Volume 3, Issue 7, 2025

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

GROWTH PARAMETERS IN TRANSFUSION DEPENDENT THALASSEMIA PATIENTS ON REGULAR CHELATION VS NON-CHELATION THERAPY

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DOI: https://doi.org/10.5281/zenodo.18347531

Keywords
Thalassemia major, growth failure, iron overload, chelation therapy, HAZ score, WAZ score, transfusion-dependent anemia, pediatric endocrinology, Pakistan.

Article History
Received: 15 July 2025
Accepted: 22 August 2025
Published: 02 September 2025

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Abstract

Objective: *To assess and compare growth parameters in children with transfusion-dependent thalassemia receiving regular chelation therapy versus those not receiving chelation.*

Design: *Descriptive cross-sectional study.*

Setting: *Department of Pediatrics, Dr. Akbar Niazi Teaching Hospital, Islamabad, conducted over from April 2025 to July 2025.*

Subjects: *Ninety-five children aged 5 to 12 years, diagnosed with transfusion-dependent beta-thalassemia.*

Main Outcome Measures: *Frequency of short stature, height-for-age Z (HAZ) scores, and weight-for-age Z (WAZ) scores.*

Results: *Children on regular chelation therapy demonstrated significantly better growth parameters. The frequency of short stature was lower in the chelation group compared to the non-chelation group. HAZ and WAZ scores were also significantly improved in the chelation group.*

Conclusion: *Regular iron chelation therapy is associated with improved growth outcomes in transfusion-dependent thalassemia patients, underscoring the importance of adherence to treatment.*

Introduction

Thalassemia syndromes rank among the most prevalent monogenic disorders worldwide, with beta-thalassemia major representing the most severe, transfusion-dependent form. Global estimates from the World Health Organization indicate that approximately 1.5% of the population—equivalent to 80–90 million individuals—carry the beta-thalassemia trait[1]. Each year, around 60,000 children are born with the major form of the disease, with the highest burden concentrated in the Mediterranean, South Asia, Southeast Asia, and the Middle East[2].

In high-prevalence countries such as India, Iran, and Pakistan, carrier rates range from 5% to 12%, rendering thalassemia a pressing public health concern[3]. In Pakistan, more than 100,000 patients are currently registered with thalassemia major, and approximately 5,000 new cases emerge annually—largely attributable to high rates of consanguineous marriage and inadequate premarital screening programmes[4].

Lifelong regular blood transfusion remains the cornerstone of treatment for beta-thalassemia major, maintaining hemoglobin levels and preventing the severe sequelae of anemia.[5] Yet this essential intervention carries the unavoidable consequence of progressive iron overload—a pathological accumulation in vital organs such as the liver, heart, and endocrine glands. Without effective removal, excess iron precipitates multi-organ dysfunction, including

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

liver cirrhosis, cardiomyopathy, endocrine failure, and growth retardation[6].

Effective control of iron overload relies on timely initiation and consistent administration of iron chelation therapy, typically using agents such as deferoxamine, deferasirox, or deferiprone. These drugs promote the excretion of excess iron through urinary and fecal pathways. The therapeutic success of chelation is contingent upon early commencement, appropriate dosing, and sustained adherence[7]. However, in many low- and middle-income countries, adherence remains suboptimal due to high treatment costs, adverse effects, and limited awareness, thereby compromising long-term outcomes[8].

Impaired physical growth represents one of the earliest and most visible manifestations of chronic iron overload. Children with transfusion-dependent thalassemia commonly present with short stature, delayed puberty, and reduced body mass index (BMI), consequences often linked to pituitary dysfunction, diminished insulin-like growth factor-1 (IGF-1) production, and broader metabolic disturbances[9]. International studies report the prevalence of short stature in thalassemia major to range between 30% and 65%, with the highest rates occurring in populations lacking reliable access to chelation therapy[10].

In South Asia, several studies have highlighted the association between poor compliance to chelation therapy and growth failure. A multicenter Indian study reported that 48% of transfusion-dependent thalassemia patients had height below the 3rd percentile[11]. Similarly, a study from Pakistan showed that only 51.4% of adolescents with thalassemia had good adherence to iron chelation therapy, contributing to widespread growth retardation[12].

Despite this, there remains a lack of local data comparing growth parameters between children on regular chelation therapy and those who are non-compliant or not receiving chelation at all. Such comparative data are essential to inform clinical decisions and encourage timely intervention. Therefore, this study aims to assess and compare height and weight outcomes—measured by HAZ and WAZ scores—among transfusion-dependent thalassemia patients receiving regular chelation versus those not on chelation therapy. The results aim to guide pediatricians and public health practitioners toward improving adherence and mitigating growth-related complications in thalassemia management.

