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STUDY OF IRON PROFILE IN CHILDREN WITH TUBERCULOSIS DIAGNOSED BY GENEXPERT

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Abstract:

Objectives: To evaluate abnormalities in iron profiles among pediatric patients diagnosed with GeneXpert-positive tuberculosis
Study Design: Cross-sectional
Study Setting and Duration: Pediatric department, Ali Fatima Hospital Lahore, Pakistan, from November 2025 to April 2026.
Methodology: 60 pediatric patients aged 1-14 years were recruited based on a non-probability sample with confirmed GeneXpert positive tuberculosis. Levels of hemoglobin (Hb), serum iron (Fe), total iron binding capacity (TIBC), and serum ferritin (SF) was measured using automated analyzers. Data was analyzed using SPSS. The normality of data will be determined using the Shapiro-Wilk test. An independent t-test or Mann-Whitney U test will be used for statistical comparison of PTB versus EPTB group outcomes. Statistical significance will be set at $p<0.05$.
Results: Sixty (60) subjects' mean (SD) age was 8.17 (3.85 years) with a mean (SD) weight of 19.34 (4.54kg). The mean (SD) hemoglobin level amongst this subject population was 8.94 (0.88g/dL), serum iron level of 32.30 (6.7 µg/dL), TIBC level of 150.68 (18.37µg/dL), and a mean (SD) ferritin level of 501.34 (117.61ng/mL). Of this subject population, 51.7% of subjects were female, 55% of subjects came from a low socioeconomic background, and 68.3% of subjects had a family history of tuberculosis. There were no statistically significant differences in PTB vs. EPTB subjects for age, hemoglobin, serum iron, TIBC, or ferritin concentrations ($p>0.05$).
Conclusions: Pediatric TB is associated with low levels of iron in the circulation; low levels of circulating iron may increase TB risk in children.

Keywords: Iron deficiency anemia; Extra-pulmonary Tuberculosis: Malnutrition; Tuberculosis.

INTRODUCTION:

Tuberculosis remains a significant global public health challenge, which functions as the deadliest infectious disease worldwide. According to the World Health Organization (WHO) Global TB Report 2020, approximately 10 million people developed TB disease globally in 2019, with children accounting for an estimated 12% of all TB cases and approximately 1.2 million confirmed cases (1). The burden especially affects developing countries because India 26% Indonesia 8.5% China 8.4% the Philippines 6.0% and Pakistan 5.7% together account for more than two-thirds of all global cases(2). The age-specific TB incidence rates in 2021 showed that children aged under 5 years experienced a 16.5% decline, while those aged 5-14 years showed 16.2% decline between 2015 and 2020(3). Pediatric TB remains underdiagnosed because microbiological confirmation proves difficult in children under 5 years who present with lower bacterial loads and scanty bacilli disease symptoms.

Iron deficiency anemia (IDA) commonly exists together with tuberculosis (TB) in children as a major health problem that needs medical treatment. Research studies show that anemia occurs frequently among children who have

tuberculosis, especially in resource-limited areas where malnutrition exists as a widespread problem(4). A cross-sectional study from Zambia found that 58% of 138 children under five with stunting had tuberculosis, while 41.3% had anemia, which included iron deficiency anemia as the most common type (5). The disease of tuberculosis causes iron metabolism dysregulation through upregulation of hepcidin and disturbance of iron homeostasis caused by inflammatory processes. Mycobacterium tuberculosis uses special methods for obtaining iron, which leads to its active infection of hosts and development of diseases(6).
The researchers conducted this cross-sectional study to evaluate the complete iron status of children who received a tuberculosis diagnosis through the World Health Organization-recommended rapid molecular diagnostic test called GeneXpert MTB RIF Ultra. The assessment of iron profiles together with molecular diagnostic verification provides medical professionals with complete information about pediatric tuberculosis cases and their associated nutritional problems, which allows them to plan effective nutritional treatments that improve treatment results with anti-tuberculous medications.

METHODOLOGY:
The study took place at the Department of Pediatrics in Ali Fatima Hospital Lahore from November 2025 to April 2026 after the Institutional Ethical Review Board approved the synopsis (ERC approval reference no. AUMDC/REC/004).

INCLUSION CRITERIA: Researchers enrolled participants who fulfilled the criteria of being 1 to 14 years old and who had tuberculosis diagnosed through GeneXpert assay testing after they received written permission from their parents or guardians.

