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# Awareness of Rickshaw Pullers About COVID-19 Prevention in Dhaka City

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## Abstract

This study examines the level of knowledge and awareness of COVID-19 among rickshaw pullers in Dhaka, Bangladesh. Employing a qualitative research design, data were collected through in-depth interviews with 30 Male rickshaw pullers aged 20 to 65 years. The study investigated participants' understanding of the disease, their day-to-day practices, and the broader impact of the pandemic on their livelihoods. The findings reveal a strikingly low level of COVID-19 awareness, accompanied by widespread misconceptions. Notably, none of the participants initially recognized the term "COVID-19"; recognition only occurred when the disease was referred to as "coronavirus." Rather than perceiving COVID-19 primarily as a public health threat, participants held divergent beliefs-some attributed it to divine punishment, while others associated it with political agendas or state-imposed control through lockdown measures. Approximately 95% of respondents demonstrated little to no understanding of transmission routes or disease severity. Economic anxieties-particularly concerning loss of income and food insecurity-consistently took precedence over fear of infection, which in turn contributed to limited adherence to and comprehension of recommended preventive measures. These findings underscore the urgent need for context-sensitive health communication strategies tailored to the realities of economically vulnerable occupational groups such as rickshaw pullers. Community-based awareness initiatives are recommended as a practical and effective means of improving health literacy and strengthening protective behaviors within such populations.

**Keywords:** Awareness, Covid-19, Dhaka, Public Health, Rickshaw Pullers, Socio-Economic Impact

## 1. Introduction

### 1.1 The Research Problem

The emerging disease COVID-19 spread rapidly and led to thousands of deaths in many countries (Zhu et al., 2020). To avoid the tragedy where the surge of too many patients overwhelmed medical systems (World Health Organization, 2021), a simple and effective approach to slow the spread of the virus was emergently desired worldwide. Handwashing and mask-wearing are critical components to slow the transmission of SARS-CoV-2

(Choi & Ki, 2020). However, within low-resource environments, executing these preventative strategies poses severe logistical conflicts.

Bangladesh is a lower-middle-income country in South Asia with a population estimated at approximately 160 million. The country has been facing rapid urbanization over the past few decades, with more than one-third of the population currently residing in dense urban centers. A study shows that there are more than 1.1 million rickshaws running in Dhaka City alone, representing a massive informal transport sector (Asian Development Bank, 2012). Many of these operators live in localized slum areas where basic amenities cannot be fulfilled easily. During the peak waves of the pandemic, Bangladesh emerged as one of the most heavily affected countries in South Asia (BRAC, 2020; IEDCR, 2021; Sayeed, 2021).

### *1.2 Importance of the Problem*

To prevent the possible spread of this virus pandemic, the World Health Organization (WHO) recommended universal compliance with specific containment measures, including rigorous handwashing, sanitized operations, mask utilization, physical distancing, and home quarantine. However, preventing the spread of this pandemic presented steep, unfeasible barriers among rickshaw pullers of Dhaka City because of structural systemic challenges such as poor sanitation facilities, absolute poverty, and a critical lack of formal public health awareness.

This problem deserves dedicated qualitative research because blanket, top-down public health regulations are often modeled around citizens with stable incomes and private infrastructure. For informal day-laborers like rickshaw pullers, compliance with preventative health dictates directly threatens immediate daily economic survival. Understanding the unique cognitive, socio-economic, and structural barriers experienced by this highly mobile occupational group is crucial to designing effective public health communication models and crisis safety nets. Therefore, the formal purpose of this study is to qualitatively map awareness, perceptions, and lived compliance challenges regarding COVID-19 safety measures among active rickshaw pullers in Dhaka City.

### *1.3 Relevant Scholarship*

Current scholarship examining pandemic responses in developing countries frequently highlights a strong intersection between poverty and health literacy deficits. Studies across lower-middle-income contexts confirm that while basic awareness of a pandemic may exist broadly in urban sectors, the depth of medical understanding regarding transmission pathways and severe clinical outcomes remains significantly low among marginalized, low-wage laborers (Anwar et al., 2020; Islam et al., 2020; Lau et al., 2020). Furthermore, regional data from Bangladesh indicates that low-income urban and rural residents display highly divergent health behaviors due to conflicting economic anxieties and localized structural limitations (Sarwer et al., 2020; Siddikur Rahman et al., 2021).

By focusing specifically on the highly mobile, informal transport sector of rickshaw pullers, this study directly addresses a critical gap in the existing literature. It provides empirical, contextual data demonstrating the direct conflict between state-mandated safety directives and the immediate economic survival needs of urban informal workers.

### *1.4 Research Questions and Correspondence to Design*

To evaluate the specific problem, this empirical study is driven by three primary qualitative research questions:

- How do urban rickshaw pullers interpret and conceptualize the nature and terminology of the COVID-19 virus?
- What are the specific behavioral and environmental barriers that prevent regular compliance with standardized mask utilization and hand hygiene protocols?
- How do immediate socio-economic pressures and daily livelihood requirements influence or override infection anxieties?

Because these questions aim to explore internal cognitive perspectives, behavioral realities, and lived structural barriers, this study uses a qualitative phenomenological research design (Finlay, 2009). Individual face-to-face in-depth interviews were selected as the primary data collection tool. This qualitative approach allows researchers to look past rigid statistical parameters, capturing the direct narratives, linguistic nuances, and contextual realities necessary to explain the complex relationship between low health literacy, economic vulnerability, and preventative behavioral gaps.

## **2. Method**

### *2.1 Research Design*

This study employed a qualitative research design using an in-depth interview approach to explore the lived experiences, perceptions, and awareness levels of the participants regarding the COVID-19 pandemic. A qualitative framework was selected to gain an in-depth understanding of how social realities are constructed and interpreted by individuals within their specific occupational contexts.

### *2.2 Participant Characteristics and Selection Criteria*

The target population for this study consisted of active male rickshaw pullers operating within Dhaka city, Bangladesh. To be eligible for inclusion, participants had to be actively engaged in rickshaw pulling during the pandemic period and aged between 20 and 65 years. Female rickshaw pullers and individuals outside this age bracket were excluded from the study criteria. However, no female rickshaw pullers were found during data collection. This is likely because, due to cultural and social norms, female rickshaw pullers are very rare across Bangladesh.

### *2.3 Sampling Procedures and Sampling Size*

A purposive, convenience sampling strategy was utilized to select participants from various key commercial and residential areas across Dhaka city. A total sample size of 30 active male rickshaw pullers was achieved. Data collection was restricted to the geographical boundaries of Dhaka city due to practical constraints and accessibility considerations during state-imposed lockdown periods. All participation was voluntary, and written informed consent was obtained from each respondent prior to individual sessions.

### *2.4 Data Collection and Measurement Approaches*

Data were collected through semi-structured, face-to-face in-depth interviews conducted in the native language (Bengali). A pre-designed interview guide consisting of open-ended questions was used to examine three primary domains: general knowledge and recognition of COVID-19, day-to-day preventive practices (such as mask-wearing and hand hygiene), and the socio-economic impacts of pandemic restrictions on livelihoods. Quality and reliability were maintained by ensuring a uniform interview style across sessions.

## **3. Results**

### *3.1 Recruitment and Participant Demographics*

Field recruitment and data collection were carried out over a specified period from July to October 2021 across multiple high-traffic commercial and residential locations in Dhaka City, Bangladesh. A total of 30 active male rickshaw pullers were enrolled in the study. The demographic profile of the sample indicates that all respondents were male, with ages ranging between 20 and 65 years. All 30 participants successfully completed the individual face-to-face in-depth interview sessions, resulting in a 100% completion rate for primary data analysis.

### *3.2 Qualitative Data Analysis and Core Themes*

The collected interview text was analyzed to identify primary thematic trends related to COVID-19 awareness, daily safety practices, and socio-economic outcomes. The findings reveal critical trends across three primary dimensions:

### 3.2.1 Knowledge and Disease Recognition

A primary and uniform finding was that initial recognition of the term "COVID-19" was non-existent among the respondents. Participants only recognized or identified the disease when the term was colloquially substituted with "coronavirus." Furthermore, instead of seeing the virus as a biological public health threat, participants expressed divergent, non-medical perspectives.

*"I have never heard of anything called COVID-19. We only know it when people say Coronavirus. To us, it feels like a punishment from God or some political play to keep us inside."* (Participant 12, 42 years old)

The pandemic was frequently interpreted through either a fatalistic viewpoint (attributing the virus to divine punishment) or socio-political viewpoints (interpreting the virus as a tool for government control or political agendas executed via lockdowns).

### 3.2.2 Transmission Awareness and Severity Perceptions

Approximately 95% of the interviewed rickshaw pullers demonstrated an absolute deficit in understanding how the virus spreads (transmission pathways) or its clinical severity. Due to this low level of medical understanding, standard public health guidelines—such as regular hand hygiene, physical distancing, and proper mask utilization—were either poorly understood or ignored in day-to-day operations.

### 3.2.3 Economic Impact vs. Infection Anxieties

The data consistently revealed that economic survival and immediate daily livelihoods took absolute precedence over the fear of contracting the virus. Participants voiced severe anxieties regarding food insecurity and the loss of daily wages due to state-enforced lockdown measures.

*"If I do not pull my rickshaw today, my family does not eat tonight. The virus might kill me later, but hunger will kill my children tomorrow. That is why the lockdowns hurt us more than the disease."* (Participant 5, 29 years old)

This acute financial strain acted as a direct barrier to protective health behaviors, as securing a daily income was perceived as an immediate necessity that overrode compliance with preventive isolation or physical distancing protocols.

## 4. Discussion

### 4.1 Interpretation of Key Findings

The findings of this study confirm that awareness regarding COVID-19 is profoundly low among rickshaw pullers in Dhaka City, heavily influenced by non-medical beliefs and immediate socio-economic survival pressures. Unlike general urban populations who recognized standardized medical terms via mainstream public health channels, this group experienced a total disconnect, demonstrating zero recognition of the term "COVID-19" until it was colloquially named "coronavirus." This distinction highlights a critical breakdown in formal health communication. Rather than interpreting the pandemic as a biological crisis, the widespread perception of the virus as either a divine curse or political propaganda aligns with a pattern where marginalized occupational groups rationalize macro-crises through familiar fatalistic or state-distrust lenses when accessible, transparent medical data is lacking.

### 4.2 Contextualization with Existing Literature

These findings strongly mirror similar qualitative trends observed globally and regionally during the pandemic. For example, the severe lack of transmission knowledge and low practice of safety measures among the accessed informal workers corroborate observations made by Lau et al. (2020) regarding income-poor households in the Philippines, where structural vulnerabilities compromised compliance with health protocols. Furthermore, the explicit prioritization of economic survival over virus mitigation seen in 95% of our respondents directly mirrors the findings of Anwar et al. (2020) and Rahman et al. (2021), who documented how economic anxieties, food insecurity, and immediate threats to daily livelihoods consistently overrode the fear of infection in lower-middle-income occupational settings.

#### *4.3 Study Limitations and Generalizability*

Several explicit limitations must be acknowledged when evaluating the generalizability and operational context of these insights. First, because the accessed sample was selected through convenience sampling within the urban center of Dhaka City, these insights cannot be systematically generalized to represent all informal sector workers or rural transport operators throughout Bangladesh. Second, data collection was entirely restricted to male participants, meaning the distinct socio-economic vulnerabilities and pandemic awareness profiles of female informal workers remain uncaptured. Third, relying on face-to-face qualitative interviews introduces potential social desirability bias, where respondents might underreport non-compliance with state-mandated lockdown protocols.

Finally, administrative and structural constraints introduce a significant temporal gap between initial field execution and final dissemination. The primary data were gathered between July and October 2021 as a partial requirement for an institutional specialization curriculum, with an initial report compiled in May 2022. Due to extended academic graduation timelines and subsequent overseas academic relocations of key co-authors, formal publication tracking was delayed. Although the analytical findings were structurally vetted and peer-reviewed via oral presentation at an international congress in June 2024, readers should evaluate these qualitative realities as an empirical reflection of the mid-pandemic landscape.

#### *4.4 Theoretical and Practical Significance*

Despite these boundaries, the practical and public health significance of this study remains critical. The outcomes offer a clear, empirical explanation of why blanket, top-down health policies (such as digital tracking or commercial lockdowns) fail to protect marginalized communities if they are not accompanied by localized, transparent economic safety nets and tailored, context-sensitive public health education. For future pandemic preparedness, applications must center on community-led communication strategies that deploy health literacy programs in accessible languages directly at informal transport hubs.

#### *4.5 Recommendations*

Based on the lived experiences and critical gaps identified among the participants, the following actions are recommended to support marginalized community networks during public health crises:

**Tailored Health Communication:** Public health entities and mass media agencies must abandon generic, top-down medical terminology and deploy localized, community-specific terminology (e.g., substituting standardized terminology with colloquial phrasing) to optimize actual risk recognition.

**Targeted Economic Safety Nets:** Since immediate economic survival completely overrode infection anxieties for 95% of the respondents, future state-enforced lockdown protocols must be strictly integrated with targeted financial relief, food security provisions, and direct livelihood subsidies designed explicitly for informal transport laborers.

Grassroots Intervention Hubs: Decentralized health literacy campaigns and preventative resource distribution setups (such as masks and hand hygiene stations) should be actively integrated directly into structural informal hubs, including local rickshaw garages and terminal gathering zones.

Inclusive Macro Policy: Government agencies, public health professionals, and policy architects must structurally incorporate vulnerable, low-income informal sector layers into national pandemic response strategies to build resilient, equity-driven urban crisis frameworks.

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**Informed Consent Statement/Ethics approval:** All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was reviewed and overseen by the academic research supervisor at the Institute of Social Welfare and Research (ISWR), University of Dhaka. Participants were fully informed regarding the purpose of the research, the absolute anonymity of their responses, how their data would be utilized for academic reporting, and that no physical or social risks were associated with their participation.

**Data Availability Statement:** The qualitative interview data generated and analyzed during the current study are not publicly available due to ethical restrictions and the need to maintain absolute participant confidentiality and anonymity as agreed upon under the informed consent protocol. Excerpts of the analytical thematic text are included within the manuscript's results section.

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**Declaration of Generative AI and AI-assisted Technologies:** This study has not used any generative AI tools or technologies in the preparation of this manuscript.

## References

- ADB (2012). The Informal Sector and Informal Employment in Bangladesh. Available from <https://www.adb.org/publications/informal-sector-and-informal-employment-bangladesh> [Accessed on 26 Dec 2021].
- Anwar S, Araf Y, Newaz Khan A, Ullah MA, Hoque N, Sarkar B, Reshad RAI, Islam R, Ali N and Hosen MJ (2020). Women's Knowledge, Attitude, and Perceptions Toward COVID-19 in Lower-Middle-Income Countries: A Representative Cross-Sectional Study in Bangladesh. *Front. Public Health* 8:571689. doi: 10.3389/fpubh.2020.571689.
- BRAC (April 9, 2020). The rapid perception survey on COVID-19 awareness and economic impact.
- Chinese National Health Commission (NHC) (2021). Update of the outbreak of the SARS-CoV-2. [http://www.nhc.gov.cn/xcs/yqfkdt/gzbd\\_index.shtml](http://www.nhc.gov.cn/xcs/yqfkdt/gzbd_index.shtml) [Accessed on 21 Dec 2021].
- Choi S and Ki M. (2020). Estimating the reproductive number and the outbreak size of COVID-19 in Korea. *Epidemiol Health*. 2020;42: e2020011. doi: 10.4178/epih.e2020011.
- Islam S, Emran G, Rahman E, Banik R, Sikder T, Smith L, Hossain S (2020). Knowledge, attitudes and practices associated with COVID-19 among slum dwellers residing in Dhaka City: a Bangladeshi interview-based survey. *Journal of Public Health*, 43(1). doi: 10.1093/pubmed/fdaa182.
- Karim R, Salam K A (2019). Organizing the Informal Economy Workers: A Study of Rickshaw Pullers in Dhaka City. Available from <https://bilsbd.org/wp-content/uploads/2019/06/A-Study-of-Rickshaw-Pullers-in-Dhaka-City.pdf> [Accessed on 25 Dec 2021].
- Lau LL, Hung N, Go DJ, Ferma J, Choi M, Dodd W, Wei X. (2020). Knowledge, attitudes and practices of COVID-19 among income-poor households in the Philippines: A cross-sectional study. *J Glob Health*;10(1):011007. doi: 10.7189/jogh.10.011007.
- Research (IEDCR), Institute of Epidemiology, Disease Control and. করোনা ইনফো. (2021). Available from <https://www.iedcr.org/> [Accessed on 28 Dec 2021].
- Sarwer R, Hussain M, Muhammad Mossaraf N (2020). COVID- 19 Impacts on Low-Income Population. [www.innovision-bd.com](http://www.innovision-bd.com).
- Sayed A (2021), Infectious Diseases and Molecular Epidemiology Dataset on COVID-19 in Bangladesh, Mendeley Data, V2, doi: 10.17632/zbwzp4mnmd.2.
- World Health Organization (WHO) (2021). Novel coronavirus (SARS-CoV-2) situation reports. <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports/> [Accessed on 29 October 2021].
- Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, Zhao X, Huang B, Shi W, Lu R, Niu P, Zhan F, Ma X, Wang D, Xu W, Wu G, Gao GF, Tan W; China Novel Coronavirus Investigating and Research Team (2019). A Novel Coronavirus from Patients with Pneumonia in China. *N Engl J Med*;382(8):727-733. doi: 10.1056/NEJMoa2001017.

## Appendix A

The Semi-Structured Interview Schedule for Assessing COVID-19 Awareness and Prevention Barriers Among Urban Rickshaw Pullers. The following guide outlines the core qualitative thematic tracks and question frameworks utilized during the individual face-to-face in-depth interviews (N=30) conducted across Dhaka City, Bangladesh.

| Theme Track                                         | Core Inquiry Focus & Colloquial Prompts                                                                                                                                                                                                                                                                                                                                                   |
|-----------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Track 1: Basic Disease Conceptualization            | <ul style="list-style-type: none"> <li>• What do you understand by the term "Coronavirus" or "COVID-19"?</li> <li>• Where or from whom did you first hear about this disease?</li> <li>• What are the main symptoms of this sickness as far as you know?</li> </ul>                                                                                                                       |
| Track 2: Prevention Awareness & Source Literacy     | <ul style="list-style-type: none"> <li>• What specific actions has the government or doctor recommended to stay safe?</li> <li>• How effective do you believe handwashing and wearing masks are against the virus?</li> <li>• What kinds of masks do you use, and how often do you clean or replace them?</li> </ul>                                                                      |
| Track 3: Livelihood Conflicts & Structural Barriers | <ul style="list-style-type: none"> <li>• How did the state-enforced lockdown affect your daily income and family food security?</li> <li>• When pulling a rickshaw, what makes it difficult to maintain a physical distance or wash hands frequently?</li> <li>• If you feel sick or experience a fever, what steps do you take, and why might you choose to continue working?</li> </ul> |

## Appendix B

Picture 1: Glimpse of COVID-19 and Rickshaw Pullers



### COVID-19

Coronaviruses are a family of viruses that infect mammals and birds and cause sickness. Coronaviruses cause infections of the respiratory tract in humans that can vary from moderate to fatal.

Infection with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus strain causes COVID-19.

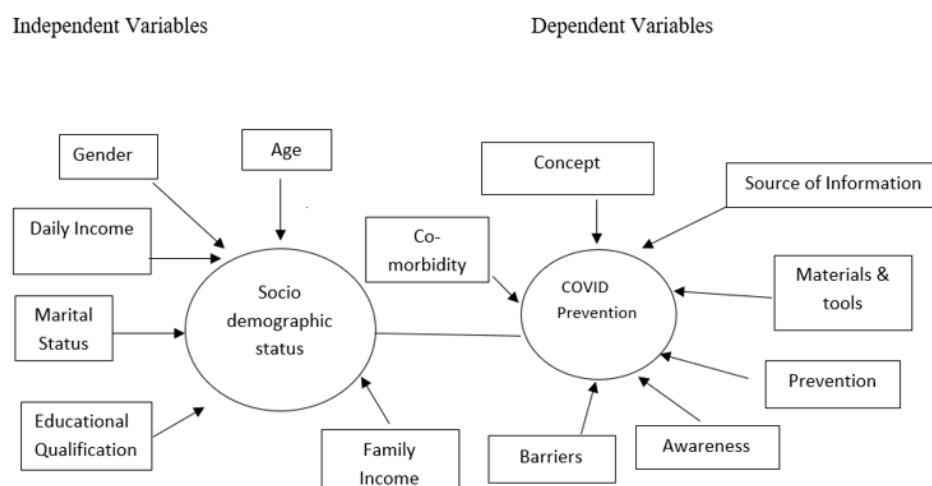
In Wuhan, China, the first SARS-CoV-2 illnesses were detected. The source of viral transmission to humans, as well as whether the virus became harmful before or after the spillover event, remained unexplained.

### Rickshaw Pullers

Rickshaw pullers are automated rickshaws, and pedal-powered cycle rickshaws, or pedicabs, are utilized for short-distance passenger transportation in many large and medium-sized cities. They go to work every day mostly to meet their families' daily subsistence needs. According to the Bangladesh Institute of Labor Studies (BILS) 2019 Survey, there are roughly 1.5 million rickshaw pullers in Dhaka.

### Awareness

The ability to directly know and perceive, feel, or be attentive to events is known as awareness. It is, more broadly, the state of being aware of something. Our discussion will be confined to COVID-19 in this study.



Picture 2: Variables of COVID-19 and Rickshaw Pullers Awareness

## Independent Variables

## Dependent Variables

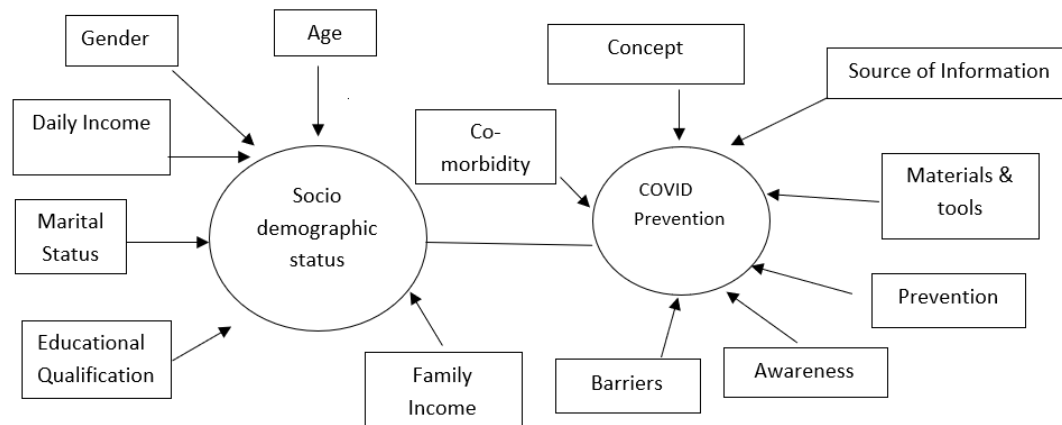


Table 1: Characteristics of Participants

| SL | Participa<br>nts | Age | Marital<br>Status | Educational<br>Qualificatio<br>ns | Reside<br>nce   | Income Per<br>Day Before<br>COVID-19<br>(BDT) | Income Per<br>Day<br>After<br>COVID-<br>19 (BDT) | Type<br>Family | of |
|----|------------------|-----|-------------------|-----------------------------------|-----------------|-----------------------------------------------|--------------------------------------------------|----------------|----|
| 1  | A1               | 27  | Married           | SSC                               | Slum            | 1000                                          | 500                                              | Single         |    |
| 2  | A2               | 33  | Married           | Class-2                           | Slum            | 900                                           | 400                                              | Joint          |    |
| 3  | A3               | 27  | Married           | SSC                               | Slum            | 800                                           | 400                                              | Single         |    |
| 4  | A4               | 27  | Married           | SSC                               | Slum            | 1000                                          | 500                                              | Joint          |    |
| 5  | A5               | 38  | Married           | Class-5                           | Slum            | 1000                                          | 500                                              | Single         |    |
| 6  | A6               | 21  | Unmarried         | SSC                               | Rented<br>House | 900                                           | 500                                              | Single         |    |
| 7  | A7               | 35  | Married           | Class-2                           | Slum            | 850                                           | 400                                              | Single         |    |
| 8  | A8               | 38  | Married           | Illiterate                        | Rented<br>House | 850                                           | 400                                              | Joint          |    |
| 9  | A9               | 35  | Married           | Class-5                           | Rented<br>House | 900                                           | 500                                              | Joint          |    |
| 10 | A10              | 27  | Married           | Class-5                           | Slum            | 1000                                          | 500                                              | Single         |    |
| 11 | A11              | 28  | Married           | SSC                               | Slum            | 1000                                          | 400                                              | Single         |    |
| 12 | A12              | 40  | Married           | Class-2                           | Slum            | 1000                                          | 500                                              | Single         |    |
| 13 | A13              | 61  | Married           | Class-5                           | Rented<br>House | 900                                           | 400                                              | Joint          |    |
| 14 | A14              | 28  | Unmarried         | Class-5                           | Rented<br>House | 850                                           | 400                                              | Joint          |    |
| 15 | A15              | 25  | Married           | SSC                               | Slum            | 900                                           | 400                                              | Joint          |    |
| 16 | A16              | 36  | Married           | SSC                               | Slum            | 1000                                          | 500                                              | Single         |    |
| 17 | A17              | 27  | Married           | Class-5                           | Slum            | 800                                           | 400                                              | Single         |    |
| 18 | A18              | 35  | Married           | Class-5                           | Rented<br>House | 800                                           | 400                                              | Single         |    |
| 19 | A19              | 62  | Married           | Illiterate                        | Rented<br>House | 900                                           | 400                                              | Single         |    |

|    |     |    |           |            |              |      |     |        |
|----|-----|----|-----------|------------|--------------|------|-----|--------|
| 20 | A20 | 30 | Married   | Class-5    | Rented House | 1000 | 500 | Single |
| 21 | A21 | 28 | Unmarried | Class-5    | Slum         | 1000 | 500 | Joint  |
| 22 | A22 | 45 | Married   | Class-2    | Rented House | 900  | 400 | Joint  |
| 23 | A23 | 65 | Married   | Illiterate | Slum         | 800  | 400 | Joint  |
| 24 | A24 | 22 | Married   | SSC        | Rented House | 1000 | 500 | Joint  |
| 25 | A25 | 35 | Married   | Class-5    | Slum         | 1000 | 500 | Single |
| 26 | A26 | 40 | Married   | Class-2    | Rented House | 1000 | 500 | Single |
| 27 | A27 | 20 | Unmarried | SSC        | Slum         | 900  | 400 | Single |
| 28 | A28 | 56 | Married   | Illiterate | Rented House | 800  | 500 | Single |
| 29 | A29 | 35 | Married   | Class-2    | Slum         | 1000 | 400 | Single |
| 30 | A30 | 32 | Married   | Illiterate | Rented House | 1000 | 500 | Single |

Table 2: Participants' Knowledge about COVID-19 Symptoms

**Symptoms of COVID-19****# of respondents' awareness**

Fever

These are the most common symptoms, but 1/3<sup>rd</sup> of respondents are aware of this fact.

Dry cough

Tiredness

Body aches and pains

Sore throat

These are fewer common symptoms and 3/4<sup>th</sup> of the respondents never heard of these symptoms before. Their knowledge about the symptoms is less and they are informed of these through the mass education program initiated by the health department.

Diarrhoea

Conjunctivitis

Headache

Loss of taste &amp; smell

Rash on skin

Discoloration of fingers or toes

Breathing difficulty

These are serious symptoms of COVID-19 that only 6 of the respondents are aware of these

Chest pain

Loss of speech or movement

Table 3: Participants' Knowledge about Precautions of COVID-19

| <b>Impacts of COVID-19</b>                     | <b>Rickshaw puller's level of awareness</b>                                                                                                                                |
|------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Wearing Mask                                   | 85% of the rickshaw puller do not wear a facemask when serving their passenger. 70% of them wear masks only when they see traffic police on the roadside.                  |
| Maintaining at least 1-meter physical distance | Maintaining physical distance outside for the rickshaw puller is almost impossible. 90% of the respondents do not aware of this physical distance as a protective measure. |
| Keep hands clean & cover cough and sneeze      | 98% of respondents do not use hand sanitizer and 82% of them do not do hand wash during their work. 37% of them use soap at home to clean their hand.                      |
| Open windows and doors for ventilation         | Ventilation facilities are not sufficient enough for 70% of respondents' residences and they have no idea about this as a precaution.                                      |
| Avoid crowd                                    | 86% of respondents do not know about the crowd to be avoided during this pandemic and they are unable to escape from the crowd due to the nature of the job.               |
| Limit time in enclosed spaces                  | 91% of the respondents are not aware of this precaution and they often spend time in congested spaces like home.                                                           |

# Gluten-Responsive Probable Pediatric Dermatitis Herpetiformis Mimicking Varicella in a Five-Year-Old Child: A Case Report

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## Abstract

**Background:** Dermatitis herpetiformis (DH) is a gluten-associated autoimmune vesiculobullous dermatosis that is rare in children and may resemble infectious eruptions, particularly varicella. **Case presentation:** A 5-year-old boy presented with persistent, painful, and intensely pruritic grouped vesicles and tense bullae, predominantly affecting the posterior trunk and upper back. Although he had a history of varicella at 3 years of age, the current episode was not preceded by known varicella exposure, fever, or prodromal symptoms. The eruption was initially diagnosed as varicella due to its vesiculobullous morphology, and a 5-day course of acyclovir was administered. Over approximately 1 month of close monitoring, some lesions transiently dried and faded, but new grouped vesicles and bullae repeatedly appeared, became more widespread, and remained painful and pruritic. Recurrent flares were subsequently observed after ingestion of gluten-containing foods. Laboratory findings were unremarkable except for eosinophilia of 14% and a serum IgE of 91.88 IU/mL. IgA-based celiac serology, histopathology, and direct immunofluorescence were not performed because the parents declined. The clinical pattern, gluten-associated recurrence, lack of sustained response to acyclovir, and improvement with gluten avoidance supported a working diagnosis of gluten-responsive probable pediatric DH. Clinical improvement was achieved with lesion-directed topical therapy, symptomatic treatment, and a strict gluten-free diet. **Conclusion:** This case underscores a varicella-mimicking, gluten-responsive probable pediatric DH presentation and highlights the importance of transparent reporting of diagnostic uncertainty when confirmatory testing is unavailable.

**Keywords:** Case Report, Dermatitis Herpetiformis, Gluten-Free Diet, Pediatric Dermatology, Topical Corticosteroid, Varicella Mimic

## 1. Introduction

Dermatitis herpetiformis (DH), also known as Duhring disease, is a chronic autoimmune blistering dermatosis strongly associated with gluten-sensitive enteropathy and celiac disease. It classically presents with intensely pruritic grouped papules, vesicles, or small bullae, most often involving extensor surfaces, the trunk, buttocks, scalp, and nuchal area. Although DH is more frequently recognized in adults, pediatric cases are clinically

important because they may present with atypical distribution, prominent excoriation, or secondary inflammation, making the eruption resemble more common infectious or allergic dermatoses (Antiga et al., 2019; Nguyen & Kim, 2021; Reunala et al., 2021; Templet et al., 2007).

The pathogenesis of DH involves gluten-driven autoimmunity, IgA antibodies directed against transglutaminase antigens, and granular IgA deposition in the dermal papillae. Neutrophil-rich inflammation contributes to subepidermal blister formation and severe pruritus. In routine pediatric practice, intact vesicles may be difficult to appreciate because repeated scratching, crusting, and post-inflammatory pigmentary change can obscure the primary morphology. These features may lead to repeated treatment for common childhood infections, including varicella, before a noninfectious vesiculobullous disorder is considered (Görög et al., 2021; Salmi & Hervonen, 2020).

The standard confirmation of DH relies on direct immunofluorescence (DIF) of perilesional skin, demonstrating granular IgA deposition, and is supported by histopathology and celiac-related serology when available. However, confirmatory testing may be limited by access, cost, child-related procedural concerns, or parental refusal of biopsy. In such circumstances, the diagnosis should be reported cautiously as suspected or probable DH rather than definite DH. A careful dietary history, recurrent grouped vesiculobullous morphology, and response to gluten avoidance may provide important clinical clues, but they do not replace IgA-based serology or DIF.

