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Blood Clues in Childhood Tuberculosis: Early Hematological Changes During the Intensive Phase of Anti-Tubercular Therapy

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ABSTRACT

Introduction: Tuberculosis remains an important cause of childhood morbidity in India, and hematological abnormalities are frequently observed at diagnosis because of chronic inflammation, nutritional compromise, marrow response and disease burden. In routine pediatric practice, complete blood count is one of the most accessible investigations available before and during anti-tubercular therapy. However, early hematological changes during the intensive phase of treatment are not always systematically documented in children, despite their potential value in monitoring response, identifying persistent inflammation and recognizing drug-related cytopenias.

Aim: To assess early changes in routine hematological parameters during the intensive phase of anti-tubercular therapy in children with tuberculosis.

Methodology: This original descriptive hospital-based study was conducted among 96 children diagnosed with tuberculosis and initiated on first-line anti-tubercular therapy in a tertiary care hospital in India. Children aged 1–18 years with clinically, radiologically or microbiologically diagnosed drug-sensitive tuberculosis were included. Children with known hematological disorders, malignancy, chronic kidney disease, chronic liver disease, HIV infection, multidrug-resistant tuberculosis, prior anti-tubercular therapy or incomplete baseline/follow-up blood reports were excluded. Hemoglobin, total leukocyte count, differential leukocyte count, platelet count and erythrocyte sedimentation rate were recorded at baseline and at the end of the intensive phase. Data were analyzed using descriptive statistics and paired comparison of hematological parameters.

Results: The mean age of the study population was 8.9 ± 4.2 years, with male predominance, 54 (56.3%). Pulmonary tuberculosis was present in 58 (60.4%) and extrapulmonary tuberculosis in 38 (39.6%) children. At baseline, anemia was observed in 62 (64.6%), leukocytosis in 31 (32.3%), thrombocytosis in 39 (40.6%) and raised erythrocyte sedimentation rate in 78 (81.3%) children. After the intensive phase, mean hemoglobin increased from 9.7 ± 1.3 g/dL to 10.6 ± 1.2 g/dL, while mean total leukocyte count, platelet count and erythrocyte sedimentation rate showed reduction. Anemia improved in 31 of 62 children (50.0%), thrombocytosis resolved in 24 of 39 (61.5%) and raised erythrocyte sedimentation rate declined in 51 of 78 (65.4%). No severe drug-related pancytopenia was observed.

Conclusion: Early hematological improvement was observed during the intensive phase of anti-tubercular therapy, particularly in hemoglobin, platelet count and erythrocyte sedimentation rate. Routine complete blood count may serve as a practical supportive tool for

monitoring early treatment response in pediatric tuberculosis, especially in Indian hospital settings.

Keywords: *Pediatric tuberculosis; Anti-tubercular therapy; Hemoglobin; Platelet count; Hematological monitoring.*

INTRODUCTION

Tuberculosis remains one of the most important infectious diseases worldwide and continues to contribute substantially to childhood morbidity and mortality, particularly in high-burden countries [1]. India carries a major share of the global tuberculosis burden, and childhood tuberculosis remains clinically important because it reflects ongoing transmission in the community and presents unique diagnostic and therapeutic challenges [2]. Under the National Tuberculosis Elimination Programme, early diagnosis, appropriate treatment initiation, nutritional support and regular monitoring are emphasized as essential components of pediatric tuberculosis care [3]. International guidelines also highlight the need for child-centered tuberculosis management, especially because children frequently have paucibacillary disease and may not always have microbiological confirmation [4]. Pediatric tuberculosis may present with prolonged fever, cough, weight loss, failure to thrive, lymphadenopathy, respiratory symptoms, abdominal complaints or extrapulmonary manifestations, and clinical judgment remains important in diagnosis and follow-up [5]. In Indian pediatric practice, diagnosis often depends on a combination of clinical features, contact history, tuberculin testing, radiology, microbiological tests where available and response to therapy [6]. Hospital-based studies from India have shown that childhood tuberculosis commonly affects nutritionally vulnerable children and that pulmonary as well as extrapulmonary forms contribute to the clinical burden [7]. Similar pediatric hospital-based observations have emphasized the variable clinical profile of childhood tuberculosis and the need for systematic baseline assessment before and during anti-tubercular therapy [8].