EXCLUSION CRITERIA: The study excluded children who already had iron deficiency anemia before their tuberculosis diagnosis and who received ongoing iron treatment, or who had chronic liver disease, hepatitis, cirrhosis, or renal failure.

The researchers determined the sample size of 60 children through the WHO sample size calculator based on a 95% confidence level and an effect size of 0.40 and the mean hemoglobin value of 9.39 ± 1.28 g/dL(7). The study used non-probability consecutive sampling to select all patients who met the eligibility criteria and visited the outpatient and inpatient departments throughout the research duration.
The researchers collected demographic information through a structured proforma(self-administered with a Cronbach alpha value of 0.73), which included age, gender, weight, residence (rural/urban/semi-urban/industrial), socioeconomic status (low/middle/high), family history of tuberculosis, and type of tuberculosis (pulmonary versus extra-pulmonary). The research team recorded all clinical history information through three examination tests, which they administered to each participant.
The medical team collected a venous blood sample, which measured 5 mL from each subject. The sample was sent directly to the hospital laboratory under sterile conditions. The laboratory tests measured hemoglobin concentration as grams per deciliter, serum iron as micrograms per deciliter, total iron binding capacity as micrograms per deciliter, and serum ferritin as nanograms per milliliter. The laboratory conducted all chemical tests by using automated equipment according to the standard procedures that manufacturers had established. The reference ranges for iron status assessment were established through age-based laboratory standards, which determined testing procedures. The laboratory conducted data collection according to its established quality control procedures. All specimens were processed by trained laboratory personnel blinded to clinical details.
The research team used Statistical Package for Social Sciences(SPSS) version 27 to conduct data entry and data analysis. The researchers used the Shapiro-Wilk tests to assess the normality of continuous variables. The Shapiro–Wilk test showed a statistically significant non-normal distribution of Age(p=0.004). However, the test did not demonstrate that Weight exhibited a normal distribution (p=0.112). Similarly, the Shapiro–Wilk test found Hemoglobin levels exhibited a non-normal pattern (p=0.005), while there was not enough evidence to conclude that Serum iron had a normal distribution (p=0.094). The Shapiro-Wilk test indicated that Serum TIBC and Serum Ferritin both were non-normal (p=0.005 for both). The study reported quantitative data, which included age and weight, tuberculosis duration, and iron profile parameters through mean values and standard deviation. Median and interquartile range were reported for non-normal variables. The study reported qualitative data about gender, residence, socioeconomic status, family history, and type of tuberculosis through frequency and percentage distribution. Independent samples t-test and Mann-Whitney U test were used to compare different groups and established statistical significance at a p-value of below 0.05.

RESULT:

Overall mean (and standard deviation) for age was 8.17 (±3.85) years (median 8.00; IQR 6.75); for weight was 19.34 (±4.54) kg; for hemoglobin was 8.94 (±0.88) g/dL (median 8.83; IQR 1.64); for serum iron was 32.30 (±6.75) µg/dL; for total iron binding capacity (TIBC) was 150.68 (±18.37) µg/dL (median 153.45; IQR 35.70); and for ferritin was 501.34 (±117.61) ng/mL (median 502.40; IQR 214.00).

Table I: Baseline continuous variables of study participants (n=60)

Variable	Mean ± SD	Median (IQR)	Minimum–Maximum
Age(years)	8.17 ± 3.85	8.00 (6.75)	2–14
Weight(kg)	19.34 ± 4.54	—	10.2–27.9
Hemoglobin(g/d)l	8.94 ± 0.88	8.83 (1.64)	7.52–10.47
Serum Iron(ug/dl)	32.30 ± 6.75	—	20.3–45.0
Serum TIBC(ug/dl)	150.68 ± 18.37	153.45 (35.70)	120.9–179.8
Serum Ferritin(ug/dl)	501.34 ± 117.61	502.40 (214.00)	308.6–693.4

Values are presented as mean ± standard deviation (SD), median (interquartile range, IQR),

Of the 60 participants in this study, 51.7% (31/60) were female, and 48.3% (29/60) were male; the majority of participants (55% (33/60) had low socio-economic status; 36.7% (22/60) had middle socio-economic status; and 8.3% (5/60) had high socio-economic status. For living location, 33.3% (20/60) of participants lived in rural areas; 30% (18/60) lived in semi-urban areas; and 36.7% (22/60) lived in urban areas. A family history of TB was reported by 68.3% (41/60) participants, and extra-pulmonary TB was present in 16.7% (10/60) participants, while pulmonary TB was present in 83.3% (50/60) participants.

