probe that is parallel to the ribs of lower thorax and upper anterior showed left lung collapse surrounded by hypoechogenic area that indicates pleural effusion (Figure 2B). Pleural lines were not visible in the collapsed lung.

This patient was managed with bronchial suction through bronchoscopy and treated in right sided position. Sputum plaque was removed from left main bronchus. Afterwards, chest x-ray appear fairly normal showing that the therapy was effective.

Figure 2



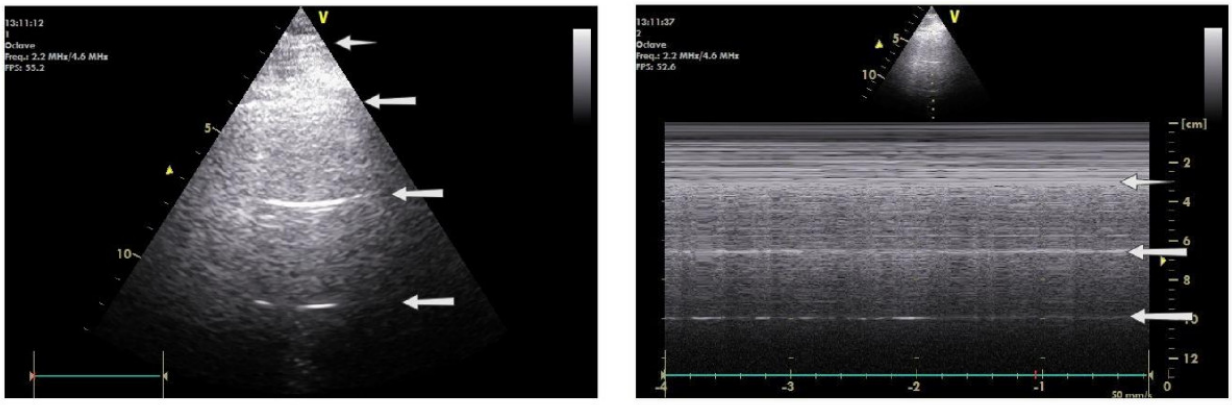
(A) (B)

Chest x-ray and ultrasound of Patient 2. *(A) Chest x-ray showed total opacification on left lung. (B) Lung ultrasound with left lung atelectasis (A) and hypoechogenic area of pleural effusion (PF).*

Discussion

The gold standard in establishing differential diagnosis in lung pathologies with chest x-ray is CT scan. To reduce undue risks to patients such as unpleasant extubation and central venous catheter dislocation during transportation, it is better to use a non-invasive bedside instrument. The accuracy of ultrasound in establishin lung pathologies like pleural effusion, consolidations or pneumothorax was shown in several studies.[1,2] In normal lung, ultrasound usually identifies pleural line. The horizontal line beneath pleural line was separated with regular intervals which are equal to the distance between the skin and pleural line. This line is an artefact line and reflects the presence of high acoustic impedance gradient elements (air and pleural tissue in this case), and they are called line A (Gambar 3). In a comparative study by Lichtensten et al., it was shown that the accuracy of ultrasound in ARDS patients was 93% for pleural effusion, 97% for consolidations and 95% for alveolar interstitial syndrome compared with 47%, 75% and 72% in respectively in chest x-ray.[2] In children, ultrasonography showed the same critical value compared to CT scan in detecting parapneumonic effusion.[3] In 2008, an algorithm (called BLUE protocol) for lung ultrasonography was established and reached a direct diagnosis in >90% acute respiratory failure.[4] We would like to promote the use of bedside ultrasound in emergency departments as well as critical units as a reliable, low-cost, and radiation-free tool for determining the differential diagnosis of a major potential lung diseases. The physical properties of ultrasonography grant a proper access to pleural space pathologies, such as air, fluids, or adhesive lung consolidations. This tool has seen significant developments in critical care for the past ten years, notably in the case of central venous line installation, echocardiography, and lung ultrasonography.

Figure 3



(A) (B)

Normal lung ultrasound. *(A) Pleural lines (arrows): Horizontal lines or lines arising from the pleural line are separated at regular intervals which are equal to the distance between the skin and the pleural line. (B) Mode M showed the pleural line. Below the pleural line is a seashore sign (sandy pattern) due to lung dynamics and sliding pleural. The horizontal lines are A lines, separated by regular intervals (arrows).*

Conclusion

Lung ultrasound is a safe and reliable tool in distinguishing pulmonary pathology in unstable critical ill patients.

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The Asian Institute of Research
Journal of Health and Medical Sciences
Vol.3, No.2, 2020: 200-207
ISSN 2622-7258

DOI: 10.31014/aior.1994.03.02.116

Combined Effects of Occupational Hazards: The Impact of Combined Stressors on Health and Work Performance

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Abstract
There exists a significant body of evidence regarding the effects of occupational hazards. These effects are often considered in isolation, yet a significant proportion of the workforce is exposed to several hazards at a time. The purpose of this study was to investigate the combined impact of workplace factors on mood, cognitive performance and physiology. Participants completed a battery of objective measures before and after work, as previous research (e.g. Broadbent et al. 1989) has shown the difference between before and after work measures to be a good indicator of workload demands during the day. The test battery was performed on the first and last days of the working week. Subjective information regarding chronic and acute (i.e. daily) exposure to hazards was also collected. Mean composite 'total negative factors' scores were created for exposure to chronic and acute stressors (e.g. noise, exposure to hazardous substances, job demand): median splits of these variables were then entered into a series of ANOVAs where mood, simple reaction time and physiology served as dependent measures. Findings indicate that chronic exposure to negative factors results in increased susceptibility to fatigue, over the course of the testing session, working day and working week.

Keywords: Psychology, Occupational medicine, Epidemiology, Stressors, Combined effects

1. Introduction

It is often difficult to obtain measures of performance efficiency at work. One method that has been applied to examine this topic is to use interpolated artificial tasks to make inferences about changes in performance over the day. This approach has been used successfully to examine the effects of fatigue and noise (Broadbent, 1979), working hours (Monk and Folkard, 1985) and workload (Parkes, 1995). Similarly, such measures are sensitive to health-related behaviours (e.g. ingestion of caffeine – Brice & Smith, 2001) and health status (e.g. upper respiratory tract illnesses- Smith et al., 2000).

A number of studies have demonstrated the usefulness of a combined effects approach to occupational hazards. Smith et al. (2004) examined physical hazards (e.g. noise, exposure to hazardous substances) in combination with working hours (e.g. night work, unsociable or unpredictable hours) and found subjective

reports of health and well-being to be lowest in combined stressor conditions. In order to test the possibility that this relationship is essentially linear, Smith et al. (2004) summed the total number of potential hazards and examined the effect of this composite variable on self-reported health outcomes. The results showed that it is an accumulation of hazards, rather than any one hazard in isolation, that causes the greatest detriment to health.

Similarly, the effects of combinations of stressors have been found in studies of accidents at work (Simpson et al. 2004). There is also some evidence to suggest that combinations of factors lead to the greatest impairments in cognitive performance. For example, Smith et al. (2001) found that workers exposed to a high number of negative factors tended to be easily distracted. However, participants in this study were only tested at the end of the working day. In a similar study of the effects of noise and night work within the seafaring population, few additive or interactive effects were observed (see Wellens et al., 2002). This may be due, however, to the relatively small sample of night workers studied or it may be the case that factors other than the physical environment or working hours lead to additive combined effects.
Previous research has concentrated on exposure to chronic stressors. Smith et al. (1999) demonstrated that chronic fatigue may lead to increased susceptibility to acute fatigue (as measured by differences in performance between the start and end of a lengthy test session). The current study also examined daily exposure to stressors, in order to determine if the pattern of effects induced by acute hazards differs from that of chronic hazards.

Given the evidence that the impact of combined stressors on subjective measures is essentially linear (Smith et al. 2001), the present study was designed to replicate this finding using objective performance measures. Furthermore, participants were tested both before and after work, in order to determine the extent of acute workload demands during the day. However, as exposure to hazards was relatively low within the current sample, a further aim was to determine whether changes in fatigue over a task or testing session were sensitive to levels of combined stressors.

2. Material and methods

2.1 Sample

One hundred and thirteen working volunteers from various occupations were recruited via internal and external advertisement. A number of participants were excluded from further analyses, due either to violation of the study criteria, or erratic working patterns, with the final sample consisting of 86 workers.

2.2 Measures

Mood and Performance:
Participants were required to complete a battery of computerised performance and mood tasks, in the same order, before and after work on the first and last day of the working week. [Test order: pre-test mood, simple reaction time, focused attention task, categoric search task, post-test mood.] Data are presented here from the mood and simple reaction time tasks because they allowed assessment of changes over the testing session and task. Two choice reaction time tasks measuring focused attention and categoric search (Broadbent et al. 1989) were also included in the battery.

Mood
Ratings of mood were taken using visual analogue scales. Participants were presented with 18 scales comprising a pair of adjectives anchored at either end of a linear scale - e.g. drowsy - alert. Participants were asked to move the display pointer, using the keys on a response box, to a position on the scale that was representative of their mood. Three main factors were then extracted from the results: alertness, anxiety and hedonic tone.

Simple Reaction Time (SRT)

A white frame was displayed in the centre of the screen and at varying intervals (1-8 seconds) a solid white square appeared inside the frame. Participants were asked to press a response key as soon as they detected the solid square. This task lasted approximately 3 minutes. Mean reaction times were calculated for the test as a whole, as well as for each minute of the task.

Physiological Measures

Salivary cortisol was measured at the beginning and end of the working day, on the first (day 1) and last day (day 5) of the working week. Systolic and diastolic blood pressure (BP) and heart rate were measured both before and after completion of the test battery on days 1 and 5 (both before and after work).

Measurement of Occupational Hazards

Participants were asked to complete a questionnaire detailing the nature of their work. Items referred to the following: hours worked, shift/night work, unpredictable hours, exposure to hazardous substances and noise, cognitive failures, minor injuries, general health, job demands, decision latitude, social support, (Karasek, 1979; Siegrist, 1986) and the home/work interface (HWI). Participants were also required to provide similar information for days 1 through to 5, in order that differences between chronic and acute exposure could be assessed.

3. Results

3.1 Demographics

The sample consisted of 41 (47.7%) males and 45 females (52.3%). The mean age of the sample was 37 years. All participants showed evidence of education, with all but 4 (4.7%) staying at school at least until the age of 16. Participants could be categorised into all six categories of the CASOC-derived social class based on occupation, although the vast majority, 66 (76.7%) were either non-manual or manual skilled workers.

3.2 Chronic Exposure to Negative Factors

A mean composite 'total negative factors' score was created, reversing items where necessary. Variables included in this score are shown in Table 1.

Table 1: Variables Included in Chronic 'Total Negative Factors' Score

Working Hours	Do you do night work?
	Do you do shift work?
	Do you work unsociable hours?
	Do you work unpredictable hours?
Physical Hazards	I am exposed to breathing fumes, dusts or other potentially harmful substances.
	I handle or touch potentially harmful substances.
	My concentration is disturbed by the level of background noise.
	I am left with a ringing in my ears or a temporary feeling of deafness.
Job Demands	I have to work very fast.
	I have to work very intensively.
	I have enough time to do everything I need to do at work.
	Do different groups demand things that are hard to combine?
Social Support	Do you get sufficient information from line management (your superiors)?
	Do you get consistent information from line management?
	How often do you get help and support from your colleagues?
	How often are your colleagues willing to listen to your work-related problems?

	How often do you get help and support from your immediate superior?
	How often is your immediate superior willing to listen to your problems?
	My tasks are such that others can help me if I do not have time.
Decision Authority	I have a choice in deciding how I do my work.
	I have a choice in deciding what I do at work.
	Others take decisions concerning my work.
	I have a great deal of say in decisions about my work
	I have a say in my work speed.
	My working time can be flexible.
	I can decide when to take a break.
	I have a say in choosing who I work with.
	I have a great deal of say in planning my work environment.
	I can take my holidays more or less when I wish.
Skill Discretion	I have the possibility of learning new things through work.
	My work demands a high skill level.
	My job requires me to take the initiative.
	I have to do the same thing over and over again.
	Does your job provide you with a variety of interesting things to do?
	Is your job boring?

3.3 Acute Exposure to Negative Factors

Mean composite 'total negative factors' scores were created for the first and last days of the working week. Variables included in these scores are shown in Table 2.

Table 2**:** Variables Included in Acute 'Total Negative Factors' Scores.

Physical Environment	The work environment was very noisy today.
	I was exposed to fumes or dusts.
	I handled or touched potentially harmful substances or materials.
	I was left with a ringing in my ears or a temporary feeling of deafness.
	My concentration was disturbed by the level of background noise.
	I felt that the air temperature was too hot/cold to work effectively.
Job Demands	I felt I had too much work to do today.
	Did you find your job required a lot of effort today?
	How stressful did you find your job today?
	Did you find your job demanding today?
Social Support	I felt that I had good support from my fellow workers today.
	I felt that management were supportive today.
	Did you have a choice in deciding what/how you did your work?

Job Satisfaction/Health	Was your job boring today?
	Did you feel satisfied with what you did at work today?
	Describe your general health today.

A total acute 'negative factors' score was also calculated from means of scores on the above variables for days 1 through 5 of the working week.

3.4 Change Scores

In order to examine the extent to which performance may vary across the task, day and working week, the following change scores were calculated: post- minus pre-test mood and physiology for day 1 am, day 1 pm, day 5 am and day5 pm. For measures of simple reaction time, mood and physiology, the following change scores were calculated: day 1 pm minus day 1 am, day 5 pm minus day 5 am, and day 5 pm minus day 1 am. In the case of simple reaction time (SRT), 'Time on task' measures were also calculated for each session, by subtracting mean scores for minute one, from mean scores for minute three.

Preliminary Analyses

Preliminary correlational analyses indicated little evidence of the impact negative factors on raw mood, performance and physiological scores. However, where the change scores described above served as dependent variables, a number of effects were observed for mood and simple reaction time, indicating that fatigue increases over the duration of the tasks, working day and working week, as a result of high exposure to chronic negative factors. The pattern of results seen for the physiological measures was not as clear however. Exposure to acute negative factors appeared to have little impact on any of the outcome variables: this may be due to the low levels of acute exposure as compared to chronic exposure. For example, measurement of acute factors did not, unfortunately, take into account daily exposure to night work, and a number of other potential stressors.

Table 3 shows the mean exposure scores for chronic negative factors, and acute negative factors for day 1, day 5 and days 1 through to 5 of the working week.

Table 3: Mean exposure scores

	Mean	SD
Chronic exposure (maximum score = 52)	26.21	9.57
Acute exposure day 1 (maximum score = 35)	18.87	6.48
Acute exposure day 5	18.56	7.66
Acute exposure days 1 through 5 (maximum score =156)	91.07	22.80

3.5 Further Analyses: ANOVA

Analyses of variance (ANOVA) were performed, where day (i.e. 1 or 5), time (i.e. am or pm) and position (i.e. pre-or post-test) served as within subjects factors, and a median split of the chronic total negative factors score served as the between subjects factor. Alertness scores were taken as an example of the effects of chronic exposure to negative factors on mood. Means and standard deviations are shown in Table 4.

Table 4: The Impact of Chronic Exposure to Negative Factors on subjective alertness (higher scores = greater alertness).

	Chronic Negative Factors	Mean	SD
Pre-test alertness Day 1 am	Low	259.4	68.0
	High	228.3	64.2
	Total	245.7	67.8
Post-test alertness Day 1 am	Low	248.7	54.4
	High	230.2	54.5
	Total	240.5	54.9
Pre-test alertness Day 1 pm	Low	262.7	55.9
	High	250.9	49.8
	Total	257.5	53.3
Post-test alertness Day 1 pm	Low	235.7	62.9
	High	216.2	51.8
	Total	227.1	58.8
Pre-test alertness Day 5 am	Low	246.6	64.3
	High	218.8	60.3
	Total	234.3	63.7
Post-test alertness Day 5 am	Low	236.9	60.3
	High	214.6	63.6
	Total	227.1	62.4
Pre-test alertness Day 5 pm	Low	254.7	55.6
	High	244.9	54.1
	Total	250.4	54.8
Post-test alertness Day 5 pm	Low	242.6	58.0
	High	209.3	65.4
	Total	227.9	63.2

A significant main effect of high chronic exposure to negative factors was observed: $F(1, 84) = 4.99$, $p<.03$. Significant within-groups effects were also found for: position (i.e. pre-or post-test): $F(1, 84) = 31.74$, $p<.0001$; time (i.e. am or pm) x position: $F(1, 84) = 23.44$, $p<.0001$, and time x position x chronic exposure to negative factors $F(1, 84) = 7.58$, $p < 0.01$. These effects demonstrate that a high chronic total negative factors score leads to a decrease in alertness generally. Furthermore, it is evident that alertness decreases significantly over the time working, an effect that is particularly marked at the end of the working day. These decreases in alertness were larger in those exposed to a high number of negative job characteristics.

The same ANOVA was performed with simple reaction time as the dependent variable. Means and standard deviations are shown in Table 5. Although no main effect of high chronic exposure to negative factors was found/ the following within-groups effects were observed: day (i.e. day 1 or 5 of the working week) x time on task (i.e. minute 1 or minute 3) x chronic negative factors: $F(1, 84) = 4.73$, $p<.03$, and time of day (i.e.am or pm) x position x chronic negative factors: $F(1, 84) = 11.79$, $p<.001$. These effects show that participants generally demonstrate slower reaction times at the end of the working day and the working week than at the beginning of the week, and are slower at the end of the task (minute 3) than the beginning (minute 1). Furthermore, high exposure to chronic negative factors results in greater slowing over the task at the end of the week. Participants in the lower median group of chronic negative factors demonstrated slower reaction speeds at the beginning of the working day, whereas those in the higher median group showed a greater slowing in reaction speed at the end of the working day.

Table 5. The Impact of Chronic Exposure to Negative Factors on Simple Reaction Time- ANOVA Means (msecs).

