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HAEMATOLOGICAL DISPARITIES IN MANTOUX POSITIVE PATIENTS: A COMPARATIVE STUDY OF PULMONARY AND EXTRAPULMONARY TUBERCULOSIS

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Abstract

Introduction

Mycobacterium tuberculosis is the causative agent of tuberculosis (TB), which is the infectious illness that is transmitted the most frequently. The study aims to comprehensively evaluate hematological parameters in Mantoux-positive patients diagnosed with pulmonary tuberculosis (PTB) and extrapulmonary tuberculosis (EPTB), and to compare the findings between these two forms of the disease.

Material and Methods

This study was conducted in a private medical college and hospital in Chennai from January 2023 to February 2024, analyzing test samples from outpatient, inpatient, and emergency departments. The research included 48 individuals who tested positive for the Mantoux skin test, categorized into pulmonary and extrapulmonary TB. Haematological manifestations included elevated ESR, leukocytosis, leukopenia, thrombocytosis, and anemia. The study excluded individuals with a history of BCG vaccination, malignant pathologies, infectious diseases, chronic inflammatory conditions, haematological disorders, autoimmune diseases, diabetes mellitus, liver, or kidney diseases, and known hypersensitivity or allergy to tuberculin or its constituents. The study used an automated Sysmex XN 1000 six-part haematology analyzer and the Wintrobe technique to assess ESR in the residual blood.

Results

Our study revealed distinct hematological patterns between pulmonary tuberculosis (PTB) and extrapulmonary tuberculosis (EPTB). PTB patients showed significantly higher neutrophil counts and erythrocyte sedimentation rates (ESR), reflecting a stronger systemic inflammatory response. In contrast, EPTB patients exhibited elevated eosinophil and basophil counts, suggesting site-specific immune activation. Hemoglobin levels, RBC counts, and platelet levels were comparable between the two groups, with no significant differences.

Conclusion

Our study highlights distinct hematological profiles in pulmonary and extrapulmonary tuberculosis, reflecting varied immune responses and emphasizing the need for tailored diagnostic and therapeutic approaches.

Keywords: Tuberculosis, Pulmonary, Extrapulmonary, Epidemiology, hematological profiles

INTRODUCTION

Mycobacterium tuberculosis is the causative agent of tuberculosis (TB), which is the infectious illness that is transmitted the most frequently. In spite of the fact that creative diagnostic methods and therapy approaches have been developed, this issue continues to be one of the most significant challenges for public health on a global scale.[1] According to estimates, there are between 9 and 11 million individuals living with TB over the world. This includes 5.8 million men, 3.2 million women, and more than a million children.[2,3] Despite the recent advancements in molecular technology, the process of diagnosing tuberculosis (TB) continues to be

extremely challenging.[4] Several factors contribute to the difficulty of diagnosing this condition, including the poor sensitivity of the technologies that are now available, the paucibacillary character of the disease, the lengthy period of time that is required to culture the bacteria, and the extensive variety of clinical symptoms that are produced by the disease.[5] The third.[6] There are roughly forty percent of people in India who are infected with tuberculosis bacilli. Patients who have cavitary lesions are the source of a significant number of infections. Generally speaking, the majority of these patients have sputum smears that are positive.[7] In order to effectively defend against mycobacteria, CD4+ T helper (Th) cells are absolutely necessary.[8]A important component that contributes to the transformation of latent tuberculosis to active tuberculosis is HIV coinfection, which targets CD4+ Th cells and increases the rates of tuberculosis reactivation from three to ten percent per lifetime to five to ten percent over the course of a lifetime. [9] When a person coughs, they generate around three thousand droplet nuclei in addition to extremely small droplets that are infectious and persist in the environment for a considerable amount of time.[10] Alveolar macrophages are the major agents responsible for the transmission of infections and diseases.[11] For this reason, it is responsible for the development of pulmonary tuberculosis (PTB), which is a chronic granulomatous illness that affects the lungs. Tuberculosis that is identified bacteriologically in parts of the body other than the lungs, such as the abdomen, lymph nodes, meninges, or genitalia, is referred to as extrapulmonary tuberculosis (ETPT). This is the word most commonly used to describe the condition.[12-15] The bacterium that causes PTB and EPTB is the same; nevertheless, the symptoms, therapy, and prognosis of these two infectious diseases are very different from one another.