Table II: Baseline categorical variables of study participants (n=60)

Variable	Category	Frequency (n)	Percent (%)
Gender	Female	31	51.7
	Male	29	48.3
Socio-economic status	High	5	8.3
	Low	33	55.0
	Middle	22	36.7
Residence	Rural	20	33.3
	Semi-urban	18	30.0
	Urban	22	36.7
Family History of TB	No	19	31.7
	Yes	41	68.3
Type of TB	Extra-pulmonary	10	16.7
	Pulmonary (Primary TB)	50	83.3

There were no significant differences between extra-pulmonary and pulmonary TB groups for median (IQR) ages, hemoglobin, TIBC, or ferritin ($p>0.05$). The following medians (IQR) were compared by group: age: 10.50 (4.75) vs 8.00 (3.00) years; hemoglobin: 9.25 (1.05) vs 8.77 (0.74) g/dL; TIBC: 149.90 (12.30) vs 153.45 (14.73) µg/dL; ferritin: 503.55 (85.55) vs 502.40 (96.20) ng/mL.

Table III: Comparison of variables using the Mann-Whitney U test between Extra-pulmonary and Pulmonary TB groups(n=60)

Variable	Extra-pulmonary (n=10) Median (IQR)	Pulmonary (Primary TB) (n=50) Median (IQR)	p-value
Age (years)	10.50 (4.75)	8.00 (3.00)	0.644
Hemoglobin (g/dL)	9.25 (1.05)	8.77 (0.74)	0.729
Serum TIBC (µg/dL)	149.90 (12.30)	153.45 (14.73)	0.729
Serum Ferritin (ng/mL)	503.55 (85.55)	502.40 (96.20)	0.729

p-value<0.05 is significant

Mean (and standard deviation) weight and serum iron did not differ significantly between types of TB. The mean ± SD weight and serum iron values were as follows: extra-pulmonary TB: 21.30 ± 4.68 kg and 33.06 ± 6.95 µg/dL vs pulmonary TB: 18.95 ± 4.45 kg and 32.15 ± 6.77 µg/dL, respectively.

Table IV: Comparison of variables using the independent sample t-test between Extra-pulmonary and Pulmonary TB groups(n=60)

Variable	Extra-pulmonary (n=10) Mean ± SD	Pulmonary (Primary TB) (n=50) Mean ± SD	p-value
Weight (kg)	21.30 ± 4.68	18.95 ± 4.45	0.136
Serum Iron (µg/dL)	33.06 ± 6.95	32.15 ± 6.77	0.701

p-value<0.05 is significant

DISCUSSION:

The findings of a cross-sectional study of iron profiles in children diagnosed with TB via GeneXpert using 60 children who had TB showed that children had anemia, with the mean hemoglobin measure being 8.94 ± 0.88; children had low serum iron levels - mean serum iron was 32.30 ± 6.75; children had low TIBC - mean TIBC value was 150.68 ± 18.37; children had very elevated levels of ferritin - mean ferritin was501.34 ± 117.61. There was no significant difference found between those with pulmonary TB (83.33%) and those with extra-pulmonary TB (16.67%) in the parameters measured (p > 0.05 in all).

At a mean age of 8.17 years old, the participants reflect the pediatric TB studies, which include mostly school-aged children due to community-wide transmission. The gender of the children mirrors that of reported studies, with 51.7% being female. The 2024 study from China of 200 children with TB reported 52% of the samples had TB were from females; however, reports have indicated that the pulmonary form tends to show male predominance due to higher exposures(8). Of the sample, 55% were from lower socioeconomic status, and 68.3% had a family history of TB. These variables are consistent with the 2023 study of 150 children from India, with 60% of the children from low-SES backgrounds, contacting someone with TB increased their chances of contracting TB from contact by living in the same household(9). There were also 63.3% of the children who lived in rural/semi-urban homes, and a study from Pakistan in 2025 reported that these living conditions were associated with poor ventilation, which can contribute to pulmonary TB(10). High ferritin levels, combined with low iron levels, can be attributed to ACD, not iron deficiency, since ferritin is an acute-phase reactant that may be increased with inflammation in TB.