	Chronic Negative Factors	Mean	SD
Mean SRT min 1 Day 1 am	Low	300	49
	High	314	67

	Total	306	57
Mean SRT min 3 Day 1 am	Low	322	58
	High	311	46
	Total	317	53
Mean SRT min 1 Day 1 pm	Low	318	49
	High	316	76
	Total	317	62
Mean SRT min 3 Day 1 pm	Low	320	51
	High	325	80
	Total	322	65
Mean SRT min 1 Day 5 am	Low	308	48
	High	322	82
	Total	312	65
Mean SRT min 3 Day 5 am	Low	316	49
	High	332	75
	Total	323	62
Mean SRT min 1 Day 5 pm	Low	327	62
	High	318	58
	Total	323	60
Mean SRT min 3 Day 5 pm	Low	326	54
	High	339	66
	Total	331	59

Analyses of the physiological measures failed to reveal significant effects of combinations of negative job characteristics.

4. Discussion

The results generally indicate that chronic exposure to negative factors, such as long hours and high job demand, results in increased susceptibility to fatigue over the course of the test session, the working day and the working week. The findings provide further support for the "after-effects" technique (Broadbent, 1979) in that the paradigm described in this study was shown to be sensitive to fluctuations in workload and demand. As discussed, a number of studies have provided evidence to suggest that the relationship between chronic exposure to negative factors and self-reported health and well-being is linear (e.g. Smith et al., 2001). The findings reported in this paper suggest that the relationship also exists between chronic exposure to negative factors and cognitive performance and mood.

It would appear therefore, that a combined effects approach to the study of workplace stressors is valid, as it seems to be an accumulation of negative factors, rather than exposure to any one hazard in particular, that causes the greatest impairments to health and performance. Of particular interest, is the fact that this approach to the measurement of combined effects is sensitive enough to predict the influence of relatively low levels of certain stressors. In this particular sample, the number of individuals who reported regular night or shift work, or exposure to harmful substances in the workplace, was negligible and levels of other negative job characteristics moderate.

Consistent with previous research (e.g. Smith et al., 1999) the current findings suggest that chronic problems result in greater susceptibility to acute fatigue. However, no discernable pattern of results was observed for acute exposure. This is more than likely due to the comparatively low exposure levels reported on a daily basis, as opposed to those reported generally (see Table 3).

Unfortunately, due to the design of the questionnaire, it was not possible to compile acute negative factors scores in exactly the same way as for chronic negative factors. It is of particular importance to note that no working hours measures were included in the acute negative factors scores. No effects were observed where physiological measures served as dependent variables: it may well be the case that only relatively extreme exposure to negative

factors (either chronic or acute), or exposure to particular types of stressor - for example night work - are necessary before changes in physiology are noted.

In conclusion, the study outlined in this paper highlights the need to consider workplace stressors in combination, if their true impact on performance and health is to be determined. Future research might wish to consider a similar experimental paradigm, with a more diverse sample, in order to determine the effect of negative factors on cognitive performance, as the current sample consisted largely of nine to five office workers. In addition, the current sample was rather small.

Acknowledgement: This research was funded by the UK Health and Safety Executive (HSE).

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The Asian Institute of Research
Journal of Health and Medical Sciences
Vol.3, No.2, 2020: 208-215
ISSN 2622-7258

DOI: 10.31014/aior.1994.03.02.117

Combinations of Workplace Stressors and Work-Related Injuries

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Abstract
Consideration of factors associated with increased accident likelihood has tended to concentrate on the influence of one specific factor (for example, noise) and other influences are either not considered or are controlled for. The aim here was to examine the influence of combinations of stressors on the prevalence of workplace accidents using self-report measures of exposure, health and work outcomes. Logistic regression analyses were carried out, with 'work-related/non-work-related accident' as the dependent variable. The main predictors were combinations of physical agents (noise, fumes, hazardous substances) and temporal stressors (night and shift work, long working hours). Additional predictors - the job demand-control-support model (Karasek 1979; Johnson and Hall 1988) and home-work interface (HWI) were also investigated. Other measured predictors (i.e., age, sex and social class based on occupation) were included in all analyses. There was some evidence for an increased likelihood of work-related accidents in those exposed to combinations of stressors - increased likelihood was largely due to independent effects of stressors, particularly noise. Certain stressors were also associated with a decreased risk of having a work-related accident (i.e. unpredictable work hours). Job-demand-control-support did not have a major impact on predicting work-/nonwork-related accident likelihood. Prevalence of accidents at work largely reflected social class based on occupation - 'skilled manual workers' or 'partly skilled workers' were most likely to have an accident.

Keywords: Occupational Medicine, Accidents, Noise, Working Hours, Combined Effects

1. Introduction

The purpose of this paper is to describe a preliminary investigation into the association of self-reported measures of occupational factors and the likelihood of suffering an accident at work. In this investigation, an accident at work is defined as an 'injury deemed severe enough by employee/employer to warrant a visit to the emergency unit at University Hospital Wales in Cardiff, which is subsequently categorised as a work-related injury during triage by a nurse'. The motivation for undertaking this research was to address the issue of the extent to which certain stressors are associated with work-related accidents and whether there is any evidence of the combined exposure to more than one stressor in the workplace being significantly more strongly associated with work-related accidents than exposure to single stressors.

There has been some suggestion for the role of occupational noise exposure in work-related accidents, although it is often felt that there is little real evidence of a relationship due to potential confounding

influences that may not have been considered (for a review: see Smith 1990). There is considerable information however that suggests a role of temporal stressors in increased accident risk. On a societal level, many of the major man-made disasters of the last 20-30 years have to some extent been attributed to tiredness or other outcomes of workplace temporal stressors such as night work, shift work or long working hours. Temporal stressors have been implicated in Chernobyl, Exxon Valdez, Three-Mile Island and Bhopal (Matthews et al. 2000). On the individual level, the role of tiredness in increased risk of error is well established and a circadian rhythm of accidents has been suggested (Folkard 1997). However, accurately modelling the cause of accidents is impaired by the inability to control for potential confounders. For example, accidents are more likely to occur at night in many jobs but the work done at night is often very different in a number of other ways - i.e. people often work alone and on different tasks compared to day workers (for a review see: Sparks et al. 1997). The workplace is a complicated environment and the general approach of studying, say, the effects of noise or night work on accident risk does not necessarily reflect the reality of the workplace. This survey intends to provide enough information so that simple questions concerning whether there is a significant increase in work accident likelihood associated with exposure to specific combinations of stressors can be addressed with more confidence.

2. Material and methods

2.1 Survey Content

The questionnaire was designed to ask about the physical, temporal and psychosocial stressors associated with the workplace. Physical and temporal stressors were measured by a series of items that asked whether the individual's job involved exposure to loud noise, disturbing background noise, exposure to fumes, having to handle hazardous substances, night work, shift work, unsociable working hours, unpredictable working hours or long working hours. Each of these items was measured on a four-point scale – 'often', 'sometimes', 'seldom' and 'never' – except long working hours which was measured by the question 'how many hours do you work per week?' which was subsequently categorised into quartiles and those in the top quartile (>48 hours per week, in line the council of the European Union working time directive number 93/104/EC) were considered as working long hours. Items were taken from the Bristol Health and Safety at Work Study (Smith et al. 2000).

Psychosocial work factors were assessed by using the job (iso-)strain model (Karasek 1979; Johnson and Hall 1988). This model can be assessed by 25 items which make up 3 scales, job demand (4 items), work social support (6 items) and decision latitude [Also termed 'job control', reflecting the amount of control one has over how they do their job.] (15 items). It is postulated that the relationship between these scales influences health, with a situation of low support, low decision latitude and high demand having the most negative outcome on health. Home/work interface (HWI) was measured using a scale adapted from the Whitehall II studies (Marmot et al. 1991). The questionnaire also included an item asking what the individual's current job was. From this, 'social class based on occupation' could be calculated - a reflection of both socioeconomic status and job type. Other demographic details were gathered from the hospital records.

2.2 Participants/Procedure

After being approved by the hospital's ethical committee, the questionnaire was distributed to 2,000 individuals randomly selected from the hospital records of the last 3 months with the assistance of hospital staff. 1,000 of these selected individuals had been categorised by staff at triage as having suffered work- related accidents and 1,000 had been categorised as having suffered nonwork- related accidents (i.e. RTA's, accidents at home, sports injuries).

2.3 Response Rate

The sample consisted of 367 (18.4%) participants. This was a poor response rate and subsequent investigation will need to greatly improve this. 162 of these reported work-related accidents and 205 non-work-related accidents. The mean age of the sample was 40.0 (Std. Dev = 11.7), ranging from 16 to 70 years old. The sample consisted

of 200 men and 115 women, due to incomplete hospital records, gender of 66 questionnaire returners was not available

3. Results

Physical stressors and temporal stressors were considered in terms of their combined effects on work-related accident likelihood.

3.1 Statistical Methods

Firstly, physical and temporal stressors were examined for an intuitive factor structure using principal components analysis in SPSS. These items grouped on to 3 factors, representing physical stressors, temporal stressors and hours of work respectively (Table 1). Physical stressors explained more of the variance (27.2%) than temporal stressors (24.0%) and hours of work (12.1%), 63.3% being accounted for in all.

Table 1: Factor analysis of the predictor variables

	Factor 1	Factor 2	Factor 3
Shift Work		.889	
Night Work		.885	
Unsociable hours of work		.856	
Unpredictable hours of work		.520	.500
Long work hours			.885
Noisy work environment	.742		
Exposed to breathing fumes	.729		
Handle dangerous substances	.611		
Left with ringing in ears	.678		
Disturbed by background noise	.773		
Unsuitable air temperature	.643		

The next set of analyses examined associations between the predictor variables and the outcomes. All analyses were carried out using SPSS binary logistic regression. The first analysis was designed to give an overview of the approximate influence of (a) physical workplace stressors, (b) temporal workplace stressors and (c) these stressors in combination. Scores on the factor 1 and factor 2 groupings were summed individually and split into quartiles. These quartiles were recoded into dichotomous variables, with quartiles 1-3 = low/medium exposure, and quartile 4 = high exposure. These 2 variables were then used to group participants into 1 of 4 categories:

1. Low exposure to both physical and temporal stressors
2. Low exposure to physical stressors, high exposure to temporal stressors
3. High exposure to physical stressors, low exposure to temporal stressors
4. High exposure to both physical and temporal stressors

A simple indicator contrast was used in the analysis, comparing the likelihood ratio of each level of the predictor to the effect associated with the first group. Subsequent analyses included an 8-level predictor variable outlining the various permutations of the job (iso-) strain model (i.e. combinations of high and low job demand, job control and social support).Home/work interface was also included as a 3-level predictor variable, (1) little or no problem, (2) moderate problems and (3) considerable problems integrating work and home life. Age, gender and social class based on occupation were all included as predictors in the logistic regression analyses. A simple indicator contrast was used for this predictor, comparing the likelihood ratio of each level of the predictor to the effect associated with the first group. Analysis of three models was

undertaken. Model 1 consisted of the key predictor alone (i.e. physical/temporal stressors). Model 2 included the demographic covariates (i.e. age, gender and social class based on occupation). Model 3 also included 'other job characteristics' (i.e. job (iso-) strain, HWI). After looking at the summed physical agents and temporal stressors, median splits of stressors were considered in pairs - 1 physical stressor and 1 temporal stressor in each analysis.

3.2 Descriptive Statistics

Descriptive statistics for age are shown in Table 2. Work-related accident cases were marginally older and had a greater age range.

Table 2: Age and accidents

	N	Mean	SD	Min	Max	Range
Work-related accident	169	39.6	12.5	16	70	54
Non-work-related accident	212	38.4	10.8	17	60	43

Descriptive statistics for gender are shown in table 3. More men had returned the questionnaire. More of the work-related accident sample were male than the non-work-related accident sample.

Table 3: Gender

	Work-related accident	Non-work-related accident
Male (N/%)	105 (69.1%)	95 (58.3%)
Female (N/%)	47 (30.9%)	68 (41.7%)

Descriptive statistics for social class based on occupation are shown in table 4. 'Skilled: manual', 'partly skilled' and 'unskilled' workers are better represented in the work-related accidents sample. 'Professional', 'managerial & technical' and 'skilled: non-manual' workers are better represented in the non-work- related accidents sample.

Table 4: Social Class Based On Occupation

	Work-related accident	Non-work-related accident
Professional (N/%)	3 (1.9%)	17 (8.3%)
Managerial & Technical (N/%)	32 (19.8%)	56 (27.3%)
Skilled non-manual (N/%)	19 (11.7%)	42 (20.5%)
Skilled manual (N/%)	57 (35.2%)	33 (16.1%)
Partly skilled (N/%)	35 (21.6%)	26 (12.7%)
Unskilled (N/%)	12 (7.4%)	5 (2.4%)
Missing data (N/%)	4 (2.5%)	26 (12.7%

The exposure to physical and temporal workplace stressors is shown in Table 5. Of the temporal stressors, the most frequent was shift work (29.7%). Of the physical stressors, a ‘noisy working environment’ was the most frequently reported condition (57.8%). Some information about the accidents is described below. Where the non-work injury was sustained is shown in Table 6. Although a considerable number of non-work- related accidents were poorly described in hospital records (33.7%), the single biggest recorded percentage was accidents in the home (27.0%). The type of injury sustained is shown in Table 7. The most frequent reason amongst the work-related injury sample was 'laceration/cut' (20.4%) and 'abrasion/bruise' (18.4%). The most frequent reasons amongst the non-work-related injury sample were 'abrasion/bruise' (19.0%) and 'sprain' (17.8%).

Table 5: Workplace exposure

	Low/Medium exposure	High exposure
Shift Work	265 (70.3%)	112 (29.7%)
Night Work	293 (78.3%)	81 (21.7%)
Unsociable hours of work	274 (67.5%)	109 (25.8%)
Unpredictable hours of work	296 (78.5%)	218 (57.8%)

Long work hours (> 48 hours per week)	313 (74.2%)	109 (25.8%)
Noisy work environment	159 (42.2%)	218 (57.8%)
Exposed to breathing fumes	240 (63.7%)	137 (36.3%)
Handle dangerous substances	274 (73.7%)	98 (26.3%)
Left with ringing in ears	329 (87.3%)	48 (12.7%)
Disturbed by background noise	268 (71.3%)	108 (28.7%)
Unsuitable air temperature	174 (46.0%)	204 (54.0%)

Table 6**:** Where the non-work injury was sustained

Road Traffic Accident	17 (10.4%)
Sport	13 (8%)
Home	44 (27.0%)
Public Place	34 (20.9%)
Other/poorly described	55 (33.7%)

Table 7: Type of injury

	Work-related	Non-work-related
Abrasion/Bruise	28 (18.4%)	31 (19.0%)
Laceration/cut	31 (20.4%)	11 (6.7%)
Sprain	13 (8.6%)	29 (17.8%
Soft tissue injury	16 (10.5%)	16 (9.8%)
Fracture	19 (12.5%)	16 (9.8%)
Burn/scald	10 (6.6%)	1 (0.6%)
Local infection	2 (1.3%)	3 (1.8%)
Foreign body	8 (5.3%)	1 (0.6%)
Other	24 (15.8%)	43 (26.4%)
Missing information	1 (0.7%)	12 (7.4%)

What the outcome of the visit to the emergency unit was is shown in table 8. More of the non-work-related accidents were of a severity/complexity to require admittance (11.0%) compared to the work-related accidents (4.0%), although generally minor injuries not requiring a stay as an inpatient are seen in this sample.

Table 8: Outcome of visit to emergency unit

	Work-related accident	Non-work-related accident
Sent home	142 (93.4%)	141 (86.5%)
Admitted to hospital	6 (4.0%)	18 (11.0%)
Did not wait	3 (2.0%)	4 (2.5%)
Unspecified	1 (0.7%)	0 (0%)

3.3 Summed Physical and Temporal Stressors

Table 9 shows the accident rates for the different stressor conditions. Univariate non-parametric analysis using Pearson chi-square showed significant differences between the categories of the summed physical and temporal stressors predictors against accident type (chi square =16.69 $p < 0.001$). Individuals reporting high exposure to physical and temporal stressors were more likely to have been admitted to the emergency unit with a work-related accident than a non-work-related accident. Looking at multivariate analysis using binary logistic regression, a test of the full model with all predictors against a constant-only model was statistically reliable (chi square

(17, N = 266) = 43.53, p<0.001). This indicated that the predictors as a set reliably distinguished between those who had suffered work-related accidents and those who had suffered non-work-related accidents. The variance accounted for however was relatively small, RL= .12. Predictive success was however quite impressive. The constant-only model correctly classified 51.9% of cases, model 1 60.2%, model 2 65.4% and model 3 67.3%. This was a 30.0% increase overall. There was no problem with outlying studentized residuals (<2). Investigation of collinearity diagnostics showed that there was no concerns regarding multicollinearity between the predictor variables. The combined stressors category was significant in all 3 models. The 'high physical stressors only' category was significant in model 1 only, but subsequently removed when additional predictors were added in models 2 and 3 (see Table 10).

Table 9: Chi-square analysis for accidents in different stressor conditions

	Non-work-related accidents	Work-related Accidents
Neither stressor	O=56; E=43.3; 27.2%	O=22; E=34.7; 13.3%
High temporal stressor	O=23; E=20.5; 20.5%	O=14; E=16.5; 8.5%
High physical stressor	O=70; E=69.4; 34.0%	O=55; E=55.6; 33.3%
Both stressors	O=57; E=72.7; 27.7%	O=74; E=58.3; 44.8%

Table 10: Odds Ratios (Exp (B)) and Confidence Intervals (CI) for the Physical/Temporal Stressors Predictors

	Model 1[a] Exp(B) (95% CI)	Model 2[b] Exp(B) (95% CI)	Model 3[c] Exp(B) (95% CI)
Neither Stressor			
High temporal stressor	1.256 (0.48, 3.27)	1.09 (0.39, 3.07)	1.40 (0.48, 4.04)
High Physical stressor	2.26 (1.10, 4.61)*	1.80 (0.84, 3.86)	2.02 (0.92, 4.44)
Both stressors	3.33 (1.62, 6.82)**	3.35 (1.08, 5.09)*	2.54 (1.11, 5.80)*

a. Physical and temporal stressors predictor only

b. Physical and temporal stressors predictor, age, gender and social class based on occupation

c. Physical and temporal stressors predictor, age, gender, social class based on occupation and job-strain

*p < 0.05 **p < 0.01

Of the other predictors included in models 2 and 3, contrast comparisons within social class based on occupation revealed that (a) skilled-manual and (b) partly-skilled workers were more likely to have suffered a work-related accident than a non-work-related accidents.

