AKENTEN APPIAH- MENKA UNIVERSITY OF SKILLS TRAINING AND ENTREPRENEURIAL DEVELOPMENT, MAMPONG.

FACULTY OF ENVIRONMENT AND HEALTH EDUCATION

DEPARTMENT OF PUBLIC HEALTH EDUCATION

MPHIL THESIS

COMPARATIVE DIAGNOSIS OF TYPHOID FEVER USING TYPHIDOT AND WIDAL METHODS WITH CULTURE AT THE KORLE BU TEACHING HOSPITAL IN THE GREATER ACCRA REGION, GHANA

BY

EUNICE ASAGA

2025

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(8238000009)

A thesis submitted to the Department of Public Health Education of the Faculty of Environment and Health Education, Akenten Appiah-Menka University of Skills Training and Entrepreneurial Development, Mampong, in partial fulfilment of the requirements for the award of a Master of Philosophy Degree in Public Health.

SEPTEMBER, 2025

DECLARATION

I hereby declare that this thesis, with the exception of quotations and references contained in published works which have been duly acknowledged; is the result of my own original work and that no part of it has been presented for another degree at this university or elsewhere.

Candidate's Name: Eunice Asaga

Signature: ……………………………… Date: ……………………..

Supervisors' Declaration

We hereby declare that the preparation and presentation of the thesis were supervised in accordance with the guidelines on supervision of thesis laid down by the Akenten Appiah-Menka University of Skills Training and Entrepreneurial Development.

Principal Supervisor's Name: Rev. Dr. Denis Dekugmen Yar (PhD)

Signature: ………………………… Date: ……………………......

Co-Supervisor's Name: Dr. Daniel Hayford (PhD)

Signature: ………………………….. Date: ………………………..

ABSTRACT

Typhoid fever remains a persistent public health challenge in many low- and middle-income countries, including Ghana. Accurate and timely diagnosis is crucial for effective case management and prevention of antimicrobial resistance. Although stool culture is considered the gold standard, limited laboratory capacity has necessitated reliance on rapid serological methods such as Widal and Typhidot tests, whose diagnostic accuracy remains uncertain in the Ghanaian context. The current study compared the diagnostic performance of Typhidot and Widal tests with stool culture for the detection of typhoid fever at Korle-Bu Teaching Hospital, Accra. Furthermore, this study examined the relationships between socio-demographic factors, clinical symptoms, personal hygiene practices, antibiotic use, and typhoid infection. A cross-sectional study was conducted among 234 suspected typhoid patients. Blood and stool samples were tested using Widal, Typhidot, and stool culture methods. Sensitivity, specificity, predictive values, and agreement were calculated. In addition, logistic regression was used to examine the associations between infection and risk factors. The prevalence of typhoid fever varied widely by method: Typhidot (50.4%), Widal (35.9%), and stool culture (5.1%). Typhidot detected all culture-positive cases, showing 100% sensitivity and 52.3% specificity, while Widal recorded 83.3% sensitivity and 32.4% specificity. Both tests had poor PPVs (approximately 10.2% and 6.3% respectively) but high NPVs (>97%). Agreement between Typhidot and Widal was moderate ($\kappa = 0.47$, $p < 0.001$). Socio-demographic variables (age, sex, marital status, and insurance status) and most clinical symptoms showed no significant associations with infection. However, a prior history of typhoid was associated with a higher positivity rate (AOR = 2.06, $p = 0.008$). Typhidot outperformed Widal in terms of sensitivity; however, both tests exhibited low specificity and predictive values compared to stool culture, thereby limiting their reliability as standalone diagnostic tools. Strengthening culture-based diagnostics and promoting rational antibiotic use are crucial for enhancing case management and reducing antibiotic resistance.

Keywords: Typhoid fever, Widal, Typhidot, stool culture, diagnostic accuracy, Korle-Bu Teaching Hospital, Ghana

DEDICATION

This thesis is dedicated first and foremost to Almighty God, whose grace, guidance, and protection have been my constant source of strength throughout this academic journey.

I also dedicate this work to my beloved parents and family for their unwavering love, encouragement, and sacrifices that made this achievement possible. Finally, I dedicate this research to all patients and healthcare workers battling typhoid fever in Ghana and beyond, with the hope that the findings from this study will contribute to improving diagnosis, treatment, and public health outcomes.

ACKNOWLEDGEMENT

My deepest gratitude goes to my supervisors, Rev. Dr. Denis Dekugmen Yar and Dr Daniel Hayford, for their exceptional guidance, constructive feedback, and mentorship throughout this research project. Their expertise, patience, and commitment greatly enriched this work.

I also thank the Department of Public Health Education, Faculty of Environment and Health Education, Akenten Appiah-Menka University of Skills Training and Entrepreneurial Development, for providing the academic platform and support that enabled me to undertake this study.

Special thanks to the management and staff of the Korle-Bu Teaching Hospital, particularly the Central Laboratory, for their cooperation, technical assistance, and for granting me access to conduct this research, especially Dr Philip Adom Yeboah.

I am also grateful to my colleagues and friends who contributed in diverse ways, from data collection to encouragement during challenging moments.

Finally, to my family, whose prayers, patience, and love gave me the strength to persevere, this achievement is as much yours as it is mine.

ACRONYMS

AOR – Adjusted Odds Ratio

AUC – Area Under the Curve

CI – Confidence Interval

COR – Crude Odds Ratio

DNA – Deoxyribonucleic Acid

HBM – Health Belief Model

IgG – Immunoglobulin G

IgM – Immunoglobulin M

IRB – Institutional Review Board

KBTH – Korle-Bu Teaching Hospital

NPV – Negative Predictive Value

OPD – Outpatient Department

PCR – Polymerase Chain Reaction

PPV – Positive Predictive Value

ROC – Receiver Operating Characteristic

SDH – Social Determinants of Health

SPSS – Statistical Package for the Social Sciences

SS Agar – *Salmonella-Shigella* Agar

TSI – Triple Sugar Iron (test)

UTI – Urinary Tract Infection

WASH – Water Sanitation and Hygiene

WHO – World Health Organisation

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11th August, 2025

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SCIENTIFIC AND TECHNICAL COMMITTEE APPROVAL PROTOCOL IDENTIFICATION NUMBER: KBTH-STC 000108/2025

The Korle Bu Teaching Hospital Scientific and Technical Committee (KBTH-STC), on 11th August, 2025 reviewed and approved your submitted study protocol.

Title of Protocol: **"Comparative Diagnosis of Typhoid Fever Using Typhidot and Widal Methods with Culture at the Korle-Bu Teaching Hospital"**

This approval requires that you forward your approved document to Korle Bu Teaching Hospital – Institutional Review Board (KBTH-IRB) for the ethical aspect of the proposal to be assessed before the project may be initiated.

PRINCIPAL INVESTIGATOR: **Eunice Asaga**

This STC approval is valid till 30th July, 2026

You may, however, request extension of the approval period, or renewal as the case may be, should the study extend beyond the stated period.

Upon completion, you are required to submit a final report on the study to the STC. This is to enable the STC ensure among others that, the project has been implemented as per the approved protocol. You are also required to inform the KBTH-STC and Research Directorate of any publications that may emanate from the research findings.

Kindly note that, should the need arise, the KBTH-STC or IRB may institute appropriate measures to satisfy itself that study is being conducted according to the highest scientific and ethical standards.

Please note that any modification to the study protocol without Scientific Technical Committee (STC) approval renders this Approval invalid.

Prof. G. Obeng Adjei
Chairman, KBTH-STC

Cc: The Chairman, KBTH-IRB

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INSTITUTIONAL APPROVAL: KORLE BU TEACHING HOSPITAL-SCIENTIFIC AND TECHNICAL COMMITTEE/INSTITUTIONAL REVIEW BOARD (KBTH-STC/IRB/000108/2025

Following approval of your study entitled "**Comparative Diagnosis of Typhoid Fever Using Typhidot and Widal Methods with Culture at the Korle-Bu Teaching Hospital**" by the Korle Bu Teaching Hospital-Scientific and Technical Committee/Institutional Review Board.

I am pleased to inform you that institutional approval has been granted for the conduct of your study in Korle Bu Teaching Hospital.

Please contact the **Head of Department** to discuss the commencement date of the study.

Please note that, this institutional approval is rendered invalid if the terms of the Institutional Reviewed Board/Scientific and Technical Committee approval are violated.

Sincere regards,

Dr. Frank Owusu-Sekyere
Director of Medical Affairs

Cc: The Chief Executive, Korle Bu

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"COMPARATIVE DIAGNOSIS OF TYPHOID FEVER USING TYPHIDOT AND WIDAL METHODS WITH CULTURE AT THE KORLE-BU TEACHING HOSPITAL"

KBTH-IRB /000108/2025

INVESTIGATOR: **EUNICE ASAGA**

The Korle Bu Teaching Hospital Institutional Review Board (KBTH IRB) reviewed and granted approval to the study entitled: **"Comparative Diagnosis of Typhoid Fever Using Typhidot and Widal Methods with Culture at the Korle-Bu Teaching Hospital"**

Please note that the Board requires you to submit a final review report on completion of this study to the KBTH-IRB.

Kindly, note that, any modification/amendment to the approved study protocol without approval from KBTH-IRB renders this certificate invalid.

Please report all serious adverse events related to this study to KBTH-IRB within seven days verbally and fourteen days in writing.

This IRB approval is valid till 28th July, 2026. You are to submit annual report for continuing review.

Sincere regards,

DR DANIEL ANKRAH
VICE CHAIR (KBTH-IRB)
FOR: CHAIR (KBTH-IRB)

Cc: The Chief Executive Officer, KBTH
The Director of Medical Affairs, KBTH

CHAPTER ONE

INTRODUCTION

1.1 Background

Enteric fever continues to be a pressing threat to public health (Piovani *et al.*, 2024). Each year, over 11 to 21 million cases, and more than 161,000 deaths occur in developing nations such as Asia, sub-Saharan Africa and South America (Katyar *et al.*, 2024). Typhoid fever, for example, is a community-acquired bacteraemia infection common in tropical nations. It occurs mainly where health infrastructure and sanitary conditions are poor due to inadequate public health facilities and low socioeconomic status (Shah, 2021).

Salmonella, a Gram-negative bacterium, whose subgroups include paratyphi A, B, and C, and *Salmonella enterica* serovar Typhi, is the cause of typhoid fever (Abd-Aljabar & Aljanaby, 2021). Among these, *Salmonella enterica serovar* Typhi is the most prevalent and is linked to serious illnesses (Chatterjee *et al.*, 2023). Humans are considered possible reservoirs for Salmonella, alongside domestic and wild animals, reptiles and poultry, and environmental sources such as soil and water. However, in endemic areas, the disease is primarily thought to spread by contact with faeces-contaminated food and water (Shayo *et al.*, 2023). Typhoid has symptoms that are similar to other infections, such as hepatitis and malaria (Mahmoud *et al.*, 2023). These signs and symptoms include fever, anorexia, headache, constipation, unexplained stomach discomfort, and malaise (Paul, 2024). Rapid urbanisation and limited access to infrastructure, health systems, and drinkable water are risk factors linked to typhoid fever (Thalia, 2024).

Several laboratory-based tests are available for diagnosing typhoid infections in cases with non-specific symptoms. These consist of molecular techniques like PCR, culture, and serological testing, such as Widal and immunochromatographic tests (Yemeli Piankeu *et al*., 2024). The Widal test is one of the earliest and most widely used diagnostic methods developed for detecting typhoid fever (Ousenu, Ali, Sama, Ndam, Tchouangueu, Tume, *et al*., 2021). Historically, the Widal test was developed in 1896 by Georges Fernand Widal as a diagnostic method for detecting typhoid fever. The basis for this test is a macroscopically visible serum-mediated agglutination response between the *S. typhi* flagellar H antigens and the somatic lipopolysaccharide O antigens (Yusuf & Allerberger, 2021). The Widal test has several advantages, such as being comparatively inexpensive, easy to administer, requiring minimal training, and not requiring any sophisticated equipment (Tegene & Eshetie, 2025). Due to cross-reactivity with other Gram-negative organisms in endemic regions and the delayed rise in antibody titre during the first week of infection, the Widal test may produce false-positive or false-negative results, thereby limiting its reliability as a standalone diagnostic tool (Vaca *et al*., 2022). This method has significant drawbacks, including low to moderate sensitivity and specificity. (Igiri *et al*., 2023).

While the Widal test has long served as a conventional and widely used serological method for typhoid diagnosis, advancements in diagnostic technology have led to the development of alternative techniques that offer improved speed and sensitivity. One such method is the Typhidot test, which utilizes immunochromatographic principles to detect specific antibodies against Salmonella antigens and can be completed quickly (Kirti *et al*., 2024).

In contrast, a study shows that the Widal test correctly detects antibodies within two weeks of infection, whereas the Typhidot method can identify antibodies as early as four days after infection (Ousenu *et al.*, 2021). Nevertheless, as with the Widal test, the increasing availability of various immunochromatographic kits on the market has led to reports of inconsistent diagnostic accuracy (Manta *et al.*, 2021).

To place these serological methods in context, it is important to note that traditional culture-based diagnostics have long been considered the benchmark for confirming typhoid fever. Urine, stool, and blood specimens analysed through culture and sensitivity tests were once regarded as the most reliable diagnostic options (Diwaker *et al.*, 2024). Even so, prolonged turnaround times and labour-intensive isolation procedures remain major limitations (Kidd & Weldhagen, 2022). More recently, bone marrow cultures have been proposed as the gold standard due to their superior sensitivity compared to blood cultures; on the other hand, their use in routine or research settings is limited by their invasive nature (Sapkota *et al.*, 2022).

This study therefore compares the agglutination-based Widal assay and the chromatographic Typhidot method to provide insight into their diagnostic performance for typhoid fever.

1.2 Problem Statement

Typhoid fever continues to be a public health concern in Ghana (Ayin *et al.*, 2023). Accurate diagnosis is crucial for effective treatment and disease control. The cultural method (using blood or stool) has long been considered the gold standard diagnostic method for typhoid fever. However, many health facilities in Ghana lack the capacity to perform culture-based diagnostic methods. As a result, most rely on serological tests such as the Widal and Typhidot, which are more cost-effective and suitable for use at various levels of healthcare delivery. These diagnostic methods, however, are prone to misdiagnosis due to cross-reactivity with other febrile illnesses, variability in antibody responses during different stages of infection, and inconsistencies in test kit quality and interpretation. Misdiagnosis can result in incorrect treatment, leading to overuse of drugs, which may contribute to antibiotic resistance. Increased antibiotic typhoid resistance can potentially spread with dire public health consequences in Ghana. Furthermore, limited studies have examined the reliability of Typhidot and Widal tests in Ghana, despite their widespread use and adoption as diagnostic methods in most health facilities. Therefore, it is imperative to evaluate the reliability of these methods compared to the stool culture method in Ghanaian health settings.

1.3 Study Objectives

The present study evaluates the laboratory diagnosis of typhoid fever using the typhidot and Widal tests compared to the gold standard (stool culture) at the Korle-Bu Teaching Hospital in Accra.

1.4 Specific Objectives

Specifically, this study sought to:

1. Determine rates of typhoid fever using the Typhidot and Widal methods.
2. Evaluate the sensitivity, specificity, positive predictive value, and negative predictive value of the Typhidot and Widal tests in detecting typhoid fever using stool culture as the gold standard.
3. Assess the association between socio-demographics, clinical symptoms, personal hygiene practices and antibiotic use with typhoid infection.

1.5 Research Question

1. What are the rates of typhoid fever detected using the Typhidot and Widal diagnostic methods among patients at Korle-Bu Teaching Hospital?
2. What is the sensitivity, specificity, positive predictive value, and negative predictive value of the Typhidot and Widal tests in detecting typhoid fever when compared to stool culture as the gold standard among patients at Korle-Bu Teaching Hospital?
3. What is the association between selected socio-demographic, clinical symptoms, personal hygiene practices and antibiotic use with typhoid infection?

1.6 Justification

Due to inadequate sanitation and water quality, typhoid fever remains a serious public health issue in many low- and middle-income countries, including Ghana (Boakye Okyere *et al*., 2024). Accurate diagnosis is essential for timely treatment. This, however, remains challenging due to the limitations of commonly used diagnostic methods, such as the Widal test and Typhidot (Sapkota *et al*., 2023). The Widal test, which detects agglutinating antibodies against *Salmonella* antigens, has been criticised for its low sensitivity and specificity, especially in endemic areas where cross-reactivity with other infections is common (Essam *et al*., 2025). On the other hand, the Typhidot test, a rapid diagnostic test, is faster but also prone to variability in accuracy across different settings (Njokuobi, 2024). Stool culture is considered the gold standard for diagnosing typhoid, but it requires specialised equipment and longer processing times, which limits its use in resource-constrained settings (Jasuja, 2024).

In a study, the Typhidot test had higher sensitivity but lower specificity (Muhammad *et al*., 2023). Similarly, the Widal test remains widely used, but its reliability is questioned due to false positives in endemic areas (Tegene & Eshetie, 2025). Despite these studies, there is a limited body of research comparing these diagnostic methods in sub-Saharan Africa, particularly in Ghana. This study aims to fill the gap in the literature by evaluating and comparing the sensitivity, specificity, and accuracy of the Widal and Typhidot tests with stool culture at Korle-Bu Teaching Hospital in Ghana. The findings will provide valuable evidence to guide clinicians in selecting the most appropriate diagnostic tool, ultimately improving regional patient outcomes. In addition, antibiotic resistance may be less of an issue since patients will not be treated for previous infections (IgG) because the Typhidot can detect both IgG and IgM antibodies. Instead, therapy will be based on the patient's current infection.

1.7 Significance

This study is significant as it addresses the critical need for accurate, reliable, and accessible diagnostic tools for typhoid fever in resource-limited settings such as Ghana. Typhoid fever, caused by *Salmonella* species, remains a leading cause of morbidity and mortality in many developing countries. Misdiagnosis or delayed diagnosis can lead to severe complications, increased transmission, and misuse of antibiotics, contributing to antimicrobial resistance. By comparing the Widal and Typhidot tests with stool culture as the gold standard, this research would provide valuable insights into the diagnostic accuracy of the two commonly used serological tests in the Ghanaian context.

The findings support better diagnostic choices at Korle-Bu, reducing misdiagnosis and antibiotic misuse, improving accuracy, and enhancing patient outcomes through timely detection.

This study would also aid in the accurate surveillance and monitoring of typhoid fever, providing valuable data for public health planning and response. Additionally, it would provide empirical data to support policy formulation agents, such as the Ghana Health Service, in their policy development and decision-making. Finally, this research will contribute to the global body of knowledge, filling a gap in the existing literature regarding typhoid diagnostics in sub-Saharan Africa.

1.8 Limitations

Although this study was carefully designed and executed, some limitations must be acknowledged. The research was conducted among 234 suspected typhoid fever patients at the Korle-Bu Teaching Hospital. Although a major referral centre, it may not fully represent populations in other regions of Ghana with different sanitation conditions, diagnostic capacities, and antibiotic-use patterns. The single-site design and cross-sectional approach limited the generalizability of findings and prevented causal inferences between socio-demographic, behavioral, and clinical variables.

The study relied solely on stool culture as the gold standard, which may not detect all true positive cases compared to more sensitive methods such as blood or bone marrow culture. Self-reported data on hygiene and antibiotic use were subject to recall and social desirability biases, while serological cross-reactivity with other endemic infections, such as malaria, could have contributed to false positives. Despite these limitations, the study provides valuable context-specific evidence to guide improvements in typhoid diagnosis and underscores the need for future multi-centre research incorporating advanced diagnostic techniques.

1.9 Scope of Study

This study encompasses those patients visiting Korle-Bu Teaching Hospital during the study period. The study's target group comprises individuals with presumed febrile illnesses from the outpatient department (OPD) and wards (inpatients) of the study site.

