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ORIGINAL ARTICLE

Serum ferritin-based assessment of iron deficiency in individuals with β-thalassemia trait.

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ABSTRACT… Objective: To evaluate the potential coexistence of iron deficiency and BTT. Additionally, this study assesses the effect of iron deficiency on haematological indices of individuals with BTT. **Study Design:** Cross-sectional study. **Setting:** Noor Thalassemia Foundation, Lahore. **Period:** May 2024 to May 2025. **Methods:** Model involved the random selection of 74 participants, including parents of known beta thalassemia major cases and patients with beta thalassemia trait (HbA2 >3.5%), who visited the OPD department of Noor Thalassemia Fondation in Lahore. 5ml venous blood was drawn and subjected to complete blood count (CBC), HLPC, and serum ferritin measurement. **Results:** Out of 74 participants, 65 were females and 9 were males. Iron deficiency, characterized by a serum ferritin concentration below 15 ng/mL, was found in 23 individuals, while 42 individuals had a serum ferritin concentration above 15 ng/mL. Mean levels of HbA_2 were 5.6±0.4%, mean haemoglobin concentration was 10.24±1.36g/dL, mean MCV was 64.73±7.32fL, and mean MCH was 19.94±4.04%. The mean value of serum ferritin levels in our study population was 34.74±32.27 ng/mL. **Conclusion:** A total of 23 individuals (31%) were found to be iron deficient. Iron deficiency reduced the red blood cell count, haemoglobin concentration, and MCV while it increased the RDW in BTT individuals ($p<0.05$), indicating that iron deficiency significantly affects the haematological indices in carriers of BTT.

Key words: Beta Thalassemia Trait, Iron Deficiency in BTT, Iron Deficiency, Serum Ferritin.

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INTRODUCTION

β-thalassemia trait, also called β-thalassemia minor, is a heterozygous genetic condition that results from mutations in the HBB gene, encoding the beta globin chain of hemoglobin. The normal ranges of haemoglobin are from 13.5 to 17.5 g/dL for adult males and 11.5 to 15.5 g/dL for adult females.[1] Although individuals with β-thalassemia trait do not have any symptoms, they are characterized by low to normal haemoglobin, low mean corpuscular hemoglobin (MCH), and low mean corpuscular volume (MCV). β-thalassemia trait is widely distributed in various regions, particularly South Asian, Middle Eastern, Mediterranean, and African populations.[2] In Pakistan, around 10 million people are carriers of beta thalassemia.[3]

Iron deficiency anemia is an acquired form of anemia generally caused by chronic blood loss, such as gastrointestinal bleeding[4] and menorrhagia in females; impaired iron absorption due to GI reasons such as Celiac disease and gluten enteropathy; poor dietary intake. It is the most prevalent type of anemia, especially in children under 5 and women of reproductive age worldwide. A 2018 study found that iron deficiency anemia affected 28.6% of children under five and 18.2% of women of reproductive age in Pakistan.[5]

Both β-thalassemia trait and iron deficiency anemia exhibit the hematological features of hypochromic, microcytic anemia, making their differentiation challenging solely based on blood indices. However, despite these overlapping features, the pathophysiology of β-thalassemia trait and iron deficiency anemia differ significantly. The β-thalassemia trait has no medical management, but iron deficiency anemia can be managed by iron therapy. β-thalassemia trait is associated with a positive iron balance due to increased iron absorption, a compensatory response to ineffective erythropoiesis. Therefore, in β-thalassemia trait, iron supplementation is not required unless iron deficiency for identifiable reasons is present.

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In such cases, an improved iron-enriched diet can also help correct iron deficiency.

Serum ferritin, along with other markers of iron profile such as serum transferrin saturation, serum iron, and TIBC, are used in the differential diagnosis of hypochromic, microcytic anemia. Serum ferritin represents the body's iron stores and is considered a reliable biomarker to diagnose iron deficiency. It is instrumental in differentiating between iron deficiency and BTT when hematological indices are inconclusive. It also plays a critical role in detecting iron deficiency in patients diagnosed with BTT. The World Health Organization (WHO) recommends that serum ferritin levels below 15 ng/mL in adults and below 12 ng/mL in children under 5 years are significant diagnostically for iron deficiency.[6] Investigating coexistent iron deficiency in patients with β-thalassemia trait in vulnerable groups, such as women and children, is necessary. Omitting iron therapy can exacerbate anemia and worsen clinical conditions such as fatigue, reduced exercise capacity, and decline of neurocognitive function.[7]

The coexistence of iron deficiency in BTT has been reported in many population-based studies. Still, its prevalence varies widely depending on the geographical region and socioeconomic status of the patients. This study aims to investigate whether iron deficiency coexists with β-thalassemia trait or not, and also to find the prevalence of iron deficiency, assessed through ferritin levels, in patients with BTT. Along with differentiating between BTT and coexistent iron deficiency in BTT, this study also explores the effect of iron deficiency on hematological indices in subjects with β-thalassemia trait. This study will contribute to the more accurate identification of iron deficiency in individuals with BTT, thereby aiding in the improvement of anemia and overall well-being.

