

KNOWLEDGE AND PRACTICES OF PEDIATRICIANS ABOUT CHELATION THERAPY IN TRANSFUSION-DEPENDENT THALASSEMIA MAJOR

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ABSTRACT

Objective: To evaluate the knowledge regarding chelation therapy among pediatricians treating transfusion-dependent thalassemia major children and to improve treatment strategies in order to better manage this disorder.

Study Design: A Cross-Sectional Study

Place and Duration of Study: The study was conducted at the Department of Pediatrics, Bolan Medical College/Hospital, located in Quetta, Pakistan. The data collection took place over a period of six months From December 2023 To May 2024.

Methods: 94 participants at Department of Pediatrics Bolan Medical Complex Hospital Quetta. Baluchistan. The data was collected by a structured questionnaire which included three major sections including sociodemographic characteristics, knowledge and practices. Scores were ranged poor (0–4), fair (5–8), and satisfactory (9–12). Data were analyzed with SPSS version 24. Normality was tested by Shapiro–Wilk test and we used chi-square or Fisher’s exact test to examine associations with significance set at $p < 0.05$.

Results: The means±s.d.m of knowledge score was 7.8 ± 2.2 and satisfactory knowledge was found in 16.3%. Years of experience and the association with the knowledge scores had significant associations $p = 0.03$. Practices differed considerably, with 82.7% of practices preferring combination therapy.

Conclusions: There is high variability in pediatricians’ knowledge and practice about chelation therapy in TDT. Though some showed sufficient understanding, many lacked important knowledge. There is a need for more rigorous adherence to guidelines and training sessions to improve the competency of pediatricians in the management of TDT. This will promote compliance, decrease side effects, and provide better outcomes.

Keywords: Thalassemia, chelation therapy, pediatricians, knowledge

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INTRODUCTION

Beta-thalassemia is a group of inherited blood disorders caused by impaired hemoglobin synthesis that is a major global health burden. It is most common in areas of high consanguinity like Pakistan, where an estimated 5,000 to 9,000 infants are born each year with transfusion-dependent thalassemia major (TDT) (1, 2). TDT is the most severe disease type, and those individuals require regularly blood transfusions every month to survive for life. While this has allowed for the treatment of sickle cell disease, the repeated blood transfusions can result in iron overload, requiring iron chelation therapy to avoid complications including cardiac and hepatic dysfunction (3). Chelation therapy is a treatment that tries to achieve this balance between iron accumulation and iron excretion as a result of repeated blood transfusions. The available chelators are desferrioxamine, deferiprone, and deferasirox, either alone or in combination (4). Various guidelines, including those published by the Thalassemia International Federation (TIF), stress the rational use of chelation therapy, including when, how much and how to monitor. Although there are guidelines advocating the implementation, adherence remains suboptimal, and the impact of therapy is largely driven by provider knowledge, attitude and practice (KAP). Previous studies in similar settings have similarly found that gaps exist in pediatricians' knowledge and practice of chelation therapy. For example, in a multicenter study conducted in Rawalpindi, the satisfactory knowledge about chelation therapy was found in only 16.3% of the pediatricians (7). Management of iron overload, which requires proper knowledge of iron metabolism, is important not only to prevent and/or treat the early and late effects of iron overload but also to avoid adverse effects from either excessive or inappropriate chelation (8). Moreover, adherence to treatment regimens, particularly in pediatric patients, continues to update as a major challenge that requires appropriate counseling and monitoring by healthcare professionals (9). Pediatricians play a key role in the management of TDT, emphasising the need to assess their knowledge and practices. The objective of the study was to assess the KAP regarding chelation therapy in children with TDT among pediatricians. This research aims to identify gaps

in these areas and help devise focused training and awareness that can improve patient outcomes (10).

METHODOLOGY

Study Design and Setting:

A hospital-based cross-sectional study was conducted in the Department of Diagnostic Radiology, Bolan Medical Complex Hospital, Quetta, over six months from January to June 2023.

Study Population:

The study included 94 patients with suspected bladder carcinoma based on clinical presentation or initial imaging, all of whom underwent contrast-enhanced CT scans followed by histopathological confirmation via TURBT. Pediatric residents (at least 6 months of training) and consultants working in tertiary care hospitals. Pediatricians who chose not to participate were excluded. Data were gathered with a questionnaire regarding knowledge (12 questions) and practices (4 questions) towards chelation therapy. Knowledge scores were classified as poor (0–4), fair (5–8) and satisfactory (9–12), whereas practices were analyzed descriptively.

