Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/jptcp.v30i18.3418

A RETROSPECTIVE CROSS-SECTIONAL STUDY TO ASSESS THE TREATMENT PATTERN AMONG THALASSEMIA PATIENT IN A TERTIARY CARE HOSPITAL; A SINGLE CENTRAL STUDY

Alia Yousaf[1], Aqna Malik[2*], Asim Raza[3], Iram Iqbal[4], Maham Irshad[5], Dr. Ashfaq. Ul. Hassan (Pharm-D) M.Phil.[6], Muhammad Zafar Siddiq[7]

[1]Department of pharmacy, University of Lahore, aliyay658@gmail.com
[2*]Department of Pharmacy, University of Chenab, Gujrat.
Department of pharmacy, University of Lahore, Cell no:03335522120, Email: Insharahbatool@yahoo.com
ORCID no: 0000-0002-1365-3225
[3]Assistant Professor (Epidemiology and Biostatistics), School of Allied Health Sciences, CMH, Lahore Medical College and Institute of Dentistry, Email: asimrazathakur@gmail.com
[4]Department of pharmacy, University of Lahore, Email: binteiqbal794@gmail.com
[5]Department of pharmacy, University of Lahore, mahamirshad0786@gmail.com
[6]Department of Pharmacy, University of Chenab, Gujrat. Social Security Hospital Gujrat
[7]Department of pharmacy, University of Lahore, Email: muhammadzafar5830@gmail.com

***Corresponding Author:** Aqna Malik
*****Department of Pharmacy, University of Chenab, Gujrat. Department of Pharmacy, University of Lahore, Lahore.0333-5522120, Insharahbatool@yahoo.com

Abstract

Background: Thalassemia characterized by a defect in the synthesis of haemoglobin (Hb) or its globin subunits. This study was conducted to evaluate the treatment pattern of thalassemia in public hospital.

Methodology: Retrospective study was conducted to assess thalassemia treatment pattern in Holy Family Hospital Rawalpindi, from September 2022 to December 2022. Total 430 registered thalassemia patients were included in this study. Data were collected and analyzed by using software SPSS version 24.

Results: Participants included in this study have 1:1 of male and female. Among 430 participants, the majority of participants belonged to <3 age (years) group 219(50.9%). 322 (74.9%) belong to the rural areas, 11 (2.6%) were from elite background. 24 (5.6%) among partcipants belong to capital and 352(81.90) belong to Punjab. It was noticed that the consanguinity of the thalassemia was 306 (71.2%) of total cases, due to first cousin marriages. Type of thalassemia which was diagnosed in patients have different types in which, 31 (7.2%) were diagnosed with β-thalassemia minor, 308 (71.6%) β-thalassemia major, 85 (19.8%) homozygous β-thalassemia, 5 (1.2%) hemolytic anemia and 1 (0.2%) intermedia thalassemia. Among total 430 thalassemia patients, 427 (99.3%) received blood transfusion and 3 (0.7%) didn't. 150 (34.9%) receive iron chelation therapy and 280 (65.1%) didn't. 35 (8.1%) administered the iron antidote desferoxamine and 395 (91.9%) didn't. 312 (72.6%) took

iron chelator deferasirox and 118 (27.4%) didn't. 85 (19.8%) were advised folic acid, 81 (18.8%) were advised calcium supplement, 10 (2.3%) thalassemia patient taking vitamin supplement, Deferiprone is an iron chelator that was 17 (4.0%) prescribed to the patients, 2 (0.5%) were taking ceclor (antibiotic), 2 (0.5%) advised Hepa-Merz which is used as a supportive therapy in liver disease, 1 (0.2%) patient taking Aceclofenac which is a non-steroidal agent,1(0.2%) patient was taking Ondansetron, 2 (0.5%) were advised Hydroxyurea, used in chronic myeloid leukemia (CML).
Conclusion: Each patient should have a medical file with precise documentation of blood transfusion requirements, iron chelation therapy requirements and CBC, haemophilia, electrophoresis monitoring, and transfusion reactions. Patients and relatives should be informed about thalassemia. Before getting married, couples should do a quick blood test to check for thalassemia to see if they are carriers or not.

Keywords: Thalassemia, Deferiprone, Deferasirox, Desferoxamine, Holy Family Hospital, Treatment.