1.10 Thesis Organisation

The study is divided into six main chapters. The first chapter addresses the background of the study, including the problem statement, objectives, hypothesis, justification, significance, scope, organisation, and conceptual framework. In the second chapter, relevant literature related to this research topic was thoroughly examined. Chapter Three presents the study area and the methodology employed in conducting the research. Moving on to Chapter Four, the study data are presented. Chapter Five covers the discussions of the study's major findings. Lastly, Chapter Six presents a summary of the results, conclusions based on the main findings and recommendations based on the study's outcomes.

CHAPTER TWO

LITERATURE REVIEW

2.1 Overview

Typhoid fever, caused by *Salmonella enterica* serovar Typhi, remains a serious global health concern despite advances in diagnostic technology, treatment, and public health interventions (Singh *et al*., 2024). It is estimated that between 11 and 21 million cases occur annually, with 128,000–161,000 deaths worldwide (Acha *et al*., 2025). The disease disproportionately affects populations in low- and middle-income countries (LMICs), where inadequate sanitation, poor access to clean water, and limited healthcare infrastructure continue to drive transmission (Kim *et al*., 2022). While largely controlled in industrialised nations, typhoid fever persists as a neglected tropical disease in South Asia, sub-Saharan Africa, and parts of Latin America (Stanley *et al*., 2023). In terms of classification and nomenclature, typhoid fever is caused by *Salmonella enterica* subspecies *enterica* serovar Typhi, a Gram-negative, facultative intracellular bacillus belonging to the family Enterobacteriaceae (Yada, 2023). The genus *Salmonella* is divided into two recognised species: *Salmonella enterica* and *Salmonella bongori* of which *S. enterica* is further subdivided into six subspecies and over 2,600 serovars, classified based on somatic (O), flagellar (H), and capsular (Vi) antigens (Saad, 2022). *S. enterica* serovar Typhi is highly adapted to humans as its only natural host, distinguishing it from other non-typhoidal *Salmonella serovars* that have a broader host range (Darboe, 2022). This taxonomic classification is essential for understanding its pathogenicity, transmission dynamics, and the development of targeted diagnostic and therapeutic strategies.

2.1.1 Global Burden of Typhoid Fever

Globally, the epidemiology of typhoid fever is shaped by geographical, socioeconomic, and infrastructural factors. Countries in South Asia, including India, Pakistan, and Nepal, account for nearly 70% of all reported cases (Garrett *et al.*, 2022). Recent estimates suggest incidence rates of 500–700 per 100,000 population annually in some regions of Sub-Saharan Africa, highlighting the disease's entrenched nature despite improvements in water supply and sanitation (Cao *et al.*, 2021).

In addition to its prevalence, the disease presents challenges due to the emergence of antimicrobial resistance (AMR) (Carey *et al.*, 2022). The increasing spread of multidrug-resistant (MDR) *Salmonella Typhi* strains has been reported in South Asia and parts of Africa, complicating treatment protocols and threatening the efficacy of first-line antibiotics such as ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole (da Silva *et al.*, 2022). Extensively drug-resistant strains (XDR), resistant to both first- and second-line antibiotics, were first reported in Pakistan and are now an emerging concern in Africa (Habib, 2023). The global burden is therefore not only measured in terms of prevalence and mortality, but also in the growing challenge of resistance, which directly relates to diagnostic accuracy and the implementation of appropriate antimicrobial stewardship.

2.1.2 Epidemiology of Typhoid Fever in Africa

In Africa, typhoid fever continues to be a significant cause of morbidity and mortality, particularly among children and young adults(Marks *et al.*, 2024). Epidemiological studies have reported prevalence rates ranging from 3% to 10% based on culture methods. In contrast, serological tests, such as the Widal test, often yield an inflated prevalence of 14.6% (Rufai *et al*., 2023). The highest burden of typhoid fever is concentrated in the Southern part of Asia and Africa (Tariq & Mushtaq, 2023).

Ghana, Nigeria, and Cameroon have consistently reported typhoid fever as one of the leading causes of outpatient febrile illness (Rufai *et al*., 2023).In Ghana, data from both regional and tertiary hospitals reveal that suspected typhoid fever accounts for up to 3.2% of febrile hospital consultations (Kungu *et al*., 2025).However, culture-confirmed rates are substantially lower, suggesting that overdiagnosis is common due to reliance on serological methods (Branda & Steere, 2021).

The epidemiological challenge is compounded by frequent antibiotic use before hospital presentation, which reduces the sensitivity of culture-based diagnostics (Banerjee & Patel, 2023). As a result, prevalence data are often unreliable, and health systems struggle to differentiate true typhoid fever from other febrile illnesses such as malaria and viral hepatitis.

2.1.3 Typhoid Fever in Ghana

In Ghana, typhoid fever is a significant public health issue and remains among the top causes of hospital admissions, particularly in urban centres such as Accra and Kumasi. The burden is closely tied to rapid urbanisation, poor sanitation, and contaminated water supply systems (Boakye Okyere, Twumasi-Ankrah, Newton, Nkansah Darko, Owusu Ansah, Darko, Agyapong, Jeon, Adu-Sarkodie, Marks, *et al*., 2025). Outbreaks have been frequently documented in peri-urban and rural communities where open defecation, unsafe drinking water, and inadequate waste management persist (Fielmua *et al*., 2023).

In some studies, the Widal test remains the most widely used diagnostic method in Ghana, despite repeated concerns about its accuracy (Lawal *et al*., 2025). While stool and blood cultures are considered the gold standard, these methods are rarely employed outside tertiary centres due to cost, turnaround time, and infrastructure limitations. Korle-Bu Teaching Hospital (KBTH), as the country's largest tertiary facility, provides an ideal setting for evaluating diagnostic methods, as it receives referrals from across the Greater Accra Region and beyond. The hospital also manages a diverse patient population, allowing for a robust analysis of diagnostic accuracy across different socio-demographic groups (Kissi *et al*., 2025).

Ghana has also witnessed a rise in antimicrobial resistance among *S. Typhi* strains. Studies conducted since 2020 report increasing resistance to fluoroquinolones and third-generation cephalosporins (Biswas *et al*., 2022). This trend highlights the crucial need for accurate diagnosis, as misdiagnosis leads to unnecessary or inappropriate antibiotic use, thereby exacerbating resistance patterns.

2.1.4 Clinical Presentation and Diagnostic Challenges

The clinical features of typhoid fever are usually nonspecific. Patients typically present with prolonged fever, abdominal pain, malaise, headache, anorexia, and occasionally constipation or diarrhoea (O'Neill *et al*., 2024).These symptoms overlap with other endemic febrile illnesses, particularly malaria, making clinical diagnosis alone unreliable. Misclassification based on clinical symptoms contributes to inappropriate antimicrobial therapy and delays in effective management.

Laboratory methods are therefore indispensable for confirming a diagnosis. The gold standard remains culture methods, including blood, stool, urine, and bone marrow cultures (Igiri *et al.*, 2021). Bone marrow culture has the highest sensitivity but is invasive and impractical in most clinical settings. Blood culture is widely used in research but is limited in practice due to its cost, the need for specialised technical expertise, and the requirement for multiple samples. Stool culture is less sensitive during acute infection, but remains critical for identifying carriers and is more feasible in resource-limited settings (Saha *et al.*, 2023).

In Ghana, stool and Blood culture are often used as the gold standard for research purposes. However, due to low availability, most hospitals continue to rely heavily on serological tests. The two most common are the Widal test and the Typhidot test. Widal detects agglutinating antibodies against the O and H antigens of *S. Typhi*, while Typhidot is a rapid immunochromatographic test that detects IgM and IgG antibodies specific to *S. Typhi* outer membrane proteins (Igiri *et al.*, 2023).

2.1.5 Limitations of Current Diagnostic Methods

Each diagnostic method has limitations:

- **Widal test:** While inexpensive and easy to perform, its specificity is poor in endemic regions due to cross-reactivity with other Gram-negative bacteria and prior exposure to non-typhoidal *Salmonella* species (Neupane *et al.*, 2021). The test is also less reliable in the first week of illness when antibody titres are low.
- **Typhidot test:** Offers faster results and higher sensitivity in some settings, detecting antibodies as early as four days post-infection. However, variability

in performance across different populations and issues with quality control of commercial kits undermine its reliability (Sam *et al.*, 2024).

- **Stool culture:** While considered the gold standard in many Ghanaian research studies, its sensitivity is reduced by prior antibiotic use, low bacterial loads, and challenges in laboratory infrastructure (Geteneh *et al.*, 2023).
- **Blood culture:** Highly sensitive in acute cases but impractical for widespread use in Ghana due to cost and infrastructure requirements.(Ofori *et al.*, 2024).

These limitations have significant implications for public health. Misdiagnosis not only skews prevalence estimates but also results in inappropriate treatment and excessive antibiotic use. This creates conditions favourable for the emergence and spread of multidrug-resistant *S. Typhi*, further complicating disease management in Ghana and similar endemic settings (Buzilă *et al.*, 2025).

2.1.6 Importance of Accurate Diagnosis

Accurate diagnosis is essential for effective case management, antimicrobial stewardship, and public health surveillance. Overreliance on Widal inflates prevalence estimates, leading to overreporting of typhoid fever in Ghanaian health records (Kungu *et al.*, 2025). This misrepresentation impacts policy decisions, resource allocation, and health system planning. Furthermore, patients wrongly diagnosed with typhoid may receive unnecessary antibiotics, accelerate resistance and delay correct treatment for the actual underlying illness (Olagunju *et al.*, 2025).

Comparative evaluations of diagnostic methods are therefore crucial. By systematically assessing Widal and Typhidot against stool culture in a large tertiary hospital such as

KBTH, researchers can provide empirical evidence to guide clinical decision-making, improve surveillance data, and inform national policy. Such studies also help clarify the role of socio-demographic, clinical, and behavioural risk factors in shaping diagnostic outcomes, further enriching the evidence base for typhoid control in Ghana.

2.2 Empirical Review

2.2.1 Prevalence of Typhoid Fever Using Typhidot, Widal, and Stool Culture

2.2.1.1 Global Prevalence of Typhoid Fever

Typhoid fever remains a significant public health concern worldwide, particularly in low- and middle-income countries, where poor sanitation infrastructure exacerbates the issue. Global estimates suggest over 11to 12 million cases and 161,000 deaths annually, with the highest burden recorded in South Asia and sub-Saharan Africa(Gautam *et al.*, 2021). The prevalence of the disease is typically measured using stool or blood culture as the reference standard; however, serological tests such as Widal and Typhidot are more commonly used in endemic regions due to their availability and affordability.

Globally, studies reveal a striking discrepancy between prevalence rates measured by culture-based methods and those measured by serological tests. For example, in a study, Typhidot confirmed 35.33% of suspected cases, while Widal tests recorded positivity rates exceeding 24% within the same populations (R. Singh & G. J. M. J. o. M. S. Singh, 2021).

2.2.1.2 Prevalence Based on the Widal Test

The Widal test has been in use for over a century and remains one of the most widely used diagnostic tools in resource-limited settings. However, its prevalence estimates are consistently inflated compared to those based on culture. According to Teferi *et al.* (2022) a study in Ethiopia found that Widal detected more than 33% of suspected cases, while stool culture confirmed less than 7%. Similar findings have been documented across multiple Asian studies, where Widal positivity is often three to six times higher than culture confirmation.

The primary reason for these discrepancies lies in the Widal test's tendency to cross-react with other Gram-negative bacteria, malaria, and previous *Salmonella* exposures. In endemic settings, background antibody levels are high, meaning that a large proportion of individuals test positive despite not having active typhoid infection. This explains why prevalence estimates based on Widal testing alone cannot reliably reflect the actual burden of the disease (Rahman, 2025).

2.2.1.3 Prevalence Based on Typhidot

Typhidot was developed as a more advanced rapid serological test intended to overcome the limitations of Widal's test. It detects IgM and IgG antibodies against *Salmonella enterica serovar* Typhi antigens, providing results within a few hours. Despite these advantages, Typhidot prevalence figures remain significantly higher than those from culture-based methods (Rahman, 2025). In India, (R. Singh & G. J. M. J. o. M. S. Singh, 2021) reported Typhidot positivity of 35.33% compared to 24% confirmed by the Widal test. Although Typhidot generally reports higher prevalence than Widal, its tendency to produce false positives still results in an overestimation of the actual disease burden. These findings suggest that Typhidot, although more specific than the Widal test, cannot replace stool culture as a confirmatory method. It nevertheless offers a more reliable option for rapid screening in endemic contexts, notably where laboratory facilities for culture are lacking.

2.2.1.4 Prevalence Based on Stool Culture

Najib *et al*. (2021) indicated that the stool and blood culture techniques remain the gold standard for typhoid fever diagnosis. Culture-confirmed prevalence is consistently lower than serological test results, making it the most reliable indicator of true disease burden. A meta-analysis confirms that stool culture prevalence was 3% among febrile patients (Teferi *et al*., 2022). In Africa, the trend is similar. In Ethiopia, Simion *et al*. (2024) confirmed that stool culture prevalence was 3.3% among febrile patients. In Cameroon, stool culture confirmed 12.9% compared to 57.7% by Widal and 15.59% by Typhidot (Ousenu, Ali, Sama, Ndam, Tchouangueu, Tume, *et al*., 2021). These studies demonstrate that culture consistently identifies fewer cases, but these are more accurate representations of infection. Yet, stool culture is constrained by several challenges: it is time-consuming, requires skilled laboratory personnel, and is influenced by prior antibiotic use. In endemic regions, patients often self-medicate with antibiotics before presenting at hospitals, reducing the likelihood of a positive culture result (Almutairy, 2024).

2.2.1.5 Evidence from African Contexts

Across sub-Saharan Africa, serological methods dominate typhoid diagnosis due to infrastructural and financial constraints. This has resulted in inflated prevalence figures in most hospital-based studies. Chidzwondo and Mutapi (2024) in a systematic review, reported average culture-confirmed prevalence rates of 3–5% compared to 20–40% using Widal and 15–25% using Typhidot. In Cameroon, Ndip *et al*. (2021) documented a stool culture prevalence of 20.9% among febrile patients, while Typhidot and Widal reported prevalences of 34% and 50%, respectively. These findings consistently emphasise the overestimation of typhoid fever prevalence when reliance is placed on serological diagnostics. Importantly, such inflated prevalence figures have significant implications for both clinical management and public health planning.

2.2.1.6 Prevalence of Typhoid Fever in Ghana

In Ghana, the use of Widal testing has contributed to the overestimation of typhoid fever prevalence rates. District hospitals report a higher Widal positivity rate, while stool culture studies confirm fewer cases, often below 7% (Domfeh *et al.*, 2023; Rufai *et al.*, 2023). Typhidot use is increasing in some facilities, but prevalence estimates remain in the 20–35% range, still far above stool culture confirmation rates (Domfeh *et al.*, 2023).

Hospital surveillance data in Ghana are primarily derived from Widal results, meaning national prevalence figures may be grossly overestimated (Kungu *et al.*, 2025). This has profound consequences for policy and practice, as it can lead to the misallocation of resources and the use of inappropriate treatment strategies.

2.2.1.7 Implications of Diagnostic Method on Prevalence Estimates

The discrepancies in typhoid fever prevalence rates based on different diagnostic methods highlight critical issues:

1. **Clinical Mismanagement and Health Misrepresentation:** Overreliance on serological tests leads to misdiagnosis and unnecessary antibiotic use (Panditrao *et al.*, 2025). Again, Inflated prevalence data mislead policymakers, resulting in inappropriate planning and intervention strategies (DeSalvo *et al.*, 2021).

2. **Antimicrobial Resistance:** Overdiagnosis contributes to the misuse of antibiotics, accelerating the spread of resistant strains of *S. Typhi* (Dhyani *et al*., 2025).
3. **Surveillance Limitations:** Inaccurate prevalence figures undermine surveillance systems and complicate outbreak detection (Folasole, 2023).

2.2.2 Diagnostic Accuracy of Typhidot and Widal Compared to Stool Culture

Accurate diagnosis is central to the effective management and control of typhoid fever. Although stool and blood cultures are considered the gold standards, many healthcare facilities in endemic areas rely on serological methods, such as the Widal and Typhidot tests, due to their cost, speed, and accessibility. However, the diagnostic performance of these methods has been questioned for decades. This section reviews the accuracy of Typhidot and Widal compared to stool culture, focusing on sensitivity, specificity and predictive values, drawing evidence from global, African, and Ghanaian contexts.

2.2.2.1 Sensitivity of Widal and Typhidot

Sensitivity measures the ability of a test to identify those with the disease (true positives) correctly. High sensitivity is desirable in screening tools, as it ensures that few cases are missed. Globally, the Widal test has shown variable sensitivity. In India, Shahapur *et al*. (2021) reported sensitivity around 90%. In Pakistan, Jahan *et al*. (2021) reported sensitivity of up to 96.9%. However, an African study done in Ethiopia reported a lower Widal sensitivity of 80.8% (Abdela and Tamirat (2023). These inconsistencies imply that the test's performance relies heavily on local epidemiological contexts, including baseline antibody levels and the presence of co-infections.

Typhidot generally demonstrates different sensitivity compared to the Widal test. Muhammad *et al*. (2023) observed a Typhidot sensitivity of 72.46%, while in India, Goenka *et al*. (2025) reported values above 91%. African studies also support these findings, with Sam *et al*. (2024) reporting a Typhidot sensitivity above 53% in Cameroon, and Igiri *et al*. (2021) documenting a sensitivity of 29.4% in Nigeria. These results suggest that Typhidot is less likely to miss actual cases, making it a more reliable screening tool in endemic regions.

2.2.2.2 Specificity of Widal and Typhidot

Specificity refers to a test's ability to correctly identify individuals without the disease (true negatives). High specificity is crucial for minimising false positives and ensuring that patients are not misdiagnosed. Widal's specificity is poor, particularly in endemic regions. In sub-Saharan Africa, it is often reported to be low. This is mainly due to cross-reactivity with other *Salmonella* species, malaria, and non-typhoidal infections (Faruku *et al*.). For example, Abdela and Tamirat (2023) reported Widal specificity at 53% in Ethiopia. In Ghana, Domfeh *et al*. (2023) found specificity as low as 29.3, reinforcing Widal's limitations as a confirmatory diagnostic tool.

2.2.2.3 Positive Predictive Value (PPV) and Negative Predictive Value (NPV)

Predictive values are critical in clinical decision-making, as they indicate the likelihood that a patient's test result reflects their true disease status.

- Widal has consistently low PPV, often below 10% in Ghana and other African contexts **PPV:** Widal has consistently low PPV, often below 10% in Ghana and other African contexts (Domfeh *et al*., 2023; Gidudu, 2021). This means that a positive Widal result rarely indicates true infection. Typhidot fares slightly better, with PPV higher than Widal in African studies (Ousenu, Ali, Sama, Ndam, Tchouangueu, Tume, *et al.*, 2021; Tegene & Eshetie, 2025). However, both tests remain unreliable in predicting true positives, particularly in areas with high background antibody prevalence.

- **NPV:** Both Widal and Typhidot demonstrate high NPVs, often above 95%. This suggests that negative results are considerably reliable in excluding infection. In Ethiopia, Simion (2024) reported NPVs of 98.9% for Widal and 99.4% for Typhidot. In Ghana, NPVs above 96.1 % have also been reported for the Widal (Domfeh *et al.*, 2023). Clinically, this means that these tests are more helpful in ruling out infection than confirming it.

2.2.2.4 Contextual Factors Affecting Diagnostic Accuracy

Several contextual factors influence the diagnostic performance of Widal and Typhidot:

1. **Antibiotic Use:** Widespread self-medication reduces bacterial load, leading to false negatives in stool culture and distorted sensitivity/specificity calculations (Buonavoglia *et al.*, 2021).
2. **High Endemicity:** Background antibody levels in endemic areas cause elevated false positives in serological tests, lowering specificity (Vengesai *et al.*, 2021).
3. **Cross-Reactivity:** Widal reacts with antibodies from other Gram-negative bacteria and malaria, both of which are highly prevalent in Africa (Faruku *et al.*).
4. **Variability in Test Kits:** Lack of standardisation and differences in Typhidot kit quality affect reproducibility across laboratories (Matsumura *et al.*, 2025).
5. **Host Immunity:** Immunocompromised patients, such as those with HIV, may have reduced antibody responses, lowering test sensitivity(Netto *et al.*, 2022).