This report presents a 5-year-old boy with a persistent, painful, and pruritic vesiculobullous eruption predominantly involving the posterior trunk and upper back. The patient had a history of varicella at age 3, and the current episode was not preceded by fever, prodromal symptoms, or known contact with a person with varicella. The eruption was initially managed as presumed varicella with a 5-day course of acyclovir. During approximately 1 month of close monitoring, some lesions transiently dried and faded, but this partial improvement was not sustained; new vesicles and bullae subsequently reappeared in larger numbers and became more extensive, particularly after the child consumed gluten-containing foods. Clinical improvement was observed following lesion-directed topical therapy and gluten avoidance. The diagnosis is deliberately classified as probable pediatric DH because IgA testing, histopathology, and DIF were not performed. This transparent terminology aligns with structured case-report principles and prevents overstatement of diagnostic certainty (Gagnier et al., 2013).

## **2. Case Presentation**

### *2.1 Patient Information*

A 5-year-old boy presented with grouped vesicles and large tense bullae accompanied by severe pruritus and pain. The clinically relevant episode began at age 5. The child had previously had varicella at 3 years of age. During the current vesiculobullous episode, the parents reported no known contact with a varicella patient, no fever before lesion onset, and no preceding systemic prodrome. No other household member was reported to have a similar acute vesicular eruption. The eruption was initially treated as presumed varicella with acyclovir for 5 days, followed by approximately 1 month of close clinical monitoring. During this observation period, several lesions appeared to dry and fade gradually; however, this mild improvement was temporary. New bullae then reappeared in greater numbers, remained painful and intensely pruritic, and extended predominantly over the posterior trunk and upper back. After the parents carefully reviewed the child's dietary pattern, recurrent flares were repeatedly noticed after consumption of gluten-containing foods. Importantly, the parents did not report a history of similar chronic or recurrent bullous eruptions since infancy or at age 1. No significant past medical history other than previous varicella was documented, and there was no known family history of autoimmune disease, celiac disease, or gluten-sensitive disorders.

To ensure confidentiality, the patient is described without initials or identifying personal information. Clinical photographs were selected to depict the posterior trunk and back, thereby minimizing the risk of facial identification.

### *2.2 Clinical Findings*

According to the parents, clusters of large, tense bullae appeared repeatedly and were most numerous on the posterior trunk, especially the upper and mid-back. Additional lesions involved the posterior neck, shoulders, and limited areas of the extremities. The lesions were associated with marked itching, pain, excoriation, crusting, and post-inflammatory hyperpigmentation. The current episode was not accompanied by fever before lesion onset, and there was no known varicella contact. During the 1-month close monitoring period, the family initially observed that some lesions gradually became drier and less prominent, but new lesions subsequently appeared in greater numbers. When the child's meals were reviewed more carefully, the recurrence was temporally associated with intake of gluten-containing foods, including bread, noodles, nuggets, and other processed wheat-based foods. Conversely, the eruption tended to improve when these foods were restricted and worsened when they were reintroduced.

Physical examination during an active flare revealed multiple grouped erythematous papules, vesicles, and tense bullae on an erythematous base, with the highest lesion burden on the back. Several lesions showed excoriation, crusting, secondary inflammatory change, and residual hyperpigmentation (Figure 1). No systemic symptoms, urinary complaints, or signs of severe dehydration were documented at presentation. No gastrointestinal manifestations were recorded in the available clinical summary.

### 2.3 Timeline

Table 1: Clinical timeline

| Time point                                                         | Clinical course                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|--------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Age 3 years                                                        | The child reportedly had varicella at 3 years of age.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| Age 5 years                                                        | The patient developed persistent painful and intensely pruritic grouped vesicles and tense bullae, predominantly on the posterior trunk, especially the upper and mid-back. There was no known contact with a patient with varicella and no fever or prodromal symptoms before lesion onset.                                                                                                                                                                                                                                                                                                          |
| Initial diagnosis, 5-day antiviral therapy, and 1-month monitoring | The eruption was assumed to represent varicella because of its vesicubullous morphology. Oral acyclovir was administered for 5 days. After completion of antiviral therapy, the patient was monitored closely for approximately 1 month; during this period, several lesions gradually dried and faded, but new grouped vesicles and bullae subsequently reappeared in larger numbers, remained painful and pruritic, spread predominantly over the posterior trunk, and showed no sustained clinical improvement. The recurrence was later noticed to occur after intake of gluten-containing foods. |
| Supportive and antimicrobial therapy                               | The patient received compounded ibuprofen for pain, loratadine syrup for pruritus, and cefadroxil syrup when crusted or suspected secondarily infected lesions were present.                                                                                                                                                                                                                                                                                                                                                                                                                          |
| Available laboratory assessment                                    | Urinalysis was within normal limits. Routine blood examination was within normal limits except for eosinophilia of 14%. Serum IgE was 91.88 IU/mL. Total serum IgA, tissue transglutaminase IgA, and endomysial IgA antibodies were not performed.                                                                                                                                                                                                                                                                                                                                                    |
| Diagnostic limitation                                              | Histopathologic examination and DIF were proposed but were not performed because the parents declined skin biopsy; therefore, the case was classified as probable rather than definite pediatric DH.                                                                                                                                                                                                                                                                                                                                                                                                  |

|                        |                                                                                                                                                                                                                                                                                                                                                                             |
|------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Therapeutic adjustment | Treatment was adjusted to lesion-directed clobetasol propionate 0.05% cream, mupirocin 2% cream for crusted or suspected secondarily infected lesions, symptomatic therapy, and a strict gluten-free diet.                                                                                                                                                                  |
| Follow-up              | After reassessment and treatment adjustment, clinical improvement was reported, with drying of lesions and reduced inflammation at approximately 2-4 weeks (Figure 2), followed by sustained improvement during longer follow-up while gluten avoidance was maintained (Figure 3). The family noted recurrence or worsening when gluten-containing foods were reintroduced. |

Note. DH = dermatitis herpetiformis; DIF = direct immunofluorescence; IgA = immunoglobulin A; IgE = immunoglobulin E.

#### 2.4 Diagnostic Assessment

The eruption was initially treated as presumed varicella because of its vesiculobullous morphology. The patient reportedly received oral acyclovir for 5 days. After completion of the antiviral course, the child was monitored closely for approximately 1 month. During this period, some bullae transiently dried and became less prominent, but the improvement was incomplete and short-lived. New grouped vesicles and tense bullae then reappeared in greater numbers, remained painful and intensely pruritic, and became more extensive over the posterior trunk. Several clinical details made uncomplicated primary varicella less likely: the child had previously had varicella at 3 years of age, there was no known recent contact with a varicella case, there was no fever or prodromal illness before the eruption, and the course was relapsing rather than self-limited. The family subsequently recognized that repeated flares tended to occur after the child ate gluten-containing foods. The absence of sustained improvement after completion of acyclovir therapy, together with a relapsing course during follow-up and a gluten-related temporal pattern, prompted reconsideration of the diagnosis.

Available laboratory data showed urinalysis and routine blood examination within normal limits, except for eosinophilia of 14%. Serum IgE was recorded as 91.88 IU/mL in the available laboratory document; because laboratory reference ranges may vary, this value was interpreted cautiously. No IgA-based assessment was performed; specifically, total serum IgA, tissue transglutaminase IgA, and endomysial IgA antibodies were not checked. Histopathologic examination and DIF were proposed but not performed because the parents declined a skin biopsy after discussion.

Because IgA-based serologic testing, histopathology, and DIF were unavailable, a definitive diagnosis of DH could not be established. The case was therefore classified as gluten-responsive probable pediatric DH based on grouped vesiculobullous morphology, severe pruritus and pain, dominant posterior trunk involvement, previous varicella at 3 years of age, absence of known varicella contact or fever before lesion onset, recurrent flare after gluten-containing food intake, worsening despite a 5-day acyclovir course and 1-month observation, and reproducible family-reported clinical improvement during gluten avoidance. Differential diagnoses included varicella, bullous impetigo, allergic or contact dermatitis with secondary infection, linear IgA bullous dermatosis, childhood bullous pemphigoid, epidermolysis bullosa acquisita, insect-bite hypersensitivity, and other pediatric autoimmune blistering diseases (Table 2).

The presence of eosinophilia and elevated IgE supported consideration of allergic or hypersensitivity-associated disorders in the differential diagnosis. However, the grouped bullous morphology, posterior truncal clustering, chronicity, and family-reported dietary relationship with gluten made DH a significant clinical consideration. The absence of histopathology and DIF was acknowledged as a major limitation, and the diagnostic terminology was deliberately maintained as probable DH.

Table 2: Differential diagnostic considerations

| <b>Differential diagnosis</b>                           | <b>Findings supporting consideration</b>                                                                                                                                            | <b>Findings less compatible with the final working diagnosis</b>                                                                                                                                                                             |
|---------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Varicella                                               | Childhood vesicular eruption; initial vesiculobullous morphology prompted empiric acyclovir.                                                                                        | Previous varicella at 3 years of age, no known varicella contact, no fever or prodrome before lesions, relapsing 1-month course, posterior trunk clustering, recurrent flare after gluten intake, and no sustained response after acyclovir. |
| Bullous impetigo or secondary bacterial infection       | Crusting, erosion, and secondary inflammatory change were present in several lesions.                                                                                               | Grouped recurrent tense bullae and gluten-associated fluctuation were not explained by primary bacterial infection alone; mupirocin and cefadroxil were used only for crusted or suspected secondarily infected lesions.                     |
| Allergic or contact dermatitis with secondary infection | Pruritus, eosinophilia, and crusting supported consideration of allergic or hypersensitivity-associated disease.                                                                    | Large grouped tense bullae on the posterior trunk, recurrent flares after gluten exposure, and sustained improvement during gluten avoidance supported DH within the differential, although not definitively.                                |
| Linear IgA bullous dermatosis                           | Age group and tense bullae may overlap with this diagnosis.                                                                                                                         | DIF was unavailable, so a linear IgA pattern could not be confirmed or excluded; the family-reported gluten relationship favored probable DH clinically.                                                                                     |
| Childhood bullous pemphigoid                            | Tense bullae and pruritus can occur in children.                                                                                                                                    | No confirmatory histopathology or DIF; distribution and gluten-related recurrence were more suggestive of probable DH in this clinical context.                                                                                              |
| Dermatitis herpetiformis                                | Grouped vesicles and tense bullae, severe pruritus and pain, posterior trunk predominance, recurrent flares after gluten-containing foods, and improvement during gluten avoidance. | No IgA-based celiac serology, histopathology, or DIF; therefore, the appropriate diagnostic term is probable DH, not confirmed DH.                                                                                                           |

Note. DH = dermatitis herpetiformis; DIF = direct immunofluorescence.

### 2.5 Therapeutic Intervention

During the initial presumed varicella episode, the patient received a 5-day course of acyclovir, which did not result in meaningful sustained improvement. Over approximately 1 month of close monitoring, some lesions appeared to dry and fade gradually, but this partial improvement was followed by recurrent crops of new vesicles and bullae that became more numerous and remained painful, pruritic, crusted, and inflamed. The parents subsequently reported that these recurrences were most noticeable after the child consumed gluten-containing foods, which reinforced the rationale for dietary intervention. Symptomatic and supportive medications included compounded ibuprofen powder for pain, loratadine syrup for pruritus, and cefadroxil syrup when crusted and inflamed lesions raised concern for secondary bacterial infection. Following reassessment, treatment was redirected toward controlling inflammation, preventing secondary infection, relieving symptoms, and implementing dietary intervention.

Clobetasol propionate 0.05% cream was applied in a lesion-directed manner to active inflammatory vesiculobullous plaques, while mupirocin 2% cream was used on crusted or suspected secondarily infected lesions. The family was counseled to use potent topical corticosteroid cautiously because of the patient's young age and the risk of local adverse effects with prolonged or extensive use.

A strict gluten-free diet was recommended, with avoidance of wheat, rye, barley, bread, noodles, nuggets, and other gluten-containing or potentially cross-contaminated processed foods. Practical counseling included reviewing food labels, identifying hidden sources of gluten, and preventing cross-contamination at home.

Dapsone was not initiated. Although dapsone can provide rapid symptomatic relief in confirmed DH, its use requires diagnostic confidence and baseline monitoring for hemolysis, methemoglobinemia, and other adverse effects, especially in children (Antiga & Caproni, 2015; Görög et al., 2021). Given the absence of confirmatory IgA testing and parental refusal of biopsy for histopathology and DIF, topical therapy and dietary management were prioritized, with an emphasis on the need for confirmatory evaluation if symptoms recur or worsen.

### *2.6 Follow-up and Outcomes*

After initiation of clobetasol propionate 0.05% cream, mupirocin 2% cream, symptomatic therapy, and gluten avoidance, the patient showed progressive clinical improvement, as reported by the family and documented in serial clinical photographs. This improvement contrasted with the preceding 1-month period of close monitoring after the 5-day acyclovir course, during which lesions had only partially dried and faded before recurring in greater numbers, especially after gluten-containing foods. Within approximately 2-4 weeks after treatment adjustment, the posterior trunk lesions became drier and less inflamed, with reduced pruritus, pain, and crusting. No new large tense bullae were reported during early follow-up when gluten avoidance was maintained (Figure 2).

Longer follow-up showed sustained improvement of the back with minimal residual post-inflammatory change (Figure 3). The family reported better disease control during periods of dietary adherence and worsening after reintroduction of gluten-containing foods. This pattern was particularly noted after consuming foods such as bread, noodles, nuggets, and other wheat-based processed products. No severe systemic complications were documented in the available clinical summary. Because IgA-based serology was not checked, serologic monitoring of disease activity or dietary adherence could not be reported.

## **3. Discussion**

### *3.1 Diagnostic Challenge and Varicella Mimicry*

This case illustrates a practical diagnostic challenge in pediatric vesiculobullous disease. Varicella is a common cause of vesicular eruption in children, and empiric antiviral treatment may be reasonable when the morphology appears infectious. However, several clinical features in this case argued against uncomplicated primary varicella: the child had previously had varicella at 3 years of age, there was no known contact with a patient with varicella, no fever or prodromal symptoms preceded the eruption, and the lesions followed a recurrent course after a completed 5-day acyclovir regimen and approximately 1 month of close observation. Several lesions initially appeared to dry and fade, but recurrent crops of grouped vesicles and bullae subsequently appeared in larger numbers. Posterior trunk clustering, grouped vesiculobullous morphology, increasing lesion burden during follow-up, and a family-observed relationship between gluten exposure and recurrent flares supported consideration of DH or another noninfectious vesiculobullous disorder rather than uncomplicated varicella.

Pediatric DH is uncommon and can be difficult to recognize because primary vesicles are often disrupted by scratching, crusting, and secondary inflammation. Lesions may therefore resemble bullous impetigo, allergic dermatitis, insect-bite hypersensitivity, or other autoimmune blistering disorders. This case reinforces that dietary history can be a useful clinical clue when gastrointestinal symptoms are absent or not prominent (Nguyen & Kim, 2021; Reunala et al., 2021).

### 3.2 Novelty and Educational Value

The educational value of this report is derived from its real-world diagnostic context rather than from introducing a novel treatment or definitively establishing a rare entity. This case documents a 5-year-old child with a varicella-mimicking vesiculobullous eruption, despite a history of varicella at 3 years of age, no known varicella contact, and no fever before lesion onset. The eruption persisted after a completed 5-day course of acyclovir and approximately 1 month of close monitoring. Although some lesions initially dried and faded, new painful and pruritic bullae subsequently reappeared in larger numbers, predominantly on the posterior back. Careful parental observation identified recurrent flares after gluten-containing foods, and improvement was observed following combined topical anti-inflammatory, antimicrobial, symptomatic, and dietary management. This sequence provides a practical clinical indicator: persistent, recurrent, or progressive grouped bullae with pruritus, pain, lack of sustained response to antiviral therapy, absence of typical varicella epidemiologic or systemic features, and possible dietary fluctuation should prompt reconsideration of noninfectious vesiculobullous disorders, including probable DH.

A second educational point is the transparent classification of the case as probable rather than definite DH. Because IgA assessment, histopathology, and DIF were not performed, the diagnosis was intentionally not overstated. This approach strengthens the scientific integrity of the report and aligns with case-report standards requiring clear diagnostic reasoning, explicit uncertainty, and limitations (Gagnier et al., 2013).

### 3.3 Diagnostic Limitation and Need for Confirmation

The diagnosis of DH is usually supported by granular IgA deposition in dermal papillae on DIF of perilesional skin. Serologic tests, especially IgA tissue transglutaminase and IgA endomysial antibodies, may support the diagnosis and help monitor adherence to gluten avoidance. Total serum IgA is also relevant because IgA deficiency may cause false-negative IgA-based serologic results (Görög et al., 2021; Salmi & Hervonen, 2020).

In this patient, none of the IgA-based tests were performed. Skin biopsy for histopathology and DIF was proposed but not performed because the parents declined the procedure. Therefore, the case cannot be presented as confirmed DH. The most scientifically appropriate wording is "probable pediatric DH" or "suspected DH" in the clinical differential diagnosis. If the disease recurs, referral for celiac serology (total IgA, tissue transglutaminase IgA, and endomysial IgA) and for a perilesional skin biopsy with DIF would be recommended. If IgA deficiency is suspected or confirmed, IgG-based celiac serology may be required.

The elevated eosinophil percentage and recorded IgE value also require cautious interpretation. Eosinophilia can occur in allergic, parasitic, drug-related, or other inflammatory conditions and is not specific for DH. These findings do not exclude DH but support maintaining a broad differential diagnosis. Their inclusion prevents selective reporting and helps readers understand the uncertainty of the case.

### 3.4 Management Implications

The main long-term management of confirmed DH is a strict gluten-free diet, which targets both cutaneous disease and underlying gluten-sensitive enteropathy. Dietary treatment can reduce medication requirements over time and may reduce systemic complications associated with celiac disease (Nguyen & Kim, 2021; Pasternack et al., 2021; Reunala et al., 2021). In this patient, the family-reported pattern of slight temporary improvement followed by recurrent flares after gluten-containing foods, together with subsequent improvement during gluten avoidance, supports the clinical suspicion but should be interpreted as supportive rather than diagnostic.

Topical clobetasol propionate 0.05% may reduce inflammation and pruritus in localized inflammatory lesions, but it does not treat the underlying gluten-driven autoimmune mechanism of DH. In children, potent topical corticosteroids should be used carefully, for a limited duration, and under clinical supervision. Mupirocin 2% is appropriate when crusted lesions raise concern for secondary bacterial infection. Ibuprofen and loratadine may help address pain and pruritus, respectively, but they are supportive rather than disease-modifying therapies. These

treatments may explain short-term improvement in inflammation and crusting, whereas gluten avoidance may explain reduced recurrence during adherence.

Dapsone is an established option for rapid symptom control in confirmed DH, but it was not used in this case. This conservative approach was reasonable given the absence of confirmatory testing, parental refusal of biopsy, and the need for safety monitoring in a young child. The case therefore supports a stepwise approach: treat pain, pruritus, secondary infection, and inflammation; document dietary response; counsel the family; and pursue confirmatory testing when available or when disease activity persists.

Importantly, clinical improvement in this case cannot be attributed solely to gluten avoidance, as topical corticosteroid therapy, topical antimicrobial treatment, and symptomatic medications were used concurrently. The gluten-related fluctuation, including recurrence after intake of gluten-containing foods during close monitoring, is therefore best interpreted as supportive evidence for a probable diagnosis, not as a substitute for confirmatory DH testing.

### *3.5 Limitations*

This report has several limitations. First, IgA-based serology, total serum IgA, histopathology, and DIF were not performed. Second, histopathology and DIF were unavailable because the parents declined biopsy, limiting diagnostic certainty. Third, although the parents reported previous varicella at 3 years of age, no known varicella contact, and no fever before lesion onset, varicella vaccination status and virologic confirmation such as polymerase chain reaction testing were not available in the clinical summary. Fourth, serum IgE was recorded as 91.88 IU/mL, but interpretation should follow the reference range of the original laboratory report. Fifth, dietary adherence and response to gluten re-exposure were based on family report rather than standardized dietary assessment or supervised gluten challenge. The observed gluten-related fluctuation should therefore be interpreted as supportive clinical evidence rather than diagnostic confirmation, because topical corticosteroid, topical antimicrobial therapy, and symptomatic medications were administered during the same treatment period.

## **4. Conclusion**

Probable pediatric DH should be considered in children with persistent, intensely pruritic and painful grouped vesiculobullous eruptions that mimic varicella but do not show sustained improvement after appropriate antiviral therapy. In this case, previous varicella at 3 years of age, absence of known varicella contact, absence of fever before lesion onset, posterior trunk predominance, relapsing progression after a 5-day acyclovir course and approximately 1 month of close monitoring, recurrent lesions after gluten-containing food intake, and improvement after clobetasol propionate 0.05% cream, mupirocin 2% cream, symptomatic therapy, and a gluten-free diet supported suspicion of DH. However, the absence of IgA testing, histopathology, and DIF prevented definitive diagnosis. Clear reporting of diagnostic uncertainty is essential, and confirmatory IgA-based serology with perilesional biopsy for DIF should be pursued when available and acceptable to the family.

### **Author Contributions:**

Conceptualization, D.A.R.D.; clinical data acquisition, D.A.R.D., J.F., and S.T.W.; data curation, J.F., K.T., and S.M.; writing – original draft, J.F., K.T., and S.M.; writing – review and editing, D.A.R.D., J.F., K.T., S.M., and S.T.W.; supervision, D.A.R.D. All authors have read and approved the submitted version and agree to be accountable for the accuracy and integrity of the work.

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**Informed Consent Statement/Ethics Approval:** Written informed consent for publication of the clinical information and anonymized clinical photographs was obtained from the patient's parent/legal guardian. Skin

biopsy for histopathology and direct immunofluorescence was proposed but declined by the parents after discussion.

**Data Availability Statement:** Data supporting the case description are contained within the clinical record and are not publicly available to protect patient confidentiality.

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**Declaration of Generative AI and AI-assisted Technologies:** During manuscript preparation, generative AI was used for language editing, structural organization, and formatting assistance. The authors reviewed, edited, and verified the manuscript content and remain fully responsible for the accuracy, integrity, and originality of the submitted work.

## References

- Antiga, E., & Caproni, M. (2015). The diagnosis and treatment of dermatitis herpetiformis. *Clinical, Cosmetic and Investigational Dermatology*, 8, 257-265. <https://doi.org/10.2147/CCID.S69127>
- Antiga, E., Maglie, R., Quintarelli, L., Verdelli, A., Bonciani, D., Bonciolini, V., et al. (2019). Dermatitis herpetiformis: Novel perspectives. *Frontiers in Immunology*, 10, 1290. <https://doi.org/10.3389/fimmu.2019.01290>
- Gagnier, J. J., Kienle, G., Altman, D. G., Moher, D., Sox, H., Riley, D., et al. (2013). The CARE guidelines: Consensus-based clinical case reporting guideline development. *Journal of Medical Case Reports*, 7, 223. <https://doi.org/10.1186/1752-1947-7-223>
- Görög, A., Antiga, E., Caproni, M., Cianchini, G., De, D., Dmochowski, M., et al. (2021). S2k guidelines (consensus statement) for diagnosis and therapy of dermatitis herpetiformis initiated by the European Academy of Dermatology and Venereology (EADV). *Journal of the European Academy of Dermatology and Venereology*, 35(6), 1251-1277. <https://doi.org/10.1111/jdv.17183>
- Nguyen, C. N., & Kim, S. J. (2021). Dermatitis herpetiformis: An update on diagnosis, disease monitoring, and management. *Medicina*, 57(8), 843. <https://doi.org/10.3390/medicina57080843>
- Pasternack, C., Hervonen, K., Mansikka, E., Reunala, T., Collin, P., Kaukinen, K., & Salmi, T. T. (2021). Persistent skin symptoms after diagnosis and on a long-term gluten-free diet in dermatitis herpetiformis. *Acta Dermato-Venereologica*, 101(9), adv00555. <https://doi.org/10.2340/00015555-3914>
- Reunala, T., Salmi, T. T., Hervonen, K., Kaukinen, K., & Collin, P. (2021). Dermatitis herpetiformis: An update on diagnosis and management. *American Journal of Clinical Dermatology*, 22(3), 329-338. <https://doi.org/10.1007/s40257-020-00584-2>
- Salmi, T., & Hervonen, K. (2020). Current concepts of dermatitis herpetiformis. *Acta Dermato-Venereologica*, 100(5), 115-121. <https://doi.org/10.2340/00015555-3401>
- Templett, J. T., Welsh, J. P., & Cusack, C. A. (2007). Childhood dermatitis herpetiformis: A case report and review of the literature. *Cutis*, 80(6), 473-476.

**Figures and Figure Legends**

Figure 1. Initial presentation and progression during monitoring after presumed varicella treatment. (A) Initial clinical photograph at 5 years of age showing multiple grouped vesicles and tense bullae over the posterior neck, shoulders, and upper back, accompanied by excoriation, crusting, and early post-inflammatory change. The morphology initially led to clinical consideration of varicella, although the child had previously had varicella at 3 years of age, had no known contact with a patient with varicella, and had no fever before lesion onset. The patient received acyclovir for 5 days. (B) After approximately 1 month of close monitoring following the completed antiviral course, some lesions had transiently dried or faded, but recurrent vesiculobullous lesions remained prominent, reappeared in larger numbers, and became more extensive over the posterior trunk, especially the upper and mid-back. The family later recognized that new crops of lesions tended to occur after gluten-containing foods were consumed.



Figure 2. Early response after treatment adjustment. (A) Approximately 2 weeks after treatment was redirected to lesion-directed clobetasol propionate 0.05% cream, mupirocin 2% cream for crusted or suspected secondarily infected lesions, symptomatic therapy, and strict gluten avoidance, active inflammation was still evident; however, compared with the preceding recurrent flare, the lesions showed transition toward crusting, drying, and reduced tense bullous activity. (B) At approximately 4 weeks after treatment adjustment, vesiculobullous activity had largely dried, inflammation and crusting had decreased, and residual post-inflammatory pigmentary change became the predominant finding. This early improvement differed from the earlier monitoring period, in which partial fading was followed by recurrent flares after gluten-containing food intake.

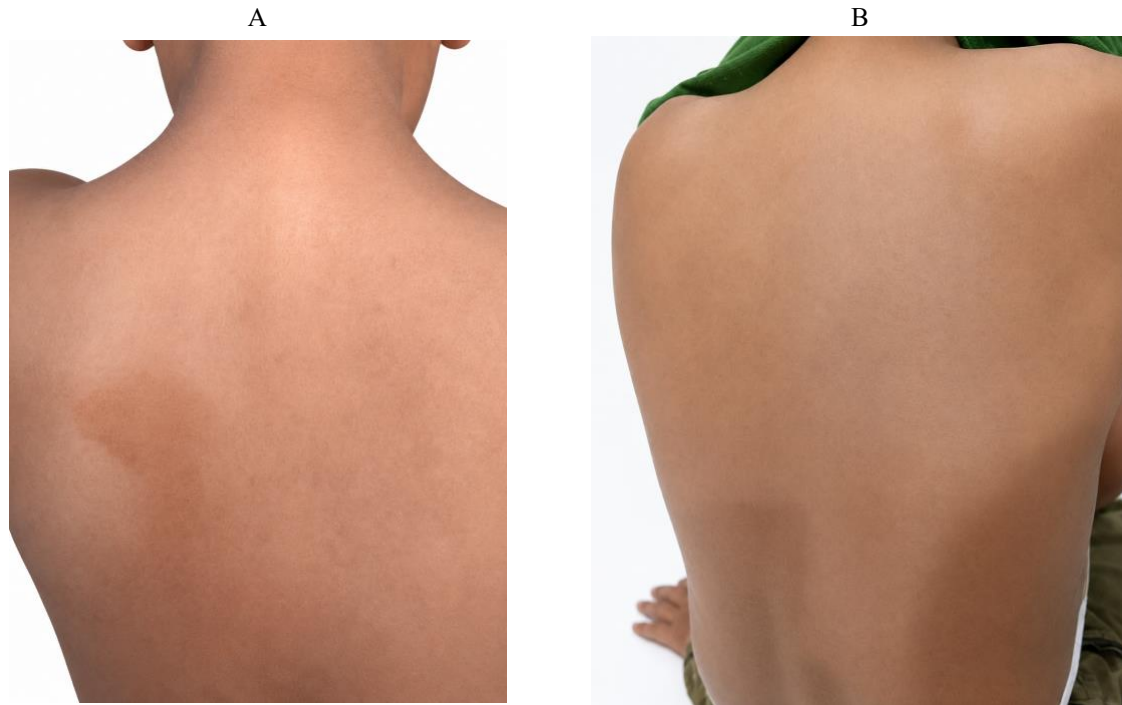


Figure 3. Late and long-term follow-up after treatment adjustment. (A) Approximately 8 weeks after treatment adjustment, the upper back showed marked clearance of active bullae with only mild residual post-inflammatory color change in the photographed area. (B) At approximately 1 year of follow-up, the back remained clinically quiet with minimal residual pigmentation or scarring and no obvious active vesiculobullous lesions.

# Correlation of HER2 Protein According to Histological Grade and Depth Invasion in Gastric Cancer

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## Abstract

The aim of this study was to determine the correlation of HER2 protein with histological grade and depth of invasion of the primary tumor with gastric cancer. Method: were used archival tissue samples of 60 gastric cancer patients who are treated by immunohistochemistry antibody to HER2 per the manufacturer's protocol and evaluated a modified scoring system HER2 positivity surgical resection sample obtained. Data were processed using the descriptive statistics, chi square test and one sample T-test, and Pearson's correlation test. Results: Statistical analysis of HER2 protein according to histological grade gastric adenocarcinoma made using chi-square test does not show a statistically significant correlation between these two variables ( $\chi^2 = 29.400$ ), the analysis using one sample t-test showed no statistically significant difference ( $t = 2.850$ ) and analysis with Pearson correlation test shows a positive correlation that is statistically significant ( $r = 0.214$ ). Statistical analysis of the HER2 protein according to the depth of invasion of gastric cancer was performed using chi-square test does not show a statistically significant association ( $\chi^2 = 59.700$ ), the analysis using one sample t-test showed no statistically significant difference ( $t = 2.900$ ), and analysis by Pearson-this test correlation shows a positive correlation that was not statistically significant ( $r = 0.021$ ). Conclusions: There is a weak positive correlation of HER2 protein according to histological grade carcinoma ( $r = 0.214$ ), and was recorded negligible positive correlation of HER2 protein according to the depth of invasion of cancer ( $r = 0.021$ ).

**Keywords:** HER2, Histological Grade, Depth of Invasion, Gastric Cancer, Correlation

## 1. Introduction

Gastric cancer is a malignant epithelial tumor of the gastric mucosa with glandular differentiation, and one of the most common tumors, and the second leading cause of cancer death in the world, although its incidence has been decreasing, especially in developed countries, since the middle of the 20th century (Kelley and Duggan, 2003). The incidence of gastric cancer depends largely on the geographical area. In Croatia, this number ranges from 35 for men and about 20 for women, and it is the third most common malignancy (Kumar et al, 2010). Generally speaking, the CFR (case fatality ratio) for gastric cancer is 0.75 and is much higher than for other malignancies, e.g. colon cancer (CFR 0.52), breast cancer (CFR 0.36), or prostate cancer (CFR 0.33). The assessment of the tumor stage is based on the basic principles of tumor growth and spread. In the initial phase of growth, the tumor

spreads within the organ in which it originated, and with further growth it can directly spread to neighboring organs. During tumor growth, tumor cells enter blood and lymphatic vessels and metastasize to lymph nodes and distant organs. Therefore, the most common elements used in tumor stage assessment are:

1. location of the tumor inside the stomach (there is a special scheme that is used to assess the expansion of the tumor),
2. the depth of tumor invasion in the stomach wall,
3. the presence of tumors in the lymph nodes and the number of affected lymph nodes,
4. presence of distant metastases.

When analyzing gastric adenocarcinoma, in addition to determining the histological type according to Lauren and the macroscopic type according to Borrmann, it is also necessary to determine the degree of differentiation and Goseki grade (Gullick, 2001). Gastric adenocarcinomas can be well / medium / poorly / undifferentiated or grade (G) 1 / 2 / 3 / 4. The depth of invasion is the morphological characteristic that has the greatest importance for the clinical outcome (Hynes and Stern, 1994). Dysplasia of the epithelium of the gastric mucosa is considered to be a precursor lesion from which "early" cancer arises, which can then progress to advanced lesions. "Early" gastric cancer is defined as a lesion limited to the mucosa and submucosa regardless of the presence or absence of metastases in the perigastric lymph nodes. Advanced gastric cancer is a neoplasm that has spread below the submucosal layer into the muscular part of the wall or even deeper. Gastric cancer is considered as "early" (pT1) or advanced ( $\geq$  pT2), based on this, a prognostic discrepancy is observed between these two levels of invasion, at the level of the TNM classification, which is currently the only prognostic factor (Dako Connection, 2010; DAKO Catalog, 2010).

