RES-130

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Evaluating the Diagnostic Value of Absolute Eosinopenia in Culture-Positive Enteric Fever: A Case-Control Study

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INTRODUCTION

Epidemiological data suggest that enteric fever affects over 21 million people each year, with an estimated 200,000 annual deaths worldwide. The highest incidence rates are found in South-Central Asia, Southeast Asia, and parts of Africa [1]. In these regions, enteric fever predominantly impacts children and young adults, with outbreaks frequently associated with poor sanitation and inadequate water supply. The disease manifests with a range of symptoms, including prolonged fever, abdominal pain, and gastrointestinal distress. Severe cases can lead to complications such as intestinal perforation and septicemia, necessitating prompt and effective treatment.

Although blood culture remains the gold standard for diagnosing enteric fever, its sensitivity varies from 40–70%, heavily influenced by prior antibiotic use, timing of sample collection, and bacterial load. Bone marrow aspirate cultures, though more sensitive, are invasive and not routinely performed in many settings [2,3]. Serological tests such as the Widal test and Typhidot (IgM and IgG) are cost-effective but have variable sensitivity and low specificity, resulting in potential misdiagnoses [4].

Hematological abnormalities, including anemia, elevated erythrocyte sedimentation rate (ESR), and thrombocytopenia, often accompany enteric fever. Leukopenia, while considered a characteristic finding, is present in only about 20–25% of cases, thus limiting its diagnostic utility [5]. Eosinopenia, characterized by a reduction in eosinophil count, has been noted in several bacterial infections including sepsis, pneumonia, and urinary tract infections, and may also be present in a significant proportion of enteric fever cases [6,7]. Specifically, absolute eosinopenia (defined as an eosinophil count of 0 cells/mm^3) has been observed in a large proportion of enteric fever cases in some studies [8,9]. The pathophysiology underlying this observation includes the arrest of myeloid maturation, reduced levels of erythroblasts and megakaryocytes, and increased phagocytosis in the bone marrow. Additionally, eosinophils are rapidly sequestered in the spleen in response to C5a and fibrin, leading to their decreased levels in peripheral circulation [8].

The potential advantages of using eosinopenia as a diagnostic marker include its rapid and straightforward measurement, which can be performed using routine hematological tests. This could provide a quicker and more accessible diagnostic option, particularly in resource-limited settings where advanced diagnostic facilities are not available

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MATERIALS AND METHODS

This retrospective case-control study was conducted from August 2023 to June 2024 at Kalinga Institute of Medical Sciences, Bhubaneswar (IRB Approval No: KIIT/KIMS/IEC/1902/2024). Informed consent was waived under retrospective exemption criteria. We included 79 culture-confirmed enteric fever cases and 80 febrile controls with non-typhoidal illnesses. Patients with hematological malignancies, asthma, filarial disease, alcohol use, or on corticosteroids/immunosuppressants were excluded. Clinical and laboratory data, including absolute eosinophil count (AEC) and Typhidot results, were collected prior to antibiotic initiation. Absolute eosinopenia was defined as 0 cells/μL. Diagnostic tools included the Sysmex XN-1000 hematology analyzer, BACTEC/BACT ALERT systems, and the VITEK identification system. Sample size (N=120) was calculated based on prior eosinopenia prevalence data; our final sample (N=159) exceeded this. Statistical analysis was performed using R 4.3.3. Group comparisons used t-tests, Mann-Whitney U, and Chi-square tests. Diagnostic performance (sensitivity, specificity, PPV, NPV) was evaluated against blood culture as the gold standard, with ROC analysis and DeLong's test for AUC comparison. Agreement was assessed using Cohen's Kappa and McNemar's test.