2.2.2.5 Clinical and Public Health Implications

The limitations of Widal and Typhidot have profound implications for clinical practice and public health (Goenka *et al.*, 2025). Clinically, reliance on serological tests leads to overdiagnosis and unnecessary antibiotic prescriptions, increasing the risk of antimicrobial resistance. At the population level, inflated prevalence figures misrepresent the actual burden of disease, undermining surveillance systems and leading to misallocation of scarce resources (Lipsitz, 2024).

Despite their limitations, serological tests remain entrenched in health systems due to their affordability, speed, and ease of use (Ofori *et al.*, 2024). In Ghana, the Widal test remains the most used test in most district hospitals, while Typhidot is increasingly being adopted in urban centres. However, without expanded access to culture-based diagnostics, these tests will continue to misguide both clinical and policy decisions.

2.2.3 Socio-Demographic, Hygiene, and Antibiotic-Use Factors in Typhoid Infection

The burden of typhoid fever cannot be fully understood without considering the socio-demographic, behavioural, and environmental factors that influence both infection risk and diagnostic outcomes. While the disease is transmitted through the faecal-oral route, its distribution in populations reflects a complex interplay of age, sex, education, socioeconomic status, hygiene practices, access to water and sanitation, and patterns of antibiotic use. In Ghana and other endemic states, these determinants are particularly critical, given widespread poverty, limited diagnostic infrastructure, and a high reliance on informal healthcare practices.

2.2.3.2 Age and Susceptibility to Infection

Age has consistently emerged as a key determinant of typhoid fever risk. Global estimates indicate that children, adolescents, and young adults bear the highest disease burden ((Khan *et al*., 2025). The reasons are both behavioural and biological. Younger individuals are more likely to consume unsafe food and water, have higher exposure in crowded environments such as schools, and engage in practices that compromise hygiene. In South Asia, studies showed an increasing occurrence of culture-confirmed typhoid cases in individuals between 20 and 40 years of age (Lin *et al*., 2021). African studies report similar trends. In Ethiopia, Atikilt Yemata *et al*. (2021) observed that most of the suspected cases were young adults between 25 and 29 years, while in Nigeria, Musa *et al*. (2025) confirmed that young adults aged 18-27 accounted for the majority of culture-positive cases. In Ghana, hospital-based studies consistently report higher prevalence among younger age groups, especially urban youth who rely heavily on street food vendors (Boakye Okyere *et al*., 2024).

2.2.3.3 Sex and Gender Differences

The role of sex in typhoid fever epidemiology is less consistent. Some studies suggest a higher prevalence among males, often linked to occupational exposures such as construction work, vending, or farming, which increase environmental contact with contaminated food and water (Sepadi *et al*., 2022). Other studies, however, have found no significant sex differences, indicating that exposure may be more related to socioeconomic and environmental conditions than biological factors (Thompson, 2021). In Ghana, available evidence suggests only slight male predominance in suspected cases, but culture confirmation does not always reveal significant differences (Boakye Okyere, Twumasi-Ankrah, Newton, Nkansah Darko, Owusu Ansah, Darko, Agyapong, Jeon, Adu-Sarkodie, & Marks, 2025)These findings underscore that gender differences in prevalence may be context-dependent, shaped by cultural roles and exposure patterns.

2.2.3.4 Education and Socioeconomic Status

Education is a critical determinant of typhoid infection, as it influences knowledge, attitudes, and practices related to hygiene and healthcare (Camilleri, 2024). Socioeconomic inequalities further compound the risk. Low-income households often reside in overcrowded urban neighbourhoods with inadequate sanitation and poor access to potable water. In Accra, Kumasi, and Tamale, urban slums report higher typhoid prevalence than planned residential (Brown *et al.*, 2023). Conversely, individuals with higher socioeconomic status often enjoy better access to healthcare, safer food, and improved water infrastructure, thereby reducing their risk of infection.

2.2.3.5 Hygiene Practices and Sanitation

Poor hygiene and sanitation remain key factors in the persistence of typhoid fever in endemic regions. The disease thrives in environments where open defecation, indiscriminate waste disposal, and contaminated water sources are common. In Nigeria, studies link higher infection rates to frequent consumption of food prepared by street vendors, many of whom operate under unhygienic conditions (Negassa *et al.*, 2023). In Ghana, Mensah (2022), found that individuals who relied on untreated surface water or sachet water from unregulated sources were more likely to test positive for typhoid compared to those with access to boreholes or piped water. Thus, the role of sanitation is important. Open defecation, common in peri-urban communities, contributes to the contamination of water bodies with *S. Typhi*. Seasonal flooding, particularly in Accra, worsens this contamination by spreading sewage into residential areas (Ntajal, 2022). The persistence of such environmental factors highlights the need for integrated water, sanitation, and hygiene (WASH) interventions as part of typhoid control strategies.

2.2.3.6 Antibiotic Use and Diagnostic Challenges

Antibiotic use before hospital presentation is one of the most important behavioural determinants influencing typhoid diagnosis in Ghana and other African countries. Widespread self-medication with antibiotics such as amoxicillin, ciprofloxacin, and cefuroxime is common, as many patients purchase drugs directly from pharmacies or chemical sellers without prescriptions (Sam *et al.*, 2024).

This practice has two major implications:

1. **Impact on Diagnosis:** Antibiotic use reduces bacterial load, lowering the likelihood of positive stool or blood culture results. This compromises diagnostic accuracy and leads to underestimation of true prevalence in culture-based studies (Montasser *et al.*, 2022).At the same time, prior antibiotic use does not reduce serological test positivity, meaning Widal and Typhidot may continue to register high rates even when cultures are negative.
2. **Antimicrobial Resistance:** Inappropriate and incomplete antibiotic use promotes the emergence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) *S. Typhi*. In West Africa, resistance to fluoroquinolones and cephalosporins is rising (Bisola Bello et al., 2024).Other studies also confirm the presence of resistant strains in both hospital and community settings, complicating treatment and raising public health concerns.

Thus, antibiotic misuse not only distorts diagnostic accuracy but also contributes directly to the global threat of antimicrobial resistance.

2.2.3.7 Cultural and Behavioural Influences

Cultural practices also significantly contribute to the epidemiology of typhoid. In many Ghanaian households, communal eating practices, inadequate washing of raw vegetables, and reliance on untreated sachet water increase the risk of exposure (Boakye Okyere *et al*., 2024). Public gatherings and festivals that involve mass food preparation under unsanitary conditions have been linked to localised outbreaks. Behavioural determinants extend to health-seeking practices. Many patients initially assume fever is malaria and delay seeking professional care, often resorting to herbal remedies or antibiotics before visiting hospitals. Such delays can increase disease severity and complicate diagnosis (Ochepo, 2022).

2.2.3.8 Urbanisation and Environmental Exposure

Rapid urbanisation in Ghana has created new environments that facilitate the transmission of typhoid fever. Overcrowded urban slums, particularly in Accra and Kumasi, often lack proper sewage systems, drainage, and safe drinking water. Seasonal flooding spreads contamination, increasing exposure to *S. Typhi*. Food vending, a key livelihood for many in these areas, is poorly regulated, further heightening the risk of outbreaks (Ainooson, 2023). Urban expansion without corresponding sanitation infrastructure, therefore, remains a major driver of typhoid prevalence in Ghana and other rapidly growing African cities.

2.2.3.9 Summary of Determinants

The literature highlights that age, education, socioeconomic status, hygiene, sanitation, and antibiotic use significantly shape the epidemiology of typhoid fever. Younger age groups and low-income households are disproportionately affected, mainly due to greater exposure to unsafe food and water. Poor hygiene and sanitation sustain the transmission of diseases, while indiscriminate antibiotic use distorts diagnostic accuracy and fosters antimicrobial resistance. These factors intersect with urbanisation and cultural practices to sustain high disease burden in Ghana and across Africa.

2.3 Theoretical Review

Theories provide essential frameworks for understanding the interplay among individual, social, and structural factors that influence health outcomes. For typhoid fever, particularly in resource-limited settings such as Ghana, theoretical perspectives help explain why diagnostic challenges persist and how socio-behavioural determinants shape infection risk and healthcare-seeking behaviour. This study is underpinned by two complementary frameworks: the **Health Belief Model (HBM)** and the **Social Determinants of Health (SDH) theory**.

2.3.1 Health Belief Model (HBM)

The Health Belief Model, first developed in the 1950s and refined over subsequent decades, explains how individuals' perceptions of health threats and benefits influence their engagement in preventive and treatment-seeking behaviours. The model is particularly relevant in contexts where diagnostic uncertainty and competing health risks such as malaria affect decision-making (Louis II, 2016).

HBM is structured around six core constructs:

1. **Perceived Susceptibility:** Individuals' beliefs about their risk of contracting typhoid fever. In Ghana, young adults and those in low-income communities often perceive themselves at higher risk due to frequent exposure to unsafe water and food sources. Such perceptions influence whether they seek diagnostic testing at hospitals or rely on self-treatment.
2. **Perceived Severity:** This refers to the seriousness attributed to typhoid fever. Communities with knowledge of fatal complications like intestinal perforation, are more likely to pursue medical confirmation. However, in endemic sites where typhoid is perceived as "common" or equivalent to malaria, the perceived severity may be misjudged, delaying health-seeking behaviour (Khanam, 2023).
3. **Perceived Benefits:** This construct reflects individuals' beliefs in the efficacy of diagnostic tests and treatment. For example, if patients believe that hospital-based diagnosis is more accurate than pharmacy consultation, they are more likely to present to tertiary facilities such as Korle-Bu Teaching Hospital.
4. **Perceived Barriers:** Barriers include the cost of testing, long waiting times, and distance to health facilities. In Ghana, limited accessibility to culture-based diagnostics and financial constraints often push patients toward cheaper but less accurate tests, such as Widal (Andrews *et al.*, 2013).
5. **Cues to Action:** Triggers that motivate individuals to seek testing, such as persistent fever, community outbreaks, or advice from peers and healthcare workers. In Accra, media campaigns during outbreaks have acted as cues for increased hospital visits.
6. **Self-Efficacy:** Confidence in one's ability to prevent or manage typhoid. Households that practice safe water storage, proper handwashing, and rational

antibiotic use demonstrate higher self-efficacy, reducing the risk of infection (Delea, 2019).

The HBM explains variations in healthcare-seeking behaviour and diagnostic choices. It highlights why many individuals may accept Widal or Typhidot as sufficient, even when aware of their limitations, due to perceived benefits and perceived barriers.

2.3.2 Social Determinants of Health (SDH)

The SDH framework emphasises the role of structural and contextual factors such as socioeconomic status, education, housing, sanitation, and health system capacity in shaping health outcomes (Hassan *et al.*, 2024). Unlike the individual-level focus of the HBM, SDH situates disease within broader social, political, and economic systems. In the context of typhoid fever:

- **Economic Inequality:** Poverty increases reliance on contaminated water sources and unhygienic food vendors. It also restricts access to accurate diagnostic tests, reinforcing dependence on cheaper, less reliable methods (Nirmalkumar *et al.*, 2024).
- **Education:** Low literacy limits awareness of disease transmission and weakens the use of preventive practices like boiling water or avoiding open defecation.
- **Urbanization:** Rapid growth of informal settlements in Accra and Kumasi without corresponding sanitation infrastructure intensifies environmental exposure to *S. Typhi*.
- **Health System Limitations:** Weak laboratory infrastructure and limited funding constrain the availability of culture-based diagnostics. This systemic gap perpetuates overreliance on Widal and Typhidot (Miglietta *et al.*, 2025).

- **Policy Environment:** Limited regulation of pharmacies allows uncontrolled antibiotic sales, contributing to widespread self-medication and resistance.

The SDH model is especially important for interpreting diagnostic performance. The poor specificity of Widal and Typhidot cannot be viewed in isolation from the structural conditions that necessitate their use. In resource-constrained contexts, health systems and societies adapt to their realities, even when diagnostic accuracy is compromised.

2.3.3 Integrative Relevance of HBM and SDH

Together, the HBM and SDH provide complementary lenses. The HBM explains how individual perceptions and motivations shape health-seeking behaviours, such as whether patients pursue confirmatory stool culture. The SDH highlights the structural barriers that make such choices difficult, including cost, access, and weak laboratory capacity. For this study, these frameworks are crucial in understanding why:

1. Patients continue to rely on rapid serological methods despite poor performance.
2. Overdiagnosis persists in Ghana's health system, inflating prevalence estimates.
3. Misdiagnosis is linked not only to test limitations but also to broader socioeconomic and systemic factors.

By combining these theoretical perspectives, the study situates diagnostic accuracy within the lived realities of patients and the structural constraints of the Ghanaian health system. This dual lens ensures that recommendations address both individual-level behaviour change and system-level reforms.

2.4 Conceptual Framework

The conceptual framework guiding this study illustrates the pathways through which socio-demographic characteristics, medical history, hygiene practices, and antibiotic use influence the diagnostic process and outcomes of typhoid fever at the Korle-Bu Teaching Hospital. These factors are hypothesised to have both direct and indirect effects on diagnostic outcomes, either by influencing exposure risk to *Salmonella Typhi* or by affecting the reliability of diagnostic tests.

Socio-demographic factors such as age, sex, level of education, and occupation influence exposure levels and health-seeking behaviours, which subsequently determine the likelihood of undergoing diagnostic testing for typhoid fever. Medical history, including prior episodes of febrile illness and comorbid conditions, may affect host immunity and the clinical presentation of typhoid, thereby influencing the performance of diagnostic methods. Personal hygiene and sanitation practices, including water source, hand washing, and food handling behaviours, are central determinants of infection risk, increasing or decreasing the probability of true positivity in diagnostic tests. Similarly, prior antibiotic use, especially self-medication before hospital attendance, reduces the bacterial load, thereby decreasing culture positivity rates and potentially altering serological responses.

These individual and behavioural-level factors interact with the chosen diagnostic methods: Typhidot, Widal, and stool culture to shape the observed diagnostic outcomes. The framework posits that stool culture serves as the gold standard for establishing typhoid infection, but the performance of Widal and Typhidot is influenced by the background factors described. The outputs of these methods are then evaluated in terms of diagnostic accuracy indices, sensitivity, specificity, positive predictive value, and negative predictive value. Ultimately, diagnostic accuracy determines the extent to which typhoid fever is correctly identified or excluded among patients suspected of having the disease. High sensitivity ensures that true cases are not missed, while high specificity reduces the number of false positives. PPV and NPV contextualise these measures in real-world prevalence settings. The outcome of this framework is the confirmation or exclusion of typhoid fever infection, which has implications for both patient management and public health surveillance. In summary, the framework highlights that diagnostic results cannot be interpreted in isolation from the socio-demographic, behavioural, and medical contexts of the patient population. By integrating these elements, the study not only compares diagnostic methods but also situates their performance within the lived realities of patients at Korle-Bu Teaching Hospital, thereby providing a holistic understanding of typhoid diagnosis in Ghana.

CONCEPTUAL FRAMEWORK

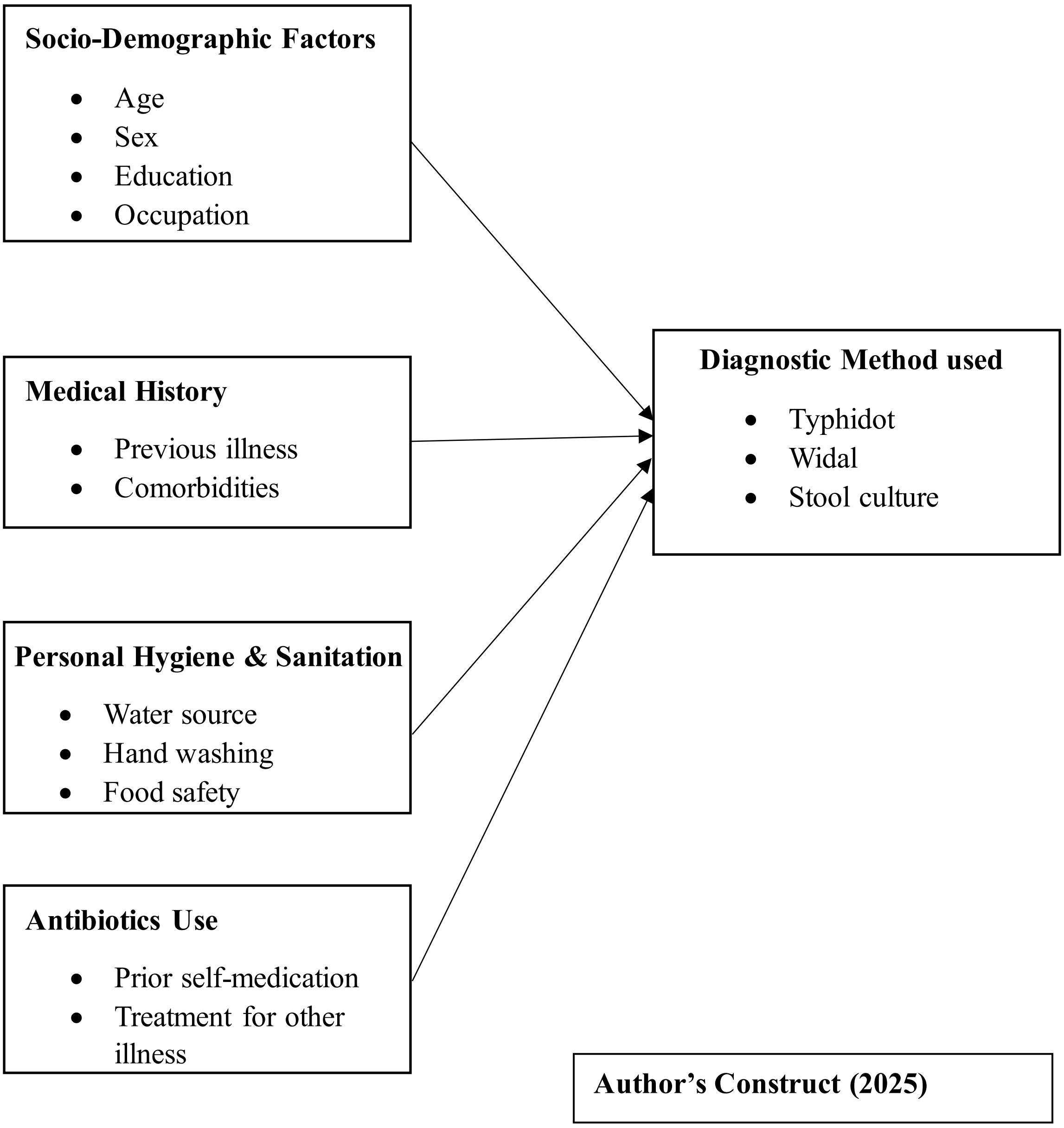

Figure 2. 1: **Conceptual framework**

2.5 Gap in Literature

Although typhoid fever is a major public health problem in many low- and middle-income countries, significant gaps persist in the literature regarding its diagnosis and epidemiology. A careful review of studies conducted globally, across Africa, and in

Ghana reveals several areas where evidence is either inconsistent, insufficient, or absent, thereby justifying the present study. One important gap is the limited number of comparative studies that simultaneously assess Widal, Typhidot, and stool culture within the same population.

Many global and African studies have examined either Widal versus culture or Typhidot versus culture, but very few have evaluated all three methods together. This limits the ability to provide clear recommendations on which diagnostic test is most appropriate for endemic contexts. In Ghana, although Widal and Typhidot are widely used, published studies directly comparing their performance with stool culture remain scarce.

A second gap lies in the inconsistent evidence surrounding the performance of Typhidot across African settings. While some studies from countries such as Cameroon and Nigeria have reported relatively high sensitivity and specificity, studies in Ghana have demonstrated significantly poorer diagnostic performance, particularly with respect to predictive values. This inconsistency suggests that Typhidot's performance is highly context-dependent and requires setting-specific evaluation rather than relying on generalizations from other regions.

