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Original Research Article

Assessment of Growth in Thalassemia Patients and Its Correlation with Pretransfusion Haemoglobin and Serum Ferritin

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Abstract:

Background: Thalassemia major causes chronic anemia and iron overload from repeated transfusions, both of which contribute to impaired growth in affected children. Elevated serum ferritin and inadequate pretransfusion hemoglobin are believed to independently and jointly worsen linear growth outcomes. This study examines their combined impact in a large pediatric cohort.

Methods: A prospective, hospital-based cohort study enrolled 174 transfusion-dependent thalassemia major patients aged 1–16 years over a 1-year period. Patients were stratified by mean pretransfusion Hb (<8 g/dL vs ≥8 g/dL), and anthropometric measurements were compared against serum ferritin levels using SPSS-based statistical analysis.

Results: Short stature was present in 35 patients (20.1%), significantly more common in the Hb <8 g/dL group (32.8%) than the Hb ≥8 g/dL group (13.8%, P = 0.045). Serum ferritin showed a strong inverse relationship with height percentile (P = 0.0004), with short-statured patients having markedly higher mean ferritin (6380 ng/mL) than taller patients (3050 ng/mL). Patients with Hb <8 g/dL also had significantly higher mean ferritin (5300 ng/mL) than those with Hb ≥8 g/dL (4230 ng/mL, P = 0.012).

Conclusion: Growth failure in transfusion-dependent thalassemia major is strongly associated with both suboptimal pretransfusion hemoglobin and elevated serum ferritin, emphasizing the need for optimized transfusion and chelation practices.

Keywords: Children, Ferritin, Hemoglobin, Growth Failure, Thalassemia.

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Introduction

Thalassemia is a group of inherited blood disorders caused by mutations in the globin genes that make up hemoglobin (Hb),[1] and is common across regions from Southeast Asia to Africa [2]. The disorder disrupts Hb synthesis through imbalanced globin chain production; in β-thalassemia, excess unpaired α-chains precipitate in red cell precursors, shortening red cell survival and driving ineffective erythropoiesis [3]. Depending on whether β-chain output is reduced or absent, this yields β+ or β0 thalassemia, respectively [4].

At the molecular level, excess globin chains promote red cell apoptosis and ineffective erythropoiesis, producing microcytic, hypochromic cells. The resulting rise in erythropoietin drives a hypermetabolic state, nutritional deficiencies (notably folate), and growth impairment, while splenomegaly from extramedullary hematopoiesis worsens anemia and increases transfusion needs, thrombocytopenia, and leukopenia [3,5].

Growth failure in thalassemia major typically progresses in three stages: early impairment driven by anemia, hypoxia, ineffective erythropoiesis, and nutritional deficits; later disturbances from endocrinopathies involving the GH-IGF-1 axis; and, from around age 10–11, pubertal delay or arrest that blunts the normal adolescent growth spurt [6].

Repeated transfusions cause iron overload and secondary hemochromatosis, with tissue iron accumulation generating free radicals and oxidative damage. Consequences include cardiac, hepatic, and endocrine complications—hypogonadism, hypothyroidism, diabetes, and disturbed calcium/bone homeostasis—along with fatigue, joint pain, and skin hyperpigmentation [7,8]. Endocrine tissues are especially sensitive to iron

deposition; pituitary iron loading within the first four years of life can impair growth hormone secretion and downstream IGF-1 and IGF-binding protein production, often compounded by hepatic hemosiderosis [9]. Together with reduced sex hormone secretion, this hormonal disruption is a key driver of short stature [10].

Additional contributors to growth retardation include hypothyroidism, reduced (especially spinal) bone density, skeletal deformities, and malnutrition linked to low socioeconomic status, gastrointestinal issues, intensive chelation regimens, and psychosocial stress. Hypermetabolism and dietary restrictions aimed at limiting iron intake—such as reduced iron-rich food or milk consumption—can further compromise intake of calories, protein, calcium, and zinc [11]. Although modern treatment and bone marrow transplantation have improved survival, growth failure continues to affect quality of life and social functioning [12].