3.4 Other predictors

Initial investigation demonstrated that sex, social class based on occupation (Table 11) and job (iso-) strain showed significant associations with the work- related/non-work-related accidents. This is why they were included as predictors in models 2 and 3. Although age did not show a significant association, this was included in models 2 and 3 because it is a standard demographic measure. HWI did not demonstrate a significant association with the work-related/non-work-related variable and was excluded from the models. As noted in the previous section, workers classified as 'skilled-manual' and 'partly-skilled' were significantly more likely to have been admitted for a work- related accident. This remained significant in models 1 and 2 but, although the trend remained, it was non-significant in model 3. Low decision latitude and high social support from the job (iso-) strain model were associated with an increased likelihood of a work-related accident (or a decreased likelihood of non-work-related accident).

Table 11: Exp (B) and C.I. for Social Class Based On Occupation

	Model 1[a] Exp(B) (95% CI)	Model 2[b] Exp(B) (95% CI)	Model 3[c] Exp(B) (95% CI)
Professional			
Managerial/technical	1.02 90.57, 1.84)	1.12 (0.61, 2.07)	1.10 (0.58, 2.084)
Skilled manual	0.67 (0.34, 1.33)	0.86 (0.42, 1.78)	0.85 (0.40, 1.78)
Skilled non-manual	2.50 (1.41, 4.43)**	2.20 (1.22, 3.96)**	2.11 (1.15, 3.89)

Partly skilled	2.23 (1.18, 4.25)**	2.09 (1.09, 4.02)*	2.16 (1.10, 4.24)
Unskilled	2.60 (0.89, 7.58)	2.14 (0.71, 6.49)	2.36 (0.74, 7.49)

a. social class based on occupation only
b. social class based on occupation, physical and temporal stressors predictor, age, and gender
c. social class based on occupation, physical and temporal stressors predictor, age, gender and job-strain
*p<.05 **p<.01

3.5 Summary of Analyses of Item Pairs

The previous analyses summarised findings from looking at the *overall* exposures to physical and temporal stressors in the workplace and other predictors. Below is a summary of further analyses that considered exposure to specific stressors in combination. Where individuals had self-reported working in a noisy environment and also often worked either nights, shifts or unsociable hours of work then there was approximately a 3-fold increase in the likelihood of the individual having had an accident at work (Table 12), in comparison to having a non-work related accident. In each case of a significant 'combined effect' there was also a significant increase in work accident likelihood associated with the noise contrast in comparison to the 'neither stressor' reference category. There was no significant difference between the likelihood ratio associated with the high noise exposure category and that associated with the combined stressors group. This can be demonstrated by observing that the odds ratio of the signficant contrasts falls within the confidence intervals of each other.

Table 12**:** Exp (b) and CI for Noisy Work Environment and Unsociable hours of work

	Model 1[a] Exp(B) (95% CI)	Model 2[b] Exp(B) (95% CI)	Model 3[c] Exp(B) (95% CI)
Neither Stressor			
Unsociable hours	1.90 (0.82, 4.38)	1.52 (0.63, 3.68)	1.68 (0.67, 4.21)
High Noise	3.41 (1.83, 6.37)**	2.59 (1.29, 5.20)**	2.73 (1.34, 5.56)**
Both stressors	4.12 (2.07, 8.18)**	3.19 (1.50, 6.81)**	3.48 (1.58, 7.67)**

a. Physical and temporal stressors predictor only
b. Physical and temporal stressors predictor, age, gender and social class based on occupation
c. Physical and temporal stressors predictor, age, gender, social class based on occupation and job-strain
*p < 0.05 **p < 0.01

All other combinations - i.e. loud noise and temporal stressors, disturbance by background noise and temporal stressors, fumes exposure and temporal stressors, hazardous substances and temporal stressors and unsuitable temperature and temporal stressors, showed no significantly increased likelihood associated with the combined stressors group. The combination of 'unpredictable work hours' and physical stressors showed a decreased risk of work-related accident compared to physical stressors alone (Table 13). Indeed, unpredictable working hours were associated with a decreased risk of accidents at work. This can also be interpreted as an increased risk of non-work-related accident in workers reporting working unpredictable hours. Noisy work was associated with increased work-related accident risk, which supports previous findings.

Table 13: Exp (B) and C.I. for Noisy Work Environment and Unpredictable Hours of Work

	Model 1[a] Exp(B) (95% CI)	Model 2[b] Exp(B) (95% CI)	Model 3[c] Exp(B) (95% CI)
Neither Stressor			
Unpredictable hors	0.52 (0.20, 1.37)	0.22 (0.56, 0.89) *	0.21 (0.49, 0.88) *
High Noise	2.63 (1.64, 4.23) **	2.23 (1.19, 4.16) *	2.045 (1.07, 3.92) *
Both stressors	2.36 (1.22, 4.55) *	1.39 (0.60, 3.25)	1.49 (0.62, 3.58)

a. Physical and temporal stressors predictor only
b. Physical and temporal stressors predictor, age, gender and social class based on occupation
c. Physical and temporal stressors predictor, age, gender, social class based on occupation and job-strain
*p < 0.05 **p < 0.01

4. Discussion

The present study provides preliminary evidence that a combination of stressors can lead to increased risk of accidents at work. Exposure was based on self-report and objective measurement is necessary in future studies. There is also the problem of missing information. For example, no information was obtained about whether people considered their job to be dangerous or whether they worked with heavy machinery. The ubiquity of increased work- related accidents being associated with 'skilled non-manual' and 'partly skilled' work shows the important role that type of job has. However,this is clearly not the whole story – as shown by the significant effect associated with the combined stressors contrast in the summed physical and temporal stressors analysis that remains even after the addition of other predictors.

It may be that as well as an increased risk depending on one's occupation, increased exposure to stressors within that workplace further increases the risk. To give an example,a factory worker may work with heavy machinery that puts them at risk of injury. This machinery may be noisy, but if their job requires them to, say, work long, unsociable hours also then the likelihood of having an accident at work may be greatly increased due to the additional strain put on the individual. In addition,the complexities of the work place – i.e. the fact that 'skilled-manual' and 'partially- skilled' occupations will often be low status jobs, with lower pay, lower job satisfaction and a more negative psychosocial environment only further increases the strain and further leads to increased accident risk.

Further adjustments that need to be made to this study are as follows: a control group needs to be added (i.e. those who have had no accident at all) as attempts to get case-controls by sending out questionnaires for participants to forward on to colleagues in comparable job roles was unsuccessful. The questionnaire does not tap into the wide variety of information that may be beneficial to a discussion of accident likelihood (i.e. risk taking, health related behaviours - alcohol, drugs etc., other health symptoms and negative affectivity - a measure of dispositional response bias). A longer questionnaire has been distributed to 5 samples of 2,000 people drawn from Hospitals around Wales. This questionnaire includes more items to allow a more in-depth analysis of the data.

Acknowledgement: This research was supported by the UK Health & Safety Executive.

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The Asian Institute of Research
Journal of Health and Medical Sciences
Vol.3, No.2, 2020: 216-222
ISSN 2622-7258

DOI: 10.31014/aior.1994.03.02.118

Childcare Before Birth: The Role of the Pediatrician

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Abstract
In all phases of their growth and development, from conception to senility, the human being counts on different care in health promotion and disease prevention offered by professionals through health care programs at different levels of care. Specifically in child health care, pediatricians have a fundamental role and their work, traditionally, starts from birth and develops for two decades, until their patient reaches adulthood. This article highlights a set of activities that the pediatrician can initially offer to the woman and the family, since the preconception period, and accompanying the entire pregnancy, called Antenatal Childcare.

Keywords: Puericulture, Childcare, Antenatal Care, Pediatric Health Care

Introduction

Since conception to the end of puberty, the human being goes through different stages of growth and development (embryo, fetus, newborn, child, adolescent, and adult), each with specific characteristics and which, succeeding harmoniously, will take to the stage of final maturity, that is, the adult individual.

From the medical point of view, so that each stage of life is overcome in good condition, it is necessary to incorporate health care that can help human beings to overcome obstacles and face adversity, in order to reach the next stage and continue their evolution. Preventive pediatrics, and especially primary health care, has as one of its objectives to promote the physical, mental and social well-being of children and adolescents through interaction between doctor-child-family, in an effort to prevent harm and promote health for all, because children reside in families and their care must involve family members and caregivers who maintain responsibility for daily contact with children (Pratt K, van Forsen, Didericksen, Amar & Berge 2018).

In this context, one of the most important activities developed by the pediatrician is the so-called anticipatory guidance, that is, a counseling technique that focuses on the needs of children at different stages. Anticipatory guidance is one of the bases of primary care pediatrics, as it provides parents with information about the expected development of children and issues related to safety and health promotion (Barkin, Scheidlin, Nrown, Ip, Finch & Wasserman 2015).

Childcare has long been practiced as a health activity that aims to provide longitudinal, and continuous monitoring, in which experienced pediatric professionals perform skillful observations of children during child health meetings with the mutual participation of parents and health professionals in the discussion about childcare (Lurshay 2017). In other words, childcare comprises a set of rules of action aimed at children to achieve the maximum of their potential capacities and avoid harmful actions that may affect them (Suchder & Howard 2018).

Antenatal care

From the beginning of the 20th century to the present, health care for pregnant women and the fetus has achieved many advances worldwide with the incorporation of actions and programs for the prevention of health problems and health promotion (Al-Gailani, Davis 2014 & Yan 2020). Prenatal care is a standard for preventive, health promotion, diagnostic and curative actions simultaneously during pregnancy, aiming at maternal and child outcomes and reducing complications in childbirth and postpartum (World Health Organization 2016, Le Tinier , Billieux, Pfister, De Tejada 2020, Andrade-Romo, Heredia-Pi, Fuentes-Rivera, Alcalde-Rabanal, Cacho, Jurkiewicz et al 2019, Leal, Esteves-Pereira, Viellas, Domingues, Gama 2020). The care offered to the pregnant woman follows protocols that are developed by obstetricians, general practitioners and nurses and follows defined protocols both for situations of normal pregnancy and for cases with complications or considered to be at higher risk

The pediatrician and the puericulture

Pediatric practices are unique among medical specialties because the child always requires the presence of parents when seeking medical assistance. Therefore, the role of the pediatrician with the family must begin when the couple plans the pregnancy (Schor 2003, Martins 2008).

The period of the first 1000 days of life (which begins at conception and ends when the child is two years old) is fundamental to the health of the child and the future adult, since growth and development are subject to many influences that can determine their future standard of living (Szostak-Wegierek 2014, Blackmore & Ozanne 2015, Cunha, Leite, Almeida 2015, Fall & Kumari 2019, Lacagnina 2019, Villares, Collado, Larqué, Trabazo, De Pipaón & Aznar 2019, Humphrey, Hagan, Suresh & Sundgren 2019). The birth, which marks the passage of the gestational period to the outside world, represents an exchange of environment and relationships, establishing two phases that deserve the attention of health professionals. While for the second phase, that is, after birth, childcare is directed at the child, for the previous phase, during the gestational period, pregnancy care is basically practiced by obstetricians and general practitioners.

In their role as advocate for children and families, pediatricians are in position to help parents during the gestational period, establishing a relationship of trust and support at this stage of life (Ioannides 2017). Thus, during the gestational period, the participation of the pediatrician in the development of preventive activities with the trinomial pregnant-fetus-family is fully feasible, which can be called Antenatal Childcare. These activities, with specific objectives and different from those of the traditional prenatal, will occur in parallel with the care offered by the care program for pregnant women, and should start from the stage of pregnancy planning, with the preconception consultation.

Preconceptional care

Preconceptional care is the first stage of the Antenatal Care. Medical care during the pregnancy planning period is a fundamental step in health actions that aim to contribute to the quality of life of the mother and the fetus. In this service, information is gathered to identify and modify, whenever possible, individuals at risk of having children affected by genetic conditions or congenital anomalies, reproductive risk factors, in addition to treating diseases that may alter the natural evolution of pregnancy (Brundage 2002, Brent 2011, Konje 2018, Dorney & Black 2018, Griejer 2020). Before their infant is born parents may be concerned about risks of some environmental exposures, hereditary diseases and other factors that may interfere with pregnancy. Therefore,

advising parents on these aspects requires the participation of the pediatrician as the doctor who for a long time will interact with the family offering health care to the child from conception. In this sense, the objectives of preconception consultation are (Wilkinson & Carroll 2018, Pacheco 2020, Chun, Leung, Wen, McDonald & Shin 2020, Oie 2020, Miller, Anderson & Lindley 2020):

a) Obtain information on genetic and / or chromosomal abnormalities and history of previous neonatal losses;
b) Genetic counseling regarding inbreeding, inborn errors of metabolism, ethnicity;
c) Reduce birth defects due to advanced or low maternal age and advanced paternal age;
d) Know aspects related to the parents' occupation and exposure to radiation or toxic chemical elements;
e) Nutritional habits and harmful lifestyle (alcohol, tobacco, drugs).

All information obtained during this service serves to support counseling and actions that must be implemented already in the preconception period and continue throughout the pregnancy.

Antenatal Childcare

After the pregnancy is confirmed the pediatrician starts to relate to the future mother and family directing educational activities, health promotion, and anticipatory guidance with objectives to serving as a reference and offering support. The direct participation of the pediatrician during pregnancy aims to (Cronin 2003, Leal, Esteves-Pereira, Viellas, Domingues & Gama 2020):

a) Establishing the relationship physician-family and starting child health care before birth; stimulating the mother-child bond. Parents are the most central and enduring influence in children's life and their interaction with pediatricians is fundamental for the good development of the child
b) Identifying needs and difficulties of first-time mothers; clarifying about perinatal events (hospitalization, type of delivery, nursery, rooming-in); understand concerns and doubts and help increase the safety of pregnant women with emotional support
c) Providing information and advice, building parenting skills for mothers and fathers
d) Identifying high-risk situations: (adolescent mother, single mother, domestic violence, harmful habits such as alcohol consumption, smoking, drugs of abuse)
e) Assist and facilitate the relationship with the obstetrician regarding the preparation of the pregnant woman for childbirth
f) Advise on the importance of puericulture

The number of meetings and its frequency can be flexible, varying according to the needs or interests of the pregnant woman. In order that a minimum program can be developed, a list of topics to be discussed at each meeting should be offered, as described below:

a) Early mother-infant interaction:
   Mother-infant bonding (M-Ib) is defined as the emotions and feelings experienced by a mother toward her child, with mutual influences by hormonal mechanisms that start in the utero and continue after birth by way sensory stimulation (skin-to-skin contact, visual, olfactory, etc) and that contribute to the adaptative changes in both mother and child (Daglar & Nur 2018). M-Ib is considered important for a positive socio-emotional-development because it serves as a model for various relationships in later stages of life (Tichelman, Westerneng, Witteveen, van Bar, van der Horst, Jong et al. 2019). Furthermore, this interaction increases the child's protection against abuse, neglect, and domestic violence, consolidating the child's social role in the family (Saisto & Halmesmak 2003, Loundes, Borkowski & Whitman 2006, Miller 2011, Coskuner, Mamuk, Dermici & Hamlac 2017, Glover & Capron 2017, Farré-Sender, Torres, Gelabert, André, Roca, Lasheras et al. 2018, Kayris 2020, Gressier, Letranchant, Glatigny-Dallay, Fallisard & Sutter-Dallay 2020, Brannigan, Tanskanen, Huttunen, Cannon, Leacy & Clarke MC 2020).
b) Assist in the preparation of motherhood
   Some pregnant women not yet had any preparation for motherhood. Thus, this motherhood preparation can start during the gestational period especially in cases of unplanned pregnancy, to avoid rejection and

prepare to offer the necessary care to the newborn (Cronin 2003, Javadifar, Majlesi, Nikbakht, Nedjat & Montazeri 2016, Brummelte & Galea 2016, Osono-Castaño, Carvajal-Carrascal & Rodriguez-Gazquez 2017). The principal objective is to improve understanding, involvement, and satisfaction with pregnancy and the neonatal period since maternal and family parenting style is essential for a health maturation of an infant's cognitive, behavioral, and social skills (Atrash, Johnson, Adams, Cordero & Howse 2006, Miller 2011, Walsh 2020).

c) Birth planning and postpartum feelings

Patient should be informed about care options and participate in decision making regarding the type of delivery, possibilities of the parents' presence during delivery, and regulation of rooming-in and nursery (Demsas, Svetina, Verdenick, Tul, Blickstein & Velikonja 2017, Nieuwenhuijze & Leahy-Warren 2019). Such guidance aims to reduce the anxiety and fear that unknown situations can cause in this stage of pregnancy. Some patients have tokophobia (fear of childbirth) – psychological disorder which ranges from insignificant to extreme fear of childbirth (Bell & Andersson 2016 and need to be supported more carefully to avoid situations that may interfere with childbirth.

It is also essential to develop actions aimed at preventing postpartum depression, a problem that affects 10 to 15% of women and impairs mother-infant interactions. This condition has multifactorial causes (interaction of adrenal, placental, sex, and peptides hormones) and neurobiological mechanisms, and when present, it must be identified as early as possible and treated appropriately (Desauny, Perrin & Gerardin 2016, Binns, Lee & Low 2016, Walsh 2020).

d) General childcare issues

1. Breastfeeding: the antenatal period is an excellent opportunity to provide guidance on breastfeeding, highlighting the benefits for the child and the mother and demystifying cultural aspects that may interfere with this practice. Breastfeeding is the most important and effective action for the child's good health, contributing to reduce childhood morbidity and mortality (Mosca & Gianni 2017, Bunik 2017, Meek 2017, McClure, Cataldi JR & O'Leary 2017, Sattari, Serwint & Levine 2019, Quesaja, Méndez & Martin-Gil 2020,
2. Vaccines: advise on the importance of vaccines for protection against infectious diseases, resolving doubts and fears about their effectiveness and safety, and increasing vaccination coverage (Nitsch-Osuk 2017, Schaeffer & Asnes 2018, De St Maurice, Edwards & Hackell 2018, Kennedy 2020, Charron, Gautier & Jestin 2020). In addition to the vaccines that must be applied to children, vaccination of contact persons is a strategy to avoid risks (cocoon vaccination), immunizing adults to preventing the spread of an illness in children, to minimize the risk of transmission of pathogens in the environment of a patient who is susceptible to an infection (Le Tinier, Billieux, Pfister, De Tejada 2020, Kennedy 2020).
3. Accident prevention: non-intentional injuries are an important preventable cause of morbidity and mortality in infancy and the best way to reduce its impact on the lives of children and family members is the prevention. According to the different stages of the child's neuromotor development, guidance should be offered on protection against falls, intoxication, asphyxiation, burns and drowning (Ehrhardt, Xu, Khoury, Yolton, Lanphear & Phelan 2017, Weismiller 2017).
4. Neonatal screening: advise on the tests that are part of the neonatal screening and its importance to detect disorders that are threatening to life or long-term health before they come symptomatic. These include hemoglobinopathies, congenital heart defects, hearing loss, inborn errors of metabolism, cystic fibrosis, immunodeficiencies, and endocrine disorders (Barca, Mazzuca & Borghi 2017, Therrell & Padilla 2018).
5. Newborn physiology: resolve doubts regarding physiological issues of the newborn such as crying, breathing pattern, infantile colic, reflexes and neuromotor development, care for the umbilical stump, sleep, pacifier, evacuation habit, bathing, more appropriate clothes and mental hygiene (Johnson & Hunt 2019, Shimko 2019, Paladinen, Blenningn & Strangas 2019). These are aspects whose ignorance can generate anxiety and motivate the search for information in inappropriate sources on the internet, at the risk of misinterpreting due to the lack of medical and scientific terms

(Paladinen, Blenningn & Strangas 2019, Kumar, Biswas, Lyengar & Kumar 2015, Kodman 2018).