Aim

To comprehensively evaluate hematological parameters in Mantoux-positive patients diagnosed with pulmonary tuberculosis (PTB) and extrapulmonary tuberculosis (EPTB), and to compare the findings between these two forms of the disease.

Objective

To compare hematological parameters including complete blood count (CBC), including white blood cell count (WBC), red blood cell indices, platelet count, and differential leukocyte counts and erythrocyte sedimentation rate (ESR), between patients diagnosed with pulmonary tuberculosis and those diagnosed with extrapulmonary tuberculosis, both confirmed with a positive Mantoux test.

To compare the distribution and severity of anemia, leukocytosis, thrombocytosis, and other hematological abnormalities between PTB and EPTB groups.

MATERIALS AND METHOD

This research was performed in the Haematology and Clinical Pathology laboratory at a private medical college and hospital in Chennai from January 2023 to February 2024, after the acquisition of appropriate clearance from the Institutional Review Board (IRB approval number…). This is a retrospective analytical research analysing test samples from the outpatient (OP) department, inpatient (IP) department, and emergency department. The research population consisted of people who tested positive for the Mantoux skin test. This study comprised 48 individuals (N=48), categorised into two groups: pulmonary and extrapulmonary TB. The research encompassed the complete blood counts (CBC) and Erythrocyte Sedimentation Rate (ESR) acquired at the time of diagnosis. Haematological manifestations were categorised as follows: elevated ESR (in males exceeding 15 mm/hr and in females exceeding 20 mm/hr); leukocytosis (leukocyte count > 11,000/mm3); leukopenia (leukocyte count < 4,000/mm3); thrombocytosis (platelet count > 450/mm3); and anaemia (haemoglobin < 12 g/dL in females and < 14 g/dL in males).[13,15] The inclusion criteria comprised Mantoux positive patients diagnosed with pulmonary or extrapulmonary tuberculosis, as well as those with a confirmed diagnosis of tuberculosis via appropriate diagnostic methods (e.g., sputum examination, chest X-ray, culture), and patients with positive Mantoux skin test results whose samples were submitted for CBC and ESR analysis. The exclusion criteria encompassed individuals with a history of Bacillus Calmette-Guerin (BCG) vaccination within the past five years, as this may result in false positive Mantoux test outcomes; individuals with malignant pathologies, infectious diseases, chronic inflammatory conditions, haematological disorders, or autoimmune diseases; individuals with diabetes mellitus, liver, or kidney diseases that affect haematological parameters; and individuals with known hypersensitivity or allergy to tuberculin or its constituents, which compromises the reliability of the Mantoux test.[16]

Approximately 4 millilitres of venous blood samples were collected using aseptic approach into suitable anticoagulant tubes (Ethylene Diamine Tetra Acetic acid tubes). The whole blood count was evaluated with an automated Sysmex XN 1000 six-part haematology analyser, utilising 2 millilitres of blood from an EDTA tube. The Wintrobe technique was employed to assess the ESR in the residual 2 millilitres of blood. Employing the single intradermal (SID) method, 1 mg of pure protein derivative (PPD) per millilitre (20,000 tuberculin units) was generated from the M. bovis strain AN-5. Intradermal injection of 0.1 ml (2,000 units) of tuberculin was

administered to the patients.[16] The pertinent history, clinical particulars, and investigative facts concerning the samples were extracted from the test request forms and the MIAS (Medical Information Archiving Software) database of our institution.

Statistical analysis

Descriptive statistics were reported as mean (SD) for continuous variables, frequencies (percentage) for categorical variables. Independent t test was used to find the association between the continuous variables of two groups. Data were statistically evaluated with IBM SPSS Statistics for Windows, Version 26.0., IBM Corp., Chicago, IL.

