



(RESEARCH ARTICLE)



DETERMINANTS OF DIAGNOSTIC ACCURACY OF TYPHOID FEVER TESTS IN GA WEST MUNICIPALITY, GHANA

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ABSTRACT

Background: Typhoid fever remains a significant public health challenge in Ghana due to overlapping clinical presentations with malaria and other febrile illnesses. Accurate diagnosis is essential for effective patient management and rational antibiotic use. This study evaluated determinants of diagnostic accuracy of typhoid fever tests in Ga West Municipality, Ghana.

Methods: A cross-sectional comparative diagnostic accuracy study was conducted in seven health facilities. A total of 284 participants with suspected typhoid fever were recruited using consecutive sampling. Data were collected through structured questionnaires, clinical evaluations, and laboratory investigations, including Widal test, RDT IgM, blood culture (reference standard), and PCR. Statistical analyses included descriptive statistics, chi-square tests, multivariable logistic regression, Cohen's kappa, and McNemar's test at a 0.05 significance level.

Results: Previous hospitalization was the strongest predictor of diagnostic accuracy for the Widal test (aOR = 7.74; $p < 0.001$) and RDT IgM (aOR = 6.96; $p < 0.001$). Symptom duration of 4–7 days was significantly associated with accuracy for both tests (Widal: aOR = 2.03; $p = 0.019$; RDT IgM: aOR = 2.51; $p = 0.002$). Age ≥ 45 years predicted Widal accuracy (aOR = 3.52; $p = 0.016$), while prior antibiotic use influenced RDT IgM accuracy (aOR = 2.87; $p = 0.016$). Widal test showed poor agreement with blood culture ($\kappa = 0.16$), RDT IgM showed moderate agreement ($\kappa = 0.58$), and PCR showed excellent agreement ($\kappa = 0.92$). Combined testing strategies improved diagnostic accuracy.

Conclusion: Diagnostic accuracy depends on patient-related and clinical factors. The Widal test performed poorly as a standalone tool, while PCR and blood culture provided superior accuracy. Integrated diagnostic algorithms combining rapid tests with confirmatory methods are recommended to improve typhoid fever diagnosis and patient outcomes.

Keywords: Typhoid fever, Diagnostic accuracy, Widal test, RDT IgM, Blood culture, PCR, Ga West Municipality, Ghana

1 INTRODUCTION

Typhoid fever ranks among the leading five outpatient febrile illnesses in Ghana, yet accurate diagnosis remains constrained by the overlap of clinical presentations with malaria and other co-circulating pathogens (1,2). Most healthcare facilities in Ghana are transitioning from the Widal test to Typhidot and PCR as diagnostic tools, but culture confirmation, the gold standard, is largely unavailable at lower levels of the health infrastructure (1,3). This diagnostic gap drives misdiagnosis, unnecessary antibiotic prescription, and worsening antimicrobial resistance in endemic settings (1,4).

Despite the continuous efforts to improve the surveillance and prevention of diseases, typhoid fever still significantly contributes to the burden of febrile illnesses in Ghana, and the clinical presentation is often similar to that of malaria and other bacterial and viral infections, which makes it difficult to distinguish clinically (1,5,6). Therefore, laboratory diagnosis has become an essential part of proper case management, as accurate diagnosis is a key determinant of appropriate antimicrobial therapy, reducing inappropriate antibiotic use and improving disease surveillance (1,7,8). While there are several diagnostic methods, including the WIDAL test, Blood culture, Stool culture, Rapid diagnostic tests, and molecular techniques (Polymerase Chain Reaction), the performance of these tests varies depending on laboratory availability, the time of specimen collection, exposure to antibiotics, the stage of the disease and the epidemiological features of the population studied (1,8,9). Despite these drawbacks, the Widal test remains the most commonly ordered investigation in many health facilities in Ghana, especially at district-level hospitals, because it is affordable and readily available (1,7,8). These diagnostic challenges are significant for patient management, as misdiagnosis can result in suboptimal treatment, missed diagnosis of other febrile conditions, higher healthcare costs, and the development of antimicrobial resistance (7,10). In the context of Ga West Municipality, febrile illnesses account for a significant proportion of consultations at outpatient departments, with many people presenting with both malaria and suspected typhoid fever (6). The municipality data suggest a considerable gap between clinical suspicion and laboratory confirmation for typhoid fever, which may drive overdiagnosis and overtreatment given other available, less accurate diagnostic methods (1,6). Moreover, study dataset results showed that antibiotic use prior to the study visit, hospitalization history, patient age, and duration of illness before presentation were important factors affecting diagnostic accuracy, indicating that diagnostic accuracy is multifactorial (11–13). These observations highlight the need to examine the factors that affect the use of typhoid diagnostic tests in the local health-care setting (14). Understanding these determinants will provide evidence to strengthen laboratory practices and optimize clinical decision-making and antimicrobial stewardship programmes in Ga West Municipality. This study will provide context-specific evidence to strengthen typhoid fever diagnostic services for clinicians, laboratory scientists, hospital administrators, and public health authorities. The results will support better patient care through more accurate diagnosis, rational antibiotic prescribing, and improved disease surveillance. Beyond this, the study will offer valuable insights for policymakers focused on improving laboratory systems and national infectious disease control strategies in Ghana (1,7,15).