Conclusions

Pediatricians are the first caregivers for babies after hospital discharge and probably the first doctors that mothers see after birth (Sayres & Visentin 2018). However, childcare starts long before the baby is born, as many social, cultural, emotional, biological, demographic, and economic factors influence child health from conception.

Therefore, it is essential that actions are developed to reduce maternal and child morbidity and mortality by anticipating preventive measures associated with prenatal and childcare (Aris, Fleisch & Oken 2018). In this context, during the gestational period the pediatrician can play an important role as an educator with the pregnant woman to expand self-care and assist the future mother with the difficulties inherent to the neonatal period.

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The Asian Institute of Research
Journal of Health and Medical Sciences
Vol.3, No.2, 2020: 223-227
ISSN 2622-7258

DOI: 10.31014/aior.1994.03.02.119

Right Coronary Artery: Abnormal Birth and Literature Review

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Abstract
The birth defect of the right coronary artery from the aorta is an anatomical malformation characterized by the abnormal birth of the right coronary artery from the antero-left sinus. It has an abnormal initial path between the aorta and the pulmonary artery and is most often intramural in the aortic wall. It represents 0.1 to 0.3% of the population and exposes to a high risk of sudden death on exertion. The mechanism retained for sudden death is the occurrence of stress myocardial ischemia by compression of the abnormal artery between the two large vessels. The diagnosis can be confirmed by a careful echocardiographic examination. The coronarography confirms the diagnosis. Surgical treatment presents a very low risk and eliminates the risk of stress myocardial ischemia. It therefore appears necessary to look for this anatomical anomaly systematically, at least in all young adults who engage in intense sports activities.

Keywords: Right Coronary Artery, Sudden Death, Coronarography

1. Introduction

Among the various anomalies of birth and initial path of the coronary arteries, some are important to detect and correct because they expose them to a risk of sudden exertional death. These are, in particular, malformations in which a coronary artery arises from the contralateral coronary sinus and presents an initial path between the aorta and the pulmonary artery. These anomalies are not uncommon and affect 0.1 to 0.3% of the total population. Their interest is due to the fact that they are responsible for 15 to 20% of the sudden deaths observed in young athletes (Houyel & Plate. 2002).

The most frequent mode of discovery remains a sudden "recovered" death, occurring during or immediately after a very intense physical effort. Often there are warning signs before the acute episode: chest pain, syncope or abnormal exercise heart rate. More and more often, the anomaly is detected during a systematic echocardiographic assessment or carried out for another reason cardiovascular. (Taylor, Rogan & Virmani. 1992).

A careful echocardiographic examination can confirm the diagnosis, especially in children and adolescents. In adults, making the diagnosis can be more difficult and any suspicion must be confirmed by an imaging technique

(coronary angiography, CT or MRI). In asymptomatic patients, additional examinations are necessary to reveal possible effort ischemia (echocardiography or effort scintigraphy). (Brothers, Whitehead, Keller & al. 2015).

The operating indications remain discussed. It is currently recognized that all patients with an abnormality of the left coronary artery should be operated whether symptomatic or not. (Garcia-Rinaldi, Sosa & Olmedo. 2004). Several surgical techniques have been described (Vouhé. 2014). Some are aimed at removing the pulmonary

artery from the abnormal coronary artery. Others aim to open the intramural path or create a coronary neostostium at the appropriate coronary sinus.

2. Clinical observation

It was a 74-year-old patient who was referred to us for surgical treatment of aortic valve disease with a tight aortic stricture type.

In his history there was a chronic obstructive pulmonary disease, a transient ischemic attack and a bilateral treatment of varicose veins of the pelvic limbs. Her cardiovascular risk factors were hypertension and a notion of coronary inheritance.

Clinically she had grade 2 to 3/4 effort dyspnea (NYHA) and a typical breath of aortic stenosis. The doppler of the supra-aortic trunks did not show any hemodynamically significant lesion of the supra-aortic trunks intended for the brain. On coronary angiography, there were no significant lesions. The left coronary artery and its branching branches had a classic anatomical arrangement (Figure 1).

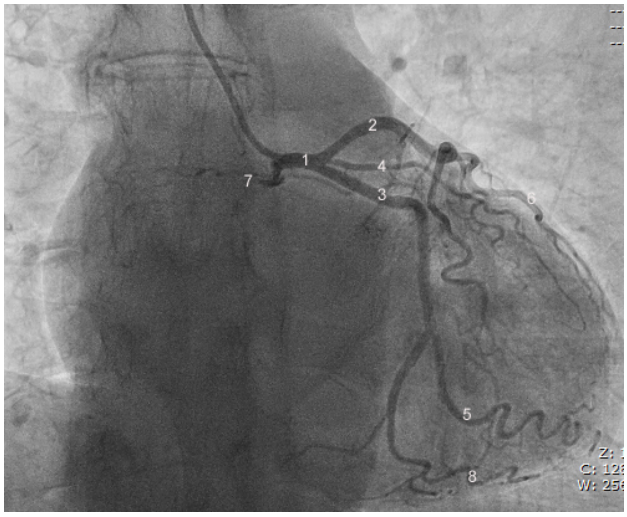

Figure 1 : **showing the left coronary artery and its branching branches on a coronarographic image**

1.trunk of the right coronary artery; 2. anterior interventricular artery; 4. bisecting artery; 5. left posterior ventricular artery (marginal); 6. Left anterior ventricular artery (diagonal); 7. Aortic sinus
In contrast, the right coronary artery originated from the antero-left sinus (Figure 2).

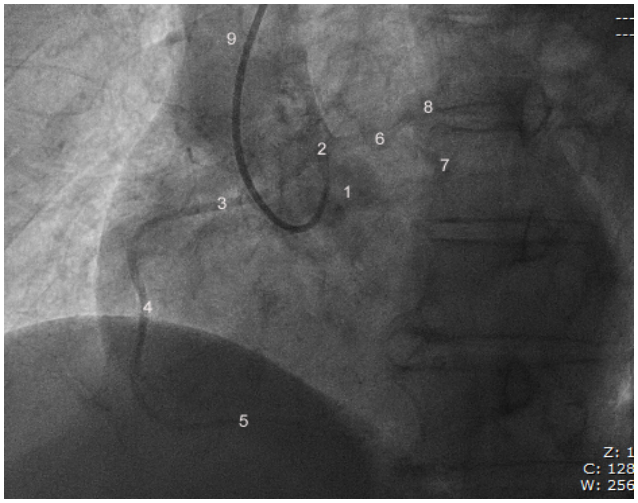

Figure 2: showing the birth of the right coronary of the antero-left sinus on a coronarographic image.

1.Aortic sinus ; 2. origin of birth of the right coronary artery in the antero-left sinus ; 3. first of the right coronary artery; 4. second segment of the right coronary artery; 5. Third segment of the right coronary artery; 6. common core of the left coronary artery; 8. anterior interventricular artery; 8. Circumflex artery; 9. Ascending aorta
The birth defect of the right coronary was clearly visible on the scanner (**Figure 3**).

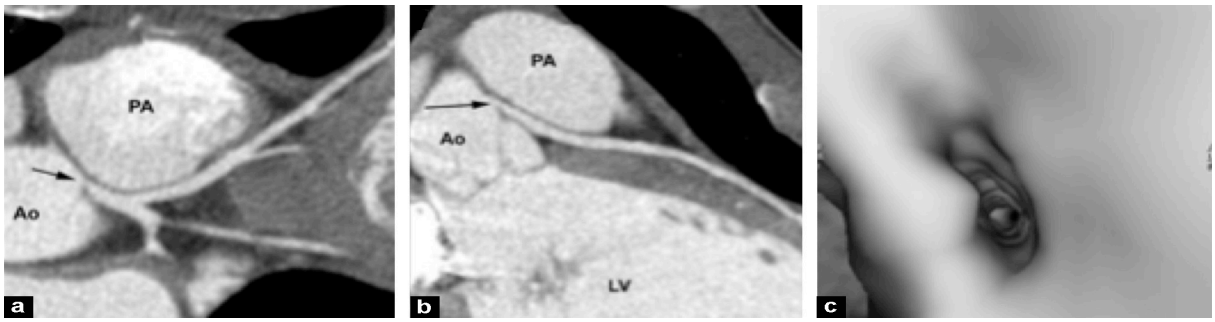

Figure 3. Birth of the left coronary of the right sinus with slit like ostium ostial stenosis and virtual angiography. Ao = ascending aorta; PA = pulmonary artery; LV = left ventricle

Functional respiratory tests were standard. Echocardiography noted an aortic stenosis with an average gradient measured at 52 mmHg, an aortic surface measured at 0.52cm² / m², a tubular aorta at 28mm, and a left ventricular function retained at 70%.

The patient's dental care was performed before surgery and she underwent aortic valve replacement with a bioprosthesis. No action has been taken on the birth anomaly of the right coronary artery due to the absence of related symptoms. On the other hand, the knowledge of its abnormal position helped us in the strategies of cardioplegia. The aftermath was simple. She left our service on D8 postoperatively.

3. Discussion

The normal coronary artery arises at the center of "its" coronary sinus. The abnormal artery arises from the same sinus (an abnormal right coronary artery arises from the antero-left sinus and vice versa). The ostium of the abnormal artery is often deformed into a slit and narrowed. The abnormal artery presents an initial path between the aorta and the pulmonary artery, most often intramural, incorporated into the aortic wall (Ou, Khraiche, Celermajer & al. 2013.) (Figure 4). This intramural segment is generally closely related to the adjacent valve commissure. The abnormal artery then resumes a normal epicardial course.

The birth defect of the right coronary artery is 5 to 6 times more frequent than that of the left coronary artery (Brothers, Whitehead, Keller M & al. 2015).

It is clearly established that the birth anomaly of the right coronary artery can be responsible for sudden death, in particular during or after intense effort (La Vecchia, Favero & Fontanelli. 2002).

Although the pathophysiology remains poorly explained, the most likely mechanism is that of an acute myocardial ischemia by compression of the abnormal artery, between the aorta and the pulmonary artery, while the large vessels dilate during effort. This dynamic compression is undoubtedly aggravated by associated anatomical factors: deformation and stenosis of the coronary ostium, anomaly of the angle of emergence of the coronary, autonomous stenosis of the intramural path, in particular with regard to the valve commissure.

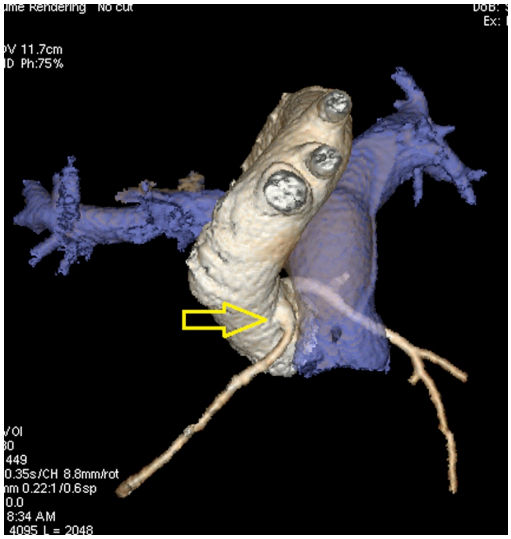

Figure 4: **Birth of the right coronary of the antero-left sinus with inter-aorto-pulmonary path.**

4. Conclusion

The presence of an aortic birth defect in a coronary artery exposes the patient to a certain risk of sudden exercise death. The diagnosis can almost always be confirmed by a careful echocardiographic examination. Surgical treatment presents a very low risk and eliminates the risk of stress myocardial ischemia. It therefore appears necessary to look for this anatomical anomaly systematically, at least in all young adults who engage in intense sports activities.

Declaration of interest links

The authors state that they have no interest links.

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The Asian Institute of Research
Journal of Health and Medical Sciences
Vol.3, No.2, 2020: 228-259
ISSN 2622-7258

DOI: 10.31014/aior.1994.03.02.120

Scoping Review of the Effects of Dietary Supplements on Postpartum Depression

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Abstract
Postpartum depression (PPD) can emerge as one of many maternal risks during the postpartum period. Though antidepressants have traditionally treated PPD, dietary supplements have been increasingly studied as a more accessible remedy, focusing on prevention. The goal of this study is to consolidate information about the effects of dietary supplements on PPD. A scoping review was conducted to identify a possible relationship between various supplements and PPD, using relevant studies on PubMed and Medline published between January 1, 2010 and February 1, 2020. Only English language literature with human subjects was included. 39 articles (from 606 articles originally retrieved) were included and summarized under headings related to: vitamins; minerals; fatty acids; antibiotics and probiotics; and, combination of supplements. The results revealed that dietary supplementation with Vitamin D, multivitamins, selenium, n-3 polyunsaturated fatty acids (PUFA), or probiotics generally lead to decreased PPD risk. Supplementation with calcium, magnesium, zinc, iodine, iron, or any B-vitamins has no effect on PPD, although there are conflicting reports regarding folate, Vitamin D, and n-3 PUFA. Furthermore, antibiotic usage and n-6 PUFA intake have correlated with increased PPD risk. Studies assessing supplement co-exposure were limited. The results of this review are mixed, with some dietary supplements having a positive effect and others having a negative or no association with PPD. This review highlights the limited knowledge regarding the effects of selenium, iodine, probiotics, and antibiotics. Further research is needed to study the combined effects of various supplements on PPD, as mothers often take multiple supplements during pregnancy.

Keywords: Antibiotic, Dietary Supplement, Maternal Mental Health, Mineral, Omega-3 Fatty Acid, Omega-6 Fatty Acid, Postpartum Depression, Probiotic, Vitamin

1. Introduction

1.1 Postpartum Depression

Postpartum depression (PPD) is a common mental disorder that affects mothers with a variety of symptoms. Differing from the 'baby blues' which requires no treatment, PPD is defined in the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-V) as a major depressive disorder that has an onset within 1 month of childbirth (American Psychiatric Association, 2013). However, cases of PPD can start during the pregnancy period and/or may have onset beyond the first postpartum

month (Gavin et al., 2005). Symptoms of PPD often include sleep disturbances beyond those associated with baby care, overwhelming anxiety, a loss of energy, feelings of worthlessness or guilt, and in more severe cases, thoughts of suicide and harm to the baby (American Psychiatric Association, 2013).

The prevalence of PPD varies between countries, with higher ranges among lower- and middle- income nations. In 2012, a cross-sectional study found a point prevalence of approximately 7.48% in Canadian women, while other studies have found that the global prevalence of PPD is approximately 17.7%, ranging from 3% in Singapore to 38% in Chile (Dennis, Heaman, & Vigod, 2012; Hahn-Holbrook, Cornwell-Hinrichs, & Anaya, 2018). Nations with higher rates of income inequality, maternal and infant mortality, or women of childbearing age working ≥40 hours a week have higher rates of PPD (Hahn-Holbrook et al., 2018). The global prevalence is set to rise over time, with differences in wealth inequality and maternal health factors explaining the majority of prevalence variation among countries.

Many individual risk factors also increase the risk of a mother developing PPD. The strongest risk factor for PPD is a history of mood or anxiety disorders, especially if left untreated during pregnancy (Stewart & Simone, 2016). In these cases, mothers can be 2-3 times more likely to develop PPD (Dennis et al., 2012; D. Nielsen, Videbech, Hedegaard, Dalby, & Secher, 2000). Likewise, if a mother has a positive family history of PPD, she tends to be more at risk for the disease, with an odds ratio (OR) of approximately 1.6 (D. Nielsen et al., 2000). Furthermore, social risk factors for PPD can include low household income, low partner support, incidences of interpersonal violence, marital conflict, poor self-perceived maternal health, and young maternal age (Dennis et al., 2012; Stewart & Simone, 2016).

Early screening and detection of PPD are widely known to be beneficial for the mother in reducing the severity of her symptoms. However, the best method for detecting postpartum depression remains controversial, and many diagnostic tools are used around the world. Most commonly used is the Edinburgh Postnatal Depression Scale (EPDS), where a score ≥13 is often used as an indicator of PPD (Boyd, Le, & Somberg, 2005). Its widespread use has led it to be translated into numerous languages and modified according to specific national guidelines (Boyd et al., 2005). Another common self-report instrument is the Beck Depression Inventory (BDI); a score ≥30 is usually indicative of PPD (Boyd et al., 2005). Similar to the EPDS, it has been translated and used in many different languages. Many other diagnostic tools are available, including the Bromley Postnatal Depression Scale (BPDS) and the Self-Rating Depression Scale (SDS), but these are less used due to low sensitivity and low positive predictive values (Boyd et al., 2005).

