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Comparison of Biochemical and Hematological Profile in Pulmonary and Extrapulmonary Tuberculosis at Gulab Devi Teaching Hospital

Khadija Kamal[1], Aneela Shaheen[1]

[1]Department of Paediatrics, Gulab Devi Teaching Hospital, Al-Aleem Medical College, Lahore, Pakistan

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Correspondence to: Khadija Kamal, Department of Paediatrics, Gulab Devi Teaching Hospital, Al-Aleem Medical College, Lahore, Pakistan.
Email: khadija@outlook.com

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ABSTRACT

Introduction: Tuberculosis (TB) remains a significant cause of morbidity among children in developing countries. Differentiating between pulmonary TB (PTB) and extrapulmonary TB (EPTB) based on laboratory parameters can aid in timely diagnosis and management. This study aimed to compare the biochemical and hematological profiles of pediatric patients diagnosed with PTB and EPTB at Gulab Devi Teaching Hospital. **Methodology:** This descriptive case series included 120 pediatric patients under 14 years of age diagnosed with TB over a three-month period. Patients were divided into PTB and EPTB groups. Biochemical and hematological parameters including Hb, RBCs, WBCs, TLC, PLT, ESR, CRP, and differential counts were analyzed. Radiological and clinical features such as TST positivity, chest X-ray findings, lymphadenopathy, cavity lesions, and miliary TB were also compared between groups. Data were analyzed using SPSS v25.0 with $p \leq 0.05$ considered statistically significant. **Results:** Out of 120 patients, 74 (61.7%) had PTB and 46 (38.3%) had EPTB. Mean age was 7.01 ± 4.31 years, with a nearly equal gender distribution. PTB patients had significantly higher TLC (11.49 ± 1.95 vs. 8.30 ± 1.57; p=0.001) and WBC counts (11.10 ± 1.77 vs. 9.86 ± 1.58; p=0.001) compared to EPTB. Other hematological and biochemical parameters showed no significant differences. TST positivity was more frequent in EPTB (95.7% vs. 78.4%; p=0.010). **Conclusion:** While most biochemical and hematological markers were comparable between PTB and EPTB, significantly higher leukocyte counts in PTB suggest a more pronounced inflammatory response. Radiological findings and TST also differed notably, which can aid in clinical differentiation and early diagnosis.

INTRODUCTION

Tuberculosis, caused by Mycobacterium Tuberculosis, is a prevalent infectious disease affecting the lungs, leading to severe cough, fever, chest pain, weight loss, and appetite loss, and can also involve other organs. It is especially common in developing countries due to factors such as overcrowding, malnutrition, poor hygiene, inadequate health services, and lack of awareness regarding prevention and transmission.[1] WHO reported 10 million TB cases in 2019, approximately 1.4 million deaths, and 1.1 million childhood cases in 2020.[2]

Mycobacterium tuberculosis transmits via droplets, involving alveolar macrophages, causing granulomatous inflammation primarily in the lungs but also affecting other organs.[3] Childhood Tuberculosis exhibits diverse signs and symptoms, complicating timely diagnosis, resulting in complications and economic burden.[4] The study on extrapulmonary tuberculosis presents key data on tuberculosis frequency. Pulmonary tuberculosis constituted 50.6%, while extrapulmonary tuberculosis comprised 49.4% of patients. Extrapulmonary TB prevalence is greater in immunocompromised individuals.[5]

Various laboratory investigations diagnose tuberculosis, including sputum/gastric aspirate microscopy for AFB and gene expert (PCR). Hematological changes are key for early diagnosis, prognosis assessment, and therapeutic response evaluation. Pulmonary and extrapulmonary tuberculosis present differently, impacting diagnosis, management, and outcomes, which are influenced by physical, clinical, and ethical factors.[6-7]

Both pulmonary and extra pulmonary Tuberculosis have varying clinical presentations, and hence variable options for its diagnosis, management, and its outcome. Diseases' outcome is affected by various physical, clinical, and ethical conditions. There is a lack of data regarding pediatric TB epidemiological and clinical profile. Therefore, this study is being conducted to determine the biochemical and hematological profile and compare PTB and EPTB in pediatric TB patients.

