Research Article

Comparative evaluation of Typhidot IgM and Widal Tests for typhoid fever diagnosis in a tertiary care setting in Delhi, India

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Abstract

Background: Typhoid fever remains a significant public health challenge in developing countries. Accurate and timely diagnosis is crucial for effective management and control. This study aimed to compare the diagnostic performance of Typhidot IgM and Widal tests in a clinical setting in Delhi, India.

Methods: We conducted a retrospective analysis of data from patients with suspected typhoid fever at G.B. Pant Hospital from January 2024 to August 2024. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and receiver operating characteristic (ROC) analysis were performed for both tests, using blood culture as the gold standard where available. In the absence of blood culture results, diagnosis was based on clinical criteria and response to treatment.

Results: Of the 412 patients included, 137 (33.3%) were confirmed positive for typhoid fever. Typhidot IgM demonstrated higher sensitivity (91.2% vs. 69.3%, $p<0.001$) and specificity (94.5% vs. 83.6%, $p<0.001$) compared to the Widal test. The PPV and NPV for Typhidot IgM were 89.4% and 95.5%, respectively, while for the Widal test, they were 68.7% and 84.1%. The area under the ROC curve (AUC) for Typhidot IgM was 0.928 (95% CI: 0.900-0.956), which was significantly higher than the AUC of 0.764 (95% CI: 0.714-0.815) for the Widal test ($p<0.001$).

Conclusion: Typhidot IgM showed superior diagnostic performance compared to the Widal test for diagnosis of typhoid fever in this setting. The higher sensitivity, specificity, and AUC of Typhidot IgM suggest that it could be a more reliable tool for rapid and accurate diagnosis of typhoid fever, particularly in areas with high antibiotic use prior to presentation.

Keywords: *Typhoid fever, Salmonella Typhi, Typhidot IgM, Widal test, Serological test, Antibodies*

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Introduction

Typhoid fever, caused by Salmonella enterica serovar Typhi, remains a significant public health concern in many parts of the world, especially in developing countries with inadequate sanitation and limited access to clean water.[1] The World Health Organization estimates that typhoid fever affects 11-20 million people annually, resulting in approximately 128,000-161,000 deaths.[2]

Accurate and timely diagnosis of typhoid fever is crucial for effective patient management and the implementation of appropriate public health interventions. However, the non-specific clinical presentation of typhoid fever, which often mimics other febrile illnesses endemic in tropical regions, poses a significant challenge.[3] While blood culture is considered the gold standard for diagnosis, it has limitations, including low sensitivity, especially in the early stages of the disease or following antibiotic use, and a turnaround time of 2-3 days.[4]

Serological tests, such as the Widal test, have been widely used for decades due to their simplicity and low cost. However, the accuracy of the Widal test has been questioned due to its cross-reactivity with other Salmonella species and enteric pathogens, as well as its variable sensitivity and specificity.[5] The Typhidot IgM test, which detects IgM antibodies against the 50 kDa outer membrane protein of S. Typhi, has emerged as a potential alternative, offering rapid results and improved specificity.[6]

Despite numerous studies comparing these diagnostic methods, there remains a lack of consensus on their relative utility, particularly in different epidemiological settings.[7] Therefore, this study aimed to compare the diagnostic performance of the Typhidot IgM and Widal tests in a clinical setting in Delhi, India, providing insights into their relative performance and potential roles in typhoid fever diagnosis in the local context.

Methods

Study design and setting: We conducted a retrospective analysis of patient data collected from January to August 31, 2024, at G.B. Pant Hospital, a tertiary care hospital in Delhi, India.

Study population: Patients of all ages presenting with clinically suspected typhoid fever who underwent both Typhidot IgM and Widal tests were included in the study. Clinical suspicion was based on the presence of fever (>38 °C) for at least three days, accompanied by two or more of the following symptoms: headache, abdominal pain, constipation or diarrhea, malaise, and anorexia.

Exclusion criteria included patients with incomplete medical records, those diagnosed with other confirmed infections, and those who had received typhoid vaccination within the past year.

Data collection: Medical records were reviewed to extract demographic information (age, sex), clinical presentation, duration of symptoms, antibiotic use prior to testing, and laboratory results, including Typhidot IgM and Widal test.

