

FACTORS AFFECTING ADHERENCE TO IRON CHELATION THERAPY IN THALASSEMIA MAJOR PATIENTS

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INTRODUCTION

One of the most widespread inherited hemoglobinopathies worldwide is thalassemia major, which is prevalent in South Asia and the Middle East.¹ The majority of patients with β -thalassemia cannot survive without regular blood transfusions, which in turn causes progressive iron overload. An overload of iron in important body parts like the heart, liver, and endocrine glands causes serious complications, like cardiomyopathy, liver cirrhosis, and endocrine dysfunction, posing a significant risk to morbidity and mortality.^{2,3} Iron chelation therapy is important in preventing iron overload and enhancing survival in such patients.⁴ Existing chelating agents such as Deferoxamine, Deferiprone, and Deferasirox have proven effective in lowering serum ferritin levels and iron load. Despite these treatment improvements, compliance with iron chelation therapy remains a major challenge, especially in resource-constrained settings.⁵ Non-adherence to chelation therapy has been widely reported and is associated with poor clinical outcomes, increased risk of complications, and reduced quality of life.⁶ Several factors have been implicated in poor

ABSTRACT

OBJECTIVES

This study aimed to determine the factors affecting adherence to iron chelation therapy among patients with thalassemia major.

METHODOLOGY

This is a cross-sectional analytical study conducted at a tertiary care hospital. 97 patients with 97 cases of 2 thalassemia major were recruited using a non-probability, consecutive sampling method. The structured questionnaire and medical record review were used to collect data. Compliance was classified as good, moderate, and poor. SPSS version 25 was used to analyze the data. Associations were tested using the chi-square test, and p-values of 0.05 or less were considered statistically significant.

RESULTS

The mean age of participants was 15.6 ± 7.0 years. Good adherence was observed in 46.4% of patients, while 53.6% showed suboptimal adherence. No statistically significant association was found between adherence and demographic or clinical variables ($p > 0.05$). The most common reasons for non-adherence were forgetfulness (28.8%) and painful injections (25.0%), followed by high cost of therapy (19.2%) and side effects (17.3%).

CONCLUSION

Adherence to iron chelation therapy is suboptimal among thalassemia patients and is mainly influenced by behavioral and treatment-related factors. Strategies focusing on patient education, adherence support, and simplified treatment regimens are essential to improve compliance and clinical outcomes.

KEYWORDS: Thalassemia Major, Iron Chelation Therapy, Adherence, Ferritin, Compliance, Pakistan

adherence, including complex treatment regimens, adverse drug effects, high cost of therapy, psychological factors, and lack of patient awareness. In addition, injectable therapies such as Deferoxamine are often associated with discomfort and inconvenience, further contributing to poor compliance.^{7,8} The lack of healthcare facilities, financial limitations, and insufficient patient education in low and middle-income countries such as Pakistan only exacerbate this in these countries. Even though numerous international studies have examined adherence patterns, little local information is available on the factors that specifically affect adherence in patients with thalassemia in this area. Therefore, this study was conducted to assess adherence to iron chelation therapy and identify key factors affecting compliance among patients with thalassemia major.

METHODOLOGY

This cross-sectional analytical study assessed factors affecting adherence to iron chelation therapy among patients with thalassemia major. The study was conducted at the Thalassemia Care Unit of a tertiary