Ethical Approval Statement .

The College of Physicians and Surgeons Pakistan (CPSP) Research and Ethical Unit (**Approval No. CPSP/REU/PAD/-2021-001-6664**) granted Ethical approval to this research under the authorship of Muhammad Hanif.

Inclusion Criteria

- Pediatric residents with at least six months of training.
- Pediatric consultants continuing their work in tertiary care medical facilities.
- Pediatricians who treat patients with transfusion-dependent thalassemia major join actively in their health management.

Exclusion Criteria

- Pediatricians who declined to participate.
- The research excludes pediatricians who do not take care of patients with transfusion-dependent thalassemia major.

DATA COLLECTION

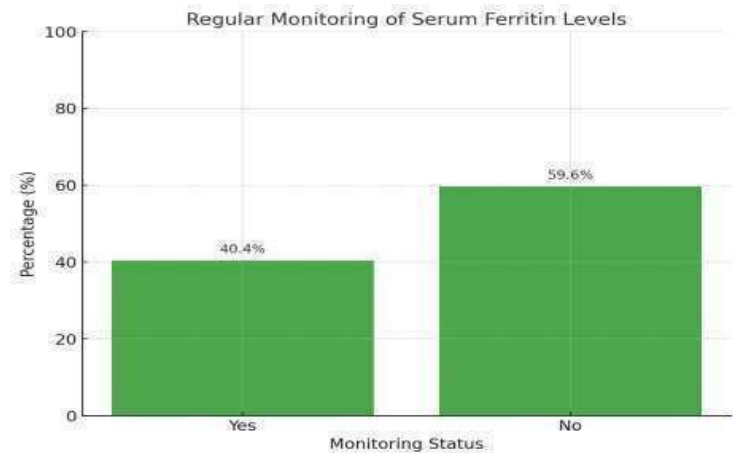
The questionnaire was prepared with 3 sections, one regarding demographic data, the second pertaining to knowledge-based questions and the third concerning practice-based questions. Before contacting participants, permission were obtained from heads of departments.

STATISTICAL ANALYSIS

Statistical analysis was conducted using SPSS 24.0. Descriptive analysis was performed with quantitative variables expressed as means and standard deviations and qualitative variables; as frequencies and percentages. Crosstab analyses were performed to evaluate associations between variables using Chi-square or Fisher’s exact test, with $p < 0.05$ regarded as statistically significant.

RESULTS

94 pediatricians participated (62% were residents and 38% were consultants). The mean knowledge score was 7.8 ± 2.17 , of which 16.3% had satisfactory knowledge, 61.2% fair, and 22.4% poor. Pediatricians with more than 5 years of experience outperformed significantly their junior counterparts $p = 0.03$. For practices, 82.7% preferred combination therapy, and the most used combination was desferrioxamine and deferasirox. Oral chelators were preferred instead of parenteral therapy due mainly to ease (65%) and better compliance (20%) with therapy. However, only 40% of the physicians reported that they monitor serum ferritin levels regularly, which is an important part of effective chelation therapy. Statistical analysis showed a significant association between the years of practice and preferred treatment choices in favor of combination therapy ($p = 0.04$).



Although recommendations are available, only 50% of the participants were aware of the Thalassemia Federation of Pakistan recommendations. Such substantial gaps in knowledge and practice that impact patient outcomes must be addressed. The study included 94 pediatricians, with a fairly balanced gender distribution: 47.9% (45) were male and 52.1% (49) were female. Regarding their professional status, 61.2% (58) were residents and 38.8% (36) were consultants. In terms of years of experience, 41.5% (39) of the pediatricians had ≤ 5 years of experience, while 58.5% (55) had more than 5 years of experience. This distribution provides insights into the experience levels and professional roles of pediatricians, which may influence their knowledge and practices related to the study topic.