Another gap is the underrepresentation of data from tertiary facilities. Much of the existing Ghanaian research on typhoid fever diagnosis has been conducted in district or primary healthcare settings, where diagnostic infrastructure is limited. As a referral centre, the Korle-Bu Teaching Hospital receives patients from diverse backgrounds, making it an important setting for generating nationally relevant data. Nevertheless, few studies have systematically investigated diagnostic accuracy at this level.

The literature also reveals a neglect of socio-demographic and behavioural factors in diagnostic research. While some studies report prevalence by age or sex, very few go beyond descriptive statistics to explore how factors such as education, hygiene practices, or prior antibiotic use affect test performance. This is particularly important because antibiotic self-medication, which is widespread in Ghana, is known to reduce culture sensitivity and distort diagnostic outcomes. Furthermore, there is an overreliance on serological test data for surveillance. National and hospital records in Ghana continue to depend heavily on Widal results, despite their poor specificity and tendency to inflate prevalence figures. This creates a distorted picture of the actual disease burden and has implications for policy and resource allocation. However, few studies have attempted to quantify the magnitude of this distortion in Ghana.

A methodological gap also exists in the limited use of advanced accuracy metrics. Many studies report sensitivity and specificity but fail to include predictive values, Cohen's kappa, or ROC/AUC analyses, which offer a full assessment of diagnostic performance in real-world contexts. Finally, most studies on typhoid fever diagnosis have lacked theoretical grounding. The absence of frameworks such as the Health Belief Model or the Social Determinants of Health reduces the explanatory power of findings, as it becomes difficult to link diagnostic outcomes with broader behavioural and structural factors. Closely related to this is the insufficient exploration of how inaccurate diagnostics contribute to antimicrobial resistance, an area of growing global concern.
Taken together, these gaps demonstrate an urgent need for comprehensive, context-specific studies that evaluate Widal and Typhidot against stool culture, while integrating socio-demographic and behavioural determinants. This study seeks to address these

gaps by generating evidence from Ghana's largest tertiary hospital, applying robust statistical measures, and grounding the analysis in relevant theoretical frameworks

CHAPTER THREE

MATERIALS AND METHODS

3.0 Introduction

This chapter focused on the study area and the methodology employed. It discussed the following sections: Study design, study area, study site, population, inclusion and exclusion criteria, sample size estimation, sampling techniques, data collection tools and techniques, data collection procedures, stool sample collection, sample processing, serological testing, data management, analysis, and ethical review and clearance.

3.1 Study Design

This hospital-based study employed a cross-sectional design at the Korle-Bu Teaching Hospital, Accra. It compared typhoid fever diagnosis using the Typhidot and Widal methods, with stool culture as the gold standard.

3.2 Study site/Study area

The study was conducted at the Korle-Bu Teaching Hospital in the Greater Accra region. Korle Bu Teaching Hospital (KBTH) is a public hospital located in the Ablekuma South Metropolitan District of Accra, Ghana. It is one of the public tertiary hospitals in the southern part of the country. It is a teaching hospital affiliated with the University of Ghana's medical school. KBTH (5.5366° N, 0.2264° W) has an elevation of 19 meters above sea level. The hospital has about 2,000 beds and 21 clinical and diagnostic Departments/Units. It has an average daily attendance of 1,500 patients and about 250 patient admissions (Ministry of Health, 2022). The study was conducted at the Central Laboratory, primarily in the Department of Microbiology and the Serology

Laboratory. These departments are responsible for conducting diagnostic tests for infectious diseases, including typhoid fever, and are equipped with facilities for both culture-based and serological diagnostic methods. Study participants were recruited from patients referred to the Central Laboratory for typhoid fever testing.

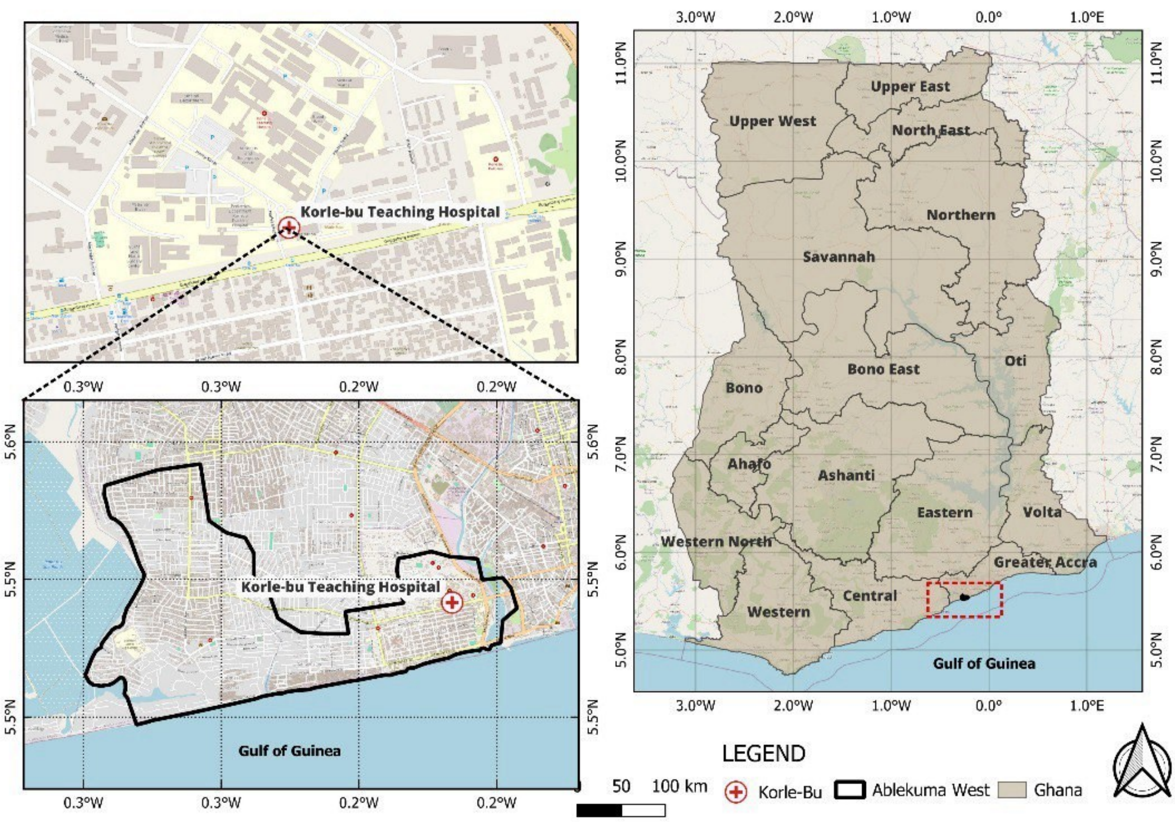

Figure 3. 1: The map of Korle-Bu Teaching Hospital.

3.3 Study Population

The study population consisted of patients presenting with clinical signs and symptoms suggestive of typhoid fever and was referred for laboratory investigation at the Central Laboratory of the Korle-Bu Teaching Hospital. As a tertiary referral hospital, Korle-Bu received both outpatients and inpatients from medical, emergency, and paediatric units who were suspected of typhoid fever and referred by clinicians for Widal, Typhidot, or stool culture testing.

3.3.1 Inclusion Criteria

1. Patients aged above 5 years and of both sexes with clinical symptoms consistent with typhoid fever (e.g., prolonged fever, abdominal pain, headache, malaise).
2. Patients referred to the Central Laboratory for typhoid diagnostic testing.
3. Patients (or guardians, in the case of minors) who provided informed consent/assent to participate in the study.

3.3.2 Exclusion Criteria

1. Patients who had taken antibiotics for more than 48 hours prior to the sampling (as this could have affected culture results).
2. Patients who declined to give informed consent/assent.
3. Patients with a confirmed alternative diagnosis for febrile illness, such as a positive malaria test, diagnosed UTI, dengue fever or other viral infection.
4. Patients who had severe medical conditions or were experiencing intense pain or distress at the time of data collection were excluded from the study.

3.4 Sample Size Estimation

The sample size for this study was calculated using Buderer's Formula (1996)

$$n = \frac{Z^2 \bullet Se \bullet (1 - Se)}{d^2}$$

Z = 1.96 (for 95% confidence)

Se = Expected sensitivity or specificity

D = Margin of error (0.07)

Assuming a sensitivity of 61% and a specificity of 53% based on previous diagnostic studies (Sam *et al*., 2024), the required sample size was:

For sensitivity:

$$n = \frac{1.96^2 \cdot 0.61 \cdot (1 - 0.61)}{0.07^2}$$

n =186

For specificity:

$$n = \frac{1.96^2 \cdot 0.53 \cdot (1 - 0.53)}{0.07^2}$$

n =195

The larger of the two values, 195, was used as the base sample size. To accommodate potential attrition and non-response rate, a 20% contingency was added to the 195. This resulted in a final sample size of **234** participants.

3.5 Sampling Technique

Participants were recruited using a purposive sampling technique from the Medical Wards, Emergency Unit, and Paediatric Unit of Korle Bu Teaching Hospital. Patients who presented with febrile illness that had lasted at least three days and exhibited symptoms suggestive of typhoid fever (such as persistent fever, abdominal pain, headache, and malaise) were identified by attending clinicians and referred to the researcher and the assistants. The team screened the patients using the standardised checklist based on the study's inclusion and exclusion criteria. Eligible individuals were informed about the study, and written informed consent (or assent with parental consent for minors) was obtained. Each enrolled participant then underwent blood sample collection for Typhidot and Widal tests, as well as a stool sample for stool culture tests.

3.6 Data collection Tool(s)

3.6.1 Data Collection Tool(s)

This study used a structured questionnaire to collect data from the participants. The questionnaires included sections on the participants' socio-demographic characteristics, knowledge of how the disease can be prevented, and other risk factors, such as personal hygiene. This instrument was crucial in gathering relevant and key data for the study.

3.6.2 Data Collection Procedure

Data was collected through face-to-face interviews using a structured, pre-tested questionnaire. The questionnaire was administered by the researcher and a trained assistant to ensure consistency and reliability of responses. During the interview, the participants were asked about their sociodemographic characteristics, including age, sex, and marital status. Data on potential typhoid risk factors were collected, including toilet practices, handwashing, drinking water sources. Each interview lasted approximately five minutes. All questionnaires were administered privately and respectfully to ensure confidentiality and encourage honest responses.

3.7 Sample Collection

Approximately 5 mL of venous blood was drawn into an appropriately labelled serum separator test tube, and 4 g of a stool sample was also collected. The blood sample was centrifuged at 2500 rpm for 5 minutes to separate the serum, and the stool sample was taken to the microbiology laboratory for culture.

3.8 Laboratory Examination

3.8.1 Widal slide agglutination test

Qualitative slide agglutination and semi-quantitative tube agglutination (titration) tests were performed using antigen kits of *Salmonella* Typhi procured from a Huichao medical (lianyungang) Company limited with catalogue number 202503003. The patient's serum was screened using the slide agglutination test for anti-O and anti-H antibodies. For the slide agglutination test, a drop of *S.* Typhi O and H antigens were mixed with 80 µL of patient serum on a Widal glass slide and rocked for one minute. The result was reported as reactive or nonreactive based on the presence of macroscopic agglutination. The titre value indicated the slide agglutination results, which were categorised as reactive, weakly reactive, or nonreactive. In the tube agglutination test (titration), serum samples were serially diluted in tubes with anti-O and anti-H antibodies. The test tubes were then filled with equal O and H antigen drops. Antibody titres of 1:80 and higher for anti-O and 1:160 and higher for anti-H antibodies were used as a cutoff value to suggest a recent infection with typhoid fever based on the manufacturer's instructions.

3.8.2 Typhidot Test / Serological Testing

This quick card test employed the lateral flow chromatographic immunoassay concept on a nitrocellulose membrane with two test bands (the G and M bands) and a control band (C line). The test kit was acquired from Huichao medical (lianyungang) Company limited with catalogue number 202503993. Following the manufacturer's instructions, one drop (30–45 µL) of the patient's serum sample was dispensed into the sample well, and then one drop of sample diluent was added. After 15 minutes, the outcome was read. Where positive, the immunoglobulin (IgM) antibody indicated a current infection, and a positive IgG antibody demonstrated prior exposure to the infection. A positive IgM or IgG result was indicated by the formation of a pink to pink-purple colour band at the test region and the presence of the C-band. The presence of the C-band and the lack of any other coloured band indicated a negative outcome.

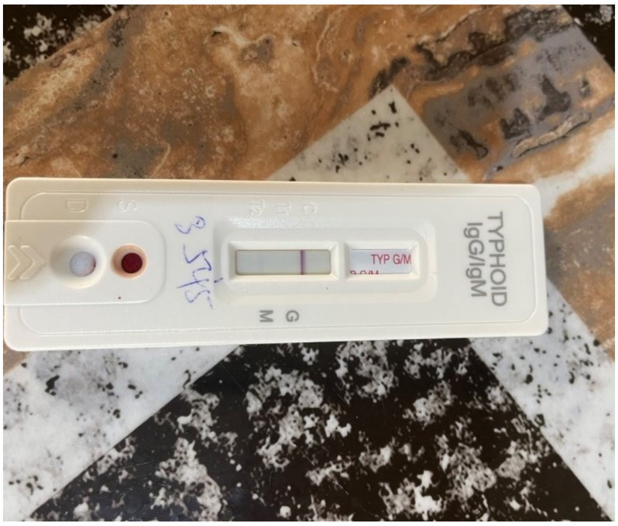

***Plate 3. 1*: Image of Typhidot test results of a selected sample**

3.8.3 Isolation and identification of *Salmonella Typhi* using Stool Culture Methods

Stool samples were inoculated into selenite broth and incubated at 37°C for 24 hours to enrich for the *Salmonella* species. Following incubation, the enriched samples were sub-cultured onto *Salmonella-Shigella* (SS) agar and incubated at 37 °C for an additional 24 hours. *Salmonella* colonies typically appear as colourless or pale colonies with black centres on SS agar due to hydrogen sulphide production.

Suspected colonies underwent further identification, involving biochemical testing using standard phenotypic microbiological techniques and were confirmed through serotyping with *Salmonella* type-specific antisera. Biochemical testing involved the use of standard assays, including triple sugar iron (TSI) agar, urease, indole, citrate utilisation, and motility tests. These tests helped in differentiating *Salmonella* species from other enteric bacteria by assessing their sugar fermentation patterns, gas and hydrogen sulphide production, enzyme activity, and motility characteristics. Serotyping was done using the slide-agglutination method. A smooth suspension of each isolate was mixed with Salmonella O and H antisera on a glass slide and gently rocked. Visible agglutination with the specific antisera confirmed the Salmonella serotype.

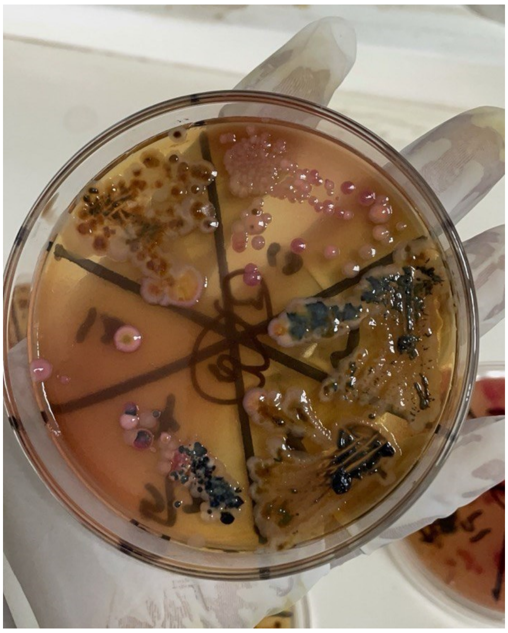

***Plate 3. 2*: Image of isolates**

3.9 Data Management Statistical Analysis

3.9.1 Data Management

The data collected from the study period was checked for completeness and consistency. The data was entered into a Microsoft Excel (version 2016) database and cleaned. Microsoft Excel 2016 was used for data organisation and preliminary processing in a spreadsheet. The clean dataset, derived from the survey data and laboratory results, was exported into IBM SPSS version 27.0 for comprehensive statistical analysis.

3.9.2 Statistical Analysis

The data were entered and analysed using the Statistical Package for the Social Sciences (SPSS), version 27.0. Descriptive statistics, such as frequencies and percentages, were used to estimate rates. The rates were calculated as the number of positive cases divided by the total number of cases, expressed as a percentage.

The diagnostic performance of the Typhidot and Widal tests were compared with that of the stool culture method, which serve as the gold standard for comparison. For each diagnostic method, 2×2 contingency tables were constructed to determine the number of true positives, false positives, true negatives, and false negatives.

Sensitivity, specificity, positive predictive value (PPV), and negative predictive values (NPV) were calculated for both Typhidot and Widal tests. Additionally, McNemar's test was used to assess the significance of the differences in paired proportions between each test and the gold standard. Cohen's kappa statistic was also computed to evaluate the level of agreement beyond chance between the diagnostic methods and the gold standard. In addition, inferential statistical methods, including cross-tabulation, the chi-square test of independence, and regression analysis, were used to assess the risk of typhoid fever among the participants. Specifically, the chi-square test of independence and binary logistic regression were applied to examine the association between typhoid fever infection and potential risk factors. Before conducting the logistic regression analysis, model fitness was evaluated using the Hosmer–Lemeshow goodness-of-fit test, with a *P-value* > 0.05 indicating a good fit (Assoah *et al.*, 2025). Furthermore, the Nagelkerke R^2 statistic and the model's classification accuracy were assessed to evaluate the explanatory power and predictive capability of the model.

For the multivariate logistic regression analysis, all variables with a *P-value* < 0.05 in the univariate analysis were considered for inclusion. Variables with more than two levels were treated as categorical variables and coded using dummy variables in SPSS (Assoah *et al*., 2025). Additionally, variables of known epidemiological relevance were retained in the final model regardless of their statistical significance. A *P-value* of less than 0.05 and a 95% confidence interval were used to determine statistical significance.

3.10. Ethical Review and Clearance

Ethical clearance for this study was acquired from the Korle Bu Teaching Hospital Institutional Review Board (KBTH IRB-STC 000108/2025). All participants were provided with detailed information regarding the study's purpose, procedures, potential risks, and benefits. Participation was entirely voluntary, and participants were informed of their right to withdraw from the study at any time without consequence. Informed consent was obtained from each participant by having them review and signa consent form before sample collection and study-related activities.

CHAPTER FOUR

RESULTS

4.0 Introduction

This section presents the results of the current study. The results of the analysis were presented in tables and figures, organised according to the specific objectives.

4.1 Demographic Characteristics of Study Participants.

The mean and median ages of the 234 participants were 31.7 and 31.9 years, respectively. Additionally, 40.6% of the participants were aged between 21 and 35 years, and 38.9% were above 35 years. Males constituted 52.1% and females were 47.9%. Most respondents identified as Christians (85.47%), followed by 11.97% who were Muslim, and 2.56% who identified as Traditional/Spiritualists. Based on their marital status, 48.7%, 44.9%, and 6.4% were married, single, and cohabiting, respectively. Regarding occupation, 29.5% were civil servants, 28.6% were students, and 22.2% were traders, while 2.1% and 6.4% were Farmers and retirees, respectively. Most of the participants (73.9%) had no medical health insurance. This information is presented in Table 4.1.