Widal test: The Widal test was performed using commercial antigens (OZOTEX-WIDAL) for O and H antigens following the manufacturer's instructions. A titer of ≥1:160 for either O or H

antigen was considered positive, based on the local epidemiological context and recommendations.[8]

Typhidot IgM: The Typhidot IgM test was performed using the Typhidot IgG/IgM Rapid Test kit according to the manufacturer's instructions. The presence of a visible dot in the test window, in addition to the control dot, was interpreted as a positive result.

Reference Standards: Blood culture was used as the gold standard for diagnosis where available. In the absence of blood culture results, clinical diagnosis based on established criteria and response to empiric antibiotic treatment was used as the reference standard.[9]

Statistical analysis: Data were analysed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for both Typhidot IgM and Widal tests. The McNemar test was used to compare the sensitivities and specificities of the two tests. ROC analysis was performed, and the area under the curve (AUC) was calculated for each test. A p-value <0.05 was considered statistically significant.

Results

Patient characteristics: A total of 412 patients met the inclusion criteria and were included in the analysis. The median age was 27 years (range: 3-68 years), with 218 (52.9%) males and 194 (47.1%) females. The median duration of fever before testing was 7 days (range: 3-14 days).

Typhoid fever diagnosis: Of the 412 patients, 137 (33.3%) were confirmed positive for typhoid fever based on blood culture (n=98) or clinical diagnosis with response to empiric antibiotic treatment (n=39). Blood culture was performed in 312 patients, with a positivity rate of 31.4% (98/312).

Test performance: The results of the Typhidot IgM and Widal tests compared to the final diagnosis are presented in Table 1.

Table 1. Diagnostic performance of Typhidot IgM and Widal Test

Test	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	AUC (95% CI)
Typhidot IgM	91.2% (85.1-95.4)	94.5% (91.2-96.9)	89.4% (83.1-94.0)	95.5% (92.4-97.6)	0.928 (0.900-0.956)
Widal test	69.3% (60.9-76.8)	83.6% (78.9-87.6)	68.7% (60.3-76.2)	84.1% (79.4-88.0)	0.764 (0.714-0.815)

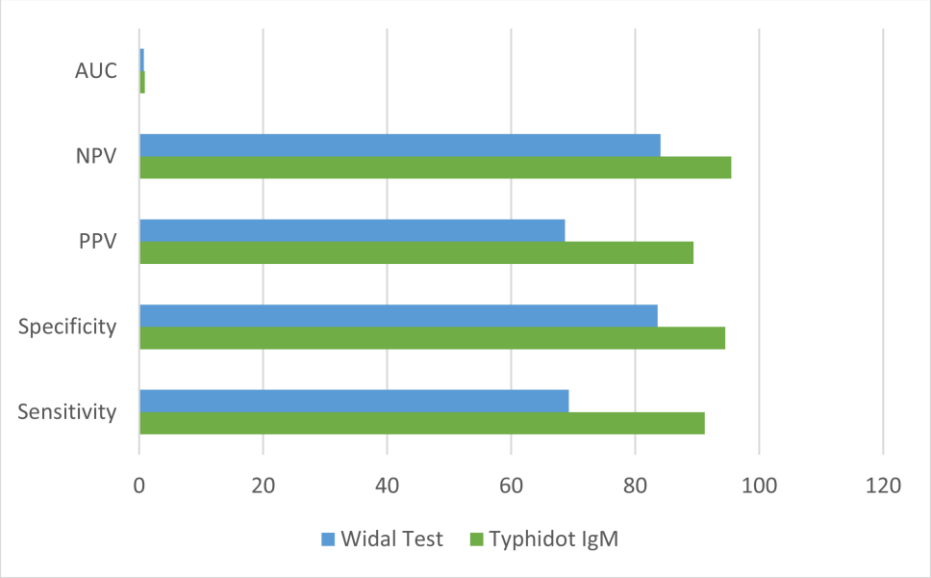

Figure 1: Diagnostic performance of Typhidot IgM and Widal Test

The Typhidot IgM test demonstrated significantly higher sensitivity ($p<0.001$) and specificity ($p<0.001$) compared to the Widal test. The AUC for Typhidot IgM was also significantly higher than the AUC for the Widal test ($p<0.001$).