### *1.2. Molecular prognostic parameters*

Overexpression of HER 2 protein in gastric cancer (which occurs in about 20% of gastric cancer cases) has been shown to be an indicator of poor prognosis in gastric cancer (Jorgensen, 2010). However, such cancer cases may respond favorably to combined chemotherapy and trastuzumab (targeted therapy) (Hofmann et al, 2008). In contrast to breast cancer, basolateral membrane staining instead of circular membrane staining is sufficient to qualify positive c-erbB-2 immunostaining in gastric cancer (Hetzel et al, 1992).

HER2 is a transmembrane glycoprotein essential in growth factor signaling. HER2 expression has also been found in colon, bladder, ovarian, endometrial, lung, cervical, head and neck, esophageal, and gastric cancers. Increased expression correlates with clinical outcome, conferring a poor prognosis, and is also a predictive factor for poor response to chemotherapy and endocrine therapy. The greatest value of determining HER2 status lies in predicting response to HerceptinR -Trastuzumab therapy (HERCEPTIN F.Hoffmann-La Roche Ltd, Basel, Switzerland and Genetech, Inc., South San Francisco, CA), in that the efficacy of anti-HER2 therapy correlates with the degree of HER2 positivity, and Herceptin therapy has revolutionized the treatment of breast cancer (Hetzel et al, 1992; Hirashima et, 2001; Douglass and Nava, 1985).

The TNM classification is currently the most important prognostic factor for gastric cancer. However, the prognosis in different patients with the same stage of the disease is not the same. Therefore, it is necessary, along with the TNM classification and classic pathological characteristics of the tumor, to identify biological prognostic factors, which are often derived from genetic processes and which are considered to be a key step in the prognosis of gastric cancer.

There are opinions that the expression of HER2 plays a key role in the development of gastric cancer, its progression and metastasis. However, little is known about its expression, because a limited number of papers have been published on this topic in the world. Given that the majority of stomach cancers, nowadays, unfortunately, are diagnosed at an advanced stage of the disease, it is still unclear whether the expression of the HER2 protein in this cancer is related to any of the proven prognostic factors, and whether it can have a potential role in the prognosis of the disease and possibly provide guidelines for therapeutic treatment.

The aim of the work was to determine the correlation of HER2 protein expression with the histological grade and the depth of invasion of the primary tumor in gastric cancer.

## **2. Material and methods**

The research conducted and presented in this paper represents a fundamental or basic type of research with an observational method of obtaining data used in the study.

### *2.1. Material*

This study used archival tissue samples of gastric carcinoma from 60 patients obtained after subtotal or total gastrectomy with regional lymphadenectomy of the lymph nodes of the perigastric fatty tissue along the lesser and greater curvature of the stomach, then the lymph nodes of the celiac tripus region and the hepatoduodenal ligament region. Pathohistological diagnostics of all gastric carcinoma samples included in this study was performed at the Department of Pathology and Cytodiagnostics of the Travnik Hospital, in the period from the beginning of 2022 to the end of 2025. In the prospective part, a pathohistological profile of HER2 amplifying gastric carcinomas was constructed based on a retrospective study, which was applied in the selection of pathohistologically verified gastric carcinomas in which immunohistochemical detection of HER2 protein was performed. Data on clinicopathological parameters of histological grade and depth of invasion of the primary tumor were obtained by individual microscopic observation of tissue samples of cancer tissue from all samples.

### *2.2. Methods*

This is a retrospective-prospective (ambispective) study. The condition for including samples in this study is that the patients had an operable tumor with a known status of regional lymph nodes and without evident distant dissemination at the time of diagnosis. The same number, i.e. 60 samples of normal stomach tissue, were used as a control group.

Pathohistological processing of biopsy material obtained by subtotal or total gastrectomy with regional lymphadenectomy involved taking tissue samples according to dissection rules, and their standard histochemical processing and, in the first act, staining with the standard hematoxylin-eosin method as well as with the special histochemical method of staining PAS (Periodic Acid Schiff) for mucin. Microscopic interpretation of tissue samples stained with these methods resulted in clinical-pathological parameters: histological grade and depth of invasion of the primary tumor. In the following procedure, the most representative tissue samples of gastric carcinoma tissue that were embedded in paraffin blocks were re-cut on a microtome and immunohistochemically stained, i.e. treated with an antibody to HER2 according to the manufacturer's protocol, and then evaluated by light microscopy and scored using a modified scoring system for HER2 positivity of surgical resections.

### *2.3. Guide to HercepTest scoring in gastric carcinoma*

Tests to examine the consistency, i.e. validity, of results between immunohistochemical staining and in situ hybridization pre-Toga studies showed that the HER2 IHC test is suitable for staining gastric carcinoma cells, but differences appeared in relation to breast carcinoma, and changes were required in the scoring system for gastric carcinoma. Pre-ToGA and ToGA (Trastuzumab for Gastric Cancer) studies have shown that a modified HER2 positivity scoring system should be used for gastric cancer samples.

### *2.4. Ethical aspects of the study*

The use of archival gastric cancer tissue samples in this study was approved by the Ethics Committee of the Travnik Hospital, the institution where the study was conducted, for the purpose of using the data for scientific purposes.

### *2.5. Statistical data processing*

After microscopic processing of the material, the obtained data were entered into MS Excel 2007. The stored data were transported to the SPSS 16.0 software package for statistical processing. Descriptive statistics, non-parametric significance tests, namely Chi square test and One sample T-test, as well as correlation tests, namely Pearson's correlation test, were used in data processing.

### 3. Results

Out of the total number of cancer tissue samples in the experimental group, none of the samples had histological grade I, or the grade of well-differentiated cancer. A total of 10 samples had moderate differentiation, or histological grade II, which is 16.7% of the total number of samples in the experimental group, while the largest number of samples, 50 of them, had histological grade III, or poor differentiation, which is 83.3% of the total number of samples in the experimental group, which is shown numerically and in percentages in Chart 1. Since no cancer tissue sample in the experimental group was well-differentiated, or had histological grade I, the slice for this group of samples in the pie chart is not shown, but the data on this group are given numerically and in percentages in order to complete the analysis of the stage of differentiation of cancer tissue in the samples of the experimental group.

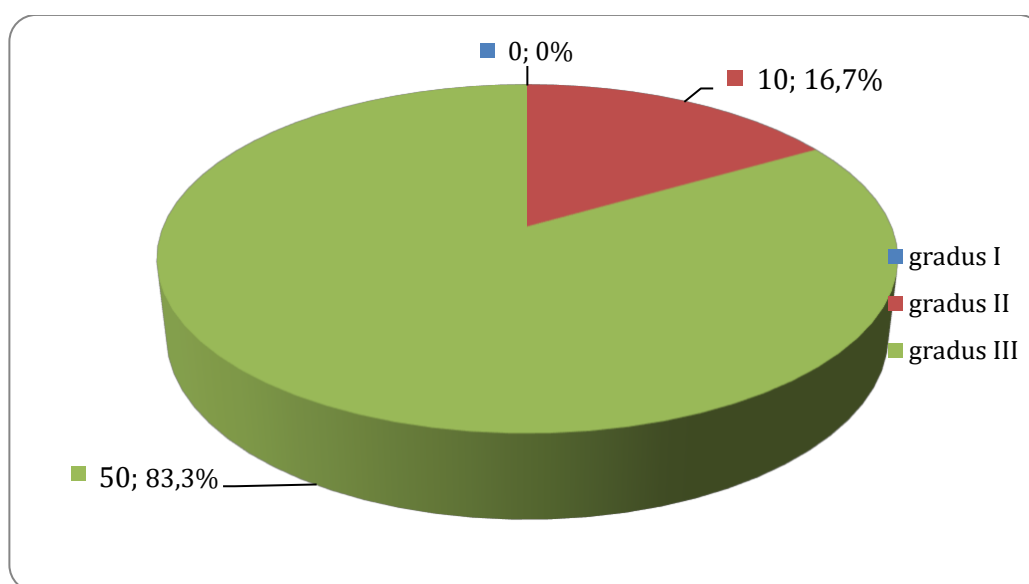


Chart 1: Structure of the differentiation stage the cancer tissue samples of experimental groups

Microscopic analysis of the depth of invasion of each sample of cancer tissue in the experimental group revealed that no cancer sample had a pT1 stage, i.e. was not limited to the mucosa or submucosa. A total of 9 samples, i.e. 15% of the total number of samples in the experimental group, had a pT2 stage, and in these samples, cancer cells infiltrated and remained limited to the muscular layer of the stomach wall, while in 48 samples, i.e. 80% of the total number of samples in the experimental group, infiltration of cancer tissue into the subserosa of the stomach wall, i.e. pT3 stage, was recorded. The remaining 3 samples, i.e. 5% of the total number of samples in the experimental group, had a pT4 stage, and perforation of the stomach wall serosa and/or infiltration of stomach cancer cells into surrounding structures was present. Data on the depth of invasion of cancer tissue samples of the experimental research group classified by pT classification are numerically and percentageally shown in chart 2. Given that none of the cancer tissue samples of the experimental group were limited to the mucosa or submucosa, i.e. did not have a pT1 stage, the section for this group of samples is not shown in the pie-graph, but the data on this group are listed numerically and percentageally in order to complete the whole analysis of the depth of invasion of cancer tissue samples of the experimental group.

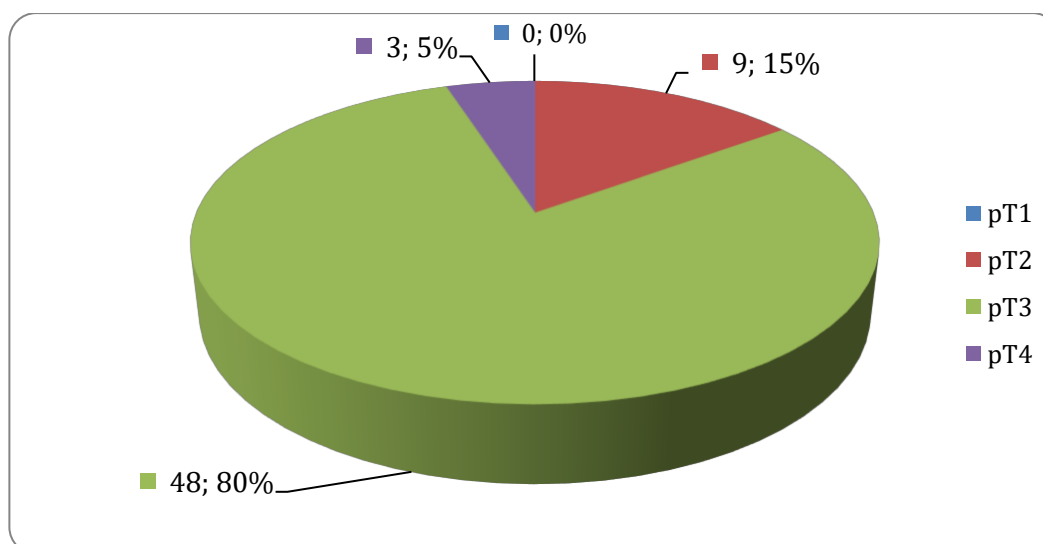


Chart 2. Structure of the depth of invasion and pT classification of the cancer tissue samples of the experimental group research

After processing and analyzing the characteristics of the cancer samples of the studied group of patients, such as the histological grade or degree of differentiation of the cancer and the depth of invasion of the primary tumor, immunohistochemical staining and analysis of all samples of the experimental and control groups of samples are performed.

The immunohistochemical analysis of the application of Herceptest on the experimental group of gastric cancer biopsy samples yielded results showing that the largest number of gastric cancers showed HER2 negative immunoreactivity, that is, that the largest number of gastric cancers did not show immunoreactivity in the expression of the HER2 protein, and out of a total of 60 samples that made up the experimental group, 36 of them, or 60%, showed HER2 negative immunoreactivity (Figure 1). Furthermore, weak or barely visible membrane activity, some of which are only in parts of the cell membranes of the cancer cells, is shown by a total of 9 samples, or 15% of the total number of samples in the experimental group (Figure 2).

Ambiguous membrane activity was shown by 8 samples of the experimental group, i.e. 13.33% of the total number of samples of the experimental group (Figure 3), and these samples in further work should be retested by the method of in situ hybridization in the light microscopic field (CISH).

And finally, what is most important and why the research was done, hyperreactivity, i.e. basolateral or lateral membrane reactivity in HER2 protein expression, was shown by 7 samples, i.e. 11.67% of the total number of samples of the experimental group (Figure 4).

One sample showed apical membranous activity, with no evident basolateral or lateral membranous activity in HER2 protein expression, and that sample was considered a HER2-negative immunoreactivity sample (Figure 5). All samples of the control group of samples represented by samples of histologically regular stomachs showed HER2 negative immunoreactivity (Figure 6).

Analyzing the histological grading of gastric cancer, where in the experimental group none of the samples had the histological grade of well-differentiated cancer, and even 50 of them had the histological grade of poorly differentiated gastric cancer, and putting them in relation to the reactivity of cell membranes in the expression of the HER2 protein, the result was that hyperreactivity in the expression of the HER2 protein was shown exclusively by poorly differentiated gastric cancers, i.e. all 7 samples with basolateral or lateral membrane activity in with HER2 protein expression belonged to the group of poorly differentiated cancers, which is 11.7% of the total number of samples of the experimental group, while pathohistologically verified cancers of moderate and good differentiation did not show hyperreactivity in the expression of HER2 protein. An almost identical result was

obtained with ambiguous membrane activity, where moderately and well-differentiated gastric carcinomas did not show this kind of membrane activity, while 8 samples of poorly differentiated gastric carcinomas, i.e. 13.3% of the total number of samples of the experimental group, showed ambiguous membrane activity in the expression of HER2 protein, which is numerically and percentageally shown in chart 3.

The control group of samples is without pathohistologically verified cancer tissue, so their histological grade was not determined either.

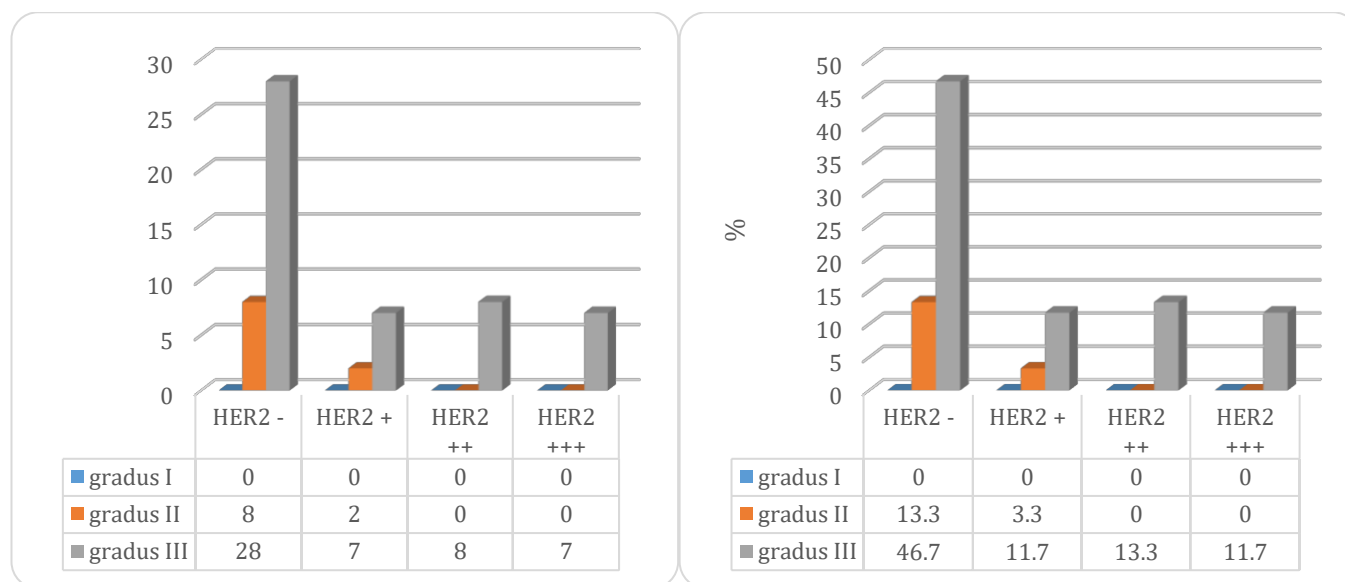


Chart 3: The expression of HER2 protein compared histological grade of gastric cancer studied groups

Statistical analysis of HER2 protein expression according to the stage of differentiation of gastric adenocarcinoma performed using the chi-square test does not show a statistically significant relationship between these two variables ( $\chi^2=29.400$ ; statistically significant relationship is if  $p<0.05$ ), analysis using the one sample T-test does not show a statistically significant difference ( $t=2.850$ ; the difference is not statistically significant if  $p>0.05$ ), and analysis using the Pearson correlation test shows a positive correlation that is not statistically significant ( $r=0.214$ ) between these two examined parameters.

Taking into account the depth of invasion of gastric cancer in the samples of the experimental group, in which as many as 48 samples, or 80% of the total number of samples, have the pT3 stage, i.e. the cancer cells in these samples infiltrate the subserosa, and no sample has the pT1 stage, and comparing them with the membrane immunoreactivity in the expression of the HER2 protein, the result was that the highest number of hyperreactivity is shown by cancers with the pT3 stage, as many as 5 of them, or 8.3% of the total number of samples of the experimental group, while one sample each showing hyperreactivity in the expression of the HER2 protein has the pT2 and pT4 stages. Ambiguous membrane activity was shown by 7 samples, or 11.7% of the total number of samples in the experimental group with the pT3 stage, and 1 sample, or 1.7% of the total number of samples in the experimental group with the pT2 stage, which is numerically and in percentages shown in chart 4.

The control group of samples consisted of samples of histologically regular gastric mucosa without pathohistologically verified cancer cells, and they were in the pT0 stage, and were not taken into account in relation to membrane immunoreactivity in the expression of the HER2 protein.

Statistical analysis of HER2 protein expression according to the depth of gastric cancer invasion performed using the chi-square test does not show a statistically significant relationship between these two variables ( $\chi^2=59.700$ ; a statistically significant relationship is if  $p<0.05$ ), analysis using the one sample T-test does not show a statistically significant difference ( $t=2.900$ ; the difference is not statistically significant if  $p>0.05$ ), and analysis using the

Pearson correlation test shows a positive correlation that is not statistically significant ( $r=0.021$ ) between these two parameters examined.

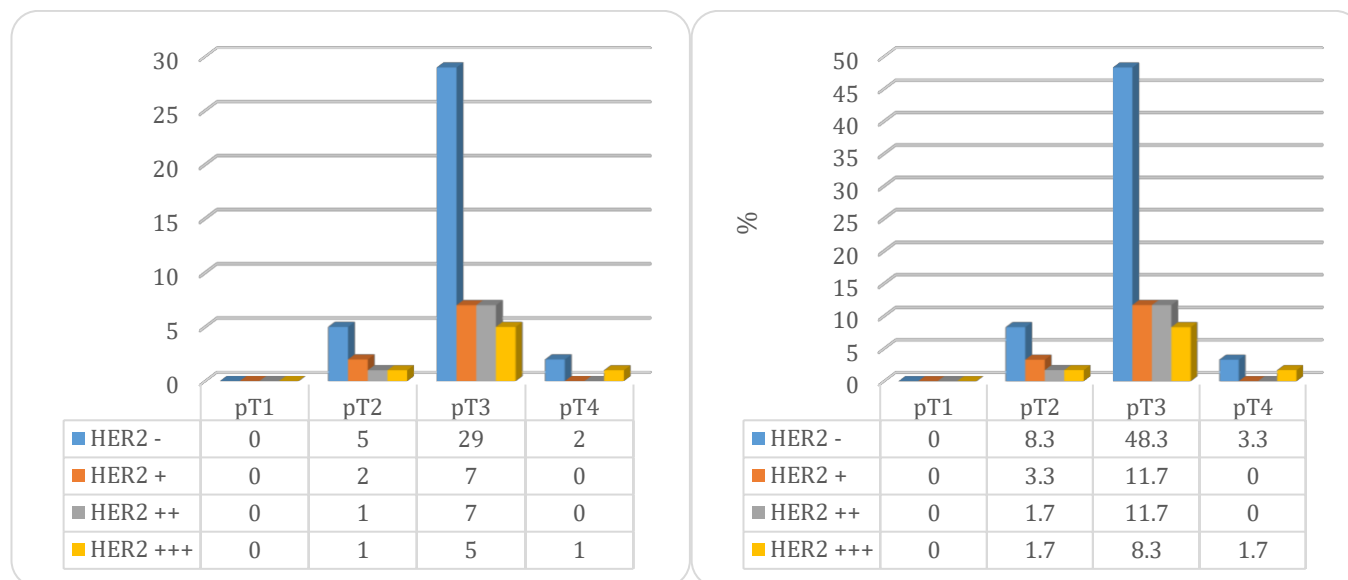


Chart 4: The expression of HER2 protein in relation to the depth of invasion of gastric cancer studied groups

#### 4. Discussion

The aim of the study was to qualitatively and quantitatively determine the possible expression of HER2 protein in gastric cancer, and to examine the correlation of HER2 protein expression with the examined clinical-pathological parameters of gastric cancer: histological grade and depth of invasion of the primary tumor.

Before discussing the main objectives of this study, we need to discuss the basic characteristics, i.e. clinical-pathological parameters of the experimental research group.

When we talk about the histological grade, i.e. the stage of differentiation of gastric cancer in our experimental research group, out of the total number of cancer tissue samples, not a single sample had histological grade I, i.e. the grade of well-differentiated cancer. A total of 10 samples had moderate differentiation, i.e. histological grade II, which is 16.7% of the total number of samples in the experimental group, while the largest number of samples, 50 of them, had histological grade III, i.e. poor differentiation, which is 83.3% of the total number of samples in the experimental group. The depth of invasion of cancer cells in the stomach wall of each individual sample of the experimental group of the study was determined by detailed and decisive microscopic analysis, and we obtained data that no cancer sample had the pT1 stage, that is, it was not limited only to the mucosa or submucosa. A total of 9 samples, or 15% of the total number of samples of the experimental group, had the pT2 stage and in these samples the cancer cells infiltrated and remained limited to the muscular layer of the stomach wall, while in 48 samples, or 80% of the total number of samples of the experimental group, infiltration of cancer tissue into the subserosa of the stomach wall was recorded, that is, the pT3 stage. The remaining 3 samples, or 5% of the total number of samples of the experimental group, had the pT4 stage and they had perforation of the serosa of the stomach wall and/or infiltration of cancer cells of the stomach into the surrounding structures.

Analyzing the above-mentioned discussion on the basic characteristics, that is, clinical-pathological parameters of the experimental research group, it can be concluded that the experimental group of our research is objectively variegated in all parameters, which is important in a studious approach to the given research goals.

The results of our study, which was conducted on an experimental group of 60 samples of pathohistologically verified gastric cancer, showed hyperexpression of HER2 protein on the cell membranes of cancer cells in 7 samples, which is

11.67% of the total number of samples, while ambiguous membrane activity was shown by a total of 8 samples, which is 13.33% of the total number of samples of the experimental group. Also, the results of our study show weak membrane activity in 9 samples, which is 15% of the total number of samples of the experimental group, and negative HER2 immunoreactivity was found in the largest number of samples, i.e. in 36 samples, which is 60% of the total number of samples of the experimental group.

So far, HER2 expression has been investigated in studies with a relatively small number of samples and the results of these studies are very controversial, as can be seen from a recent review by Gravalos et al. (Gravalos and Jimeno, 2008). The frequencies of HER2 protein expression in published studies vary enormously from 8% to 91%. One of the first studies on this topic was conducted in 2000 when Allgayer et al., examining the frequency of HER2 protein expression in gastric cancer, obtained an extremely high expression of 91%. However, both in this and in other initially conducted studies on this topic, tumor heterogeneity was neglected, which is extremely pronounced in gastric cancer compared to breast cancer (4.80%:1.40%), and the malignant cell scoring system used was for breast cancer. These data can be taken as the reason for such a high percentage of HER2-positive gastric cancers (Van Cutsem et al, 2009).

Newer studies that were conducted after the pre-ToGa and large multicenter ToGa studies, took into account the heterogeneity of gastric cancers, as well as a modified tumor cell scoring system adapted for gastric cancer. In our study, these two parameters were also taken into account and we obtained 11.67% of HER2-positive cancers, which is similar and different from the findings of previous studies: the large multicenter ToGa (Trastuzumab for GAstriaC Cancer) study in which there were 22.10%, the results of the Chinese study conducted by Guan Zhen Yu et al. which had overexpression of HER2 protein in 28% of the primary gastric adenocarcinomas examined, as well as the results of the largest, most recent study conducted to date on 924 patients in which there were 7% HER2 positive cancers (Heike et al, 2010).

The results of the comparative analysis of HER2 protein expression and cancer differentiation stage in our study showed that hyperreactivity in HER2 protein expression is shown only by poorly differentiated gastric cancers, i.e. all 7 samples with basolateral or lateral membrane activity in HER2 protein expression belonged to the group of poorly differentiated cancers, which is 11.7% of the total number of samples of the experimental group, while pathohistologically verified cancers of moderate and good differentiation did not show hyperreactivity in HER2 protein expression. An almost identical result was obtained with ambiguous membrane activity, where moderately and well-differentiated gastric carcinomas did not show this kind of membrane activity, while 8 samples of poorly differentiated gastric carcinoma, i.e. 13.3% of the total number of samples of the experimental group, showed ambiguous membrane activity in the expression of HER2 protein. Weak membrane activity in the expression of HER2 protein was obtained in 2 samples of moderately differentiated carcinomas, which is 3.3% of the total number of samples, and in 7 samples of poorly differentiated carcinomas, which is 11.7% of the total number of samples in the experimental group. Negative HER2 immunoreactivity was shown by 8 samples of moderately differentiated carcinomas, which is 13.3% of the total number of samples, and 28 samples of poorly differentiated carcinomas, which is 46.7% of the total number of samples in the experimental group of our study. Statistical analysis of HER2 protein expression according to the stage of differentiation of gastric adenocarcinoma performed using the chi-square test does not show a statistically significant relationship between these two variables ( $\chi^2=29.400$ ; a statistically significant relationship is if  $p<0.05$ ), analysis using the one sample T-test does not show a statistically significant difference ( $t=2.850$ ; the difference is not statistically significant if  $p>0.05$ ), and analysis using the Pearson correlation test shows a positive correlation that is not statistically significant ( $r=0.214$ ) between these two examined parameters.

The results of our study regarding the depth of invasion of gastric cancer showed that no sample of cancer with stage pT1 showed hyperreactivity of HER2 protein expression, while 1 sample of cancer with stage pT2 and pT4 showed such reactivity, which is 1.7% of the total number of samples, and 5 samples of gastric cancer with stage pT3, which is 8.3% of the total number of samples. Ambiguous membrane activity was obtained in one pT2 stage gastric cancer sample, which is 1.7% of the total number of samples, and in 7 pT3 stage cancer samples, which is 11.7% of the total number of samples. Almost identical results with ambiguous membrane activity were obtained by the samples of our experimental group with weak membrane activity, so 2 samples of cancer stage pT2, which is 3.3% of the total number of samples, and 7 samples of cancer stage pT3, which is 11.7% of the total number of samples, had this activity, and 5 pT2 stage cancer samples, which is 8.3% of the total number of samples, had negative HER2 immunoreactivity, followed by 29 pT3 stage cancer samples, which is 48.3% of the total number of samples, and 2 pT4 stage cancer samples, which is 3.3% of the

total number of samples of the experimental group. Statistical analysis of HER2 protein expression according to the depth of gastric cancer invasion performed using the chi-square test does not show a statistically significant relationship between these two variables ( $\chi^2=59.700$ ; statistically significant relationship is if  $p<0.05$ ), analysis using the one sample T-test does not show a statistically significant difference ( $t=2.900$ ; the difference is not statistically significant if  $p>0.05$ ), and analysis using the Pearson correlation test shows a positive correlation that is not statistically significant ( $r=0.021$ ) between these two examined parameters.

HER2 protein expression is also correlated with the control group, which in absolutely all samples showed a completely negative immunoreaction to HER2 protein expression.

#### *4.1. Limitation of the study*

Until now, HER2 expression has been examined through studies with a relatively small number of examined samples and the results of those studies are very controversial, and the frequencies of HER2 protein expression through published studies vary enormously from 8% to 91%.

Our study was also conducted on a relatively small number of samples, due to the smaller number of gastric cancer samples that met the given conditions, as well as the costs of the examination, which came from personal financial resources.

### **5. Conclusions**

The results of the correlation of HER2 protein expression with the examined clinicopathological parameters show that there is only a weak positive correlation of HER2 protein with the histological grade or stage of differentiation of the cancer ( $r=+0.214$ ), and a negligible positive correlation of HER2 protein with the depth of cancer invasion ( $r=+0.021$ ).

Therefore, the expression of HER2 protein correlated with other clinicopathological parameters in our study did not show statistical significance, which is the same as in the study by Heike Grabasch et al.<sup>15</sup> who correlated HER2 protein expression with the degree of differentiation, depth of tumor invasion, lymph node status, and lymphovascular invasion. The results of the study by Guan Zhen Yua et al. are similar. which obtained a non-significant relationship with gender, depth of tumor invasion, tumor grade, lymph node status (Guan et al, 2009).

A weak positive correlation without statistical significance in our study was found between HER2 protein expression and histological grade of gastric cancer. Namely, all samples that showed hyperexpression of HER2 protein.

A weak positive correlation without statistical significance was found in our study between HER2 protein expression and histological grade of gastric cancer. Namely, all samples that showed HER2 protein hyperexpression were poorly differentiated carcinomas, i.e. carcinomas of histological grade III, while none of the samples of histological grades I and II showed either HER2 protein hyperexpression or ambiguous membrane activity.

HER2 protein expression showed a negligible positive correlation without statistical significance with the depth of invasion of gastric cancer, i.e. its pT stage, using the univariate statistical method according to Pearson, where 71.43% of all samples with HER2 protein hyperexpression had the pT3 stage, which is again 8.3% of the total number of samples in the experimental group.

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**Conflict of Interest:** The authors declare no conflict of interest.

**Informed Consent Statement/Ethics Approval:** Not applicable.

**Declaration of Generative AI and AI-assisted Technologies:** This study has not used any generative AI tools or technologies in the preparation of this manuscript.

## References

- Dako Connection. HER2 in gastric cancer. 2010: 15-25.
- DAKO Catalog. Products and Services: HercepTest 2010: 162-3.
- Douglass Jr HO, Nava HR. Gastric adenocarcinoma. Management of the primary disease. *Semin Oncol* 1985; 12: 32-45.
- Gravalos C, Jimeno A. HER2 in gastric cancer: a new prognostic factor and a novel therapeutic target. *Annals of Oncology* 2008;19(9): 1523–9.
- Guan ZY, Ying C, Jie JW. Overexpression of Grb2/HER2 signaling in Chinese gastric cancer: their relationship with clinicopathological parameters and prognostic significance. *J Cancer Res Clin Oncol*, 2009; 135: 1331–9.
- Gullick WJ. Update on HER-2 as a target for cancer therapy: alternative strategies for targeting the epidermal growth factor system in cancer. *Breast Cancer Res* 2001; 3: 390-4.
- Heike G, Shivan S, Sally G, Helmut E. Gabbert and Wolfram Müller HER2 expression in gastric cancer: Rare, heterogeneous and of no prognostic value – conclusions from 924 cases of two independent series. *Cellular Oncology* 2010; 32: 57–65.
- Hetzel DJ, Wilson TO, Keeney GL. HER-2/neu expression: a major prognostic factor in endometrial cancer. *Gynecol Oncol* 1992; 47: 179–85.
- Hirashima N, Takahashi W, Yoshii S. Protein overexpression and gene amplification of c-erb B-2 in pulmonary carcinomas: a comparative immunohistochemical and fluorescence in situ hybridization study. *Mod Pathol* 2001; 14: 556–662.
- Hofmann M, Stoss O, Shi D, Buttner R, Kim W, Ochiai A, et al. Assessment of a HER2 scoring system for gastric cancer: results from a validation study. *Histopathology* 2008; 52: 797-805.
- Hynes NE, Stern DF. The biology of erbB-2/neu/HER-2 and its role in cancer. *Biochim Biophys Acta* 1994;1198: 165-84.
- Jorgensen JT. Targeted HER2 treatment in advanced gastric cancer. *Oncology* 2010; 78: 26-33.
- Kelley JR, Duggan JM. Gastric cancer epidemiology and risk factors. *J Clin Epidemiol* 2003; 56:1-9.
- Kumar V, Abbas AK, Fausto N, Mitchell R. *Osnove patologije, osmo izdanje*. DataStatus Beograd, 2010; 15: 597-9.
- Martin HM, Filipe MI, Morris RW, Lane DP, Silvestre F. p53 Expression and prognosis in gastric carcinoma. *Int J Cancer* 1992; 50: 859-62.
- Van Cutsem E, Kang Y, Chung H, Sawaki A, Lordick F, Hill J, et al. Efficacy results from the ToGA trial: A phase III study of trastuzumab added to standard chemotherapy (CT) in first-line human epidermal growth factor receptor 2 (HER2)-positive advanced gastric cancer (GC). *J Clin Oncol* 2009;27: 18.