This study aimed to assess growth patterns in children with thalassemia major by comparing those with mean pretransfusion Hb <8 g/dL versus ≥8 g/dL, and to evaluate the effect of average serum ferritin on growth in transfusion-dependent thalassemia major.

Materials and methods

Study Design, Setting, and Duration: This prospective, hospital-based cohort study was conducted over a 1-year period at the Thalassemia Day Care Center, Department of Pediatrics, in a tertiary healthcare centre.

Study Population: Of 350 registered thalassemia patients at the center, 174 transfusion-dependent children aged 1–16 years were enrolled. Children below 1 year or above 16 years, those whose families declined consent, and those with associated comorbidities or a history of splenectomy were excluded.

Data Collection: Baseline demographic data—age, age at diagnosis, disease duration, sex, family history, perinatal and developmental history, and immunization status—were recorded for all participants. General and systemic examinations, including grading of hepatosplenomegaly by Hackett's classification, were performed at enrollment and repeated three-monthly.

Anthropometric and Growth Assessment: Height/length, weight, and head circumference were measured at each visit and plotted against reference standards using the IAP Growth Charts app (WHO standards for children up to 5 years; IAP standards beyond 5 years)—a low-cost, widely accessible tool suited to resource-limited settings. Patients were stratified by mean pretransfusion Hb over the preceding five transfusions into two groups: <8 g/dL and ≥8 g/dL.

Laboratory Investigations: Both groups were evaluated for total leukocyte count, platelet count, serum ferritin, and biochemical parameters including random blood glucose, serum calcium and magnesium, alkaline phosphatase, inorganic phosphate, SGOT, and SGPT. Serum 25(OH) Vitamin D and thyroid hormone levels were assessed at baseline and every three months thereafter; these tests are generally available through district-level or referral laboratory networks.

Transfusion and Chelation Protocol: Details of iron chelator use along with frequency and volume of transfusions were documented. Most patients received non-Leuk depleted packed red blood cells at a standard dose of 10 mL/kg, up to a maximum of 350 mL per transfusion—a simple, reproducible protocol requiring no specialized blood-bank processing.

Statistical Analysis: Mean values for each parameter were computed annually using Microsoft Excel, with between-group comparisons performed in SPSS (version 20). Categorical variables were expressed as frequencies and percentages, and continuous variables as mean ± SD or median with interquartile range, as appropriate. A p-value <0.05 was considered statistically significant.

Ethical Considerations: Approval for the study was granted by the Gujarat Adani Institute of Medical Sciences Institutional Ethics Committee (Letter No.- GAIMS/IEC/APPROVAL/2023/60, Dated- 17/05/2023) and written informed consent was obtained from parents/guardians of all participants.

Results

Among the 174 transfusion-dependent thalassemia patients studied, general anthropometric assessment showed that 35 patients (20.1%) had short stature (height <3rd percentile), while the majority, 78 patients (44.9%), had heights between the 3rd and 50th percentiles, indicating that growth impairment was common across the cohort even though outright short stature affected only about a fifth of patients. Only 8 patients (4.6%) achieved heights above the 75th percentile, reflecting an overall leftward shift in the growth distribution typical of transfusion-dependent thalassemia major. When stratified by pretransfusion hemoglobin, short stature was significantly more prevalent in the Hb <8 g/dL group (32.8%) compared to the Hb ≥8 g/dL group (13.8%) (P = 0.045), and this group also showed a higher concentration of patients in the lower height percentile bands (3rd–25th percentile), whereas patients maintaining Hb ≥8 g/dL were more evenly distributed toward the higher percentile categories (Table 1).