RESULTS

Table 1: Distribution of demographic details among the study participants (N=48)

Slno	Age	Pulmonary (n=21)	Extra-pulmonary (n=27)	Total
1	10-20	2 (9.5)	1 (3.7)	3 (6.3)
2	21-30	5 (23.5)	5 (18.5)	10 (20.8)
3	31-40	7 (33.3)	10 (37)	17 (35.4)
4	41-50	3 (14.3)	5 (18.5)	8 (16.7)
5	51-60	3 (14.3)	3 (11.1)	6 (12.5)
6	61-70	0 (0)	2 (7.4)	2 (4.2)
7	>70	1 (4.8)	1 (3.7)	2 (4.2)

This table 1 illustrates the age distribution of 48 participants diagnosed with pulmonary tuberculosis (PTB) and extrapulmonary tuberculosis (EPTB). The majority of cases fall within the 31–40 age group, with 33.3% of PTB cases and 37% of EPTB cases, accounting for 35.4% of the total participants. This finding highlights that TB is most prevalent among adults in their productive years, which may be related to higher exposure to environmental and occupational risk factors, as well as immune challenges during this stage of life. The 21–30 age group is the second most affected (20.8% of total cases), followed by the 41–50 age group (16.7%). The older age groups (61–70 and >70 years) together represent only 8.4% of the total cases, suggesting that younger to middle-aged adults are more vulnerable to both PTB and EPTB. The distribution between PTB and EPTB across these age groups highlights a similar trend, with slightly higher cases of EPTB in older age groups (7.4% in 61–70 and 3.7% in >70).

Table 2: Distribution of gender among the study participants (N=48)

Slno	Gender	Age	Pulmonary (n=21)	Extra-pulmonary (n=27)
1	**Female**	10-20	1 (10)	0 (0)
2		21-30	1 (10)	2 (!5.4)
3		31-40	4 (40)	8 (61.5)
4		41-50	2 (20)	2 (51.4)
5		51-60	1 (10)	1 (7.7)
6		61-70	0 (0)	0 (0)
7		>70	1 (10)	0 (0)
1	**Male**	10-20	1 (9.1)	1 (7.1)
2		21-30	4 (36.4)	3 (21.4)
3		31-40	3 (27.3)	2 (14.3)
4		41-50	1 (9.1)	3 (21.4)
5		51-60	2 (18.2)	2 (14.3)
6		61-70	0 (0)	2 (14.3)
7		>70	0 (0)	1 (7.1)

The table 2 illustrates the age and gender distribution of the study participants across PTB and EPTB categories. Among females, the highest prevalence for PTB (40%) and EPTB (61.5%) is observed in the 31–40 age group. For males, the highest prevalence is also in the 31–40 age group for PTB (27.3%) but shifts to the 21–30 age group for EPTB (21.4%). These findings suggest that females in their third and fourth decades of life are more susceptible to TB, particularly EPTB, potentially due to biological or hormonal factors affecting

immunity. In males, younger adults are more affected by both forms of TB. Interestingly, no cases are observed in females over 61 years, while males exhibit a slight prevalence in older age groups. This difference could reflect gender-specific exposure, lifestyle, or healthcare-seeking behaviors.

Table 3:Hematological parameters among the study participants (N=48)