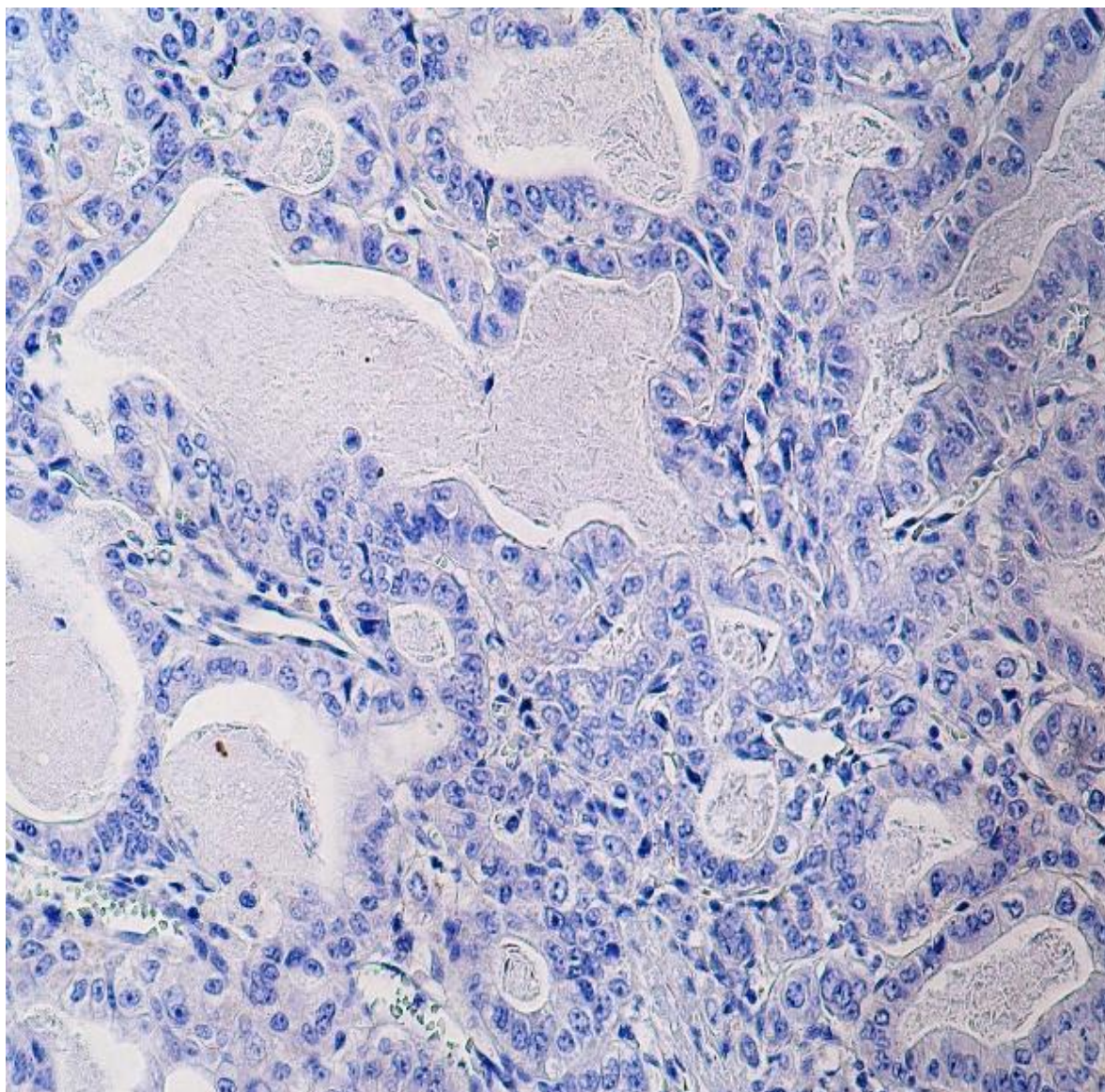


Figure 1: The negative reactivity of the HER2 protein (0) (40x)

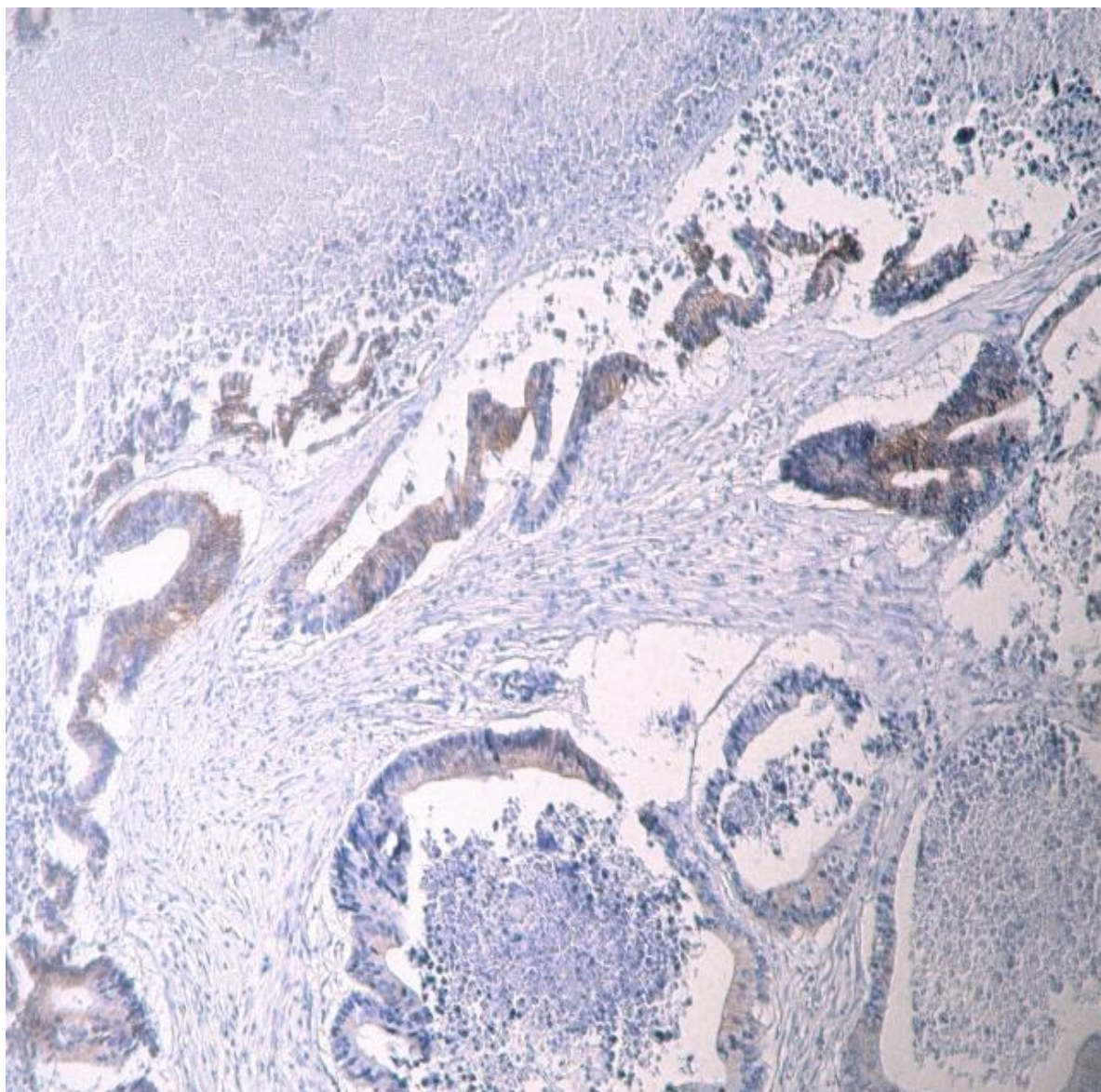


Figure 2: Light HER2 expression (+) (40x)

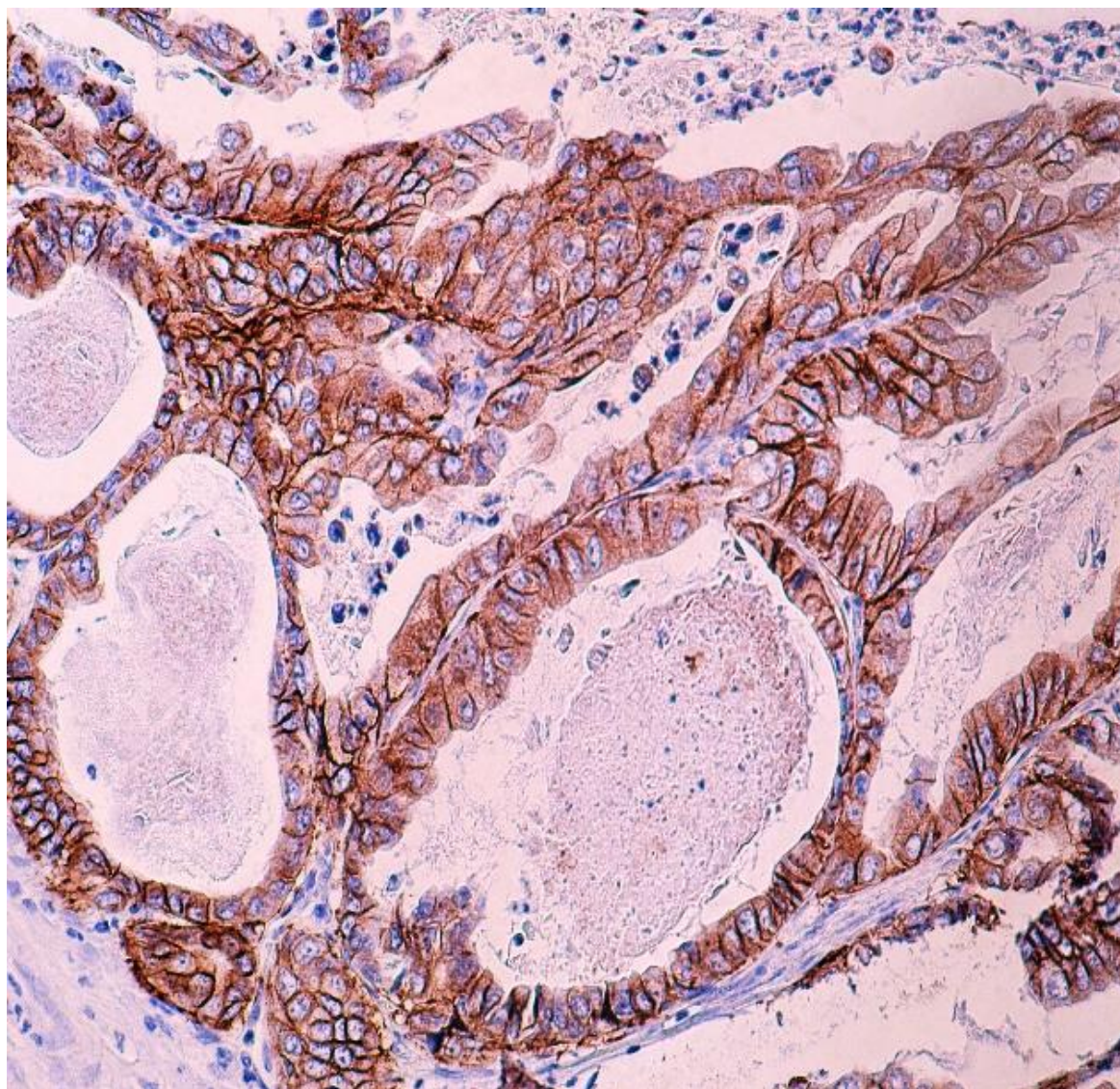


Figure 3: Ambiguous HER2 positivity (++) (40x)

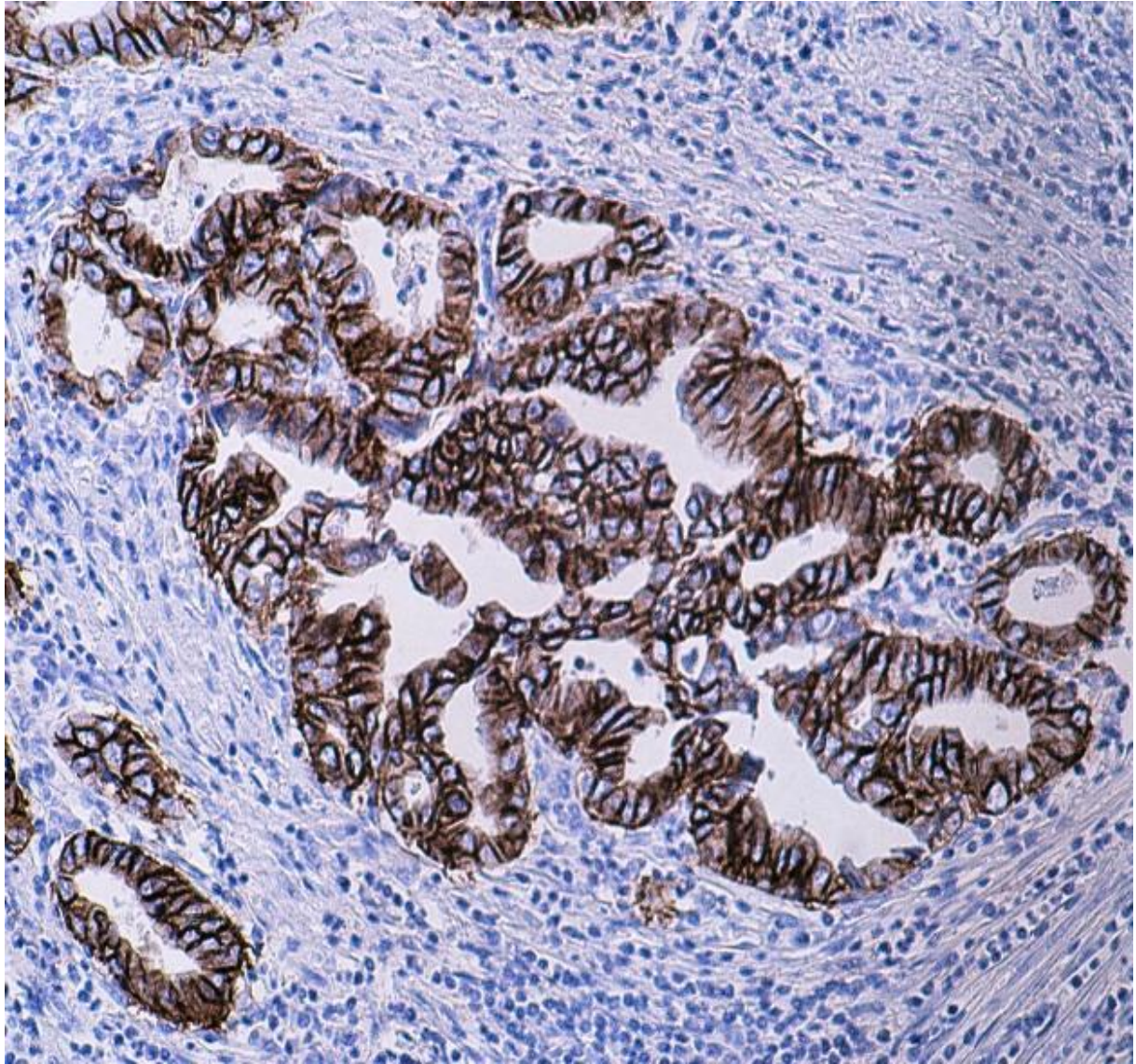


Figure 4: A strong expression of HER2 protein or hyperreactivity in the expression of HER2 protein (40x)

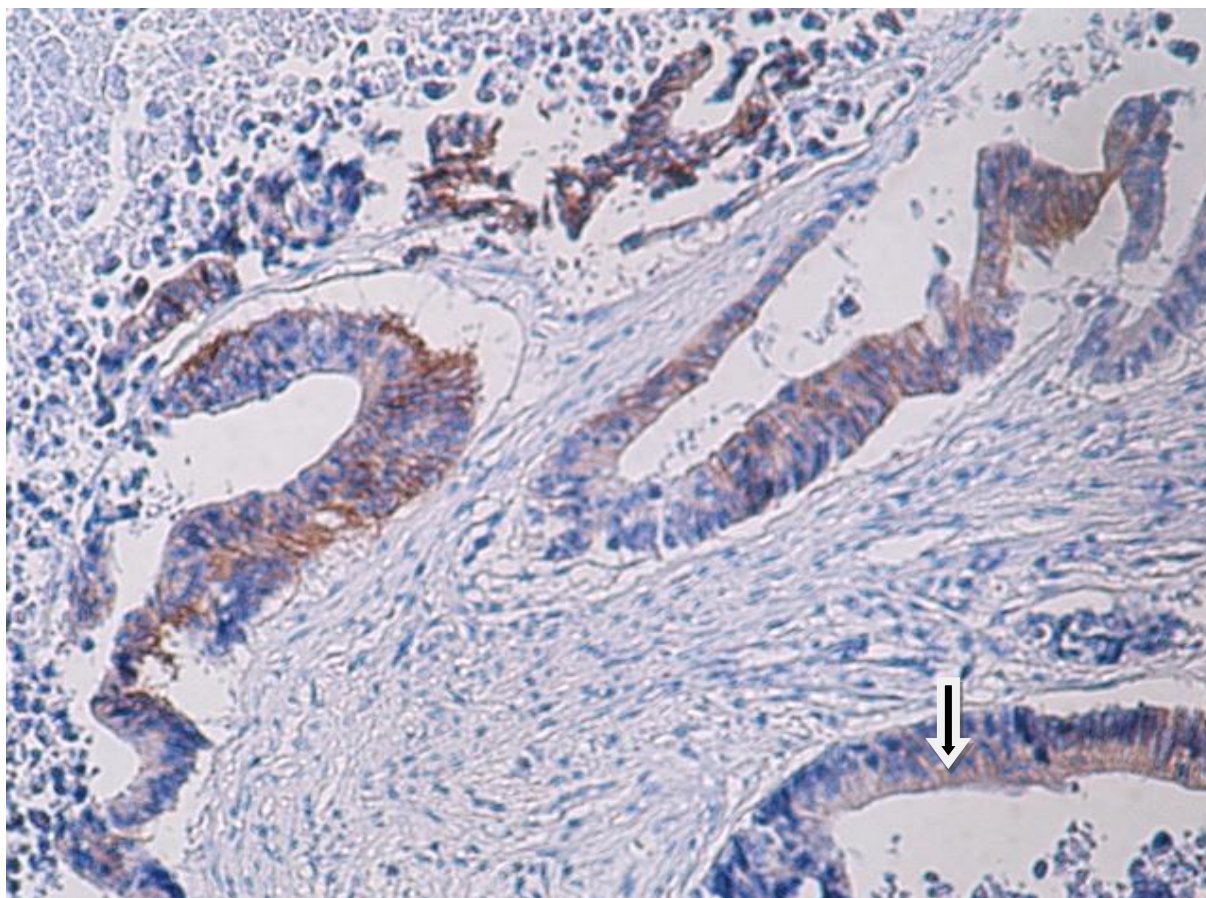


Figure 5: Apical membrane activity in HER2 protein expression (40x)

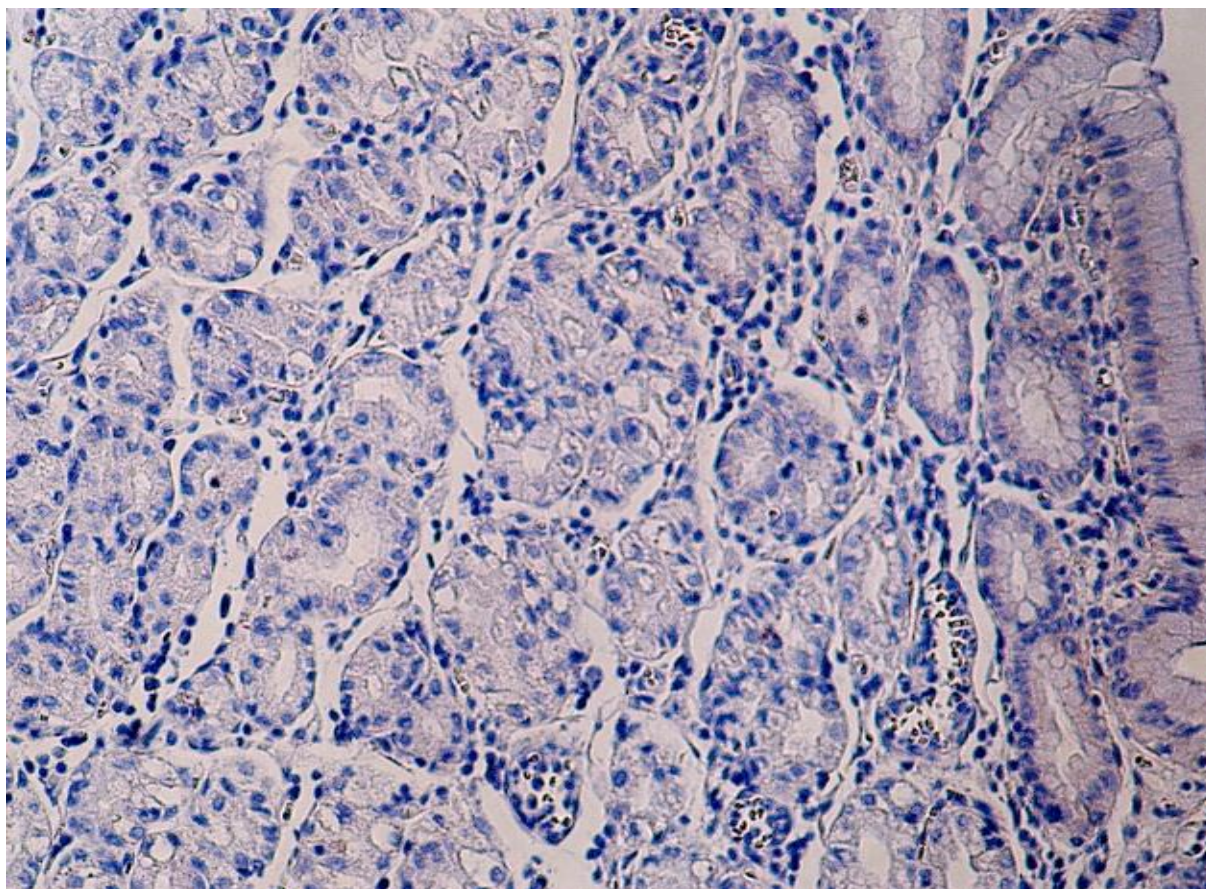


Figure 6: Negative expression of HER2 protein in control samples (40x)

# Effectiveness of Improving Home Environment as A Measure to Prevent the Transmission of Pulmonary Tuberculosis in Badung Regency: A Quasi-Experimental Study

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## Abstract

Pulmonary tuberculosis (TB) remains a public health problem in Indonesia, including in Badung Regency, Bali. A physical home environment that does not meet health standards, such as poor ventilation, insufficient lighting, high humidity, and inappropriate room temperatures, can increase the risk of TB transmission. The objective of this study was to improve the home environmental quality, including room temperature, lighting, humidity, and ventilation rates, before and after environmental improvement interventions in the homes of pulmonary TB patients. The study employed a quasi-experimental design with a pre-posttest approach. The study sample consisted of 10 households of pulmonary TB patients located within the service areas of 10 community health centers (Puskesmas) in Badung Regency, Bali. The instrument used a digital thermo-hygrometer to measure temperature and humidity; a lux meter to measure lighting; and an anemometer to measure ventilation rate. The analysis used the McNemar test at a 95% significance level. The results show that before the intervention, the majority of homes did not meet the criteria for room temperature (70%), lighting (70%), humidity (90%), and ventilation rate (80%). After intervention, the proportion of homes that met the criteria increased to 90% for room temperature and lighting, 80% for humidity, and 80% for ventilation rate. The McNemar test showed significant differences in room temperature ( $p=0.031$ ), lighting ( $p=0.031$ ), humidity ( $p=0.016$ ), and ventilation rate ( $p=0.031$ ). In conclusion, enhancing natural ventilation, natural lighting, and humidity control in homes where people with pulmonary TB live improves the physical environment.

**Keywords:** Environmental Quality, Lighting, Temperature And Humidity, Tuberculosis, Ventilation Rate

## 1. Introduction

Tuberculosis (TB) is an infectious disease that remains a global health problem. Data from the World Health Organization (WHO) show that in 2018 there were approximately 10 million cases of TB worldwide, with Indonesia ranking among the eight countries with the highest number of cases, along with India, China, the Philippines, Pakistan, Nigeria, Bangladesh, and South Africa (World Health Organization, 2019). Even before the

COVID-19 pandemic, TB surpassed HIV/AIDS as the leading cause of death (Suryanti & Ahmed, 2025). According to data from the Ministry of Health of the Republic of Indonesia, the number of TB cases detected in 2019 reached 543,874, while in 2018 there were 566,623 cases (Ministry of Health of Indonesia, 2020). In Bali Province, the number of TB cases in 2020 reached 2,873, with Badung Regency being one of the regions with the highest number of cases at 400 (Dinas Kesehatan Provinsi Bali (Bali Department of Health), 2021). The transmission of pulmonary TB is influenced by interactions among the pathogen, the host, and the environment. The physical environment of a home plays a crucial role in determining the survival of *Mycobacterium tuberculosis* (Cut Fidha Balkis et al., 2026; Ehrt & Schnappinger, 2009; Lili Amaliah et al., 2022). Homes with poor ventilation, low lighting, inappropriate temperatures, and high humidity can create conditions that support the long-term survival of TB bacteria (Fahdhienie et al., 2024; Marni et al., 2024; Meliyanti, 2026).

A study showed that poor home lighting increases the risk of pulmonary TB by 6.67 times compared to homes with good lighting. A study also showed that housing density, ventilation, lighting, and humidity are significantly associated with the incidence of pulmonary TB (Sahadewa et al., 2019). A previous study conducted by (Suyasa et al., 2024) in Badung Regency showed that the knowledge and behaviors of pulmonary TB patients remain low. A total of 90.3% of respondents had insufficient knowledge, and 68.2% exhibited inadequate TB prevention behaviors. The analysis results indicated a significant association between knowledge and behavior and the incidence of pulmonary TB ( $p=0.001$ ). Previously, research about the environment in TB patients was conducted. In (Metri, 2025), a study of the related physical environment with TB prevention was performed, where the homelighhting, home cleanliness was identified as the most influential factors in preventing pulmonary TB transmission. Besides, research about the correlation between clean and healthy living behavior and the condition of the home environment was conducted. It shows that TB patients have a moderate level of clean and healthy living behavior (39.2%), and they live in unhealthy homes (57.9%) (As et al., 2025). A study about counseling has also been conducted to improve public knowledge and behavior in preventing TB transmission. It revealed that the counseling has increased the participants' knowledge by 37.7% with positive behavioral changes (Sirait et al., 2025). However, these studies analyzed only the correlation between the factors, and there is a gap in the implementation or intervention to change the home environment condition. A home environment that does not meet health standards allows TB bacteria to survive longer in the air, thereby increasing the risk of transmission to other family members. Therefore, interventions aimed at improving the quality of the home environment are needed as part of family-based efforts to prevent TB transmission.

This study aims to measure changes in room temperature, lighting, humidity, and ventilation rates before and after improvements were made to the home environment of pulmonary TB patients in Badung Regency.

## 2. Method

This study employed a quantitative method with a quasi-experimental pre-posttest control group design. An experimental study is defined as the most comprehensive quantitative research approach, meaning it meets all requirements for testing cause-and-effect relationships (Sahir, 2021). The study population consists of all subjects or objects with specific characteristics under investigation. This study population consists of all households with pulmonary TB patients located within the service areas of the 10 Community Health Centers (*Puskesmas*) in Badung Regency, Bali. The study sample comprised 10 households with pulmonary TB patients, selected through purposive sampling based on predetermined inclusion criteria. The intervention involved improving natural ventilation in the homes, optimizing natural lighting, controlling indoor humidity, and providing education on maintaining a healthy environment. The study variables included room temperature ( $^{\circ}\text{C}$ ) with a quality standard of 18–30 $^{\circ}\text{C}$ , lighting (lux) with a minimum quality standard of 60 lux, humidity (%) with a quality standard of 40–60%, and ventilation rate (m/second) with a standard requirement of 0.15–0.25 m/second.

Data collection is a research activity aimed at gathering data. Before conducting data collection, it is necessary to consider the data collection instruments to strengthen the research results. These data collection instruments may include questionnaires, observations, interviews, or a combination of all three. The research variables, room temperature and humidity, were measured using a digital thermohygrometer in the morning and afternoon in the main room; room temperature was measured in degrees Celsius ( $^{\circ}\text{C}$ ) and humidity in percent (%). The lighting

variable was measured using a lux meter during the day (10:00 a.m.–2:00 p.m.) in lux, while the ventilation rate was measured using an anemometer in m/s. The data were analyzed univariately to describe the characteristics of the respondents and the quality of the home environment. Bivariate analysis used the McNemar test to determine differences in environmental quality before and after the intervention at a 95% confidence level ( $\alpha = 0.05$ ).

### 3. Results

#### 3.1 Characteristics of Respondents

Characteristics of the study respondents are categorized by gender, age, education, occupation, and income. The youngest respondent was 15 years old, and the oldest was 88 years old, with an average age of  $50.6 \pm 23.99$  years; the average number of household members was  $4.3 \pm 1.57$ . The distribution of respondents by gender, education, occupation, and income is presented in Table 1.

Table 1: Characteristics of respondents

| Characteristics       | Frequency (n) | Percentage (%) |
|-----------------------|---------------|----------------|
| <b>Gender</b>         |               |                |
| Male                  | 8             | 80             |
| Female                | 2             | 20             |
| Total                 | 10            | 100            |
| <b>Education</b>      |               |                |
| Elementary School     | 4             | 40             |
| Junior High School    | 4             | 40             |
| Senior High School    | 2             | 20             |
| Total                 | 10            | 100            |
| <b>Occupation</b>     |               |                |
| Unemployed            | 3             | 30             |
| Farmer                | 2             | 20             |
| Laborer               | 3             | 30             |
| Entrepreneur          | 2             | 20             |
| Total                 | 10            | 100            |
| <b>Monthly income</b> |               |                |
| Rp1.5–2 million       | 5             | 50             |
| >Rp2–2.5 million      | 4             | 40             |
| >Rp2.5–3 million      | 1             | 10             |
| Total                 | 10            | 100            |

Based on Table 1, the majority of respondents were male (80%). In terms of educational attainment, elementary and junior high school graduates each accounted for 40% of the respondents, while high school graduates accounted for 20%. Meanwhile, in terms of employment, the majority of respondents worked as laborers (30%) or were unemployed (30%). Family income was mostly in the range of Rp1.5–2 million per month (50%).

#### 3.2 Environment Quality

Environmental quality was assessed through observations conducted before and after the intervention on air quality, using the parameters of room temperature, lighting, humidity, and ventilation rate. The results of the environmental quality assessment are shown in Table 2.

Table 2: Environmental quality in the respondents' home before and after the intervention

| Variable                | n (%) Before Intervention | n (%) After Intervention |
|-------------------------|---------------------------|--------------------------|
| <b>Room temperature</b> |                           |                          |
| Unqualified             | 7 (70.0)                  | 1 (10.0)                 |
| Qualified               | 3 (30.0)                  | 9 (90.0)                 |
| <b>Lighting</b>         |                           |                          |
| Unqualified             | 7 (70.0)                  | 1 (10.0)                 |
| Qualified               | 3 (30.0)                  | 9 (90.0)                 |
| <b>Humidity</b>         |                           |                          |
| Unqualified             | 9 (90.0)                  | 2 (20.0)                 |
| Qualified               | 1 (10.0)                  | 8 (80.0)                 |
| <b>Ventilation rate</b> |                           |                          |
| Unqualified             | 8 (80.0)                  | 2 (20.0)                 |
| Qualified               | 2 (20.0)                  | 8 (80.0)                 |

Table 2 shows that before environmental improvements were made, most of the respondents' homes had environmental conditions that did not meet health standards, including indoor or room temperature (70.0%), lighting (70.0%), humidity (90.0%), and ventilation rate (80.0%). Following interventions involving improvements to natural ventilation, increased natural lighting, and humidity control, there was an increase in the proportion of homes meeting health standards. The proportion of homes with temperature and lighting that met the standards rose to 90.0%, while those with humidity and ventilation rates that met the standards rose to 80.0% each.