METHODS

This cross-sectional study was conducted at the Hematology outpatient department at Noor Thalassemia Foundation, Lahore, between May 2024 and May 2025 after approval from ethical review committee (NTF-R04-24-19/4/24). A random selection of parents of β-thalassemia major and patients of β-thalassemia trait diagnosed on the basis of haemoglobin electrophoresis (HbA_2 >3.5%) was made. The inclusion criteria comprised individuals aged greater than 18 years with no history of iron supplementation or blood transfusion in the recent 3 months. Individuals with chronic inflammatory disease, liver or kidney disorders, or a history of blood transfusion or iron supplementation were excluded from the study. After obtaining informed consent from the patients, 5 ml of blood was drawn for laboratory evaluation. Laboratory investigations involved CBC performed using Sysmex Kx21 (Sysmex corporation, Kobe Japan), HPLC using BioRad D10 Hemoglobin testing system (Bio-Rad laboratories, USA)and serum ferritin level assessment performed on Siemens Atellica using chemiluminescence immunoassays (Siemens,Medical Solutions, USA).

All the data were recorded and assessed through IBM SPSS version 25.0. The occurrence of iron deficiency in BTT subjects was determined descriptively. Furthermore, Independent T-test was employed to compare mean values of HbA_2, Red Blood Cells (RBC), Haemoglobin (Hb), Mean Corpuscular Volume (MCV), Mean Corpuscular Haemoglobin (MCH), Mean Corpuscular Haemoglobin Concentration (MCHC), Red cell distribution width (RDW) and ferritin in two groups; one group with BTT and other group with coexistent iron deficiency.

RESULTS

Our study population enrolled 74 subjects diagnosed with β-thalassemia trait. Out of these, 65 were females (88%) and 9 were males (12%). The female-to-male ratio in our study was approximately 7.3:1. Participants ranged from 18 to 57 years of age, with the majority (92%) falling within the 20 to 49 years age group.

The haematological parameters, including HbA_2, RBC count, Hb, MCV, MCH, MCHC, RDW, and Serum ferritin levels, were measured and recorded as mean ± standard deviation and are presented in Table-I.

Out of these 74 participants, Iron deficiency (serum ferritin <15ng/mL) was identified in 23 subjects (31%), all of them were females (100%), while

no males exhibited iron deficiency- a statistically significant difference ($p<0.05$). Latent iron deficiency (serum ferritin 15 to 30 ng/mL) was identified in 22 subjects (29%). Among them, 3 were males (14%) and 19 were females (86%). A total of 29 subjects (40%) had serum ferritin >30ng/mL, indicating normal iron status.

Our study participants were categorized into two groups: Group A included individuals with β-thalassemia trait only, and Group B included those with concurrent iron deficiency.

Independent t-test showed statistically significant differences in values of hematological indices and serum ferritin between both groups (Table-II)

TABLE-I

Haematological Parameters

Parameters	Mean±S.D
HbA_2 (%)	5.6±0.4
RBC ($x10^{12}$/L)	5.32±0.79
Hb(g/dL)	10.24±1.36
MCV(fL)	64.73±7.32
MCH(%)	19.94±4.04
MCHC(%)	30.22±2.20
RDW(fL)	41.21±4.36
Ferritin(ng/mL)	34.74±32.27

TABLE-II

Differences in values of hematological indices

	Group A BTT Only	Group B Concurrent Iron Deficiency	P-Value
HbA_2 (%)	5.57±0.87	3.95±0.3	$<0.05^S$
RBC ($x10^{12}$/L)	5.46±0.79	5.2±0.79	0.21^{NS}
Hb(g/dL)	10.09±1.03	9.2±1.4	$<0.05^S$
MCV(fL)	65.84±7.09	61.6±7.4	$<0.05^S$
MCH(%)	20.17±3.5	19.20±5.02	0.35^{NS}
MCHC(%)	30.42±2.25	29.79±2.01	0.27^{NS}
RDW(fL)	38.5±3.8	46.6±7.2	$<0.05^S$
Ferritin(ng/mL)	46.16±32.91	9.3±3.69	$<0.05^S$

DISCUSSION

The study evaluated the iron status, assessed through serum ferritin, among individuals with β-thalassemia trait. Our findings revealed the significant frequency of iron deficiency in individuals carrying β-thalassemia trait, and highlighted the hematological differences between BTT carriers and those with concurrent iron deficiency.

