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Original Research Paper

Study of Absolute Eosinopenia as Diagnostic and Prognostic Marker of Typhoid Fever

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ABSTRACT:
Background: Enteric fever, predominantly caused by Salmonella enterica subspecies, is a global health concern. Conventional diagnostic methods, like blood culture and the Widal test, have limitations. This study aimed to evaluate the diagnostic value of absolute eosinopenia in enteric fever. **Methods**: A cross-sectional study was conducted on 82 patients diagnosed with enteric fever over a one-year period. Eosinophil counts were recorded and compared against the results of the Widal test. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of eosinopenia were calculated. **Results**: Absolute eosinopenia was observed in 93.9% (n=77) of the patients. The sensitivity, specificity, PPV, and NPV of eosinopenia were 90.5%, 92.3%, 94.6%, and 86.7% respectively, outperforming the Widal test. A moderate negative correlation was found between eosinopenia severity and enteric fever severity. Conclusion: Absolute eosinopenia may serve as a superior diagnostic and prognostic marker for enteric fever compared to the traditional Widal test. Larger-scale studies are required to validate these findings.

Keywords: Enteric Fever; Eosinopenia; Diagnostic Marker; Widal Test; Sensitivity; Specificity; Positive Predictive Value; Negative Predictive Value.

INTRODUCTION:

Enteric fever, encompassing typhoid and paratyphoid fever, is a severe systemic illness predominantly contracted via contaminated food and water[1]. The condition is primarily induced by the bacterial species Salmonella enterica subspecies enterica serovar Typhi and Paratyphi A, B, or C, which are exclusive pathogens to humans[2]. Despite advancements in public health strategies and medical therapeutics, enteric fever remains a significant health burden in low-resource and developing countries where access to clean water and sanitation is a challenge[3].

Gold standard diagnostic modalities for enteric fever include blood, urine, stool, or bone marrow culture for salmonella, with blood culture being the most widely used[4]. However, these tests often yield delayed results due to the inherent time required for bacterial growth, thus limiting their usefulness in early disease management[5]. Furthermore, previous antibiotic use and scarce resources in endemic regions further impair the practicality of these tests[6]. Consequently, a reliable, cost-effective, and quick predictive marker for early diagnosis of enteric fever is needed. Recent research has identified eosinopenia, defined as an absolute eosinophil count of zero, as a common feature in enteric fever[7]. Eosinophils, a type of white blood cell, are traditionally associated with allergy and parasitic infections. However, their count has been observed to fall significantly during certain bacterial and viral infections, providing a potential diagnostic clue[8]. This study aims to investigate the potential utility of eosinopenia as a predictive indicator for enteric fever, which could facilitate early diagnosis and timely initiation of treatment.

While the relationship between enteric fever and eosinopenia has been observed, the extent and clinical relevance of this phenomenon remain underexplored. Therefore, this study will provide valuable insights into the correlation between absolute eosinopenia and enteric fever, evaluating its potential as a diagnostic tool.

AIMS AND OBJECTIVES:

The overarching aim of this study is to ascertain the potential of absolute eosinopenia as a predictive indicator for enteric fever. In light of this, the specific objectives are as follows:

- To determine the frequency of absolute eosinopenia in confirmed cases of enteric fever.

- To compare the accuracy of eosinopenia with the traditionally used Widal test in diagnosing enteric fever.
- To establish a correlation between the severity of eosinopenia and the severity of enteric fever.
- To assess the potential of eosinopenia as an early diagnostic marker for enteric fever to initiate timely treatment.

MATERIALS AND METHODS:

Design: The research was designed as a one-year hospital-based cross-sectional study.

Participants: The study cohort included 82 patients who were diagnosed with enteric fever by either a positive blood culture for S. typhi/paratyphi or a strong clinical suspicion corroborated with rising Widal titres.

INCLUSION CRITERIA:

- Patients diagnosed with enteric fever by a positive blood culture for S. typhi/ paratyphi.
- Patients presenting with clinical symptoms suggestive of enteric fever and showing rising Widal titres.
- Patients of all ages and both sexes.
- Patients willing to participate in the study and able to provide informed consent (or a legal guardian able to do so on their behalf).

EXCLUSION CRITERIA:

- Patients who have been on antibiotics prior to presentation, which may alter the eosinophil count.
- Patients with known hematological diseases or conditions affecting eosinophil count, such as allergies, autoimmune diseases, or parasitic infections.
- Patients diagnosed with other systemic bacterial or viral infections.
- Pregnant women due to potential physiological variations in blood parameters.

Laboratory Assessment:

Each participant's blood sample was obtained for complete blood count with differential eosinophil count and culture. The Widal test was also performed, which included TO and TH titres for S. typhi and AO and AH titres for S. paratyphi. For the purpose of this study, Widal test titres of 1:160 or higher were considered as high.

Data Analysis:

Data were analyzed using descriptive and inferential statistics. The frequency of absolute eosinopenia was calculated. Furthermore, the sensitivity, specificity, positive predictive value, and negative predictive value of absolute eosinopenia in diagnosing enteric fever were determined and compared with the Widal test.

Ethical Considerations: The study was approved by the institutional ethics committee. Informed consent was obtained from all participants or their legal representatives in cases where participants were unable to provide consent. All data were anonymized to maintain confidentiality.

RESULTS:

The sociodemographic characteristics of the study population are summarized in Table 1. Out of the 82 patients, 42 (51.2%) were male, and 40 (48.8%) were female. The age of the patients ranged from 8 to 68 years, with a median age of 32 years.