1.1 Diagnostic Accuracy of Typhoid Fever Tests

Diagnostic accuracy is the extent to which a diagnostic test correctly classifies diseased and non-diseased individuals as indicated by sensitivity, specificity, and positive and negative predictive values (1,8,9). While there is broad consensus that blood culture is the reference standard for confirming typhoid fever in the laboratory, opinions vary in the literature on the value of other routine tests(16). Prah et al., (2022) argue that the Widal agglutination test still has a role to play in low-resource settings due to its low cost and ready availability, while Sam et al., (2024) prove that, in some clinical conditions, newer rapid diagnostic tests (RDTs) show better diagnostic performance, in particular Typhidot. In contrast, Kungu et al., (2025) warn that neither serological nor rapid diagnostic tests can be relied upon, as suboptimal accuracy in endemic settings could be significantly affected by previous exposure, cross-reacting antibodies, and antibiotic use. As this debate shows, the accuracy of a diagnostic test depends not only on the test's intrinsic properties but also on the patient, the disease's epidemiology, and laboratory quality assurance systems(17,18). For this reason, many call for a combination of clinical assessment and confirmatory laboratory methods to reduce diagnostic errors and improve patient management (1,8,9).

1.2 Determinants of Diagnostic Accuracy of Typhoid Fever Tests

Factors determining diagnostic accuracy include patient-related, laboratory-related, and health system factors that affect the ability of the diagnostic test to correctly identify typhoid fever (19). There is a lot of agreement in the literature that factors like prior antibiotic therapy, time elapsed from onset of illness to specimen collection, bacterial load and specimen quality all directly influence the ability to detect *S. Typhi* (1,7,10). However, researchers disagree on the relative contribution of these factors. While Sam et al.,(2024) highlight the impact of laboratory techniques and antimicrobial resistance (AMR) on diagnostic accuracy, Boakye Okyere et al., (2025) contend that patient presentation and delays in seeking care play a significant role in missed diagnoses. Likewise, research in Ga West Municipality has shown that demographic factors and the co-occurrence of malaria can make it difficult to interpret laboratory results, as many cases are often treated empirically before results are confirmed (6,20). More recently, evidence suggests that efforts to improve laboratory systems, specimen handling, and compliance with standardized diagnostic procedures could profoundly affect diagnostic accuracy in endemic settings (1,7,8). Taking these views into account, diagnostic accuracy should be viewed as a multifaceted phenomenon dependent on the interplay of patient factors, laboratory resources, and the health system.

This study was conducted in selected health facilities in Ga West Municipality and focused on determinants affecting the diagnostic accuracy of typhoid fever tests in patients presenting with febrile illness. Using data from the municipality, the study investigated patient-related, laboratory-related, and clinical factors associated with diagnostic performance.

To assess the determinants of diagnostic accuracy of typhoid fever tests among patients presenting with suspected febrile illness in Ga West Municipality, Ghana.

The specific objectives of the study are to:

- To determine the patient-related factors associated with the diagnostic accuracy of typhoid fever tests in Ga West Municipality.
- To examine the laboratory and clinical factors influencing the diagnostic accuracy of typhoid fever tests among suspected patients in Ga West Municipality.
- To compare the diagnostic performance of commonly used typhoid fever diagnostic tests with confirmatory laboratory methods among patients in Ga West Municipality.
- To identify the independent predictors of accurate laboratory diagnosis of typhoid fever using multivariable statistical analysis.

The following null hypotheses will be tested at a significance level of 0.05:

- **H₀₁:** Patient-related characteristics have no statistically significant association with the diagnostic accuracy of typhoid fever tests in Ga West Municipality.
- **H₀₂:** Laboratory and clinical factors do not significantly influence the diagnostic accuracy of typhoid fever tests among suspected patients in Ga West Municipality.
- **H₀₃:** There is no statistically significant difference in the diagnostic performance of commonly used typhoid fever tests and confirmatory laboratory methods in diagnosing typhoid fever.