Hematological abnormalities are frequently observed in tuberculosis because of chronic inflammation, nutritional deficiency, altered iron metabolism, bone marrow response and disease severity. Anemia is one of the most common findings and may be mild, moderate or severe depending on the duration of illness, nutritional status and inflammatory burden. Recent pediatric evidence has shown that tuberculosis-related anemia in children is associated with inflammation and may improve after initiation of anti-tubercular therapy [9]. Tuberculosis-associated anemia is not only a marker of nutritional compromise but also reflects persistent immune activation, and inflammatory hematological changes may continue even after treatment has been started [10]. Indian clinical literature has also documented tuberculosis-associated anemia and its predictors, supporting the importance of recognizing anemia as a relevant comorbidity in tuberculosis patients [11]. Apart from anemia, changes in total leukocyte count, differential leukocyte count and platelet count may also occur during active tuberculosis and may change after anti-tubercular therapy [12]. Studies assessing the impact of anti-tuberculosis treatment on hematological parameters have reported improvement in several blood indices after treatment, suggesting that routine blood parameters may provide supportive information during monitoring [13]. The prevalence and evolution of anemia during tuberculosis treatment have also been studied, showing that anemia may improve with anti-tubercular therapy, although recovery may be incomplete in some patients [14]. Reviews on tuberculosis-associated anemia further support that hematological abnormalities in tuberculosis are multifactorial and should be interpreted in relation to inflammation, nutritional status, disease burden and treatment response [15]. In this background, the present study was undertaken to assess early changes in routine hematological parameters during the intensive phase of anti-tubercular therapy in children with tuberculosis in an Indian hospital-based setting.

AIM

To assess early changes in routine hematological parameters during the intensive phase of anti-tubercular therapy in children with tuberculosis.

METHODOLOGY

This descriptive hospital-based study was conducted in the Department of Pediatrics of a tertiary care hospital in India over a period of **January 2025to December 2025**, among 96 children diagnosed with tuberculosis and initiated on first-line anti-tubercular therapy. The study was conducted after obtaining approval from the Institutional Ethics Committee. Written informed consent was obtained from parents or legal guardians, and assent was obtained from older children wherever applicable. Children aged 1–18 years with clinically, radiologically or microbiologically diagnosed drug-sensitive tuberculosis who were started on standard first-line anti-tubercular therapy under programmatic or institutional protocol were included. Both pulmonary and extrapulmonary tuberculosis cases were included. Children with previously treated tuberculosis, multidrug-resistant or rifampicin-resistant tuberculosis, known HIV infection, malignancy, chronic kidney disease, chronic liver disease, known inherited or acquired hematological disorder, severe acute bleeding, recent blood transfusion, concurrent immunosuppressive therapy, or incomplete baseline and follow-up hematological records were excluded.

Relevant demographic and clinical details including age, sex, nutritional status, type of tuberculosis, presenting symptoms, history of contact, microbiological confirmation wherever available and treatment category were recorded using a

structured proforma. Routine hematological parameters including hemoglobin, total leukocyte count, differential leukocyte count, platelet count and erythrocyte sedimentation rate were recorded at baseline before initiation of anti-tubercular therapy and repeated at the end of the intensive phase, defined as completion of two months of first-line therapy. Anemia was interpreted using age-appropriate hemoglobin cut-offs. Leukocytosis, leukopenia, thrombocytosis and thrombocytopenia were defined according to standard pediatric laboratory reference ranges used by the institution. Raised erythrocyte sedimentation rate was considered as per age-appropriate laboratory interpretation.

Children were followed clinically during the intensive phase for symptom improvement, drug tolerance, adherence and need for treatment modification. The primary outcome was change in routine hematological parameters from baseline to the end of the intensive phase. Secondary observations included the frequency of baseline hematological abnormalities, proportion of children showing improvement in anemia, leukocytosis, thrombocytosis and erythrocyte sedimentation rate, and occurrence of clinically significant drug-related hematological adverse events. Data were entered in Microsoft Excel and analyzed using appropriate statistical methods. Categorical variables were expressed as frequency and percentage, while continuous variables were expressed as mean and standard deviation. Paired comparison of baseline and post-intensive phase hematological parameters was performed using paired t-test or appropriate non-parametric test depending on data distribution. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 96 children diagnosed with tuberculosis and initiated on first-line anti-tubercular therapy were included in the present study. The results were organized into four tables to cover the demographic and clinical profile, baseline hematological abnormalities, early hematological changes during the intensive phase and monitoring pattern after two months of therapy.

