

Diagnostic Value of Absolute Eosinopenia as an Early Surrogate Marker in Enteric Fever – A Retrospective Observational Study

Rammohan G¹, Suresh K¹, Felix Fernandus S¹

¹Department of General Medicine, Sri Venkateshwaraa Medical College Hospital and Research Centre, Ariyur, Puducherry, India

*Corresponding Author: Dr. Suresh K, Dr. Felix Fernandus S

E-mail ID: sureshsuchu@yahoo.co.in; inform2felix@gmail.com

ABSTRACT

INTRODUCTION: India has the highest enteric fever burden in Southeast Asia. Currently, blood culture is the gold standard, however, its value is limited due to delayed results. Widal is used in low-resource settings despite its low specificity. This study tends to ascertain the potential of absolute eosinopenia as an early marker in laboratory-confirmed cases of enteric fever; to analyse its association with in-hospital events; and to obtain its occurrence in different serovars of *Salmonella*.

METHODS: This is a two-year hospital-based retrospective observational study involving 39 patients in a Tertiary Care Hospital at Puducherry. Patients with enteric positive bodily fluid culture or Widal were included. Those with known comorbidities affecting eosinophil counts, mixed growth in culture, antibiotic usage before admission, and antenatal women were excluded. AEC of 0 was considered significant. Data was analyzed using descriptive and inferential statistics. A *p*-value of <0.05 was considered significant.

RESULTS: Absolute eosinopenia was observed in 71.80% (n=39). Significant correlation was observed between eosinopenia and systemic signs, with the most common being abdominal tenderness in 12 patients. No significant correlation of eosinopenia with in-hospital events or type of serovar was observed.

DISCUSSION: This study demonstrated a strong correlation between absolute eosinopenia and enteric fever. With the right clinical suspicion, absolute eosinopenia has a prospective use as a viable diagnostic marker of enteric fever for physicians with limited resources.

Keywords: Enteric fever, absolute eosinopenia, typhoid fever

INTRODUCTION:

“Enteric fever” is a common clinical diagnosis that refers to a bacterial infection comprising two infections: Typhoid and Paratyphoid fever. This illness is brought on by *Salmonella enterica*, a gram-negative bacterium that is a member of the Enterobacteriaceae genus. Compared to *Salmonella* serovars Typhi (typhi) and Paratyphi A, serovars B and C are less commonly seen in clinical settings.¹

By ingesting tainted food or water, humans can acquire the organism through the feco-oral route.² The amount consumed, the acidity of the stomach, and the host's intestinal integrity all have a significant impact on how severe the disease is.³ After passing through the intestinal mucosa, the organism penetrates the M cell and is phagocytosed by the macrophages. The ileal lymphatics then allow it to enter the reticuloendothelial system, which includes the bone marrow, lymph nodes, liver, and spleen. Even though the majority of cases are symptomatic, some carriers may not exhibit any symptoms and still spread the disease.⁴

India alone is responsible for 75% of enteric fever deaths and 82% of cases in South Asia.⁵ However, the supplied data is primarily limited to the public healthcare system and comes from a small portion of the population. The private sector provides a sizable amount of the nation's outpatient care. However, this sector's case surveillance is either inadequate or nonexistent.⁶ Additionally, over-the-counter antibiotics are easily accessible to the general public, which further reduces the likelihood of identification and effective case reporting.⁷ Consequently, these figures are likely to be greatly underestimated. According to the WHO/UNICEF Joint Reporting Form on Immunization (JRF), which was released in 2023, India has the greatest enteric fever burden of any country in Southeast Asia.⁸

Disease endemicity has been exacerbated by a number of factors, including inadequate human waste management, limited access to clean water supplies, rapid population increase, increasing urbanization,

and overburdened healthcare systems.⁹ Early diagnosis and appropriate treatment should be the main approaches to managing enteric fever in these circumstances.¹⁰

Most people with enteric fever are found and treated in the community. In 1 in 3 to 1 in 10 cases, hospitalization is necessary because of a complication, a decrease in the clinical status, or failure in defervescence.¹¹

In a secondary and tertiary care setup, blood culture is most commonly utilized as the gold standard diagnostic modality for enteric fever, along with other bodily fluid cultures like urine, stool, and bone marrow.¹² The value of these tests in early disease management is limited because they often yield delayed results due to the slow bacterial growth. In addition, these tests are less useful if antibiotics have been used in the recent past. Consequently, antibiotic resistance could develop as a result of inappropriate treatment.⁹

In healthcare settings where more precise diagnostic methods for enteric fever are unavailable, the Widal test is only the most widely used technique despite its low sensitivity and moderate specificity.^{13,14}

PCR-based tests and ELISA are also commercially accessible, but their high cost is unsuitable in developing nations such as India.¹⁵ Whilst a small number of patients also exhibit hematological indicators such as high erythrocyte sedimentation rate (ESR), thrombocytopenia, and neutropenia, their sensitivity and specificity are debatable.¹⁶

So in most instances, physicians need to rely on their experience and have to depend on the presenting clinical symptoms, which are indistinguishable from those of other febrile illnesses. To overcome these difficulties, a rapid, precise, and inexpensive predictive marker for early diagnosis is required.

Recent research has identified absolute eosinopenia as a common occurrence in enteric fever while others have observed normal or above normal eosinophil count.^{17,18}

Traditionally, increased eosinophil levels have been linked to allergies and parasite infections. We already know that eosinopenia is a subsequent stress reaction to an acute illness.¹⁹ The eosinophil cut-off values are still unknown, though. Eosinopenia, which has been frequently seen in some bacterial infections linked to sepsis, is strongly correlated with procalcitonin and C-reactive protein.^{20,21}

On the other hand, little is known about the relationship between eosinopenia and the disease's clinical progression. Furthermore, little is known about the connection between various *Salmonella* serovars and eosinopenia. When assessing a case of Pyrexia of Unknown Origin (PUO) or Acute Undifferentiated Febrile Illness (AUI), this could significantly aid doctors in reducing the differential diagnosis.

Therefore, this study intends to investigate the correlation between eosinopenia and enteric fever, and thus assess the possibilities of using absolute eosinopenia as an early diagnostic and predictive marker of enteric fever.