Slno	Parameters	Pulmonary tuberculosis (N=21)	Extrapulmonary tuberculosis (N=27)	P value
1.	Haemoglobin	12.081±1.94	12.87±1.57	0.12
2.	RBC	4.66±0.55	4.88±0.51	0.16
3.	PCV	39.05±4.95	40.85±3.92	0.16
4.	MCV	83.90±6.79	84.17±7.89	0.90
5.	MCH	25.92±3.03	26.59±3.06	0.46
6.	MCHC	30.78±1.63	31.79±1.97	0.06
7.	TLC	10605.71±6532.24	8879.62±2498.40	0.21
8.	Neutrophils	67.86±11.59	60.39±10.42	0.02
9.	Lymphocytes	24.49±11.35	29.38±9.83	0.11
10.	Monocytes	5.09±2.52	4.51±1.69	0.32
11.	Eosinophils	2.38±1.65	4.93±3.69	0.005
12.	Basophils	0.20±0.15	0.36±0.17	0.002
13.	Absolute neutrophil count	7653.33±6329.74	5549.62±2358.06	0.118
14.	ESR	73.09±34.98	46.37±33.61	0.01
15.	PLT	3.09±0.96	3.05±0.67	0.84

Table 3 highlights the hematological profiles of patients with pulmonary tuberculosis (PTB) and extrapulmonary tuberculosis (EPTB), shedding light on the differences in immune and systemic responses between the two conditions. Although mean hemoglobin levels and RBC counts are slightly higher in EPTB patients (12.87 g/dL and 4.88 million/µL, respectively) compared to PTB patients (12.08 g/dL and 4.66 million/µL), these differences are not statistically significant. Similarly, packed cell volume (PCV), mean corpuscular volume (MCV), and mean corpuscular hemoglobin (MCH) are comparable between the two groups, with no notable differences.

The total leukocyte count (TLC) is higher in PTB patients (10605.71/µL) than in EPTB patients (8879.62/µL), though this is not statistically significant. However, a significant distinction is observed in the neutrophil counts, which are higher in PTB patients (67.86%) compared to EPTB patients (60.39%, $p = 0.02$), indicating a more pronounced inflammatory response in PTB. Conversely, eosinophil and basophil counts are significantly elevated in EPTB patients (4.93% and 0.36%, respectively) compared to PTB patients (2.38% and 0.20%, $p = 0.005$ and $p = 0.002$). These findings may reflect variations in immune responses based on the site of infection, with EPTB involving different immunopathological mechanisms.

The erythrocyte sedimentation rate (ESR), a marker of systemic inflammation, is significantly higher in PTB patients (73.09 mm/hr) than in EPTB patients (46.37 mm/hr, $p = 0.01$), further supporting the idea of heightened systemic inflammation in PTB. In contrast, lymphocyte percentages, monocyte counts, and platelet levels are similar between the two groups, with no statistically significant differences. These results underscore the distinct hematological patterns of PTB and EPTB, with PTB showing stronger neutrophilic and systemic inflammatory responses, while EPTB demonstrates elevated eosinophil and basophil counts, suggesting site-specific immune activation.

DISCUSSION

Our study provides a detailed analysis of hematological parameters in patients with pulmonary tuberculosis (PTB) and extrapulmonary tuberculosis (EPTB), offering insights into the distinct immune responses associated with these conditions.

In our study, the highest prevalence of TB was observed in the 31–40 age group for both PTB and EPTB, with females showing a greater susceptibility to EPTB (61.5%) compared to males. This trend aligns with Gebreweld

et al[17]., who reported the highest TB prevalence in the 25–34 age group (34.8%). Kurup et al[18]. similarly observed that most TB cases occurred in younger to middle-aged adults, with a mean age of 40 years. Gender differences in TB prevalence were also evident, with male dominance reported in Kurup et al[18]. and Gebreweld et al[17]., whereas Ongwae et al[19]. observed a nearly equal distribution between males and females.

Hemoglobin Levels and RBC Counts

In our study, the mean hemoglobin levels and RBC counts were slightly higher in EPTB patients (12.87 g/dL and 4.88 million/µL) compared to PTB patients (12.08 g/dL and 4.66 million/µL), but the differences were not statistically significant. Similarly, Shyama S et al[20]. observed higher RBC counts in EPTB cases compared to PTB (4.47 vs. 4.24 million/µL; p=0.036), aligning with our findings. Kurup et al[18]. and Ongwae et al[19]., however, reported significantly lower hemoglobin and RBC levels in PTB patients compared to healthy controls, highlighting the anemia commonly associated with PTB. Ongwae et al[19]. specifically noted that hemoglobin levels (11.93 g/dL) and RBC counts (4.37 million/µL) were significantly lower in PTB cases than in controls (p<0.001). These differences across studies may reflect regional variations, sample sizes, and the prevalence of comorbidities like nutritional deficiencies or chronic inflammation.