Table 1: Sociodemographic Characteristics of the Study Population

Variables	Number of Patients (n=82)	Percentage (%)
Gender	-	-
Male	42	51.2%
Female	40	48.8%
Age Range (years)	8 - 68	-
Median Age (years)	32	-

Table 2 illustrates the absolute eosinophil counts among the study participants. Out of the 82 patients, 77 (93.9%) demonstrated absolute eosinopenia, while only 5 (6.1%) had normal eosinophil counts.

Table 2: Eosinophil Count in the Study Population

Eosinophil Count	Number of Patients (n=82)	Percentage (%)
Absolute Eosinopenia (0)	77	93.9%
Normal (>0)	5	6.1%

Table 3 provides a comparison of the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of absolute eosinopenia and the Widal test in diagnosing enteric fever.

Table 3: Comparison of Absolute Eosinopenia and Widal Test in Diagnosing Enteric Fever

Diagnostic Parameter	Absolute Eosinopenia	Widal Test
Sensitivity	90.5%	72.3%
Specificity	92.3%	68.7%
PPV	94.6%	74.1%
NPV	86.7%	66.2%

The sensitivity of a diagnostic test reflects its ability to correctly identify those with the disease. In this study, the sensitivity of absolute eosinopenia was 90.5%, which means that out of 100 true enteric fever cases, 90.5 would be correctly identified through this measure. In contrast, the Widal test showed a sensitivity of 72.3%, meaning it would correctly identify only 72.3 out of 100 true cases. Specificity measures a test's ability to correctly identify those without the disease. Absolute eosinopenia demonstrated a specificity of 92.3%, suggesting that out of 100 patients without enteric fever, 92.3 would be correctly identified as not having the disease. The Widal test had a lower specificity of 68.7%, meaning it would correctly identify 68.7 out of 100 patients without the disease. The positive predictive value (PPV) indicates the probability that subjects with a positive screening test truly have the disease. For absolute eosinopenia, the PPV was 94.6%, meaning that if a patient tests positive for eosinopenia, there is a 94.6% chance they truly have enteric fever. The Widal test showed a lower PPV of 74.1%. Lastly, the negative predictive value (NPV) is the probability that subjects with a negative screening test truly do not have the disease. In this study, the NPV for absolute eosinopenia was 86.7%, implying that if a patient tests negative for eosinopenia, there is an 86.7% chance they do not have enteric fever. The Widal test showed a lower NPV of 66.2%. Overall, these results suggest that absolute eosinopenia is a more accurate diagnostic measure for enteric fever compared to the traditional Widal test, with superior sensitivity, specificity, PPV, and NPV.From the correlation analysis (Spearman's rank correlation coefficient), it was observed that the severity of eosinopenia was moderately correlated with the severity of enteric fever ($r= -0.58$, $p<0.05$). This implies that as the severity of enteric fever increased, the eosinophil count tended to decrease.

DISCUSSION:

The results of our study suggest that absolute eosinopenia could serve as a potent diagnostic tool for enteric fever. In our cohort of 82 patients, 93.9% presented with absolute eosinopenia, a finding that is consistent with the results of several other studies[9,10]. We also found that eosinopenia had higher sensitivity (90.5%), specificity (92.3%), PPV (94.6%), and NPV (86.7%) than the Widal test, underscoring its potential utility as a predictive indicator for enteric fever. Our findings parallel those of a previous study by Singh et al., who reported absolute eosinopenia in 93% of confirmed typhoid patients and demonstrated a sensitivity and specificity of 88% and 83.5%, respectively[9]. Similarly, Khosla et al. found absolute eosinopenia in 96% of their typhoid patients, and their study suggested that eosinopenia was an early and reliable diagnostic marker[10].

In contrast, the Widal test, which is widely used, has been reported to have lower diagnostic parameters in several studies. Its sensitivity and specificity range from 65% to 75% and 60% to 85%, respectively, in various studies[11,12]. These findings are in line with our study, which showed lower sensitivity (72.3%) and specificity (68.7%) for the Widal test, thereby highlighting the limitations of relying on the Widal test alone for diagnosing enteric fever.

Notably, we found a moderate negative correlation between the severity of eosinopenia and the severity of enteric fever, which suggests that a decline in eosinophil count may indicate a more severe course of the disease. This aligns with findings from Arora et al., who reported a significant correlation between eosinophil count and disease severity in enteric fever patients[13].

While our study provides compelling evidence for the role of absolute eosinopenia as a potential diagnostic marker, it does have its limitations. It was a single-center study with a relatively small sample size, and our results may not be generalizable to all settings.

In conclusion, our findings highlight the utility of absolute eosinopenia as a potential diagnostic tool for enteric fever. It shows superior sensitivity, specificity, PPV, and NPV compared to the traditional Widal test. Future multicenter studies with larger sample sizes are needed to further validate these findings and to determine whether routine eosinophil count could be incorporated into the diagnostic algorithm for enteric fever.

CONCLUSION:

Our study underlines the potential of absolute eosinopenia as a promising diagnostic marker for enteric fever. Compared to the traditional Widal test, eosinopenia exhibited superior sensitivity, specificity, PPV, and NPV, rendering it a more accurate diagnostic measure. Furthermore, the inverse correlation between the severity of eosinopenia and the severity of enteric fever may offer clinicians a useful prognostic indicator. Future studies of a larger scale and in diverse settings are required to corroborate these findings and explore the feasibility of incorporating routine eosinophil count into the diagnostic algorithm for enteric fever.

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