Current treatment for PPD includes psychotherapy and antidepressants, but studies are increasingly reporting that these therapies have milder effects on PPD than initially believed. Selective serotonin reuptake inhibitors, such as fluoxetine, sertraline and paroxetine, are the most commonly used antidepressants, but studies are now doubting their efficacy. In a systematic review by Shama & Sommerdyk (2013), antidepressant usage failed to show significant improvements in PPD symptoms compared to a placebo or psychotherapy alone (Sharma & Sommerdyk, 2013). Furthermore, some antidepressants were found to have higher PPD remission rates compared to the placebo-control groups (Sharma & Sommerdyk, 2013). In a meta-analysis by Cuijpers, Brännmark, & van Straten (2008), results showed that psychological treatments, including psychotherapy, have smaller effect sizes on PPD compared to those usually found for treatment on other types of depression (Cuijpers, Brännmark, & Straten, 2008). Similarly, evidence showed that psychological treatment often does not have a significant long-term effect on PPD (i.e. 6-12 months follow-up) (Cuijpers et al., 2008).

Unfortunately, compliance with PPD treatment is not deemed optimal either. Boath, Bradly, & Henshaw's (2004) observational study found that nearly 50% of breastfeeding participants with PPD did not take their prescribed antidepressants for various reasons (Boath, Bradley, & Henshaw, 2004). The most common explanations for a lack of compliance were misunderstandings about medication, including the belief that the antidepressants were addictive and can impact child development, or a lack of perceived benefit (Boath et al., 2004). Other studies have highlighted that obstacles to psychotherapy also limit patient compliance, including stigma, cost, and limited access to psychotherapists (Stewart & Simone, 2016).

The conflicting results regarding the lack of efficacy and compliance to current treatment highlights the need for more effective remedies with which women are likely to comply.

1.2 Dietary Supplements

Since the turn of the century, there has been a sudden growth in interest in the use of dietary supplements to treat various ailments, including depression. According to the 'WHO Traditional Medicine Strategy 2014-2023', over 100 million Europeans regularly use complementary medicine, including dietary supplements; this number increases in Africa, Asia, Australia and North America (World Health Organization [WHO], 2013). Furthermore, one New Zealand study reported that over 63% of participants with current depressive episodes take at least one supplement daily, with an average of 2.8 dietary supplements taken daily (Silvers, Woolley, & Hedderley, 2006). Many people around the world use daily dietary supplements; however, these supplements can also be taken in addition to traditional prescribed pharmaceuticals when used as a potential remedy for an illness like depression. Nevertheless, there is a general dearth of information regarding the combinatory effects of the two when taken together. These findings suggest that dietary supplements are generally considered by the public to be beneficial for health problems, including depression, possibly due to the belief that it is 'more natural.' Despite the public's perception, there are relatively few studies that assess the effects of various supplements on ailments, in particular PPD.

1.3 Current Study

We are interested in the effects of various common dietary supplements, taken by the mother during the prenatal or early postpartum period, on postpartum depression. A clearer view is urgently needed to better understand and clarify the effects of various dietary supplements on PPD. This knowledge can then be applied to help increase adherence to treatment, using scientifically proven effective supplements, although future correlational studies will be needed to verify this potential relationship.

This scoping review aims to assess the positive and negative effects of various common dietary supplements, taken prenatally or postpartum, on maternal PPD. It will explore the possibility of different supplements as risk or protective factors for developing postpartum depression among reproductive age women. More specific research objectives include: (1) to determine whether present literature supports a link between various supplements and postpartum depression; (2) to assess whether specific supplements provide a higher risk for postpartum depression, and thus whether pregnant women should avoid these supplements; and, (3) to assess whether specific supplements help provide protection against postpartum depression, and thus whether pregnant women should use these supplements. As there is currently no study outlining this potential relationship, a scoping review was chosen over a systematic review to provide an overview of the current knowledge and to act as a potential precursor to a more vigorous systematic review.

2. Methods

2.1 Eligibility Criteria

For inclusion as part of this review, the following were fulfilled:

1. Studies: journal articles (peer-reviewed), randomized-controlled trials, prospective studies, retrospective studies, cross-sectional studies, case-control studies, exploratory studies, and analysis of primary data.
2. Participants: women, single or married, first-time pregnancy or otherwise, and vaginal or Caesarean birth.
3. Interventions (dietary supplement exposure): Vitamin B, Vitamin D, multivitamins, omega-3 fatty acids, omega-6 fatty acids, calcium, zinc, magnesium, iodine, selenium, iron, folate, antibiotics, *Lactobacillus rhamnosus* HN001 probiotics, multi-nutrients and a combination of supplements.
4. Outcome: all types of methods for the potential diagnosis of PPD symptoms were considered: Edinburgh Postnatal Depression Scale (EPDS), Beck's Depression Inventory (BDI), Centre for Epidemiologic

Studies-Depression (CES-D) scores, the Bromley Postnatal Depression Scale (BPDS) and the Self-Rating Depression Scale (SDS), and self-diagnosed PPD.

Studies were excluded if maternal PPD scores or symptoms were not the primary measured outcome.

2.2 Search Strategy

Comprehensive literature searches were conducted to retrieve articles of interest from 2 databases: Medline and PubMed.

A list of key words was developed to correspond with terms related to the fields of interest —postpartum depression and dietary supplements — based on preliminary research on common supplements mothers take during the pregnancy period. Trial and error was then used to identify the best key words and subject headings for each database. The key words for dietary supplements included both vague and specific terms (e.g. 'Dietary Supplements' and 'Docosahexaenoic Acids'). The complete lists of key words used for the Medline search is found in Table A in the Appendix. The complete lists of key words for PubMed is found in Table B in the Appendix.

2.3 Data Extraction

Covidence (Veritas Health Innovation Ltd, Melbourne, Australia), an online systematic review managing program, was used to import and evaluate the extracted studies from the two databases. Duplicate articles were automatically removed by Covidence, and one reviewer evaluated the removed duplicates to ensure that the proper articles were excluded.

Two review stages were then completed to assess and select the articles used in this review. Firstly, titles and abstracts were evaluated by one reviewer based on the following exclusion criteria: (1) publication date before January 1, 2010; (2) neither titles nor abstracts described any type of dietary supplement nor PPD. Secondly, a full-text review was completed by one reviewer to determine the included articles, based on the eligibility criteria listed below. See Figure 1 for a visual representation of the article screening process.

2.4 Eligibility Criteria

All studies included in this analysis: (1) involved human models; (2) included direct or indirect exposure to vitamins, minerals, fatty acids, antibiotics, or probiotics; (3) had a primary outcome involving PPD symptoms or diagnosis at any timepoint postpartum, using tests such as, but not limited to, the EPDS, BDI, and self-reported diagnosis; and, (4) analyzed quantitative data, whether primary source or secondary source data.

Studies were excluded from this analysis during the full-text screening if: (1) animal or rat models were used; (2) interventions other than exposure to vitamins, minerals, fatty acids, antibiotics, or probiotics were used; (3) maternal PPD scores or symptoms were not the primary measured outcome; (4) the study was grey literature or a literature review (scoping review or systematic review); (5) any remaining duplicate articles remained; (6) the study was written in a language other than English; or, (7) the full text was not available.

Studies were included irrespective of their definition of PPD. Likewise, studies were included regardless of the geographic location or type of PPD test that was used. The ten-year time frame for eligible articles in this review was set to include articles that likely used more modern diagnostic criteria, while also including as much information as possible, due to the novelty of this topic.

2.5 Data Analysis

Given our interest in looking at different types of studies, and the varied outcomes associated with each of these studies, we decided to conduct a narrative synthesis. This approach allowed us to include as many studies as possible, as well as provide a comprehensive analysis of the studied supplements.

3. Results

The initial search strategy yielded 606 articles from the two databases. After automatic de-duplication, 366 articles were admitted to level 1 screening. After both screening phases, 39 articles were included in the review. See Figure 1 for a PRISMA diagram outlining the screening process. Of the 39 included articles, one focused on antibiotics, one focused on probiotics, 15 studied fatty acids, four investigated minerals, and 19 focused on vitamins. Four studies focused on a combination of various minerals and vitamins on PPD. Note that this number exceeds 39 as some articles researched multiple supplements simultaneously.

3.1 Quality Assessment

The quality of the cohort studies (n=25) was assessed using the CASP (Critical Appraisal Skills Programme) checklist. Of the 25 articles, 2 had poor overall quality, 11 had a satisfactory level of overall quality, and 12 had a good of overall quality. Please refer to Table C in the Appendix for the overall quality assessment of each of the cohort studies.

The quality of the case-control studies (n=2) was assessed using the Downs and Black Checklist. Both the Abedi et al. (2018) and N. O. Nielsen et al. (2013) studies were considered to be of satisfactory quality. The Abedi et al. (2018) study had a Downs and Black Checklist score of 22 out of a possible 32 points, while the N. O. Nielsen et al. (2013) study had a score of 25 out of 32. Please see Table D in the Appendix.

The quality of the cross-sectional studies (n= 2) was assessed using the Downs and Black Checklist. Please refer to Table D in the Appendix for the overall quality assessment of each of the cross-sectional studies. Both the Cosatto, Else, & Meyer (2010) and Lin et al. (2019) studies were of satisfactory quality. The Cosatto, Else, & Meyer study (2010) had a Downs and Black Checklist score of 22 out of a possible 32 points, while the Lin et al. (2019) study had a score of 25 out of 32.

The quality of the randomized-controlled trials (n=9) was assessed using the Cochrane Risk of Bias tool. The judgement for each entry was labelled with a risk of bias of 'low risk', 'high risk', or 'unclear risk', with the 'unclear risk' category indicating either a lack of information or uncertainty of the potential for bias. Of the articles, Amini et al. (2020), Fard et al. (2017), Makrides et al. (2010), Nguyen et al. (2017), and Slykerman et al. (2017) were considered to have low risk of bias, with zero or one classification of 'unclear risk' of bias. Williams et al. (2016) had one classification of 'high risk' for potential reporting bias, while Paoletti et al. (2013), Vaz et al. (2017), and Vaziri et al. (2016) likely have high risk of bias in their respective articles. Please refer to Table E in the Appendix for the overall quality assessment of each of the randomized-controlled trials.

3.2 Analysis of Results

3.2.1 Vitamin D

Fourteen studies investigated the effects of Vitamin D on postpartum depression, nine of which focused specifically on 25-hydroxycholecalciferol, or 25(OH)-D, a pre-hormone produced by the hydroxylation of Vitamin D3. Typically, Vitamin D supplementation has been shown to decrease hypertensive disorders and other, especially musculoskeletal, comorbidities of pregnancy (Mithal & Kalra, 2014). The mothers in each of the included studies had no known prior health issues, but it is not known whether they had also ingested other supplements, as the studies did not inquire about other supplementation. Results from these studies were mixed,

with some articles indicating protective effects of Vitamin D, while others concluded that it has no effect on PPD risk (Table 1). Note that serum 25(OH)-D levels were used as an objective measure of maternal vitamin intake.

Using prospective cohort designs, three articles concluded that Vitamin D was ineffective in reducing PPD symptoms, while five articles determined that Vitamin D was protective against the depression. Of the three articles with statistically insignificant results, Gould et al. (2015) compared umbilical cord 25(OH)-D levels with EPDS scores at 6 weeks and 6 months postpartum. At both times, vitamin levels were not significantly different between mothers with PPD and mothers without PPD (Gould et al., 2015). In the Leung et al. (2013) and Miyake et al. (2016) studies, Vitamin D supplementation during gestation was self-reported by mothers to determine possible correlations with EPDS scores ≥10 and Centre for Epidemiologic Studies-Depression (CES-D) scores ≥50, respectively (Leung et al., 2013; Miyake et al., 2016). Neither study reported significant relationships between supplementation and PPD at their respective follow-up periods, stipulating that Vitamin D produced no benefits (Leung et al., 2013; Miyake et al., 2016).

Of the prospective cohort studies that produced significant results, all five of them used maternal serum 25(OH)-D as their supplement of interest. Accortt et al. (2016), Gur et al. (2015), Lamb et al. (2018), and Robinson et al. (2014) measured 25(OH)-D at various points during the gestational period prior to childbirth, and compared these levels in women with and without PPD, diagnosed using the EPDS (Accortt, Schetter, Peters, & Cassidy-Bushrow, 2016; Gur et al., 2015; Lamb et al., 2018; Robinson et al., 2014). Gur et al. (2015) found a negative correlation between the two variables at 1 week, 6 weeks, and 6 months postpartum, with r values of -0.2, -0.2, and -0.3 ($p<0.05$) respectively (Gur et al., 2015). Similarly, Lamb et al. (2018) found a negative relationship between serum levels taken 14 weeks into gestation ($r=-0.23$, $p<0.05$) and 6 weeks postpartum ($r=-0.22$, $p<0.05$), and EPDS scores at 10 weeks postpartum; however, there was no significant correlation between 25(OH)-D levels measured at 32 weeks into gestation and EPDS scores at 10 weeks postpartum (Lamb et al., 2018). Robinson et al. (2014) determined that low gestation 25(OH)-D levels were a significant risk factor for PPD immediately after childbirth, with an odds ratio of 2.1 ($p<0.05$) (Robinson et al., 2014). In Fu et al.'s (2015) cohort, serum 25(OH)-D levels were taken 24-48 hours postpartum, as opposed to during gestation (Fu, Liu, Tu, Yang, & Cao, 2015). The authors reported that 25(OH)-D levels were higher in women without PPD, and thus were potentially protective against the depression (OR=0.74, $p<0.05$) (Fu et al., 2015).

Two of the included studies had case-control designs, separating women with PPD from those who did not have it. In the Abedi et al. (2018) study, serum 25(OH)-D levels were compared to the presence or absence of depression, using a BDI score ≥17 (Abedi, Boyari, Fakhri, & Jahanfar, 2018). Women with PPD were found to have lower 25(OH)-D levels compared to women without PPD, with the study citing an OR=3.30 ($p<0.05$) for those with lower 25(OH)-D (Abedi et al., 2018). However, the cut-off level for 25(OH)-D was not defined in the article. In the second article, N. O. Nielsen et al. (2013) also used maternal blood concentrations to study a potential relationship between Vitamins D2 and D3, and PPD. Unlike the previous study, authors found no significant relationship between either vitamin and PPD (N. O. Nielsen et al., 2013).

A cross-sectional study by Lin et al. (2019) investigated potential Vitamin D and retinol relationships with PPD. Using serum 25(OH)-D and retinol levels at 6-8 weeks postpartum, no significant relationship was found between vitamin levels and presence of PPD (Lin et al., 2019).

The two randomized controlled trials (RCT) produced contradicting results. Vaziri et al. (2016) exposed pregnant women to either 0 or 2000IU of Vitamin D3 daily from 26-28 weeks into gestation until childbirth (Vaziri et al., 2016). The resulting data suggested that Vitamin D3 supplementation was protective against PPD at 4 and 8 weeks postpartum (Vaziri et al., 2016). At each time point, the mean EPDS scores of the trial group were lower than the scores of the placebo group, with an average score difference of 2.88 ($p<0.05$) (Vaziri et al., 2016). In comparison, Williams et al. (2016) exposed pregnant women to either ≥20 ng/mL of Vitamin D per day or <20ng/mL of Vitamin D daily (Williams et al., 2016). After 6-8 weeks postpartum, no significant association was present between the two groups, indicating that Vitamin D is ineffective against PPD (Williams et al., 2016).

The exploratory study by Murphy et al. (2010) used a convenience sample to determine the ability of maternal 25(OH)-D to predict PPD diagnosis based on EPDS scores. Results showed a significant relationship between low

25(OH)-D levels and high EPDS scores, indicating that Vitamin D is protective against the depression (Murphy, Mueller, Hulsey, Ebeling, & Wagner, 2010).

3.2.2 Vitamin B

Of the studies researching Vitamin B, results showed that supplementation with Vitamins B1, B3, B6 and B12 had no effect on PPD; however, data involving folate, also known as Vitamin B9, were mixed. B-vitamin supplements are often taken by mothers to reduce anemia in the mother during pregnancy, as well as promote healthy neurodevelopment in the newborn, including the prevention of neural tube defects (Dror & Allen, 2012). The mothers in each of the included studies had no known prior health issues, but it is not known whether they had also ingested other supplements, as the studies did not inquire about other supplementation.

The Blunden et al. (2012) study looked at the effects of Vitamins B6, B12 and folate on PPD. Self-reported maternal intake levels of these vitamins pre- and during gestation were compared to EPDS scores at 6 months and 1 year postpartum. Results showed no relation between vitamin intake at any timepoint during gestation and EPDS scores at any time postpartum (Blunden et al., 2012).

Another prospective study by Chong et al. (2014) researched Vitamin B12 and its potential association with PPD. Maternal plasma vitamin concentrations were taken 26-28 weeks into gestation and compared to EPDS scores at 3 months postpartum (Chong et al., 2014). No statistically significant relationship was found between plasma Vitamin B12 levels and EPDS scores in mothers, supporting the results from the Blunden et al. (2012) study (Chong et al., 2014).

The aforementioned Leung et al. (2013) study also investigated Vitamins B1, B3, B6, B12 and folate, in addition to Vitamin D. In this cohort, no statistically significant associations were present between any of the B-vitamins and EPDS scores at 12 weeks postpartum either (Leung et al., 2013).

A fourth article, authored by Lewis et al. (2012), used a British cohort of pregnant women to study the effects of folate. The women self-reported folate supplementation 32 weeks into gestation, and were followed-up at 8 weeks, 8 months, and 21 months postpartum (Lewis, Araya, Leary, Davey Smith, & Ness, 2012). Although no statistically significant relationship was found between folate intake and PPD, measured by EPDS scores, at 8 weeks or 8 months postpartum, results found a significant inverse correlation between supplementation and EPDS scores at 21 months postpartum (Lewis et al., 2012). Mothers who took the supplements had a smaller increase in EPDS scores compared to mothers who did not take the supplements (Lewis et al., 2012).

Yan et al. (2017) also investigated folate, using a self-reported questionnaire about supplementation during the pregnancy period to investigate a possible relationship with PPD, measured with the Self-Rating Depression Scale (SDS) at 6-12 weeks postpartum (Yan et al., 2017). The authors reported that folate was protective against PPD if taken for more than six months during the pregnancy period (OR=0.76, $p<0.05$) (Yan et al., 2017).

3.2.3 Multivitamins

In the multivitamin study, Dagher & Shenassa (2012) explored a possible correlation between multivitamin intake at various timepoints in pregnancy and PPD. Although supplementation during the second and third trimesters had no significant impact on EPDS scores, supplementation during the first trimester had a significant and inversed correlation with EPDS scores ($r= -1.37$, $p<0.05$) (Dagher & Shenassa, 2012). This indicates that multivitamin supplementation during the first trimester was somewhat protective against PPD, although intake at other timepoints was ineffective.