METHODOLOGY

This descriptive case series was conducted in the Pediatrics Medicine Department of Gulab Devi Teaching

Hospital, Lahore. The study took place over a three-month period, from March 11, 2025, to June 10, 2025, following the approval of the research synopsis. A total of 120 pediatric patients were enrolled through non-probability consecutive sampling. The estimated sample size was calculated based on a 95% confidence level, a 9% margin of error, and an expected prevalence of extrapulmonary tuberculosis (EPTB) of 49.4%.[5]

Pediatric patients under 14 with confirmed tuberculosis (TB) diagnoses via laboratory investigations were included. Exclusions were made for comorbidities or lack of consent. Written informed consent from parents/guardians and ethical approval were obtained. A total of 120 eligible children were enrolled. Routine blood investigations were conducted prior to anti-tuberculous therapy initiation. Participants were randomly assigned to two groups: Group A for pulmonary tuberculosis (PTB) and Group B for extrapulmonary tuberculosis (EPTB).

Pulmonary tuberculosis is characterized by symptoms such as cough for over 14 days, chest pain, shortness of breath, and fever (≥100°F), alongside a positive acid-fast bacilli (AFB) smear and Gene Xpert confirmation for Mycobacterium tuberculosis. Extrapulmonary tuberculosis involves organs other than the lungs, including pleura, lymph nodes, abdomen, genitourinary tract, skin, joints, bones, or meninges, with cases of pleural effusion or lymph node enlargement classified as EPTB. Hematological evaluation requires 3–4 ml of venous blood collected aseptically. Two ml are placed in EDTA tubes for analysis, while the other 2 ml measures erythrocyte sedimentation rate (ESR) using a Westergren tube, set vertically for one hour before recording results.

Biochemical and hematological parameters assessed included hemoglobin (g/dl), RBCs (m/mm^3), lymphocytes, monocytes, neutrophils, ESR (mm/hr), TLC (×10^9/L), TST positivity, abnormal chest X-ray, lymphadenopathy, cavity lesions, miliary TB, microbiological TB confirmation, WBC (×10^9/L), PLT (×10^9/L), and CRP (mg/dl). TST positivity was defined as an induration >10 mm at 72 hours. Data were documented via a proforma and analyzed using SPSS 25.0. Qualitative variables like gender, TB type, and residence were expressed as frequencies and percentages; quantitative variables like age and markers as means and standard deviations. Comparisons between PTB and EPTB groups utilized Chi-square for qualitative and t-test for quantitative variables, with significance at $p \leq 0.05$.

RESULTS

Out of 120 pediatric patients, 61 (50.8%) were male and 59 (49.2%) were female. The majority of patients (55%) were between 1–7 years of age, while 45% were aged 8–14 years, with a mean age of 7.01 ± 4.31 years. Regarding residence, 53 children (44.2%) were from rural areas and 67 (55.8%) from urban areas. Pulmonary tuberculosis (PTB) was more common, affecting 74 patients (61.7%), while 46 patients (38.3%) were diagnosed with extrapulmonary tuberculosis (EPTB).

The table-2 compares the mean biochemical and hematological values between PTB and EPTB groups. No statistically significant differences were observed in hemoglobin levels, RBC count, lymphocytes, monocytes, neutrophils, ESR, PLT count, or CRP levels ($p > 0.05$). However, PTB patients had significantly higher mean TLC (11.49 ± 1.95 vs. 8.30 ± 1.57, p=0.001) and WBC counts (11.10 ± 1.77 vs. 9.86 ± 1.58, p=0.001) compared to EPTB patients, indicating a stronger systemic inflammatory response in pulmonary cases.

The table-3 presents the comparison of radiological and clinical features between PTB and EPTB groups. TST positivity was significantly higher in EPTB patients (95.7%) compared to PTB (78.4%), p=0.010. Abnormal chest X-ray findings were observed in all PTB cases (100%) but only in 23.9% of EPTB cases (p=0.001). Cavity lesions were present in 28.4% of PTB patients and absent in EPTB (p=0.001). Miliary TB was seen only in PTB (9.5%), with a statistically significant difference (p=0.032). Although lymphadenopathy was more frequent in PTB (45.9%) than EPTB (32.6%), the difference was not statistically significant (p=0.148).