Table 1: Demographic and Clinical Profile of Study Participants

Variable	Category	Frequency (n=96)	Percentage (%)
Age group	1–5 years	24	25.0
	6–10 years	34	35.4
	11–18 years	38	39.6
Sex	Male	54	56.3
	Female	42	43.8
Type of tuberculosis	Pulmonary tuberculosis	58	60.4
	Extrapulmonary tuberculosis	38	39.6
Nutritional status	Normal nutrition	29	30.2
	Moderate undernutrition	43	44.8
	Severe undernutrition	24	25.0
History of TB contact	Present	31	32.3
	Absent/not known	65	67.7
Microbiological confirmation	Present	37	38.5
	Clinico-radiological diagnosis	59	61.5

The above table shows that most children belonged to the 11–18 years age group, 38 (39.6%), followed by 6–10 years, 34 (35.4%), and 1–5 years, 24 (25.0%). Males constituted 54 (56.3%) and females 42 (43.8%) of the study population. Pulmonary tuberculosis was present in 58 (60.4%) children, while extrapulmonary tuberculosis was present in 38 (39.6%). Moderate or severe undernutrition was observed in 67 (69.8%) children, reflecting the close clinical relationship between childhood tuberculosis and nutritional compromise in Indian hospital settings.

Table 2: Baseline Hematological Profile Before Initiation of Anti-Tubercular Therapy

Hematological Parameter	Frequency / Mean Value	Percentage / Range
Hemoglobin, mean ± SD	9.7 ± 1.3 g/dL	7.1–12.4
Anemia	62	64.6%
Mild anemia	29	30.2%
Moderate anemia	27	28.1%
Severe anemia	6	6.3%
Total leukocyte count, mean ± SD	11,840 ± 3,260/mm³	5,200–21,600
Leukocytosis	31	32.3%
Leukopenia	4	4.2%
Platelet count, mean ± SD	4.32 ± 1.18 lakh/mm³	1.42–7.85
Thrombocytosis	39	40.6%
Thrombocytopenia	3	3.1%
ESR, mean ± SD	54.6 ± 18.9 mm/hr	14–108

Raised ESR	78	81.3%

The above table demonstrates that anemia was the most frequent baseline hematological abnormality, observed in 62 (64.6%) children. Among them, mild anemia was seen in 29 (30.2%), moderate anemia in 27 (28.1%) and severe anemia in 6 (6.3%). Leukocytosis was present in 31 (32.3%), thrombocytosis in 39 (40.6%) and raised erythrocyte sedimentation rate in 78 (81.3%) children. These findings indicate that children with tuberculosis frequently showed hematological evidence of inflammation, nutritional compromise and systemic disease activity at treatment initiation.

Table 3: Early Hematological Changes at the End of Intensive Phase of Anti-Tubercular Therapy

Parameter	Baseline Mean ± SD	End of Intensive Phase Mean ± SD	Mean Change	p-value
Hemoglobin (g/dL)	9.7 ± 1.3	10.6 ± 1.2	+0.9	<0.001
Total leukocyte count (/mm³)	11,840 ± 3,260	9,620 ± 2,410	-2,220	<0.001
Neutrophil count (%)	66.4 ± 10.8	59.2 ± 9.7	-7.2	0.002
Lymphocyte count (%)	25.1 ± 8.9	31.6 ± 8.3	+6.5	0.004
Platelet count (lakh/mm³)	4.32 ± 1.18	3.54 ± 0.91	-0.78	<0.001
ESR (mm/hr)	54.6 ± 18.9	32.8 ± 14.7	-21.8	<0.001

The above table shows significant early hematological improvement after completion of the intensive phase of anti-tubercular therapy. Mean hemoglobin increased from 9.7 ± 1.3 g/dL to 10.6 ± 1.2 g/dL. Mean total leukocyte count decreased from 11,840 ± 3,260/mm³ to 9,620 ± 2,410/mm³. Platelet count declined from 4.32 ± 1.18 lakh/mm³ to 3.54 ± 0.91 lakh/mm³, while mean ESR decreased from 54.6 ± 18.9 mm/hr to 32.8 ± 14.7 mm/hr. These findings suggest reduction in inflammatory activity and partial hematological recovery during the intensive phase.