Table 1: Comparison of height percentile category between pretransfusion Hb <8 g/dL vs ≥8 g/dL (N=174)

Height percentile	Hb <8 g/dL (n=58), n (%)	Hb ≥8 g/dL (n=116), n (%)	Total, n (%)	p-value
<3rd (short stature)	19 (32.8)	16 (13.8)	35 (20.1)	0.045
3rd–10th	17 (29.3)	24 (20.7)	41 (23.6)	
10th–25th	6 (10.3)	31 (26.7)	37 (21.3)	
25th–50th	12 (20.7)	25 (21.6)	37 (21.3)	
50th–75th	4 (6.9)	12 (10.3)	16 (9.2)	
>75th	0 (0.0)	8 (6.9)	8 (4.6)	
Total	58 (100)	116 (100)	174 (100)	

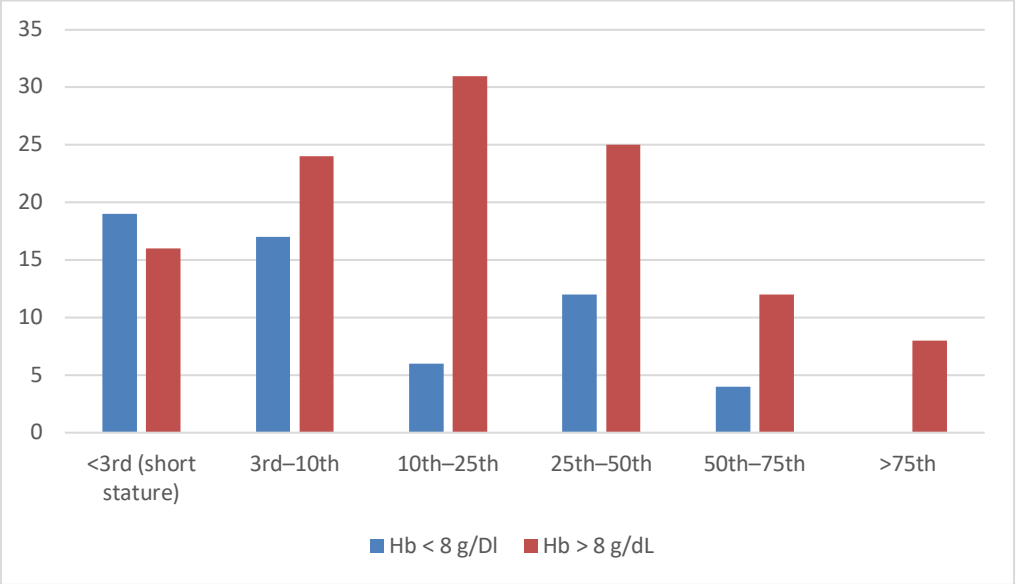

Figure 1: Height Percentile Distribution Stratified by Pretransfusion Hemoglobin Level.

Serum ferritin levels showed a clear inverse relationship with height percentile across the cohort (P = 0.0004). Patients with short stature (<3rd percentile) had the highest mean ferritin levels (6380 ± 1890 ng/mL), which progressively declined with increasing height percentile, reaching a mean of 3050 ± 1650 ng/mL in patients above the 50th percentile. This graded decline suggests a dose-dependent effect of chronic iron overload on growth, consistent with the hypothesis that elevated ferritin reflects cumulative iron deposition in the pituitary and other endocrine tissues, thereby impairing the growth hormone–IGF-1 axis and contributing to stunted linear growth in more heavily iron-loaded patients (Table 2).

Table 2: Association of average serum ferritin (ng/mL) with height percentile category (N=174)

Height percentile	n	Mean ± SD ferritin	Median (IQR)	p-value
<3rd percentile	35	6380 ± 1890	6050 (5450–7550)	0.0004
3rd–10th	41	4900 ± 2400	4850 (3000–6400)	
10th–25th	37	4350 ± 2350	3900 (2800–5900)	
25th–50th	37	3800 ± 1750	3850 (2350–4500)	
>50th	24	3050 ± 1650	2900 (1900–4600)	
Total	174	4550 ± 2280	4450 (2700–5950)	

Mean serum ferritin was significantly higher in patients with pretransfusion Hb <8 g/dL (5300 ± 1970 ng/mL) compared to those with Hb ≥8 g/dL (4230 ± 2380 ng/mL, P = 0.012), with a similarly higher median ferritin level in the low-Hb group (5450 ng/mL vs. 4250 ng/mL). This finding indicates that patients who are unable to maintain adequate pretransfusion hemoglobin levels tend to require more frequent or larger-volume transfusions, resulting in a greater cumulative iron burden despite ongoing chelation therapy, and further supports the interlinked relationship between suboptimal transfusion practice, iron overload, and downstream growth compromise observed in this cohort (Table 3).