### 3. Statistical Analysis on Environmental Quality

An analysis of differences in environmental quality before and after the intervention was conducted using the McNemar test. Table 3 shows the results of the statistical test.

Table 3: McNemar test results on environmental quality changes

| Variable         | N (%)<br>Unqualified<br>Intervention | Before | N (%)<br>Qualified<br>Intervention | After | p-value |
|------------------|--------------------------------------|--------|------------------------------------|-------|---------|
| Room temperature | 7 (70.0)                             |        | 9 (90.0)                           |       | 0.031   |
| Lighting         | 7 (70.0)                             |        | 9 (90.0)                           |       | 0.031   |
| Humidity         | 9 (90.0)                             |        | 8 (80.0)                           |       | 0.016   |
| Ventilation rate | 8 (90.0)                             |        | 8 (80.0)                           |       | 0.031   |

Based on the results of the analysis using the McNemar test on Table 3, there are significant changes in all indoor environmental quality parameters following the intervention. Significant changes are found in room temperature ( $p=0.031$ ), lighting ( $p=0.031$ ), humidity ( $p=0.016$ ), and ventilation rate ( $p=0.031$ ). These results indicate that improvements in the home environment are effective in enhancing the physical quality of the homes of patients with pulmonary TB.

### 4. Discussion

The study results show that the majority of respondents were male (80%), with an average age of  $50.6 \pm 23.99$  years. These findings are consistent with the epidemiological profile of tuberculosis (TB) in Indonesia and worldwide, which indicates that men are at higher risk of developing TB than women. According to a WHO report,

approximately 56% of global TB cases occur in adult men. The high proportion of men in this study may be attributed to behavioral factors, high occupational mobility, exposure to occupational risk factors, smoking habits, and delays in seeking healthcare (Jiang et al., 2026; World Health Organization, 2025).

Most respondents had a low level of education, with 40% being elementary school graduates and 40% junior high school graduates. Education is one of the social determinants of health that influences an individual's ability to understand health information, adopt clean and healthy living behaviors, and take steps to prevent disease. Previous research has shown that a low level of education is associated with limited knowledge about TB, delayed diagnosis, and low adherence to behaviors that prevent the transmission of TB (Suyasa et al., 2024). Regarding occupation, most respondents were laborers (30%) or unemployed (30%). This indicates that the majority of respondents came from lower-middle socioeconomic groups. Low socioeconomic status is often associated with poor housing quality, high housing density, and limited ability to improve the home environment. According to a study conducted by (Sulidah et al., 2024), low socioeconomic status is a factor contributing to an increased risk of TB because it is associated with an unhealthy living environment.

The study results show that before the intervention, the majority of respondents' homes had physical environmental conditions that did not meet health standards. A total of 70% of homes had indoor temperatures that did not meet standards, 70% had inadequate lighting, 90% had high humidity, and 80% had ventilation rates that did not meet health standards. These conditions indicate that the homes of most people with pulmonary TB still contain environmental factors that could potentially increase the risk of disease transmission. A closed-off home environment with insufficient sunlight and inadequate ventilation can allow *Mycobacterium tuberculosis* bacteria to survive longer in the air and increase the likelihood of transmission to other family members (World Health Organization, 2025).

Following interventions such as improvements to natural ventilation, increased natural lighting, and humidity control, there is a significant improvement in all parameters of indoor environmental quality. The percentage of homes meeting indoor temperature standards increased from 30% to 90%, lighting improved from 30% to 90%, humidity levels rose from 10% to 80%, and ventilation rates increased from 20% to 80%. These improvements indicate that simple environmental interventions in the homes of people with TB can have a tangible impact on the physical quality of the home environment. The results of this study align with research (Nada Zahra et al., 2025) showing that home ventilation, lighting, and humidity are key factors influencing the incidence of pulmonary TB in the community. Improving home environmental conditions can reduce exposure to infectious droplets containing *Mycobacterium tuberculosis*, thereby contributing to efforts to prevent disease transmission.

The study results show that improving the quality of the home environment can significantly enhance the physical conditions of the homes of people with pulmonary TB. Before the intervention, most homes had inadequate ventilation, poor lighting, high humidity, and suboptimal room temperatures. The increase in appropriate room temperatures following the intervention indicates that improvements in ventilation and lighting were able to enhance indoor air circulation. Good air circulation helps reduce the concentration of droplets containing *Mycobacterium tuberculosis*, thereby lowering the risk of transmission. Research findings indicate that interventions to improve the home environment can significantly improve the physical conditions of people with pulmonary TB. Improvements in ventilation and natural lighting have been shown to improve indoor air quality, thereby potentially reducing the risk of TB transmission. These results are consistent with studies showing that inadequate ventilation increases the risk of pulmonary TB due to limited air circulation and increased concentrations of droplets containing *Mycobacterium tuberculosis* (Nurjannah & Yuantari, 2024).

According to the Ministry of Health of the Republic of Indonesia, the ideal indoor temperature ranges from 18–30°C. Temperatures that are too high or too low can affect indoor air quality and contribute to an increased risk of environment-related diseases (Ministry of Health of Indonesia, 2024). The results of this study indicate that improving the physical environment of homes can be an effective strategy for creating healthier temperature conditions for residents.

Lighting is one of the environmental factors that has a significant impact on TB transmission. In this study, the proportion of homes with adequate lighting increased from 30% to 90% following the intervention. The results of the McNemar test showed a significant change ( $p=0.031$ ). The improvement in lighting was achieved through the optimization of window openings, the reduction of barriers to sunlight, and the utilization of natural lighting. Sunlight contains ultraviolet rays, which are known to damage the DNA structure of *Mycobacterium tuberculosis*, thereby reducing the bacteria's ability to survive in the environment. These findings are consistent with a study (Kencana, 2024) that concluded that homes with inadequate lighting have a higher risk of pulmonary TB compared to homes with good lighting. Another study conducted by (Fitriani, 2020) also showed that the quality of home lighting has a significant association with the incidence of pulmonary TB. Therefore, increasing access to sunlight inside the home is a simple yet effective environmental intervention to support TB prevention. Improvements in natural lighting have also shown significant results. Sunlight contains ultraviolet radiation that can inhibit or even kill TB bacteria in the environment. These findings align with a study by (Sahadewa et al., 2019), which states that home lighting is associated with the incidence of pulmonary TB. The increase in natural lighting that occurred following the intervention also supports TB prevention efforts. Sunlight, particularly ultraviolet rays, is known to inhibit the growth of TB bacteria in the home environment. Several studies indicate that homes with poor lighting have a higher risk of TB cases compared to homes with lighting that meets health standards.

Humidity was the parameter that showed the greatest change in this study. Before the intervention, 90% of homes had humidity levels that did not meet health standards. After the intervention, the proportion of homes meeting the standards increased to 80%. The analysis results indicate a statistically significant change ( $p=0.016$ ). High humidity can increase bacteria's ability to survive longer in the home environment. Additionally, high humidity is often associated with the growth of mold, other microorganisms, and a decline in indoor air quality. These conditions can worsen the respiratory health of household occupants.

Research indicates that household humidity is one of the environmental factors associated with the incidence of pulmonary TB. By improving ventilation and natural lighting, indoor humidity can be controlled, thereby creating an environment less conducive to the survival of *Mycobacterium tuberculosis* (Nurjannah & Yuantari, 2024). The decrease in indoor humidity following the intervention indicates that improved ventilation can enhance air exchange, thereby reducing indoor water vapor levels. High humidity is known to support the survival of *Mycobacterium tuberculosis* for longer periods. The significant decrease in indoor humidity observed in this study indicates that ventilation modifications can improve air exchange and reduce water vapor levels inside the home. Humid conditions are known to provide an environment that supports the survival of TB bacteria for a longer period of time.

Ventilation rate is a critical factor in controlling TB transmission because it is directly related to the process of air exchange. Research findings show that the proportion of homes with adequate ventilation increased from 20% to 80% following the intervention. The McNemar test revealed a significant change ( $p=0.031$ ). Good ventilation reduces the concentration of infectious droplets in the air through dilution and the expulsion of contaminated air to the outside environment. The WHO emphasizes that ventilation is one of the key strategies in environment-based TB transmission prevention, particularly in homes with family members who have active TB (World Health Organization, 2025). These findings are supported by a meta-analysis by (Jannah et al., 2023), which showed that inadequate home ventilation significantly increases the risk of TB cases. Similar results were also reported by (Nada Zahra et al., 2025), who found that homes with poor ventilation are more likely to experience TB cases compared to homes with adequate ventilation. Increased ventilation rates also indicate that modifications to natural ventilation effectively improve air exchange between the interior and exterior of the home. These findings are supported by a study by (Perdana & Putra, 2018), which states that home ventilation is a major risk factor for pulmonary TB.

The results of this study indicate that interventions to improve the home environment are an effective strategy for improving the quality of the physical environment in the homes of people with TB. TB control programs have traditionally focused primarily on case detection and treatment. However, controlling environmental factors needs to be an integral part of TB elimination strategies. Interventions such as improving natural ventilation, optimizing lighting, and controlling humidity are relatively easy to implement, low-cost, and can be sustained by the

community. Therefore, community health centers and local governments need to develop support programs for families of TB patients that focus not only on treatment adherence but also on home environment improvements as a means of preventing transmission at the household level.

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**Informed Consent Statement/Ethics approval:** All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Poltekkes Kemenkes Denpasar No. DP.04.02/F.XXIV.26/542/2026.

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## References

- As, A., Sabriadi, R., Mukty, M. I., & Sanas, N. T. (2025). Integration of Clean and Healthy Living Behavior and Home Environment: A Holistic Approach to Controlling Pulmonary Tuberculosis. *EcoVision: Journal of Environmental Solutions*, 2(2). <https://doi.org/10.61511/evojes.v2i2.2025.2142>
- Cut Fidha Balkis, Mardi Fadillah, Ernawati, & T.M Rafsanjani. (2026). Determinants of Home Environmental Health Related to Pulmonary Tuberculosis Score in The Working Area of UPTD Johan Pahlawan Public Health Center. *MEDALION Journal: Medical Research, Nursing, Health and Midwife Participation*, 6(4), 536–545. <https://doi.org/10.59733/medalion.v6i4.256>
- Dinas Kesehatan Provinsi Bali (Bali Department of Health). (2021). *Profil Kesehatan Provinsi Bali 2020 (Bali Health Profile in 2020)*.
- Ehrt, S., & Schnappinger, D. (2009). Mycobacterial Survival Strategies in The Phagosome: Defence Against Host Stresses. *Cellular Microbiology*, 11(8), 1170–1178. <https://doi.org/10.1111/j.1462-5822.2009.01335.x>
- Fahdhienie, F., Mudatsir, M., Abidin, T. F., & Nurjannah, N. (2024). Risk Factors of Pulmonary Tuberculosis in Indonesia: A Case-Control Study in A High Disease Prevalence Region. *Narra J*, 4(2), e943. <https://doi.org/10.52225/narra.v4i2.943>
- Fitriani, H. U. (2020). The Differences of Ventilation Quality, Natural Lighting and House Wall Conditions to Pulmonary Tuberculosis Incidence in The Working Area of Sidomulyo Health Center, Kediri Regency. *Jurnal Kesehatan Lingkungan*, 12(1), 39–47. <https://doi.org/10.20473/jkl.v12i1.2020.39-47>
- Jannah, R. Z., Azizah, R., Jalaludin, J. B., Sulistyorini, L., & Lestari, K. S. (2023). Meta-Analysis Study: Environmental Risk Factors of Tuberculosis (TB). *Jurnal Kesehatan Lingkungan*, 15(2), 84–91. <https://doi.org/10.20473/jkl.v15i2.2023.84-91>
- Jiang, F., Li, X., Qiao, Q., Zhang, M., Tian, Y., Zhou, S., Li, Y., Ni, R., an, Y., Liu, Y., Zhang, L., & Gong, W. (2026). Global, Regional, and National Burden of Tuberculosis, 1990–2050: A Systematic Comparative

- Analysis Based on Retrospective Cross-sectional of GBD 2021 and WHO Surveillance Systems. *International Journal of Surgery*, 112(1), 250–269. <https://doi.org/10.1097/JS9.00000000000003412>
- Kencana, Y. T. (2024). Studi Meta-Analisis Tentang Hubungan Ventilasi, Kelembaban, Pencahayaan dan Kepadatan Hunian Dengan Kejadian TB Paru di Indonesia (2015 –2020). *Jurnal Kesehatan VisiKes*, 23(1), 104–117.
- Lili Amaliah, Arie Ardiyanti Rufaedah, Sri Nurcahyati, R. Nur Abdurakhman, & Abas Hidayat. (2022). The Relationship between The Physical Home Environment and The Event of Tuberculosis. *World Journal of Advanced Research and Reviews*, 14(3), 623–628. <https://doi.org/10.30574/wjarr.2022.14.3.0627>
- Marni, L., Muchtar, B., Fatimah, S., Barlian, E., Razak, A., & Putra, A. (2024). Home Environment Physical Conditions With Incidence of Tuberculosis (TB) Due to Mycobacterium Tuberculosis (M.tb). *Journal of Sustainability Science and Management*, 19(3), 140–146. <https://doi.org/10.46754/jssm.2024.03.010>
- Meliyanti, F. (2026). Association Between Physical Housing Conditions and Pulmonary Tuberculosis Incidence: A cross-Sectional Study. *Lentera Perawat*, 7(1), 169–180. <https://doi.org/10.52235/lp.v7i1.714>
- Metri, D. (2025). Physical environment increase the transmission of tuberculosis. *Malahayati International Journal of Nursing and Health Science*, 8(9), 1231–1237. <https://doi.org/10.33024/minh.v8i9.1711>
- Ministry of Health of Indonesia. (2020). *Profil Kesehatan Indonesia 2019 (Indonesia Health Profile 2019)*.
- Ministry of Health of Indonesia. (2024). *Profil Kesehatan Indonesia 2023 (Indonesia Health Profile 2023)*.
- Nada Zahra, R., Indah Dewi Aurora, W., & Harahap, H. (2025). The Relationship between Household Environmental Health and the Incidence of Pulmonary Tuberculosis Community Health Center in Jambi City Electronic Journal. *E-SEHAD (Scientific of Environmental Health and Diseases)*, 5(2), 130–137.
- Nurjannah, S., & Yuantari, MG. C. (2024). Analisis Faktor Internal, Pencahayaan, Kelembapan dan Suhu Rumah dengan Kejadian Tuberkulosis. *Faletehan Health Journal*, 11(03), 217–326. <https://doi.org/10.33746/fhj.v11i03.717>
- Perdana, A. A., & Putra, Y. S. (2018). Hubungan Faktor Lingkungan Fisik Rumah terhadap Kejadian TB Paru di Wilayah Kerja Puskesmas Panjang, Lampung. *Jurnal Kesehatan*, 9(1), 46–50. <https://doi.org/10.26630/jk.v9i1.739>
- Sahadewa, S., Eufemia, E., Edwin, E., Niluh, N., & Shita, S. (2019). Hubungan Tingkat Pencahayaan, Kelembaban Udara Dan Ventilasi Udara Dengan Kebajian Tb Paru BTA Positif Di Desa Jaticalang Kecamatan Krian Kabupaten Sidoarjo. *Jurnal Ilmiah Kedokteran Wijaya Kusuma*, 8(2), 118–130. <https://doi.org/10.30742/jikw.v8i2.617>
- Sahir, S. H. (2021). *Metodologi Penelitian* (Vol. 1). Penerbit KBM Indonesia.
- Sirait, R. A., Sinurat, J. L., & Sinurat, J. L. (2025). Healthy Home Education Free from Tuberculosis: Efforts to Prevent TB Transmission in the Pantai Labu Public Health Center, Deli Serdang Regency. *Jurnal Pengmas Kestra*, 5(2), 462–469. <https://doi.org/10.35451/68fr9122>
- Sulidah, Irwan, M., Elmania, Fadlilah, S., Hamdani-Rahil, N., & Nugroho, A. (2024). Home Environment as a Risk Factor for Increasing Tuberculosis Incidence: A Case-Control Study. *Ciencia y Enfermeria*, 30(5), 1–9. <https://doi.org/10.29393/ce30-5hesa60005>
- Suryanti, & Ahmed, I. A. (2025). Letter to the Editor Recent Review Tuberculosis in Indonesia: Burden and the Challenge of Under-Reporting Dear Editor-in-Chief. *Iran J Public Health*, 54(2), 445–446. <https://creativecommons.org/licenses/by-nc/4.0/>
- Suyasa, I. N. G., Dharmawati, I., Jirna, I. N., Purna, I. N., Sundari, C. D. W. H., & Mastra, I. W. S. N. (2024). Correlation between Environmental Factors, Knowledge, and Behavior towards Pulmonary Tuberculosis Incidents. *Journal of Health and Medical Sciences*, 7(3). <https://doi.org/10.31014/aior.1994.07.03.322>
- World Health Organization. (2019). *Global Tuberculosis Report*. <https://iris.who.int/server/api/core/bitstreams/48b446af-11ff-4817-8750-d723c8f70787/content>
- World Health Organization. (2025). *Global Tuberculosis Report 2025*. <https://iris.who.int/server/api/core/bitstreams/e97dd6f4-b567-4396-8680-717bac6869a9/content>

# Factors Associated with the Decline in Health Facility Utilization for Childbirth in Ekiti State, Nigeria: Empirical Evidence from a Mixed-Methods Survey

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## Abstract

**Introduction:** Despite targeted investments in maternal health services, Ekiti State, Nigeria, has experienced a decline in health facility-based deliveries. This study explores the contextual factors influencing the non-utilization of health facilities for deliveries as well as evaluates the vulnerability factors that influence general health-seeking behaviour by women of childbearing age in Ekiti State. **Methods:** A comprehensive mixed-methods evaluation involving desk reviews, quantitative household surveys, and stakeholder interviews was adopted for the study. Local government areas with the highest trends in drop-off for facility deliveries informed the selection of the six study sites. The quantitative household survey involved 529 respondents and collected data on sociodemographic characteristics, past delivery experiences, perceptions of maternal healthcare services, and the drivers of women's choice of place of delivery. The qualitative component provided deeper insights into stakeholders' perspectives and the contextual factors influencing delivery decisions. **Findings:** Key findings indicate that the most significant determinant for delivery decisions is spousal influence, whilst the provision of respectful maternal care (RMC) is an additional factor. A follow-up study engaging male partners through Computer-Assisted Telephone Interviewing (CATI) revealed that 50% of men whose wives delivered outside health facilities cited "cost of care" as the main barrier. Other factors included parental pressure, religious beliefs, and the appeal of traditional birth attendants (TBAs). **Conclusion:** Addressing the identified factors through policy interventions, community engagement, and health system improvements is essential to reversing the decline in facility deliveries and improving maternal and neonatal outcomes in Ekiti State. Actionable recommendations are provided to enhance service quality, build community trust, and strengthen referral pathways.

**Keywords:** Maternal Health, Facility-Based Deliveries, Spousal Influence, Cost of Care, Traditional Birth Attendants, Nigeria, Mixed-Methods Survey

## 1. Introduction

Despite decades of policy attention and investment, maternal mortality remains a persistent public health challenge in sub-Saharan Africa, where over two-thirds of global maternal deaths occur annually (WHO, 2022; Say et al., 2014). Nigeria, as Africa's most populous country, accounts for nearly 20% of these deaths, with an estimated maternal mortality ratio (MMR) of 512 per 100,000 live births as of 2021 (NDHS, 2021; WHO, 2022). These figures are particularly concerning given that most maternal deaths are preventable through timely access to quality antenatal care (ANC), skilled birth attendance, and postnatal care (Campbell & Graham, 2006; Montagu et al., 2011).

Utilization of maternal health services in Nigeria has improved only modestly over the past two decades, with persistent gaps in facility-based childbirth. Nationally, the proportion of births occurring in health facilities increased from about one-third in the early 2000s to 39.4% in 2018, reflecting slow progress despite repeated policy efforts to improve maternal health service uptake (NDHS 2003; NDHS 2008; NDHS 2013; NDHS 2018 & NDHS, 2023). Between 2013 and 2018 alone, facility delivery increased only marginally from 35.8% to 39.4% nationally. However, this national trend masks important subnational variations, including reversals in states that had previously recorded relatively high levels of maternal service utilization. In Ekiti State, evidence from the NDHS trend suggests that facility-based delivery declined between 2013, 2018, and 2023 despite relatively high antenatal care coverage. This pattern reflects a critical "continuum-of-care drop-off," where contact with the formal health system during pregnancy does not consistently translate into childbirth in a health facility. The Ekiti paradox is therefore not merely one of low service awareness or low ANC contact, but of women disengaging from facility-based care at the point of delivery. Understanding the socio-economic, health-system, cultural, and experiential factors driving this decline is essential for designing interventions that go beyond ANC attendance to address the barriers that shape women's final choice of place of birth.

While national and state governments have prioritized increasing service availability, evidence suggests that access alone is insufficient. The persistent gap between ANC attendance and institutional delivery underscores the need to understand what prevents women from transitioning to facility-based births even after engaging with the health system. This transition is a critical inflexion point in the maternal health continuum, where household dynamics, perceptions of care, and financial considerations often override clinical recommendations or public health messaging. If policy interventions continue to treat supply-side constraints as the sole barrier, they risk failing the very women they are designed to protect.

This study seeks to move beyond surface-level statistics by examining the deeper structural and contextual determinants of delivery location in Ekiti State. In particular, it investigates how household financial constraints and spousal decision-making power intersect to influence maternal health-seeking behaviour. These factors are especially salient in southwestern Nigeria, where traditional gender norms remain entrenched, and economic hardship disproportionately affects rural households. By foregrounding these issues, this research contributes to a more grounded and actionable understanding of maternal health service utilization, with implications for program design, policy reform, and future research.

## **2. Review Related Literature**

### *2.1 Trends in Maternal Health in Sub-Saharan Africa and Nigeria*

Sub-Saharan Africa remains the epicentre of the global maternal mortality crisis, with mortality ratios exceeding 500 deaths per 100,000 live births in some countries (WHO, 2022). Nigeria contributes nearly 25% of all maternal deaths in the region, reflecting deep systemic issues in access, quality, and continuity of care (UNFPA, 2022; FMoH, 2020). Despite multiple health sector reforms and global commitments like the Sustainable Development Goals (SDGs) and Every Woman Every Child initiative, maternal mortality remains unacceptably high.

There has been notable progress in increasing antenatal care (ANC) attendance and skilled birth attendance (SBA). For example, national ANC coverage in Nigeria rose from 58% in 2013 to 67% in 2021, while SBA increased from 43% to 50% over the same period (NPC & ICF, 2023). However, these improvements have not always

translated into increased facility-based deliveries, particularly in states like Ekiti. A growing number of women receive ANC from skilled providers but still opt to deliver at home, often assisted by traditional birth attendants (TBAs) (Fagbamigbe et al., 2017; Okonofua et al., 2018). This paradox signals deeper barriers beyond access—related to experience of care, socio-cultural factors, and trust in the health system.

## *2.2 Barriers to Facility-Based Deliveries*

A wide range of barriers undermine women's access to facility-based deliveries.

**Economic barriers**—including formal user fees, cost of transportation, and opportunity costs (e.g., lost income, childcare)—disproportionately affect low-income households and rural populations (Borghi et al., 2006; Kruk et al., 2010). In rural Nigeria, financial constraints were identified as the top reason for home births by Ononokpono and Odimegwu (2014).

**Cultural norms and gender dynamics add a further layer of constraint.** In many communities, childbirth is considered a routine, natural process best handled within the home or by familiar caregivers. Patriarchal structures often assign decision-making authority to male partners or elder relatives, limiting women's autonomy to choose institutional care (Adamu & Salihu, 2002; Osuor et al., 2006; Izugbara et al., 2020). These social expectations remain deeply entrenched even among educated or urban households.

Spousal influence, in particular, has been recognized as a decisive factor in maternal health service utilization. Men's perceptions of cost, necessity, and quality of care directly shape whether their partners deliver in health facilities (Yaya et al., 2018; Doctor et al., 2019). In settings where men dominate household decisions, the likelihood of facility-based delivery rises significantly if the male partner is positively inclined toward skilled maternity care.

However, even when women do reach health facilities, the experience of care itself can be a powerful deterrent to return or recommend facility use. This brings into focus the emerging priority of Respectful Maternity Care (RMC). RMC refers to care that upholds the dignity, privacy, and autonomy of women, avoids harm or mistreatment, and ensures informed consent and continuous support during childbirth (WHO, 2018). In Nigeria, reports of verbal abuse, neglect, denial of care, and discrimination remain widespread and underreported (Bohren et al., 2015; Okafor et al., 2020). These experiences can shape women's future health-seeking behaviour and ripple through communities via word of mouth.

Neglecting the importance of RMC risks undermining gains in coverage. Women may opt for TBAs not only because of proximity or affordability but because these caregivers often provide emotional support, familiarity, and respectful interactions, qualities sometimes lacking in overstretched health facilities. As such, poor experience of care should be viewed not just as a quality issue, but as a structural barrier to maternal survival.

## *2.3 The Role of Antenatal Care and Health Education*

ANC remains a critical entry point into the formal health system, offering opportunities for early risk detection, health promotion, and preparation for skilled birth attendance (Tura et al., 2013; Moyer & Mustafa, 2013). However, its impact on subsequent delivery choices hinges on the quality and content of services received. Several studies report that when ANC is limited to routine checks without meaningful education on birth preparedness, danger signs, or the benefits of skilled care, its influence on delivery behaviour is minimal (Bohren et al., 2014; Warren et al., 2017).

Furthermore, the engagement of male partners during ANC has been shown to increase women's likelihood of delivering in a facility. Community-based interventions that include men, through education campaigns, peer groups, or counselling, have successfully increased demand for skilled care (Ditekemena et al., 2012; Mullany et al., 2007). These strategies also promote more equitable decision-making, gradually shifting patriarchal norms.

Ultimately, bridging the gap between ANC and facility-based delivery requires a holistic approach that addresses both clinical care and the interpersonal dynamics within health systems. This includes strengthening RMC, promoting birth preparedness, engaging families and communities, and ensuring that every touchpoint, particularly ANC, is leveraged to build trust and continuity in maternal care

### **3. Methodology**

#### *3.1 Study Design*

A cross-sectional mixed-methods design was used to explore the factors influencing facility-based deliveries in Ekiti State. This approach allowed triangulation of quantitative and qualitative data, enabling a more robust understanding of both measurable trends and contextual nuances (Creswell & Plano Clark, 2017).

#### *3.2 Desk Review*

Secondary data from the District Health Information System (DHIS 2) and other government sources were analyzed to identify patterns in ANC attendance, facility deliveries, and postnatal care (PNC) coverage across LGAs [FMOH/DHIS 2, 2023]. This analysis informed the selection of high-priority LGAs for deeper investigation.

#### *3.3 Quantitative Household Survey*

A structured questionnaire was administered to 529 women of reproductive age (15–49 years) across six LGAs exhibiting the most significant drop-off between ANC and facility-based deliveries. The survey instrument, adapted from previous validated maternal health tools (MEASURE DHS, 2019), captured demographic details, delivery history, health-seeking behaviours, and perceptions of healthcare quality. Data were analyzed using SPSS, with chi-square and logistic regression techniques used to assess associations between sociodemographic variables and delivery location.

#### *3.4 Qualitative Interviews and Focus Group Discussions*

To explore cultural, social, and systemic factors in-depth, key informant interviews (KIIs) and focus group discussions (FGDs) were conducted with community stakeholders, including health workers, TBAs, religious leaders, and local government officials. Thematic analysis was carried out using Atlas.ti software, following a grounded theory approach (Strauss & Corbin, 1998). Codes were developed both inductively and deductively based on emerging themes and the study objectives.

#### *3.5 Measurement of Respectful Maternal Care*

The Mothers on Respect Index (MORi) was employed to measure the level of respectful maternal care (RMC) received by women during delivery. This tool, developed and validated for low-resource settings, assesses communication, autonomy, and perceived discrimination during childbirth (Vedam et al., 2017). The MORi provides insight into how provider attitudes and interpersonal care influence health service utilization and satisfaction (Afulani et al., 2020).

#### *3.6 Inclusion and Exclusion Criteria*

Participants were selected based on the following:

- i. Women aged 15–49 who were currently pregnant or had delivered within the past two years.
- ii. Stakeholders with operational knowledge of maternal health services in Ekiti.
- iii. Enumeration areas compromised by security issues or non-consenting individuals were excluded.

## 4. Discussion and Presentation of Results

This section presents the findings from the mixed-methods analysis of the study. The results integrate quantitative and qualitative evidence to provide a comprehensive understanding of the factors influencing the utilization of health facilities for delivery. The quantitative findings are presented first, highlighting the statistical patterns associated with health facility delivery utilization. These findings are complemented by qualitative insights from key informant interviews and community stakeholders, which provide deeper explanations of the underlying social, cultural, economic, and institutional factors shaping maternal healthcare-seeking behaviours. Therefore, this section presents the findings from the mixed-methods analysis, beginning with the quantitative results and followed by the qualitative findings, which help to explain and contextualize the quantitative patterns.

### *4.1 Access to Maternal Health Services:*

The survey examined respondents' access to healthcare services across six LGAs in Ekiti State, with a focus on the availability of primary health care (PHC) facilities, distance to care, 24-hour service availability, maternal health service utilization, and quality perceptions.

#### **Availability of Health Facilities:**

A vast majority of respondents (96.8%) reported having a PHC facility in their community, with slightly higher availability in rural areas. However, gaps remained in some LGAs, particularly Ikere (6.7%), Ido-Osi (6.3%), and Ikole (5.9%), where respondents reported the absence of PHCs. In terms of additional functional health facilities beyond PHCs, only 69% confirmed the presence of such facilities in their communities, with Ise/Orun (56.5%) and Ikere (52.6%) reporting the least access.

#### **Facility Utilization and Operating Hours:**

More than half (56.3%) of respondents received care from PHCs, while 21.9% used general hospitals. Only 63% of PHCs reportedly operated 24 hours, with rural areas having more limited round-the-clock services. Notably, Efon Alaye (49%), Ekiti West (41%), and Ise/Orun (37.6%) had high proportions of non-24-hour facilities.

#### **Proximity to Healthcare Services:**

The average walking time to a health facility was 22.3 minutes, but 14.8% of respondents walked more than 30 minutes—particularly in Ikole (26%) and Ikere (21.1%). Less vulnerable women had a longer average walking time (25.7 minutes) compared to their more vulnerable counterparts.

#### **Perception of Service Quality:**

Only 48% of respondents believed that PHC services were improving. The most positive ratings came from Ikole, while respondents from Efon Alaye and Ekiti West were most likely to say services were worsening. Interestingly, more vulnerable women were generally more satisfied with care quality, whereas less vulnerable women reported unmet expectations.

#### **Utilization of Maternal and Neonatal Health Services:**

Antenatal care (ANC) attendance was high overall, with 93.2% attending at least once. However, ANC non-attendance was highest in Ikole and, surprisingly, among less vulnerable women (15.4%) compared to more vulnerable women (5.3%). Postnatal care (PNC) utilization within 2–3 days of delivery stood at 83.4%, with the highest uptake in Efon Alaye (93.9%) and Ise/Orun (91.8%), and the lowest in Ido-Osi (66.3%). Again, less vulnerable women were more likely to miss PNC visits.

#### **Cord Care Practices:**

Most respondents (81.9%) used methylated spirit with cotton wool for cord care. Chlorhexidine gel use was reported by only 9%, primarily in Efon Alaye and Ikere, and not at all in Ikole. A small proportion reported traditional or harmful practices, including hot substances, herbal mixtures, or kerosene.

#### **Health Complications During Pregnancy:**

Malaria in pregnancy was the most frequently reported health challenge among respondents (41.4%), with a higher prevalence observed in rural areas and Efon Alaye. Other maternal health complications, including preterm labour, postpartum haemorrhage, and anaemia, were reported at considerably lower proportions. The distribution of reported health challenges among respondents is presented in Table 1.