3.2.4 Minerals

The studies investigating minerals found no relationship between minerals and PPD overall, although one study found selenium to potentially have a protective effect against PPD. The other studies had statistically insignificant results, indicating that zinc, magnesium, calcium, iron and iodine generally have no relationship with PPD symptoms (Table 2). Typically, calcium, iron and magnesium help promote healthy neural development and tissue construction in the baby, while also reducing the risk of pre-eclampsia in the mother (Khayat, Fanaei, & Ghanbarzehi, 2017). Likewise, iodine also has a role in fetal neural development, but has an additional role in regulating maternal thyroid hormone levels, while selenium regulates fetal growth and development (Khayat et al., 2017). The mothers in each of the included studies had no known prior health issues, but it is not known whether they had also ingested other supplements, as the studies did not inquire about other supplementation.

In one triple blind randomized-controlled trial, Fard et al. (2017) used pregnant mothers to determine whether zinc and/or magnesium had an effect on EPDS scores at 8 weeks postpartum. Mothers were randomly assigned to an intervention group of either one zinc sulfate tablet daily, one magnesium sulfate tablet daily, or a placebo daily for 8 weeks (Fard et al., 2017). However, neither intervention group had significant difference in EPDS scores when compared to the placebo group, with authors concluding that magnesium and zinc did not influence PPD risk (Fard et al., 2017).

Another study using a retrospective cohort model investigated the effects of iron, zinc and calcium on self-reported PPD diagnosis based on diet during gestation. Similar to the Fard et al. study, neither iron, zinc, nor calcium intake had a significant impact on PPD (Hogg-Kollars, Mortimore, & Snow, 2011). Mothers with self-diagnosed PPD ingested similar amounts of the aforementioned minerals compared to mothers without PPD (Hogg-Kollars et al., 2011).

In addition to studying Vitamin D, Miyake et al. (2016) explored the effects of calcium on PPD, using the same prospective cohort. Mothers self-reported dietary intake of calcium during the gestation period and were monitored for PPD at 3-4 months postpartum with the CES-D scale (Miyake et al., 2016). Again, the authors noted no statistically significant relationship between calcium intake in the pregnancy period and PPD, indicating that calcium does not have an effect on PPD (Miyake et al., 2016).

In the Leung et al. (2013) study, a cohort of 475 pregnant women was monitored for any relationship between dietary intake of iodine, magnesium, selenium and zinc, and PPD. EDPS scores were taken at 12 weeks postpartum, where scores ≥12 were indicative of PPD, and compared to self-reported maternal supplement intake during the prenatal period. There were no significant relationships between iodine, iron, magnesium or zinc intake and EPDS scores (Leung et al., 2013). However, the authors reported a significant inverse relationship between selenium and EPDS (Leung et al., 2013). The mean ingestion of selenium in mothers later diagnosed PPD was approximately 19mcg, while the mean ingestion of selenium in mothers not diagnosed with PPD was approximately 25mcg ($p<0.05$), suggesting that selenium may be protective against PPD (Leung et al., 2013).

3.2.5 Fatty Acids

Fifteen articles researched the effects of long-chain polyunsaturated fatty acids (LC-PUFA), particularly n-3 PUFA and n-6 PUFA, as well as docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) on PPD. DHA and EPA specific studies were included in this review as they are commonly used examples of n-3 PUFA. These fatty acids are often used during the pregnancy period to improve newborn neurodevelopment and to regulate inflammation (Greenberg, Bell, & van Ausdal, 2008). The mothers in each of the studies had no known prior health issues, but it is not known whether they had also ingested other supplements, as the studies did not inquire about other supplementation. Results from these articles were mixed, with seven articles claiming protective effects, while the other eight suggesting no significant effects (Table 3).

Hoge et al. (2019), Markhus et al. (2013) and Parker et al. (2015) used similar protocols to each other, measuring n-3 PUFA and n-6 PUFA levels in maternal erythrocytes at various points in the gestation period. Hoge et al.

(2019) measured the fatty acid profile at an unspecified time in early pregnancy, while Markhus et al. (2013) analyzed the profile at 28 weeks into gestation, and Parker et al. (2015) used fatty acid profiles taken 36 weeks into gestation (Hoge et al., 2019; Markhus et al., 2013; Parker et al., 2015). The studies produced similar results, identifying a potential significant and negative correlation between total n-3 PUFA, DHA and EPA levels, and PPD (Hoge et al., 2019; Markhus et al., 2013; Parker et al., 2015). Hoge et al. (2019) indicated that DHA (OR=0.55, $p<0.05$) and total n-3 PUFA levels (OR=0.58, $p<0.05$) were strongly protective against PPD (Hoge et al., 2019). Correlation coefficients of -0.39 ($p<0.05$) between total n-3 PUFA and PPD, and of -0.41 ($p<0.05$) between DHA and PPD were also calculated (Markhus et al., 2013).

A n-6 PUFA/n-3 PUFA ratio was also found to be positively correlated with PPD (OR=2.09, $p<0.05$), indicating that high ratios may be a risk factor for PPD diagnosis (Hoge et al., 2019). Additionally, Parker et al. (2015) concluded that increased n-6 PUFA levels were related to an increased risk of PPD; women with EPDS scores ≥10 had approximately 27.1% of their erythrocyte fatty acid profile consisting of n-6 PUFA, compared to 26.8% in women with EPDS scores <9 (Parker et al., 2015). Note that serum levels were used as an objective measure of fatty acid intake by mothers during the gestation period. However, it should also be noted that research has shown significant decreases in n-3 PUFA and n-6 PUFA during normal pregnancy that are not associated with PPD alone, suggesting a potential confounder (Kitamura et al., 2017).

Three prospective cohorts found statistically significant results using self-reported questionnaires. Hamazaki et al. (2019) administered a questionnaire at an unspecified time in the mid-late gestational period on a cohort of 84 181 pregnant Japanese women (Hamazaki et al., 2019). Intake of foods high in n-3 PUFA was found to lower the risk of PPD in mothers at 6 months and 1 year postpartum (OR=0.80 at both time points, $p<0.05$). Likewise, Leung et al. (2013) found that the mean intake of n-3 PUFA in mothers with PPD was substantially less than the mean intake in mothers without PPD (Leung et al., 2013). Whereas mothers with PPD had an average intake of 90mg of n-3 PUFA during gestation, mothers without PPD ingested an average of 180mg ($p<0.05$) (Leung et al., 2013). The third study, by da Rocha & Kac (2012), compared self-reported intake of n-3 PUFA and n-6 PUFA in the first trimester to EPDS scores at least 30 days after childbirth (da Rocha & Kac, 2012). No significant relations were found between total n-3 PUFA or total n-6 PUFA intake and PPD, but the authors did conclude that increased ratios of n-6 PUFA/n-3 PUFA in mothers can be predictive of PPD (da Rocha & Kac, 2012). In mothers with n-6 PUFA/n-3 PUFA ratios greater than 9:1, the prevalence ratio of PPD was 2.72 ($p<0.05$) (da Rocha & Kac, 2012). In the Lin et al. (2019) cross-sectional study, maternal fatty acid profiles were taken at 6-8 weeks postpartum and referenced to EPDS scores, where a score ≥10 indicated PPD (Lin et al., 2019). The authors discovered that increased total n-3 PUFA levels (OR=0.994, $p<0.05$) and n-3 PUFA/n-6 PUFA ratios (OR=0.764, $p<0.05$) may be protective against PPD (Lin et al., 2019). As well, mothers with higher total n-6 PUFA levels were at a greater risk of PPD (OR=1.005, $p<0.05$) (Lin et al., 2019). However, despite being statistically significant, the calculated odds ratios were close to 1, potentially rendering the effects negligible. Note that fatty acid profiles in erythrocytes were used as an objective measure of maternal fatty acid intake during pregnancy, assuming that diet did not drastically change within the first 6-8 weeks after childbirth. However, it should also be noted that research has shown significant decreases in n-3 PUFA and n-6 PUFA during normal pregnancy that are not associated with PPD, suggesting a potential confounder (Kitamura et al., 2017).

Four of the studies finding no effects used prospective cohorts, one used a retrospective cohort, two used double-blind RCTs, and one used a cross-sectional design. Chong et al. (2015) and Sallis et al. (2014) investigated maternal LC-PUFA profiles in blood samples during the gestation period, comparing them to EPDS scores measured at 3 months and 8 weeks postpartum, respectively (Chong et al., 2015; Sallis, Steer, Paternoster, Davey Smith, & Evans, 2014). Both articles concluded that neither LC-PUFA, DHA, nor EPA were associated with a significant risk for PPD (Chong et al., 2015; Sallis et al., 2014). Note that antenatal maternal serum fatty acid profiles were used as objective measures of maternal fatty acid supplementation during the gestational period. However, it should also be noted that research has shown significant decreases in n-3 PUFA and n-6 PUFA during normal pregnancy that are not associated with PPD, suggesting a potential confounder (Kitamura et al., 2017).

Hamazaki et al. (2018) and Kobayashi et al. (2017) also used prospective cohorts, but measured fatty acid supplementation using self-reported questionnaires administered prior to childbirth (Hamazaki et al., 2018; Kobayashi et al., 2017). Pregnant women reported intake of fatty acid supplements at any dosage during the

gestational period, and then completed the EPDS questionnaire postpartum. Self-reported intake of any fatty acid did not affect the risk of PPD in mothers, regardless of dosage (Hamazaki et al., 2018; Kobayashi et al., 2017).

One study conducted in Austria asked mothers to complete questionnaires about diet during gestation, with a particular interest in n-3 PUFA. In this retrospective cohort, maternal intake was analyzed against self-diagnosis of PPD (Hogg-Kollars et al., 2011). There was no significant difference in n-3 PUFA intake between mothers who diagnosed themselves with PPD and mothers without PPD, concluding that there was no association between the two variables (Hogg-Kollars et al., 2011).

Another study investigated self-reported daily n-3 PUFA intake in mothers, using a cross-sectional design. Comparing mothers with EPDS scores ≥10 with mothers with lower EPDS scores, Cosatto, Else, & Meyer (2010) found no significant correlation between daily n-3 PUFA intake during and post childbirth, and a PPD diagnosis (Cosatto, Else, & Meyer 2010).

One double blind RCT used pregnant women to identify potential protective effects of n-3 PUFA against PPD, measured by EPDS scores. Pregnant women were either exposed to three n-3 PUFA rich capsules per day, for a daily total of 800mg of DHA and 100mg of EPA, or one placebo daily (Makrides et al., 2010). Using follow-up EPDS tests at 6 weeks and 6 months postpartum, significant differences in the total percent of women with EPDS scores >12 between each intervention group at either timepoint were not reported (Makrides et al., 2010). Again, n-3 PUFA did not produce any protective effect against PPD.

Vaz et al. (2017) used a similar protocol, exposing pregnant women to either six 1.8g capsules of n-3 PUFA daily, for a daily total of 1.08g of EPA and 0.72g of DHA, or six placebo pills daily (Vaz, Farias, Adegboye, Nardi, & Kac, 2017). Comparing EPDS scores of the two intervention groups at 4-6 weeks postpartum, no significant differences were found (Vaz et al., 2017). Treatment did not affect the risk of PPD in pregnant women, as also found in the previous study (Vaz et al., 2017).

3.2.6 Antibiotics and Probiotics

There were a limited number of studies investigating the effects of antibiotics and probiotics on postpartum depression; however, the two included studies produced significant results suggesting that antibiotic usage is a risk factor for PPD while probiotic supplementation may be protective (Table 4).

In the one study evaluating antibiotics, Murphy et al. (2018) used a prospective cohort of 120 pregnant mothers, comparing self-reported intake of antibiotics with follow-up EPDS scores at 1 month, 2 months, 3 months and 6 months postpartum (Murphy, Paul, Dunlop, & Corwin, 2018). The included cohort of mothers had antibiotic exposure during the intrapartum or postpartum period, and had no other known health issue (Murphy et al., 2018). The reasons provided for antibiotic usage included group B streptococcus positivity, uterine infection, premature rupture of membranes, fever, uterine tract infection, and upper respiratory infection; furthermore, exposure could be single or multiple dosage, taken enterally or parenterally (Murphy et al., 2018). However, the study did not separate study participants based on the ingested classes of antibiotics. Likewise, it is not known whether the mothers had ingested any other supplement, as the study did not inquire about other supplementation. Results determined a significant relationship between antibiotic intake and EPDS scores in the short-term post-childbirth (at 1 month and 2 months postpartum), where increased intake was correlated with increased EPDS scores (ß=1.69 at 1 month postpartum and ß=1.55 at 2 months postpartum, $p<0.05$) (Murphy et al., 2018). No significant relationship between the two variables was determined in the long-term, with no statistically significant correlation at 3 months or 6 months postpartum (Murphy et al., 2018). Since the authors did not distinguish the specific types of antibiotics that were taken by in their cohort though, it is difficult to determine whether certain types of antibiotics produced greater effects compared to others.

Slykerman et al. (2017) used pregnant mothers to monitor EPDS scores at 6 months postpartum, following the administration of *Lactobacillus rhamnosus* HN001 probiotics (Slykerman et al., 2017). Mothers were separated into treatment groups exposed to 0 or $6x10^9$ colony forming units (cfu) of HN001 per day starting from enrollment

at 14-16 weeks gestation and ending at 6 months postpartum (Slykerman et al., 2017). It is not known whether the mothers had ingested any other supplement, as the study did not inquire about other supplementation, though the cohort of mothers reportedly had no known health issues (Slykerman et al., 2017). Results from this study suggested that probiotic intake with HN001 may have a protective effect against PPD. Mothers from the treatment group reported lower EPDS scores at 6 months postpartum compared to the placebo group (Slykerman et al., 2017). Whereas the HN001 group had a mean EPDS score of 7.7 at 6 months postpartum, the placebo group had a mean EPDS score of 9.0 ($p<0.05$) (Slykerman et al., 2017).

3.2.7 Combination of Supplements

A limited number of studies investigated the combined effects of dietary supplements on PPD. However, based on the included studies, results were mixed (Table 6). Most recently, Amini et al. (2020) used a double blind RCT to determine whether a combination of Vitamin D3 and calcium carbonate had a protective effect against PPD. Pregnant women were exposed to either a combination of Vitamin D3 and calcium carbonate daily, or one Vitamin D3 supplement daily, or one calcium carbonate supplement daily (Amini et al., 2020). Based on EPDS scores at 8 weeks postpartum, there was a significant reduction in EPDS scores in the treatment groups who were exposed to a combination of supplements or solely Vitamin D3; however, there was no significant reduction in EPDS scores in the treatment group exposed to only calcium carbonate (Amini et al., 2020). Furthermore, there was a greater mean reduction in EPDS scores in the vitamin only group (mean reduction of 4.16, $p<0.05$) than in the combination supplement group (mean reduction of 1.70, $p<0.05$), suggesting that Vitamin D3 was more effective at reducing PPD symptoms when taken individually rather than when combined with calcium (Amini et al., 2020).

Another study, conducted by Nguyen et al. (2017), exposed pregnant women to a mixture of vitamins and minerals. Women were randomly provided with one of three interventions, each taken weekly: a multiple micronutrient supplement containing 15 different micronutrients plus 2 800µg of folate and 60mg of iron; a supplement containing only 2 800µg of folate and 60mg of iron; or, a supplement containing solely 2 800µg of folate (Nguyen et al., 2017). EPDS scores were compared at 3 months postpartum, with no significant differences among the first two interventions when compared to the folate group (Nguyen et al., 2017).

A third RCT by Paoletti et al. (2013) compared a commercially available multi-nutrient tablet with a tablet containing Vitamin D3 and calcium carbonate, each taken daily (Paoletti et al., 2013). The researchers used Elevit® (Bayer Pharmaceuticals, Leverkusen, Germany), a pregnancy multivitamin and mineral supplement, as the commercial tablet (Paoletti et al., 2013). At 15 and 30 days postpartum, the Elevit® group had significantly greater reductions in EPDS scores compared to the other intervention group (Paoletti et al., 2013).

The sole prospective cohort study investigating a combination of supplements studied whether a mixture of multivitamins and iodine was more effective at preventing PPD compared to solely multivitamins or a placebo. Wang et al. (2020) exposed pregnant women to either one multivitamin and 150 µg of iodine per day, or one multivitamin with no iodine per day, or one placebo pill daily for at least three months during the gestational period (Wang et al., 2020). EPDS scores measured at one month after childbirth found that the intervention group exposed to a combination of multivitamins and iodine had significantly higher EPDS scores (mean EPDS score=5.0, $p<0.05$) compared to the other two intervention groups (mean EPDS score in multivitamin group=3.5, mean EPDS score in placebo group=3.0, $p<0.05$) (Wang et al., 2020). There were no significant differences between the multivitamin group and the placebo group (Wang et al., 2020). Although the authors did not specify which multivitamins were included in the supplements, this study contradicts other articles included in this scoping review, indicating that a combination of multivitamins and iodine may exacerbate the maternal risk of developing PPD.

4. Discussion

4.1 Main Findings

Many mothers with PPD cite a number of reasons for a lack of compliance with current treatments. Resultantly, dietary supplements are increasingly being looked at as an alternative remedy, focusing on prevention rather than treatment, for mothers who prefer naturopathic medicine over allopathic care. With the purpose of examining possible protective effects of various dietary supplements on PPD using current literature, the results from this review produced conflicting results.