OBJECTIVES OF THE STUDY:

Primary Objective:

1. To ascertain the potential of absolute eosinopenia as an early surrogate marker in laboratory-confirmed cases of enteric fever.

Secondary Objective:

1. To determine the frequency of absolute eosinopenia in patients with enteric fever.
2. To analyze the association between absolute eosinopenia and in-hospital events.
3. To obtain the occurrence of absolute eosinopenia in different serovars of *Salmonella enterica*.

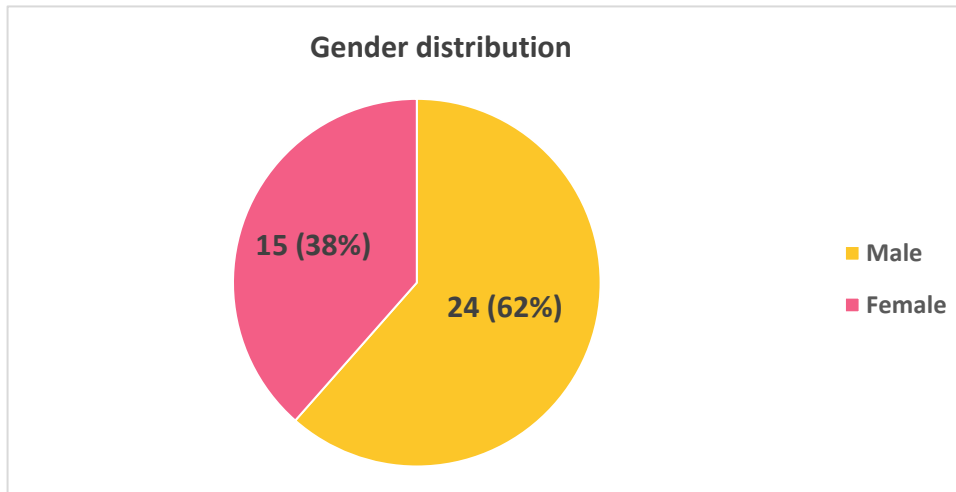
MATERIALS AND METHODS:

This research is a two-year hospital-based retrospective observational study involving 39 patients who were admitted and diagnosed with enteric fever in a Tertiary Care Hospital at Puducherry between 01/01/2023 and 15/02/2025.

Patients diagnosed with enteric fever by Widal test or one culture positive for *Salmonella* in any bodily fluid (blood, urine, or stool), age more than 13 years and both Genders were included in the study. Patients with known comorbid conditions affecting eosinophil count such as allergies, autoimmune diseases, or parasitic infestations; cultures with positive for a second organism at the same time; who had taken antibiotics before getting admitted to the hospital and antenatal women were excluded from the study.

Data collection:

Retrospective data from the MRD was collected after the Institute's SRC and IEC approval (Ref no: 42/SVMCH/IEC-Cert/May.25). The patient's brief medical history and examination findings along with reports of total count, percentage of eosinophils, Widal, and bacterial culture were collected from the case sheets. Widal titers of 1:160 or higher (strong positive) in the second week of illness were considered significant. Absolute Eosinophil Count (AEC) was calculated using the formula: $AEC = \text{Total counts} * \text{Percentage of eosinophils}$. Absolute eosinopenia i.e. AEC of 0 was considered significant.



STATISTICAL ANALYSIS:

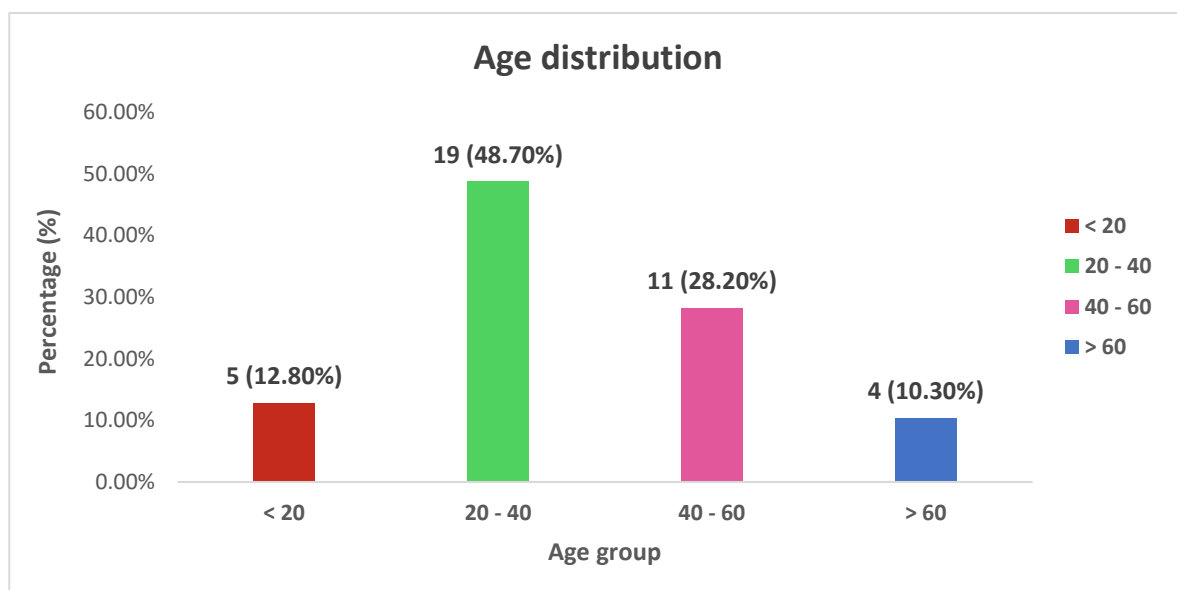
Data was entered in MS Excel and analyzed using SPSS software version 23.0. Data was analyzed using descriptive and inferential statistics. Quantitative data was analyzed using frequency distribution and mean standard deviation. Association was analyzed using chi-square and ANOVA tests. A p-value of <0.05 is considered significant.

RESULTS:

Figure 1: Frequency distribution of Age among the participants (n=39)

Figure 1 shows the bar chart representing the distribution of age among the participants. It shows that the maximum cases i.e. 19 (48.70%) belong to the age group of 20 - 40 years followed by 11 (28.20%) in 40 - 60 years, 5 (12.80%) in < 20 years, and 4 (10.30%) in > 60 years of age.