Among 74 participants, females showed a marked preponderance. BTT is known to have equal gender predisposition. The female predisposition in our studies may reflect the sample bias, the willingness of females to participate, and the greater number of females in society.

The mean HbA_2 levels (5.6±0.4%) align with the diagnostic criterion for BTT (HbA_2 >3.5%).[8] The mean value of haemoglobin (10.24±1.36g/dL) indicates a mild degree of anemia that is consistent with BTT.[9] Mean values of MCV (64.73±7.32fL) and MCH (19.94±4.04%) show microcytosis and hypochromia that are characteristic features of BTT.[10]

Iron deficiency affected 31% of participants, all of them were females. This substantial rate of iron deficiency observed in females reinforces the known gender disparity in iron deficiency. A similar study conducted by Salman et al. found that 34.7% of females with BTT were iron deficient.[11] Almost all the women suffering from iron deficiency in our study were in their reproductive years (20 to 45 years). Women in their reproductive ages are at higher risk of iron deficiency, where factors such as menstrual blood loss, pregnancy, and increased iron requirements contribute to the iron depletion.[12] Additionally, 29% of individuals showed latent iron deficiency, and 86% of them were females, showing broader patterns of latent iron deficiency in females. The high prevalence of iron deficiency and latent iron deficiency demands the need for routine iron assessment in BTT patients, especially females.

Individuals were stratified into two groups: Group A (individuals with BTT only) and Group B (BTT individuals with concurrent iron deficiency).

Group B showed significantly lowered HbA_2 levels (3.95±0.3%) as compared to Group A (5.57±0.87%) ($p<0.05$), reaffirming that iron deficiency can suppress HbA_2 levels. This phenomenon has been documented in many study cohorts[13] and highlights the need to rule out iron deficiency before diagnosing

BTT based on HPLC or Hb electrophoresis, to avoid misdiagnosis and enhance diagnostic accuracy.

Group B showed significantly lowered levels of haemoglobin as compared to group A (9.2±1.4 g/dL) vs (10.09±1.03 g/dL), ($p<0.05$), indicating more severe anemia in those with concurrent iron deficiency. This suggests that the compounded erythropoietic impairment because of iron deficiency and thalassemia leads to reduced haemoglobin synthesis in individuals with concurrent iron deficiency. An existing literature states that carriers typically present with mild anemia, i.e, their haemoglobin ranges from 9 to 12 g/dL.[14] These findings suggest that if BTT individuals exhibit moderate anemia (haemoglobin <10g/dL), they must be screened for iron deficiency. Improving concurrent iron deficiency can improve the level of haemoglobin in BTT patients, as documented in studies.[15]

Significantly reduced MCV in group B relative to group A ($p<0.05$) shows the additive microcytic effect of iron deficiency on thalassemic RBCs. Elevated RDW in group A (46.6±7.2 fL) as compared to group B (38.5±3.8fL) shows the significant differences ($p<0.05$) and marked anisocytosis- a feature associated with iron deficiency.[16]

While the RBC count was higher in group A relative to group B, this difference lacked statistical significance ($p = 0.21$). BTT typically involves a compensatory increase in erythropoiesis due to chronic mild anemia[17], resulting in increased RBC count. However, the concurrent iron deficiency impairs the red cell production and haemoglobin synthesis, potentially normalizing or reducing RBC count despite the underlying β-thalassemia trait.

MCH and MCHC were also reduced in group B, indicating increased hypochromia. However, differences were not statistically significant, suggesting that though hypochromia is increased in the presence of iron deficiency, it may not consistently reflect the significant variation in the study population.

The study had a few limitations. It included a small number of males (n=9) that limited the gender based comparison. Only one marker of iron profile, i.e., serum ferritin, was evaluated. It is suggested to conduct a study that includes a balanced number of males and females to better assess the iron levels in males. Moreover, a comprehensive iron profile including serum transferrin saturation, serum iron, and TIBC should be incorporated to enhance diagnostic accuracy.

CONCLUSION

Our findings confirmed that iron deficiency can coexist with the beta thalassemia trait. Iron deficiency was found in 31% participants, and all of them were females. Additionally, 29% individuals, comprising 14% males and 86% females, were found to have latent iron deficiency. Women of reproductive age emerged as a group showing the most susceptibility to iron deficiency due to physiological processes such as menstruation, pregnancy, and increased nutritional requirements.

The high prevalence of iron deficiency in our study underlines the clinical significance of monitoring iron status in individuals with BTT, particularly women of reproductive age. Iron deficiency has significantly reduced the RBC count, haemoglobin, and MCV, and raised RDW ($p<0.05$) in BTT participants.