care hospital over 6 months, from May 2022 to November 2022. Ethical approval for the study was obtained from the Research Evaluation Unit, College of Physicians and Surgeons Pakistan (CPSP) prior to data collection (Ref No: CPSP/REU/PED-2020-022-6040; dated May 21, 2022). Written informed consent was obtained from all participants, and in the case of pediatric patients, consent was obtained from their parents or legal guardians. Confidentiality and anonymity of patient information were strictly maintained throughout the study. The sample size for this study was calculated using the World Health Organization (WHO) formula for estimating a proportion, considering adherence to iron chelation therapy as the primary outcome variable. A confidence level of 95% was used, corresponding to a Z value of 1.96. Because adherence to iron chelation therapy varies across studies, an expected proportion (p) of 50% was assumed to ensure a maximum sample size.⁹ The margin of error (d) was set at 10%. Based on these parameters, the calculated sample size was 96 participants. To ensure adequacy and account for potential data inconsistencies, 97 patients were included in the study. The sampling method used was a non-probability, consecutive sampling method, in which patients who presented to the thalassemia center during the study period were recruited. The patients were eligible if they were 4 years of age or older, had a confirmed diagnosis of β -thalassemia major, had been on iron chelation treatment for at least 6 months, and were willing to take part in the study. Patients with other hemoglobinopathies not under chelation therapy, with severe comorbid conditions that may hinder adherence assessment, and with incomplete medical records were excluded. A structured, pre-tested questionnaire was used to collect data, and medical records were reviewed. Demographic variables (age, gender, residence, socioeconomic status), clinical (duration of disease, frequency of blood transfusions, serum ferritin levels), and treatment-related variables (type and duration of chelation therapy) were collected in the questionnaire. The adherence to iron chelation therapy was evaluated using patient responses and classified as good, moderate, or poor. Other factors such as side effects, level of knowledge, and non-adherence causes were also recorded. Face-to-face interviews were conducted during regular hospital visits to collect the data. Hospital records and clinical data, such as serum ferritin levels and treatment history, were confirmed to achieve accuracy and reduce recall bias. The questionnaire was pre-tested by hematology and medical education experts to ensure validity. A pilot study comprising about 10% of the sample was conducted to assess the instrument's clarity, feasibility, and reliability, and required changes were made. IBM

SPSS Statistics version 25 was used to enter the data and analyze it. The mean and standard deviation of quantitative variables, such as age and serum ferritin levels, were provided; the mean and percentage frequencies of qualitative variables were provided. The chi-square test was used to determine the relationship between adherence and independent variables, including gender, socioeconomic status, type of chelation therapy, side effects, and level of knowledge. Cramer's V was used to determine the strength of association. A p-value ≤ 0.05 was considered statistically significant.

RESULTS

A total of 97 patients with thalassemia major were included in the study. The mean age of participants was 15.6 ± 7.0 years (range: 4-28 years). The majority of patients belonged to the 10–18 years age group (40.2%), followed by >18 years (36.1%) and <10 years (23.7%). A slight female predominance was observed (56.7%). Most participants were from urban areas (51.5%), while 45.4% had low socioeconomic status, indicating a considerable burden on lower-income groups. The clinical profile showed that most patients had a longer disease duration, with 36.1% each in the 5-10 years and >10 years categories. A majority of patients (72.2%) required ≥ 2 blood transfusions per month, indicating severe disease burden. Regarding treatment, Deferiprone (40.2%) and Deferoxamine (38.1%) were more commonly used compared to Deferasirox (21.6%). Slightly more than half of the patients (53.6%) had been on chelation therapy for less than 2 years. The mean serum ferritin level was 3343.8 ± 1053.0 ng/mL (range: 1604-4984 ng/mL), reflecting significant iron overload among the study population. Assessment of adherence to iron chelation therapy showed that fewer than half of patients demonstrated optimal adherence. A total of 46.4% of patients showed good adherence, while 26.8% each had moderate and poor adherence. Overall, 53.6% of patients exhibited suboptimal adherence (moderate + poor), indicating a significant gap in effective disease management. The relationship between demographic and clinical factors and adherence to iron chelation therapy was evaluated with the Chi-square test. No significant association was found between adherence and gender, socioeconomic status, type of chelation therapy, side effects, or knowledge level ($p > 0.05$). Effect sizes were weak because the variables were associated with small effect sizes. Among patients with suboptimal adherence (moderate and poor), the most common reason for non-adherence was forgetfulness (28.8%), followed by painful injections (25.0%). Other important contributing factors included high cost of therapy

(19.2%) and side effects (17.3%), while lack of awareness (9.6%) was the least reported reason.