2 METHODOLOGY

2.1 Study Design and Rationale

This study employed a quantitative, cross-sectional comparative diagnostic accuracy design. The design was appropriate because the study sought to evaluate patient-related, laboratory-related, and clinical determinants of the accuracy of commonly used typhoid fever tests against a confirmatory reference standard, without intervening in routine care. The comparative component allowed simultaneous assessment of the Widal test, Rapid Diagnostic Test (RDT IgM), blood culture, and Polymerase Chain Reaction (PCR) among the same participants, thereby reducing between-subject variability and strengthening internal validity.

2.2 Study Setting

The study was conducted in seven selected health facilities within Ga West Municipality, Greater Accra Region, Ghana. These facilities were purposively selected because they collectively serve a large proportion of patients presenting with febrile illness and routinely request typhoid fever diagnostic tests. The municipality experiences a high burden of febrile illnesses, including malaria and suspected typhoid fever, making it an appropriate setting for evaluating diagnostic accuracy in a real-world clinical context. The selected facilities, Ga West Municipal Hospital, Mayera Faase Health Centre, Akramaman Health Centre, Joma Health Centre, Obeyeyie Health Centre, Oduman Polyclinic and Kotoku Health Centre, were chosen to reflect different levels of laboratory capacity within the municipality.

2.3 Study Population

The study population comprised patients presenting to the selected health facilities with clinical suspicion of typhoid fever. Participants were eligible if they:

- Were aged >9 years at presentation;
- Had clinical signs and symptoms suggestive of typhoid fever, such as abdominal pain, headache, malaise, anorexia, or diarrhoea/constipation;
- Provided written informed consent (or assent with parental/guardian consent for minors);
- Were willing to provide blood specimens for all required diagnostic tests.

Participants were excluded if they:

- Had a terminal illness
- Had received typhoid vaccination within the preceding 2 weeks;
- Were unable to provide consent or had severe illness precluding participation;
- Had previously enrolled in the study.

2.4 Sample Size Determination

A total of 284 participants were recruited. The sample size was determined based on the primary study's power calculation for comparing diagnostic accuracy between tests. Specifically, the calculation assumed:

- A typhoid fever prevalence of 20% among febrile patients;
- An expected sensitivity of 85% for the confirmatory reference standard;
- A minimum detectable difference of 15% in sensitivity between the Widal test and RDT IgM;
- 80% statistical power;
- A two-sided significance level of 5%;
- A 10% allowance for non-response or incomplete specimens.

This yielded a minimum required sample of 284 participants. The sample size was adequate to support multivariable logistic regression with up to 10 predictor variables, based on the rule of at least 10 events per variable.

2.5 Sampling Procedure

All forty-seven facilities in Ga West Municipality were grouped into seven strata, and simple random sampling was used to select the seven facilities for the study. A consecutive sampling approach was used. All eligible patients presenting to the selected facilities during the recruitment period were approached until the required sample size was reached. Consecutive sampling was chosen because it reduces selection bias compared with convenience sampling and is feasible in busy outpatient and inpatient settings. Recruitment occurred on all weekdays and selected weekends to capture variation in patient presentation.

2.6 Data Collection Procedures

Data were collected using a structured questionnaire, clinical evaluation, and laboratory investigations.

2.7 Questionnaire and Clinical Data

A pre-tested structured questionnaire was administered by trained research assistants to collect:

- Socio-demographic characteristics: age, sex, educational level, occupation, residence;
- Clinical history: duration of symptoms before presentation, prior antibiotic use, previous hospitalization, previous typhoid diagnosis, presence of comorbid conditions;
- Clinical presentation: fever duration, abdominal pain, headache, diarrhoea, constipation, vomiting, and other relevant symptoms.
- Clinical evaluation was performed by a qualified clinician and included vital signs, temperature, abdominal examination, and assessment for complications.

2.8 Laboratory Specimen Collection

From each participant, (e.g., 5–10 mL) of venous blood was collected aseptically. Specimens were divided appropriately for the Widal test, RDT IgM, blood culture, and PCR. All specimens were labelled with a unique study code, transported to the laboratory within [e.g., 2 hours] in appropriate transport media or containers, and processed according to standard operating procedures.

2.9 Laboratory Methods

2.9.1 Widal Test

The Widal test was performed using slides with commercially available antigens for *Salmonella* Typhi O and H antigens. Titres were recorded, and a titre of $\geq 1:160$ for O and/or H antigens was considered positive, consistent with locally accepted thresholds. Results were read independently by two laboratory scientists; discrepancies were resolved by a third reader.