Table 3: Comparison of average serum ferritin between pretransfusion Hb <8 g/dL vs ≥8 g/dL (N=174)

Average serum ferritin (ng/mL)	Hb <8 g/dL (n=58)	Hb ≥8 g/dL (n=116)	Total	p-value
Mean ± SD	5300 ± 1970	4230 ± 2380	4590 ± 2290	0.012
Median (25th–75th)	5450 (4000–6450)	4250 (2100–5550)	4450 (2650–5900)	
Range	1750–9150	210–11,050	210–11,050	

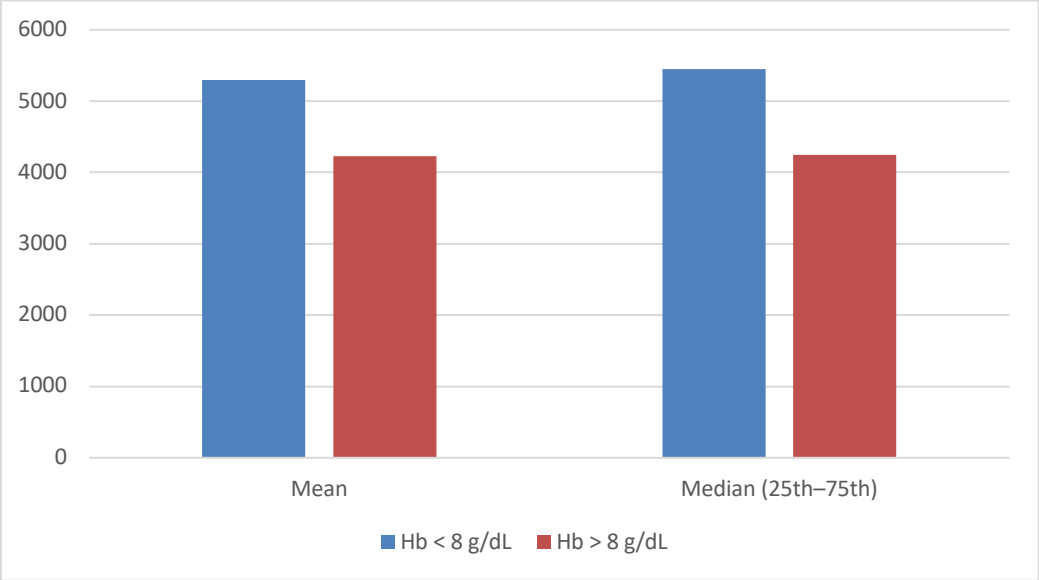

Figure 2: Serum Ferritin Levels (Mean and Median) by Pretransfusion Hemoglobin Group.

Discussion

In this study of 174 transfusion-dependent thalassemia major patients, 20.1% exhibited short stature, a proportion comparable to that reported by Rathaur et al. [13], though somewhat lower than the 62–67% short stature rates reported by other studies [14,15]. The majority of our cohort (44.9%) fell between the 3rd and 50th height percentiles, reflecting a general leftward shift in growth distribution rather than overt stunting in most patients, a pattern consistent with earlier reports describing growth impairment as a spectrum rather than a binary outcome in thalassemia major [11,12]. None of our patients were overweight or obese, in keeping with the findings of Moiz et al. [16]. Differences in the magnitude of short stature across studies likely reflect variation in transfusion adequacy, age at diagnosis, and chelation practices between centers, as has been noted previously [13,15].