The findings highlight the need of evaluating iron status in BTT individuals presenting with low haemoglobin concentration, increased microcytosis (reduced MCV) and Raised RDW, must be evaluated to correct the iron deficiency and improve the haematological indices in individuals with BTT.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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REFERENCES

1. Hoffbrand AV. **Hoffbrand's essential haematology.** John Wiley & Sons. 2024 Jun 25.

2. Zhang S, Chen Z, Chen M, Huang H. **Current status and trends in thalassemia burden across South, East and Southeast Asia, 1990–2021 a systematic analysis for the global burden of disease study 2021.** BMC Public Health. 2024 Dec 18; 24(1):34-72.
3. Khaliq S. **Thalassemia in Pakistan.** Hemoglobin. 2022 Jan 2; 46(1):12-4.
4. Kumar A, Sharma E, Marley A, Samaan MA, Brookes MJ. **Iron deficiency anaemia: Pathophysiology, assessment, practical management.** BMJ Open Gastroenterology. 2022 Jan 1; 9(1):e000759.
5. Habib A, Kureishy S, Soofi S, Hussain I, Rizvi A, Ahmed I, et al. **Prevalence and risk factors for iron deficiency anemia among children under five and women of reproductive age in Pakistan: Findings from the National Nutrition Survey 2018.** Nutrients. 2023; 15(15):3361.
6. Daru J, Colman K, Stanworth SJ, De La Salle B, Wood EM, Pasricha SR. **Serum ferritin as an indicator of iron status: what do we need to know?.** The American Journal of Clinical Nutrition. 2017 Dec 1; 106:1634S-1639S.
7. Benson CS, Shah A, Stanworth SJ, Frise CJ, Spiby H, Lax SJ, et al. **The effect of iron deficiency and anaemia on women's health.** Anaesthesia. 2021 Apr; 76:84-95.
8. Colaco S, Nadkarni A. **Borderline HbA2 levels: dilemma in diagnosis of beta-thalassemia carriers.** Mutation Research/Reviews in Mutation Research. 2021 Jul 1; 788:108387.
9. Langer AL. **Beta-thalassemia.** 2000 Sep 28.
10. Sain A, Bhake A, Agrawal A, Thomas S. **Discriminant red cell indices for microcytic hypochromic anaemia in distinguishing beta thalassaemia trait and iron deficiency anaemia: A systematic review.** Journal of Clinical & Diagnostic Research. 2021 Jan 1; 15(1):EE01-EE06.
11. Salman F, Fahim F, Saleem A. **Prevalence of iron deficiency in individuals with-thalassemia trait.** Pak J Pathol. 2022 Mar. 31; 33(1):5-8.
12. Makade, Jagadish; Tiwade, Yugeshwari R; Bahadure, Sweta Dilip; Badge, Ankit K. **Exploring the association between iron deficiency anemia and pregnancy outcomes: A narrative review.** Journal of Medical Society. May–Aug 2024; 38(2):159-61. | DOI: 10.4103/jms.jms_39_24
13. Hafeez A, Nadeem S, Robert HM, Jabeen S, Tasneem A. **Evaluation of effect of iron deficiency anemia on HbA2 levels.** Pakistan Armed Forces Medical Journal. 2023 Aug 2; 73.
14. Tahir N, Khattak SA, Shaikh GM, Sajjad Z, Hanif TB, Jamal N. **Red cell parameters in beta thalassemia trait; Comparison between iron deficient and non-deficient carriers.** Journal of Bahria University Medical and Dental College. 2024 Apr 25; 14(02):113-7.
15. Moeen SM, Thabet AF, Thabet MM. **Effect of iron therapy on red cell indices and hemoglobin subtypes on patients with beta-thalassemia trait who developed iron-deficiency anemia: a tertiary center experience.** The Egyptian Journal of Internal Medicine. 2019 Dec; 31:741-5.
16. Soliman AR, Kamal G, Mohamed TS. **Blood indices to differentiate between-thalassemia trait and iron deficiency anemia in adult healthy Egyptian blood donors.** The Egyptian Journal of Haematology. 2014 Jul 1; 39(3):91-7.
17. Alhussain A H, Alquwayi WA, Alameer Alkuwaiti YA, Almehainy AM, Alqahtani BM. **Disorders of red and white blood cells, such as anemia and leukemia.** International Journal of Health Sciences. 2017; 1(S1):130-47.

AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Muhammad Irtza Tanveer:** Conceptualization of study, data interpretation, literature search.
2	**Saima Mansoor Bugvi:** Study design, proofreading, data analysis.
3	**Areeba Manzoor:** Literature search, data collection.