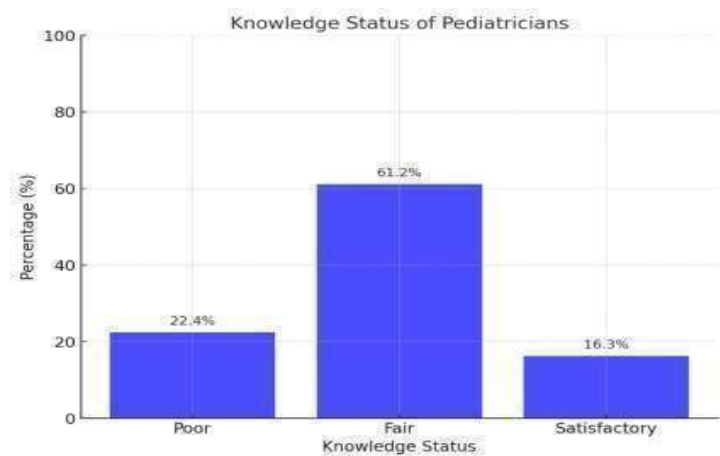


Table 1: Demographic Information of Participants

Variable	Category	Frequency (n)	Percentage (%)
Gender	Male	45	47.9%
	Female	49	52.1%
Status of Pediatrician	Resident	58	61.2%
	Consultant	36	38.8%
Experience (Years)	≤ 5	39	41.5%
	> 5	55	58.5%

The knowledge status of the pediatricians in the study was distributed as follows: 22.4% (21) had poor knowledge, scoring between 0-4; 61.2% (58) had fair knowledge, with scores between 5-8; and 16.3% (15) had satisfactory knowledge, scoring between 9-12. This suggests that the majority of pediatricians have a fair level of knowledge on the subject, while a smaller proportion have either poor or satisfactory knowledge, indicating potential areas for improvement in education or training regarding the topic.

Table 2: Knowledge Scores of Pediatricians

Knowledge Status	Frequency (n)	Percentage (%)
Poor (0-4)	21	22.4%
Fair (5-8)	58	61.2%
Satisfactory (9-12)	15	16.3%

The distribution of chelation drug use among pediatricians in the study was as follows: 23.4% (22) of pediatricians reported using desferrioxamine, 42.6% (40) used deferasirox, 14.9% (14) used deferiprone, and 19.1% (18) utilized combination therapy. This indicates that deferasirox was the most commonly used chelation drug, followed by desferrioxamine, while combination therapy and deferiprone were used less frequently. The variation in drug choices may reflect individual preferences, treatment protocols, or patient-specific factors influencing the choice of chelation therapy.

Table 3: Preferred Chelation Therapy Drug

Chelation Drug	Frequency (n)	Percentage (%)
Desferrioxamine	22	23.4%
Deferasirox	40	42.6%
Deferiprone	14	14.9%
Combination Therapy	18	19.1%

In the study, 40.4% (38) of pediatricians reported monitoring their patients while on chelation therapy, whereas 59.6% (56) did not engage in regular monitoring. This suggests that a majority of pediatricians may not be consistently monitoring patients during chelation therapy, highlighting potential gaps in clinical practice or a need for improved guidelines on patient monitoring during treatment.

Table 4: Regular Monitoring of Serum Ferritin Levels

Monitoring	Frequency (n)	Percentage (%)
Yes	38	40.4%
No	56	59.6%

DISCUSSION:

While the results of this study on awareness and practice of pediatricians about chelation therapy in TDT patients are concordant with many previous studies, they have shown significant area of concern. Despite the fair knowledge shown by the pediatricians (61.2%), and the high percentage of preference for combination therapy (82.7%), the gaps in reaching guideline adherence as well as in monitoring of therapy suggest that current practice requires further attention. Our knowledge scores indicate that only 16.3% of pediatricians implemented sufficient knowledge of chelation therapy. This is in accordance with a study done by Fakih et al. majority of pediatricians showed poor knowledge about iron chelation therapy in TDT children as reported in 2022 (11). Another study by Riaz et al. Healthcare professionals, especially in developing countries like Pakistan, are not well aware of the details of chelation process (12). These results imply that despite expectations that Substantial improvements have been made in recent years, many pediatricians remain unaware of current chelation protocols, including optimal dosing, drug interactions and monitoring. In contrast, more than two-thirds of adult participants (68.8%) preferred monotherapy while a higher proportion of pediatricians (82.7%) preferred combination therapy, particularly with desferrioxamine and deferasirox. This is in keeping with other studies, such as those by Shander et al. Monotherapy reached also, as reported in Giardina & Forget (2008) and in Rougier et al. (2009), rates of balance that were more suboptimal and associated with higher effects by pharmaceutical agents (13, 14). Combination therapy regimens, particularly tailored to the requirements of the individual patient, reduce the risk of iron load- associated complications (eg, cardiac and hepatic dysfunction). Nevertheless, the concern is that only 40.4% of pediatricians said they monitored serum ferritin levels regularly, though combination therapy