Figure 2: Frequency distribution of Gender among the participants (n=39)



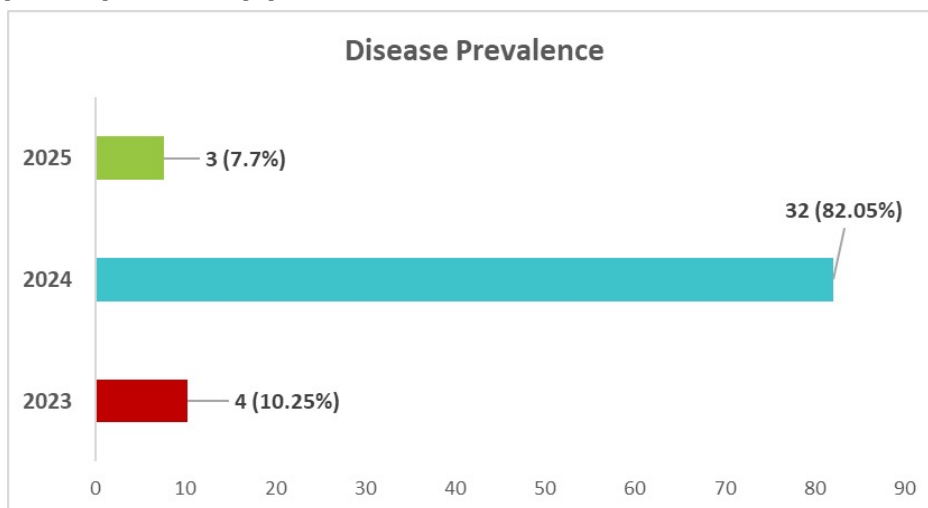


Figure 2 shows the pie chart determining the frequency distribution of gender among the participants. It shows that the majority of participants were male 24 (62%) and the remaining 15 (38%) were female.

Figure 3: Frequency distribution of Residence of the participants

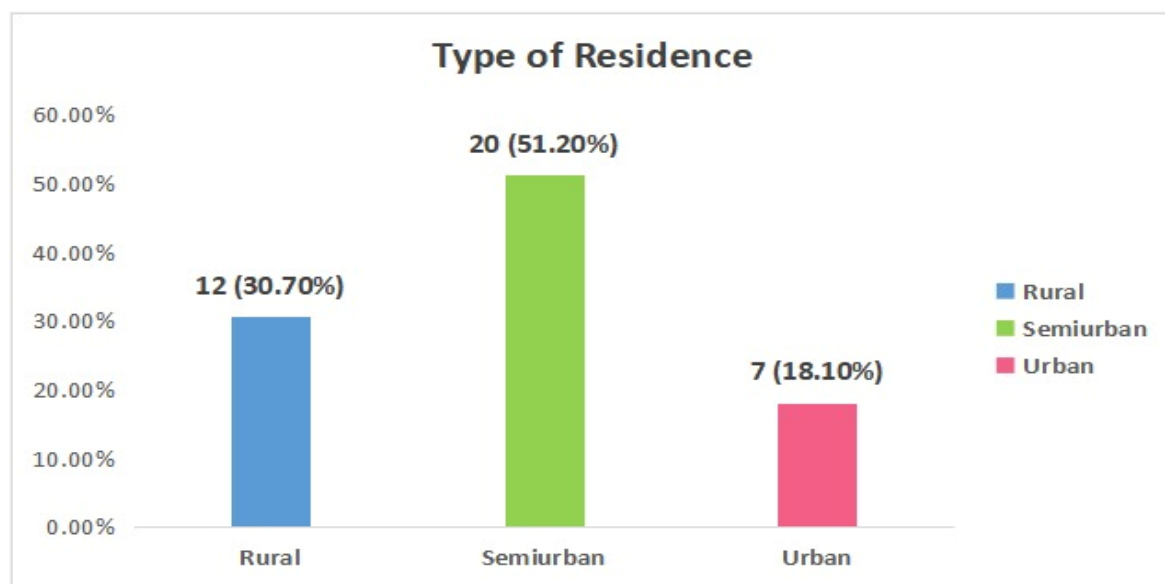


Figure 3 shows the frequency distribution of residence of the participants. It shows that the majority of the participants i.e. 20 (51.20%) belong to semi-urban areas, followed by 12 (30.70%) from rural areas and 7 (18.10%) from urban areas.

Figure 4: Frequency distribution of Disease prevalence (n=39)

Figure 4 shows the frequency distribution of disease prevalence from 2023 to 2025. It shows that the majority of cases i.e. 32 (82.05%) were in 2024, followed by 4 (10.25%) in 2023 and 3 (7.70%) in 2025.

Table 1: Frequency distribution of presenting symptoms among the participants (n=39)

Presenting symptoms	Frequency	Percentage (%)
Fever	35	89.70%
Loose stools	15	38.40%
Vomiting	14	35.89%
Abdominal pain	9	23.07%
Headache	5	12.82%

Body pain	5	12.82%
Productive cough	4	10.25%
Joint pain	3	7.69%
Weight loss	2	5.12%
Burning micturition	2	5.12%
Breathlessness	1	2.56%
Dry cough	1	2.56%

Table 1 determines the frequency distribution of presenting symptoms among the participants. It shows that the majority i.e. 35 (89.70%) of participants presented with fever as a presenting symptom followed by loose stools among 15 (38.40%), vomiting in 14 (35.89%), abdominal pain in 9 (23.07%), headache in 5 (12.82%), body pain in 5 (12.82%), productive cough in 4 (10.25%), joint pain in 3 (7.69%), weight loss in 2 (5.12%), burning micturition in 2 (5.12%), breathlessness in 1 (2.56%) and dry cough in 1 (2.56%) participant.

