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Knowledge, Attitude, and Practice of Young Paediatricians About Chelation Therapyin Transfusion-Dependent Thalassemia Major Children

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ABSTRACT

Objective: To determine the knowledge, attitude, and practice of young paediatricians about chelation therapy in transfusion-dependent thalassemia major children.

Study Design: KAP survey

Place and Duration of Study: Six different hospitals in Rawalpindi and Islamabad Pakistan, from Jul 2019 to Jan 2020.

Methodology: We study enrolled a sample of 98 doctors. The study included all residents (R1, R2, R3, and R4) and senior registrars of the six hospitals, while those on leave for any reason like maternity or others were excluded. A pre-validated questionnaire was used to collect the data.

Results: Out of 98, maximum residents were of third-year (R3) 27(27.6%), followed by the second-year resident (R2) and senior registrar (SR) 19(19.4%). About 52(53.1%) residents reported that they did not have any thalassemia centre in their facility, with a maximum from Rawalpindi 65(66.3%). The study revealed that 61.2% study population had fair knowledge and attitude towards chelation therapy, while 22(22.4%) had poor and 16(16.3%) had satisfactory scores. The study revealed varied practices except for combination therapy, where 82.7% preferred it. The study showed a significant association between different categories of knowledge and attitude with professional levels, (p-value = 0.014).

***Conclusion*:** The majority had a fair knowledge and attitude towards chelation therapy, while the practice varies mostly, except for the maximum preferred combination therapy for chelation. The study further concluded that with an increase in professional experience, knowledge, attitude and practice improved towards better treatment.

Keywords: Blood transfusion, Chelation therapy, Iron overload, Thalassemia.

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INTRODUCTION

Beta thalassemia is at the top of the list of associated genetic disorders for haemoglobin synthesis in terms of prevalence.[1,2] In Pakistan, it is estimated that an average of 5000-9000 children with β-thalassemia are born per year with 5-7% of the carrier proportion.[3] Intensive iron chelation therapy is a crucial part of managing such children.[4]

Literature from recent studies revealed that the optimum use of chelation therapy reduces complications related to iron overload, and for which doctors dealing with such children must have sound knowledge, attitude, and practising experience.[5-7] According to guidelines for the Management of Transfusion Dependent Thalassaemia (TDT),[8] the chelation therapy aims to balance the accumulation of iron (accumulated due to continuous blood transfusion) by increasing the excretion of the iron through urine and faeces with the help of chelators. As per the guidelines, the key target of chelation therapy is to balance the benefits of coping with iron overload and the detriment of the harmful effects of excessive use of chelation therapy. Many knowledge-based aspects are addressed in the guidelines appropriately, like dosage, drug used (alone or in combination), monitoring, and clinical diagnosis.[9] These guidelines must be available in all Thalassemia centres/clinics. All doctors related to such paediatric setups must ensure their practicality while dealing with such patients and address a major challenge in chelation therapy which aims to achieve regular adherence to treatment regimens throughout a lifetime. Evidence reveals that the stage of initiating iron chelation therapy is supposed to be a key factor in their survival.[10]

Adequate knowledge of chelation therapy can help maintain a "safe" iron status at all times in children on a regular transfusion regime and minimize the effects of iron overload while optimising their growth and development. Keeping in view this study aimed to determine the knowledge, attitude, and practice of young Paediatricians about chelation therapy in transfusion-dependent thalassemia major children.

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METHODOLOGY

This KAP survey was conducted after ethical approval (vide No: A/28/PEHH/19/EC/05, dated 10/06/2019) from the Ethical Committee of Pak Emirates, Military Hospital, Rawalpindi Pakistan. The study was conducted in six different hospitals of Rawalpindi and Islamabad after taking all administrations on board, namely: 1) Military Hospital, 2) Fauji Foundation Hospital, 3) Railway Hospital, 4) Shifa International Hospital, 5) Pakistan Institute of Medical Sciences, and 6) Benazir Bhutto Hospital Rawalpindi Pakistan, from July 2019 to January 2020. The population of young paediatricians from all six hospitals was 132 (residents plus senior registrar). A sample of 98 was calculated and enrolled based on the formula (CI=95%, p=0.5%, e=0.05, n= 132).[11]

Inclusion Criteria: The study included all paediatric residents (R1, R2, R3, and R4) and senior registrars.

Exclusion Criteria: Doctors who were on leave for any reason were excluded from the study.