Table 1: Demographic Characteristics of Participants (n = 97)

Variable	Category	Frequency (%)
Age (years)	-	15.6 ± 7.0 (4-28)
Age Group	<10 years	23 (23.7%)
	10-18 years	39 (40.2%)
	>18 years	35 (36.1%)
Gender	Male	42 (43.3%)
	Female	55 (56.7%)
Residence	Urban	50 (51.5%)
	Rural	47 (48.5%)
Socioeconomic Status	Low	44 (45.4%)
	Middle	31 (32.0%)
	High	22 (22.7%)

Table 2: Clinical and Treatment Characteristics (n = 97)

Variable	Category	Frequency (%)
Duration of Disease	<5 years	27 (27.8%)
	5-10 years	35 (36.1%)
	>10 years	35 (36.1%)
Blood Transfusion Frequency	<2/month	27 (27.8%)
	≥2/month	70 (72.2%)
Type of Chelation Therapy	Deferasirox	21 (21.6%)
	Deferiprone	39 (40.2%)
	Deferoxamine	37 (38.1%)
Duration of Chelation Therapy	<2 years	52 (53.6%)
	≥2 years	45 (46.4%)
Serum Ferritin (ng/mL)	-	3343.8 ± 1053.0(1604-4984)

Table 3: Adherence to Iron Chelation Therapy (n = 97)

Adherence Level	Frequency (%)
Good Adherence	45 (46.4%)
Moderate Adherence	26 (26.8%)
Poor Adherence	26 (26.8%)

Table 4: Association of Factors with Adherence to Iron Chelation Therapy (n = 97)

Variable	Category	Good n (%)	Moderate n (%)	Poor n (%)	χ ² value	p-value	Cramer's V
Gender	Male	22(52.4%)	07(16.7%)	13(31.0%)	3.888	0.143	0.20
	Female	23(41.8%)	19(34.5%)	13(23.6%)			
Socioeconomic Status	High	11(50.0%)	08(36.4%)	03(13.6%)	3.774	0.438	0.14
	Low	20(45.5%)	12(27.3%)	12(27.3%)			
	Middle	14(45.2%)	06(19.4%)	11(35.5%)			
Type of Chelation Therapy	Deferasirox	11(52.4%)	04(19.0%)	06(28.6%)	2.623	0.623	0.12
	Deferiprone	20(51.3%)	09(23.1%)	10(25.6%)			
	Deferoxamine	14(37.8%)	13(35.1%)	10(27.0%)			
Side Effects	Present	19(51.4%)	08(21.6%)	10(27.0%)	0.918	0.632	0.09
	Absent	26(43.3%)	18(30.0%)	16(26.7%)			
Knowledge Level	Good	19(47.5%)	10(25.0%)	11(27.5%)	0.113	0.945	0.03
	Poor	26(45.6%)	16(28.1%)	15(26.3%)			

Table 5: Reasons for Non-Adherence (n = 52)

Reason	Frequency (%)
Forgetfulness	15 (28.8%)
Painful injections	13 (25.0%)
High cost of therapy	10 (19.2%)
Side effects	09 (17.3%)
Lack of awareness	05 (9.6%)

DISCUSSION

The present study evaluated adherence to iron chelation therapy among patients with thalassemia major and identified factors influencing compliance. The findings revealed that only 46.4% of patients demonstrated good adherence, while 53.6% exhibited suboptimal adherence, highlighting a significant gap in effective disease management. These findings are consistent with recent international literature, which indicates that adherence rates among thalassemia patients remain suboptimal, typically ranging from 40–60% depending on healthcare access and treatment modalities.^{10,11} The study's demographic profile was dominated by adolescents (10-18 years), a crucial age group for adherence issues. The results of the studies by Musallam et al. (2025) and Lee Wan et al. (2023) demonstrated that adolescents tend to be less adherent to treatment due to psychosocial factors, caregiver treatment fatigue, and reliance.^{12,13} Similarly, the slight female predominance observed in this study aligns with regional data; however, no significant association between gender and adherence was found, which is

