

## Prevalence of Typhoid Fever and Limitations of Blood Culture in Guiding Empirical Antibiotic Therapy in an Endemic Setting.

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### Abstract

#### Background:

Typhoid fever remains a major public health concern in India. Although blood culture is the gold standard for diagnosis, its diagnostic utility is often limited in routine clinical settings due to prior antibiotic use, low bacterial load, and delayed presentation. Consequently, empirical antibiotic therapy is frequently initiated based on serological tests.

#### Methods:

A retrospective observational study was conducted over three months in a tertiary care hospital in Western Uttar Pradesh. A total of 110 clinically suspected cases were analyzed. Diagnosis was based on the Typhi Dot test detecting IgM and IgG antibodies against *Salmonella Typhi* and blood culture, where available. IgM positivity, with or without IgG, was considered indicative of recent or ongoing infection. Demographic and clinical variables were statistically analyzed.

#### Results:

Out of 110 cases, 27 (24.5%) were positive. Higher positivity was observed among females (30.0%) and elderly patients (>60 years, 33.3%). The Medicine department showed the highest positivity (27.7%). IPD patients had higher positivity (29.1 %) compared to OPD (12.9 %). Blood culture yield was low, limiting its role in guiding targeted therapy.

#### Conclusion:

Typhoid fever shows a considerable burden in this region. Limited culture positivity necessitates reliance on empirical antibiotic therapy, highlighting the need for improved diagnostics and rational antimicrobial use.

**Keywords-** Typhoid Fever , Enteric Fever, Disease Prevalence , Blood Culture Yield , Empirical Antibiotic Therapy , Antimicrobial Resistance (AMR), Serological Diagnosis , Typhi Dot

### INTRODUCTION

Typhoid fever is a potentially life-threatening systemic infection caused by *Salmonella enterica* serotype Typhi, a Gram-negative bacillus that infects only humans<sup>1</sup>. Transmission primarily occurs through ingestion of food or water contaminated with human fecal matter, reflecting poor sanitation and hygiene practices<sup>2</sup>. The disease remains endemic in many low- and middle-income

countries, particularly in South Asia, where rapid urbanization and population density facilitate sustained transmission.

After an incubation period of approximately 6–30 days, patients usually present with prolonged fever, abdominal discomfort, headache, anorexia, and gastrointestinal disturbances. In severe cases, complications such as intestinal perforation, encephalopathy, and septicemia may occur<sup>1</sup>. A proportion of infected individuals may become chronic carriers, contributing to continued transmission within the community<sup>3</sup>.

Despite improvements in public health infrastructure, enteric fever—caused by *Salmonella Typhi* and *Salmonella Paratyphi*—remains a substantial global burden. Recent estimates indicate millions of cases annually, with India accounting for a significant share<sup>3,7,8,11</sup>. Regional epidemiological studies have shown heterogeneity in disease distribution, with higher prevalence in densely populated, resource-limited settings<sup>4,6</sup>. Furthermore, recent Indian studies underscore the growing public health concern and the need for strengthened preventive strategies<sup>5</sup>.

Laboratory diagnosis of typhoid fever traditionally relies on blood culture, which remains the reference standard for definitive diagnosis. However, its sensitivity is limited in routine clinical practice due to prior antibiotic use, low levels of bacteremia, and delayed presentation of patients. Blood culture is most useful during the first week of illness, after which the likelihood of isolating the organism decreases significantly. These constraints significantly limit its effectiveness in routine clinical decision-making. In contrast, serological tests such as Typhi Dot, which detect IgM and IgG antibodies, are widely used due to their rapid turnaround time and ease of performance. IgM antibodies indicate recent or acute infection, while IgG antibodies suggest past exposure or later stages of disease. However, variability in sensitivity and specificity, particularly in endemic settings, remains a concern.

In routine clinical practice, these diagnostic limitations often necessitate early initiation of empirical antibiotic therapy before microbiological confirmation. While this approach is clinically justified, it contributes to the emergence of antimicrobial resistance (AMR), as highlighted in recent Indian surveillance studies<sup>9</sup>.

Recent advancements in prevention, particularly the introduction of typhoid conjugate vaccines, have shown promise in reducing disease burden in endemic regions<sup>10</sup>.

Given these challenges, the present study was undertaken to determine the prevalence and demographic distribution of typhoid fever in a tertiary care hospital in Western Uttar Pradesh and to assess the practical limitations of blood culture in guiding antibiotic therapy.

## MATERIALS AND METHODS

### Study Design and Setting:

This retrospective observational study was conducted in the Department of Microbiology at a tertiary care teaching hospital in Western Uttar Pradesh, India, over a period of three months.

**Study**

A total of 110 clinically suspected cases of enteric fever were included in the study. Samples were received from both inpatient (IPD) and outpatient (OPD) departments and processed in the microbiology laboratory.