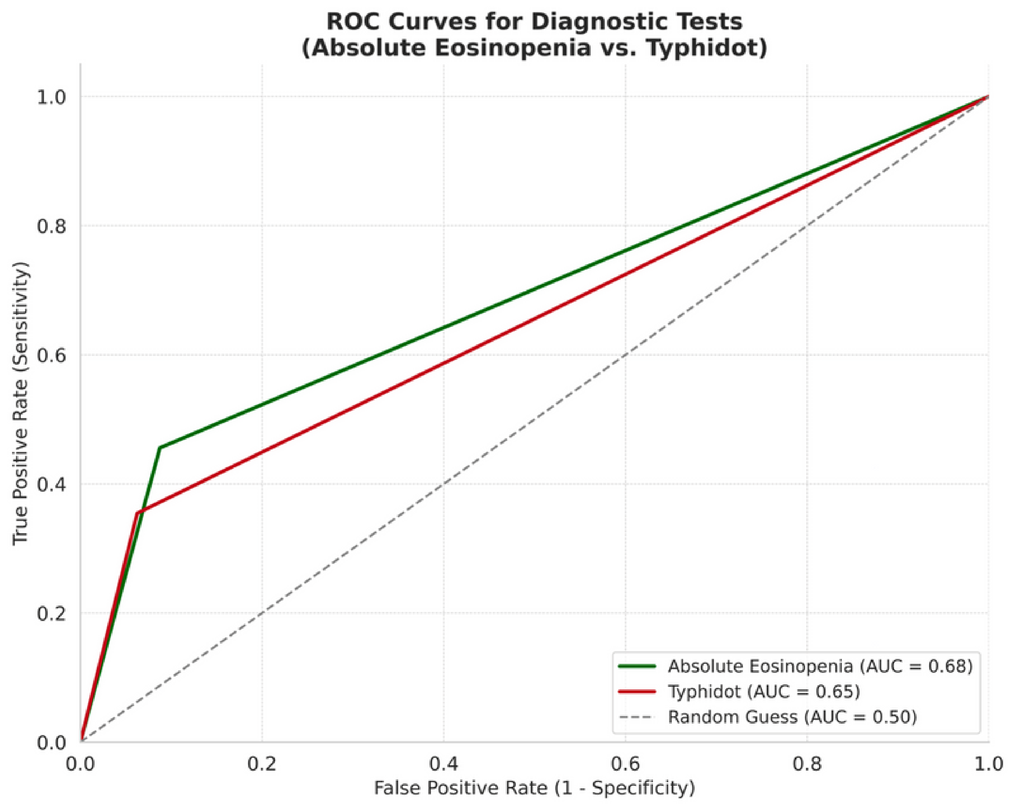

FIGURE 1: Receiver Operating Characteristic (ROC) Curves for Absolute Eosinopenia and Typhidot

This chart compares the ROC curves of absolute eosinopenia and Typhidot tests, illustrating their relative diagnostic strengths. Area under the curve (AUC) values help determine which test offers better discrimination between cases and controls.

RESULTS

A total of 159 patients were included, with a mean age of 31 years and a male predominance (75%). Culture-positive enteric fever cases had significantly lower eosinophil counts compared to controls (0.60 vs. 1.12 cells/μL, p = 0.001), and absolute eosinopenia was present in 46.8% of cases. Both Widal (p = 0.0107) and Typhidot (p < 0.0001) showed significant associations with culture positivity.

Diagnostic accuracy analysis demonstrated that all three tests had high specificity (≥91%), though sensitivity was modest: Absolute eosinopenia (45.6%), Widal (44.4%), and Typhidot (35.4%). Absolute eosinopenia had a PPV of 83.7% and NPV of 62.9%, similar to Typhidot (PPV 84.9%, NPV 59.5%) and Widal (PPV 36.4%, NPV 93.6%). ROC analysis indicated moderate predictive power (AUC: eosinopenia 0.68, Widal 0.64, Typhidot 0.62). McNemar's test highlighted significant differences in diagnostic distributions between eosinopenia and Typhidot, while Cohen's Kappa showed only moderate agreement, suggesting the tests are not interchangeable. DeLong's test revealed no significant difference in AUCs, confirming comparable diagnostic power. Overall, absolute eosinopenia emerges as a cost-effective tool with strong specificity, offering diagnostic performance comparable to conventional serological tests.

DISCUSSION

Despite significant progress in public health, enteric fever continues to affect over 21 million people annually, with nearly 200,000 deaths worldwide, particularly in regions with poor sanitation and limited access to clean water [1]. This study evaluated the diagnostic performance of Absolute Eosinopenia, Typhidot, and Widal tests in 159 patients (mean age: 31 years; 75% male). Culture-positive cases showed significantly lower eosinophil counts compared to controls (0.60 vs. 1.12 cells/μL, p = 0.001), and absolute eosinopenia was observed in 46.8% of confirmed cases. Diagnostic accuracy analysis revealed that Absolute Eosinopenia had a sensitivity of 45.6% and specificity of 91.3% (PPV: 83.7%, NPV: 62.9%), comparable to Widal (44.4%/91.3%) and Typhidot (35.4%/93.7%). ROC analysis confirmed moderate predictive ability (AUC: eosinopenia 0.68, Widal 0.64, Typhidot 0.62). Prior studies in India and abroad support these findings, consistently reporting eosinopenia as a highly specific but moderately sensitive marker for enteric fever, with particular value in early diagnosis when culture results are delayed or unavailable. Overall, Absolute Eosinopenia emerges as a cost-effective, rapid, and accessible tool with diagnostic performance comparable to conventional serological tests, but given its moderate sensitivity, it should be used as a complementary marker alongside clinical evaluation and other diagnostics.

Table 1 : Diagnostic Accuracy Measures.

Test	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Absolute Eosinopenia	45.57	91.25	83.72	62.93
Typhidot	35.44	93.74	84.85	59.52
Widal	44.44	91.25	36.36	93.59

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