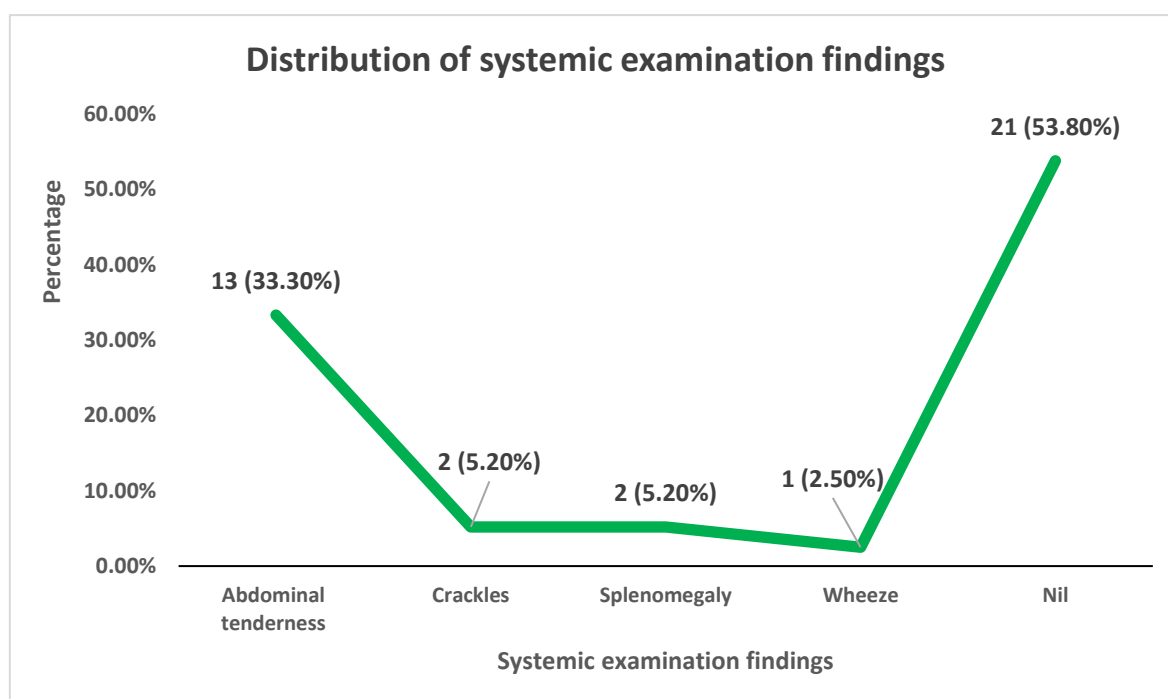
Figure 5: Frequency distribution of systemic examination findings among the participants (n=39)

Figure 5 shows the line diagram representing the frequency distribution of systemic examination findings among the participants. The majority of participants 21 (53.80%) had no findings. Around 13 (33.30%) participants were found to have abdominal tenderness followed by crackles in 2 (5.20%), splenomegaly in 2 (5.20%), and wheeze in 1 (2.50%).

Figure 6: Frequency distribution of hospital admission among the participants (n=39)

Figure 6 shows the frequency distribution of hospital admission among the participants. The majority of participants 34 (87.20%) got admitted into the Ward while only 5 (12.80%) got admitted into the intensive care unit.

Figure 7: Frequency distribution of the presence of complications among the participants (n=39)



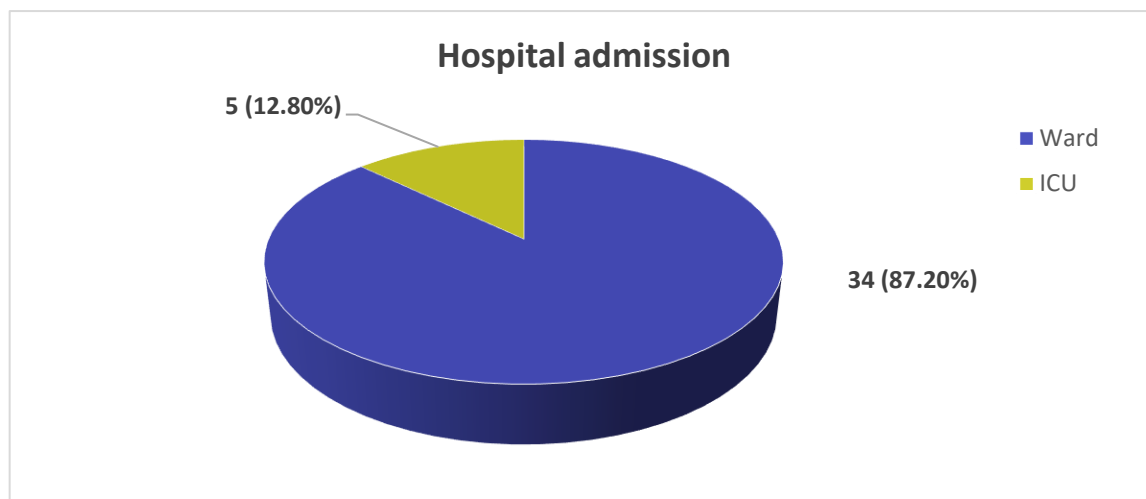


Figure 7 shows the frequency distribution of the presence of complications among the participants. It reveals that about 22 (56.50%) had one or the other complication while 17 (43.60%) had no complications.

Figure 8: Frequency distribution of complications among the participants (n=39)

Figure 8 shows the frequency distribution of complications among the participants. Among 39 participants, 22 (56.4%) had complications as depicted in the bar chart above. Bowel wall edema was detected in 6 (15.30%) followed by hypovolemic shock in 5 (12.80%), acute kidney injury in 3 (7.60%), mesenteric lymphadenitis in 2 (5.20%), appendicitis in 2 (5.20%), reactive arthritis in 2 (5.20%), metabolic acidosis in 1 (2.50%) and hepatitis in 1 (2.50%) participant.