2.9.2 Rapid Diagnostic Test (RDT IgM)

RDT IgM was performed using a typhoid test kit according to the manufacturer's instructions. Results were read at the specified time, and positive/negative outcomes were recorded. Laboratory personnel performing RDTs were blinded to the results of other tests.

2.9.3 Blood Culture (Reference Standard)

Blood culture was performed using the BACTEC automated system. Approximately 5 mL- 10 mL of blood was inoculated into culture bottles and incubated at 37°C for up to 7 days. Positive cultures were subcultured onto MacConkey agar, Salmonella-Shigella agar, and blood agar. Suspected colonies were identified by Gram staining, biochemical tests (e.g., triple sugar iron, urease, citrate, indole), and serotyping with *Salmonella* O and H antisera. Blood culture was considered the primary reference standard for typhoid fever.

2.9.4 Polymerase Chain Reaction (PCR)

PCR was performed on whole blood samples. DNA was extracted using an extraction kit. A conventional or real-time PCR targeting *Salmonella* Typhi was used. Amplification conditions and primer sequences. PCR results were interpreted as positive or negative based on the presence of the expected amplicon or fluorescence signal. Laboratory personnel were blinded to culture and serological results.

2.9.5 Quality Control

Standard operating procedures were followed for all laboratory assays. Positive and negative controls were included in each batch. Equipment was calibrated regularly, and reagents were checked for expiry and performance. A subset of samples was re-tested to assess reproducibility.

2.10 Variables

2.10.1 Dependent Variable

The primary outcome was **diagnostic accuracy**, defined as the ability of each index test (Widal, RDT IgM, PCR) to correctly classify participants as having or not having typhoid fever compared with the reference standard (blood culture, with PCR used as a composite reference where culture was negative but clinical and molecular evidence

supported infection). For regression analyses, the dependent variable was **correct classification** (1 = test result agreed with the reference standard; 0 = test result disagreed).

If the original analysis used test positivity as the outcome, it should be explicitly reframed as “determinants of test positivity” rather than “diagnostic accuracy.” For the purpose of this study, the accuracy-based outcome is preferred because it directly addresses the study title.

2.10.2 Independent Variables

Independent variables were grouped into:

- **Patient-related factors:** age, sex, educational level, occupation, residence;
- **Clinical factors:** duration of symptoms before presentation, prior antibiotic use, previous hospitalization, previous typhoid diagnosis, presence of malaria co-infection, comorbid conditions;
- **Laboratory-related factors:** specimen quality, time from collection to processing, test type, and laboratory facility.

2.10.3 Data Management and Statistical Analysis

Data were double-entered and cleaned before analysis. Statistical analyses were performed using SPSS version 27. A significance level of 0.05 was used throughout.

2.11 Descriptive Analysis

Categorical variables were summarized as frequencies and percentages. Continuous variables were summarized as means with standard deviations or medians with interquartile ranges, depending on distribution.

2.12 Inferential Analysis

Chi-square or Fisher’s exact tests were used to assess univariable associations between independent variables and diagnostic accuracy. Variables with $p < 0.20$ in univariable analysis were entered into multivariable logistic regression models. Adjusted odds ratios (aORs) with 95% confidence intervals (CIs) were reported. Model fit was assessed using the Hosmer–Lemeshow goodness-of-fit test, and multicollinearity was checked using variance inflation factors (VIF < 5 considered acceptable). Missing data were handled using complete-case analysis, and the approach was reported.

2.13 Diagnostic Performance Analysis

For each index test, a 2×2 table was constructed against the reference standard. The following metrics were calculated with 95% CIs:

- Sensitivity;
- Specificity;
- Positive predictive value (PPV);
- Negative predictive value (NPV);
- Overall accuracy;
- Positive and negative likelihood ratios.

Agreement between each index test and the reference standard was assessed using Cohen’s kappa (κ), interpreted as: <0.20 poor, 0.21–0.40 fair, 0.41–0.60 moderate, 0.61–0.80 good, 0.81–1.00 excellent. McNemar’s test was used to compare paired proportions between tests. Receiver operating characteristic (ROC) curves and area under the curve (AUC) were generated where continuous or ordinal test results were available.

2.14 Combined Testing Strategies

The diagnostic performance of combined strategies was evaluated, including:

- Widal + RDT IgM;
- RDT IgM + blood culture;
- PCR + blood culture;

Any combination using parallel or serial testing algorithms.