Table 4. 1: Sociodemographic characteristics of study participants

Variable	Frequency (n)	Percentage (%)
Median Age	**31.89**	
Mean Age	**31.72**	
Age group		
<12 years	10	4.27
12 to 20 years	38	16.24
21 to 35 years	95	40.60
> 35 years	91	38.89
Sex		
Male	122	52.14
Female	112	47.86
Religion		
Christian	200	85.47
Muslim	28	11.97
Traditional/Spiritualist	6	2.56
Marital status		
Married	114	48.72
Co habiting	15	6.41
Single	105	44.87
Occupation		
Farmer	5	2.14
Retired	15	6.41
Student	67	28.63
Trader	52	22.22
Civil servant	69	29.49
Unemployed	26	11.11
Health insurance		
Yes	61	26.07
No	173	73.93

(Source: Field Data, 2025)

4.2 Positivity Rates of Suspected Typhoid Fever Cases using Typhidot, Widal, and Stool Culture Methods.

Figure 4.1 shows that the Typhidot method detected 50.4% of all suspected typhoid cases as positive, whereas the Widal test detected 35.9% of cases, and the stool culture method detected 5.1% positive cases.

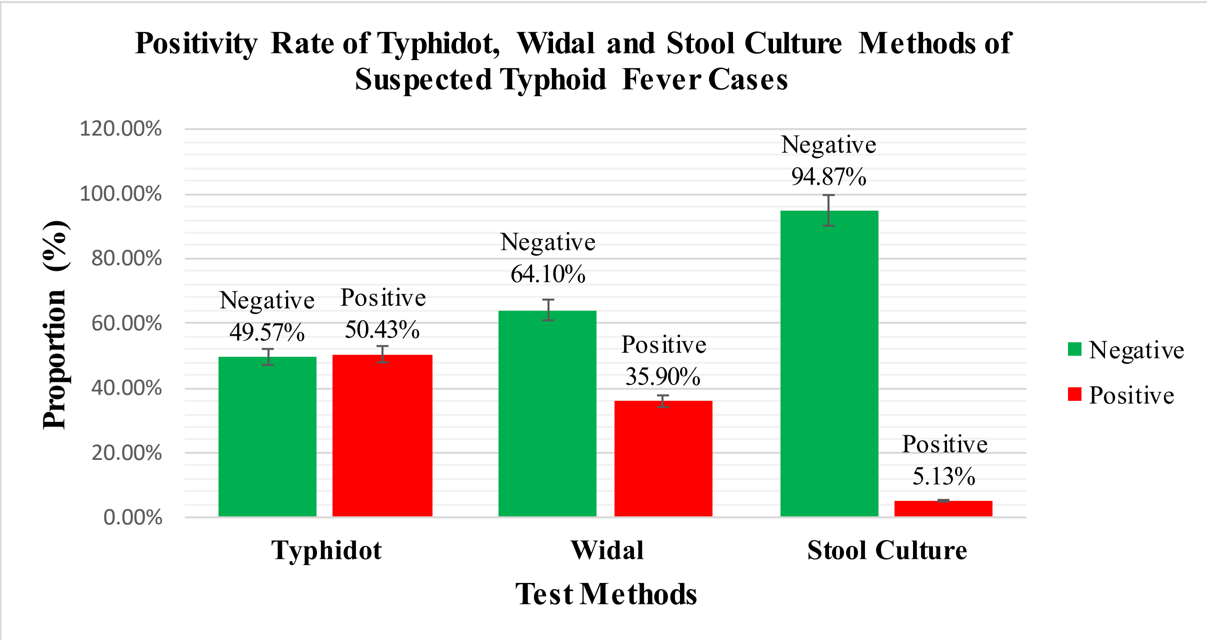

Figure 4. 1: Positivity Rate of Typhidot, Widal and Stool Culture Methods of Suspected Typhoid Fever Cases

4.3.0 Sensitivity, Specificity, PPV, and NPV of the Typhidot and Widal Tests in detecting Typhoid Fever using Stool Culture as the Gold Standard.

4.3.1 Concordance of Typhoid Fever cases Detection using Stool Culture, Typhidot, and Widal Methods

Table 4.2 illustrates the performance of the three laboratory tests used in detecting cases of typhoid fever. Out of the 234 suspected typhoid fever cases examined, 5% (12) were confirmed positive by stool culture. Stool culture results, compared with Typhidot and Widal tests, revealed varied patterns of concordance and discordance. Among the 12 culture-confirmed cases, 10 were positive for both Typhidot and Widal, while 2 cases were positive for Typhidot. All stool culture-positive cases were detected with both Typhidot and Widal tests. In contrast, among the 222 stool culture-negative cases, 100 tested positive with both Typhidot and Widal tests, whereas 6 cases that tested positive for Typhidot tested negative for Widal. Additionally, 66 stool culture-negative cases tested negative for both the Typhidot and Widal tests. However, 50 stool culture-negative cases tested positive for Typhidot and negative for Widal.

Table 4. 2: Cross-tabulation of Stool Culture, Typhidot, and Widal Test Results for Typhoid Diagnosis

Group	Stool Positive (n=12)	Stool Negative (n=222)	Total
Typhidot + / Widal +	10	100	110
Typhidot + / Widal –	2	6	8
Typhidot – / Widal +	0	50	50
Typhidot – / Widal –	0	66	66
Total	**12**	**222**	**234**

(Source: Field Data, 2025)

4.3.2 Comparison of Typhidot and Widal test with stool culture among suspected typhoid fever cases

Table 4.3 shows that of the 234 patients suspected of having typhoid fever, stool culture confirmed 12 as positive cases. On the other hand, the Typhidot test identified 118 positive cases, which included all 12-stool culture-confirmed positives, and correctly classified 116 cases as negative, consistent with the stool culture-negative results. In comparison, the Widal test detected 82 positive cases, including only 10 of the culture-confirmed positives, and reported 150 suspected cases as negative, most of which were also negative by stool culture. The Typhidot test detected all stool culture-confirmed cases (12) compared with 10 of 12 instances detected by the Widal test. Furthermore, the Typhidot test indicated 118 positive cases compared to 82 positive cases observed through the Widal test. In comparison with the stool, there were false negatives. In contrast, Widal test-positive case detection yielded fewer positive results among culture-negative patients, resulting in a larger number of negative outcomes (150 compared to 116 with Typhidot).

Table 4. 3: Comparison of the Typhidot test and Widal test with stool culture among suspected typhoid fever cases (N = 234)

Diagnostic Test	Stool Culture Positive n (%)	Stool Culture Negative n (%)	Total
Typhidot Positive	12 (10.2)	106 (89.8)	118
Typhidot Negative	0 (0.0)	116(100.0)	116
Total (Typhidot)	12 (5.1)	222 (94.9)	234
Widal Positive	10 (12.2)	72 (87.8)	82
Widal Negative	2 (1.3)	150 (98.7)	152
Total (Widal)	12 (5.2)	222 (94.8)	234

(Source: Field Data, 2025)

4.3.3 Distribution of Typhoid Cases by Typhidot, Widal Test, and Stool Culture

Table 4.4 indicates how the diagnostic outcomes were examined in combination across the three tests, revealing eight distinct groups among the 234 suspected cases. In Group A, 48 cases (21%) tested positive only with the Typhidot test, and in Group B, 14 cases (6%) tested positive only with the Widal test. Group C (0%) had no stool culture-positive cases. In Group AB, 58 cases (25%) tested positive for both Typhidot and Widal only. In Group AC, 2 (1%) individuals tested positive for both Typhidot and stool culture only, and in Group BC, there were no positive cases for both Widal and stool culture. Group ABC shows that 10 patients (4%) tested positive for all three diagnostic methods, whereas 102 patients (44%) tested negative for all three methods.

Table 4. 4: Distribution of Typhoid Cases by Typhidot, Widal Test, and Stool Culture Results (N = 234)

Group	Diagnostic Combination	n (%)
I	Typhidot positive only	48 (21)
II	Widal positive only	14 (6)
III	Stool culture is positive only	0 (0)
IV	Typhidot + Widal positive (Stool negative)	58 (25)
V	Typhidot + Stool positive (Widal negative)	2(1)
VI	Widal + Stool positive (Typhidot negative)	0 (0)
VII	Positive on all three tests	10 (4)
VIII	Negative on all three tests	102 (44)
Total		**234 (100)**

(Source: Field Data, 2025)

4.3.4 Sensitivity, Specificity of Widal and Typhidot Tests Compared to Stool Culture (Gold Standard)

In **Table 4.5,** Typhidot was 100% sensitive (95% CI: 73.5–100) in detecting all confirmed stool culture-positive cases, while Widal was 83.3% sensitive (95% CI: 62.2–100) in detecting 10 out of 12. The Widal test demonstrated a specificity of 32.4% (95% CI: 26.6–38.8), indicating that 150 (64%) false positives occurred. Its positive predictive value (PPV) was only 6.3% (95% CI: 4.7–15.6), while the negative predictive value (NPV) was 97.3% (95% CI: 96.9–100). Overall accuracy was 35.0%, with a χ^2 value of 4.20 (p = 0.040), and the ROC/AUC was 0.57, reflecting poor discriminatory ability. In contrast, Typhidot performed somewhat better. Its specificity was 52.3% (95% CI: 45.7–58.7) and PPV 10.2% (95% CI: 5.9–16.9), while maintaining an NPV of 100% (95% CI: 98.3–100). The overall accuracy reached 54.7%, with a χ^2 value of 10.43 (p = 0.0012). However, its ROC/AUC was 0.55, like that of Widal, and still indicative of limited diagnostic utility.

Table 4.5: **Diagnostic Performance of Widal and Typhidot Tests Compared to Stool Culture (Gold Standard) 95% CI;**

Test	TP	FP	TN	FN	Sensitivity	Specificity	PPV	NPV	Accuracy	χ^2 (*P-value*)	ROC/AUC
Widal	10	150	72	2	83.3% (62.2–100)	32.4% (26.6-38.8)	6.3% (4.7-15.6)	97.3% (93.6–100)	35.0%	4.20 (p=0.040)	0.57
Typhidot	12	106	116	0	100% (73.5–100)	52.3% (45.7-58.7)	10.2% (5.9-16.9)	100% (98.3–100)	54.7%	10.43 (p=0.0012)	0.55

Key: TP= True Positive, FP=False Positive, TN= True Negative, FN= False Negative, PPV= Positive Predictive value, NPV= Negative Predictive Value, χ^2 = Chi-square, ROC/AUC= Receiver Operating Characteristic Value/Area Under the Curve

(Source: Field Data, 2025)

4.3.5 Agreement Between Typhidot and Widal Tests

The level of agreement between the Typhidot and Widal diagnostic tests for typhoid fever was assessed using Cohen's kappa statistic. Table 4.6 shows that the observed proportion of agreement between the two tests was 73.50%, while the agreement expected by chance alone was 49.88%. The kappa coefficient was 0.4714 (SE = 0.0626), indicating a moderate agreement between the two methods according to the Landis and Koch interpretation scale. This agreement was statistically significant ($Z = 7.53$, $p < 0.001$), indicating that the concordance observed was unlikely to be due to chance.

Table 4. 6: **Agreement between the Typhidot test and the Widal test in detecting Typhoid fever cases**

Statistic	Value	95% CI	Interpretation
Observed agreement (%)	73.50	–	
Expected agreement (%)	49.88	–	
Kappa	0.4714	0.348 – 0.595	Moderate agreement
Standard error	0.0626	–	
Z	7.53	–	
P-value	<0.001	–	Statistically significant

(Source: Field Data, 2025)

4.4.0 Association Between Socio-Demographic, Medical History, Personal Hygiene and Antibiotic Use and Typhoid Fever Infection.

4.4.1 Association between Socio-Demographic Factors and Typhoid Fever Infection

Table 4.7 shows there is no significant associations between age ($\chi^2 = 0.198, p = 0.978$), gender ($\chi^2 = 0.150, p = 0.699$), religion ($\chi^2 = 0.812, p = 0.666$), marital status ($\chi^2 = 0.199, p = 0.928$), and health insurance status ($\chi^2 = 0.005, p = 0.943$) and the likelihood of testing positive for typhoid fever.

Table 4. 5: **Association between Socio-Demographic Factors and Typhoid Fever Infection**

Factors	Positive Typhidot(%)	Independence X^2	*P-value*
Age			
< 12 Years	5(50.0)	0.198	0.978
12-20 Years	18(47.4)		
21-35 Years	48(50.5)		
> 35 Years	47(51.6)		
Gender			
Male	63(51.6)	0.150	0.699
Female	55(49.1)		
Religion			
Christian	101(50.5)	0.812	0.666
Muslim	13(46.4)		
Traditionalist	4(66.7)		
Marital Status			
Married	59(51.8)	0.199	0.928
Divorced/Widowed	7(46.7)		
Single	52(49.5)		
Health Insurance Status			
Not Insured	31(58.8)	0.005	0.943
Insured	87(50.3)		

(Source: Field Data, 2025)

4.4.2 Association Between Symptoms and Typhoid Fever Infection

Table 4.8 and table 4.9 shows that fever, headache, vomiting, diarrhoea, body weakness, loss of appetite, and abdominal pain were not significantly associated with the likelihood of testing positive for typhoid fever. For example, fever ($\chi^2 = 0.983$, $p = 0.321$) and headache ($\chi^2 = 0.187$, $p = 0.665$) did not show significant differences in the likelihood of testing positive. Furthermore, abdominal pain ($\chi^2 = 2.627$, $p = 0.105$) and body weakness ($\chi^2 = 1.787$, $p = 0.181$) did not reach statistical significance either. However, individuals with a history of being diagnosed with typhoid fever were significantly more likely to test positive (AOR = 2.059, 95% CI [1.12, 3.18], $p = 0.008$).

Table 4. 6: **Association between symptoms and typhoid fever infection**

Symptoms	**Positive Typhidot(%)**	**X^2 (*P-value*)**	**COR (95%CI) *P-value***	**AOR (95%CI) *P-value***
Fever				
No	3(75.0)	0.983 (0.321)	Ref:	
Yes	115(50.0)		0.47 (0.03, 6.53) 0.577	0.47(0.03,6.53)0.57
Headache				
No	3(60.0)	0.187 (0.665)	Ref:	
Yes	115(50.2)		0.67 (0.11, 4.10) 0.67	0.67(0.11,4.10)0.670
Vomit				
No	46(48.4)	0.258 (0.612)	Ref:	
Yes	72(51.8)		1.10(0.834,1.97)0.164	2.11(0.44,10.03)0.348
Diarrhoea				
No	30(44.1)	1.527 (0.217)	Ref:	
Yes	88(53.0)		1.56(0.83,2.92)0.170	0.254(0.044,1.47)0.126
Body weakness				
No	4(80.0)	1.787 (0.181)	Ref:	
Yes	114(49.8)		0.25 (0.27, 2.25) 0.248	2.557(0.021,9.29)0.943

(Source: Field Data, 2025)

Table 4.9: **Association between symptoms and typhoid fever infection (Con't)**

Symptoms	**Positive Typhidot(%)**	**X^2 (*P-value*)**	**COR (95%CI) *P-value***	**AOR (95%CI) *P-value***
Loss of appetite				
No	41(46.6)	0.830 (0.362)	Ref:	
Yes	77(52.7)		1.27(0.71,2.25)0.419	0.279(0.055,1.411)0.123
Abdominal pain				
No	10(71.4)	2.627 (0.105)	Ref:	
Yes	108(49.1)		0.38 (0.10, 1.42) 0.152	0.625(0.283,1.380)0.0.244
Diagnosed with typhoid in past				
No	49(41.5)	7.546 (**0.006**)	Ref:	1.575(0.339,7.310)0.562
Yes	69(59.5)		2.059 (1.12, 3.18) **0.008**	

4.4.3 Association between Personal Hygiene Practices and Typhoid Fever Infection

Table 4.10 shows that handwashing before eating ($\chi^2 = 0.987$, $p = 0.320$), using soap ($\chi^2 = 0.282$, $p = 0.596$), and using different toilet facilities ($\chi^2 = 1.849$, $p = 0.39$) were not significantly associated with testing positive for typhoid fever. The consumption of raw foods (e.g., salad, fruits, or eggs) and drinking water sources (e.g., sachet water, bottled water) also did not show significant associations with typhoid fever infection. For example, the use of water from sachets (51.8% positive) was not significantly associated with testing positive ($\chi^2 = 1.803$, $p = 0.406$).

Table 4. 7*:* Personal hygiene practices and typhoid fever infection

Factors	**Positive Typhidot (%)**	**Independence X^2**	***P-value***
Wash your hands before eating.			
No	1(100)		
Yes	117(50.2)	0.987	0.320
Wash your hands with soap.			
No	31(53.4)		
Yes	87(49.4)	0.282	0.596
Toilet facility used			
Water closet	62(46.6)	1.849	0.39
KVIP	31(54.4)		
None	25(56.8)		
Wash your hands after using the washroom.			
No	1(100)		
Yes	60(48.8)	1.063	0.588
Sometimes	57(51.9)		
Cutting of fingernails			
Regularly	23(51.1)	0.010	0.919
Sometimes	95 (50.3)		
Primary source of drinking water			
Pipe/well/Stream	30(50.0)	1.803	0.406
Bottle	3(30.0)		
Sachet	88(51.8)		
Eat salad/fruits/eggs.			
No	6(54.5)	0.078	0.768
Yes	112(50.0)		
Eat sausage/kebab/pork.			
No	18(45.0)	0.596	0.453
Yes	100(51.5)		
Bite figure nails			
No	23(41.5)	0.741	0.389
Yes	95(51.9)		
Drink raw/unpasteurized milk			
No	55(47.4)	0.836	0.361
Yes	63(53.4)		

(Source: Field Data, 2025)

4.4.4 Antibiotic Use and Typhoid Fever Infection

Table 4.11 and **Table 4.12** shows that a prior typhoid diagnosis was significant, $\chi^2(1) = 6.83$, $p = .006$; AOR = 1.99, 95% CI [1.19, 3.34], $p = .009$. The diagnostic method mattered, with Typhidot-diagnosed cases having higher odds of positivity than those diagnosed with Widal, AOR = 23.65, 95% CI [1.88, 297.34], $p = .014$. Antibiotic use showed no chi-square significance, $\chi^2(1, N = 234) = 0.00$, $p = .982$; however, logistic regression indicated increased odds, AOR = 1.84, 95% CI [0.72, 5.76], $p = .020$. The type of antibiotic used was not a significant factor. Treatment duration of 5–7 days was associated with reduced odds, AOR = 0.01, 95% CI [0.001, 0.53], $p = .026$. Self-medication was nonsignificant, $\chi^2(1, N = 234) = 2.10$, $p = .147$; AOR = 2.87, 95% CI [0.61, 13.56], $p = .184$. The frequency of self-medication showed a trend, with an AOR of 17.77, 95% CI [0.76, 414.70], $p = .073$. Awareness of self-medication effects, χ^2 (1, N = 234) = 0.57, $p = .449$, and treatment-seeking factors were not significant.