Table 1: Distribution of Reported Health Challenges Among Respondents

| Health Challenge       | % Respondents |
|------------------------|---------------|
| Malaria in Pregnancy   | 41.4          |
| None                   | 35.9          |
| Uncomplicated Delivery | 13.8          |
| Preterm Labour         | 2.1           |
| Low Birth Weight       | 1.9           |
| Postpartum Hemorrhage  | 1.7           |
| Anemia                 | 1.3           |
| Complicated CS         | 1.1           |

#### Facility Delivery and Willingness to Recommend:

A notable 26.1% of respondents delivered outside health facilities. Ido-Osi had the highest rate of non-facility deliveries (35%). Urban and rural differences were negligible, but from a vulnerability perspective, 43.3% of less vulnerable women delivered outside facilities—more than double the rate of more vulnerable women. Despite this, 95.1% of all respondents were willing to recommend their delivery location to others; of the 4.9% who were not, most had delivered at home.

Figure 1: Respectful Maternal Care (RMC)

The overall MORi score for Ekiti State was 81.4%, indicating a moderate level of respectful care. Although the state excelled in preventing abuse and discrimination, significant gaps were observed in professional care standards and provider-mother rapport. For example, 45.2% of respondents experienced painful vaginal examinations, and 61% reported being denied a birth companion during labour (Afulani et al., 2020).

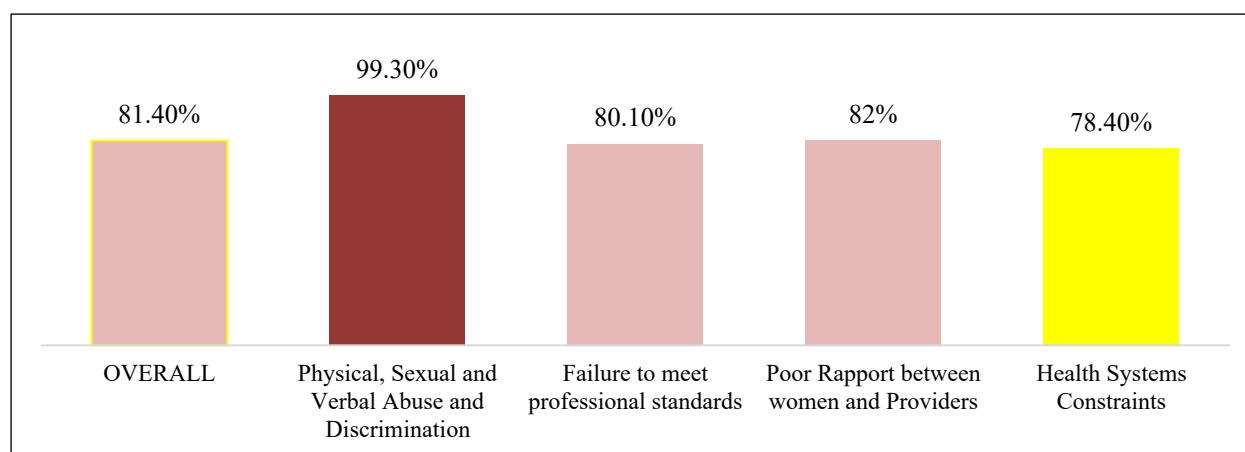


Figure 1: Index of Mothers on Respectful Maternal Care according to the 4 domains

Figure 2: Key Drivers of Non-Utilization

The findings presented in Figure 2 further underscore the dominant influence of spousal decision-making and economic constraints on the utilization of health facilities for delivery. The fact that 71.5% of respondents identified husbands as key decision-makers highlights the continued influence of household power dynamics in maternal healthcare choices, which is consistent with previous evidence on the role of male partners in maternal health decision-making (Kruk, Mbaruku, Rockers, & Galea, 2010; Izugbara et al., 2020).

Similarly, the finding that 50% of male respondents cited the cost of care as the primary barrier among women who delivered outside health facilities reflects the importance of financial constraints in shaping access to facility-based delivery (Izugbara, Wekesah, Tilahun, Amo-Adjei, Dimbuene, 2020). These findings suggest that improving maternal healthcare utilization requires interventions that address not only health system barriers but also household decision-making structures and financial limitations.

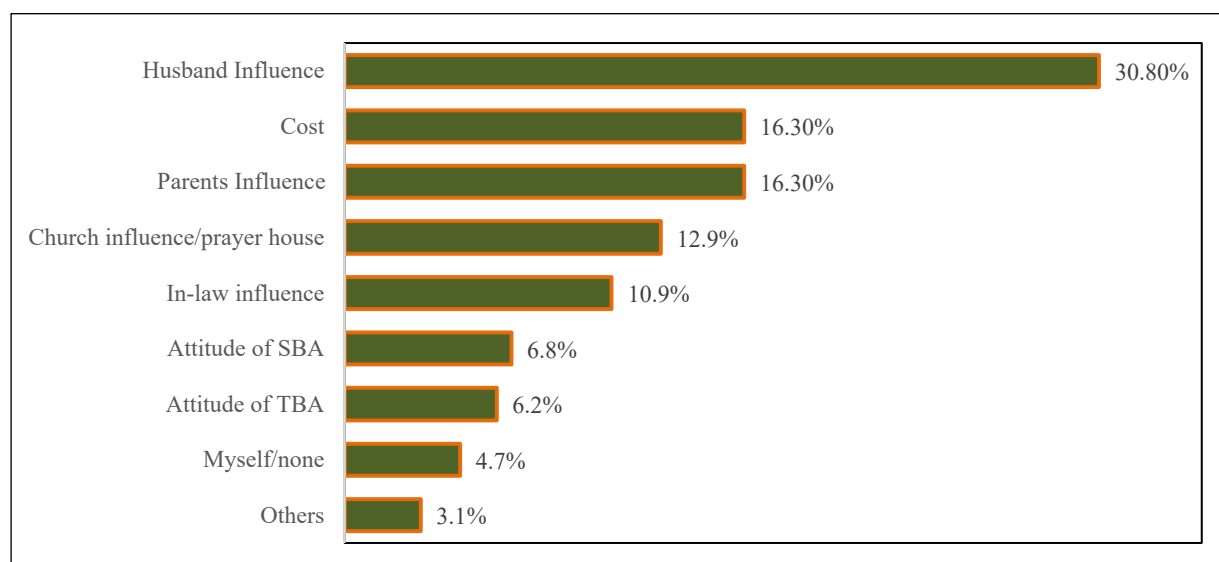


Figure 2: Drivers of choice of place of Delivery in Ekiti State

Figure 3: Community and Health System Factors

Figure 3 illustrates that despite high ANC attendance (93.2%), only 74% of respondents delivered in a health facility. Rural women and those classified as less vulnerable—often with greater decision-making autonomy—were more likely to deliver outside facilities. Logistical challenges, including long travel times and limited transport options, further compounded this disparity (Afulani, Phillips, Aborigo, Moyer, & Asante, 2019; Bohren, Vogel, Hunter, Lutsiv, Makh, Souza, & Gülmezoglu, 2015)

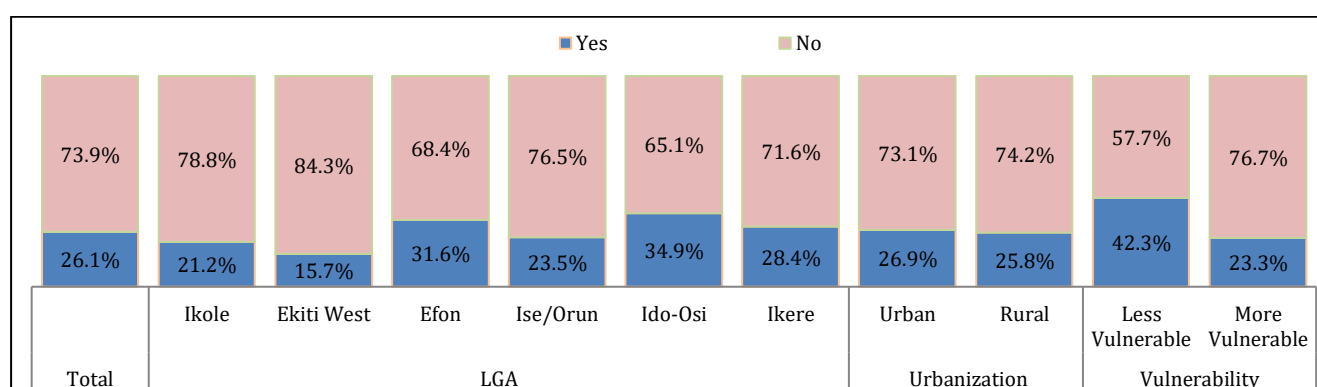


Figure 3: Facility vs. Non-Facility Delivery Rates in Ekiti State

#### 4.2 Contextual Factors Influencing Non-Utilization of Health Facilities for Delivery: Qualitative Findings

Qualitative findings further reinforce the identified drivers of non-utilization of health facilities for delivery. The findings revealed that social, psychological, and socio-economic factors influence women's decisions regarding the choice of delivery location.

##### Influence of husbands, parents, and in-laws

One prominent factor identified was the influence of husbands, parents, and in-laws in maternal healthcare decision-making. Participants indicated that husbands often have a dominant role in determining the place of delivery, particularly because they are responsible for financing delivery-related costs. As noted from the qualitative responses: *“The final decision is always the husband’s because they are the person that will pay for the cost of delivery.”* This highlights how financial responsibility and gendered decision-making dynamics shape women’s autonomy and choices regarding place of delivery.

### **Psychological Factors**

Respondents were of the view that many pregnant women make efforts to hide their pregnancy from others for fear of spiritual attacks. Participants explained that this fear creates an opportunity for TBAs to attract pregnant women by providing spiritual support. Another scenario from the qualitative component of the research reported that *“The TBAs usually capitalize on this fear to offer prayers as a solution, which gradually woo the pregnant women away from the health facility.”*

### **Socio-Economic Factors**

Participants also identified socio-economic challenges as important drivers of non-utilization of health facilities for delivery. This includes TBAs’ “fight” for survival in the face of economic hardship and insufficient financial risk protection. This is in line with the respondents’ views in the qualitative arm of the study, which reported that *“The TBAs are also struggling to survive because this is their means of livelihood.”* These findings demonstrate that non-utilization of health facilities for delivery is influenced by a combination of household decision-making structures, psychological concerns, and economic realities within the community.

## **5. Discussion**

The study reveals a multifaceted challenge. While respectful maternal care is an important factor, its impact is overshadowed by the dominant role of spousal influence and the economic barrier of cost. The finding that husband’s control 71.5% of delivery decisions aligns with existing literature on male involvement in maternal health (Borghi, Ensor, Somanathan, Lissner, & Mills, 2006). In addition, the fact that 50% of men identify cost as a primary barrier underscores the economic constraints that impede access to facility-based care (Bohren, Vogel, Hunter, Lutsiv, Makh, Souza, & Gulmezoglu, 2015).

### *5.1. Spousal Influence and Economic Barriers*

Male partners play a pivotal role in healthcare decision-making in many Nigerian communities (Campbell & Graham, 2006). The high reliance on spousal influence necessitates those interventions extend to male-targeted education and involvement programs. Cost barriers, as identified by half of the male respondents, indicate that financial constraints—both actual and perceived—are critical deterrents to facility-based deliveries. Addressing these issues through subsidized care and transport support is essential (Doctor, Nkhoma, Abdulsalam-Anibilowo, 2019).

### *5.2. Systemic and Logistical Challenges*

The gap between high ANC attendance and lower facility-based deliveries highlights significant systemic weaknesses. Inadequate transport limited 24-hour service availability, and logistical inefficiencies contribute to the delivery gap. Strengthening referral systems and ensuring consistent service quality are vital steps towards improving facility utilization (Izugbara, Wekesah, Tilahun, Amo-Adjei, & Dimbuene, 2020).

### *5.3. Implications for Policy and Practice*

The findings suggest that policy interventions should prioritize the following areas:

**Male Involvement:**

Tailored education programmes and community outreach initiatives should be developed to engage male partners and promote supportive roles in maternal healthcare decision-making.

**Financial Support:**

Expansion of health insurance schemes, provision of transport subsidies, and enhanced funding for free maternal care programmes are essential to reduce financial barriers to facility-based delivery.

**Health System Strengthening:**

Investments in healthcare infrastructure, staffing, and operational improvements are required to ensure the availability of reliable 24-hour maternal health services.

**Integration of Traditional Birth Attendants (TBAs):**

The cultural role of TBAs should be leveraged by integrating them into the formal health system through appropriate training, referral networks, and collaboration with healthcare facilities (Adamu & Salihu, 2002; Fagbamigbe, Idemudia, & Adebawale, 2017).

*5.4. Limitations*

This study is limited by its cross-sectional design, which precludes causal inference. Self-reported data are subject to recall bias, and the findings from selected LGAs may not be generalizable nationwide. Future research should consider longitudinal designs and broader geographic sampling to validate these findings (Fagbamigbe, Idemudia, & Adebawale, 2017).

**6. Conclusion and Recommendations**

The findings of this study demonstrate that reversing the decline in facility-based deliveries in Ekiti State requires a comprehensive and context-specific approach that addresses the socio-cultural, economic, and health system barriers influencing maternal healthcare-seeking behaviour. The evidence highlights the critical roles of household decision-making dynamics, financial constraints, cultural practices, and community-level factors in shaping women's choices regarding place of delivery. Addressing these interconnected challenges is essential for improving the utilization of health facilities and advancing maternal health outcomes in the state. Based on these findings, the following recommendations are proposed to strengthen facility-based delivery utilization in Ekiti State.

**Promote Male Involvement**

Develop and implement targeted education programs for male partners to underscore the benefits of facility-based deliveries. Utilize community forums and media campaigns to engage men in maternal health decision-making and shift social norms around childbirth.

**Expand Financial Access**

Scale up health insurance schemes and introduce transport subsidies to reduce the cost burden associated with facility-based deliveries. Ensure that free maternal care programs are efficiently implemented and effectively reach rural and underserved populations.

**Enhance Respectful Maternal Care**

Implement comprehensive training for health workers on patient-centred care and respectful communication. Establish robust feedback and grievance redress systems to improve accountability and ensure women feel safe and respected in health facilities.

**Strengthen Health System Infrastructure**

Invest in upgrading health facilities to provide reliable, 24-hour services, especially in rural areas. Improve transport networks and referral systems to ensure timely access to emergency obstetric care.

By addressing these determinants, particularly the dominant role of spousal influence and the economic constraints identified, Ekiti State can enhance facility-based delivery rates, ultimately improving maternal and neonatal health outcomes and reducing preventable deaths.

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**Informed Consent Statement/Ethics Approval:** Ethical approval for the study was obtained from the Ekiti State Ministry of Health and the Ekiti State Health Insurance Agency. Verbal informed consent was obtained from all study participants prior to their participation in the study.

**Declaration of Generative AI and AI-assisted Technologies:** This study has not used any generative AI tools or technologies in the preparation of this manuscript.

## References

- Adamu, Y. M., & Salihu, H. M. (2002). Barriers to the use of antenatal and obstetric care services in rural Kano, Nigeria. *Journal of Obstetrics and Gynaecology*, 22(6), 600–603. <https://doi.org/10.1080/014436102100000407>
- Afulani, P. A., Phillips, B., Aborigo, R. A., Moyer, C. A., & Asante, K. P. (2019). Person-centred maternity care in low-income and middle-income countries: Analysis of data from Kenya, Ghana, and India. *The Lancet Global Health*, 7(1), e132–e142. [https://doi.org/10.1016/S2214-109X\(18\)30403-0](https://doi.org/10.1016/S2214-109X(18)30403-0)
- Bohren, M. A., Vogel, J. P., Hunter, E. C., Lutsiv, O., Makh, S. K., Souza, J. P., & Gülmezoglu, A. M. (2015). The mistreatment of women during childbirth in health facilities globally: A mixed-methods systematic review. *PLoS Medicine*, 12(6), e1001847. <https://doi.org/10.1371/journal.pmed.1001847>
- Borghi, J., Ensor, T., Somanathan, A., Lissner, C., & Mills, A. (2006). Mobilising financial resources for maternal health. *The Lancet*, 368(9545), 1457–1465. [https://doi.org/10.1016/S0140-6736\(06\)69383-5](https://doi.org/10.1016/S0140-6736(06)69383-5)

- Campbell, O. M. R., & Graham, W. J. (2006). Strategies for reducing maternal mortality: Getting on with what works. *The Lancet*, 368(9543), 1284–1299. [https://doi.org/10.1016/S0140-6736\(06\)69381-1](https://doi.org/10.1016/S0140-6736(06)69381-1)
- Ditekemena, J., Koole, O., Engmann, C., Matendo, R., Tshefu, A., Ryder, R., & Colebunders, R. (2012). Determinants of male involvement in maternal and child health services in sub-Saharan Africa: A review. *Reproductive Health*, 9, 32. <https://doi.org/10.1186/1742-4755-9-32>
- Doctor, H. V., Nkhoma, D., & Abdulsalam-Anibilowo, M. (2019). Male involvement in maternal health care: Evidence from Anambra State, Nigeria. *BMC Public Health*, 19, 761. <https://doi.org/10.1186/s12889-019-7089-3>
- Federal Ministry of Health. (2020). *Nigeria Every Newborn Action Plan: 2020–2024*. Federal Ministry of Health.
- Fagbamigbe, A. F., Idemudia, E. S., & Adebawale, A. S. (2017). Maternal health care service utilization in Nigeria: A comparative analysis of rural and urban women. *International Journal of Women's Health*, 9, 681–690. <https://doi.org/10.2147/IJWH.S125652>
- Izugbara, C. O., Wekesah, F. M., Tilahun, T., Amo-Adjei, J., & Dimbuene, Z. T. (2020). Family, reproductive health, and care-seeking behaviour in Africa: A review of the literature. *African Journal of Reproductive Health*, 24(3), 27–41. <https://doi.org/10.29063/ajrh2020/v24i3.3>
- Kruk, M. E., Mbaruku, G., Rockers, P. C., & Galea, S. (2010). User fee exemptions are not enough: Out-of-pocket payments for “free” delivery services in rural Tanzania. *Tropical Medicine & International Health*, 15(12), 1457–1463. <https://doi.org/10.1111/j.1365-3156.2010.02620.x>
- Montagu, D., Yamey, G., Visconti, A., Harding, A., & Yoong, J. (2011). Where do poor women in developing countries give birth? A multi-country analysis of demographic and health survey data. *PLoS ONE*, 6(2), e17155. <https://doi.org/10.1371/journal.pone.0017155>
- Moyer, C. A., & Mustafa, A. (2013). Drivers and deterrents of facility delivery in sub-Saharan Africa: A systematic review. *Reproductive Health*, 10, 40. <https://doi.org/10.1186/1742-4755-10-40>
- Mullany, B. C., Becker, S., & Hindin, M. J. (2007). The impact of including husbands in antenatal health education services on maternal health practices in urban Nepal: Results from a randomized controlled trial. *Health Education Research*, 22(2), 166–176. <https://doi.org/10.1093/her/cyl060>
- National Population Commission [NPC] [Nigeria] & ICF. (2023). *Nigeria demographic and health survey 2023: Key indicators report*. NPC and ICF.
- National Population Commission [NPC] [Nigeria] & ICF International. (2014). *Nigeria demographic and health survey 2013*. NPC and ICF International.
- Okafor, I. I., Ugwu, E. O., & Obi, S. N. (2020). Disrespect and abuse during facility-based childbirth in a low-income country. *International Journal of Gynecology & Obstetrics*, 148(1), 110–116. <https://doi.org/10.1002/ijgo.13096>
- Okonofua, F., Ntoimo, L., Ogu, R., Galadanci, H., Gana, M., Okike, O., & Abdus-Salam, R. (2018). Assessing the knowledge and skills on emergency obstetric care among health providers: Evidence from a multicenter study in Nigeria. *PLoS ONE*, 13(1), e0192347. <https://doi.org/10.1371/journal.pone.0192347>
- Olaniran, A., Msuya, S. E., & Cholongola, J. O. (2019). The role of traditional birth attendants in maternal health care in Nigeria. *African Journal of Reproductive Health*, 23(1), 26–34. <https://doi.org/10.29063/ajrh2019/v23i1.3>
- Olorunsaiye, C. Z., Degge, H. M., & Abegunde, D. O. (2016). Maternal and child health service utilization in Nigeria: Implications for intervention. *Pan African Medical Journal*, 24, 1–12. <https://doi.org/10.11604/pamj.2016.24.1.9630>
- Osubor, K. M., Fatusi, A. O., & Chiwuzie, J. C. (2006). Maternal health-seeking behavior and associated factors in a rural Nigerian community. *Maternal and Child Health Journal*, 10(2), 159–169. <https://doi.org/10.1007/s10995-005-0037-z>
- Say, L., Chou, D., Gemmill, A., Tunçalp, Ö., Moller, A. B., Daniels, J., & Alkema, L. (2014). Global causes of maternal death: A WHO systematic analysis. *The Lancet Global Health*, 2(6), e323–e333. [https://doi.org/10.1016/S2214-109X\(14\)70227-X](https://doi.org/10.1016/S2214-109X(14)70227-X)
- Tura, G., Afework, M. F., & Yalew, A. W. (2013). The effect of health facility delivery on neonatal mortality: Systematic review and meta-analysis. *BMC Pregnancy and Childbirth*, 13, 18. <https://doi.org/10.1186/1471-2393-13-18>
- United Nations Population Fund. (2022). *State of world population report 2022*. United Nations Population Fund.
- Warren, C. E., Mwangi, A., Owuya, E., Kamunya, R., & Koskei, N. (2017). Safeguarding maternal and newborn health: Improving the quality of postnatal care in Kenya. *International Journal for Quality in Health Care*, 29(2), 183–190. <https://doi.org/10.1093/intqhc/mzx003>
- World Health Organization. (2018). *WHO recommendations: Intrapartum care for a positive childbirth experience*. World Health Organization.
- World Health Organization. (2022). *Trends in maternal mortality 2000 to 2020: Estimates by WHO, UNICEF, UNFPA, World Bank Group and the United Nations Population Division*. World Health Organization.

Yaya, S., Uthman, O. A., Amouzou, A., & Bishwajit, G. (2018). Inequalities in maternal health care utilization in Benin: A population-based cross-sectional study. *BMC Pregnancy and Childbirth*, 18, 194. <https://doi.org/10.1186/s12884-018-1833-x>

# Comparison of Public and Private Healthcare Seekers in a Resource-Limited Country: Utility Indices, Consequences, Associations, and Predictors

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## Abstract

Even with free 24-hour public healthcare (PHC), many choose not to access healthcare. This study explored the use/non-use of PHC, the consequences of non-utilisation, and the factors associated with and predictors of PHC access. The study included 308 adults seeking medical attention using prescriptions or seeking over-the-counter medications at pharmacies for personal use. Through convenience sampling, data were collected face-to-face at selected pharmacies from 10 March to 31 May 2024 using an 18-item questionnaire. Data were analysed using SPSS based on descriptive and inferential methods. Most participants were female; many reported comorbidities, including depression, overweight, diabetes mellitus, and hypertension. The utility index (PHC) was 0.296; the affordability index was 0.328. The absolute non-affordability index was 0.603. The affordability of private healthcare was limited to one-third of participants and was strongly associated with higher income and socioeconomic status. Place of treatment (public or private) was associated with education level, employment status, and monthly income. Consequences that were higher among non-afforders included being less able to engage in vacations/socializing/leisure time because of funds, increased burden on family who may have to use their own funds, interruptions to daily routines or activities of daily living, and reduced hobbies/activities. Many reported resorting to home remedies or alternative treatments. The low utility index of PHC and low affordability reflect systemic imbalances in the health systems of a resource-limited country. Negative consequences were particularly prevalent among non-afforders.

**Keywords:** Healthcare Access, Utility Index, Affordability Index, Non-Afforders, Negative Consequences

## 1. Introduction

Many countries provide free 24-hour public healthcare (PHC) services to improve access to healthcare. Gulliford et al. (2002) emphasised the complex nature of access and conceptualised access as comprising four aspects of evaluation: availability, adequate supply, opportunity to access services, and having access to services. However, Levesque et al. (2013) described access as 'health systems with dimensions of approachability, acceptability, availability/accommodation, affordability and appropriateness'. The World Health Organization (WHO) describes access as 'people's perceptions to their ease in reaching health services or health facilities in terms of location, time, and ease of approach' (World Health Organization, n.d.).

The WHO emphasises access as a quality outcome and reflects the overall state of health received. It is based on 'the timely use of personal health services to achieve the best possible health outcomes' (Institute of Medicine, 1993). Our study defines access narrowly as patients presenting themselves 'to receive the treatment required' (National Academies of Sciences, Engineering, and Medicine, 2018). Although PHC is free in many countries, private healthcare (PrHC) use remains significant: for instance, countries like Pakistan (82.5%) (Khalid et al., 2021) and Nigeria (52%) (Basu et al., 2012) report significant rates of PrHC use. PrHCs in Canada and USA account for 28.8% (Canadian Institute for Health Information, 2024) and 40% (Centers for Medicare and Medicaid Services, n.d.), respectively of the total health budget. PrHC users, especially non-afforders, may face additional challenges and consequences such as financial (Smolderen et al., 2010), social, and disease complications (Gordon et al., 2020; Smolderen et al., 2010).

Similar to the rest of the world, healthcare research in Trinidad and Tobago has focused on PHC users with little emphasis on non-users. PrHC users remain outside the scope of most healthcare analyses, policies, and practical developments (Hoon et al., 2017). Although utilisation is a pre-requisite for initiation of optimisation of healthcare (Oladipo, 2014), understanding and improving successful access has not yet been emphasised. PrHC non-afforders suffer additional unfair infringement, resulting in treatment delays and financial and social problems. Many are forced to make decisions that may harm them (Allegheny County Health Department, n.d.) or their loved ones (Allegheny County Health Department, n.d.). PrHC users end up paying out-of-pocket (Institute of Medicine, 2003), or using their savings (Agha & Lyford, n.d.) and their children's savings (Agha & Lyford, n.d.) to obtain healthcare. Other consequences include unnecessary treatment delays (Allegheny County Health Department, n.d.), disease complications (Dockstader, 2023), need for more medications (Dockstader, 2023) and even death (Dockstader, 2023). The lack of prompt treatment affects employment, leisure, social life, and the overall quality of life (Martin et al., 2005). This study explores the utility of health services and the consequences of non-affordability and identifies key associations and predictors in a resource-limited country.

## 2. Methods

This cross-sectional study included persons aged 18 years and older seeking medication at five selected pharmacies in South Trinidad using at least one prescription originating from PHC or PrHC, or seeking over-the-counter (OTC) self-medication. This methodology is similar to another study on barriers to healthcare conducted by the authors. An 18 item-questionnaire measuring sociodemographic variables (9 items), medical conditions and lifestyle diseases (1 item), type of healthcare received (3 items), and consequences (1 item: disease, treatment, social, or financial) was used. Data were collected over a ten-week period from 10 March to 31 May 2024 via face-to-face interviews. Data analysis comprised both descriptive and inferential statistical methods. The former included frequencies and percentages, graphs, and/or charts for qualitative variables as well as minimum and maximum values, medians, and means with corresponding standard deviations (SD) for providing single number summaries of quantitative variables. Inferential methods included 95% Confidence Intervals (CIs) for means and proportions and hypothesis testing at the 5% significance level, including Analysis of Variance (ANOVA) and Multiple Comparison procedures.

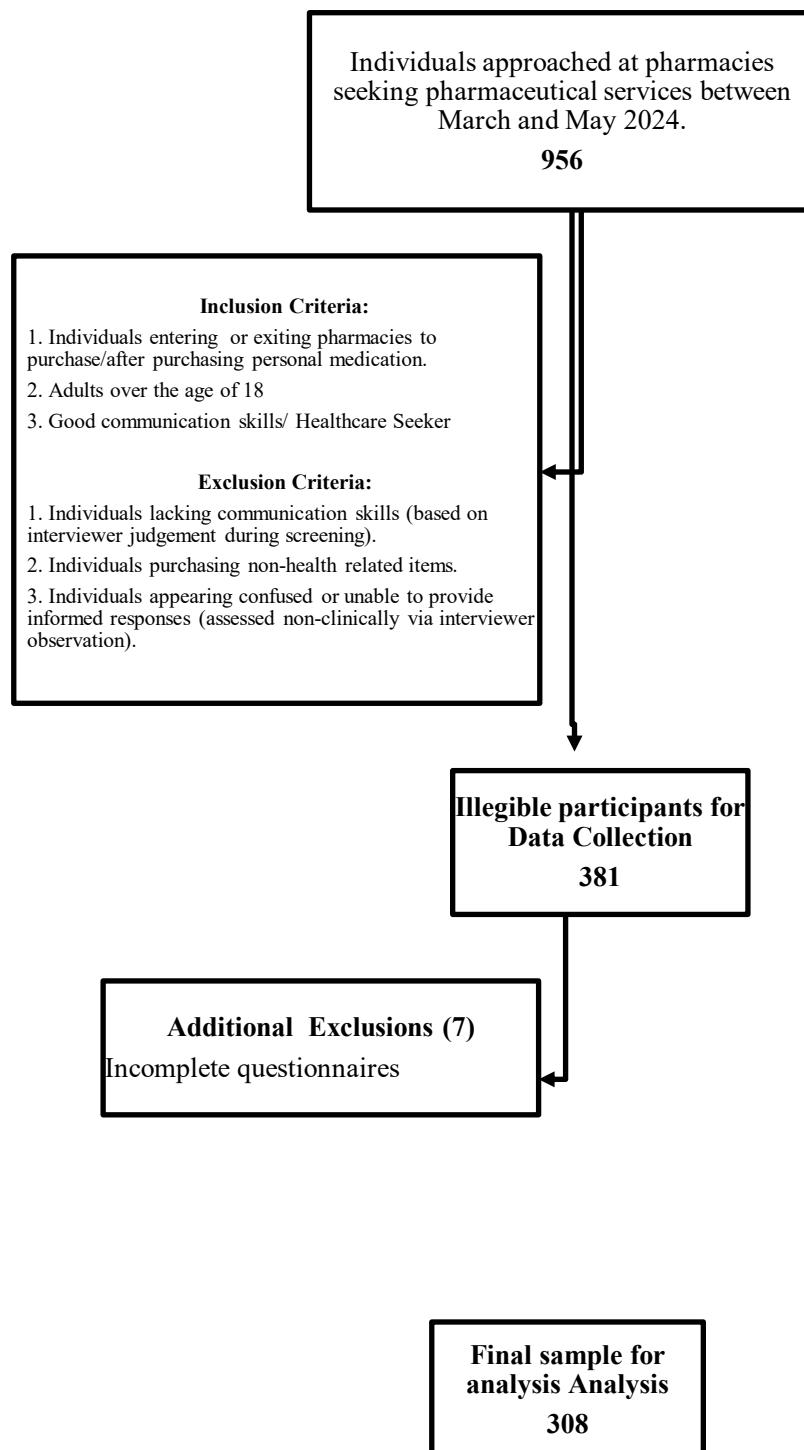


Figure 1: Participant selection process and determination of study sample

### 2.1 Definition: Indices

- 1) Utility Index (PHC): The proportion of participants who exclusively used the public healthcare (PHC) system.
- 2) Non-Utility Index (PHC): The proportion of participants who did not use the public system ( $1 - \text{Utility Index}$ ).
- 3) Affordability Index: The proportion of participants who reported that they can afford private healthcare.
- 4) Relative non-Affordability Index: The proportion of participants who receive (opt for) private healthcare despite reporting 'being unable to afford healthcare and experience challenges in seeking private care'.
- 5) Absolute non-affordability Index: The proportion of participants who either receive public healthcare or receive private healthcare despite reporting being unable to afford it.

### 2.2 Other definitions

Afforders were defined as patients who could fund their private hospital stay without difficulty or assistance. Non-afforders were patients who faced financial difficulties when paying for their healthcare.

### 2.3 Ethics

Ethical approval for the study was obtained from the Ethics Committee of the University of the West Indies on 21 March 2024. All participants provided verbal consent to participate in the study; participants were not rewarded for participation.

## 3. Results

### 3.1 Section I

#### 3.1.1 Descriptive Statistics

Usable data were obtained from 308 participants. Women ( $n = 195$ ; 63.3%), aged 30–50 years ( $n = 136$ ; 44.2%), and Indo-Trinbagonians ( $n = 150$ ; 48.7%) comprised the largest group in the various categories. Table 1. More than half of the participants ( $n = 155$ ; 51.3%) had a tertiary level education, and 205 (66.6%) were employed.