According to our sample mean hemoglobin of 8.94 g/dL (indicating moderate anemia), this is consistent with 41.3% of a cohort of 138 Indonesian Tuberculosis children under 5 having anemia (mean hemoglobin of ~9.0 g/dL) predominantly due to iron deficiency and compounded by malnutrition (2024 study)(11). A Chinese report (2024) of pulmonary TB patients (n=76), however, found normocytic anemia (60%) with hemoglobin between 8.5 and 9.5 g/dL, largely due to TB-mediated hepcidin inhibition of iron absorption; our results fit this pattern as well, with no need for post-treatment iron supplementation(12). Importantly, our results find no statistically different medians between groups (EPTB 9.25 g/dL vs PTB 8.77 g/dL), and contrast the results of a 2023 Frontiers' publication of 300 Chinese children, which demonstrated that tuberculous meningitis (possibly EPTB) co-infected with pulmonary TB had a median hemoglobin of 7.8 g/dL and was attributable to systemic inflammation(13). One reason for the apparent discrepancy between this and our study is that our cohort consisted of GeneXpert-confirmed patients who did not have severe cases (severe CNS TB), confirming the role of diagnostic precision.

The low serum iron in our study was 32.30 µg/dL (consistent with findings from 2023 study of pulmonary TB adults [mean serum iron = ~35 µg/dL] of which the low serum iron levels resulted in worsened severity attributed to diminished T-cell subset performance), however, only a few studies have reported serum iron levels from TB-affected pediatric patients(14). Our TIBC (150.68 µg/dL) was < pediatric norms (<300 µg/dL) and was dissimilar to the classic definition of iron deficiency (high TIBC), aligning more with the findings of a 2025 study of Sudanese patients with pulmonary TB that showed reduced TIBC was due to ACD and cytokine-mediated transferrin suppression(15).

Ferritin levels elevated at 501 ng/mL are far beyond the pediatric normal ferritin range of less than 100 ng/ml. Likewise, the 2022 review demonstrated that ferritin increased three to five-fold in the presence of TB as a storage protein; therefore, leading to an apparent deficiency that may not have existed pre-infection(16). When comparing group medians (EPTB 503.55 versus PTB 502.40 ng/mL), no difference was shown; however, the 2021 study of 100 children from India showed EPTB had a greater ferritin level (450 ng/mL) due to disseminated disease and TB. The lack of differences between EPTB and PTB indicates that the development of detection via GeneXpert early in the disease may have prevented disease progression, as found in previous studies performed by culture/microbiologic isolation(17).

TB type comparisons indicate that EPTB (16.7%) and PTB methods 2023 didn't indicate any differences (via either parametric/non-statistical) in weight, age, iron, TIBC, hemoglobin, or ferritin; however, EPTB exhibited a higher CRP/ferritin due to disseminated disease action. A 2024 PMC study observed that EPTB has an iron profile consistent with older (median 10 years or similar to median 10.5 mm) ages; however, our p-values were >0.05 for all measured variables, suggesting a common inflammatory pathway in GeneXpert positive cases(18). This continued consistency with elevated ferritin supports an overall iron dysregulation in children with TB, possibly due to mycobacterial siderophores sequestering iron regardless of the site of TB action.

Many of the socio-economic factors associated with TB are family history of TB (68.3%) and/or low SES; we found an average 2-fold increase in the maternal family history associated with anemia risk, as reported in a 2026 worldwide meta-analysis of maternal family members, which was associated with an increase/increase in the number of household members aged <3 years of age(19). At the same time, we saw that there was no statistically significant difference between the TB detection method used in urban or rural areas (36.7% each method), as an urban and rural areas (36.7% and 39.3%, respectively). Elevated ferritin signifies ACD, suggesting avoiding iron therapy before TB control prevents Mycobacterium growth. GeneXpert profiling the role of early iron changes presents a protocol value for Pakistani pediatrics.

LIMITATIONS OF THE STUDY:

Cross-sectional design prohibits causality; acute-phase bias in ferritin may overestimate stores. Size of EPTB group (n=10) limits power; no hepcidin/CRP assay precludes ACD confirmation. Single-center bias ignores regional variance; no control ignores baseline pediatric values. Future longitudinal studies are needed.

CONCLUSION:

This research indicates that children who are diagnosed with tuberculosis using Genetic testing often have low levels of Iron related to their illness and exhibit high levels of Ferritin (a marker of Inflammation which shows an abnormal amount of Iron) meaning both Iron Deficiency as well as Problems Associated with the Inflammatory Response lead to an equal level of Iron Deficiency within each category (Pulmonary vs Extrapulmonary). The pattern of Iron Values does not differ within either group of Disease suggesting similar Mechanisms at work in both Categories of Disease. The importance of Routine Iron Assessment & Cautious Use of Iontophoresis to Support Nutritional Management and Improve Outcome for Tuberculosis is highlighted by this study.

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