Table 4. 8: **Association of antibiotic use and typhoid fever infection**

Factors	**Positive Typhidot (%)**	**X² (*P-value*)**	**COR (95% CI) *P-value***	**AOR (95% CI) *P-value***
Diagnosed with typhoid fever before				
No	48(41.7)	6.828(0.006)	Ref.	
Yes	70(58.8)		1.994(1.185,3.335)0.009	0.47(0.03,6.53)0.577
Method used for diagnosis				
Widal test	5(100)	5.243(0.073)	Ref.	
Typhidot test	7(77.8)		2.013(2.012, 2.019)0.240	23.646(1.880,297.34)**0.014**
Not sure	58(55.8)			
Used Antibiotic				
No	3(60.0)	0.001(0.982)	Ref.	
Yes	69(59.5)		0.979(0.157,6.084) 0.979	1.842(0.723,5.763)**0.020**
Type of antibiotic used				
Azithromycin	9(90.0)	6.367(0.173)	Ref.	
Amoxicillin	8(66.7)		0.123(0.11,1.023) 0.053	2.041(0.723,5.763)0.178
Ciprofloxacin	7(63.6)			
Ceftriaxone	1(33.3)			
None	40(52.6)			

(Source: Field Data, 2025)

Table 4. 12: **Association of antibiotic use and typhoid fever infection (Con't)**

Factors	**Positive Typhidot (%)**	**X^2 (*P-value*)**	**COR (95% CI) *P-value***	**AOR (95% CI) *P-value***
The treatment duration of antibiotics				
<5 days	38(60.3)	1.347(0.510)	Ref.	
5-7 days	23(52.3)		0.537(0.042,6.845)0.32	0.005(0.001,0.532)0.026
8-14 days	1(33.3)			
Self-medication				
No	16(40.0)	2.099(0.147)	Ref.	
Yes	102(52.6)		0.974(0.73,12.917)0.974	2.866(0.606,13.558)0.184
Frequency of self-medication				
Often	13(36.1)	7.289(0.026)	Ref.	
Sometimes	68(48.6)		3.275(0.292,36.732)0.336	17.766(0.761,414.7)0.073
Never	37(63.8)			
Awareness of effect of self-medication				
No	110(51.2)	0.573(0.449)	Ref.	
Yes	8(42.1)		0.770(0.284,2.085)0.607	1.603(0.465,5.529)0.455

(Source: Field Data, 2025)

CHAPTER FIVE

DISCUSSION

5.0 Introduction

This chapter presents a critical interpretation of the findings reported in Chapter Four, relating them to the study's objectives and situating them within the existing empirical and theoretical literature. The study compared the diagnostic performance of the Typhidot and Widal serological tests with stool culture, which served as the gold standard, in detecting typhoid fever among patients at the Korle-Bu Teaching Hospital in Accra. Additionally, the study examined the associations between socio-demographic factors, clinical symptoms, personal hygiene practices, and antibiotic use with the likelihood of testing positive for typhoid fever.

5.1 Demographic Characteristics of Study Participants

Most participants were young to middle-aged adults, particularly those between 21–35 years and those above 35 years. This age pattern is consistent with findings reported in other studies in Ghana, where typhoid fever disproportionately affects the economically active population(Konkor, 2023) Studies conducted in settings such as Accra, Kumasi, and the Bono Region similarly observed higher suspicion or diagnosis of typhoid among adults in their productive years, largely due to increased exposure to contaminated water, food sources, and crowded environments typical of workplaces and urban social activities (Thalia, 2024). This supports the assertion that adults face greater risk because of occupational mobility and higher likelihood of consuming food prepared outside the home.

Sex distribution in this study showed a slightly higher proportion of males than females, a trend that aligns with several Ghanaian investigations reporting marginal male predominance among suspected typhoid cases explanations include gender differences in occupational exposure, where men often work in environments with increased contact with unsafe water and food sources. However, some local studies have reported no significant sex differences (Biswas *et al.*, 2021).suggesting that in endemic settings, exposure risk affects both males and females relatively equally.

Religious affiliation in the present study was dominated by Christians, reflecting Ghana's national religious composition rather than any epidemiological association with typhoid fever. Marital status was almost evenly distributed between married and single individuals, consistent with earlier studies that found no strong link between marital status and typhoid risk (Siddique *et al.*, 2024). This reinforces the notion that environmental and behavioral determinants rather than household or social structure play a more significant role in shaping typhoid exposure in endemic regions.

Occupationally, a substantial proportion of participants were students, traders, and civil servants. Similar occupational patterns have been observed in studies from Kumasi and Tamale, where students and workers frequently appeared among typhoid-suspected or confirmed cases. These groups often depend on commercial food vendors, a recognized risk factor for typhoid transmission in urban Ghana due to inconsistent food hygiene and challenges with water quality. Farmers and retired individuals were less represented, likely reflecting their relatively lower reliance on urban food vending systems(Boakye Okyere *et al.*, 2024).

Health insurance status also revealed an important public health implication. Only a minority of participants had active insurance coverage, while most were uninsured. Other Ghanaian studies have similarly reported low insurance coverage among febrile patients, particularly in peri-urban or low-income communities and this pattern may delay healthcare seeking and increase reliance on presumptive diagnostic methods such as Widal and Typhidot, which are commonly used in resource-limited settings(Sigamoney & Singh, 2023).

Overall, the demographic profile observed in this study mirrors earlier Ghanaian research, showing that typhoid suspicion and diagnosis commonly involve young to middle-aged adults, slightly more males than females, and occupational groups with greater exposure to unsafe water and food sources. These consistencies reaffirm that typhoid fever in Ghana remains a significant public health concern affecting individuals with high environmental exposure and limited access to safe water, sanitation, and timely diagnostic services.

5.2 Positivity Rates of Typhidot, Widal, and Stool Culture

The present study found substantial variation in positivity rates across the three diagnostic methods employed. The Typhidot method identified a much larger proportion of suspected cases as positive compared to the Widal test, while stool culture the gold standard confirmed only a very small fraction as true infections. This pattern underscores a critical diagnostic dilemma in Ghana and similar endemic regions, where rapid serological tests frequently overestimate the true prevalence of typhoid fever.

5.2.1 Overestimation by Serological Tests

The high positivity rate of Typhidot and Widal compared to stool culture is consistent with evidence from other endemic regions. In Ghana, Widal positivity rates have been reported at over 60%, whereas stool culture positivity often remains below 10% (Domfeh *et al.*, 2023). Similarly, in India, (Nirmal *et al.*, 2023) reported Widal test positivity rates exceeding 17% compared with culture-confirmed cases of less than 1%. This suggests that serological assays may be detecting cross-reacting antibodies rather than true infections, particularly in areas with overlapping endemic diseases such as malaria, brucellosis, and non-typhoidal salmonellosis.

Typhidot's detection of half of all suspected cases is particularly striking. While the test is designed to identify IgM and IgG antibodies to *Salmonella Typhi*, the persistence of IgG antibodies from previous infections or vaccinations may inflate positivity rates. In Ghana, where recurrent exposure to contaminated food and water is a daily occurrence, antibody persistence can complicate the interpretation of Typhidot results. (Sam *et al*., 2024). It is noted that in endemic sites, Typhidot positivity may represent past exposure rather than acute infection, raising concerns about misdiagnosis, unnecessary antibiotic use, distorted surveillance data, and poor resource allocation, ultimately weakening effective typhoid control and public health decision-making.

5.2.2 The Reliability of Stool Culture

Stool culture identified only 12 out of 234 suspected cases (5.1%) as true positives. This low detection rate aligns with evidence that culture-based methods are less sensitive in stool than in bone marrow or blood specimens (Misra & Powell, 2024). The limited yield of stool cultures may be attributed to prior antibiotic use among patients, improper sample collection, and the intermittent shedding of bacteria in faeces during infection. Metreveli *et al*. (2022) emphasise that stool culture, while specific, may underestimate acute infection when compared to bone marrow culture, which is rarely feasible in resource-constrained settings. Nevertheless, the culture-confirmed prevalence reported here is consistent with Ghanaian epidemiological data, where confirmed typhoid rates typically range below 10% in febrile populations (Domfeh *et al*., 2023). This highlights the need to interpret serological positivity with caution, as overestimation can distort public health surveillance figures and lead to misallocation of resources.

5.2.3 Implications for Prevalence Estimation in Ghana

The discrepancy between serological and culture results has significant implications for estimating disease burden. In Ghana, reliance on Widal and, increasingly, Typhidot in primary and secondary healthcare facilities means that many patients are misclassified as typhoid positive. This inflates prevalence rates and complicates the interpretation of surveillance data. Misdiagnosis not only contributes to unnecessary treatment but also obscures the accurate epidemiological profile of typhoid fever in the country.

Studies in Accra and Kumasi have highlighted this challenge. For instance, Ipadeola *et al*. (2024) observed that in urban Ghana, Widal-based prevalence estimates often exceeded 30%, whereas stool cultures confirmed less than 10% of suspected cases. Such discrepancies are problematic for public health planning, as they overstate the burden of typhoid relative to other febrile illnesses, particularly malaria, which remains the leading cause of fever in Ghana (Kungu *et al*., 2025).

5.2.4 Clinical and Public Health Risks of False Positives

From a clinical perspective, high positivity rates of serological tests carry significant risks. False positives may lead to unnecessary antibiotic prescriptions, exposing patients to drug side effects and antimicrobial resistance. In Ghana, fluoroquinolone and third-generation cephalosporin resistance in *Salmonella Typhi* has already been reported (Sarkodie-Addo *et al*., 2025). Overdiagnosis exacerbates this problem by increasing inappropriate antibiotic use. Furthermore, false positives may delay the diagnosis of alternative causes of fever, such as malaria, viral hepatitis, or urinary tract infections, leading to poorer patient outcomes. Misdiagnosis also imposes economic burdens on families, as patients may spend scarce resources on unnecessary treatments.

For uninsured patients, who made up nearly three-quarters of the respondents in this study, this represents a significant financial strain.

5.2.5 Comparison Between Typhidot and Widal Positivity

Although both tests overestimated prevalence, Typhidot detected a substantially higher proportion of positives than Widal (50.4% vs. 35.9%). This finding supports the evidence that Typhidot had 35.5% and Widal had 24% (R. Singh & G. Singh, 2021). This means Typhidot had a higher sensitivity Notably, Widal's lower sensitivity may reflect its reliance on antibody titres that take longer to rise after infection, whereas Typhidot can detect antibodies as early as four days post-infection (Takaya, 2024). Nevertheless, neither test offers an accurate picture of current infection in endemic contexts, reinforcing the need for culture-based confirmation.

5.3 Diagnostic Performance of Typhidot and Widal

The results of this study, which found that Typhidot demonstrated higher sensitivity than Widal but both tests showed poor specificity and positive predictive value against stool culture, are consistent with findings from other investigations in Ghana reported that although Widal showed relatively high sensitivity (81.8%), its specificity (29.3%) and PPV (7.1%) were extremely low, indicating significant overestimation of typhoid cases (Tegene & Eshetie, 2025). Also, another similar study documented low Widal sensitivity and specificity reinforcing its poor diagnostic accuracy in endemic populations.Sam *et al.* (2024) observed typhidot had sensitivity and specificity values of 35% and 45%, respectively, when compared with combined culture methods, concluding that Typhidot was also unreliable as a standalone diagnostic tool. Broader reviews of rapid serological assays further note that although Typhidot may perform slightly better than Widal in terms of sensitivity, its specificity remains inadequate in endemic settings. Collectively, these external findings support the present study's conclusion that both Typhidot and Widal tests lack sufficient accuracy for effective clinical decision-making in Ghana

5.3.1 Sensitivity, Specificity, and Predictive Values

The Typhidot test demonstrated a sensitivity of 100%, correctly identifying all 12-stool culture-confirmed cases of typhoid fever. This indicates that the test is highly effective at detecting true positives, making it a valuable tool for screening suspected cases. In contrast, the Widal test achieved a sensitivity of 83.3%, identifying 10 out of 12 culture-confirmed cases. Although still relatively high, Widal's lower sensitivity compared to Typhidot increases the risk of false negatives, which could result in missed diagnoses and delayed treatment. However, sensitivity alone is insufficient to evaluate diagnostic performance. Specificity results reveal significant limitations. Typhidot had a specificity of 52.3%, while Widal's specificity was even lower at 32.4%. The high sensitivity of Typhidot observed in this study is consistent with reports from other endemic settings, where Typhidot has been shown to detect a greater proportion of true typhoid cases than Widal. A study found that although Typhidot sensitivity was lower (35%) when compared with combined culture methods, it still outperformed Widal in detecting confirmed infection(Ousenu, Ali, Sama, Ndam, Tchouangueu, & Tume, 2021). Widal often produces moderate to low sensitivity (81.8% and 40.9%, respectively), reinforcing its tendency to miss true case an observation that aligns with its lower sensitivity (83.3%) in the present study.

The positive predictive values (PPVs) of both tests were notably low: 10.2% for Typhidot and 6.3% for Widal. In practice, this means that fewer than one in ten patients who tested positive with these serological assays were truly infected with typhoid fever. Such poor predictive capacity highlights the risk of overdiagnosis and overuse of antibiotics in endemic regions where these tests are widely employed. By contrast, the negative predictive values (NPVs) of Typhidot and Widal were 100% and 97.3%, respectively. These high NPVs suggest that both tests are relatively reliable at ruling out typhoid fever when results are negative, although Typhidot performs slightly better. These findings relate to previous studies. For instance, (R. Singh & G. Singh, 2021) reported that Typhidot had higher sensitivity than Widal but was compromised by low specificity in endemic regions. Similarly, (Tegene & Eshetie, 2025) found that the Widal test had poor specificity and produced numerous false positives in India. In Ghana, (Abduljalil *et al*., 2024) highlighted that Typhidot and Widal produced inflated positivity rates when compared to stool culture, reinforcing the limitations observed in this study.

From a clinical standpoint, these results suggest that Typhidot may be preferable to Widal as a screening tool, given its superior sensitivity and NPV. However, its low specificity and PPV prevent it from being used as a confirmatory test. Clinicians who rely solely on Typhidot risk diagnosing many uninfected patients with typhoid, leading to overtreatment. This highlights the crucial role of stool culture in confirming a diagnosis, despite its higher cost and resource requirements.

5.3.2 Accuracy and ROC/AUC

The findings of this study show that Typhidot demonstrated better overall diagnostic accuracy than the Widal test, correctly classifying a greater proportion of cases. However, despite this relative advantage, both tests still fell short of the reliability required for confident clinical decision-making, underscoring their limitations as standalone diagnostic tools.

The ROC/AUC (Receiver Operating Characteristic/Area Under the Curve) analysis further underscores the limited diagnostic utility of both tests. Typhidot achieved an AUC of 0.55, while Widal recorded an AUC of 0.57. In diagnostic science, an AUC value of 0.5 suggests a test performs no better than chance, while values above 0.7 are considered acceptable, and those above 0.9 reflect excellent discrimination (Staartjes & Kernbach, 2021). Both Typhidot and Widal, with AUCs only slightly above 0.5, fall into the category of poor discriminatory tests. These findings are comparable to that of Tegene and Eshetie (2025) who noted that the Widal test, despite its historical use, often performs poorly in endemic regions due to cross-reactivity with other infections. Typhidot, although somewhat better, also exhibits limited discriminative power in practice. The similarity in ROC/AUC values suggests that, despite Typhidot's advantage in sensitivity, its overall diagnostic reliability remains comparable to that of Widal, and both are inadequate substitutes for stool or blood culture.

Clinically, the poor ROC/AUC values imply that these tests cannot reliably distinguish between actual cases of typhoid fever and other febrile illnesses common in Ghana. This diagnostic weakness complicates case management, particularly in regions where malaria, viral hepatitis, and other bacterial infections produce overlapping symptoms.

Patients may therefore be misclassified, leading to inappropriate treatment regimens and delayed identification of the actual underlying illness.

5.3.3 Implications for Diagnostic Pathways in Ghana

The diagnostic performance highlights a pressing dilemma for Ghana's healthcare system. Although serological tests such as Typhidot and Widal are widely accessible, inexpensive, and rapid, making them attractive in resource-limited settings, their poor specificity, PPV, and overall accuracy compromise their reliability and contribute to systemic misdiagnosis. Furthermore, while this study suggests that Typhidot may have a role as a preliminary screening tool in suspected cases of typhoid fever, particularly in primary healthcare settings where culture is unavailable, reliance on Typhidot or Widal alone for definitive diagnosis is not advisable. Confirmatory testing, such as stool or blood culture, remains indispensable for accurate diagnosis and effective treatment. Strengthening laboratory capacity to conduct culture-based diagnostics in Ghanaian hospitals is therefore an urgent priority. Moreover, given that nearly three-quarters of participants lacked health insurance, the affordability and accessibility of gold-standard diagnostics continue to be a challenge. This reinforces the importance of health policy interventions aimed at expanding insurance coverage and subsidising culture-based diagnostics to ensure equitable access to reliable diagnostic services.

5.4 Agreement Between Diagnostic Methods

A key objective of this study was to assess the level of agreement between the Typhidot and Widal diagnostic tests for the diagnosis of typhoid fever. The results revealed a moderate agreement ($\kappa = 0.4714$, SE = 0.0626, $p < 0.001$) between the two serological methods. The proportion of agreement was 73.5%, while the expected agreement by chance alone was 49.9%. These results indicate that Typhidot and Widal occasionally classify patients similarly, but their concordance is far from strong or consistent.

5.4.1 Interpretation of Cohen's Kappa

Cohen's kappa statistic is widely used to measure inter-test or inter-rater reliability, adjusting for agreement that might occur by chance. According to the Landis and Koch (1977) scale, a kappa value between 0.41 and 0.60 is considered moderate agreement, 0.61–0.80 as substantial, and above 0.81 as almost perfect. Thus, the kappa value obtained in this study places Typhidot and Widal within the "moderate agreement" range, suggesting that while they do not produce completely divergent results, their overlap is insufficient to imply equivalence. This finding has clinical implications. Moderate agreement suggests that the two tests may occasionally reinforce each other in diagnostic practice; however, their inconsistencies indicate that one cannot be substituted for the other. More importantly, neither can replace stool culture as the gold standard for typhoid confirmation.

The results of this study are consistent with findings from other endemic regions. Ousenu, Ali, Sama, Ndam, Tchouangueu, Tume, *et al.* (2021) observed a moderate agreement between Typhidot and Widal, but emphasised that this concordance was not strong enough to validate their joint use as substitutes for culture. Similarly, Pasha *et al.* (2025) found a kappa of 0.43 between Widal and Typhidot, again reflecting moderate agreement. These studies collectively highlight that while both tests may occasionally align, their variability undermines diagnostic reliability.

In Ghana, few studies have formally evaluated kappa statistics between Typhidot and Widal. However, anecdotal evidence from clinical practice suggests that there are frequent discrepancies between the two methods, leading to confusion in case management. For example, patients who test positive on one test but negative on the other may still be treated presumptively for typhoid, reflecting clinician reliance on serological outcomes in the absence of culture. This practice amplifies the risks of misdiagnosis and inappropriate treatment.

5.4.4 Implications for Public Health Surveillance

Beyond individual patient management, discordance between Typhidot and Widal undermines the reliability of surveillance data. In many Ghanaian health facilities, Widal remains the primary diagnostic tool, while Typhidot is increasingly being adopted where resources allow. If these tests produce discordant results in a significant proportion of cases, aggregated prevalence figures derived from health facility data will be inconsistent and misleading. Overestimation of prevalence by either or both tests could inflate the perceived burden of typhoid fever, while underestimation in certain contexts might mask outbreaks.

5.4.5 Policy and Clinical Considerations

The moderate agreement observed in this study emphasises the need for diagnostic algorithms that incorporate confirmatory culture testing. While resource limitations make universal culture testing challenging, a tiered approach may be a feasible alternative. For example, Typhidot could serve as an initial screening tool given its higher sensitivity, while culture confirmation could be prioritised for cases with discordant Typhidot and Widal results or for patients not responding to empirical treatment. Such an approach would optimise resource use while enhancing diagnostic accuracy. Again, the findings underscore the need for clinicians to receive training on the interpretation of serological results. Awareness of the limitations and discordance of Typhidot and Widal can inspire more cautious diagnostic decision-making, reducing reliance on single-test outcomes and prompting further investigation when necessary.

5.5 Association Between Risk Factors and Typhoid Infection

One objective was to study the link between selected socio-demographic variables, clinical symptoms, personal hygiene practices, and antibiotic use with the likelihood of testing positive for typhoid fever. This analysis offers insight into the broader epidemiology of typhoid in Ghana and helps to contextualise diagnostic outcomes.

5.5.1 Socio-Demographic Factors

The study revealed that socio-demographic variables, including age, sex, marital status, religion, and health insurance status, were not significantly associated with testing positive for typhoid fever. For example, positivity rates were similar across different age groups: 50.5% among those aged 21–35 years and 51.6% among those aged 35 years or older. Likewise, males and females recorded nearly identical positivity rates (51.6% and 49.1%, respectively). These findings indicate that demographic attributes may not solely or necessarily drive typhoid fever in Ghana. Environmental and infrastructural conditions expose the entire population to risk. Emanche (2022), for example, argues that in endemic regions, typhoid is more strongly associated with unsafe water supplies, inadequate sanitation, and food contamination than with individual demographic characteristics. The present study reinforces this view, suggesting that regardless of age, sex, or social status, individuals in Ghana remain vulnerable to typhoid if they are exposed to contaminated environments.