Introduction

"Thalassemia" comes from the Greek words "Thalassa" (sea) and "Haema" (blood), (Rachmilewitz & Giardina, 2011). It is a global public health problem in which due to absence of Globin chains α and β thalassemia termed as α, β and decreased thalassemia (Forget & Bunn, 2013). 95% of thalassemia births have been reported worldwide (Weatherall & Clegg, 2001). Both types are transmitted in an autosomal recessive pattern. Thalassemia major (TM), often known as Cooley anemia (Bajwa & Basit, 2019) and thalassemia intermedia are 2 forms of thalassemia based on severity (Haddad et al., 2014). β-Thalassemia major is noted to be 73.9% of all thalassemia types (Kadhim et al., 2017) and is characterized by moderate to severe symptoms including low Hb levels after 6 months of birth (Bajwa & Basit, 2019). Parents who have the mutant thalassemia gene can transmit the disease to their offspring. One faulty gene is all it takes for a child to be a carrier, often known as the "thalassemia trait" (Unissa et al., 2018). Despite availability of no accurate data regarding incidence, prevalence, and mortality rates of inherited blood disorders like thalassemia, some researchers found β thalassemia trait in Pakistan prevalent between 5%-8% (Ansari et al., 2011) with over ten million carriers according to (Black et al., 2010). In case both parents will be carriers, child will surely be thalassemic and every year nearly 5000 children found to be carriers of β-Thalassemia major (Asif & Hassan, 2014), contrary to alpha thalassemia, which is very common in Asia and the Mediterranean while in Pakistan, 8.3 % of the population has α-thalassemia (Shahid et al., 2017). Many factors including transfusion-dependent thalassemia, consanguineous and early marriages, sharp birth rate, low literacy rate and low level of cooperation from patients are contributing factors for such high rate of thalassemia carriers in children in Pakistan (Khalid et al., 2019).

People with β thalassemia major exhibited severe anemia within the first 2 yrs. of life and need frequent blood transfusions (Galanello & Origa, 2010). Regular blood transfusion is necessary to maintain Hb levels for better growth and development alongside reduction of hepatosplenomegaly (Cappellini et al., 2014). Chronic anemia and iron overload mainly responsible for growth retardation and endocrinopathies, especially hypogonadism, are common in people with thalassemia (Chatterjee & Bajoria, 2010). Endocrine insufficiencies may cause hypogonadotropic hypogonadism which may lead to in-fertility (Fica et al., 2005). Hormonal replacement is indicated for hormonal imbalance (Lasco et al., 2001).

Osteopenia and osteoporosis are main cause of morbidity in thalassemia patients with passage of time (Agarwal, 2009). These bone deformities can be managed by monitoring of chelation therapy to over-come iron overload (Lucarelli & Gaziev, 2015). Lifestyle modifications including increased calcium intake and physical activity along with Vit D therapy (Piga, 2017). Cessation of smoking is another life style medication can be adopted for thalassemia patients (Rund & Rachmilewitz, 2005). Tretament modality of iron chelation therapy has increased life expectancy for patients with β-

thalassemia (Davis & Porter, 2002). Thalassemia studies observed effectiveness of deferasirox (Cappellini et al., 2006) Desferrioxamine (Olivieri et al., 1990) and deferiprone (Pennell et al., 2006).However patients with thalassemia intermedia were treated with additional folic acid to avoid deficiencies brought on by overactive bone marrow (Origa et al., 2007).

Materials and methods:

This cross-sectional study was carried out using two year's (2020-2022) retrospective secondary data of 430 thalassemia patients who were registered in a thalassemia centre of Holy Family Hospital, Rawalpindi which is ranked as the second highest thalassemia centre in Pakistan. Investigators visited to the thalassemia center for the collection of data after the ethical approval from the Institutional Review Board (IRB) of Holy Family Hospital, Rawalpindi. Consent was also taken from the in-charge of hospital's thalassemia center. All registered patients were included in this study. Patients with additional disorders like thrombocytopenia, anaemia, sickle cell anaemia were excluded from the study. Uncompleted information was also excluded from the study.

Ethical approval and consent:

Ethical approval was taken from the Institutional review board (IRB) of University of Lahore. All collected data and information were kept private. Hard copies of the data were kept in registers. The consultants in charge of the thalassemia units at each institution retained hard copies in a secured cabinet.

Data collection tools:

Data regarding age, gender, ethnicity, residency, degree of consanguinity between their parents and treatment patterns of the thalassemia patients from the medical record of their files were collected from September, 2022 to December 2022.

Data collection procedure:

Permission was taken from the respective hospital authority for the collection of data from their reports. Verbal informed consent was taken from the selected participants. On the basis of inclusion criteria 430 patients were selected as study population by using non-probability convenient sampling technique. All records of registered thalassemia patients were reviewed at the thalassemia center. Patient registers, and clinical records were available and patients were interviewed where possible.

Data Analysis:

After the data collection, the data was analyzed by using IBM SPSS (Statistical package for social sciences). SPSS version 24 would be used for the analysis of the data and compilation of results. Descriptive analysis, Correlation and chi-square were applied for the statistics. All results were calculated at 95% confidential interval and p-value <0.05 considered as significant value.

Results:

Retrospective study was conducted to assess the treatment pattern of thalassemia in tertiary care hospital**.** Total 430 thalassemia patients were selected as study population by using non-probability convenient sampling technique.