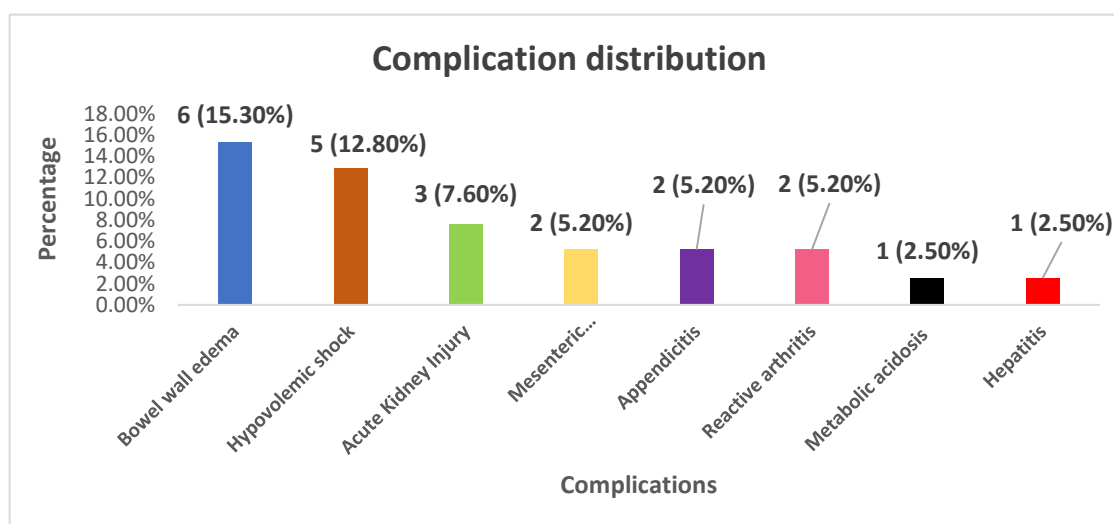
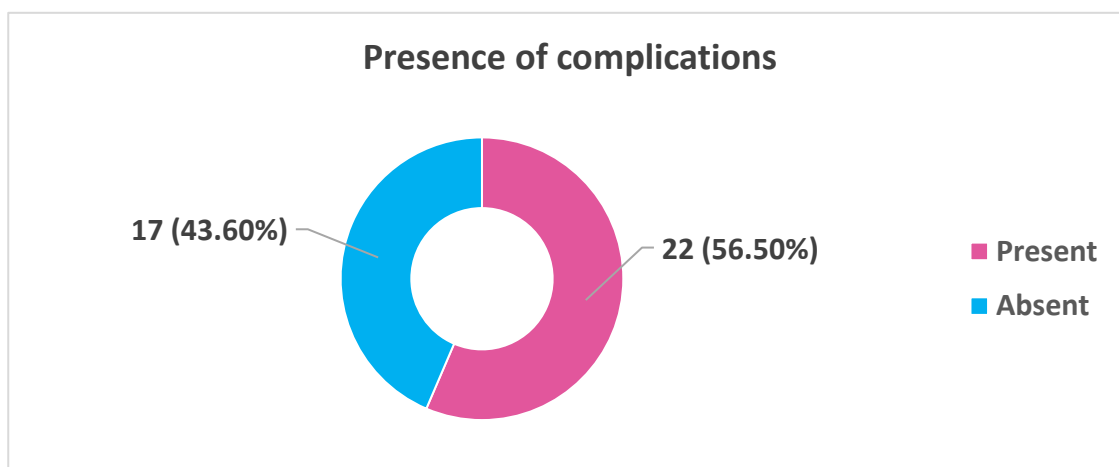
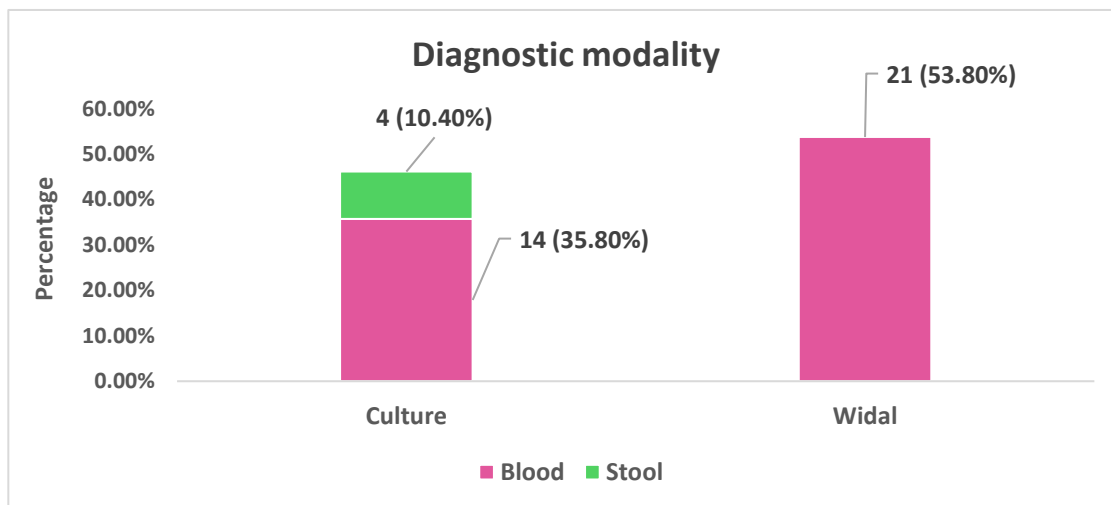


Figure 9: Frequency distribution of diagnostic modalities among the participants (n=39)

Figure 9 shows the frequency distribution of diagnostic modalities among the participants. Among 39 participants, the majority 21 (53.80%) had undergone Widal test for diagnosis while culture was done for the



remaining 18 (46.2%) participants. Of the 18 participants, 14 (35.80%) were diagnosed with blood cultures while 4 (10.40%) with stool cultures.

Table 2: Frequency distribution of type of serovar among the participants (n=39)

Type of serovar	Frequency	Percentage (%)
Typhi	26	66.60%
Paratyphi A	7	17.90%
Paratyphi B	6	15.50%

Table 2 shows the frequency distribution of type of serovar among the participants. It depicts that about 26 (66.60%) were diagnosed with Typhi serovar followed by 7 (17.90%) Paratyphi A and 6 (15.50%) Paratyphi B.

Figure 10: Frequency distribution of Absolute eosinopenia among the participants (n=39)

Figure 10 shows the frequency distribution of absolute eosinopenia among the participants. It shows that the majority 28 (71.80%) had absolute eosinopenia and 11 (28.20%) did not.