Table 1: Distribution of socio-demographic variables

| Variable          | n   | %    |
|-------------------|-----|------|
| Age group         |     |      |
| < 30              | 75  | 24.4 |
| 30-50             | 136 | 44.2 |
| > 50              | 91  | 30.1 |
| No response       | 6   | 1.9  |
| Gender            |     |      |
| Male              | 113 | 36.7 |
| Female            | 195 | 63.3 |
| Ethnicity         |     |      |
| Afro-Trinbagonian | 69  | 22.4 |
| Indo-Trinbagonian | 150 | 48.7 |
| Mixed             | 83  | 26.9 |
| Other             | 4   | 1.3  |
| No response       | 2   | 0.6  |

|                            |     |      |
|----------------------------|-----|------|
| Highest level of education |     |      |
| No formal education        | 2   | 0.6  |
| Primary                    | 22  | 7.1  |
| Secondary                  | 123 | 39.9 |
| Tertiary                   | 155 | 51.3 |
| No response                | 3   | 1.0  |
| Employment status          |     |      |
| Employed                   | 205 | 66.6 |
| Unemployed                 | 46  | 14.9 |
| Retired                    | 49  | 16.1 |
| Never employed             | 4   | 1.3  |
| No response                | 4   | 1.3  |
| Lives alone                |     |      |
| No                         | 250 | 81.2 |
| Yes                        | 55  | 17.9 |
| No response                | 3   | 1.0  |
| Monthly income (\$TT)      |     |      |
| < 5000                     | 66  | 21.4 |
| ≥ 5000                     | 96  | 31.2 |
| No response                | 146 | 47.4 |

Figure 2 shows that 18.0% (n = 55) of the study participants lived alone; and 16.3% (n = 50) lived with a spouse.

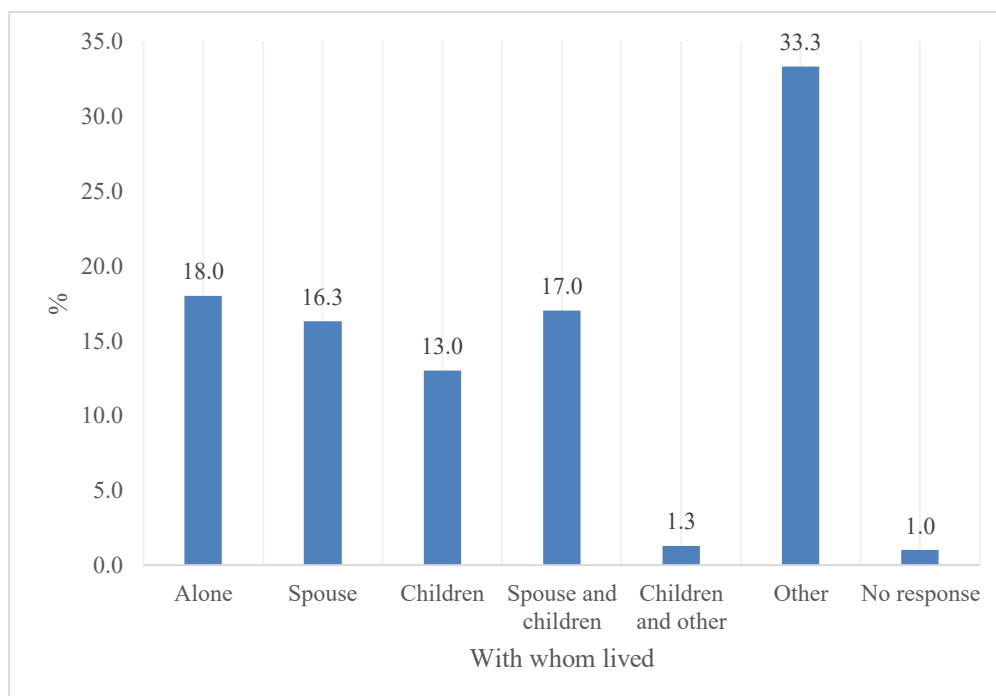


Figure 2: With whom patient lived

Table 2: Distribution of participants by type of care

| Type of Healthcare                                             | n   | %    |
|----------------------------------------------------------------|-----|------|
| Private healthcare (afforders)                                 | 101 | 32.8 |
| Private healthcare (non-afforders)                             | 103 | 33.4 |
| Public healthcare (PHC)                                        | 91  | 29.6 |
| Other (self-medicated without clinic or hospital intervention) | 13  | 4.2  |

Table 3 shows the frequency and percentage distribution of participants' sociodemographic characteristics by type of care, with p-values from association tests. Highest level of education, (Chi-square = 19.975, df = 3,  $p \leq 0.001$ ), employment status, (Chi-square = 715.072, df = 3,  $p = 0.010$ ), and monthly income (Chi-square = 8.055, df = 2,  $p = 0.018$ ) were the only socio-demographic variables that were associated with healthcare category. However, ordinal and nominal logistic regression analyses showed that none of these three variables predicted the type of healthcare category.

Table 3: Type of care by socio-demographic characteristics

| Variable           | n   | Type of hospital |               |           | p-value |
|--------------------|-----|------------------|---------------|-----------|---------|
|                    |     | Private          |               | Public    |         |
|                    |     | Afforders        | Non-afforders |           |         |
| Age group          | 302 |                  |               |           |         |
| < 30               |     | 29 (38.7)        | 20 (26.7)     | 18 (24.0) | 0.063   |
| 30-50              |     | 42 (31.6)        | 41 (30.1)     | 35 (25.7) |         |
| > 50               |     | 26 (29.7)        | 22(24.2)      | 37 (40.7) |         |
| Gender             | 308 |                  |               |           |         |
| Male               |     | 42 (37.2)        | 38 (33.6)     | 33 (29.2) | 0.297   |
| Female             |     | 57 (29.2)        | 80 (41.0)     | 58 (29.7) |         |
| Ethnicity          | 306 |                  |               |           |         |
| Afro-Trinbagonian  |     | 25 (36.2)        | 21 (30.4)     | 22 (31.9) | 0.494   |
| Indo Trinbagonian  |     | 46 (30.7)        | 55 (36.7)     | 48 (32.0) |         |
| Mixed              |     | 26 (31.3)        | 36 (43.4)     | 21 (25.3) |         |
| Other              |     | 1 (25.0)         | 3 (75.0)      | 0 (0.0)   |         |
| Level of education | 305 |                  |               |           |         |
| Primary            |     | 1 (4.5)          | 5 (22.7)      | 16 (72.7) | ≤ 0.001 |
| Secondary          |     | 28 (22.8)        | 47 (38.2)     | 46 (37.4) |         |
| Tertiary           |     | 68 (43.0)        | 63 (39.9)     | 27(17.1)  |         |
| None               |     | 1 (50.0)         | 0 (0.0)       | 1 (50.0)  |         |
| Employment status  | 304 |                  |               |           |         |
| Employed           |     | 76 (37.1)        | 82 (40.0)     | 45 (22.0) | 0.010   |
| Unemployed         |     | 10 (21.7)        | 16 (34.8)     | 20 (43.5) |         |
| Never employed     |     | 0 (0.0)          | 2 (50.0)      | 2 (50.0)  |         |
| Retired            |     | 13 (25.6)        | 15 (30.6)     | 21 (42.9) |         |
| Monthly income     |     |                  |               |           |         |
| < TT\$5,000        | 162 | 13 (19.7)        | 40 (60.6)     | 13 (19.7) | 0.018   |
| TT\$5000 and over  |     | 39 (40.6)        | 45 (46.9)     | 12 (12.5) |         |

### 3.1.2 Presenting Health Conditions

Figure 3 shows that depression (n = 86; 27.9%), overweight (n = 82; 26.6%), diabetes mellitus (n = 61, 19.8%), and hypertension (n = 61; 19.8%) were the four main self-reported health conditions among participants intending to fill a prescription or to purchase OTC medication.

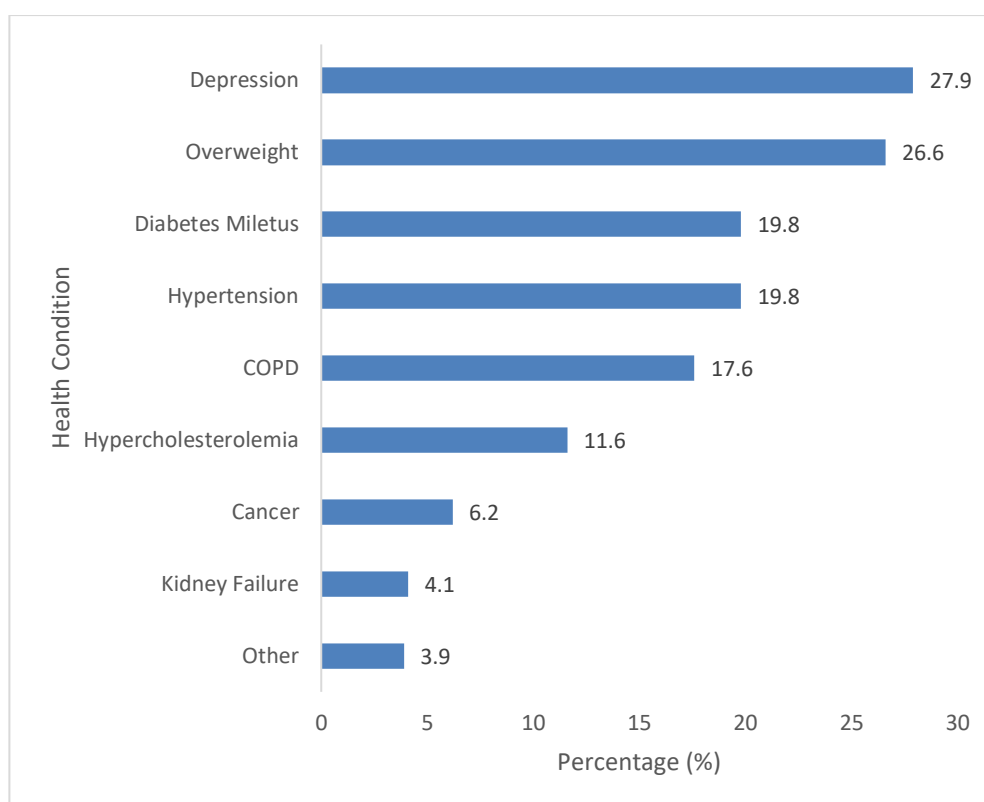


Figure 3: Percentage distribution of health conditions

Among afforders, personal savings ( $n = 90$ , 81.1%) was the main source of funding, followed by medical insurance ( $n = 72$ , 64.9%). Among non-afforders, personal savings ( $n = 85$ , 85.0%) was also the main funding source. The difference between the number of afforders and non afforders using personal savings was not statistically significant.

### 3.1.3 Utility Indices

The Utility Index (PHC) was 0.296, and the Non-Utility Index PHC (= 1-Utility Index) was 0.704, with an affordability index of 0.328.

Table 4: Selected healthcare indices

| Index                                          | Numerator<br>(a) | Denominator (n) | Index<br>(a/n) |
|------------------------------------------------|------------------|-----------------|----------------|
| 1. Utility index (PHC)                         | 91               | 308             | 0.296          |
| 2. Non-utility index (PHC) (= 1-utility index) | 217              | 308             | 0.704          |
| 3. Affordability index                         | 101              | 308             | 0.328          |
| 4. Relative non-affordability index            | 103              | 308             | 0.334          |
| 5. Absolute non-affordability index            | 194              | 308             | 0.630          |

## 3.2 Section II

### 3.2.1 Consequences

The non-afforders of PrHC reported the most common consequences. These included increased burden on family who may need to use personal savings ( $n = 63$ ; 54.3%); reduced hobbies/activities ( $n = 62$ ; 53.4%); reduced

financial ability to engage in vacations/socializing/leisure (n = 61; 52.6%); use of home remedies or alternative treatment (n = 61; 52.6%); and interruptions to daily routine or activities of daily living (n = 61; 52.6%).

Table 5: Consequences faced by patients due to barriers in healthcare

| Variable                 | Consequence                                                                     | PHC       | Afforders | Non-Afforders | All        |
|--------------------------|---------------------------------------------------------------------------------|-----------|-----------|---------------|------------|
|                          |                                                                                 | n, %      | n, %      | n, %          | n, %       |
| Treatment                | 1. Delay/less effective/ treatment                                              | 5 (5.5)   | 11 (11.1) | 48 (41.4)     | 64 (20.8)  |
|                          | 2. Use home remedies or alternative treatment                                   | 17 (18.7) | 34 (34.3) | 61 (52.6)     | 112(35.3)  |
|                          | 3. Did not receive treatment                                                    | 5 (5.5)   | 12 (12.1) | 30 (35.9)     | 47 (15.3)  |
| Disease                  | 1. Longer time to improve health/or get better                                  | 11 (12.1) | 18 (8.2)  | 49 (42.2)     | 78 (25.3)  |
|                          | 2. Worsening of medical condition/development of complications                  | 5 (5.5)   | 13 (13.1) | 36 (31.0)     | 54 (17.5)  |
|                          | 3. Development of physical problems such as mobility/vision problems            | 6(6.6)    | 10(10.1)  | 16 (13.8)     | 32 (10.4)  |
| Other (social/financial) | 1. Less able to engage in vacations/socializing/leisure time because of funds   | 9(9.9)    | 34 (34.3) | 61 (52.6)     | 104 (33.8) |
|                          | 2. Increased burden on the family who may have to use their own funds           | 7 (7.7)   | 31 (31.3) | 63 (54.3)     | 101(32.8)  |
|                          | 3. Interruptions to daily routine or activities of daily living                 | 8 (8.8)   | 34 (34.3) | 61 (52.6)     | 103 (33.4) |
|                          | 4. Cut down on hobbies/activities                                               | 8 (8.8)   | 30 (30.3) | 62 (53.4)     | 100 (33.5) |
|                          | 5. Cut down on use of basic items (food, clothing, etc.) because of diversion   | 5 (5.5)   | 28 (28.3) | 58 (50.0)     | 91 (29.5)  |
|                          | 6. Cut down on schooling/housing because of diversion of finances to healthcare | 5 (5.5)   | 25 (25.3) | 43 (37.1)     | 73 (23.7)  |
|                          | 7. Other (not specified)                                                        | 5(5.5)    | 22 (22.4) | 45 (39.4)     | 72 (23.4)  |

All three pairs of the total consequence scores were correlated pairwise. Analysis of Variance (ANOVA) of total number of consequences showed that type of hospital care was the only variable with significant pairwise differences among mean scores ( $p \leq 0.001$ ). Specifically, afforders' mean number of consequences was lower than that of non-afforders ( $p = 0.003$ ); additionally, non-afforders' mean number of consequences was higher than that of public care patients ( $p \leq 0.001$ ). Table 6.

Table 6: Pairwise correlations

| Consequences | Consequences           |                        |                        |
|--------------|------------------------|------------------------|------------------------|
|              | Disease                | Treatment              | Financial              |
| Disease      | 1                      | 0.668 ( $\leq 0.001$ ) | 0.491 ( $\leq 0.001$ ) |
| Treatment    | 0.668 ( $\leq 0.001$ ) | 1                      | 0.528 ( $\leq 0.001$ ) |
| Financial    | 0.491( $\leq 0.001$ )  | 0.528 ( $\leq 0.001$ ) | 1                      |

## 4. Discussion

### 4.1 Section 1

#### 4.1.1 Demographics and Association with Type of Healthcare

Participants were mostly female ( $n = 195$ , 63.3%) aged 30–50 years ( $n = 136$ , 44.2%). In a similar study conducted in 2015 in rural Nigeria, the respondents were primarily male, and 34.4% were aged 41–50 years (Omonona et al., 2015). The most common co-morbidities were depression ( $n = 86$ ; 27.9%), overweight ( $n = 82$ ; 26.6%), diabetes mellitus ( $n = 61$ , 19.8%), and hypertension ( $n = 61$ ; 19.8%), similar to the findings reported by Gabrani et al. (2020). More than two-thirds (63%) of the respondents reported suffering from at least one chronic illness. In Canada and USA (Blackwell et al., 2009), the prevalence of overweight as a risk factor is 32.7% and 32.5% respectively.

Most participants ( $n = 204$ ; 66.2%) in our study were healthy (Table 2), equally distributed between afforders ( $n = 101$ , 32.8%) and non-afforders ( $n = 103$ , 33.4%). Similarly, Rout et al. (2019) found that in India, the use of PrHCs was nearly three times greater than that of PHC. Conversely, in China (Tang et al., 2016), nearly 78.9 % preferred large public hospitals to private hospitals.

Our findings revealed that education level ( $p < 0.001$ ), employment status ( $p = 0.010$ ), and monthly income ( $p = 0.018$ ) were associated with the type/place of healthcare (PHC or PrHC). Afforders had higher education levels, and they were employed; thus, they were wealthier than their non-afforders or PHC counterparts. This is consistent with the findings reported by Awoke et al. (2017), highlighting the correlation between higher education and private care services, stating that the use of private healthcare providers increased with wealth in Ghana. Similarly, a study (Bourne et al., 2010) assessing trends in PrHC and PHC among Jamaicans highlighted the increased use of PrHC with increasing wealth and showed that using public services is still much cheaper overall; thus, people with lower incomes tended to choose more affordable public options. In contrast to other studies, there was no association with patients' residence, type of support, or source of funding by user type (Awoke et al., 2017; Hossain et al., 2021).

#### 4.1.2 Utility indices

In this study, the utility index (PHC) was 0.296 (or 29.6%), that is, those who sought PHC. This contradicts a study conducted in India in which the reliance on the public sector for outpatient care ranged as low as 8.5% in Punjab to 78.8% in Assam (Rout et al., 2019). This is similar to a study in Brazil (Bastos et al., 2011) whereby the use of PHC was 42.0%. Further, 70.45% of patients resort to non-PHC or PrHC (Non-Utility Index (PHC) is 0.704), which contrasts with another study which reported that 17.8% of people seek PrHC (Awoke et al., 2017). Further, Wambiya et al. (2021) found that 47% used private facilities and a further 20% used complementary medicine. This compares well with a study by Bagchi et al., which revealed that 88% reported that their family members did not use public healthcare (Bagchi et al., 2022).

Affordability index (0.328 or 32.8%) compares well with other high-income countries such as USA (30.7%, 2016) (Emanuel et al., 2017). Affordability may be related to private insurance availability and a relatively high disposable income. In our study, 31.2% ( $n = 96$ ) earned more than \$5000 per month; this population may reflect afforders of PrHC (32.8%,  $n = 101$ ). The absolute non-affordability index is 63% ( $n = 194$ ); this may reflect non-afforders of PrHC or PHC users who may earn less than \$5000/month (21.4%,  $n = 66$ ).

The users of PHC and the non-afforders of PrHCs exhibit continual oscillations, similar to that of a pendulum between the two sectors, contingent on prevailing financial and social circumstances. During periods of financial stability, such individuals may be inclined to access PrHCs in pursuit of higher-quality services or expedited care.

Conversely, economic constraints may necessitate a return to PHC, thereby interrupting the continuity of care. PHC users may also seek PrHCs because of the unavailability of resources offered at public facilities.

## 4.2 Section 2

### 4.2.1 Consequences

Our findings reveal that the major complications caused by the failure to access PHC are patients being 'less able to engage in vacations/socializing/leisure time because of funds' (n = 104, 33.8%), or experiencing 'increased burden on the family who may have to use their own funds' (n = 101, 32.8%), 'interruptions to daily routine or activities of daily living' (n = 103, 33.4%) and having to 'cut down on hobbies/activities' (n = 100, 32.5%'. Kissoon (2016) also reported increased burden on family and emphasised that emotional and financial stress affect family dynamics and overall wellbeing (Kissoon, 2016).

Disease-related consequences included a longer time to improve health/or get better (n = 78, 25.3%) and worsening of medical conditions/development of complications (n = 54, 17.5%). Schwarz et al. (2022) reported that patients with chronic illnesses encountered barriers such as poor care coordination, long waiting times, and financial constraints. These in turn contributed to delayed diagnosis and treatment, leading to treatment delays, disease progression, and adverse social and financial effects. Similarly, another study reported that 'increases in privatisation frequently corresponded with worse health outcomes for patients' (Goodair & Reeves, 2024). The psychological consequences of such health-related outcomes have not been studied.

In our study, many participants resorted to CAM as alternative or complimentary treatment, including home remedies (n = 112, 36.3%). Similarly, in Switzerland, 64.4% of patients used home remedies and 38.5% did so to avoid PHC (Winkler et al., 2022). However, this was not significantly associated with the types of healthcare accessed.

## 5. Conclusion

In our study, only approximately one-third of healthcare seekers were afforders. The majority (about two-thirds) used either PHC or PrHC with difficulty in similar proportions. Non-afforders seeking PrHC experience major problems that affect or limit their participation in social, leisure, or recreational activities, increase their financial burden on family members, and disrupt their daily functioning. The systemic imbalance in the receipt of public healthcare has led to inequity. This is corroborated by another study, which reported that, '...health disparities are not only based on racial, ethnic, and cultural differences within the population. Lifestyle choices, age, sexual orientation, lack of access, and personal, socioeconomic, and environmental characteristics are also to be included' (Riley, 2012). Therefore, the low affordability index with its consequences and inequity necessitates an even better PHC system to ensure the availability of quality healthcare.

## 6. Limitations

The limitations of this study must be acknowledged. First, our study did not include patients seeking dental care. Second, the selected pharmacies may not be representative. Third, because of the small sample size, sub-analysis was not possible. Fourth, a subset of the population, termed 'self-carers', may opt **not** to engage with formal healthcare services. Instead of seeking PHC or PrHC, these individuals rely on self-directed care, including home remedies, OTC medication, traditional medicine, and alternative therapies.

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**Informed Consent Statement/Ethics Approval:** Ethics approval for the study was obtained from the Ethics Committee of the University of the West Indies on March 21st, 2024. All participants gave verbal consent to participate in the study; and participants were given no rewards for participation.

**Data Availability Statement:** Data supporting the findings of this study will be made available from the corresponding author upon reasonable request.

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## References

- Agha, Z., & Lyford, S. New survey finds large number of people skipping necessary medical care because of cost [Internet]. *Chicago: NORC at the University of Chicago*. <https://www.norc.org/research/library/new-survey-finds-large-number-of-people-skipping-necessary-medic.html>
- Allegheny County Health Department. Allegheny County: Always inspiring [Internet]. Allegheny County Health Department. [https://www.alleghenycounty.us/uploadedFiles/Allegheny\\_Home/Health\\_Department/Resources/Data\\_and\\_Reporting/Chronic\\_Disease\\_Epidemiology/HEB-ACCESS.pdf](https://www.alleghenycounty.us/uploadedFiles/Allegheny_Home/Health_Department/Resources/Data_and_Reporting/Chronic_Disease_Epidemiology/HEB-ACCESS.pdf)
- Awoke, M. A., Negin, J., Moller, J., Farell, P., Yawson, A. E., Biritwum, R. B., & Kowal, P. (2017). Predictors of public and private healthcare utilization and associated health system responsiveness among older adults in Ghana. *Global Health Action*, 10(1), Article 1301723. <https://doi.org/10.1080/16549716.2017.1301723>
- Bagchi, T., Das, A., Dawad, S., & Dalal, K. (2022). Non-utilization of public healthcare facilities during sickness: A national study in India. *Journal of Public Health*, 30(4), 943–951. <https://doi.org/10.1007/s10389-020-01363-3>
- Bastos, G. A. N., Duca, G. F. D., Hallal, P. C., & Santos, I. S. (2011). Utilization of medical services in the public health system in the Southern Brazil. *Revista de Saúde Pública*, 45(3), 475–454. <https://doi.org/10.1590/s0034-89102011005000024>
- Basu, S., Andrews, J., Kishore, S., Panjabi, R., & Stuckler, D. (2012). Comparative performance of private and public healthcare systems in low- and middle-income countries: A systematic review. *PLOS Medicine*, 9(6), Article e1001244. <https://doi.org/10.1371/journal.pmed.1001244>
- Blackwell, D. L., Martinez, M. E., Gentleman, J. F., Sanmartin, C., & Berthelot, J.-M. (2009). Socioeconomic status and utilization of health care services in Canada and the United States: Findings from a binational health survey. *Medical Care*, 47(11), 1136–1146. <https://doi.org/10.1097/MLR.0b013e3181adcbe9>
- Bourne, P. A., Eldemire-Shearer, D., Paul, T. J., Lagrenade, J., & Charles, C. A. (2010). Public and private health care utilization differences between socioeconomic strata in Jamaica. *Patient Related Outcome Measures*, 1, 81–91. <https://doi.org/10.2147/PROM.S11868>
- Canadian Institute for Health Information. (2024–)snapshot [Internet]. National health expenditure trends. CIHI. <https://www.cihi.ca/en/national-health-expenditure-trends-2024-snapshot>
- Centers for Medicare and Medicaid Services. NHE fact sheet [Internet]. CMS. <https://www.cms.gov/data-research/statistics-trends-and-reports/national-health-expenditure-data/nhe-fact-sheet>
- Dockstader, W. (2023). The consequences of delaying medical care [Internet]. *Plano HealthC2U*. <https://healthc2u.com/the-consequences-of-delaying-medical-care/>
- Emanuel, E. J., Glickman, A., & Johnson, D. (2017). Measuring the burden of health care costs on US families: The affordability index. *JAMA*, 318(19), 1863–1864. <https://doi.org/10.1001/jama.2017.15686>
- Gabrani, J., Schindler, C., & Wyss, K. (2020). Factors associated with the utilisation of primary care services: A cross-sectional study in public and private facilities in Albania. *BMJ Open*, 10(12), Article e040398. <https://doi.org/10.1136/bmjopen-2020-040398>

- Goodair, B., & Reeves, A. (2024). The effect of health-care privatisation on the quality of care. *The Lancet. Public Health*, 9(3), e199–e206. [https://doi.org/10.1016/S2468-2667\(24\)00003-3](https://doi.org/10.1016/S2468-2667(24)00003-3)
- Gordon, T., Booysen, F., & Mbonigaba, J. (2020). Socio-economic inequalities in the multiple dimensions of access to healthcare: The case of South Africa. *BMC Public Health*, 20(1), Article 289. <https://doi.org/10.1186/s12889-020-8368-7>
- Gulliford, M., Figueroa-Munoz, J., Morgan, M., Hughes, D., Gibson, B., Beech, R., & Hudson, M. (2002). What does “access to health care” mean? *Journal of Health Services Research and Policy*, 7(3), 186–188. <https://doi.org/10.1258/135581902760082517>
- Hoon, E., Pham, C., Beilby, J., & Karnon, J. (2017). Unconnected and out-of-sight: Identifying health care non-users with unmet needs. *BMC Health Services Research*, 17(1), Article 80. <https://doi.org/10.1186/s12913-017-2019-4>
- Hossain, B., James, K. S., Nagargoje, V. P., & Barman, P. (2021). Differentials in private and public healthcare service utilization in later life: Do gender and marital status have any association? *Journal of Women and Aging*, 35(2), 183–193. <https://doi.org/10.1080/08952841.2021.2011562>
- Institute of Medicine (US) Committee on Monitoring Access to Personal Health Care Services. (1993). Access to health care in America [Internet]. National Academies Press. <https://www.ncbi.nlm.nih.gov/books/NBK235890/>
- Institute of Medicine (US) Committee on the Consequences of Uninsurance. (2003). Chapter 3. Hidden costs, values lost: Uninsurance in America [Internet]. *Spending on Health Care for Uninsured Americans: How Much, and Who Pays*. National Academies Press. <https://www.ncbi.nlm.nih.gov/books/NBK221653/>
- Khalid, F., Raza, W., Hotchkiss, D. R., & Soelaeman, R. H. (2021). Health services utilization and out-of-pocket (OOP) expenditures in public and private facilities in Pakistan: An empirical analysis of the 2013–14 OOP health expenditure survey. *BMC Health Services Research*, 21(1), Article 178. <https://doi.org/10.1186/s12913-021-06170-4>
- Kissoon, N. (2016). Healthcare costs to poor families: An agonising burden. *Indian Journal of Pediatrics*, 83(10), 1063–1064. <https://doi.org/10.1007/s12098-016-2170-7>
- Levesque, J.-F., Harris, M. F., & Russell, G. (2013). Patient-centred access to health care: Conceptualising access at the interface of health systems and populations. *International Journal for Equity in Health*, 12, 18. <https://doi.org/10.1186/1475-9276-12-18>
- Martin, L. R., Williams, S. L., Haskard, K. B., & DiMatteo, M. R. (2005). The challenge of patient adherence. *Therapeutics and Clinical Risk Management*, 1(3), 189–199.
- National Academies of Sciences, Engineering, and Medicine. (2018). Chapter 2. Health-care utilization as a proxy in disability determination [Internet]. *Factors That Affect Health-Care Utilization*. National Academies Press. <https://www.ncbi.nlm.nih.gov/books/NBK500097/>
- Oladipo, J. A. (2014). Utilization of health care services in rural and urban areas: A determinant factor in planning and managing health care delivery systems. *African Health Sciences*, 14(2), 322–333. <https://doi.org/10.4314/ahs.v14i2.6>
- Omonona, B. T., Obisesan, A. A., & Aromolaran, O. A. (2015). Health-care access and utilization among rural households in Nigeria. *Journal of Development and Agricultural Economics*, 7(5), 195–203. <https://doi.org/10.5897/JDAE2014.0620>
- Riley, W. J. (2012). Health disparities: Gaps in access, quality and affordability of medical care. *Transactions of the American Clinical and Climatological Association*, 123, 167–172; discussion 172.
- Rout, S. K., Sahu, K. S., & Mahapatra, S. (2019). Utilization of health care services in public and private healthcare in India: Causes and determinants. *International Journal of Healthcare Management*, 14(2), 509–516. <https://doi.org/10.1080/20479700.2019.1665882>
- Schwarz, T., Schmidt, A. E., Bobek, J., & Ladurner, J. (2022). Barriers to accessing health care for people with chronic conditions: A qualitative interview study. *BMC Health Services Research*, 22(1), Article 1037. <https://doi.org/10.1186/s12913-022-08426-z>
- Smolderen, K. G., Spertus, J. A., Nallamothu, B. K., Krumholz, H. M., Tang, F., Ross, J. S., Ting, H. H., Alexander, K. P., Rathore, S. S., & Chan, P. S. (2010). Health care insurance, financial concerns in accessing care, and delays to hospital presentation in acute myocardial infarction. *JAMA*, 303(14), 1392–1400. <https://doi.org/10.1001/jama.2010.409>
- Tang, C., Xu, J., & Zhang, M. (2016). The choice and preference for public–private health care among urban residents in China: Evidence from a discrete choice experiment. *BMC Health Services Research*, 16(1), Article 580. <https://doi.org/10.1186/s12913-016-1829-0>
- Wambiya, E. O. A., Otieno, P. O., Mutua, M. K., Donfouet, H. P. P., & Mohamed, S. F. (2021). Patterns and predictors of private and public health care utilization among residents of an informal settlement in Nairobi, Kenya: A cross-sectional study. *BMC Public Health*, 21(1), Article 850. <https://doi.org/10.1186/s12889-021-10836-3>

- Winkler, N. E., Sebo, P., Haller, D. M., & Maisonneuve, H. (2022). Primary care patients' perspectives on the use of non-pharmacological home remedies in Geneva: A cross-sectional study. *BMC Complementary Medicine and Therapies*, 22(1), Article 126. <https://doi.org/10.1186/s12906-022-03564-7>
- World Health Organization. Health systems strengthening [Internet]. World Health Organization. <https://www.who.int/docs/default-source/documents/health-systems-strengthening-glossary.pdf>

# From Next-Generation Sequencing to Clinical Decisions in Lung Cancer: Five-Patient Case Series

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## Abstract

Precision oncology increasingly relies on next-generation sequencing (NGS) to support treatment decisions, yet clinically meaningful findings do not always translate into timely care. This retrospective descriptive molecular case series reviewed five de-identified lung cancer NGS reports generated between July 2024 and February 2026 together with available clinicopathological records. Formalin-fixed paraffin-embedded tumour tissue was analysed using the OncoPrint Comprehensive Assay on the Ion GeneStudio™ S5 Plus System, with bioinformatic processing in Ion Reporter™ Software. Each case was evaluated for clinicopathological concordance, need for orthogonal verification or complementary biomarker testing, clinical actionability, treatment-access implications, and the next organisational step. The five profiles included EML4::ALK and TPM3::ROS1 fusions and complex profiles involving BRCA2/PIK3CA, ATR/POLE/MSH2/SETD2, and NF1/MSH2/TSC2. The ALK-rearranged case showed the most pronounced morphology–molecular discordance: earlier records included squamous-cell classification, EGFR-negative and ALK-negative results, and PD-L1 expression of 0%, whereas later surgical pathology documented poorly differentiated adenocarcinoma and comprehensive NGS detected EML4::ALK. After reassessment and confirmation, ALK-inhibitor therapy was introduced. Recurrent barriers included pathology reassessment, verification of unexpected findings, distinction between biological significance and validated lung-cancer actionability, molecular tumour board review, and early evaluation of treatment access. These findings support treating NGS as the beginning of a clinical implementation pathway rather than as a stand-alone therapeutic recommendation. A structured pathway integrating quality review, clinicopathological interpretation, parallel confirmation and access assessment, molecular tumour board review, defined responsibilities, target timelines, and outcome tracking may improve regional precision-oncology practice but requires prospective validation.