Leukocyte Parameters

Our study showed that the total leukocyte count (TLC) was higher in PTB patients (10,605/µL) than in EPTB patients (8,879/µL), although not statistically significant. Neutrophil counts were significantly elevated in PTB patients (67.86%) compared to EPTB patients (60.39%, p=0.02), indicating a pronounced inflammatory response in PTB. Similarly, Gebreweld et al.[17] observed significantly elevated WBC, neutrophil, and systemic immune-inflammation (SII) indices in male TB patients compared to controls. Ongwae et al[19]. also reported elevated neutrophil levels in PTB patients compared to controls (p=0.044). Shyama S et al.[20] further highlighted higher total WBC levels in pediatric cases compared to adults, which may explain the variability in leukocyte parameters based on age.

Eosinophils and Basophils

In our study, eosinophil and basophil counts were significantly higher in EPTB patients (4.93% and 0.36%) compared to PTB patients (2.38% and 0.20%; p=0.005 and p=0.002, respectively). This finding highlights the distinct immune activation in EPTB, potentially related to its diverse organ involvement and chronic nature. Such a detailed comparison was not provided in the other studies reviewed, indicating that our study adds a unique dimension to the understanding of immune responses in TB.

ESR Levels

The erythrocyte sedimentation rate (ESR), a marker of systemic inflammation, was significantly higher in PTB patients in our study (73.09 mm/hr) compared to EPTB patients (46.37 mm/hr; p=0.01). This finding aligns with Ongwae et al[19]., who reported significantly elevated ESR in PTB patients (69.18 mm/hr) compared to controls (14.34 mm/hr; p<0.001). Gebreweld et al.[18] similarly documented higher ESR in TB patients than in healthy controls, reflecting active inflammation.

Platelet Counts

Platelet counts in our study were comparable between PTB and EPTB patients, with no significant difference (3.09 and 3.05 × 10^3/µL, respectively). In contrast, Shyama S et al[20]. and Ongwae et al[19]. observed significantly higher platelet counts in PTB patients (337 × 10^3/µL and 328.61 × 10^3/µL, respectively) compared to EPTB cases or controls. This discrepancy might be attributed to variations in study populations and methodologies, as platelet elevation is often linked to inflammatory responses in TB.

Biochemical Parameters

Although our study did not evaluate serum calcium or sodium levels, Shyama S et al[20]. found significant differences in these parameters between PTB and EPTB cases. Serum calcium was higher in PTB cases (11.65 vs. 9.18 mg/dL; p<0.001), while sodium was elevated in EPTB cases (139.49 vs. 130.10 mmol/L; p<0.001). These findings suggest metabolic alterations specific to TB localization and merit further investigation in our cohort.

Our study's limitations include a small sample size and the absence of biochemical parameters like serum calcium and sodium, which restricts the depth of analysis. The single-center design limits the generalizability of

findings across diverse populations. Additionally, the lack of data on HIV coinfection and healthy controls constrains the broader applicability and comparative insights.

CONCLUSION

Distinct hematologic patterns are demonstrated by our study in pulmonary tuberculosis versus extrapulmonary tuberculosis, with enhanced neutrophilia and systemic inflammatory response in pulmonary tuberculosis, and elevated eosinophils and basophils in extrapulmonary tuberculosislikely indicating site specific immune activation. The differences with other studies highlight how TB-related hematological and biochemical changes are not the same across studies, depending on the study population, disease localization, or coexistence of other diseases. More comprehensive studies with a wider array of biochemical endpoints, in larger cohorts, may be informative not only with respect to the underlying pathophysiology of TB, but with the implications for applying our findings to the clinical population.

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