Materials and Methods

Subjects and Apparatus

This was a descriptive, cross-sectional study conducted in the Pediatric Department of Dr. Akbar Niazi Teaching Hospital, Islamabad. The study included 95 children aged 5 to 12 years diagnosed with transfusion-dependent beta-thalassemia, confirmed by hemoglobin electrophoresis showing HbA <90% and HbA2 >3%. Only patients receiving at least three transfusions per month were included to ensure consistency in disease severity.

Children with irregular transfusions (<3/month), cardiomyopathy, positive hepatitis B or C serology, or previous splenectomy were excluded due to the potential influence of these factors on growth.

Data were collected using a structured and pre-tested proforma specifically developed for this study. The tool captured demographic information (age, gender, residence), clinical details (transfusion frequency and duration, chelation therapy type and adherence), socioeconomic status, and family history including consanguinity. Height was measured to the nearest 0.1 cm using a wall-mounted stadiometer with participants barefoot and positioned in the Frankfurt horizontal plane. Weight was recorded to the nearest 0.1 kg using a calibrated digital scale. Each measurement was taken twice, and the mean was used for analysis. HAZ and WAZ scores were calculated using WHO AnthroPlus software.

Study Design and Sampling

A total of 95 patients were selected using non-probability consecutive sampling during April 2025 and July 2025, following synopsis approval from CPSP.

The sample size was calculated using the WHO sample size calculator, assuming a 43.1% prevalence of short stature in transfusion-dependent thalassemia patients as reported by Pathania et al. (2020), with a 95% confidence level and a 7% margin of error. This yielded a required sample size of 95 participants.

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ISSN: (e) 3007-1607 (p) 3007-1593

Data Collection Procedure

Informed written consent was obtained from parents or guardians. The proforma recorded participant demographics (age, gender, residence), transfusion details (frequency, duration), chelation therapy information (status, chelator type, adherence level), socioeconomic classification, and family history including the presence or absence of consanguineous marriage.

Participants were divided into two groups:

- **Chelation group**: receiving regular iron chelation therapy (≥80% adherence)
- **Non-chelation group**: not receiving chelation or with poor adherence

Each child's weight and height were recorded, and HAZ/WAZ scores were computed using WHO AnthroPlus software.

Statistical Analysis

Data were entered and analyzed using SPSS version 25. Descriptive statistics (mean ± SD) were calculated for continuous variables, and categorical variables were expressed as frequencies and percentages.

Normality of the data was tested using the Shapiro-Wilk test. Independent sample t-tests were used to compare HAZ and WAZ scores between chelation and non-chelation groups. The Chi-square test was applied to assess the association between chelation status and the presence of short stature. A p-value <0.05 was considered statistically significant.

Results

A total of 95 children diagnosed with transfusion-dependent thalassemia were enrolled in the study, with a mean age of 8.92 ± 2.45 years. Among these, 52 (54.7%) were male and 43 (45.3%) were female. The children were stratified into two groups based on chelation therapy status: 55 children (57.9%) were receiving regular chelation therapy, while 40 (42.1%) were not on any chelation regimen or had irregular compliance (Refer to Figure 1).

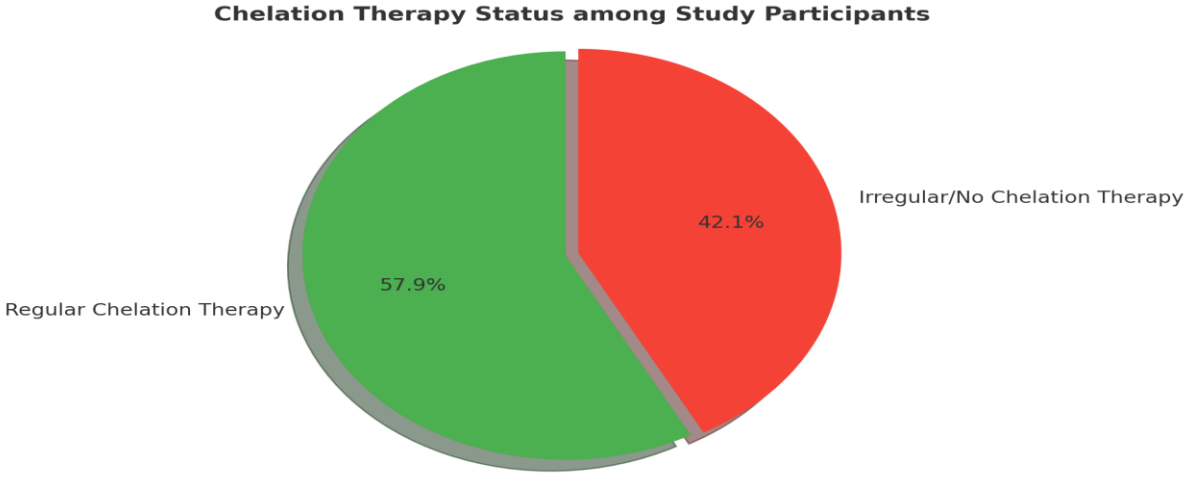

Figure 1: Chelation Therapy Statues among Study Participants (Source: Compiled by Author)

The mean height-for-age Z score (HAZ) in the chelation group was –1.27 ± 0.91, while in the non-chelation group, it was significantly lower at –2.13 ± 1.05 (p = 0.001). Similarly, the weight-for-age Z score (WAZ) was also significantly different between the two groups: children on chelation therapy had a mean WAZ score of –1.41 ± 0.94 compared to –2.31 ± 1.08 in those not receiving chelation (p = 0.002).