We observed that patients with pretransfusion Hb <8 g/dL had a significantly higher prevalence of short stature (32.8%) compared to those maintaining Hb ≥8 g/dL (13.8%, P = 0.045), reaffirming that suboptimal hemoglobin control before transfusion is an important modifiable determinant of linear growth. This is consistent with prior work showing that inadequate transfusion regimens perpetuate chronic hypoxia, ineffective erythropoiesis, and increased metabolic demand, all of which suppress growth velocity in children with thalassemia major [11]. Adolescents are particularly vulnerable in this respect, as advancing age increases transfusion requirements due to alloimmunization and compensatory splenic activity, further compromising hemoglobin stability [17,18].

Our study also demonstrated a strong inverse relationship between serum ferritin and height percentile (P = 0.0004), with mean ferritin levels of 6380 ng/mL in short-statured patients compared to 3050 ng/mL in those above the 50th percentile. This graded association mirrors findings from Fadlyana et al. and Shalitin et al., who similarly reported that serum ferritin above a threshold value was strongly associated with impaired growth and pubertal delay [15,19], and is consistent with the Malaysian cohort of Hamidah et al., which found significantly higher ferritin in short-statured versus normal-statured patients [20]. The proposed mechanism involves early pituitary iron deposition disrupting growth hormone secretion and IGF-1 production, an effect compounded by liver hemosiderosis and iron-induced gonadal dysfunction [1,21]. Similarly, patients with Hb <8 g/dL had significantly higher mean ferritin (5300 ng/mL) than those with Hb ≥8 g/dL (4230 ng/mL, P = 0.012), suggesting that patients requiring more frequent or larger-volume transfusions to compensate for poor hemoglobin maintenance accumulate greater cumulative iron burden despite ongoing oral chelation, a pattern also described by Pemde et al., who reported persistently elevated mean serum ferritin levels (3112 ng/mL)

despite adequate pretransfusion hemoglobin maintenance and regular chelation therapy, emphasizing that iron overload remains a major determinant of growth impairment in transfusion-dependent thalassemia [22].

Taken together, these findings underscore that growth failure in transfusion-dependent thalassemia major is not attributable to anemia or iron overload in isolation, but rather to their combined and interdependent effects on the growth hormone–IGF-1 axis and skeletal maturation. Ensuring both adequate pretransfusion hemoglobin levels and effective, compliant iron chelation therapy appears critical to mitigating growth retardation, particularly as children approach adolescence when endocrine vulnerability to iron toxicity is greatest [6,22]. These results reinforce the need for individualized transfusion protocols and closer ferritin surveillance as part of routine thalassemia care.

Conclusion

This study of 174 transfusion-dependent thalassemia major patients confirms that growth failure is a significant, largely preventable complication closely linked to inadequate pretransfusion hemoglobin and chronic iron overload. Short stature affected one-fifth of the cohort, disproportionately among those with Hb <8 g/dL, while serum ferritin showed a strong inverse relationship with height, reflecting iron-mediated disruption of the growth hormone–IGF-1 axis. Optimizing transfusion adequacy and chelation compliance, alongside regular growth and ferritin monitoring, is essential to minimizing growth retardation in these children.