The lack of significant association with religion or marital status further highlights that typhoid transmission transcends sociocultural divisions. While one might hypothesise that married individuals or households with more stable living conditions would face a reduced risk, the findings here indicate otherwise. This could be due to widespread contamination in urban sites such as Accra, where even households that practice good hygiene cannot fully escape exposure to unsafe water or food (Kwarteng *et al.*, 2025).

The lack of a significant difference based on health insurance status is also of interest. While uninsured patients may face barriers to healthcare access, this study found no association between insurance coverage and infection. This suggests that typhoid exposure is widespread, and health insurance does not protect against environmental factors that contribute to infection. However, as discussed earlier, insurance status likely influences the diagnostic methods patients can afford, shaping clinical pathways rather than infection risk.

5.5.2 Clinical Symptoms

Another important finding was that common clinical symptoms were not significantly associated with confirmed typhoid fever. Symptoms such as fever ($\chi^2 = 0.983$, $p = 0.321$), headache ($\chi^2 = 0.187$, $p = 0.665$), abdominal pain ($\chi^2 = 2.627$, $p = 0.105$), diarrhoea, and vomiting showed no statistical significance in predicting typhoid infection. This reflects one of the enduring challenges of typhoid diagnosis: its clinical presentation overlaps extensively with other febrile illnesses. Malaria, viral hepatitis, and a range of gastrointestinal infections present with similar symptoms, making clinical diagnosis unreliable. Boakye Okyere *et al.* (2024) emphasise that clinical diagnosis of typhoid is nearly impossible without laboratory confirmation, especially in sub-Saharan Africa, where malaria co-endemicity is high. However, a notable exception in this study was the finding that individuals with a history of previous typhoid diagnosis were significantly more likely to test positive again (AOR = 2.059, 95% CI [1.12, 3.18], $p = 0.008$). This could reflect reinfection, given the persistence of environmental risk factors, or false positives resulting from antibody persistence, particularly in Typhidot testing. Typhidot detects both IgM and IgG antibodies, and the presence of IgG from past infections may contribute to higher positivity among those with prior diagnoses. These finding relates to earlier work in India, where individuals with a history of typhoid were more likely to test positive on serological assays despite culture negativity (Najib *et al*., 2021). These results highlight the limitations of relying on symptoms or history for diagnosis. In Ghana, where presumptive treatment based on symptoms remains common, this could lead to mismanagement of febrile illnesses.

5.5.3 Hygiene Practices and Water Sources

Personal hygiene and water consumption practices are often considered central to typhoid prevention. Surprisingly, this study found no statistically significant associations between hygiene practices and the incidence of infection. For example, washing hands before eating ($\chi^2 = 0.987, p = 0.320$) or with soap ($\chi^2 = 0.282, p = 0.596$) did not significantly reduce the risk of infection. Similarly, the type of toilet facility (water closet, KVIP, or none) and primary water source (pipe, sachet, or bottled) were not significantly associated with typhoid positivity. This counterintuitive finding may be explained by the pervasive environmental contamination in Accra and similar urban centres. Even individuals who practice good personal hygiene may be exposed to contaminated municipal water supplies, street food, or communal environments (Emanche, 2022). In endemic settings, structural and infrastructural factors such as municipal water safety and sanitation systems are stronger predictors of typhoid risk than individual hygiene practices. The finding that sachet water consumption was not significantly associated with infection is particularly notable, as previous studies in Ghana have implicated sachet water in outbreaks of waterborne diseases (Dongdem *et al.*, 2025). This suggests that contamination may be widespread across multiple water sources, making distinctions between them less meaningful. It is also possible that self-reported hygiene practices were subject to social desirability bias, with participants overreporting good practices such as handwashing. This could have obscured any true associations between hygiene and infection. Regardless, the lack of significant associations emphasises the need for systemic interventions at the community and municipal levels rather than solely focusing on individual behaviours.

5.5.4 Antibiotic Use and Self-Medication

Antibiotic use was another important variable examined. While chi-square analysis showed no significant association between prior antibiotic use and infection (p = 0.982), logistic regression analysis revealed that antibiotic use was associated with an increased odds of testing positive (AOR = 1.84, p = 0.020). This apparent contradiction suggests that antibiotics may have altered the clinical course of infection without entirely eradicating bacteria, leading to persistent positivity on Typhidot. Prior antibiotic use can also reduce the sensitivity of stool culture, as partially treated infections may not yield bacterial growth (Sam *et al.*, 2024). Interestingly, treatment duration was significantly associated with infection status. Patients who reported using antibiotics for 5–7 days had reduced odds of positivity (AOR = 0.01, 95% CI [0.001, 0.53], p = 0.026). This suggests that adherence to appropriate treatment regimens may reduce the persistence of infections. At the same time, incomplete or irregular use of antibiotics may lead to false negatives in culture and persistent antibody detection in serological tests. This finding aligns with Mo *et al.* (2023) for adequate antibiotic duration to prevent relapse and resistance.

Self-medication emerged as a common practice among participants, though it was not statistically significant. Those who self-medicated often had higher odds of positivity, with an AOR of 2.87 (p = 0.184). Moreover, frequent self-medication showed a concerning trend toward a higher likelihood of infection (AOR = 17.77, p = 0.073). Although not statistically significant, the large odds ratio highlights the risks associated with unregulated antibiotic use, which contributes to antimicrobial resistance and complicates diagnosis. This finding resonates with Musa *et al.* (2025) who highlighted that antibiotic misuse is a growing public health threat in Ghana, particularly in relation to typhoid fever. Furthermore, awareness of the consequences of self-medication did not appear to reduce the practice, as infection rates were similar among those who reported being aware of the risks and those who did not. This highlights a gap between knowledge and practice, underscoring the need for more robust regulatory and educational interventions.

5.6 Implications for Public Health and Clinical Practice

The findings of this study have important implications not only for clinical practice at the patient level but also for public health policy, surveillance systems, and healthcare financing in Ghana. The comparative evaluation of Typhidot, Widal, and stool culture underscores the urgent need to reassess diagnostic strategies for typhoid fever in endemic settings, particularly in resource-constrained environments.

5.6.1 Implications for Clinical Practice

From a clinical perspective, the study demonstrates that both Typhidot and Widal are inadequate as standalone diagnostic tools for typhoid fever. Typhidot's superior sensitivity and high negative predictive value suggest that it may be a useful initial screening tool, especially in primary health facilities where culture is unavailable. Its ability to rule out infection when results are negative can help clinicians avoid unnecessary antibiotic prescriptions for patients who are not infected. However, the poor specificity and positive predictive value of both Typhidot and Widal imply that a positive result from these tests cannot be relied upon to confirm active infection. Overdiagnosis exposes patients to unnecessary treatments, delays the identification of alternative causes of fever, and contributes to antibiotic resistance. Clinicians must therefore interpret positive results with caution and, where possible, seek confirmatory stool or blood cultures.

The study's findings on clinical symptoms further complicate matters. Since fever, headache, diarrhoea, and abdominal pain were not statistically associated with confirmed typhoid infection, clinicians cannot rely on symptoms alone to distinguish typhoid from other febrile illnesses such as malaria. This reinforces the need for laboratory confirmation in all suspected cases, even when classic symptoms are present. Additionally, the significant association between prior antibiotic use and persistent positivity highlights the need for clinicians to take detailed drug histories and to interpret diagnostic outcomes in that context. For example, a negative stool culture in a patient with a history of prior antibiotic use should not immediately exclude typhoid, as antibiotic suppression may have reduced bacterial growth. This nuance must be integrated into diagnostic algorithms to prevent missed diagnoses.

5.6.2 Implications for Public Health Policy

At the policy level, the findings call for an urgent reassessment of Ghana's reliance on serological methods in typhoid surveillance and case management. Widal remains the dominant diagnostic method in many government and private facilities due to its low cost; however, the evidence from this study confirms its poor reliability. Typhidot, while marginally better, still inflates prevalence figures. Over-reliance on these tests therefore risks misinforming public health authorities about the actual burden of typhoid fever. Inflated prevalence statistics can also lead to misallocation of scarce health resources. For example, overestimation of typhoid cases may divert attention and resources from other febrile illnesses such as malaria, viral hepatitis, or urinary tract infections. It may also lead to the unnecessary procurement of antibiotics, contributing to stock wastage and increased costs within the healthcare system. Therefore, strengthening laboratory infrastructure is essential. Investments are needed to expand culture-based diagnostic capacity in regional and district hospitals across Ghana. This is pivotal because while stool and blood cultures require more resources than serological tests, their specificity ensures accurate diagnosis, better treatment, and more reliable epidemiological data. Policymakers should consider subsidising culture tests under the National Health Insurance Scheme (NHIS) to reduce the financial barriers observed in this study, where nearly three-quarters of participants were uninsured.

5.6.3 Implications for Surveillance and Research

At the surveillance level, reliance on inaccurate serological data undermines efforts to track typhoid incidence and detect outbreaks. Since Typhidot and Widal often overestimate the prevalence of typhoid, public health authorities may assume a constant burden of typhoid, obscuring actual fluctuations in incidence. This has consequences for outbreak detection and response, as well as for monitoring progress toward control goals. Furthermore, the current study highlights gaps for further research. The absence of associations between hygiene practices and typhoid infection suggests that environmental contamination may override individual behaviours in Accra. Future studies should therefore focus on microbial testing of municipal water, sachet water, and street foods to better understand transmission pathways. Additionally, given the strong association between antibiotic misuse and infection persistence, research into local resistance patterns of *Salmonella Typhi* is urgently needed.

5.6.4 Implications for Antimicrobial Stewardship

One of the most significant implications of this study is the issue of antimicrobial resistance. The low specificity and poor PPV of Typhidot and Widal mean that large numbers of patients are falsely diagnosed with typhoid fever and prescribed antibiotics. Over time, this practice fuels the emergence of resistant strains. Already, studies in Ghana have documented increasing resistance of *S. Typhi* to fluoroquinolones and cephalosporins (Konyali *et al.*, 2023). If unchecked, this trend will undermine treatment efficacy and increase morbidity and mortality. To address it, antimicrobial stewardship programmes must be strengthened at both the hospital and community levels. Clinicians should be trained to interpret serological test results cautiously and confirm diagnoses with cultures whenever possible. At the same time, public education campaigns should discourage self-medication with antibiotics, a practice that this study found widespread and associated with higher odds of positivity. Regulatory authorities must also tighten controls on the sale of over-the-counter antibiotics, which remain common in Ghana.

5.6.5 Broader Public Health Significance

Ultimately, the current study highlights the broader importance of enhancing diagnostic accuracy for typhoid fever in Ghana. Accurate diagnosis not only improves patient outcomes but also enhances surveillance, guides resource allocation, and strengthens public health preparedness. Inaccurate diagnosis, by contrast, perpetuates a cycle of mismanagement, wasted resources, and resistance. Addressing these challenges requires a multi-pronged approach that integrates improved laboratory infrastructure, clinician training, health insurance reform, and public education.

5.7 Summary of Discussion

This chapter presents the study's findings in relation to the stated objectives. The results showed that socio-demographic traits such as age, sex, marital status, and religion were not significantly associated with typhoid infection, suggesting that exposure is more environmental than individual. Positivity rates differed markedly across diagnostic methods: Typhidot (50.4%) and Widal (35.9%) yielded inflated results compared to stool culture, which confirmed only 5.1% of cases. This reflects the tendency of serological tests to overestimate prevalence in endemic settings. In terms of diagnostic performance, Typhidot was more sensitive (100%) than Widal (83.3%), but both had poor specificity, low positive predictive values, and weak overall accuracy. Their ROC/AUC values (~0.55) confirmed limited discriminatory power. Agreement between the two tests was moderate ($\kappa = 0.47$), further underscoring their variability. Clinical symptoms were not reliable predictors of typhoid infection, while prior history of typhoid showed a significant association. Hygiene practices and water sources showed no significant correlation, indicating widespread environmental contamination. Antibiotic use and self-medication posed key challenges, with evidence of incomplete treatment and risk of resistance. Overall, the findings emphasise that Typhidot and Widal are inadequate as confirmatory tools and that stool culture remains the gold standard. Strengthening laboratory capacity, expanding access to reliable diagnostics, and enforcin

CHAPTER SIX

SUMMARY OF FINDINGS, RECOMMENDATIONS, AND CONCLUSION

6.0 Introduction

This chapter presents a synthesis of the major findings, discusses their implications, and outlines recommendations and conclusions drawn from the study.

6.1 Summary of Findings

The findings of this study provide a comprehensive evaluation of the diagnostic performance of the Typhidot and Widal serological tests compared with stool culture, as well as the influence of socio-demographic factors, clinical symptoms, hygiene practices, and antibiotic use on typhoid fever infection among suspected patients at the Korle-Bu Teaching Hospital. The study revealed considerable discrepancies in positivity rates across the three diagnostic methods. Typhidot recorded the highest positivity rate of 50.4%, followed by the Widal test with 35.9%, whereas stool culture, the gold standard, detected only 5.1% of cases. The markedly higher positivity from the serological tests indicates substantial overestimation of typhoid fever prevalence, suggesting that most positive results from Typhidot and Widal were false positives. This finding underscores the limitations of serological tests in endemic settings where background antibody levels and cross-reactivity are common.

An assessment of diagnostic accuracy demonstrated that the Typhidot test had a sensitivity of 100%, meaning it detected all culture-positive cases, while the Widal test showed a lower sensitivity of 83.3%. However, the specificity of both serological tests was poor, with Typhidot recording 52.3% and Widal 32.4%. The positive predictive values were extremely low, at approximately 10.2% for Typhidot and 6.3% for Widal, implying that a positive result from either test had a very poor likelihood of representing a true infection. Nonetheless, both tests had negative predictive values above 97%, indicating that negative results were more reliable for excluding typhoid fever. A moderate level of agreement was observed between Typhidot and Widal ($\kappa = 0.47$, $p < 0.001$), suggesting both tests often produced similar outcomes, although these outcomes were not necessarily accurate when compared with stool culture.

The analysis of socio-demographic factors, clinical symptoms, personal hygiene practices, and antibiotic use revealed that these variables did not significantly influence typhoid fever infection in the study population. Age, sex, marital status, education, and NHIS enrolment were not associated with positive stool culture results. Similarly, common clinical symptoms such as fever, headache, abdominal pain, diarrhoea, constipation, and malaise did not show statistically significant associations with confirmed infection. Personal hygiene behaviours, including handwashing practices and water sources, along with patterns of antibiotic use before hospital presentation, also showed no significant relationships with infection status. The only variable that demonstrated a statistically significant association with typhoid positivity was a prior history of typhoid fever (AOR = 2.06, $p = 0.008$), suggesting either residual antibodies influencing serological results or a predisposition to recurrent infection.

Overall, the findings highlight profound limitations in the diagnostic reliability of Typhidot and Widal tests in endemic settings such as Ghana. While Typhidot demonstrated excellent sensitivity, both serological tests performed poorly in terms of specificity and predictive accuracy, leading to notable overdiagnosis. This has important clinical and public health implications, particularly regarding inappropriate antibiotic use and its contribution to antimicrobial resistance. The very low stool culture positivity further suggests that many suspected cases may be misclassified due to reliance on serological tests rather than culture-based confirmation. The absence of significant associations between most demographic or behavioural factors and confirmed infection emphasises the need for improved diagnostic capacity rather than assumptions based on patient characteristics. These findings collectively point to the necessity of strengthening laboratory culture infrastructure, refining diagnostic algorithms, and promoting rational antibiotic use to enhance typhoid fever diagnosis and management in Ghana.

6.2 Conclusion

The findings of this study demonstrate that although the Typhidot and Widal tests remain widely used in Ghana for the diagnosis of typhoid fever, their diagnostic performance is significantly limited when compared with stool culture, the gold standard. The study revealed that both serological tests substantially overestimated the prevalence of typhoid fever, with Typhidot and Widal recording positivity rates of 50.4% and 35.9% respectively, against a culture-confirmed prevalence of only 5.1%. This disparity highlights the risk of misdiagnosis, unnecessary treatment, and the potential contribution to antibiotic resistance, particularly in endemic settings where background antibody levels are high. While Typhidot demonstrated excellent sensitivity by detecting all culture-positive cases, and Widal showed moderate sensitivity, both tests recorded poor specificity and very low positive predictive values. These findings indicate that although serological tests may be useful in ruling out infection due to their high negative predictive values, they cannot reliably confirm true typhoid fever cases.

Furthermore, the study found that socio-demographic characteristics, clinical symptoms, hygiene practices, and antibiotic use were not significantly associated with confirmed infection, with the exception of a prior history of typhoid fever, which was linked to higher odds of testing positive. This suggests that behavioural and demographic factors alone may not adequately explain differences in infection status within this setting. Instead, the findings point toward limitations in diagnostic tools rather than population characteristics as the primary contributor to inaccurate diagnosis. Overall, the study concludes that Typhidot and Widal tests have limited utility as standalone diagnostic

6.3 Recommendations

Drawing on the findings, several recommendations are proposed for clinical practice, health policy, public health interventions, and future research.

6.3.1 Policy Level

1. The Ministry of Health (MoH) and Ghana Health Service (GHS) should revise national diagnostic guidelines, reducing reliance on serological tests.
2. MoH should invest in laboratory infrastructure, including staff training and supply of culture media, reagents, and equipment.
3. GHS should establish national diagnostic quality assurance programmes to standardise and monitor practices across health facilities.

6.3.2 Practice Level

6.3.2.1 Clinical Practice

1. Hospital management should prioritise stool culture as the confirmatory diagnostic method for suspected typhoid cases.
2. Clinicians should use Widal and Typhidot only as preliminary screening tools, not as the sole basis for antibiotic therapy.

3. Medical superintendents should ensure rational antibiotic prescribing by requiring laboratory confirmation where possible.

6.3.2.2 Antibiotic Stewardship

1. Hospital boards should set up antibiotic stewardship committees to monitor prescribing and promote rational drug use.
2. The Pharmacy Council of Ghana should intensify inspections and enforce regulations on antibiotic dispensing.
3. The Ghana Medical Association (GMA) and Pharmaceutical Society of Ghana (PSGH) should organise continuous professional development (CPD) training for clinicians and pharmacists on rational antibiotic use.
4. The Food and Drugs Authority (FDA) should strengthen surveillance of antimicrobial resistance (AMR) and link resistance trends with diagnostic practices.

6.3.2.3 Public Health Interventions

1. The Health Promotion Unit of GHS should implement community health education campaigns discouraging self-medication and encouraging early hospital visits.
2. Food and Drugs Authority (FDA), in collaboration with local assemblies, should monitor food vendors, ensuring compliance with hygiene standards.
3. Community leaders should be engaged in sensitisation programmes to promote safe food handling and reduce risk exposures.

6.4 Future Research Directions

1. Future studies should be conducted on a larger scale and across multiple sites to improve the generalizability of findings and allow subgroup analyses by age, sex, and socio-economic status.
2. Further investigations are needed to evaluate molecular and newer rapid diagnostic methods, such as PCR-based tests, and compare their performance with stool and blood culture.
3. Research linking diagnostic performance with antimicrobial resistance patterns is essential to gain a better understanding of the consequences of misdiagnosis on public health.
4. Longitudinal and community-based studies should be undertaken to capture the true burden of typhoid fever and assess patient outcomes over time.