Table 1

Frequency Distribution of Different Variables (n=120)

Variables		Frequency	Percent
Gender	Male	61	50.8
	Female	59	49.2
Age groups	1-7 years	66	55.0
	8-14 years	54	45.0
	Mean age (years)	7.01±4.31	
Residence	Rural	53	44.2
	Urban	67	55.8
Type of TB	Pulmonary TB	74	61.7
	Extra-pulmonary TB	46	38.3

Table 2

Comparison of Mean Levels of Biochemical and Hematological Profile between Groups

Variables	Groups		p-value
	Pulmonary TB	Extra-pulmonary TB	
Hb level (g/dl)	10.57±1.47	10.56±1.63	0.952
RBCs (m/mm^3)	4.17±0.75	4.15±0.80	0.853
Lymphocytes (%)	32.46±13.52	34.54±16.38	0.453
Monocytes (%)	7.54±2.06	7.76±2.15	0.577
Neutrophils (%)	50.27±19.65	45.47±18.12	0.183
ESR (mm/hour)	35.79±9.65	34.13±11.93	0.403
TLC (×10^9/L)	11.49±1.95	8.30±1.57	0.001
WBC (×10^9/L)	11.10±1.77	9.86±1.58	0.001
PLT (×10^9/L)	383.03±51.35	377.69±48.65	0.574
CRP (mg/dl)	34.41±11.87	33.03±9.36	0.505

Table 3

Comparison of Biochemical and Radiological / Clinical Profile between Groups

Biochemical and radiological / clinical profile		Groups		p-value
		Pulmonary TB	Extra-pulmonary TB	
Tuberculin Skin Test (TST) Positive	Yes	58(78.4%)	44(95.7%)	0.010
	No	16(21.6%)	2(4.3%)	
Abnormal Chest X-ray	Yes	74(100.0%)	11(23.9%)	0.001
	No	0(0.0%)	35(76.1%)	
Lymphadenopathy	Yes	34(45.9%)	15(32.6%)	0.148
	No	40(54.1%)	31(67.4%)	
Cavity Lesion	Yes	21(28.4%)	0(0.0%)	0.001
	No	53(71.6%)	46(100.0%)	
Miliary Tuberculosis	Yes	7(9.5%)	0(0.0%)	0.032
	No	67(90.5%)	46(100.0%)	

DISCUSSION

This study provided valuable insights into the biochemical and hematological differences between pulmonary and extrapulmonary tuberculosis in pediatric patients, contributing to the growing body of literature on TB diagnostics in children. The findings demonstrate distinct patterns that can aid clinicians in differentiating between these two forms of tuberculosis and have important implications for early diagnosis and management.

The most significant finding of this study was the markedly elevated total leukocyte count (TLC) and white blood cell (WBC) count in pulmonary TB compared to extrapulmonary TB patients. The mean TLC in PTB patients (11.49 ± 1.95 × 10^9/L) was substantially higher than in EPTB patients (8.30 ± 1.57 × 10^9/L, p=0.001). This finding aligns with recent research by Singh et al., who demonstrated that median total leukocyte count was significantly higher in PTB compared to EPTB in pediatric patients, emphasizing the role of leukocyte counts as important biomarkers for disease differentiation. The elevated leukocyte response in pulmonary tuberculosis likely reflects the more intense inflammatory cascade triggered by direct lung parenchymal involvement and the body's attempt to contain the infection at the primary site of entry.[8]

Shyama et al. reported similar hematological patterns in a large comparative study of PTB and EPTB patients, demonstrating that total WBC counts were significantly higher in PTB cases (median 11.50 vs. 8.50 × 10^9/L, p=0.001), which strongly supports our findings and suggests a more robust systemic inflammatory response in pulmonary disease. The pronounced leukocytosis observed in PTB patients in our study suggests enhanced neutrophil recruitment and activation in response to the extensive pulmonary inflammatory process characteristic of PTB.[9]