Table 3: Association between Absolute eosinopenia and type of admission (n=39)

Absolute eosinopenia	Type of admission		P - Value (Fischer's Exact)
	Ward	ICU	
Present	24	4	0.662 (0.562)
Absent	10	1	

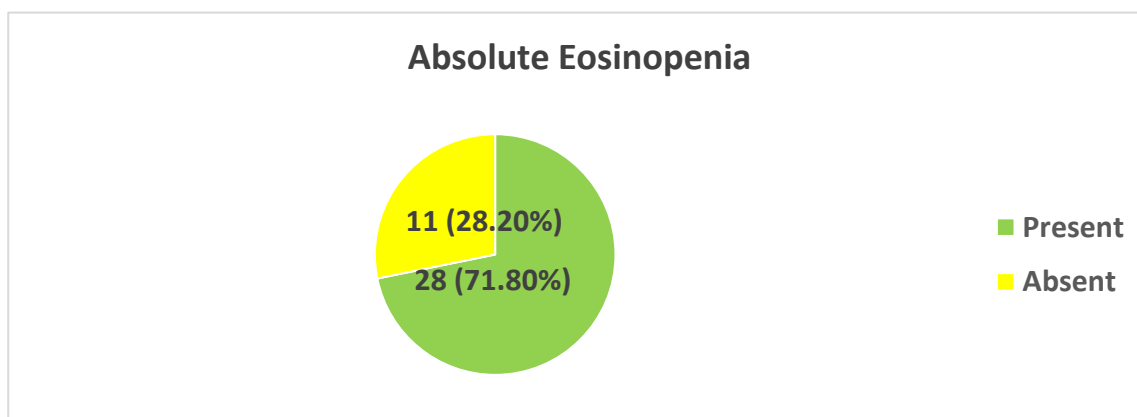


Table 3 shows the association between absolute eosinopenia and type of admission. There was no statistically significant association between absolute eosinophil count and type of admission since the p-value is not < 0.05.

Table 4: Association between Absolute eosinopenia and different types of serovar (n=39)

Absolute eosinopenia	Type of serovar			P - Value (Chi-square value)
	Typhi	Paratyphi A	Paratyphi B	
Present	17	6	5	0.451 (1.592)
Absent	9	1	1	

Table 4 shows the association between absolute eosinopenia and different types of serovar. There was no statistically significant association between absolute eosinophil count and type of serovar since the p-value is not < 0.05.

Table 5: Association between Absolute eosinopenia and systemic findings (n=39)

Absolute eosinopenia	Systemic findings					P - Value (Chi-square value)
	Abdominal tenderness	Crackles	Splenomegaly	Wheeze	Nil	
Present	12	0	1	0	15	0.029 (10.808)
Absent	1	2	1	1	6	

Table 5 shows the association between absolute eosinopenia and systemic findings. There was a statistically significant association between absolute eosinophil count and systemic findings with p-value < 0.05.

Table 6: Association between Absolute eosinopenia and development of complications (n=39)

Absolute eosinopenia	Complications		P - Value (Chi-square value)
	Present	Absent	
Present	15	13	0.103 (2.662)
Absent	9	2	

Table 6 shows the association between absolute eosinopenia and the development of complications. There was no statistically significant association between absolute eosinophil count and complication.

DISCUSSION:

Due to its high rate of death and morbidity, enteric fever is regarded as a disease of concern, especially in developing nations. It is usually a brief febrile disease with minimal complications but it can also prove potentially fatal if treatment is not received. In recent years, India has seen an increase in the number of cases of enteric fever. Estimated data shows India has the largest typhoid burden in the world, with 10 million cases of typhoid fever reported in 2021.²² Early diagnosis and treatment are crucial in combating this global menace. Considering the time-consuming nature of bacterial cultures and the low sensitivity and specificity of Widal test in endemic regions there is a lacuna for an easily affordable, quick, and specific marker to distinguish enteric fever from other febrile illnesses.^{13,14}

We enrolled 39 inpatients with laboratory-confirmed enteric fever in our study. The patients ranged in age from 14 to 70 years old, with a mean age of 36.87 ± 16.125 years. Sixty-two percent of the patients were male. In comparison to 2023 (10.25%), the diagnosis and reporting of cases increased dramatically in 2024 (82.05%). This is in line with the WHO/UNICEF JRF 2023 statistics, which shows that the number of cases with enteric fever has increased recently (4.02 lakh cases in 2022 to 5.74 lakh cases in 2023).⁸ One factor contributing to the issue may be the increase in the consumption of packaged foods and meals from street vendors. This is especially true while consuming dairy products because it provides an ideal environment for *S. typhi* to grow.²³

We observed that the majority of the patients were hailing from the semi-urban (51.20%) or rural (30.70%) localities, while only a small number of patients were reported to be from urban areas (18.10%). This geographical predilection may be a result of unplanned urbanization, inadequate water storage, poor sanitation, and environmental changes.⁹

Fever (89.70%) was the most frequent presentation, followed by vomiting (35.69%) and loose stools (38.00%). The same results were found in a research by Tulika et al. Following gastrointestinal problems (anorexia in 71.33%, vomiting in 38.67%, and loose stools in 5.33%), fever was observed in 100% of

cases.²⁴ Furthermore, our study found that abdominal soreness (33.30%) was commonly reported. The macrophages' production of cytokines in response to the bacterial products results in fever and discomfort in the abdomen. Many *S. typhi* strains emit toxins that cause intestinal mucosal inflammation and cause gastrointestinal symptoms like diarrhoea and vomiting. In severe cases, these poisons also result in multisystem involvement and unusual presentation.⁴

Only a small number of the cases (12.80%) were admitted to the intensive care units, indicating the brief course of the illness and response to therapy. 56.50% of the cases reported complications, with the most frequently encountered bowel wall edema (15.30%), hypovolemic shock (12.80%), and acute kidney injury (7.60%).