The studies examining vitamin supplementation on PPD risk found mixed results. For example, as seen in Table 1, Abedi et al. (2018) found that women with lower serum 25(OH)-D were over three times more likely to have PPD than women with higher levels of 25(OH)-D (Abedi et al., 2018). However, Gould et al. (2015) concluded that 25(OH)-D levels have no correlation with PPD presence at 6 weeks or 6 months post-childbirth (Gould et al., 2015). Furthermore, another article about Vitamin D found that its potential to produce protective effects was specific to certain times during the gestational period (Lamb et al., 2018). Regarding folate intake, two studies found no significant protective effect against PPD (Blunden et al., 2012; Leung et al., 2013), but two other articles found that increased folate intake produced lower EPDS scores under certain conditions (i.e if supplementation was for >6 months during gestation, and if EPDS scores were measured at 21 month postpartum) (Lewis et al., 2012; Yan et al., 2017). Based on the included articles though, there was replicated evidence that other B-vitamins, not including folate, had no effect on PPD risk at any dosage or time point (Blunden et al., 2012; Chong et al., 2014; Leung et al., 2013). Additionally, the articles investigating retinol and multivitamins found that retinol had no protective effect against PPD, and that only multivitamin intake in the first trimester had a significant negative correlation with EPDS scores (Dagher & Shenassa, 2012; Lin et al., 2019). However, given that there was only one article available for each regarding retinol and multivitamin supplementation, these results cannot be considered conclusive. Thus, it is currently unclear whether Vitamin D, folate, retinol and multivitamins might prevent PPD from occurring in mothers. Vitamins B1, B3, B6 and B12, on the other hand, do not seem to have any effect on PPD.

The majority of studies examining mineral supplementation found no difference in PPD risk in mothers with higher or lower intake, regardless of the mineral type (Fard et al., 2017; Hogg-Kollars et al., 2011; Leung et al., 2013; Miyake et al., 2016). Including a variety of study designs (RCT, prospective and retrospective cohort), none of the studies suggested that iron, zinc, magnesium, calcium nor iodine had a statistically significant correlation with PPD after childbirth (Fard et al., 2017; Hogg-Kollars et al., 2011; Leung et al., 2013; Miyake et al., 2016). However, one study concluded that selenium intake in the prenatal period was protective against PPD, where mothers with PPD had, on average, a lesser intake of the mineral compared to mothers without depression (Leung et al., 2013). As this was only one article investigating selenium caution must be taken when using these findings in a clinical setting.

Literature regarding treatment with fatty acids found mixed results. The majority of articles found that supplementation with total n-3 PUFA, DHA or EPA had no significant effects on PPD (Chong et al., 2015; Cosatto et al., 2010; Hamazaki et al., 2018; Hogg-Kollars et al., 2011; Kobayashi et al., 2017; Makrides et al., 2010; Sallis et al., 2014; Vaz et al., 2017). These findings were consistent despite differing study designs, geographic locations, definitions of PPD, and lengths of follow up. However, six studies found a significant inverse relationship between these fatty acids and PPD (Leung et al., 2013; Lin et al., 2019; Hoge et al., 2019; Markhus et al., 2013, Parker et al., 2015; Hamazaki et al., 2019). The strength of this relationship, though, differed between studies. Whereas Hamazki et al. (2019), Lin et al. (2019) and Markhus et al. (2013) found modest protective effects against PPD (Hamazaki et al., 2019; Lin et al., 2019; Markhus et al., 2013), Hoge et al. (2019) concluded that increased n-3 PUFA and DHA intake reduced the risk of PPD considerably (Hoge et al., 2019). Clearly, there is a lack of definitive understanding as to whether total n-3 PUFA, DHA and EPA intake can influence PPD risk. In regard to n-6 PUFA intake, increased supplementation may be a slight risk factor for PPD, although again, these effects may be minimal (Lin et al., 2019; Parker et al., 2015). The largest risk factor for PPD was an elevated n-6 PUFA/n-3

PUFA ratio (Hoge et al., 2019; da Rocha & Kac, 2012), but it is unclear how mothers could monitor this ratio via supplementation.

Although the included articles researching antibiotics and probiotics produced statistically significant findings, there were a limited number of studies. Only one article was available for each of these supplements, and thus, results were not replicated. Antibiotic usage during the gestational period produced higher EPDS scores and thus, were linked with increased risk of PPD in the first two months after childbirth (Murphy et al., 2018). This relationship was not found at 3 months and 6 months postpartum though, making it unclear how long-lasting the negative effects of antibiotics would be (Murphy et al., 2018). Given that the classes of antibiotics were not separated in this study, it is uncertain whether specific antibiotics produce more pronounced effects than others. One study reported that treatment with *L. rhamnosus* HN001 produced lower EPDS scores than in women not exposed to the probiotic (Slykerman et al., 2017). Nevertheless, other types of probiotics were not researched, and these results were not replicated. Thus, more research is needed into the effects of antibiotics and probiotics before definitive conclusions can be reached.

Regarding a combined exposure of various supplements, articles showed mixed results. Women taking commercially available Elevit® tablets, consisting of multi-nutrients, Vitamin D3 and calcium carbonate, had greater reductions in EPDS scores compared to women taking solely calcium and Vitamin D (Paoletti et al., 2013). However, these findings were not consistent in other studies, and were sometimes refuted. One study found that multivitamin and iodine supplementation produced EPDS scores higher than a placebo pill, with no significant changes between the placebo group and the group taking only multivitamins (Wang et al., 2020). Likewise, another study found that a multi-micronutrient supplement similar to Elevit® produced no differences in EPDS scores compared to folate supplementation (Nguyen et al., 2017), while a third concluded that a combination of Vitamin D3 and calcium was not as effective in reducing the risk of PPD as an individual Vitamin D3 capsule (Amini et al., 2020). Thus, it is unclear which way a combination of supplements influences PPD, if at all.

Results from this scoping review show a considerable lack of understanding regarding the effects of dietary supplements on PPD, with many studies showing mixed findings, and results regarding potential protective effects often not replicated. This dearth of evidence is noticeable in current Canadian and global guidelines, such as the 'Prenatal Nutrition Guidelines for Health Professionals' and the 'Family-Centred Maternity and Newborn Care: National Guidelines,' which were intended to provide the latest information on necessary maternal healthcare for Canadians (Canada & Health Canada, 2009; Public Health Agency of Canada, 2017). Neither of these documents provide recommendations on supplement usage for the prevention or treatment of PPD, only on its effects on other health problems (Canada & Health Canada, 2009; Public Health Agency of Canada, 2017). Likewise, in the World Health Organization's (WHO) 'WHO Recommendations on Antenatal Care for a Positive Pregnancy Experience,' there are no recommendations from the WHO regarding supplement usage for the prevention or treatment of PPD, only suggesting supplementation for other health problems (WHO, 2016). However, with the exception of n-6 PUFA and antibiotics, the included studies also did not conclude any negative impacts of supplements on PPD, meaning that although no effects may be witnessed in some women, supplement intake will often not exacerbate the risk of PPD. Resultantly, this scoping review could provide the foundation for new or updated policies regarding supplement intake, especially with selenium, HN001, folate, Vitamin D, and n-3 PUFA, to combat PPD.

4.2 Limitations

There were some limitations to this scoping review. This review was limited to two databases (Medline and PubMed) when searching for relevant articles. However, other databases may have additional articles regarding this topic. As well, this review used specific keywords and MeSH subheadings to identify relevant articles. The specific nature of the keywords and subheadings may have prevented the inclusion of other related studies.

Additionally, the studies for this review took place throughout the world and at different time points in the last 10 years. As such, different versions of PPD diagnostic tests were used in each of the studies, leading to an inconsistency in the definition of postpartum depression. For example, whereas some studies considered an EPDS score ≥10 to be classified as PPD, other studies considered an EPDS score ≥12 to be classified as PPD, and yet

other studies used different diagnostic checklists to diagnose PPD. The inclusion of these articles in this review, regardless of the administered diagnostic test, may lead to an underestimation or overestimation of the effects of certain dietary supplements on PPD, as there was no set definition of PPD applied in this scoping review given the relatively small number of studies evaluating each supplement.

Finally, many of the studies used serum levels or fatty acid profiles of erythrocytes to objectively measure maternal supplement intake. However, as previously mentioned, fatty acid profiles of erythrocytes have been determined to drastically change during pregnancy, even without the presence of PPD (Kitamura et al., 2017). Likewise, it is not known whether there are substantial changes to endogenous synthesis of fatty acids, including DHA and EPA, during the pregnancy period of a mother without PPD. Resultantly, these methods of data collection may provide some confounding bias, making the direction of the relationship between maternal fatty acid profiles/serum levels and PPD unclear.

4.3 Future Directions

This review highlights a lack of research regarding the effects of supplement co-exposure on PPD. Of the 39 included articles, only four studies analyzed the effects of multiple exposure simultaneously on PPD diagnosis. However, Health Canada recommends that multiple different supplements be taken before and during the gestational period, including Vitamin D, iron, and folic acid (Canada & Health Canada, 2009). As a result, mothers often consume numerous supplements during pregnancy, meaning that, further research is needed to better understand the combined effects of various supplement intake on PPD. Additionally, research is needed to take into account socioeconomic factors as well as effective dosage values, which may impact the efficacy of various supplement intake on PPD.

5. Conclusion

The results from this scoping review provide some understanding into the effects of various dietary supplements on PPD. Findings from the included studies support a relationship between certain supplements and PPD diagnosis, although most results are inconclusive or statistically insignificant. Future research is needed to better understand the combined effects of various supplements. This scoping review could be used to help guide new or updated policies regarding supplement intake to prevent PPD. Furthermore, this paper can lay the basis for future research to help attain greater insight into the effects of individual supplement intake and supplement co-exposure on postpartum depression.

6. Disclosure Statement

The authors have no potential conflict of interest to report.

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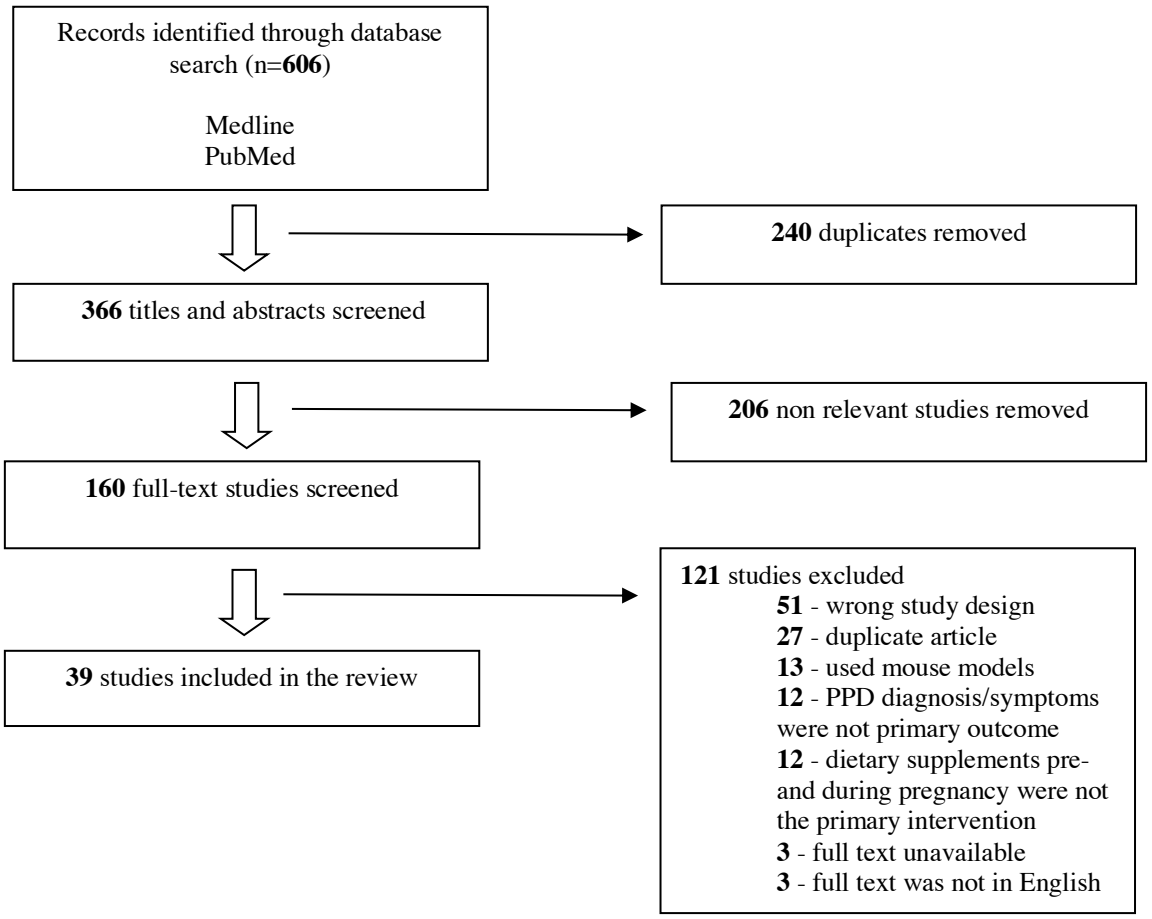

Figure 1. PRISMA diagram generated in Covidence, outlining the selection process for identifying relevant articles to include in the scoping review.

Table 1. Details of studies involving vitamin supplementation.

Study	Dietary Supplement of Interest	Study Design	Location	Participants	Intervention	Primary Outcomes	Definition of PPD	Length of Follow-Up
Abedi et al., 2018	25(OH)-D	Case-control study	Izeh, Iran	120 pregnant women (60 with PPD)	Serum 25(OH)-D levels post-birth	Women with PPD have less 25(OH)-D than women without PPD (OR=3.30)	BDI score ≥ 17	6-8 weeks postpartum
Accortt et al., 2016	25(OH)-D	Prospective cohort	Detroit, USA	91 African-American pregnant women	Serum 25(OH)-D levels pre-birth	Lower prenatal 25(OH)-D levels were associated with more PPD symptoms	EPDS scale used	4-6 weeks postpartum
Blunden et al., 2012	Folate, Vitamins B6 and B12	Prospective cohort	Southampton, England	2 856 pregnant women	Self-reported intake of vitamins pre- and during gestation	No association between vitamin intake pre- and during pregnancy, and EPDS scores	EPDS score ≥13	6 months-1 year postpartum
Chong et al., 2014	Vitamin B12	Prospective cohort	Singapore	709 pregnant women	Plasma Vitamin B12 concentrations taken between 26-28 weeks gestation	No association between plasma vitamin levels and PPD	EPDS score ≥ 13	3 months postpartum
Dagher & Shenassa, 2012	Unspecified multivitamin	Prospective cohort	Maryland, USA	526 pregnant women who took prenatal vitamins	Hospital interview at birth about vitamin intake	Only vitamin use in the first trimester had an inverse relationship with EPDS scores (r=-1.37) Vitamin intake at other trimesters were not associated with EPDS scores	EPDS scale used	8 weeks postpartum
Fu et al., 2015	25(OH)-D	Prospective cohort	Beijing, China	213 pregnant women	Serum 25(OH)-D levels at 24-48 hours postpartum	Serum 25(OH)-D levels were higher in those without PPD (OR=0.74)	EPDS score ≥ 12	3 months postpartum
Gould et al., 2015	25(OH)-D	Prospective cohort	Australia	1 040 pregnant women	Umbilical cord 25(OH)-D levels	No association between 25(OH)-D levels and PPD at 6 weeks or at 6 months	EPDS score ≥ 12	6 weeks and 6 months postpartum
Gur et al., 2015	25(OH)-D	Prospective cohort	Izmir, Turkey	179 pregnant women	Serum 25(OH)-D levels at second trimester	Significant negative correlation between 25(OH)-D and EPDS scores at 1 week, 6 weeks and 6 months postpartum (r= -0.2; r=-0.2; r=-0.3)	EPDS score ≥ 12	1 week, 6 weeks, and 6 months postpartum
Lamb et al., 2018	25(OH)-D	Prospective cohort	Southern California, USA	88 pregnant women	Maternal 25(OH)-D at 14 weeks and 32 weeks gestation, and 6 weeks postpartum	Significant inverse relationship between 25(OH)-D levels at 14 weeks gestation and 6 weeks postpartum, and EPDS scores (r=-0.23; r=-0.22)	EPDS score ≥ 10	10 weeks postpartum

						No significant relationship between 25(OH)-D levels at 32 weeks gestation and EPDS scores		
Leung et al., 2013	Vitamins B1, B3, B6, B9, B12, and D	Prospective cohort	Alberta, Canada	475 pregnant women	Self-reported prenatal supplement intake	No significant relationship between any vitamin intake and EPDS scores	EPDS score ≥ 10	12 weeks postpartum
Lewis et al., 2012	Folate	Prospective cohort	Bristol, England	6 809 pregnant women	Self-reported folate supplementation at 32 weeks gestation	No significant relationship between folate supplementation and PPD at 8 weeks or 8 months postpartum. Significant inverse relationship between folate supplementation and PPD at 21 months postpartum	EPDS scale used	8 weeks, 8 months, and 21 months postpartum
Lin et al., 2019	25(OH)-D and retinol	Cross-sectional study	Taipei, Taiwan	120 pregnant women (97 with PPD)	Serum 25(OH)-D and retinol levels at 6-8 weeks postpartum	No significant relationship between 25(OH)-D or retinol and PPD	EPDS score ≥ 10	N/A
Miyake et al., 2016	Vitamin D	Prospective cohort	Kyushu and Okinawa, Japan	1 319 mother-child pairs	Self-reported dietary intake of Vitamin D during pregnancy	No significant relationship between Vitamin D intake and PPD	CES-D score ≥ 16	3-4 months postpartum
P. K. Murphy et al., 2010	25(OH)-D	Exploratory descriptive study	Charleston, USA	97 postpartum women	Maternal 25(OH)-D levels measured monthly	Significant inverse relationship between 25(OH)-D levels and EPDS scores	EPDS score ≥ 9	Every month for first 7 months postpartum
N. O. Nielsen et al., 2013	Vitamins D2 and D3	Retrospective case-control study	Denmark	1 450 pregnant women (605 with PPD)	Maternal blood concentration of Vitamins D2 and D3	No significant relationship between either vitamin and PPD	Whoever filled prescriptions for antidepressants	N/A
Robinson et al., 2014	25(OH)-D	Prospective cohort	Perth, Australia	796 Caucasian pregnant women	Maternal blood concentration of 25(OH)-D at 18 weeks gestation	Significant inverse relationship between 25(OH)-D levels and PPD symptoms (OR=2.19)	EPDS score ≥ 6	3 days postpartum
Vaziri et al., 2016	Vitamin D3	Single-blind randomized controlled trial	Shiraz, Iran	153 pregnant women (79 in trial group, 75 in placebo group)	Either 2000IU of Vitamin D3/day from 26-28 weeks gestation to birth (trial group) or a placebo (placebo group)	Significant inverse relationship between vitamin intake and EPDS scores. (mean EPDS scores at 4 weeks: 4.59 in trial group, 7.36 in placebo group) (mean	EPDS score > 13	4 and 8 weeks postpartum

						EPDS scores at 8 weeks: 4.19 in trial group, 7.18 in placebo group)		
Williams et al., 2016	Vitamin D	Double-blind randomized controlled trial	Michigan, USA	119 pregnant women (98 in high vitamin level group, 19 in low vitamin level group)	Either ≥20ng/mL of Vitamin D per day (high vitamin group) or <20ng/mL of Vitamin D per day (low vitamin group)	No significant association between Vitamin D and BDI scores	BDI scale used	6-8 weeks postpartum
Yan et al., 2017	Folate	Prospective cohort	Tianjin, China	1 202 pregnant women	Self-reported questionnaire about folate supplementation	Significant inverse relationship between folate intake for >6 months during pregnancy and PPD (OR=0.76)	SDS score ≥ 50	6-12 weeks postpartum

All numerical data are statistically significant (p<0.05). The Accortt et al. (2016), Dagher & Shenassa (2012), Lewis et al. (2012), and Williams et al. (2016) studies used the EPDS scores as an independent variable, and thus did not define what they considered as PPD.