**Keywords:** Next-Generation Sequencing, Lung Cancer, Precision Oncology, Molecular Tumour Board, Targeted Therapy, Clinical Implementation

## 1. Introduction

Precision oncology increasingly complements morphology-based tumour classification with genomic information. In advanced solid tumours, next-generation sequencing (NGS) can identify alterations with established, investigational, or tumour-agnostic clinical relevance. However, the clinical value of NGS depends not simply on the number of detected variants, but on whether molecular findings can be interpreted correctly, verified when necessary, and translated into feasible clinical decisions (Mateo et al., 2018; Mosele et al., 2024). This issue is particularly important in regional and resource-variable oncology settings, where diagnostic confirmation, multidisciplinary review, regulatory requirements, reimbursement, procurement, and referral pathways may substantially affect the implementation of molecularly guided treatment.

Pathogenicity, biological relevance, and clinical actionability are distinct concepts. Automated molecular reports may simultaneously list therapies approved for the same tumour type, tumour-agnostic indications, off-label options, and investigational strategies. Consequently, each biomarker–drug association must be evaluated according to its level of evidence and interpreted in the context of tumour histology, disease stage, previous biomarker testing, treatment history, and current standards of care (Chakravarty et al., 2017; Mateo et al., 2018). Previous real-world precision-oncology studies have demonstrated that potentially actionable molecular findings are substantially more frequent than successfully implemented treatment recommendations, indicating that clinical implementation represents a distinct step in the precision-oncology pathway (Volders et al., 2025; Westphalen et al., 2025).

A particularly vulnerable “last-mile” gap may therefore arise between release of an NGS report and implementation of a clinical decision. Potential barriers include morphology–molecular discordance, the need for orthogonal confirmation or complementary biomarker testing, delayed communication between pathology and oncology services, molecular tumour board (MTB) review, regulatory and reimbursement constraints, drug procurement, referral logistics, and deterioration in the patient’s clinical condition. Although these individual barriers have been recognised previously, their interaction within routine regional oncology practice remains clinically relevant.

One ROS1-positive patient included in the present series was previously reported as an individual clinical case focusing on personalised treatment of ROS1-positive non-small cell lung cancer with brain metastases (Abdrashev et al., 2026). In the present study, that case is not used to provide additional treatment-efficacy evidence; instead, it is re-examined as one of five implementation scenarios to analyse the pathway from molecular detection to a documented clinical decision. Thus, the present report differs from the earlier case report by focusing on recurrent implementation barriers across multiple molecular profiles rather than on the clinical course of a single patient.

Given the retrospective descriptive design, no formal inferential hypothesis was prespecified. The primary objective was to identify recurrent failure points between NGS reporting and documented clinical decision-making across five lung cancer molecular profiles. The secondary objective was to use these observations to develop a practical implementation pathway with measurable quality indicators for regional and resource-variable oncology services. Conceptually, the study was based on the premise that molecular detectability, clinical actionability, and successful implementation represent related but distinct stages of precision oncology.

Accordingly, a retrospective descriptive molecular case-series design was selected because the aim was not to compare treatment efficacy or test causal associations, but to examine heterogeneous real-world implementation scenarios in detail. The theoretical implication of this approach is that the clinical utility of genomic testing should be considered as a multistep implementation process rather than as an intrinsic property of an individual molecular finding. Practically, identifying recurrent barriers may support more structured pathology review, timely verification, MTB discussion, treatment-access assessment, and prospective monitoring of NGS-guided decision-making.

## 2. Methods

### 2.1. Study design and data sources

We conducted a retrospective, descriptive molecular case series of five patients with a clinical diagnosis of lung cancer whose de-identified NGS reports were generated between July 2024 and February 2026. Available pathology reports, selected treatment records, prior biomarker results, and longitudinal clinical notes were reviewed together with the molecular reports. The source records indicated that four cases were managed as adenocarcinoma, while one case had an earlier squamous-cell classification that was subsequently reassessed in the context of later adenocarcinoma pathology and an ALK fusion. The series was designed to analyse implementation barriers and not to estimate treatment efficacy.

One ROS1-positive patient in this series was previously described in a separate case report focused on personalised treatment of ROS1-positive non-small cell lung cancer with brain metastases (Abdrashev et al., 2026). In the present study, that observation is included only for the distinct purpose of analysing the clinical implementation pathway. Previously published treatment-response outcomes were not re-analysed as a cohort outcome.

### 2.2. NGS workflow and molecular interpretation

Tumour profiling was performed on formalin-fixed paraffin-embedded tissue using the OncoPrint Comprehensive Assay reagent set and the Ion GeneStudio™ S5 Plus System (Thermo Fisher Scientific, USA). Bioinformatic processing, variant review, and report generation were performed using Ion Reporter™ Software. The de-identified reports did not contain a uniform set of sample-specific sequencing depth, tumour-cellularity, or orthogonal-validation metrics for all five cases; therefore, pooled analytical performance statistics were not calculated.

Each observation was assessed in five domains: (1) analytical context of the principal molecular alteration; (2) concordance with histology and clinical context; (3) level of clinical actionability; (4) need for orthogonal confirmation, complementary biomarker testing, or germline evaluation; and (5) the organisational step required to reach a documented clinical decision. Automated treatment suggestions contained in software-generated reports were not considered equivalent to a clinical prescription. Interpretation was guided by the principles of the ESMO Scale for Clinical Actionability of molecular Targets (ESCAT) and consensus standards for somatic variant interpretation (Li et al., 2017; Mateo et al., 2018).

### 2.3. Clinical data and outcome handling

Clinical data were not equally complete for all five patients. Accordingly, age, sex, stage, performance status, treatment timing, and outcome variables were not summarised as pooled cohort statistics. Where longitudinal data were available, they were used only to clarify the implementation scenario. No statistical comparisons were performed.

For the ALK-rearranged observation, the expanded longitudinal record documented a right lower-lobe lung tumour treated surgically in July 2022. The final clinical summary described poorly differentiated adenocarcinoma, grade 3, with a signet-ring cell component, stage IIIA (pT1bN2M0) and an R1 margin. The patient underwent right lower lobectomy with mediastinal lymph-node dissection, followed by eight cycles of systemic chemotherapy, thoracic radiotherapy to a total dose of 54 Gy, and six additional cycles of chemotherapy. Later records documented osseous and intracranial progression, palliative brain radiotherapy to 30 Gy in March 2026, and further systemic treatment during April–July 2026. Performance status in the available record was ECOG 1 and Karnofsky 80%. These data were used to describe the clinical route rather than to estimate effectiveness of any regimen.

### 3. Results

The five observations represented distinct implementation problems rather than a uniform series of treatment outcomes. The key clinicopathological context, molecular findings, and required actions are summarised in Table 1.

#### 3.1. Case 1: morphology–molecular discordance and delayed verification

A 56-year-old patient (sex and smoking status not documented) had discordant historical morphology labels. The treatment pathway initially included a squamous-cell classification and standard first-line chemotherapy, whereas later surgical pathology documented poorly differentiated adenocarcinoma. Molecular testing in August 2022 reported no EGFR mutation, an ALK-negative result, and PD-L1 expression of 0% (CPS 0). After subsequent disease progression, comprehensive NGS identified an EML4::ALK fusion. Because the result was unexpected in the context of the earlier record, pathology and molecular findings required re-review and confirmation. Approximately three months elapsed between NGS detection and repeat confirmation; this interval represents the verification phase rather than the complete time to treatment initiation. Following reassessment and confirmation, an ALK inhibitor was introduced.

The earlier ALK-negative result and later ALK-positive NGS result should not be labelled an analytical false-negative on the basis of the available documents. The earlier assay methodology, specimen comparability, tumour content, and temporal relationship to the later NGS specimen were not uniformly documented. The clinically relevant point is therefore the need for rapid reconciliation of discordant pathology and biomarker results.

#### 3.2. Case 2: rare ROS1 fusion and access-sensitive decision-making

A 68-year-old woman with no history of smoking presented with non-small cell lung cancer and multiple brain metastases.

A TPM3::ROS1 fusion was detected by comprehensive NGS after initial testing for common driver alterations had yielded negative results. This observation has been reported previously as a single clinical case (Abdrashev et al., 2026). In the present analysis, it demonstrates an implementation problem: a rare but potentially actionable fusion requires prompt confirmation of tumour context, consideration of central nervous system disease, and simultaneous assessment of access to ROS1-directed therapy. The molecular finding alone does not complete the treatment pathway.

#### 3.3. Case 3: BRCA2 and PIK3CA alterations without a standard lung-cancer indication

A 66-year-old woman (smoking status not documented) had right upper-lobe lung cancer, G2, pT2bN1M0, stage IIB, and underwent surgical resection with lymph-node dissection in December 2025, followed by two cycles of systemic chemotherapy. Her clinical history also included basal cell carcinoma of the facial skin. NGS identified BRCA2 p.E621Rfs\*6 at a variant allele fraction (VAF) of 4.76% together with PIK3CA p.E545K at a VAF of 49.12%. The automated report listed therapies largely supported in other tumour types. Before any treatment implication could be considered, the result required review of sample quality and tumour content, assessment of personal and family cancer history, and germline testing when clinically indicated. A low-VAF BRCA2 finding in tumour tissue cannot by itself establish a hereditary cancer diagnosis, and a biologically meaningful PIK3CA alteration does not automatically create a validated treatment indication in lung cancer (Kuzbari et al., 2023; Zhunussova et al., 2026).

#### 3.4. Case 4: DNA-repair-related variants requiring phenotype-level confirmation

A 47-year-old woman (smoking status not documented) had left lung cancer, T1cN2M0, stage IIIA, and had received five cycles of systemic chemotherapy. Her clinical history also included a second primary squamous-cell carcinoma of the middle third of the oesophagus, stage IIIC (T4aN2Mx), for which systemic chemotherapy had also been administered. The molecular profile included variants in ATR, POLE, MSH2, SETD2, and other genes. An isolated POLE or MSH2 variant does not independently establish mismatch-repair deficiency (dMMR), microsatellite instability-high (MSI-H), or tumour mutational burden-high (TMB-H) status. The appropriate clinical route is to verify the relevant biomarker phenotype using validated assays and to interpret the genomic finding together with pathology and the complete molecular context (Bartley et al., 2022).

### *3.5. Case 5: complex profile and possible germline implications*

A 77-year-old woman (smoking status not documented) had stage IV left lung cancer (T3NxM1) with brain metastases. She had received eight cycles of systemic chemotherapy combined with targeted therapy, followed by documented disease progression with continued tumour growth. NGS revealed NF1 p.Q239\* at a variant allele fraction (VAF) of 12% together with multiple variants, including MSH2 and TSC2 alterations with high VAFs. The report did not provide a single standard lung-cancer treatment assignment. Review therefore needed to focus on tumour cellularity and analytical quality, possible loss of heterozygosity, and whether the molecular pattern warranted germline evaluation based on clinical and family history (Kuzbari et al., 2023).

### *3.6. Proposed implementation pathway and quality indicators*

Across the five profiles, the recurrent failure points were: (1) morphology–molecular discordance; (2) delayed or sequential rather than parallel confirmation; (3) over-interpretation of automatically listed drugs; (4) incomplete integration of germline implications; (5) delayed MTB review; and (6) treatment-access assessment beginning only after interpretation was complete. These findings informed the proposed pathway shown in Figure 1.

Day 0 is defined as the date on which the NGS report is registered in the clinical pathway. Within three working days, a named coordinator should reconcile the molecular result with pathology, stage, prior biomarker testing, and current treatment. Potentially actionable or discordant findings should be reviewed by an MTB within seven working days. When orthogonal verification is indicated, it should proceed in parallel with evaluation of regulatory status, reimbursement, procurement, referral options, and clinical-trial access. The final decision note should document the evidence level, recommended next step, responsible clinician, and target date. Proposed audit indicators are summarised in Table 2.

## **4. Discussion**

This five-patient series shows that the principal challenge in precision oncology is not necessarily detection of a molecular alteration but completion of the clinical implementation process. Three broad scenarios emerged. The first is a validated driver alteration in the relevant tumour type, exemplified by EML4::ALK and TPM3::ROS1. The second is a biologically meaningful alteration for which treatment evidence is stronger in another tumour type, as in the BRCA2/PIK3CA profile. The third is a complex genomic profile that requires complementary phenotypic testing or possible germline evaluation before a clinical decision can be justified.

The ALK-rearranged case demonstrates why unexpected results should trigger reconciliation rather than immediate acceptance or rejection. The source record contained a historical squamous-cell label, later adenocarcinoma pathology, an earlier ALK-negative result, and a later EML4::ALK fusion by broad NGS. These observations could reflect differences in specimen, tumour heterogeneity, assay sensitivity, temporal evolution, or documentation. The available data cannot distinguish among these possibilities. The correct implementation response is to review pathology and specimen adequacy, verify the molecular result by an appropriate validated method when necessary, and discuss the case in an MTB (Lindeman et al., 2018).

The three-month detection-to-confirmation interval in this case is operationally important but should not be misrepresented as a complete “NGS-to-treatment” interval. The exact date of treatment initiation relative to each

intermediate decision was not available in a uniform form. The practical quality-improvement lesson is that pathology review, confirmation, and treatment-access assessment should occur in parallel wherever possible, because sequential processing adds delay without necessarily adding analytical value.

A second recurrent risk is over-interpretation of automated treatment suggestions. Commercial reporting systems can list drugs supported by evidence from other tumour types, tumour-agnostic approvals, early clinical trials, or biological rationale. These links are useful for hypothesis generation but must be ranked by disease-specific evidence before they are translated into treatment. ESCAT and knowledge bases such as OncoKB provide structured approaches for this distinction (Chakravarty et al., 2017; Mateo et al., 2018). Experimental molecular studies in other tumour models further illustrate this distinction. For example, miR-484-mediated inhibition of oncogenic FOXM1 signalling was shown to increase temozolomide sensitivity in both IDH-wild-type and IDH-mutant glioblastoma cells (Nurdinov et al., 2026). Such mechanistic evidence can support biological plausibility and treatment-response hypotheses, but it should not be interpreted as a disease-specific therapeutic indication without appropriate clinical validation.

A third issue is the boundary between somatic profiling and hereditary cancer assessment. Low- or high-*VAR* alterations in *BRCA2*, *MSH2*, and other cancer-predisposition genes may raise a germline question, but tumour-only testing cannot establish germline status. Clinical and family history, tumour purity, loss of heterozygosity, and testing of a non-tumour sample may be required (Kuzbari et al., 2023). Similarly, individual *POLE* or *MSH2* variants should not be substituted for validated phenotype-level evidence of dMMR, MSI-H, or TMB-H when immunotherapy decisions depend on those biomarkers (Bartley et al., 2022). Finally, the pathway must incorporate drug access as a clinical variable. Real-world precision-oncology programmes demonstrate a persistent gap between theoretically actionable alterations and implemented treatment [4, 13]. In regional services, regulatory status, reimbursement, procurement, referral, and trial availability can determine whether an otherwise appropriate molecular recommendation is actionable in practice. A named coordinator and a documented control date are therefore not administrative extras; they are components of the precision-oncology intervention itself (Tsimberidou et al., 2023; Westphalen et al., 2025).

#### *4.1. Study Limitations*

This study has several limitations. First, it is a small retrospective descriptive series of only five patients and cannot estimate prevalence, diagnostic yield, treatment benefit, or survival. Second, the completeness of clinical data differed between cases; age, sex, stage, treatment chronology, tumour cellularity, sequencing depth, confirmation method, and clinical outcomes were not uniformly available. Third, the earlier *ALK*-negative test and the later *EML4::ALK* NGS result were generated at different points in the disease course, and the available records do not permit a controlled analytical comparison of the two assays or specimens. Fourth, one *ROS1*-positive case was previously published as a single case report; it is included here only as a pathway-level implementation scenario, and its previously reported treatment outcome is not presented as new efficacy evidence. Fifth, the proposed 3- and 7-working-day targets and audit metrics are pragmatic quality-improvement benchmarks rather than validated standards. They require prospective evaluation in a larger cohort with standardised capture of biopsy date, pathology sign-out, NGS report date, MTB decision, treatment initiation, reasons for non-implementation, response, and toxicity.

### **5. Conclusion**

In this descriptive molecular case series, NGS created clinically relevant opportunities but did not itself complete diagnosis or guarantee treatment implementation. Translation of a molecular finding into a clinical decision required clinicopathological reconciliation, verification of unexpected results, evidence ranking, MTB review, attention to possible germline implications, and early assessment of treatment access. The *ALK*-rearranged case particularly illustrates the risk of delay when discordant pathology and molecular data are resolved sequentially. A structured pathway with a named coordinator, parallel verification and access assessment, target timelines, and outcome tracking may support quality improvement in regional oncology services. Prospective validation in a larger cohort is required before the proposed timelines or indicators can be considered performance standards.

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**Informed Consent Statement.** Written informed consent for publication of anonymised clinical and molecular data was obtained from all five patients included in the study.

**Data Availability Statement.** The data supporting the findings of this study are available from the corresponding author upon reasonable request, subject to ethical and patient-confidentiality restrictions. Patient-level clinical and molecular data are not publicly available because of privacy and ethical considerations.

**Conflicts of Interest.** The authors declare no conflict of interest. The funding sponsor had no role in the design of the study; in the collection, analysis, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

**Declaration Regarding the Use of AI and AI-Assisted Technologies.** During the preparation of this manuscript, the authors used OpenAI’s ChatGPT solely as a language-support tool to improve the clarity, grammar, structure, and fluency of the text. The tool was not used to generate or modify primary clinical or molecular data, perform statistical analyses, interpret molecular findings, or determine clinical outcomes. All AI-assisted content was critically reviewed and verified by the authors, who take full responsibility for the scientific content, accuracy, and integrity of the final manuscript.

## References

- Abdrashev, A. S., Musirali, D. M., Yeltay, Y. Y., Akter, A. M., Saruarov, Y. G., & Nurdinov, N. S. (2026). Personalized treatment of ROS1-positive non-small cell lung cancer with brain metastases: A case report. *Eurasian Journal of Oncology and Radiology*, (1), 50–57. <https://doi.org/10.52532/2521-6414-2026-1-663>
- Bartley, A. N., Mills, A. M., Konnick, E., Overman, M., Ventura, C. B., Souter, L., Colasacco, C., Stadler, Z. K., Kerr, S., Howitt, B. E., Hampel, H., Adams, S. F., Johnson, W., Magi-Galluzzi, C., Sepulveda, A. R., & Broaddus, R. R. (2022). Mismatch repair and microsatellite instability testing for immune checkpoint inhibitor therapy: Guideline from the College of American Pathologists in collaboration with the Association for Molecular Pathology and Fight Colorectal Cancer. *Archives of Pathology & Laboratory Medicine*, 146(10), 1194–1210. <https://doi.org/10.5858/arpa.2021-0632-CP>
- Chakravarty, D., Gao, J., Phillips, S. M., Kundra, R., Zhang, H., Wang, J., Rudolph, J. E., Yaeger, R., Soumerai, T., Nissan, M. H., Chang, M. T., Chandarlapaty, S., Traina, T. A., Paik, P. K., Ho, A. L., Hantash, F. M., Grupe, A., Baxi, S. S., Callahan, M. K., Schultz, N. (2017). OncoKB: A precision oncology knowledge base. *JCO Precision Oncology*, 2017(1), 1–16. <https://doi.org/10.1200/PO.17.00011>

- Kato, S., Kim, K. H., Lim, H. J., Boichard, A., Nikanjam, M., Weihe, E., Kuo, D. J., Eskander, R. N., Goodman, A., Galanina, N., Fanta, P. T., Schwab, R. B., Shatsky, R., Plaxe, S. C., Sharabi, A., Stites, E., Adashek, J. J., Okamura, R., Lee, S., Kurzrock, R. (2020). Real-world data from a molecular tumor board demonstrates improved outcomes with a precision N-of-One strategy. *Nature Communications*, 11(1), 4965. <https://doi.org/10.1038/s41467-020-18613-3>
- Kuzbari, Z., Bandlamudi, C., Loveday, C., Garrett, A., Mehine, M., George, A., Hanson, H., Snape, K., Kulkarni, A., Allen, S., Jezdic, S., Ferrandino, R., Westphalen, C. B., Castro, E., Rodon, J., Mateo, J., Burghel, G. J., Berger, M. F., Mandelker, D., & Turnbull, C. (2023). Germline-focused analysis of tumour-detected variants in 49,264 cancer patients: ESMO Precision Medicine Working Group recommendations. *Annals of Oncology*, 34(3), 215–227. <https://doi.org/10.1016/j.annonc.2022.12.003>
- Li, M. M., Datto, M., Duncavage, E. J., Kulkarni, S., Lindeman, N. I., Roy, S., Tsimberidou, A. M., Vnencak-Jones, C. L., Wolff, D. J., Younes, A., & Nikiforova, M. N. (2017). Standards and guidelines for the interpretation and reporting of sequence variants in cancer: A joint consensus recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists. *The Journal of Molecular Diagnostics*, 19(1), 4–23. <https://doi.org/10.1016/j.jmoldx.2016.10.002>
- Lindeman, N. I., Cagle, P. T., Aisner, D. L., Arcila, M. E., Beasley, M. B., Bernicker, E. H., Colasacco, C., Dacic, S., Hirsch, F. R., Kerr, K., Kwiatkowski, D. J., Ladanyi, M., Nowak, J. A., Sholl, L., Temple-Smolkin, R., Solomon, B., Souter, L. H., Thunnissen, E., Tsao, M. S., Yatabe, Y. (2018). Updated molecular testing guideline for the selection of lung cancer patients for treatment with targeted tyrosine kinase inhibitors: Guideline from the College of American Pathologists, the International Association for the Study of Lung Cancer, and the Association for Molecular Pathology. *Journal of Thoracic Oncology*, 13(3), 323–358. <https://doi.org/10.1016/j.jtho.2017.12.001>
- Mateo, J., Chakravarty, D., Dienstmann, R., Jezdic, S., Gonzalez-Perez, A., Lopez-Bigas, N., Ng, C. K. Y., Bedard, P. L., Tortora, G., Douillard, J.-Y., Van Allen, E. M., Schultz, N., Swanton, C., André, F., & Puzstai, L. (2018). A framework to rank genomic alterations as targets for cancer precision medicine: The ESMO Scale for Clinical Actionability of molecular Targets (ESCAT). *Annals of Oncology*, 29(9), 1895–1902. <https://doi.org/10.1093/annonc/mdy263>
- Mosele, M. F., Westphalen, C. B., Stenzinger, A., Barlesi, F., Bayle, A., Bièche, I., Bonastre, J., Castro, E., Dienstmann, R., Krämer, A., Czarnecka, A. M., Meric-Bernstam, F., Michiels, S., Miller, R., Normanno, N., Reis-Filho, J., Remon, J., Robson, M., Rouleau, E., André, F. (2024). Recommendations for the use of next-generation sequencing (NGS) for patients with advanced cancer in 2024: A report from the ESMO Precision Medicine Working Group. *Annals of Oncology*, 35(7), 588–606. <https://doi.org/10.1016/j.annonc.2024.04.005>
- Nurudinov, N., Güler, A., Albayrak, S., Kursunluoglu, G., Ulutabanca, H., Cinar, V., Memis, M., Erdem, S., Aydın, O., Sener, E. F., Taheri, S., Ozpolat, B., & Hamurcu, Z. (2026). miR-484 sensitizes IDH-wild and IDH-mutant glioblastoma cells to temozolomide by inhibiting oncogenic FOXM1 signaling. *Cancer Cell International*, 26, 200. <https://doi.org/10.1186/s12935-026-04238-x>
- Tsimberidou, A. M., Kahle, M., Vo, H. H., Baysal, M. A., Johnson, A., & Meric-Bernstam, F. (2023). Molecular tumour boards-Current and future considerations for precision oncology. *Nature Reviews Clinical Oncology*, 20(12), 843–863. <https://doi.org/10.1038/s41571-023-00824-4>
- Volders, P.-J., Aftimos, P., Dedeurwaerdere, F., Martens, G., Canon, J.-L., Beniuga, G., Froyen, G., Van Huysse, J., De Pauw, R., Prenen, H., Lambin, S., Decoster, L., Vaeyens, F., Rottey, S., Van Dam, P.-J., Decoster, L., Rutten, A., Schreuer, M., Loontjens, S., Maes, B. (2025). A nationwide comprehensive genomic profiling and molecular tumor board platform for patients with advanced cancer. *npj Precision Oncology*, 9(1), 66. <https://doi.org/10.1038/s41698-025-00858-0>
- Westphalen, C. B., Boscolo Bielo, L., Aftimos, P., Beltran, H., Benary, M., Chakravarty, D., Collienne, M., Dienstmann, R., El Helali, A., Gainor, J., Horak, P., Le Tourneau, C., Marchiò, C., Massard, C., Meric-Bernstam, F., Pauli, C., Pruneri, G., Roitberg, F., Russnes, H. E. G., Curigliano, G. (2025). ESMO Precision Oncology Working Group recommendations on the structure and quality indicators for molecular tumour boards in clinical practice. *Annals of Oncology*, 36(6), 614–625. <https://doi.org/10.1016/j.annonc.2025.02.009>
- Zhunussova, G., Omarbayeva, N., Zhunussova, A., Abdullayeva, D., Skvortsova, L., Nurudinov, N., & Oshibayeva, A. (2026). Germline PALB2 genetic variant associated with rapid metastatic progression and poor survival in two Kazakh women with breast cancer: A case study. *Genes*, 17(8), 913. <https://doi.org/10.3390/genes17080913>

## Appendix A

Table 1. Clinical and molecular characteristics of the five implementation scenarios

| Case | Clinicopathological context                                                                                                                                                                  | Key NGS finding                                                | Clinical interpretation                                                                | Documented / required action                                                                                      |
|------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------|----------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------|
| 1    | Historical squamous-cell label; later surgical pathology: poorly differentiated adenocarcinoma G3, stage IIIA, R1; prior EGFR negative, ALK negative, PD-L1 0%; later metastatic progression | EML4::ALK fusion                                               | Validated oncogenic driver, but discordant with earlier morphology / biomarker history | Pathology and specimen review; confirm unexpected finding; MTB review; ALK inhibitor subsequently introduced      |
| 2    | NSCLC with brain metastases; previously published as a single case [8]                                                                                                                       | TPM3::ROS1 fusion                                              | Rare, potentially actionable driver requiring CNS-aware interpretation                 | Contextual confirmation; rapid ROS1-directed treatment-access review; use here limited to pathway analysis        |
| 3    | Adenocarcinoma; incomplete longitudinal clinical data                                                                                                                                        | BRCA2 p.E621Rfs*6 (VAF 4.76%); PIK3CA p.E545K (VAF 49.12%)     | Biological relevance does not equal a validated lung-cancer indication                 | Review quality / tumour content; family history; germline testing if indicated; evidence ranking                  |
| 4    | Adenocarcinoma; incomplete longitudinal clinical data                                                                                                                                        | ATR, POLE, MSH2, SETD2 and other variants                      | Single gene variants do not establish dMMR / MSI-H / TMB-H phenotype                   | Validated MSI / MMR / TMB assessment as appropriate; integrated interpretation                                    |
| 5    | Adenocarcinoma; incomplete longitudinal clinical data                                                                                                                                        | NF1 p.Q239* (VAF 12%); MSH2 / TSC2 and other high-VAF variants | Complex profile without a single standard treatment assignment                         | Check tumour cellularity / sequencing quality; assess LOH; consider germline evaluation when clinically indicated |

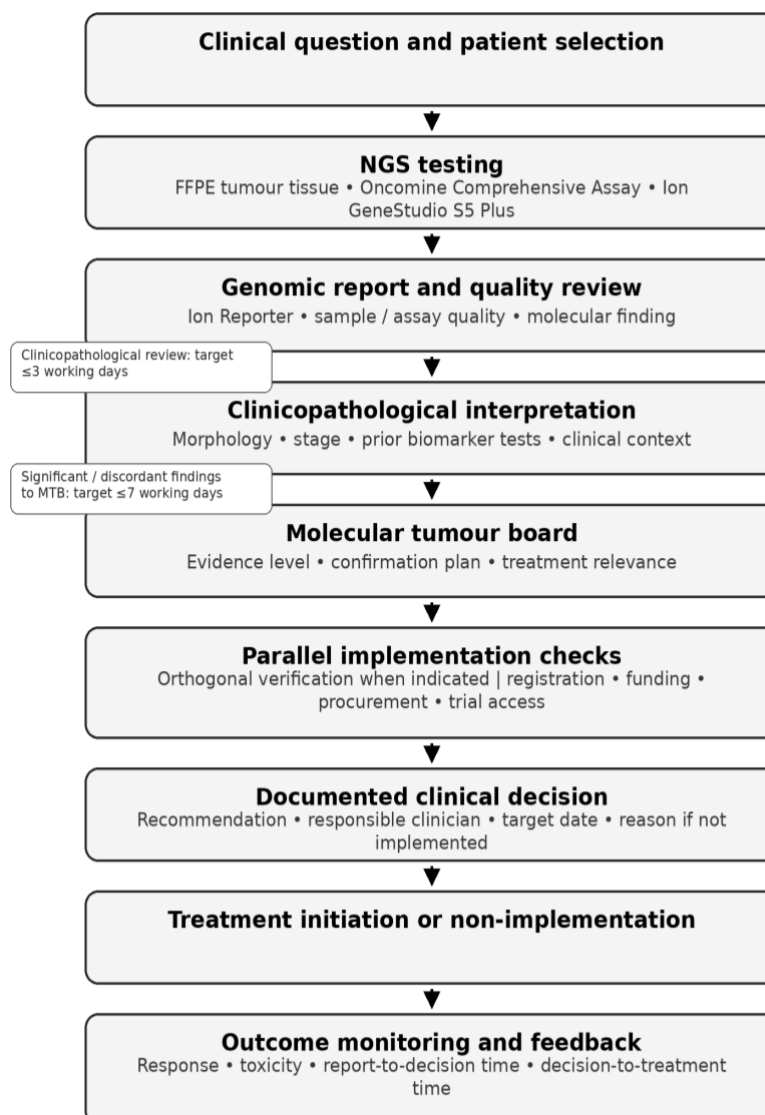
**Abbreviations:** dMMR, deficient mismatch repair; LOH, loss of heterozygosity; MSI-H, microsatellite instability-high; MTB, molecular tumour board; NSCLC, non-small cell lung cancer; TMB-H, tumour mutational burden-high; VAF, variant allele fraction.

Table 2. Proposed pilot quality indicators for NGS implementation

| Process step                                      | Proposed target                         | Audit metric                                                                              |
|---------------------------------------------------|-----------------------------------------|-------------------------------------------------------------------------------------------|
| Report registration                               | Day 0                                   | Proportion of NGS reports entered into the pathway on the day received                    |
| Clinicopathological reconciliation                | ≤3 working days                         | Time from report registration to integrated pathology / clinical review                   |
| MTB review for significant or discordant findings | ≤7 working days                         | Time from report registration to documented MTB decision                                  |
| Verification and access review                    | Parallel when indicated                 | Time to orthogonal confirmation; time to reimbursement / procurement / trial decision     |
| Decision documentation                            | At MTB / responsible-clinician decision | Proportion with evidence level, next step, responsible person, and target date documented |
| Implementation and follow-up                      | Prospective tracking                    | Report-to-decision interval; decision-to-treatment interval; implementation rate;         |

reason for non-implementation; response and toxicity

## Appendix B.



**Figure 1. Proposed pathway from NGS report to a documented clinical decision.** Orthogonal verification, when indicated, and treatment-access assessment are initiated in parallel with clinical interpretation rather than after it. The proposed 3- and 7-working-day targets are quality-improvement benchmarks that require prospective validation. *Source: compiled by the authors.*