was favored. Monitoring for efficacy is critical to avoid both under-treatment and over-treatment, in terms of iron removal during chelation therapy (15). In our study, a dramatic 59.6% of pediatricians do not follow a regular schedule for monitoring ferritin levels. This result aligns with El Beshlawy (2005) who reported that although chelation therapy is commonly utilized, routine monitoring of ferritin level is frequently overlooked due to logistical and resource limitations (16). It is essential to monitor ferritin levels, as iron overload can occur if there is a lack of effective chelation therapy and lead to irreversible damage to vital organs." Moreover, the poor adherence to guidelines found in our study also aligns with evidence from Dahlui et al. (2009), despite the existence of iron chelation guidelines, as they are poorly applied in practice due to knowledge gaps and infrastructure issues (17). In addition to this, the fact that only 50% of the pediatricians are aware of the guidelines made by the Thalassaemia International Federation conveys a higher aspect of awareness needed for understanding the purpose of the guidelines and spreading them to even higher medical professionals. Ansari et al. described a similar lack of familiarity with newly updated guidelines. (2011) stressed that education and training programs need to remain active to help care providers stay informed as best practices evolve (18). This study shows the dire need for educational campaigns to fill gaps in TDT knowledge and chelation therapy practices among pediatricians. Though combination therapy provides some indication of comfort with more advanced treatment protocols, the disconnect with monitoring and the failure to follow underlying guidelines demonstrate the need for further training. Increased awareness of the importance and necessity of regular monitoring along with the application of updated guidelines and the latest research in chelation therapy through programs targeted towards this issue could greatly improve clinical outcomes in TDT patients.

Finding of our study There is a fair level of knowledge on chelation therapy among our pediatricians, but important gaps remain in terms of the adherence to published consensus and guideline and the routine monitoring of therapy. Moreover, closing these gaps with continuing medical education and enhanced access to resources could translate to better management of TDT and improved patients outcomes(19).

CONCLUSION

Our study reported on the knowledge and practice gaps of pediatricians in terms of the chelation therapy for TDT patients which need to be addressed. Although many pediatricians are knowledgeable and prefer combination therapy, finding scared of obtaining numbers regularly or prescribing therapy according to the guidelines show that there is room to improve education needs as well as clinical practice. Further improvements in education regarding chelation therapy protocols should ultimately lead to better patient care by decreasing the risk of complications associated with iron overload.

LIMITATIONS

We conducted this study at a single hospital, and thus, these findings may not be applicable to other regions or healthcare settings. Vulnerabilities to selection bias are embedded in the convenience sample and self-reported nature of the data also would contribute to the skew of correct information of practices and knowledge.

FUTURE FINDINGS

Future research should examine the deterrents to guideline compliance as well as follow-up practices, mainly in under-resourced settings. Future work exploring the effect of enhanced training on knowledge of pediatricians and outcomes of patients would be informed by longitudinal studies. As a result, these observations would be more broadly generalizable and accompanied with the

knowledge of thresholds on which to base intervention implementation by expanding the study to include multiple centers.

ABBREVIATIONS

1. **TDT** – Transfusion-Dependent Thalassemia Major
2. **KAP** – Knowledge, Attitude, and Practices
3. **SPSS** – Statistical Package for the Social Sciences
4. **CVD** – Cardiovascular Disease
5. **HF** – Hepatic Failure
6. **TIF** – Thalassemia International Federation
7. **FDA** – Food and Drug Administration
8. **IQR** – Interquartile Range
9. **FBC** – Full Blood Count
10. **BMC** – Bolan Medical College
11. **SER** – Serum Ferritin Levels
12. χ^2 – Chi-Square Test
13. **SD** – Standard Deviation
14. **DF** – Degree of Freedom
15. **WHO** – World Health Organization

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AUTHOR CONTRIBUTIONS

MH: Conceptualization, study design, and manuscript drafting.

S: Data collection, methodology development, and critical revisions.

NH: Statistical analysis, data interpretation, and manuscript editing.

ANA: Literature review, validation, and quality assurance.

HUR: Data acquisition, manuscript formatting, and final manuscript approval.

MM: Final manuscript revisions, supervision, and overall coordination.

All authors have reviewed and approved the final version of the manuscript.

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