consistent with findings from a multicenter study conducted in the Middle East.¹⁴ The clinical characteristics revealed that a large proportion of patients required frequent transfusions (≥ 2 /month) and had elevated serum ferritin levels, indicating significant iron overload. Despite this, adherence remained suboptimal. This paradox has also been reported in recent studies, suggesting that even patients with severe disease burden fail to adhere adequately to therapy.¹⁵ The mean ferritin level in this study (3343.8 ng/mL) is comparable to that reported in a Pakistani study by Khan et al. (2022), in which poor adherence was associated with greater iron overload.¹⁶ In terms of treatment modalities, Deferiprone and Deferoxamine were more common than Deferasirox. Even though oral chelators such as Deferasirox are often associated with higher adherence due to their ease of use, this study failed to show a statistically significant relationship between chelation therapy type and adherence. Reddy et al. (2022) have reported similar findings, indicating that it depends on factors beyond the type of drug, including patient behavior and socioeconomic limitations.¹⁷ Notably, there were no statistically significant differences in adherence with gender, socioeconomic status, side effects, or level of knowledge. Even though socioeconomic status could be regarded as a key determinant of adherence, the non-significant correlation in this study might be explained by the fact that financial constraints were relatively homogenous among the study population. Lee et al. (2024) also found weak correlations between socioeconomic variables and compliance, highlighting the multifactorial nature of compliance behavior.¹⁷ The most fatal results of this research are associated with the causes of non-adherence, with forgetfulness (28.8) and painful injections (25.0) as the most common ones. Recent literature provides strong support for these findings. Forgetfulness was cited by Locke et al. (2022) in a systematic review as one of the most frequent barriers to adherence, especially in pediatric and adolescent populations.¹⁰ Similarly, pain linked to injectable medications, namely Deferoxamine, has been recurrently cited as a significant discouraging factor.¹⁸ The barriers represented by the cost of therapy (19.2%) indicate the difficulties in the low- and middle-income countries such as Pakistan. South Asian research has also emphasized that financial strain has a major impact on long-term adherence to treatment, particularly in chronic illnesses that require lifelong treatment (19,20). Even though the least reported factor in this study was lack of awareness, its presence still suggests the need to establish structured patient education programs. Overall, the results of this research support the idea that the behavioral and treatment-related factors contribute more to adherence to iron chelation therapy than the

demographic or clinical variables. The lack of robust statistical correlations indicates that treatment adherence is a multifactorial and complex problem that needs extensive interventions such as patient counseling, simplified treatment regimens, and psychosocial support.

LIMITATIONS

This study has several limitations. First, it was conducted at a single tertiary care center with a relatively small sample size, which may limit the generalizability of the findings to the broader thalassemia population. Second, the cross-sectional design prevents establishing causal relationships between identified factors and adherence to iron chelation therapy. Third, adherence was assessed primarily through self-reported responses, making the results susceptible to recall and social desirability bias. Finally, psychosocial factors such as caregiver support, mental health status, and health literacy were not explored in detail and may have influenced adherence behaviors.

CONCLUSIONS

Adherence to iron chelation therapy among patients with thalassemia major was found to be suboptimal, with more than half of the patients demonstrating moderate to poor adherence. The study highlights that adherence is primarily influenced by behavioral and treatment-related factors rather than demographic or clinical characteristics. Forgetfulness and painful administration methods emerged as the leading barriers, followed by financial constraints and treatment-related side effects. These findings emphasize the need for targeted interventions, including patient education, adherence support strategies, and the promotion of more convenient treatment options, to improve long-term compliance and reduce complications associated with iron overload.

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AUTHORS CONTRIBUTION

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The authors accept responsibility for all aspects of the work and will ensure that any concerns regarding the accuracy or integrity of any part are properly investigated and resolved.



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