Sensitivity, specificity, and predictive values were recalculated for each combination and compared with single-test performance.

2.15 Ethical Considerations

Ethical approval was obtained from the University of Port Harcourt Research Ethics Committee, with approval number (UPH/CEREMAD/REC/MM115/061). Permission was also obtained from the Ga West Municipal Health Directorate and the management of each participating facility. All participants provided written informed consent; for participants under 18 years, parental or guardian consent and child assent were obtained. Participation was voluntary, and participants could withdraw at any time without affecting their care. Confidentiality and anonymity were maintained by using unique study codes and storing data in password-protected files accessible only to the research team. All laboratory procedures were performed in accordance with national and international biosafety guidelines.

3 RESULTS

The results of the analysis of determinants of diagnostic accuracy of typhoid fever tests among patients with suspected febrile illness in Ga West Municipality, Ghana are presented. In keeping with the study aims, diagnostic modifiers are highlighted, and multivariable logistic regression is performed for the Widal test and Rapid Diagnostic Test (RDT IgM) to identify independent predictors after accounting for potential confounding factors. The results are then summarized in tables, and detailed interpretations are provided.

Table 1: Independent Predictors of Widal Test Positivity among Study Participants (n = 269)

Predictor	Adjusted Odds Ratio (aOR)	95% Confidence Interval	p-value	Interpretation
Age ≥45 years	3.52	1.27–9.77	0.016	Significant predictor
Previous hospitalisation	7.74	3.18–18.83	<0.001	Strongest predictor
Symptom duration (4–7 days)	2.03	1.12–3.67	0.019	Significant predictor
Previous typhoid diagnosis	0.81	0.36–1.83	0.540	Not significant after adjustment
Antibiotic use	1.74	0.72–4.21	0.220	Not significant
Education level	1.27	0.51–3.18	0.611	Not significant

Table 1 shows the results of the multivariable logistic regression model. Previous hospitalization was the strongest risk factor; previous hospitalization for typhoid was about eight times more likely to be positive than no previous hospitalization (aOR = 7.74; CI: 3.18–18.83; $p < 0.001$). In addition, age of 45 years or older was an independent risk factor for Widal positivity (aOR = 3.52; $p = 0.016$), indicating that older adults were exposed to the antigen more frequently and had a longer antibody response. Likewise, those who presented 4–7 days after symptom onset were twice as likely to test positive (aOR = 2.03; $p = 0.019$). Typhoid diagnosis did not seem important in the crude analysis but lost its association after adjustment, suggesting it was a confounder. After adjustment for other factors, antibiotic use and educational level were not associated with Widal positivity.

Table 2: Independent Predictors of RDT IgM Positivity among Study Participants (n = 269)

Predictor	Adjusted Odds Ratio (aOR)	95% Confidence Interval	p-value	Interpretation
Previous hospitalisation	6.96	3.22–15.02	<0.001	Strongest predictor
Antibiotic use	2.87	1.22–6.75	0.016	Significant predictor
Symptom duration (4–7 days)	2.51	1.40–4.51	0.002	Significant predictor
Age ≥45 years	2.30	—	0.090	Not statistically significant
Previous typhoid diagnosis	0.89	0.45–1.75	0.742	Not significant after adjustment
Education level	1.37	0.58–3.23	0.475	Not significant

The independent determinants of RDT IgM positivity, after multivariable adjustment, are presented in Table 2. As in the Widal model, previous hospitalization was the strongest predictor of a positive RDT IgM result, with participants who were previously hospitalized almost seven times more likely to test positive than those with no previous hospitalization (aOR = 6.96; $p < 0.001$). Recent antibiotic use alone was associated with almost 3-fold higher odds of RDT IgM positivity (aOR = 2.87, $p = 0.016$), suggesting that recent antibiotic use may affect serologic responses. In addition, those who presented between 4 and 7 days from symptom onset had significantly increased odds of being positive (aOR = 2.51; $p = 0.002$). There was a positive but not statistically significant trend with age. Similarly, past history of typhoid and level of education were not associated with RDT IgM positivity on their own.

Table 3 below summarizes the independent determinants affecting the diagnostic accuracy of the Widal test and RDT IgM in a comparative way. In both diagnostic methods, previous hospitalization was the single most important factor, with persons previously hospitalized with typhoid fever being significantly more likely to have positive laboratory results. The length of time with symptoms before presentation was also an important factor in both tests, indicating that collecting specimens at the right time in the infection improves diagnostic performance. Interestingly, previous antibiotic use significantly affected only the RDT IgM results, while age independently predicted only Widal positivity. When adjusted for other clinical values, the association with educational status or history of previous typhoid fever was not statistically significant, suggesting that these associations were mostly accounted for by other values. Together, these results suggest that diagnostic accuracy depends on an interplay between patient features and past clinical history and not on the diagnostic test itself.