Table 4: Pattern of Hematological Improvement and Monitoring Outcome After Intensive Phase

Monitoring Parameter	**Frequency**	**Percentage**
Anemia at baseline	62	64.6%
Anemia improved after intensive phase	31/62	50.0%
Anemia persisted after intensive phase	31/62	50.0%
Leukocytosis at baseline	31	32.3%
Leukocytosis resolved after intensive phase	22/31	71.0%
Thrombocytosis at baseline	39	40.6%
Thrombocytosis resolved after intensive phase	24/39	61.5%
Raised ESR at baseline	78	81.3%
ESR declined after intensive phase	51/78	65.4%
New-onset mild leukopenia during therapy	3	3.1%
Clinically significant drug-related pancytopenia	0	0.0%
Treatment interruption due to hematological toxicity	0	0.0%

The above table illustrates that among 62 children with baseline anemia, 31 (50.0%) showed improvement after the intensive phase, while anemia persisted in 31 (50.0%). Leukocytosis resolved in 22 of 31 children (71.0%), thrombocytosis resolved in 24 of 39 (61.5%) and ESR declined in 51 of 78 (65.4%). New-onset mild leukopenia was observed in 3 (3.1%) children, but no clinically significant drug-related pancytopenia or treatment interruption due to hematological toxicity was recorded.

DISCUSSION

The present hospital-based descriptive study evaluated early hematological changes during the intensive phase of anti-tubercular therapy among 96 children with tuberculosis. Childhood tuberculosis remains a major public health concern globally, and WHO has emphasized the continuing burden of tuberculosis in children and adolescents [1]. In India, where tuberculosis remains highly prevalent, pediatric cases are of particular importance because they indicate recent transmission and require structured diagnosis, treatment and follow-up [2]. In the present study, children were evaluated in a hospital setting and were treated according to standard first-line anti-tubercular therapy. This is consistent with NTEP recommendations, which emphasize appropriate diagnosis, treatment initiation and monitoring in pediatric tuberculosis [3]. WHO pediatric tuberculosis guidance also supports careful clinical follow-up during treatment because children often have paucibacillary disease and microbiological confirmation may not be possible in all cases [4].

The demographic and clinical profile of the present study showed that most children were above five years of age, with 39.6% belonging to the 11–18 years age group. Males constituted 56.3% of the study population. Pulmonary tuberculosis was observed in 60.4% of children, while extrapulmonary tuberculosis was present in 39.6%. These findings are comparable with the clinical pattern described by Jaganath et al., who noted that pediatric tuberculosis presents with variable pulmonary and extrapulmonary manifestations and requires clinical correlation for diagnosis [5]. Shah also

emphasized that pediatric tuberculosis diagnosis frequently depends on combined clinical, radiological and microbiological assessment, especially in high-burden settings [6]. In the present study, microbiological confirmation was available in 38.5% of cases, while 61.5% were diagnosed on clinico-radiological grounds, which reflects real-world pediatric tuberculosis practice.

Undernutrition was common in the present cohort, with moderate undernutrition in 44.8% and severe undernutrition in 25.0% of children. Bharani et al. reported childhood tuberculosis cases from a tertiary care DOTS center in central India and highlighted the importance of clinical and nutritional assessment during tuberculosis care [7]. Ksoo et al. also described varied clinical presentations of pediatric tuberculosis in a tertiary hospital and showed that childhood TB commonly presents with systemic symptoms and nutritional compromise [8]. The high frequency of undernutrition in the present study may partly explain the high burden of baseline anemia and other hematological abnormalities.

At baseline, anemia was observed in 62 children (64.6%), making it the most common hematological abnormality. Han et al. reported that tuberculosis-related anemia in children was associated with inflammatory activity and that hemoglobin may improve after treatment initiation [9]. In comparison, the present study also showed significant improvement in mean hemoglobin from 9.7 ± 1.3 g/dL at baseline to 10.6 ± 1.2 g/dL after the intensive phase. Gil-Santana et al. showed that tuberculosis-associated anemia is linked to a distinct inflammatory profile that may persist even after initiation of anti-tubercular therapy [10]. This supports the present finding that although hemoglobin improved after two months of therapy, anemia persisted in 50.0% of children who were anemic at baseline.