A questionnaire with 16 questions based proforma was designed with the field's experts, including,[12] choosing the best answer-based questions for knowledge and attitude and four practice-based questions. The proforma was piloted among 20 different paediatricians, and an internal consistency of >0.70 (Cronbach's Alpha) was recorded for the research tool.[12] After taking informed written consent, a prevalidated questionnaire including demographics was self-administrated among the sample population based on proportionate consecutive sampling. For interpretation, four questions of practices were reported,[12] questions for knowledge and attitude were categorized into three strata:1) Poor Status (Score 0-4), 2) Fair Status (Score 5-8), and 3) Satisfactory Status (Score 9-12).[13]

Statistical Package for Social Sciences (SPSS) version 25:00 was used for the data analysis. Quantitative variables were summarized as Mean±SD and qualitative variables were summarized as frequency and percentages. Chi-square test was applied to find out the association. The p-value lower than or up to 0.05 was considered as significant.

RESULTS

The study was conducted on 98 residents and senior registrars regarding chelation therapy in transfusion-dependent thalassemia major children. The study revealed that the maximum study participants were residents of year three (R3) 27(27.6%), followed by residents of year two (R2) and senior registrar. About 46(46.9%) respondents reported that their facility had Thalassemia Center, while 52(53.1%) had no such centre.

In this study, 65(66.3%) respondents from six different hospitals belonged to Rawalpindi, while the remaining 33(33.7%) belonged to Islamabad. The study revealed that 60(61.2%) of the study population had fair knowledge and attitude towards chelation therapy, while 22(22.4%) had poor and 16(16.3%) had satisfactory scores. Relevant answers as per knowledge and attitude were shown in the Table-I.

Table-I: Knowledge and Attitude of Study Population (n=98)

Knowledge and Attitude Related Questions:	Incorrect	Correct
The starting point of chelation?	69(70.4%)	29(29.6%)
What is the goal of chelation therapy (ferritin levels)?	62(63.3%)	36(36.7%)
Are you checking ferritin levels?	59(60.2%)	39(39.8%)
Dose of Desferrioxamine?	41(41.8%)	57(58.2%)
Dose of Deferasirox?	60(61.2%)	38(38.8%)
Dose of Deferiprone?	60(61.2%)	38(38.8%)
Why combination therapy?	38(38.8%)	60(61.2%)
Ferritin levels as the cutoff to start combination therapy?	27(27.6%)	71(72.4%)
Side effects of Desferrioxamine?	38(38.8%)	60(61.2%)
Side effects of Deferasirox?	30(30.6%)	68(69.4%)
Side effects of Deferiprone?	37(37.8%)	61(62.2%)
Guidelines of Iron Chelation Therapy by Thalassemia Federation of Pakistan (Awareness)?	46(46.9%)	52(53.1%)

The practices of the study participants with respect to the professional level were shown in the Table-II. The stratification of knowledge and attitude categories with professional, Thalassemia centre and city were shown in the Table-III.

DISCUSSION

Our study revealed that the maximum of the study population had a fair bit of knowledge and attitude towards this therapy. The practice varies among different professional levels except for the choice of therapy where the maximum favoured combination therapy. Furthermore, the study showed that the senior registrar, the most experienced in the study population, had the maximum number of participants with satisfactory scores.

Chelation therapy is an important pillar in managing Thalassemia. For major children dependent

Table-II: Practice in the Study Population for Chelation Therapy (Professional Level Wise) (n=98)

Questions	Options	R1(n=16)	R2(n=19)	R3(n=27)	R4(n=17)	SR(n=19)
Which chelation drug you use as the first line for iron overload?	Desferrioxamine	3(18.8%)	9(47.4%)	16(59.3%)	10(58.8%)	9(47.4%)
	Deferasirox	12(75%)	9(47.4%)	10(37%)	7(41.2%)	10(52.6%)
	Deferiprone	1(6.2%)	1(5.2%)	1(3.7%)	0	9(47.4%)
What is the reason you justify using oral chelator over parenteral chelator?	Better Chelation among two	5(31.3%)	0	1(3.7%)	0	2(10.5%)
	Ease of Use	7(43.8%)	9(47.4%)	12(44.4%)	9(52.9%)	12(63.2%)
	Patient's Compliance	3(18.8%)	6(31.6%)	13(48.1%)	8(47.1%)	4(21.1%)
	Non Availability of infusion pump	1(6.3%)	4(21.1%)	1(3.7%)	0	1(5.3%)
Do you practice combination therapy?	Yes	12(75%)	14(73.7%)	23(85.2%)	16(94.1%)	16(82.7%)
	No	4(25%)	5(26.3%)	4(14.8%)	1(5.9%)	3(15.8%)
What combination therapy do you prefer?	Desferrioxamine +Deferasirox	11(68.8%)	13(68.4%)	19(70.4%)	15(88.2%)	12(63.2%)
	Desferrioxaine +Deferiprone	3(18.8%)	5(26.3%)	7(25.9%)	2(11.8%)	6(31.6%)
	Deferasirox +Deferiprone	2(12.5%)	1(5.3%)	1(3.7%)	0	1(5.3%)

Table-III: Knowledge and Attitude Categories with Professional Level, Thalassemia Center, and City of the Study (n=98)