**Population:**

**Inclusion and Exclusion Criteria:**  
All samples from patients clinically suspected of enteric fever during the study period were included. Duplicate samples, samples with incomplete demographic or clinical details, and inconclusive test results were excluded from the analysis.

**Diagnostic Methods:**  
Serological testing was performed using the Typhi Dot test for qualitative detection of IgM and IgG antibodies against Salmonella Typhi.

IgM positivity, with or without IgG, was considered indicative of recent or ongoing infection. Samples showing both IgM and IgG positivity were interpreted as representing the mid to late phase of infection, while IgG positivity alone was considered suggestive of past exposure or late-stage infection.

Blood culture was performed wherever opted. In cases where blood culture was negative but IgM (with or without IgG) was positive, patients were categorized as probable typhoid cases based on serological findings and clinical correlation. The limited sensitivity of blood culture was attributed to prior antibiotic use, low bacterial load, and delayed presentation, as the culture positivity is highest during the first week of illness when bacteremia is present.

**Data Collection:**  
Relevant demographic and clinical data, including age, sex, department, and patient category (IPD/OPD), were obtained from laboratory records and entered into a structured data sheet for analysis.

**Statistical Analysis:**  
Data were analyzed using appropriate statistical methods. Categorical variables were expressed as frequencies and percentages. The Chi-square test was applied to assess associations between variables, and a p-value of <0.05 was considered statistically significant.

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**Conflict of Interest** – The authors have no conflict of interest whatsoever.

**Ethical Approval** - Approved

**RESULTS**

A total of 110 clinically suspected cases of enteric fever were analyzed during the study period. Of these, 27 cases (24.5%) were positive, while 83 cases (75.5%) were negative (Table 1).

The sex distribution showed that, of 70 female patients, 21 (30.0%) tested positive, whereas among 40 male patients, 6 (15.0%) tested positive. Thus, a higher positivity rate was observed among females compared to males (Table 2).

Age-wise analysis revealed an increasing trend of positivity with advancing age. No positive cases were observed in the 0–20 years age group. The positivity rate was 18.8% in the 21–40 years group, which increased to 29.5% in the 41–60 years group and reached the highest value of 33.3% in patients aged more than 60 years (Table 3).

Department-wise distribution indicated that the majority of cases were reported from the Medicine department, which also showed a higher positivity rate of 27.7%. Emergency cases demonstrated a comparable positivity rate of 28.6%, while minimal or no positive cases were observed in other departments (Table 4).

With respect to the patient category, 79 samples were received from IPD and 31 from OPD. A higher positivity rate was observed among IPD patients (29.1 %) compared to OPD patients (12.9 %) (Table 5).

With regard to blood culture, only 2 out of 23 IPD-positive cases underwent culture testing; both samples were collected after more than 7 days of illness, and no bacterial growth was observed. Among OPD patients, none of the positive cases underwent blood culture testing. Overall, blood culture was performed in only 2 of 27 positive cases, and no culture positivity was recorded (Table 6).

**Table 1: Overall Positivity**

Result	Number (n)	Percentage (%)
Positive	27	24.5%
Negative	83	75.5%
Total	110	100%

**Table 2: Sex-wise Distribution**

Sex	Positive (n)	Negative (n)	Total (n)	Positivity (%)
Male	6	34	40	15.0%
Female	21	49	70	30.0%
Total	27	83	110	24.5%

**Table 3: Age-wise Distribution**

Age Group	Positive (n)	Negative (n)	Total (n)	Positivity (%)
0–20	0	10	10	0%
21–40	6	26	32	18.8%
41–60	13	31	44	29.5%

>60	8	16	24	33.3%
Total	27	83	110	24.5%

**Table 4: Department-wise**

Department	Positive (n)	Negative (n)	Total (n)	Positivity (%)
Medicine	23	60	83	27.7%
Surgery	2	12	14	14.3%
Emergency	2	5	7	28.6%
ENT	0	1	1	0%
OBG	0	2	2	0%
ORTHO	0	1	1	0%
PAEDIATRICS	0	1	1	0%
CARDIO	0	1	1	0%
Total	27	83	110	24.5%

**Table 5: IPD vs OPD**

Source	Positive (n)	Negative (n)	Total (n)	Positivity (%)
IPD	23	56	79	29.1 %
OPD	4	27	31	12.9 %
Total	27	83	110	24.5%

**Table 6: Blood Culture Findings**

Source	Positive cases (n)	Culture Performed (n)	Culture Result	Culture positivity (%)	Remark
IPD	23	2	No Growth	0%	Samples collected after >7 days
OPD	04	0	Not performed	0 %	Culture not opted
Total	27	2	No growth	0 %	

## DISCUSSION

The present study demonstrated an overall positivity rate of 24.5% among clinically suspected cases, indicating a substantial burden of enteric fever in the study population. These observations are in agreement with findings from systematic reviews and meta-analyses from India, which have reported a considerable burden of enteric fever in endemic settings <sup>12</sup>. Similar estimates from

global epidemiological analyses further support the high prevalence of typhoid fever in low- and middle-income countries<sup>13</sup>.