Complete blood count analysis showed leucopenia in 30.70% and leucocytosis in 18.10% of cases while the others (51.20%) had normal Total Leucocyte Counts (TLC). Neutrophilia in 25.70%, lymphopenia in 35.80%, and lymphocytosis in 10.40% were observed in the Differential Leucocyte Count (DLC). From data by Qamar U et al, leucopenia was observed in 52%, neutropenia in 32%, neutrophilia in 23%, lymphopenia in 8%, and lymphocytosis in 12%.²⁵ Neutropenia was not seen in our investigation, despite the fact that the frequencies of neutrophilia and lymphocytosis were similar. Furthermore, our study had relatively greater rates of lymphopenia and leucocytosis. Neutropenia has been thought to be caused by dysregulated granulopoiesis and expanded margination.²⁶ Neutrophilic leucocytosis is considered a symptom of complication, whereas neutrophilia occurs after relative lymphocytosis during the recovery period.²⁷ Intestinal irritation, perforation, or subsequent infections can all result in leucocytosis.²⁸ Although lymphopenia is recognized to be caused by enteric fever the precise mechanism is yet understood.²⁹ As observed in different viral infections, it might be secondary to lymphocyte death through apoptosis, pyroptosis, autophagy, and antibody-dependent cell-mediated cytotoxicity.³⁰

Absolute eosinopenia was found in 71.80% of the samples (n = 39). This is in line with what other research has found. Absolute eosinopenia was seen in 93.33% of the patients in Gandhi et al.³¹ Mallya et al. observed absolute eosinopenia in 93.9% of cases, while Lokhandwala et al. observed it in 100% of cases.^{17,32}

Eosinophils make up 1–4% of all white blood cells in circulation. They are essential for the immunological and inflammatory reactions to normal or pathological stimuli because they stimulate tissue remodeling and local inflammation.³³ Adrenaline and adrenal glucocorticosteroids play a key role in maintaining eosinophil homeostasis. Chemotactic substances such as fibrin and C5a rapidly sequester eosinophils in the periphery during the acute stage of infection.^{19,21}

Additionally, we found a statistically significant ($p < 0.05$) association between the results of the systemic examination and absolute eosinopenia. Compared to patients with normal eosinophil levels, those with absolute eosinopenia are more likely to exhibit localizing symptoms. In 12 out of 39 patients, stomach soreness was the most often observed localizing symptom.

Numerous investigations have provided an explanation for the process by which eosinopenia results in clinical symptoms in acute bacterial infections. Gram-negative bacteria's lipopolysaccharides trigger type 1 or T helper 1 (TH1) cell-mediated inflammation. They cause harm to host tissue and phagocyte activity by releasing cytokines that set off a pro-inflammatory cascade.

However, type 2 or T helper 2 (TH2) cell-mediated inflammation results in eosinophil activation for extracellular organisms that cannot be phagocytosed. This aids in tissue healing by activating myofibroblasts and promoting angiogenesis. A loss of balance between type 1 and type 2 inflammation is associated with poor infection outcomes.³⁴ Reduced eosinophil numbers could be a sign of immunological dysregulation because they are linked to type 2 inflammation. Eosinopenia has been shown to be a reliable indication of bacteremia in patients in need of intensive care unit treatment, and there is an inverse relationship between eosinophils and bacterial burden.^(20,35,36,37,38,39,40) However, our study found no statistically significant relationship between the type of serovar, the kind of hospitalization, or the development of complications and absolute eosinopenia.

CONCLUSION:

Our current study demonstrated a strong correlation between absolute eosinopenia and enteric fever. Absolute eosinopenia has a prospective use as a viable diagnostic marker for enteric fever. With the right clinical suspicion, it may direct and narrow the diagnosis towards enteric fever, thus aiding in prompt treatment, particularly in low-resource settings. This study would become more universally applicable if similar studies involving a larger sample size and multiple centres are undertaken in the near future.

REFERENCES:

1. Loscalzo J. Harrison's Principles of Internal Medicine. 21st ed. Vol. 1. New York: McGraw Hill LLC; 2022.
2. Amsalu T, Genet C, Adem Siraj Y. Salmonella Typhi and Salmonella Paratyphi prevalence, antimicrobial susceptibility profile and factors associated with enteric fever infection in Bahir Dar, Ethiopia. *Sci Rep.* 2021 Apr 1;11:7359.
3. Farrar J. Manson's Tropical Diseases. 24th ed. China: Elsevier Saunders; 2023.
4. Bennett J. Mandell, Douglas, and Bennett's principles and practice of infectious diseases. 9th ed. Philadelphia: Elsevier; 2020.
5. GBD 2017 Typhoid and Paratyphoid Collaborators. The global burden of typhoid and paratyphoid fevers: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet Infect Dis.* 2019 Apr;19(4):369–81.
6. Phalkey RK, Butsch C, Belesova K, Kroll M, Kraas F. From habits of attraction to modes of inclusion: enhancing the role of private practitioners in routine disease surveillance. *BMC Health Serv Res.* 2017 Dec;17(1):599.
7. Pitzer VE, Meiring J, Martineau FP, Watson CH, Kang G, Basnyat B, et al. The Invisible Burden: Diagnosing and Combatting Typhoid Fever in Asia and Africa. *Clin Infect Dis Off Publ Infect Dis Soc Am.* 2019 Oct 15;69(Suppl 5):S395–401.
8. Immunization Data [Internet]. [cited 2025 Mar 9]. WHO Immunization Data portal - Detail Page. Available from: <https://immunizationdata.who.int/global/wiise-detail-page>
9. Sur D, Barkume C, Mukhopadhyay B, Date K, Ganguly NK, Garrett D. A Retrospective Review of Hospital-Based Data on Enteric Fever in India, 2014-2015. *J Infect Dis.* 2018 Nov 10;218(suppl_4):S206–13.
10. Mirza SH, Beeching NJ, Hart CA. Multi-drug resistant typhoid: a global problem. *J Med Microbiol.* 1996 May;44(5):317–9.
11. Sinha A, Sazawal S, Kumar R, Sood S, Reddaiah VP, Singh B, et al. Typhoid fever in children aged less than 5 years. *The Lancet.* 1999 Aug 28;354(9180):734–7.
12. Gilman RH, Terminiello M, Levine MM, Hernandez-Mendoza P, Hornick RB. Relative efficacy of blood, urine, rectal swab, bone-marrow, and rose-spot cultures for recovery of Salmonella typhi in typhoid fever. *Lancet Lond Engl.* 1975 May 31;1(7918):1211–3.
13. Levine MM, Grados O, Gilman RH, Woodward WE, Solis-Plaza R, Waldman W. Diagnostic value of the Widal test in areas endemic for typhoid fever. *Am J Trop Med Hyg.* 1978 Jul;27(4):795–800.
14. Pang T, Puthucherry SD. Significance and value of the Widal test in the diagnosis of typhoid fever in an endemic area. *J Clin Pathol.* 1983 Apr;36(4):471–5.
15. Abubakar I, Irvine L, Aldus CF, Wyatt GM, Fordham R, Schelenz S, et al. A systematic review of the clinical, public health and cost-effectiveness of rapid diagnostic tests for the detection and identification of bacterial intestinal pathogens in faeces and food. *Health Technol Assess Winch Engl.* 2007 Sep;11(36):1–216.
16. Khosla SN, Anand A, Singh U, Khosla A. Haematological profile in typhoid fever. *Trop Doct.* 1995 Oct;25(4):156–8.
17. B DVM, Malali DAKD. Study of Absolute Eosinopenia as diagnostic and prognostic marker of Typhoid fever. *Int J Med Sci Clin Res Rev.* 2023 Jun 27;6(03):687–90.
18. Khan M, Coovadia YM, Connolly C, Sturm AW. The early diagnosis of typhoid fever prior to the Widal test and bacteriological culture results. *Acta Trop.* 1998 May;69(2):165–73.
19. Bass DA, Gonwa TA, Szejda P, Cousart MS, DeChatelet LR, McCall CE. Eosinopenia of Acute Infection. *J Clin Invest.* 1980 Jun;65(6):1265–71.
20. Abidi K, Khoudri I, Belayachi J, Madani N, Zekraoui A, Zeggwagh AA, et al. Eosinopenia is a reliable marker of sepsis on admission to medical intensive care units. *Crit Care Lond Engl.* 2008;12(2):R59.
21. Bass DA. Behavior of eosinophil leukocytes in acute inflammation. II. Eosinophil dynamics during acute inflammation. *J Clin Invest.* 1975 Oct;56(4):870–9.
22. Mehta K, Joshi M, Omar MA. Typhoid fever in India: A growing concern requiring immediate preventive efforts. *Health Sci Rep.* 2024 Feb 15;7(2):e1899.
23. Luby SP, Faizan MK, Fisher-Hoch SP, Syed A, Mintz ED, Bhutta ZA, et al. Risk factors for typhoid fever in an endemic setting, Karachi, Pakistan. *Epidemiol Infect.* 1998 Mar;120(2):129–38.
24. Sinha SK. A Prospective Study to Examine the Clinical and Laboratory Characteristics of Typhoid Fever in Children Under 18 Years Age in Bihar Region.
25. Qamar U. Hematological changes associated with typhoid fever Children's Hospital and Institute of Child's Health. *Rawal Med J.* 1970 Jan 1;38(1):32–32.
26. Park K. Park's Textbook of Preventive and Social Medicine. 27th ed. Jabalpur: Banarsidas Bhanot; 2023.
27. Hoffbrand AV, Higgs DR, Keeling DM, Mehta AB. Postgraduate Hematology. 7th ed. New York: Oxford University Press Inc; 2015.
28. Basnyat B, Qamar FN, Rupali P, Ahmed T, Parry CM. Enteric fever. *The BMJ.* 2021 Feb 26;372:n437.
29. Shah AK. Diagnosis of Enteric Fever. *Pediatr Infect Dis.* 2021 Dec 27;3(4):165–9.
30. Guo Z, Zhang Z, Prajapati M, Li Y. Lymphopenia Caused by Virus Infections and the Mechanisms Beyond. *Viruses.* 2021 Sep 20;13(9):1876.
31. Gandhi A, Darshan A. Eosinopenia as a Diagnostic Marker of Enteric Fever: A 1-Year Observational Study. *J Clin Infect Dis Soc.* 2023 Sep;1(3):252.
32. Lokhandwala A, Athar S, Turrin N. Role of absolute eosinopenia as marker of enteric fever: Experience from a Tertiary Care Hospital in the United Arab Emirates. *Ibnosina J Med Biomed Sci.* 2012 Dec;04(06):249–53.
33. Nagata M, Nakagome K, Soma T. Mechanisms of eosinophilic inflammation. *Asia Pac Allergy.* 2020 Apr;10(2):e14.
34. Spellberg B, Edwards JE. Type 1/Type 2 immunity in infectious diseases. *Clin Infect Dis Off Publ Infect Dis Soc Am.* 2001 Jan;32(1):76–102.
35. Davido B, Makhoulouf S, Matt M, Calin R, Senard O, Perronne C, et al. Changes in eosinophil count during bacterial infection: revisiting an old marker to assess the efficacy of antimicrobial therapy. *Int J Infect Dis IJID Off Publ Int Soc Infect Dis.* 2017 Aug;61:62–6.

36. Shaaban H, Daniel S, Sison R, Slim J, Perez G. Eosinopenia: Is it a good marker of sepsis in comparison to procalcitonin and C-reactive protein levels for patients admitted to a critical care unit in an urban hospital? *J Crit Care*. 2010 Dec;25(4):570-5.
37. Agnello L, Giglio RV, Bivona G, Scazzone C, Gambino CM, Iacona A, et al. The Value of a Complete Blood Count (CBC) for Sepsis Diagnosis and Prognosis. *Diagnostics*. 2021 Oct;11(10):1881.
38. Al Duhailib Z, Farooqi M, Piticaru J, Alhazzani W, Nair P. The role of eosinophils in sepsis and acute respiratory distress syndrome: a scoping review. *Can J Anaesth*. 2021;68(5):715-26.
39. Lavoignet CE, Le Borgne P, Slimani H, Forato M, Kam C, Kauffmann P, et al. [Relevance of eosinopenia as marker of sepsis in the Emergency Department]. *Rev Med Interne*. 2016 Nov;37(11):730-4.
40. Lin Y, Rong J, Zhang Z. -Revisit Eosinopenia as a Biomarker for Diagnosis of Sepsis: A Meta-Analysis [Internet]. In Review; 2020 [cited 2025 Mar 19]. Available from: <https://www.researchsquare.com/article/rs-57239/v1>