Variables		Knowledge & Attitude			*p*-value
		Poor n(%)	Fair n(%)	Satisfac-tory n(%)	
Professional Level	R1 (n=16)	6 (37.5%)	8 (50.0%)	2 (12.5%)	0.014
	R2 (n=19)	5 (26.3%)	13 (68.4%)	1 (5.3%)	
	R3 (n=27)	5 (18.5%)	20 (74.1%)	2 (7.4%)	
	R4 (n=17)	2 (11.8%)	13 (76.5%)	2 (11.8%)	
	SR (n=19)	4 (21.1%)	6 (31.6%)	9 (47.4%)	
Thalassemia Center	Yes (n=46)	10 (21.7%)	25 (54.4%)	11 (23.9%)	0.158
	No (n=52)	12 (23.1%)	35 (67.3%)	5 (9.6%)	
City	Rawalpindi (n=65)	13 (20.0%)	40 (61.5%)	12 (18.5%)	0.623
	Islamabad (n=33)	9 (27.3%)	20 (60.6%)	4 (12.1%)	

on regular blood transfusion, studies reveal that its appropriate and timely use can prolong life.[10,11] Thus, useful information has great significance, particularly among the doctors who face such cases frequently. This study, revealed that a maximum of the study population had a fair bit of knowledge and attitude towards this therapy, which shows either lack of interest or teaching in the relevant quarter.[12,13] A review by Mobarra *et al*,[14] emphasized the importance of iron chelators, the drug used and its knowledge among healthcare workers. Proper understanding and approach of doctors towards iron chelation therapy can be lifesaving and improve the quality of life of such patients.

The study revealed different numbers for awareness regarding the diverse roles of ferritin (must be considered while starting chelation) in chelation therapy like the goal of chelation in terms of ferritin level, frequency of monitoring ferritin level, and its level used as cut off for combination therapy. As per guidelines set by the Thalassemia Federation of Pakistan,[9] the goal of chelation therapy is to keep the ferritin level up to 500 ng/dl (36.7% of participants reported it correctly), while ferritin level needed to initiate combination therapy is 2500 mg/dl (72.4% participants reported it correctly). Initiation of the chelation therapy based on ferritin level traditionally starts after two years or above/after 10-20 transfusions, or when ferritin exceeds 1,000 ng/mL, only 29.6% of the participants recorded a correct answer.[15]

The study population revealed some mixed practices for iron chelation therapy except for combination drugs, where 4/5 participants agreed to initiate combination therapy. Combination therapy is described as a variety of approaches used after the failure of the monotherapy to control iron overload and its side effects. Desferrioxamine (DFO) and Deferasirox(DFX) are popular for their effective result in controlling iron overload.[10] Different studies suggest, as per practice adopted by the doctors of this study, that combination therapy has better results than a drug used alone. However, the mode of drug administration may vary.[16,17] Similarly, a study by Kontoghiorghes,[18] in 1995 also showed a positive impact of combination therapy for iron chelation. In combination therapy, 3:4 of the professionals are practising Desferrioxamine plus Deferasirox, the most effective combination therapy as per available data.[14,19] This study shows some mixed results for first-line iron

chelator being used in which almost same numbers of professionals have recommended Deferasirox and Desferrioxamine. The available statistics also had no particular first line for iron chelation, though some studies have given the edge to Deferasirox if needed alone, followed by Desferrioxamine.[14] In this study, the professionals mostly adopted oral means of medicine due to its easier administration, which contradicts the evidence available in the literature suggesting that the few iron chelators may perform better when used intravenously or intramuscularly.[20]

The results of this study revealed that almost half of the sample population is unaware of the Iron Chelation Therapy guidelines issued by the Thalassemia Federation of Pakistan.[10] These results should encourage the availability and use of these guidelines nationally. At the return of the questionnaire, the participants were given the printout of the guidelines and web links to reinforce the correct practice. The small sample size, just involving junior-level practitioners and only two cities, was among the few limitations of this study. Nevertheless, the reason for particularly involving the budding paediatricians was to show that the professionals' knowledge is mostly based on experience from patient treatment rather than any separate training module or implementation of guidelines.

CONCLUSION

Most of the population had a fair knowledge and attitude towards chelation therapy, followed by poor and satisfactory. In practice, the situation varies mostly except in the type of therapy where maximum prefer combination therapy when serum ferritin levels are not controlled, representing ineffective chelation with monotherapy. The study further emphasizes that with an increase in professional experience, knowledge, attitude, and practice improvement, which shows that the residents are not aware or guided but mostly learn with time, reinforcing the need to follow standard guidelines at all levels to ensure proper management.

Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

MF & FB: Data acquisition, data analysis, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

SA & FI: Conception, Study design, drafting the manuscript, approval of the final version to be published.

HA & QZK: Critical review, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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