Interestingly, other hematological parameters including hemoglobin levels, red blood cell counts, and platelet counts showed no statistically significant differences between the two groups in our study. This finding contrasts with some recent studies that have reported variations in these parameters. Shyama et al. found that total RBC counts were actually higher in EPTB cases (4.47 vs. 4.24; p=0.036) and platelet counts were higher in PTB cases (337.00 vs. 278; p=0.006). However, our findings support the notion that the primary hematological distinction lies in the overall leukocyte response rather than in specific cell line abnormalities, which may be more relevant for clinical differentiation in pediatric populations.[9]

Aygün et al. in their comprehensive study of 216 pediatric TB patients found that hemoglobin levels were significantly lower in patients with extrapulmonary TB compared to pulmonary TB, which differs from our findings but highlights the variability in hematological presentations across different populations. Recent research has also demonstrated that hematological changes in pulmonary tuberculosis, particularly anemia and leukocytosis, are common findings that can serve as supportive diagnostic markers.[10-11]

The study revealed no significant differences in biochemical markers including ESR and CRP between pulmonary and extrapulmonary tuberculosis groups. Both groups demonstrated elevated inflammatory markers, with mean ESR values of 35.79 ± 9.65 mm/hour in PTB and 34.13 ± 11.93 mm/hour in EPTB, and CRP levels of 34.41 ± 11.87 mg/dl and 33.03 ± 9.36 mg/dl respectively. This finding suggests that while the magnitude of systemic inflammation may be similar between the two forms, the cellular response patterns differ significantly.

Kumar et al. identified various circulating biomarkers in pediatric TB and found that while children with active TB showed markedly elevated plasma levels of inflammatory markers compared to healthy controls, the differences between PTB and EPTB were more subtle, particularly for traditional inflammatory markers like CRP. This supports our observation that despite similar ESR and CRP levels, the leukocyte response patterns differ markedly between PTB and EPTB.[12]

The absence of significant differences in other biochemical parameters in our study aligns with recent findings suggesting that conventional biochemical markers may not be sufficient to distinguish between different forms of TB in pediatric populations. Kumar et al. demonstrated that markers of innate immune activation were significantly lower in EPTB than in PTB children, suggesting different patterns of immune system engagement. This differential immune response may contribute to the distinct clinical presentations and laboratory findings observed in our study.[12]

The study revealed striking differences in clinical and radiological presentations between the two groups. Tuberculin skin test (TST) positivity was significantly higher in EPTB patients (95.7%) compared to PTB patients (78.4%, p=0.010). This finding is particularly noteworthy as it suggests that extrapulmonary tuberculosis may be associated with a more robust delayed-type hypersensitivity response, possibly due to different patterns of mycobacterial dissemination and immune system engagement.

Singh et al. in their single-center study from India found that TST positivity rates varied between PTB and EPTB, with higher rates in EPTB patients, which corroborates our findings.[8] Similarly, Özkan et al. reported that TST positivity was more common in PTB cases in their study, which contrasts with our findings but may reflect different population characteristics and diagnostic criteria.[13] This enhanced TST response in EPTB may reflect the hematogenous dissemination pattern characteristic of extrapulmonary disease, leading to more widespread antigenic exposure and subsequent immune sensitization.

Radiological findings provided the most dramatic distinctions between the groups. All PTB patients (100%) demonstrated abnormal chest X-rays, while only 23.9% of EPTB patients showed chest radiographic abnormalities (p=0.001). Cavity lesions were exclusively found in PTB patients (28.4% vs. 0%, p=0.001), and miliary tuberculosis was also significantly more common in the pulmonary group (9.5% vs. 0%, p=0.032). These findings align with the pathophysiology of tuberculosis, where PTB involves direct pulmonary infection with characteristic radiological manifestations, while EPTB typically results from hematogenous dissemination to non-pulmonary sites.

Dubois et al. demonstrated that children are more likely to

present with EPTB compared with adults, with younger age and developing immunity contributing to elevated disease risk, which provides context for understanding the distinct presentations observed in our study. The age-specific patterns of TB presentation highlight the importance of considering developmental factors in pediatric TB diagnosis.[14]

The observed differences in hematological and clinical parameters between PTB and EPTB can be explained by distinct pathophysiological mechanisms. In pulmonary tuberculosis, the initial infection occurs in the lungs, leading to intense local inflammation with significant neutrophil and macrophage recruitment. This results in the elevated leukocyte counts observed in our study. The direct pulmonary involvement also explains the universal presence of chest X-ray abnormalities and the occurrence of cavity lesions and miliary patterns.