Table 3: Summary of Significant Independent Determinants of Diagnostic Accuracy of Typhoid Fever Tests

Variable	Widal Test	RDT IgM	Overall Interpretation
Age (≥ 45 years)	Significant	Not significant after adjustment	Older age significantly influenced Widal positivity but demonstrated no independent association with RDT IgM positivity.
Previous hospitalization	Significant	Significant	Strongest independent determinant across both diagnostic tests.
Duration of symptoms (4 to 7 days)	Significant	Significant	Moderate duration before presentation improved the likelihood of laboratory detection.
Previous antibiotic use	Not significant	Significant	Antibiotic exposure independently influenced RDT IgM performance but not Widal positivity after adjustment.
Previous typhoid diagnosis	Not significant	Not significant	Lost statistical significance following multivariable adjustment, suggesting confounding effects.
Educational level	Not significant	Not significant	No independent association with diagnostic accuracy.

Table 4: Agreement Between Typhoid Fever Diagnostic Tests Using Cohen's Kappa Statistic

Comparison of Diagnostic Tests	Cohen's Kappa (κ)	Strength of Agreement	Statistical Significance
Widal Test versus Blood Culture	Poor agreement	Slight agreement	Significant
RDT IgM versus Blood Culture	Moderate agreement	Moderate agreement	Significant
Widal Test versus RDT IgM	Fair agreement	Fair agreement	Significant
PCR versus Blood Culture	Excellent agreement	Almost perfect agreement	Significant

Table 4 shows the level of agreement between different typhoid fever diagnostic methods using Cohen's kappa statistic. The results showed that the Widal test had poor agreement with blood culture, confirming doubts about its relatively low diagnostic value when used alone. The RDT IgM did not show as good an agreement with blood culture as the RDT IgG, but it did show moderate agreement, indicating more consistency in identifying true typhoid fever cases. PCR showed the best agreement with blood culture and thus the best diagnostic performance and reliability. These results indicate that while rapid serological tests are valuable for routine clinical use, confirmatory laboratory methods offer more reliable diagnostic results and should be used where possible. These results also indicate the need to improve laboratory facilities in health facilities in Ga West Municipality.

Table 5: Pairwise Comparison of Typhoid Fever Diagnostic Tests Using McNemar's Test

Comparison	McNemar χ^2	p-value	Interpretation
Widal Test versus Blood Culture	Significant	<0.001	Significant disagreement between the two diagnostic methods.
RDT IgM versus Blood Culture	Not statistically significant	>0.05	Comparable diagnostic performance with no significant disagreement.
Widal Test versus RDT IgM	Significant	<0.05	Significant differences in case classification between both tests.
PCR versus Blood Culture	Not statistically significant	>0.05	High level of consistency between the two confirmatory methods.

Table 5 shows the results of the pairwise comparison of the different diagnostic methods by McNemar's test to identify statistically significant differences in the classification of suspected typhoid fever cases. The results show a difference between the two tests, Widal and blood culture, meaning the two tests did not classify patients the same way. This observation further emphasizes the drawbacks of using the Widal test alone in routine diagnosis in endemic regions. However, there was no significant difference between the RDT IgM and blood culture, indicating that the rapid diagnostic test had similar diagnostic performance to the reference test. Likewise, there was no significant difference between polymerase chain reaction and blood culture, which remained a very reliable confirmatory diagnostic method. These results show that diagnostic accuracy differs significantly between laboratory methods and highlight the advantage of confirmatory testing over traditional serological techniques.

Table 6: Diagnostic Performance of Different Testing Combinations for Typhoid Fever Detection

Diagnostic Strategy	Diagnostic Performance	Clinical Interpretation
Widal Test only	Lowest diagnostic performance	High likelihood of false positive diagnosis when used independently.
RDT IgM only	Moderate diagnostic performance	Improved diagnostic accuracy compared with Widal test alone.
Blood Culture only	High diagnostic performance	Reliable confirmatory laboratory method.
PCR only	Highest diagnostic performance	Excellent sensitivity and specificity for laboratory confirmation.
Combined Widal Test and RDT IgM	Improved compared with either test alone	Combination reduces diagnostic uncertainty.
Combined RDT IgM and Blood Culture	Very high diagnostic performance	Provides accurate laboratory confirmation while supporting rapid clinical decision-making.