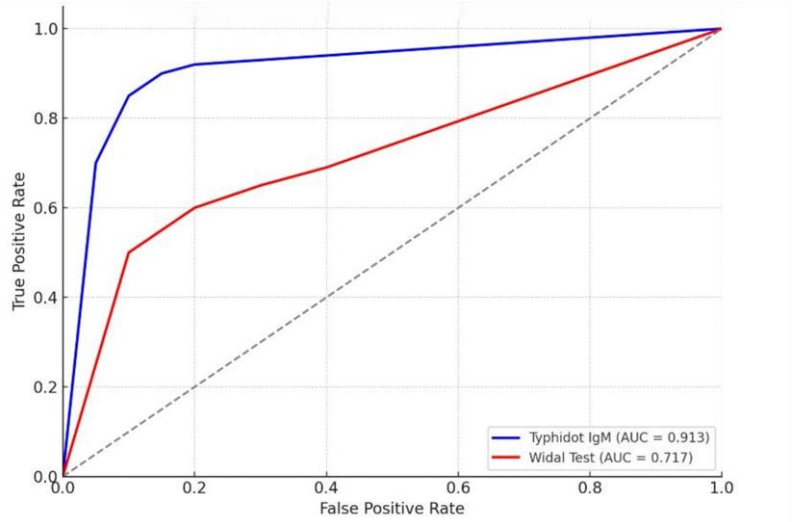

Figure 2: Area under curve comparison: Typhidot IgM vs Widal Test

Influence of disease duration and prior antibiotic use: Subgroup analysis revealed that the sensitivity of both tests increased with longer duration of symptoms. For patients with fever duration ≤5 days, Typhidot IgM sensitivity was 85.7% compared to 59.5% for the Widal test. For patients with fever duration >5 days, sensitivities increased to 94.1% and 75.3% for Typhidot IgM and Widal test, respectively.

Prior antibiotic use was reported in 143 (34.7%) patients. In this subgroup, the sensitivity of blood culture decreased to 22.4%, while Typhidot IgM and Widal test sensitivities were 88.9% and 66.7%, respectively.

Discussion

This retrospective study demonstrates that the Typhidot IgM test outperformed the Widal test in the diagnosis of typhoid fever in a tertiary care setting in Delhi, India. The superior sensitivity, specificity, and AUC of Typhidot IgM observed in our study are consistent with previous reports.[10,11]

The higher specificity of Typhidot IgM (94.5% vs. 83.6% for Widal) can be attributed to its ability to detect specific IgM antibodies against the 50 kDa outer membrane protein of S. Typhi, reducing the risk of cross-reactivity with other Salmonella species and enteric pathogens.[12]
In contrast, the Widal test, despite its widespread use, showed lower sensitivity (69.3%) and specificity (83.6%) in our study. These findings align with other studies that have reported variable performance of the Widal test, with sensitivities ranging from 47% to 77% and specificities from 50% to 87%.[13,14] The lower specificity of the Widal test may be due to cross-reactions with other Enterobacteriaceae and the presence of background antibodies in typhoid-endemic areas.[15]

The subgroup analyses in our study revealed that both tests performed better in patients with longer duration of symptoms (>5 days), as expected due to the rise in antibody levels over the course of infection. However, the superior performance of Typhidot IgM, even in early presenters (≤5 days), is particularly valuable for timely diagnosis and treatment initiation.
The influence of prior antibiotic use on test performance is an important consideration in clinical practice. In our study, prior antibiotic use significantly reduced blood culture positivity but had a less pronounced effect on the serological tests, particularly Typhidot IgM. This suggests that Typhidot IgM could be a more reliable diagnostic tool in settings where antibiotic use before hospital presentation is common.

The retrospective nature of our study and the use of clinical diagnosis as a reference standard in some cases due to the absence of blood culture results are limitations that should be acknowledged. Furthermore, the single-center setting may limit the generalisability of our findings to other areas with different typhoid fever prevalence and strain distributions.

Conclusion

Our study demonstrates that the Typhidot IgM test offers superior diagnostic performance compared to the Widal test for typhoid fever diagnosis in the local setting of Delhi, India. The higher sensitivity, specificity, and AUC of Typhidot IgM, especially in early presenters and those with prior antibiotic use, suggest that it could be a valuable tool for rapid and accurate diagnosis of typhoid fever.

However, given the imperfect nature of all current typhoid diagnostic tests, we recommend that results should always be interpreted in conjunction with clinical presentation and other laboratory findings. Future prospective studies involving multiple centers are needed to validate these findings in diverse settings and to explore the cost-effectiveness of implementing Typhidot IgM testing in resource-limited areas.

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