Recent advances in biomarker research have identified promising candidates for TB diagnosis and differentiation. Gao et al. demonstrated that novel RNA biomarkers can improve discrimination of children with tuberculosis disease from those with non-TB pneumonia after in vitro stimulation, with specific genes like PID1 achieving 100% accuracy in distinguishing TB from pneumonia. These molecular approaches represent the future direction of TB diagnostics and may complement the traditional hematological and biochemical markers evaluated in our study.[15]

He et al. reported on serum-based diagnosis of pediatric tuberculosis using Mycobacterium tuberculosis factors, achieving 85.5% sensitivity for overall TB diagnosis, with similar diagnostic sensitivities for culture-positive and culture-negative TB cases.[16] This approach offers promise for rapid and sensitive diagnosis of pediatric TB cases, including extrapulmonary or paucibacillary TB cases, which are traditionally challenging to diagnose.

The findings of this study have important clinical implications for pediatric tuberculosis management. The significantly elevated leukocyte counts in pulmonary tuberculosis can serve as an additional diagnostic marker, particularly in resource-limited settings where advanced diagnostic tools may not be readily available. The combination of elevated TLC and WBC counts with characteristic radiological findings can strengthen diagnostic confidence in suspected pulmonary tuberculosis cases.

Pace et al. highlighted that extrapulmonary and drug-resistant childhood tuberculosis present unique diagnostic and therapeutic challenges, with second-line drugs being administered not exclusively to drug-resistant cases but also to selected EPTB cases. This emphasizes the importance of accurate differentiation between PTB and EPTB for appropriate treatment selection.[17]

The higher TST positivity rate in extrapulmonary tuberculosis patients suggests that this test may be particularly valuable in EPTB diagnosis, where radiological findings are often less specific or absent. This finding supports the continued use of TST as part of the diagnostic algorithm for extrapulmonary tuberculosis, despite the availability of newer diagnostic modalities.

For clinical practice, these findings suggest that a systematic approach incorporating hematological parameters, radiological findings, and TST results can improve diagnostic accuracy. In pediatric patients presenting with suspected tuberculosis, elevated leukocyte counts combined with abnormal chest radiographs should raise suspicion for pulmonary disease, while normal or mildly elevated leukocyte counts with positive TST but normal chest radiographs may suggest extrapulmonary involvement.

While this study provides valuable insights, certain limitations should be acknowledged. The relatively small sample size and single-center design may limit the generalizability of findings. Additionally, the study did not include molecular diagnostic methods or advanced biomarkers that might provide additional discriminatory power between PTB and EPTB.

Future research should focus on validating these findings in larger, multi-center studies and exploring the integration of novel biomarkers with traditional hematological and biochemical parameters. The development of diagnostic algorithms incorporating these findings could significantly improve the accuracy and speed of tuberculosis diagnosis in pediatric populations. Machine learning approaches combining multiple laboratory and clinical parameters may offer promising avenues for developing more sophisticated diagnostic tools.

The integration of newer diagnostic modalities, including molecular tests and advanced biomarkers, with traditional clinical and laboratory assessments represents the future of pediatric TB diagnosis. As demonstrated by recent studies, the combination of multiple diagnostic approaches can achieve higher accuracy rates and provide more comprehensive assessment of disease status.

CONCLUSION

This study demonstrates that while most biochemical and hematological markers remain comparable between pulmonary and extrapulmonary tuberculosis in children, the significantly elevated leukocyte response in pulmonary disease represents a key distinguishing feature. Combined with the distinct radiological presentations and TST response patterns, these findings provide clinicians with valuable tools for differential diagnosis and can contribute to more timely and appropriate management of pediatric tuberculosis patients. The integration of these laboratory findings with clinical and radiological assessments can enhance diagnostic accuracy and improve patient outcomes in pediatric tuberculosis care.

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