References

1. Sadiq IZ, Abubakar FS, Usman HS, Abdullahi AD, Ibrahim B, Kastayal BS, Ibrahim M, Hassan HA. Thalassemia: Pathophysiology, diagnosis, and advances in treatment. Thalassemia Reports. 2024 Oct 15;14(4):81-102.
2. Musallam KM, Lombard L, Kistler KD, Arregui M, Gilroy KS, Chamberlain C, Zagadailov E, Ruiz K, Taher AT. Epidemiology of clinically significant forms of alpha-and beta-thalassemia: a global map of evidence and gaps. American journal of hematology. 2023 Sep;98(9):1436-51.
3. Shafique F, Ali S, Almansouri T, Van Eeden F, Shafi N, Khalid M, Khawaja S, Andleeb S, Hassan MU. Thalassemia, a human blood disorder. Brazilian Journal of Biology. 2021 Sep 3;83:e246062.
4. Xian J, Wang Y, He J, Li S, He W, Ma X, Li Q. Molecular epidemiology and hematologic characterization of thalassemia in Guangdong Province, Southern China. Clinical and Applied Thrombosis/ Hemostasis. 2022 Aug; 28:10760296221119807.
5. Thein SL. The molecular basis of β-thalassemia. Cold Spring Harbor perspectives in medicine. 2013 May 1;3(5):a011700.
6. Chatterjee R, Bajoria R. Critical appraisal of growth retardation and pubertal disturbances in thalassemia. Annals of the New York Academy of Sciences. 2010 Aug;1202(1):100-14.
7. Sposi NM. Oxidative stress and iron overload in β-thalassemia: an overview. IntechOpen; 2019 Dec 16.
8. Roussou P, Tsagarakis NJ, Kountouras D, Livadas S, Diamanti-Kandarakis E. Beta-thalassemia major and female fertility: the role of iron and iron-induced oxidative stress. Anemia. 2013;2013(1):617204.
9. Ashraf TS, De Sanctis V, Yassin M, Adel A. Growth and growth hormone-insulin like growth factor-I (GH-IGF-I) axis in chronic anemias. Acta Bio Medica: Atenei Parmensis. 2017;88(1):101.
10. Mohajeri-Tehrani M, Arab F, Salemkar S, Darvishian N, Mohseni F, Larijani B, et al. Investigating β Thalassemia patients and their growth: a brief review and our clinical experience. J Pediatr Rev 2024;12:87–94.
11. Merchant RH, Shirodkar A, Ahmed J. Evaluation of growth, puberty and endocrine dysfunctions in relation to iron overload in multi transfused Indian thalassemia patients. Indian J Pediatr 2011;78:679–83.
12. Skordis N, Kyriakou A. The multifactorial origin of growth failure in thalassaemia. Pediatr Endocrinol Rev 2011;8 Suppl 2:271–7.
13. Rathaur VK, Imran A, Pathania M. Growth pattern in thalassemic children and their correlation with serum ferritin. J Family Med Prim Care 2020;9:1166–9.
14. Jana A, Gupta D, Bhattyacharyya M, Sarkar BN. Correlation between nutritional status and clinical parameters among thalassemic patients: A study of West Bengal. Hum Biol Rev 2016;5:349–60.
15. Fadlyana E, Ma'ani F, Elizabeth M, Reniarti L. Correlation between serum ferritin level and growth disorders in children with thalassemia. Am J Clin Med Res 2017;5:31–5.
16. Moiz B, Habib A, Sawani S, Raheem A, Hasan B, Gangwani M. Anthropometric measurements in children having transfusion-dependent beta thalassemia. Hematology 2018;23:248–52.
17. Shah FT, Sayani F, Trompeter S, Drasar E, Piga A. Challenges of blood transfusions in β-thalassemia. Blood Rev 2019;37:100588.
18. Abdelrazik AM, Elshafie SM, El Said MN, Ezzat Ahmed GM, Al-Gamil AK, El Nahhas MG, et al. Study of red blood cell alloimmunization risk factors in multiply

transfused thalassemia patients: Role in improving thalassemia transfusion practice in Fayoum, Egypt. Transfusion 2016;56:2303–7.
19. Shalitin S, Carmi D, Weintrob N, Phillip M, Miskin H, Kornreich L, et al. Serum ferritin level as a predictor of impaired growth and puberty in thalassemia major patients. Eur J Haematol 2005;74:93–100.
20. Hamidah A, Arini MI, Zarina AL, Zulkifli SZ, Jamal R. Growth velocity in transfusion dependent prepubertal thalassemia patients: Results from a thalassemia center in Malaysia. Southeast Asian J Trop Med Public Health 2008;39:900–5.
21. Mohajeri-Tehrani M, Arab F, Salemkar S, Darvishian N, Mohseni F, Larijani B, et al. Investigating β Thalassemia patients and their growth: a brief review and our clinical experience. J Pediatr Rev 2024;12:87–94.
22. Pemde H, Jagdish Chandra J, Gupta D, Singh V, Sharma R, Dutta AK. Physical growth in children with transfusion-dependent thalassemia. Pediatr Health Med Ther 2011; 2:13–9.