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APPENDICES

APPENDIX I: WORK PLAN

Activity	March 2025	April-May 2025	June-July 2025	August-September 2025	October 2025
Choosing and approval of research topic					
Writing of research proposal					
Submission To supervisor and KTH For Ethical Clearance					
Pretesting of research instrument					
Data collection and data entry					
Data cleaning and analysis discussing of findings					
Compilation of final work					
Submission of final work					

APPENDIX II: BUDGET

ITEMS	COST (GHS)
Media (SS agar)	2,500
General printing	1,500
Other Reagent (widal and TyphI dot)	1,500
Expert/Lab Assistant motivation	1,000
Stool container (1 cost 2 cedis)	480
EDTA tubes (100 pieces cost 80 cedis)	200
T&T during sample collection	650
Ethical consideration	1,200
Others	500
Total	**9,390**

APPENDIX III: CONSENT/ASSENT FORM

	KORLE BU TEACHING HOSPITAL KBTH- **IRB CONSENT FORM**

Personal Details			
Title:	**Surname:**	**First Name:**	**Middle Name:**
Place of birth:		**Gender**	Male ☐ Female ☐
Date of Birth (dd-mm-yyyy) Please attach birth certificate			
Phone N°			
Home Address			
Email		**Postal Address**	
Nationality: Ghanaian ☐ Foreigner ☐	**If foreigner, State Country:**		
Occupation:			
Person to notify in case of emergency:	**Name:**	**Telephone:**	

Applicant Information	
Title: *[Name of research project]*	**Comparative Diagnosis of Typhoid Fever using Typhoidot and Widal Methods with Culture at the Korle-Bu Teaching Hospital in the Greater Accra Region, Ghana**
Principal Investigator: *[Name]*	**Eunice Asaga**
Address: *[Name of institution/company and complete address]*	**AAMUSTED-M, P.O.BOX 40, Mampong Ashanti**

General Information about Research :(State clearly the objective of the research in easily-understood words. There must be a statement that the study involves research, an explanation of the purpose of the research and the expected duration of the participant's participation, a description of the procedures to be followed and the identification of any procedures which are experimental and what the participant(s) is supposed to do. All information about the research must be stated) (NB: Avoid the use of technical language or jargons)

Problem Statement

Although there is a surge in typhoid fever in the country, accurate diagnosis is critical for effective treatment and control of the disease. Cultural method (blood or stool) has long been considered the gold standard diagnostic method for typhoid fever. However, due to a lack of cultural methods in many health facilities in Ghana, most rely on serological diagnostic methods such as the Widal and typhidot tests, which are cheaper and can be used at most levels of health facilities. These diagnostic methods, however, are prone to misdiagnosis. Misdiagnosis can result in incorrect treatment, leading to overuse of drugs, which may contribute to antibiotic resistance. Increased antibiotic typhoid resistance can potentially spread with dire public health consequences in Ghana. Furthermore, limited studies have examined the reliability of typhidot and widal tests in Ghana, despite their widespread use and adoption as diagnostic methods in most health facilities. Therefore, it is imperative to comprehensively evaluate the reliability of these methods compared to the stool culture method in Ghanaian health settings.

Study Objectives

The present study aims to compare the laboratory diagnosis of typhoid fever using typhidot and Widal methods with the gold standard in the Korle-Bu Teaching Hospital, Accra.

Specific Objectives

1. To determine rates of typhoid fever using the typhidot and Widal methods.

2. To compare the sensitivity, specificity, and accuracy of the Widal and typhidot techniques with the stool culture method in diagnosing typhoid fever.

3. To assess the association between socio-demographics, clinical symptoms, personal hygiene practices and antibiotic use with typhoid infection.

Inclusion and Exclusion Criteria

Patients with febrile illnesses willing to participate in the study will be provided informed consent when recruited. In addition, those who did not receive antibiotic treatment for typhoid fever or other bacterial infections will be eligible. Those who experience fever for at least two days before seeking medical attention and other clinical symptoms of typhoid fever, such as abdominal discomfort, constipation, diarrhoea, vomiting, and body and joint pains, will be eligible to participate. Patients with febrile illnesses who are on admission and undergoing antibiotic therapy and those who have been identified as having another known febrile disease, such as malaria and Individuals with severe cognitive impairments that may affect their ability to provide reliable responses or comply with study procedures will be excluded during the period of study.

Data Collection Procedure

Qualified laboratory personnel will conduct in-person interviews using a pre-tested questionnaire with study

Possible Risks and Discomforts: (Description of any reasonable foreseeable risks or discomfort to the participant. Include physical, social and psychological risk if anticipated.)

There is a minimal risk for a loss of confidentiality.

Possible Benefits: (Specific language about benefits to individuals and/or society that can be reasonably expected.)

This study is significant as it addresses the critical need for accurate, reliable, and accessible diagnostic tools for typhoid fever in resource-limited settings such as Ghana. Typhoid fever, caused by *Salmonella* species, remains a leading cause of morbidity and mortality in many developing countries. Misdiagnosis or delayed diagnosis can lead to severe complications, increased transmission, and inappropriate use of antibiotics, contributing to antimicrobial resistance. By comparing the Widal and Typhoidot tests with stool culture as the gold standard, this research will provide valuable insights into the diagnostic accuracy of the two commonly used serological tests in the Ghanaian context.

The findings of this study will help healthcare professionals at Korle-Bu Teaching Hospital make informed decisions on the best diagnostic approach to improve diagnostic accuracy, inform treatment decisions, and reduce misdiagnosis and inappropriate use of antibiotics, resulting in antibiotic resistance, which helps in improving patient outcomes through earlier and more accurate detection of typhoid fever.

Alternatives to Participation: (Disclosure of appropriate alternatives or courses of treatment, if any, that might be advantageous to the subject). (This does not apply to all studies and usually used for intervention studies)

Not applicable

Confidentiality: (A statement describing the extent, if any, to which confidentiality of records identifying the subjects will be maintained. For example, "We will protect information about you to the best of our ability. You will not be named in any reports. Some staff of [list all groups that may access the research records] may sometimes

Confidentiality of all participants' information will be strictly maintained throughout the study. Personal identifiers will not be used in any reports or publications. Data collected will be securely stored and accessible only to the research team and authorized personnel from the Korle-Bu Teaching Hospital and the institutional ethics review board, if necessary. We will protect information about participants to the best of our ability to ensure privacy and confidentiality.

Compensation: (If there are any compensation packages either in cash or kind available for participants it must be clearly spelt out in terms of the actual amount or gift to be given, conditions for receiving the package and when it will be made) Usually compensation should be given at the end of the study.

Participation in this study is entirely voluntary.

Voluntary Participation and Right to Leave the Research: (A statement that the research is voluntary and participant can withdraw without penalty).

Participation in this research is completely voluntary. You are free to decide whether or not to take part in the study. If you choose to participate, you may withdraw at any time without any penalty or loss of benefits to which you are otherwise entitled. Your decision to decline or withdraw will not affect your access to medical care or services at the Korle-Bu Teaching Hospital.

Termination of Participation by the Researcher: (Any anticipated circumstances under which the participant's participation may be terminated by the investigator without regard to the participant's consent must be specified) NB:(This does not apply to all studies)

In this study, there are no anticipated circumstances under which a participant's involvement would be terminated by the researcher without their consent. However, if it becomes evident that continued participation may pose a risk to the health or well-being of the participant, or if there is a violation of study procedures that could compromise the integrity of the research, the investigator reserves the right to withdraw the participant from the study in consultation with the supervising ethics committee

Notification of Significant New Findings: (A statement that significant new findings developed during the course of the research that may relate to the participant's willingness to continue participation will be provided to the participant) NB:(This does not apply to all studies)

Not applicable

Contacts for Additional Information (Give an explanation of whom to contact for answers to pertinent questions about the research and whom to contact in case of research-related injury. Give names and mobile numbers that are accessible to the participant)
If you have any questions concerning the study, please contact Ms. Eunice Asaga on 0552066831, and Dr. Denis Dekugmen Yar on 0243 236810.

APPENDIX III: VOLUNTEER CONSENT/ASSENT FORM

Your rights as a Participant

This research has been reviewed and approved by the Institutional Review Board of Korle Bu Teaching Hospital for Medical Research (KBTH-IRB). If you have any questions about your rights as a research participant you can contact the IRB Office between the hours of 8am-5pm through the landline ***0302666766 or email addresses:***
rdo@kbth.gov.gh

Volunteer Agreement

The above document describing the benefits, risks and procedures for the research title (name of research) has been read and explained to me. I have been given an opportunity to have any questions about the research answered to my satisfaction. I agree to participate as a volunteer.

Name and signature or mark of parent or guardian **Date**

If volunteers cannot read the form themselves, a witness must sign here:

I was present while the benefits, risks and procedures were read to the volunteer. All questions were answered and the volunteer has agreed to take part in the research.

Name and signature of witness : **Date:**

I certify that the nature and purpose, the potential benefits, and possible risks associated with participating in this research have been explained to the above individual.

Name Signature of Person Who Obtained Consent : **Date:**

APPENDIX IV: RESEARCH INSTRUMENT

OUESTIONNAIRE ON TYPHOID	
Socio-Demographic Characteristics	
1.	**How old are you?** 1. □ Below 12 years 2. □ 12 to 20 years 3. □ 21 to 35 years 4. □ Above 35 years
2.	**Sex** 1. □ Male 2. □ Female
3.	**What is your religion?** 1. □ Christian 2. □ Muslim 3. □ Traditional/Spiritualist 4. □ No religion 5. □ Other (specify)
4.	**What is your current marital status?** 1.□ Married (civil, traditional, religious) 2.□ Co habiting 3.□ Divorced 4.□ Widowed 5.□ Single
5.	**What is your Occupation?** 1.□ Student 2.□ Trader 3.□ Civil Servant 4.□ Unemployed 5.□ Others (specify)
MEDICAL HISTORY	
6.	**Do you have Health Insurance?** 1.□ Yes 2.□ No

OUESTIONNAIRE ON TYPHOID	
7.	**Do you currently have a fever?** 1. Yes 2. No
8.	**Do you have a headache?** 1. Yes 2. No
9.	**Do you vomit?** 1. Yes 2. No
10.	**Do you have Diarrhea?** 1. Yes 2. No
11.	**Do you feel weak?** 1. Yes 2. No
12.	**Do you experience loss of appetite?** 1. Yes 2. No
13.	**Do you have abdominal pain?** 1. Yes 2. No
14.	**Any previous history of typhoid infection**? 1. Yes 2. No
Personal Hygiene and Eating Habits	
15.	**Do you wash your hands before eating?** 1. Yes 2. No
16.	**Do you always use soap to wash your hands?** 1. Yes 2. No
17.	**What type of toilet facility do you use in your house?** 1. Water closest 2. KVIP 3. None
18.	**Do you wash your hands after you use the washroom?** 1. Yes 2. No 3. Sometimes
19.	**How often do you cut your fingernails?** 1. Regularly 2. Sometimes 3. Not at all

OUESTIONNAIRE ON TYPHOID	
20..	**What is your primary source of drinking water?** 1. □ Pipe/Well/Stream 2. □ Bottle 3. □ Sachet
21.	**Do you have a habit of eating already made salad/ fruits/eggs?** 1.□ Yes 2. □ No
22.	**Do you have a habit of eating sausages/kebabs/ pork?** 1. □ Yes 2. □ No
23.	**Have you ever drunk raw/unpasteurized milk from cattle**? 1. □ Yes 2. □ No
	Antibiotics use
24.	**Have you ever been diagnosed with typhoid fever before?** 1. □ Yes 2. □ No If No, skip to Q 29
25.	**If yes, what method was used to diagnose your typhoid fever?** 1. □ Widal Test 2. □ Typhidot Test 3.□ Culture 4.□ Not sure
26.	**Were you prescribed antibiotics for your typhoid fever treatment?** 1. □ Yes 2. □ No
27.	**If yes, which type of antibiotic was prescribed for you?** 1. □ Azithromycin 2. □ Ciprofloxacin 3. □Amoxicillin 4. □Ceftriaxone 5. □ Don't know
28	**How long did you take the prescribed antibiotics for your typhoid fever treatment?** 1. □ Less than 5 days 2. □ 5-7 days 3. □8-14 days 4. □ More than 14 days
29	**Before seeking a professional diagnosis for typhoid fever, have you ever self-medicated with antibiotics?** 1. □ Yes 2. □ No

OUESTIONNAIRE ON TYPHOID	
30.	**How frequently do you use antibiotics without a prescription when you suspect you have typhoid fever or similar symptoms?** 1. Often 2. Never 3. Sometimes
31.	**Are you aware of the potential side effects or risks associated with improper use of antibiotics for typhoid fever?** 1. Yes 2. No If No, skip to Q 33
32.	**If yes, can you mention one?**
33.	**What influenced your decision to seek medical help and use antibiotics for typhoid fever?** 1. Severity of symptoms 2. Cost of healthcare services 3. Advice from friends or family 4. Availability of over-the-counter antibiotics 5. Knowledge of antibiotic resistance 6. Others (Please specify) …….
	END OF INTERVIEW
	INTERVIEWER: THANK YOU FOR COMPLETING THIS INTERVIEW FORM.

APPENDIX V

PREPARATION OF CULTURE MEDIA

APPENDIX VI

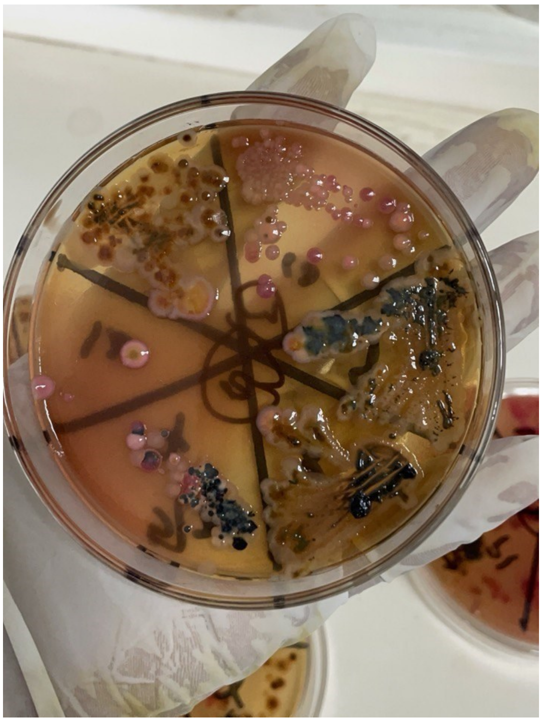

PLATE READING

APPENDIX VII: ETHICAL CLEARANCE

In case of reply the number
And the date of this
Letter should be quoted

My Ref. No. KBTH/MD/G3/25

Your Ref. No......................

KORLE BU TEACHING HOS
P. O. BOX KB 77,
KORLE BU, ACCRA.

Tel: +233 302 667759/673034-
Fax: +233 302 667759
Email: info@kbth.gov.gh
pr@kbth.gov.gh
Website: www.kbth.gov.gh

11th August, 2025

EUNICE ASAGA
AKENTEN APPIAH-MENKA UNIVERSITY OF SKILLS TRAINING
AND ENTREPRENEURIAL DEVELOPMENT
FACULTY OF ENVIRONMENT AND HEALTH EDUCATION
DEPARTMENT OF PUBLIC HEALTH EDUCATION, MAMPONG CAMPUS

SCIENTIFIC AND TECHNICAL COMMITTEE APPROVAL PROTOCOL IDENTIFICATION NUMBER: KBTH-STC 000108/2025

The Korle Bu Teaching Hospital Scientific and Technical Committee (KBTH-STC), on 11th August, 2025 reviewed and approved your submitted study protocol.

Title of Protocol: **"Comparative Diagnosis of Typhoid Fever Using Typhidot and Widal Methods with Culture at the Korle-Bu Teaching Hospital"**

This approval requires that you forward your approved document to Korle Bu Teaching Hospital – Institutional Review Board (KBTH-IRB) for the ethical aspect of the proposal to be assessed before the project may be initiated.

PRINCIPAL INVESTIGATOR: **Eunice Asaga**

This STC approval is valid till 30th July, 2026

You may, however, request extension of the approval period, or renewal as the case may be, should the study extend beyond the stated period.

Upon completion, you are required to submit a final report on the study to the STC. This is to enable the STC ensure among others that, the project has been implemented as per the approved protocol. You are also required to inform the KBTH-STC and Research Directorate of any publications that may emanate from the research findings.

Kindly note that, should the need arise, the KBTH-STC or IRB may institute appropriate measures to satisfy itself that study is being conducted according to the highest scientific and ethical standards.

Please note that any modification to the study protocol without Scientific Technical Committee (STC) approval renders this Approval invalid.

Prof. G. Obeng Adjei
Chairman, KBTH-STC

Cc: The Chairman, KBTH-IRB

APPENDIX VIII: ETHICAL CLEARANCE

In case of reply the number
And the date of this
Letter should be quoted

My Ref. No. KBTH/MD/G3/25
Your Ref. No.................

KBTH

1923

KORLE BU TEACHING HOSPITAL
P. O. BOX KB 77,
KORLE BU, ACCRA.

Tel: +233 302 667759/673034-6
Fax: +233 302 667759
Email: info@kbth.gov.gh
pr@kbth.gov.gh
Website: www.kbth.gov.gh

1st September, 2025

EUNICE ASAGA
AKENTEN APPIAH-MENKA UNIVERSITY OF SKILLS TRAINING
AND ENTREPRENEURIAL DEVELOPMENT
FACULTY OF ENVIRONMENT AND HEALTH EDUCATION
DEPARTMENT OF PUBLIC HEALTH EDUCATION, MAMPONG CAMPUS

INSTITUTIONAL APPROVAL: KORLE BU TEACHING HOSPITAL-SCIENTIFIC AND TECHNICAL COMMITTEE/INSTITUTIONAL REVIEW BOARD (KBTH-STC/IRB/000108/2025

Following approval of your study entitled "**Comparative Diagnosis of Typhoid Fever Using Typhidot and Widal Methods with Culture at the Korle-Bu Teaching Hospital**" by the Korle Bu Teaching Hospital-Scientific and Technical Committee/Institutional Review Board.

I am pleased to inform you that institutional approval has been granted for the conduct of your study in Korle Bu Teaching Hospital.

Please contact the **Head of Department** to discuss the commencement date of the study.

Please note that, this institutional approval is rendered invalid if the terms of the Institutional Reviewed Board/Scientific and Technical Committee approval are violated.

Sincere regards,

Dr. Frank Owusu-Sekyere
Director of Medical Affairs

Cc: The Chief Executive, Korle Bu

APPENDIX IX: ETHICAL CLEARANCE

In case of reply the number
And the date of this
Letter should be quoted
My Ref. No. KBTH/MD/G3/25
Your Ref. No. ....

KORLE BU TEACHING HOSPITAL
P. O. BOX KB 77,
KORLE BU, ACCRA.

Tel: +233 302 667759/673034-6
Fax: +233 302 667759
Email: info@kbth.gov.gh
pr@kbth.gov.gh
Website: www.kbth.gov.gh

29th August, 2025

EUNICE ASAGA
AKENTEN APPIAH-MENKA UNIVERSITY OF SKILLS TRAINING
AND ENTREPRENEURIAL DEVELOPMENT
FACULTY OF ENVIRONMENT AND HEALTH EDUCATION
DEPARTMENT OF PUBLIC HEALTH EDUCATION, MAMPONG CAMPUS

"COMPARATIVE DIAGNOSIS OF TYPHOID FEVER USING TYPHIDOT AND WIDAL METHODS WITH CULTURE AT THE KORLE-BU TEACHING HOSPITAL"

KBTH-IRB /000108/2025

INVESTIGATOR: **EUNICE ASAGA**

The Korle Bu Teaching Hospital Institutional Review Board (KBTH IRB) reviewed and granted approval to the study entitled: **"Comparative Diagnosis of Typhoid Fever Using Typhidot and Widal Methods with Culture at the Korle-Bu Teaching Hospital"**

Please note that the Board requires you to submit a final review report on completion of this study to the KBTH-IRB.

Kindly, note that, any modification/amendment to the approved study protocol without approval from KBTH-IRB renders this certificate invalid.

Please report all serious adverse events related to this study to KBTH-IRB within seven days verbally and fourteen days in writing.

This IRB approval is valid till 28th July, 2026. You are to submit annual report for continuing review.

Sincere regards,

DR DANIEL ANKRAH
VICE CHAIR (KBTH-IRB)
FOR: CHAIR (KBTH-IRB)

Cc: The Chief Executive Officer, KBTH
The Director of Medical Affairs, KBTH