Table 2. Details of studies involving mineral supplementation.

Study	Dietary Supplement of Interest	Study Design	Location	Participants	Intervention	Primary Outcomes	Definition of PPD	Length of Follow-Up
Fard et al., 2017	Zinc sulfate and magnesium sulfate	Triple blind randomized-controlled trial	Tabriz, Iran	99 pregnant women (33 in each intervention group)	Either one 27mg zinc sulfate tablet daily, or one 320mg magnesium sulfate tablet daily, or one placebo daily for 8 weeks	No significant difference between any of the groups	EPDS score ≥ 13	8 weeks postpartum
Hogg-Kollars et al., 2011	Iron, zinc, and calcium	Retrospective cohort	Austria	400 mothers (83 had self-reported PPD)	Self-reported questionnaire about dietary foods during pregnancy	No significant difference of iron, zinc or calcium intake between mothers with PPD and mothers without PPD	Self-diagnosis of PPD	Unspecified
Leung et al., 2013	Iodine, iron, magnesium, selenium and zinc	Prospective cohort	Alberta, Canada	475 pregnant women	Self-reported prenatal supplement intake	No significant relationship between iodine, iron, magnesium or zinc intake and EPDS scores Significant inverse relationship between selenium intake and EPDS scores (mean intake of mothers with PPD=19mcg; mean intake of mothers without PPD=25mcg)	EPDS score ≥ 10	12 weeks postpartum
Miyake et al., 2016	Calcium	Prospective cohort	Kyushu and Okinawa, Japan	1 319 mother-child pairs	Self-reported intake of calcium during pregnancy	No significant relationship between calcium and PPD	CES-D score ≥ 16	3-4 months postpartum

All numerical data are statistically significant ($p<0.05$).

Table 3. Details of studies involving fatty acid supplementation.

Study	Dietary Supplement of Interest	Study Design	Location	Participants	Intervention	Primary Outcomes	Definition of PPD	Length of Follow-Up
Chong et al., 2015	LC-PUFA	Prospective cohort	Singapore	968 pregnant women	Plasma LC-PUFA measured at 26-28 weeks gestation	No significant association between PUFA levels and PPD	EPDS score ≥ 13	3 months postpartum
Cosatto et al., 2010	n-3 PUFA	Cross-sectional study	Australia	94 mothers (76 with PPD)	Self-reported questionnaire about daily fatty acid intake	No significant association with daily n-3 PUFA intake and PPD	EPDS score ≥ 10	N/A
Hamazaki et al., 2018	n-3 PUFA	Prospective cohort	Japan	77 661 pregnant women	Self-reported questionnaire about n-3 PUFA intake	No significant association between n-3 PUFA intake and PPD	EPDS score ≥ 9	1 month postpartum
Hamazaki et al., 2019	n-3 PUFA	Prospective cohort	Japan	84 181 pregnant women	Self-reported questionnaire about n-3 PUFA intake at middle to late pregnancy	Significant inverse relationship between n-3 PUFA intake and PPD at 6 months and 1 year postpartum (OR=0.80; OR=0.80)	EPDS score ≥ 9	6 months and 1 year postpartum
Hoge et al., 2019	n-3 PUFA and n-6 PUFA	Prospective cohort	Liege, Belgium	72 pregnant women	Maternal fatty acid profile in erythrocytes in early pregnancy	Significant inverse relationship between DHA and total n-3 PUFA, and PPD (OR=0.55; OR=0.58) Significant positive relationship between n-6 PUFA/n-3 PUFA ratio and PPD (OR=2.09)	Bromley PDS used	1 year postpartum

Hogg-Kollars et al., 2011	n-3 PUFA	Retrospective cohort	Austria	400 mothers (83 had self-reported PPD)	Self-reported questionnaire about dietary foods during pregnancy	No significant difference of n-3 fatty acid intake between mothers with PPD and mothers without PPD	Self-diagnosis of PPD	Unspecified
Kobayashi et al., 2017	DHA and EPA	Prospective cohort	Tokyo, Japan	967 pregnant women	Self-reported questionnaire about DHA and EPA intake at 26-40 weeks gestation	No significant association between DHA or EPA intake and PPD at either timepoint	EPDS score ≥ 9	1 month and 6 months postpartum
Leung et al., 2013	Omega-3 fatty acids	Prospective cohort	Alberta, Canada	475 pregnant women	Self-reported prenatal supplement intake	Significant inverse relationship between omega-3 fatty acid intake and PPD (mean intake of mothers with PPD=90mg; mean intake of mothers without PPD=180mg)	EPDS score ≥ 10	12 weeks postpartum
Lin et al., 2019	n-3 PUFA and n-6 PUFA	Cross-sectional study	Taipei, Taiwan	120 pregnant women (97 with PPD)	Maternal fatty acid profile in erythrocytes at 6-8 weeks postpartum	Significant slight inverse relationship between total n-3 PUFA and n-3 PUFA/n-6 PUFA ratio, and PPD (OR=0.994; OR=0.764) Significant slight positive relationship between total n-6 PUFA and PPD (OR=1.005)	EPDS score ≥ 10	N/A
Makrides et al., 2010	DHA and EPA	Double blind randomized-controlled trial	Melbourne, Australia	2 399 pregnant women (1 197 in the trial group, 1 202 in	Either three 500mg of n-3 PUFA-rich capsules per day (total of 800mg of DHA and 100mg of	No significant difference between the percent of women with PPD at either timepoint	EPDS score > 12	6 weeks and 6 months postpartum

				the placebo group)	EPA) (trial group) or one 500mg of vegetable oil capsule per day (placebo group)	between the trial and placebo groups		
Markhus et al., 2013	DHA and EPA	Prospective cohort	Western Norway	35 pregnant women	Maternal fatty acid profile in erythrocytes at 28 weeks gestation	Significant inverse relationship between total n-3 PUFA, DHA and n-3 PUFA/n-6 PUFA ratio, and PPD (r=-0.39; r=-0.41; r=-0.31)	EPDS score ≥ 10	3 months postpartum
Parker et al., 2015	n-3 PUFA and n-6 PUFA	Prospective cohort	Australia	773 pregnant women between 34 and 37 weeks gestation	Maternal fatty acid profile in erythrocytes at 36 weeks gestation	Significant inverse relationship between EPA levels and n-3PUFA, and PPD (mean percent of EPA in erythrocyte: 0.5% in women with PPD, 0.6% in women without PPD) (mean percent of n-3 PUFA in erythrocyte: 9.1% in women with PPD, 9.3% in women without PPD) Significant positive relationship between n-6 PUFA levels and PPD (mean percent of n-6 PUFA in erythrocyte: 27.1% in women with PPD, 26.8% in women without PPD)	EPDS score ≥ 10	3 months postpartum

da Rocha & Kac, 2012	Omega-3 and omega-6 fatty acids	Prospective cohort	Rio de Janeiro, Brazil	106 pregnant women	Self-reported questionnaire about dietary intake in the first trimester	Greater prevalence ratio of PPD in women with an omega-6/omega-3 ratio > 9:1 (PR=2.72)	EPDS score ≥ 11	At least 30 days postpartum
Sallis et al., 2014	DHA and EPA	Prospective cohort	Southwest England	2 757 mothers	Maternal antenatal fatty acid profile in blood samples	No significant association between EPA or DHA and PPD	EPDS score > 12	8 weeks postpartum
Vaz et al., 2017	DHA and EPA	Double blind randomized-controlled trial	Rio de Janeiro, Brazil	32 pregnant women (15 in trial group, 17 in placebo group)	Either six 1.8g of n-3 PUFA-rich capsules per day (total of 1.08g of EPA and 0.72g of DHA) (trial group) or six capsules of soybean oil per day (placebo group). Capsule intake lasted 16 weeks starting at 22-24 weeks gestation	No significant difference between EPDS scores of trial group and placebo group	EPDS score ≥ 11	4-6 weeks postpartum

All numerical data are statistically significant ($p<0.05$).

Table 4. Details of studies pertaining to antibiotic and probiotic supplementation.

Study	Dietary Supplement of Interest	Study Design	Location	Participants	Intervention	Primary Outcomes	Definition of PPD	Length of Follow-Up
J. R. Murphy et al., 2018	Unspecified antibiotics	Prospective cohort	N/A	120 pregnant women	Self-reported antibiotic exposure between intrapartum through the first 14 days postpartum	Significant positive relationship between antibiotic intake and EPDS scores at 1 month and 2 months postpartum (ß=1.69; ß=1.55) No significant relationship between antibiotic intake and EPDS scores at 3 months and 6 months postpartum	EPDS scale used	1 month, 2 months, 3 months, and 6 months postpartum
Slykerman et al., 2017	*Lactobacillus rhamnosus* HN001 probiotic	Double blind randomized-controlled trial	Auckland and Wellington, New Zealand	380 pregnant women (193 in the trial group, 187 in the placebo group)	Either $6x10^9$ cfu of HN001 per day (trial group) or one placebo capsule per day (placebo group) from enrollment into study to 6 months postpartum	The trial group reported significantly lower EPDS scores compared to the placebo group at 6 months postpartum (mean EPDS scores: 7.7 in trial group, 9.0 in placebo group)	EPDS score > 12	6 months postpartum

All numerical data are statistically significant ($p<0.05$). The J. R. Murphy et al. (2018) study used the EPDS scores as an independent variable, and thus did not define what they considered to be PPD

Table 5. Details of studies involving a combination of dietary supplements.

Study	Dietary Supplement of Interest	Study Design	Location	Participants	Intervention	Primary Outcomes	Definition of PPD	Length of Follow-Up
Amini et al., 2020	Vitamin D3 and calcium	Double blind randomized-controlled trial	N/A	81 pregnant women at risk of PPD (had EPDS scores > 12 during gestation) (27 in each intervention group)	Either one Vitamin D3+calcium carbonate supplement per day, or one Vitamin D3+placebo supplement per day, or one placebo+calcium carbonate supplement per day	Significant reductions in EPDS scores were evident in the vitamin+calcium group (mean EPDS score reduction=1.7) and the vitamin+placebo group (mean EPDS score reduction=4.16) No significant reductions in EPDS scores were evident in the placebo+calcium carbonate group	EPDS score > 12	8 weeks postpartum
Nguyen et al., 2017	Multiple micronutrients, folate, and iron	Double blind-randomized controlled trial	Northern rural Vietnam	1 465 pregnant women at risk PPD (472 in MM group, 478 in IFA group, 515 in FA group)	Either multiple micronutrients (15 micronutrients including 2800µg folate + 60mg iron) (MM group), iron and folate (2800µg folate + 60mg iron) (IFA group), or folate (2800µg folate) (FA group) per week	No significant difference in EPDS scores when comparing MM or IFA groups with FA group	EPDS score ≥ 4	3 months postpartum
Paoletti et al., 2013	Multi-nutrients, calcium, and vitamin D3	Double-blind randomized controlled trial	Cagliari, Italy	552 pregnant women (274 in the multi-nutrient group, 278 in the calcium+vitamin D group)	Either 1 Elevit® tablet (contains several different vitamins and minerals) daily (multi-nutrient group), or 1 calcium+vitamin D	Significant reductions in EPDS scores from baseline were more evident in the multi-nutrient group than the other group at both	EPDS score ≥ 12	15 days and 30 days postpartum

					tablet (500mg of calcium and 400IU of Vitamin D3) taken daily (calcium+vitamin D group)	timepoints (mean EPDS score difference at 15 days and 30 days=-2.2 and -3.1 for multi-nutrient group compared to -1.2 and -1.6 for the other group)		
Wang et al., 2020	Multivitamins and iodine	Prospective cohort	Shenyang, China	648 pregnant women (234 in group A, 220 in group B, 195 in group C)	Either one multivitamin+150μg of iodine daily (group A) or one multivitamin with no iodine daily (group B) or placebo daily (group C) for 3+ months during pregnancy	EPDS scores of group A were significantly higher than groups B and C (mean EPDS score=5 in group A, compared to 3.5 in group B and 3 in group C) No significant difference between groups B and C	EPDS score ≥ 10	1 month postpartum

All numerical data are statistically significant (p<0.05).

Appendix

Table A. Keywords used for Medline search. Keywords and subject headings for the dietary supplements were combined with keywords and subject headings for postpartum depression via "AND".

	Keywords and Subject Headings (MeSH)
Dietary supplement search	(probiotic.mp. OR Probiotics/) OR (Iron/ OR Vitamins/ OR Dietary Supplements/ OR Vitamin D/ OR multivitamin.mp.) OR (herbal supplement.mp.) OR (Drugs, Chinese Herbal/ OR Plant Extracts/ OR Plant Preparations/ OR Plants, Medicinal/ OR herbal drug.mp. OR herbal product.mp.) OR (antibiotic.mp. OR Anti-Bacterial Agents/) OR (Fatty Acids, Omega-3/ OR Fatty Acids, Nonesterified/ OR Fatty Acids/ OR Dietary Fats/ OR Fatty Acids, Unsaturated/ OR Fish Oils/ OR Fatty Acids, Omega-6/ OR Docosahexaenoic Acids/ OR Eicosapentaenoic Acid/ OR fatty acid*.mp. OR omega 6 fatty acid*.mp. OR omega 3 fatty acid*.mp. OR dha.mp. OR epa.mp.) OR (Vitamin E/ OR Vitamin A/ OR Vitamin D/ OR Ascorbic Acid/ OR vitamin a*.mp.)
Postpartum depression search	postpartum depression.mp OR Depression, Postpartum/

Table B. Keywords used for PubMed search. Keywords and subject headings for the dietary supplements were combined with keywords and subject headings for postpartum depression via "AND".

	Keywords and Subject Headings (MeSH)
Dietary supplement search	(probiotic*) OR (((multivitamin*) OR (vitamin*)) OR (dietary supplement)) OR (((((((herbal supplement) OR (herbal product)) OR (herbal drug)) OR (chinese herbal drug)) OR (plant extract*)) OR (plant preparation*)) OR (medicinal plant*)) OR ((antibiotic*) OR (anti-bacterial agent*)) OR (((((((((fatty acid) OR (omega-3 fatty acid)) OR (omega-6 fatty acid)) OR (dietary fat*)) OR (fish oil*)) OR (unsaturated fatty acid)) OR (nonesterified fatty acid)) OR (docosahexaenoic acid)) OR (eicosapentaenoic acid))
Postpartum depression search	postpartum depression*

Table C. Summary of the quality assessments for the cohort studies included in this review, using the CASP Checklist.

Study (Author & Year)	Overall Quality
Accort et al., 2016	Good
Blunden et al., 2012	Good
Chong et al., 2014	Good
Chong et al., 2015	Good
Dagher & Shenassa, 2012	Satisfactory
Fu et al., 2015	Satisfactory
Gould et al., 2015	Satisfactory
Gur et al., 2015	Satisfactory
Hamazaki et al., 2018	Satisfactory
Hamazaki et al., 2019	Good
Hogg-Kollars et al., 2011	Poor
Hoge et al., 2019	Satisfactory
Kobayashi et al., 2017	Good
Lamb et al., 2018	Satisfactory
Leung et al., 2013	Good
Lewis et al., 2012	Good
Markhus et al., 2013	Good
J. R. Murphy et al., 2018	Satisfactory
Miyake et al., 2016	Satisfactory
Parker et al., 2015	Satisfactory
Robinson et al., 2014	Poor
da Rocha & Kac, 2012	Good
Sallis et al., 2014	Good
Wang et al., 2020	Good
Yan et al., 2017	Satisfactory

Table D. Summary of the quality assessments for the case-control and cross-sectional studies included in this review.

Study (Author & Year)	Study Design	Quality Assessment Tool	Overall Quality
Abedi et al., 2018	Case-control	Downs and Black Checklist	22/32
Cosatto et al., 2010	Cross-sectional	Downs and Black Checklist	22/32
Lin et al., 2019	Cross-sectional	Downs and Black Checklist	25/32
N. O. Nielsen et al., 2013	Case-control	Downs and Black Checklist	25/32

Table E. Summary of the quality assessments for the randomized-controlled trials included in this review, using the Cochrane Risk of Bias tool.

Study (Author & Year)	Domain	Risk of Bias
Amini et al., 2020	Selection bias	Low

	Reporting bias	Low
	Performance bias	Low
	Attrition bias	Unclear
Fard et al., 2017	Selection bias	Low
	Reporting bias	Low
	Performance bias	Low
	Attrition bias	Low
Makrides et al., 2010	Selection bias	Low
	Reporting bias	Low
	Performance bias	Low
	Attrition bias	Low
Nguyen et al., 2017	Selection bias	Low
	Reporting bias	Low
	Performance bias	Low
	Attrition bias	Low
Paoletti et al., 2013	Selection bias	Low
	Reporting bias	High
	Performance bias	Unclear
	Attrition bias	Unclear
Slykerman et al., 2017	Selection bias	Low
	Reporting bias	Unclear
	Performance bias	Low
	Attrition bias	Low
Vaz et al., 2017	Selection bias	Unclear
	Reporting bias	Low
	Performance bias	Low
	Attrition bias	Unclear
Vaziri et al., 2016	Selection bias	Low
	Reporting bias	Unclear
	Performance bias	High
	Attrition bias	Low
Williams et al., 2016	Selection bias	Low
	Reporting bias	High
	Performance bias	Low
	Attrition bias	Low