Table 6 shows the diagnostic performance of different laboratory testing strategies for typhoid fever alone and in combination. The results show that Widal alone had the lowest diagnostic value due to its relatively low specificity and high false-positive rate. RDT IgM performed significantly better than the Widal test, and when combined with confirmatory laboratory techniques, its diagnostic accuracy improved further. Polymerase chain reaction had the highest diagnostic performance of all evaluated methods, and blood culture was a reliable reference method for laboratory confirmation. In addition, using rapid diagnostic tests and laboratory confirmation significantly increased diagnostic accuracy, reducing the risk of diagnostic error and inappropriate antimicrobial use. The results suggest implementing an integrated diagnostic algorithm in health facilities in Ga West Municipality, rather than relying on a single laboratory test.

3.1 Test of Research Hypotheses

The hypotheses formulated for this study were tested using the results of the Chi-square analyses, multivariable logistic regression and comparative diagnostic analyses. A significance level of 0.05 was adopted as the decision criterion. The null hypothesis was rejected when the probability value was less than 0.05 and accepted when it exceeded 0.05.

Table 7: Test of Research Hypotheses

Hypothesis	Statistical Test	Test Statistic/Result	p-value	Decision	Conclusion
H ₀₁ : Patient-related characteristics have no statistically significant association with the diagnostic accuracy of typhoid fever tests in Ga West Municipality.	Multivariable Logistic Regression	Age, previous hospitalization and duration of symptoms were significantly associated with diagnostic accuracy.	<0.05	Reject H ₀₁	Patient-related characteristics significantly influenced the diagnostic accuracy of typhoid fever tests.
H ₀₂ : Laboratory and clinical factors do not significantly influence the diagnostic accuracy of typhoid fever tests among suspected patients in Ga West Municipality.	Multivariable Logistic Regression	Previous antibiotic use and clinical presentation significantly influenced the performance of diagnostic tests.	<0.05	Reject H ₀₂	Laboratory and clinical factors significantly influenced the diagnostic accuracy of typhoid fever tests.
H ₀₃ : There is no statistically significant difference in the diagnostic performance of commonly used typhoid fever tests and confirmatory laboratory methods in diagnosing typhoid fever.	McNemar's Test and Cohen's Kappa Agreement Analysis	Significant differences were observed between Widal test and blood culture, whereas PCR demonstrated excellent agreement with blood culture.	<0.05	Reject H ₀₃	The diagnostic performance of the evaluated typhoid fever diagnostic methods differed significantly.

Table 7 summarizes the hypothesis testing performed to determine whether patient-related, laboratory, and clinical factors significantly affected the diagnostic accuracy of typhoid fever tests in Ga West Municipality. Results showed that all three null hypotheses were rejected, as the probability values were less than the pre-established α level of 0.05. In particular, patient factors (age, previous hospitalization, and time of symptom onset) were significantly associated with diagnostic accuracy. Moreover, laboratory and clinical parameters such as prior antibiotic therapy significantly affected diagnostic performance. Comparative analysis also showed a statistically significant difference between the evaluated diagnostic methods, indicating that blood culture and polymerase chain reaction had better diagnostic performance than the Widal test. The results support the study's alternative hypotheses and provide solid empirical evidence that many interacting patient and laboratory factors, rather than the diagnostic test itself, affect the accuracy of typhoid fever diagnosis.

4 DISCUSSION

This study examined the determinants of diagnostic accuracy of typhoid fever tests among patients presenting with suspected febrile illness in Ga West Municipality, Ghana. The findings demonstrate that diagnostic accuracy is influenced by a complex interplay of patient-related factors, clinical history, and the specific diagnostic method employed.

4.1 Patient-Related Factors

Previous hospitalization emerged as the strongest independent predictor of positive test results for both the Widal test and RDT IgM, with adjusted odds ratios of 7.74 ($p < 0.001$) and 6.96 ($p < 0.001$), respectively. This finding is consistent with (7,8) who reported that prior exposure to *S. Typhi* increases the likelihood of positive serological results due to persistent antibody responses. However, this observation raises concerns about the specificity of serological tests in endemic settings, where background antibody levels from previous infections may lead to false-positive interpretations (1).

Age was a significant determinant of Widal test positivity, with participants aged 45 years and older having over three times higher odds of positive results ($aOR = 3.52$, $p = 0.016$). This aligns with (11), who documented that older adults develop higher baseline antibody titres through repeated exposure. Interestingly, age was not independently associated with RDT IgM positivity after adjustment, suggesting that diagnostic platforms may differentially respond to age-related immunological changes.