Short stature, defined as a height below the 3rd percentile for age and gender, was found in 11 (20%) children in the chelation group and in 17 (42.5%) of the non-chelation group. The association between chelation therapy and reduced prevalence of short stature was statistically significant (p = 0.018).

No significant differences were observed between the groups in terms of socioeconomic status (p = 0.68), gender distribution (p = 0.77), or history of consanguineous marriage (p = 0.59). However, there was a higher proportion of urban dwellers in the chelation group compared to the non-chelation group (p = 0.04), suggesting better access to healthcare services among urban patients.

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ISSN: (e) 3007-1607 (p) 3007-1593

A subgroup analysis also indicated that children with documented regular adherence to chelation (defined as ≥80% compliance) had higher HAZ and WAZ scores compared to those with poor adherence, even within the chelation group. This emphasizes the critical role of consistent chelation in mitigating iron overload complications affecting growth.

Discussion

This study demonstrates that regular iron chelation therapy has a statistically significant positive impact on growth outcomes in children with transfusion-dependent thalassemia. The results corroborate findings from international studies that associate chelation adherence with improved linear growth and body mass outcomes[6,9].

Growth failure is a well-documented consequence of iron overload in thalassemia major and can result from several endocrine and metabolic disruptions[13]. Iron deposition in the anterior pituitary gland can lead to deficiencies in growth hormone and gonadotropins, which in turn delays puberty and reduces final adult height[8]. Similarly, iron accumulation in the pancreas and liver can alter glucose metabolism and impair IGF-1 production, further hampering physical development.[14]

The prevalence of short stature observed in our non-chelation group (42.5%) aligns with previous studies conducted in similar populations. For instance, a study in North India reported that 40–50% of thalassemia patients had heights below the 3rd percentile[10], while research from Iran and the UAE found similar figures in patients with irregular chelation[11,20].

Our findings also reveal that chelation therapy not only reduces the frequency of short stature but also improves mean WAZ and HAZ scores. This suggests that chelation positively influences both skeletal growth and weight gain—likely due to improved endocrine function and reduced systemic inflammation associated with iron overload.[15] These findings are also supported by Miri-Moghaddam et al. (2020), who observed significant growth improvements in patients following consistent use of deferasirox[3].

The statistical significance of improved growth outcomes in urban dwellers may reflect disparities in healthcare access, education, and awareness between rural and urban settings. This observation is critical for healthcare policymakers, highlighting the need for targeted interventions in rural areas where chelation therapy remains underutilized.[16]

Although socioeconomic status was not a statistically significant factor in our study, other researchers have reported financial barriers as a major determinant of chelation adherence[7]. In many cases, families discontinue or delay treatment due to the high cost of iron chelators or a lack of insurance coverage.[17,19]

Furthermore, while our study excluded patients with other chronic complications such as cardiomyopathy or hepatitis, it is important to recognize that such conditions further compound growth retardation.[18] For instance, hepatitis C infection, common among multitransfused patients in under-resourced settings, can exacerbate liver dysfunction and impair nutrient metabolism[8].

Limitations of this study include its cross-sectional design, which precludes causal inference. The sample was drawn from a single tertiary care hospital, limiting generalizability to broader populations. Additionally, the assessment of chelation adherence was based on caregiver self-reporting rather than electronic tracking or serum ferritin levels, which could introduce recall bias.

Nevertheless, the clinical implications are substantial. Pediatricians should monitor growth parameters routinely as part of thalassemia management. Prompt initiation of chelation, especially before the onset of irreversible endocrine damage, can significantly improve the child's quality of life. Public health campaigns should focus on caregiver education, decentralization of chelation services, and subsidization of therapy to promote equitable access.

Future longitudinal studies are needed to track growth trajectories over time and explore additional variables such as pubertal onset, bone age, and quality-of-life indicators. Integration of digital health tools to monitor adherence could also help in objectively evaluating the impact of chelation.

In conclusion, this study confirms the hypothesis that regular chelation therapy in transfusion-dependent thalassemia patients leads to improved growth parameters. It

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ISSN: (e) 3007-1607 (p) 3007-1593

underscores the need for proactive chelation strategies, especially in developing countries, where the burden of thalassemia is high, and healthcare access is uneven.

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