Mukherjee et al. reported tuberculosis-associated anemia in an Indian clinical setting and identified it as an important comorbidity requiring attention during tuberculosis management [11]. The present study similarly found mild anemia in 30.2%, moderate anemia in 28.1% and severe anemia in 6.3% of children. This pattern suggests that anemia in pediatric tuberculosis may result from both disease-related inflammation and coexisting nutritional deficiency, especially in Indian hospital-based populations.

Leukocytosis was present in 31 children (32.3%) at baseline and resolved in 22 of them (71.0%) after the intensive phase. Kassa et al. observed that anti-tuberculosis drugs and treatment response may influence hematological profiles, including leukocyte parameters [12]. In the present study, mean total leukocyte count decreased significantly from 11,840 ± 3,260/mm³ to 9,620 ± 2,410/mm³ after two months of treatment. Reta et al. also reported improvement in hematological parameters following anti-tuberculosis treatment, supporting the interpretation that serial complete blood count may reflect reduction in inflammatory burden during therapy [13].

Thrombocytosis was observed in 39 children (40.6%) at baseline and resolved in 24 of them (61.5%) after the intensive phase. Mean platelet count decreased significantly from 4.32 ± 1.18 lakh/mm³ to 3.54 ± 0.91 lakh/mm³. Reactive thrombocytosis in tuberculosis is commonly attributed to inflammation-mediated stimulation of thrombopoiesis. Lee et al. reported the evolution of anemia associated with tuberculosis and showed that hematological abnormalities may improve during the course of treatment [14]. The decline in platelet count in the present study supports early reduction of inflammatory activity during the intensive phase, although persistent thrombocytosis in some children suggests that complete hematological normalization may take longer.

Raised ESR was the most frequent abnormality, present in 78 children (81.3%) at baseline. After the intensive phase, ESR declined in 51 of these children (65.4%), and mean ESR decreased from 54.6 ± 18.9 mm/hr to 32.8 ± 14.7 mm/hr. Dasaradhan et al. described tuberculosis-associated anemia as a multifactorial condition related to inflammation, nutritional deficiency and chronic disease activity [15]. The present findings are consistent with this concept, as improvement in ESR, hemoglobin, leukocyte count and platelet count occurred together in many children, suggesting reduction in systemic inflammation during treatment.

Overall, this study shows that routine hematological parameters demonstrate measurable changes during the intensive phase of anti-tubercular therapy in children. Hemoglobin improved, leukocytosis and thrombocytosis declined, and ESR decreased in a substantial proportion of cases. These findings support the practical value of complete blood count and ESR as accessible supportive tools for early monitoring in Indian pediatric tuberculosis care. However, these parameters should not be interpreted in isolation or used as substitutes for clinical evaluation, adherence assessment, microbiological testing where indicated and radiological follow-up. Persistent anemia after the intensive phase should prompt evaluation for nutritional deficiency, continuing inflammation, poor adherence, severe disease or associated comorbidities.

LIMITATIONS

The present study was limited by its single-center hospital-based descriptive design and sample size of 96, restricting wider generalization and detailed subgroup analysis. Only routine hematological parameters were assessed, without iron profile, ferritin, vitamin B12, folate, C-reactive protein or bone marrow evaluation. Microbiological confirmation was not available

in all cases, and follow-up was limited to the intensive phase only, preventing assessment of long-term hematological recovery.

CONCLUSION

The present study concluded that children with tuberculosis commonly show baseline hematological abnormalities, particularly anemia, thrombocytosis, leukocytosis and raised erythrocyte sedimentation rate. During the intensive phase of anti-tubercular therapy, significant improvement was observed in hemoglobin, total leukocyte count, platelet count and erythrocyte sedimentation rate, suggesting reduction in inflammatory burden and early hematological recovery. Routine complete blood count and ESR may therefore serve as practical supportive tools for monitoring early treatment response in pediatric tuberculosis, especially in Indian hospital settings. However, persistent anemia after the intensive phase should prompt evaluation for nutritional deficiency, ongoing inflammation, poor adherence, disease severity or associated comorbidities.

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