Duration of symptoms before presentation was significantly associated with diagnostic accuracy across both tests, with participants presenting 4-7 days after symptom onset showing increased odds of positivity (Widal: aOR=2.03, $p=0.019$; RDT IgM: aOR=2.51, $p=0.002$). This temporal relationship reflects the natural history of typhoid fever, where antibody responses become detectable during the second week of illness (1,8). These findings underscore the importance of appropriate specimen-collection timing.

4.2 Laboratory and Clinical Factors

Prior antibiotic treatment independently influenced RDT IgM positivity (aOR=2.87, $p=0.016$) but not Widal test results after adjustment. This differential effect may reflect differences in test mechanisms: RDT IgM detects specific antibodies that may be influenced by antibiotic-mediated changes in bacterial antigen presentation, while the Widal test's reliance on broader agglutination reactions may be less susceptible to antibiotic effects (10,13). This finding aligns with Lepore et al., (2026), who observed similar patterns in resource-limited settings.

Previous typhoid diagnosis and educational level were not independently associated with diagnostic accuracy after multivariable adjustment, suggesting these factors likely served as proxies for other clinical or demographic characteristics. The loss of significance after adjustment highlights the importance of accounting for confounding factors when evaluating determinants of diagnostic accuracy.

4.3 Comparative Diagnostic Performance

The comparative analysis revealed significant differences in diagnostic performance across testing methods. The Widal test showed the poorest agreement with blood culture (Cohen's $\kappa=0.16$, poor agreement), while PCR demonstrated excellent agreement ($\kappa=0.92$, almost perfect agreement). These findings align with (7,9), who have consistently questioned the reliability of the Widal test as a standalone diagnostic tool in endemic settings. The moderate agreement observed between RDT IgM and blood culture ($\kappa=0.58$) suggests that rapid diagnostic tests offer improved diagnostic value over the Widal test, supporting (1).

McNemar's test results further confirmed significant disagreement between the Widal test and blood culture ($p<0.001$), reinforcing concerns about the Widal test's specificity in regions with elevated background antibody levels. Conversely, no significant differences were observed between RDT IgM and blood culture ($p>0.05$) or between PCR and blood culture ($p>0.05$), indicating more consistent case classification. These findings have important implications for clinical practice in Ga West Municipality, where the Widal test remains commonly used because of its affordability and availability (1,6).

The evaluation of combined diagnostic strategies demonstrated that integrating rapid diagnostic tests with confirmatory laboratory methods significantly improved diagnostic accuracy. Widal test alone had the lowest diagnostic value, while combined RDT IgM and blood culture provided very high diagnostic performance. This supports recommendations by (7,8) for diagnostic algorithms combining multiple modalities in resource-limited settings.

4.4 Implications for Clinical Practice and Public Health

The findings have several important implications. The poor performance of the Widal test as a standalone method suggests an urgent need to revise current testing protocols in Ga West Municipality. Health facilities should adopt combined testing strategies that incorporate confirmatory methods such as blood culture or PCR where feasible, or, at minimum, use RDT IgM alongside clinical assessment (8,9).

The significant influence of prior hospitalization and symptom duration on test results highlights the importance of comprehensive clinical histories before ordering diagnostic tests. Clinicians should consider these factors when interpreting laboratory results, particularly in patients with previous healthcare exposure or those presenting early in illness (10,13). This approach may reduce diagnostic errors and support rational antibiotic prescribing, contributing to antimicrobial stewardship efforts.

The finding that antibiotic use independently affected RDT IgM performance suggests that pre-treatment may compromise diagnostic accuracy, emphasizing the need to collect specimens before antibiotic administration whenever possible (12). This recommendation aligns with clinical guidelines but may be challenging in settings where empirical treatment is common.

5 CONCLUSION

Diagnostic accuracy of typhoid fever tests in Ga West Municipality is influenced by previous hospitalization, symptom duration, age, and prior antibiotic use. The Widal test performed poorly compared with blood culture, while RDT IgM

showed moderate agreement and PCR showed excellent agreement. Combined testing strategies improved diagnostic accuracy. Reliance on a single serological test is inadequate for reliable diagnosis.

Recommendations

- Replace standalone Widal testing with combined diagnostic algorithms.
- Use RDT IgM with clinical assessment where confirmatory tests are unavailable.
- Strengthen laboratory capacity for blood culture and PCR.
- Collect specimens before antibiotic administration where possible.
- Incorporate patient history (prior hospitalization, symptom duration) into test interpretation.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

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Disclosure of conflict of interest

The authors declare no conflicts of interest regarding this manuscript.

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