An important observation in the present study was the higher positivity rate among females compared to males. While several earlier studies have reported male predominance, gender-based differences in enteric fever epidemiology may vary across regions due to differences in exposure risk, healthcare-seeking behavior, and sociocultural factors<sup>27</sup>. This highlights the importance of region-specific epidemiological assessments.

Age-wise distribution in the present study showed increasing positivity with advancing age, with the highest prevalence observed among elderly individuals. This finding contrasts with some global data suggesting higher incidence among children but is supported by studies indicating that disease patterns in endemic regions may shift depending on immunity, repeated exposure, and comorbid conditions<sup>15,26</sup>. The higher positivity among older age groups in this study may also reflect healthcare utilization patterns and increased likelihood of testing in symptomatic adults.

The higher positivity observed among IPD patients compared to OPD patients is consistent with hospital-based surveillance data, where more severe or clinically suspected cases are more likely to be admitted and undergo diagnostic evaluation<sup>15,16</sup>. This emphasizes that hospital-based prevalence may overrepresent more severe disease presentations.

Department-wise distribution revealed the highest burden in the Medicine department, which aligns with the clinical presentation of enteric fever as a common cause of prolonged febrile illness managed in general medical practice<sup>17</sup>. Similar observations have been reported in clinical and hospital-based studies.

A key finding of this study is the limited diagnostic yield of blood culture in routine clinical practice. Although blood culture remains the gold standard for diagnosis, its sensitivity is often reduced due to prior antibiotic use, low bacterial load, and delayed presentation of patients. As a result, a significant proportion of clinically suspected cases are diagnosed based on serological tests rather than culture confirmation. This limitation has been well documented in studies describing challenges in laboratory diagnosis of enteric fever in endemic settings<sup>18,21</sup>

The low yield of blood culture has important implications for patient management. In routine clinical practice, clinicians frequently commence empirical antimicrobial therapy before obtaining culture results or without waiting for antimicrobial susceptibility testing. While this approach is necessary to prevent complications, it reduces the opportunity for targeted therapy and contributes to inappropriate antibiotic use. Surveillance studies have highlighted evolving antimicrobial susceptibility patterns and the emergence of multidrug-resistant and extensively drug-resistant strains of *Salmonella Typhi* in India and other endemic regions<sup>14,19,22</sup>.

The increasing reliance on empirical therapy, coupled with diagnostic limitations, underscores the need for improved and rapid diagnostic tools that can guide appropriate antibiotic selection. Strengthening laboratory capacity and promoting timely sample collection before antibiotic initiation are essential steps to improve culture yield and optimize patient management<sup>21</sup>

Despite advances in prevention, including vaccination strategies, enteric fever continues to persist as a major public health problem in endemic regions. Multicentric and regional studies have demonstrated that inadequate sanitation, unsafe water supply, and high population density remain key drivers of disease transmission<sup>20,21</sup>. Globally, although some decline in incidence has been observed due to improved public health measures, enteric fever continues to pose a significant burden in low- and middle-income countries<sup>23,24</sup>

Strengthening surveillance systems, improving diagnostic capacity, ensuring rational antibiotic use, and expanding vaccination coverage are critical components of a comprehensive strategy to control enteric fever<sup>25</sup>.

## **CONCLUSION**

The present study demonstrates a considerable burden of typhoid fever in Western Uttar Pradesh, with an overall positivity rate of 24.5% among clinically suspected cases. Higher positivity observed among females, elderly individuals, and hospitalized patients highlights the influence of demographic and clinical factors on disease distribution in this setting.

A key finding of this study is the limited utility of blood culture in routine clinical practice. Factors such as prior antibiotic use, low bacterial load, and delayed presentation significantly reduce culture positivity, thereby limiting its role in guiding targeted antimicrobial therapy. Consequently, clinicians frequently rely on serological tests and initiate empirical antibiotic treatment.

While empirical therapy remains essential for timely management, it poses challenges in ensuring appropriate antibiotic selection and contributes to the growing problem of antimicrobial resistance. These findings underscore the need for improved diagnostic strategies, including timely sample collection and the development of rapid and reliable diagnostic tools.

Strengthening microbiological diagnostic facilities, promoting rational antibiotic use, and enhancing surveillance systems are critical to improving patient outcomes. In addition, public health measures such as improved sanitation, safe water supply, and expanded vaccination coverage remain essential for long-term control and prevention of typhoid fever.

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