Table 1. Demographic characteristics of participants

Characteristics	Categories	Cases n (%)	Chai square	p value
Age (years)	<3 3-6 7-10 11-14 15-18 >18	219(50.90) 97(22.60) 57(13.30) 31(7.20) 15(3.50) 11(2.60)	434	<0.001*
Residency	Urban Rural	108(25.10) 322(74.90)	106	<0.001*
Socio-economic status	Elite Moderate Low	11(2.60) 26(6.00) 393(91.40)	653	<0.001*
Ethnicity	Punjabi Pashtun Kashmiri Others	288(67.00) 102(23.70) 32(7.40) 8(1.90)	448	<0.001*
Provinces	Capital Punjab KPK Azad Kashmir Tribal areas	24(5.60) 352(81.90) 41(9.50) 10(2.30) 3(0.70)	1038	<0.001*
Consanguinity	First Cousin Second cousin /Relatives Unrelated	306(71.20) 60(14.00) 64(14.90)	276	<0.001*
Diagnosis	β-thalassemia minor β-thalassemia major Homozygous β-thalassemia Hemolytic anemia Intermedia thalassemia	319(7.20) 308(71.60) 85(19.80) 5(1.20) 1(0.20)	768	<0.001*
Blood group of participants	A+ve A-ve B+ve B-ve AB+ve AB-ve O+ve O-ve	91 (21.20) 11 (2.60) 112(26.0) 17 (4.00) 51 (11.90) 14 (3.30) 108 (25.10) 25 (5.80)	330	<0.001*

Table 1. Shows the demographic of the participants. Participants included in this study have 1:1 of male and female. Among 430 participants, the majority of participants belonged to <3 age group 219(50.9%) and >18-year age group were 11(2.6%). 322 (74.9%) were belong from the rural areas, 108 (25.1%) were from Urban areas. 11 (2.6%) were Elite in their socio-economic status, 393 (91.4%) Low in status. Majority of the participants were Punjabi 288 (67.0%) and 8 (1.9%) others. Participants belong from different provinces of Pakistan in which 24 (5.6%) were from the Capital, 352 (81.9%) from Punjab, 41 (9.5%) from KPK, 10 (2.3%) from Azad Kashmir and 3 (0.7%) from the Tribal areas. It was noticed that the consanguinity of the thalassemia was 306 (71.2%) of total patients due to first cousin marriage, 60 (14.0%) were of second cousin marriage and 64 (14.9%) families parents had no relation to each other. 31 (7.2%) of patients were diagnosed with β-thalassemia minor, 308 (71.6%) β-thalassemia major, 85 (19.8%) homozygous β-thalassemia, 5(1.2%) hemolytic anemia and 1 (0.2%) intermedia thalassemia. Blood groups of majority of partipants was B^+ 112 (26.0%), 108 (25.1%) O^+, 91 (21.2%) A^+, 51 (11.9%) AB^+.

Table 2. Blood transfusion and Iron chelation therapy

Characteristics	Categories	Cases n (%)	Chai square	p-value
Blood Transfusion	Yes No	427(99.30) 3(0.70)	418	<0.001*
Iron chelation therapy	Yes No	150(34.90) 280(65.10)	39	<0.001*

Table 2. Illustrate about the blood transfusion and Iron chelation therapy given to the participants. Among total 430 thalassemia patients, 427 (99.3%) were received Blood transfusion and 3 (0.7%) didn't. 150 (34.9%) receive Iron chelation therapy and 280 (65.1%) didn't. A statistical significant difference was found among the therapy given to the patients chi square where p <0.05.

Table 3. Distribution of used medicines for treatment

Generic name of medicines	Categories	n (%)	Chi square	p value
Desferoxamine	Yes No	35 (8.10) 395 (91.90)	301	<0.001*
Deferasirox	Yes No	118 (27.40) 312 (72.60)	87	<0.001*
Deferiprone	Yes No	17 (4.0) 413 (96.0)	364	<0.001*
Folic acid	Yes No	85 (19.8) 345 (80.2)	157	<0.001*
Calcium supplements	Yes No	81 (18.8) 349 (81.2)	167	<0.001*
Vitamin supplements	Yes No	10 (2.3) 420 (97.7)	390	<0.001*
Ceclor	Yes No	2 (0.5) 428 (99.5)	422	<0.001*
Hepa-Merz	Yes No	2 (0.5) 428 (99.5)	422	<0.001*
Aceclofenac	Yes No	1 (0.2) 429 (99.8)	426	<0.001*
Ondansetron	Yes No	1 (0.2) 429 (99.8)	426	<0.001*
Hydroxyurea	Yes No	2 (0.5) 428 (99.5)	422	<0.001*
Total	430			

Table 3. Demonstrate the Treatment pattern of thalassemia. Among total 430 participants, 35 (8.1%) were administered the iron antidote Desferoxamine, 395 (91.9%) didn't. 312 (72.6%) were gi ven iron chelator deferasirox and 118 (27.4%) didn't. 85 (19.8%) were advised folic acid and 345 (80.2%) didn't. 81 (18.8%) advised calcium supplement and 349 (81.2%) didn't. 10 (2.3%) thalassemia patient taking vitamin supplement and 420 (97.7%) didn't. Deferiprone is an iron chelator that is 17 (4.0%) prescribed to the patients and to 413 (96.0%) didn't. 2 (0.5%) taking ceclor which is used as antibiotic and 428 (99.5%) didn't. 2 (0.5%) advised Hepa-Merz which is used as a supportive therapy in liver disease and to 428 (99.5%) didn't. 1 (0.2%) patient taking Aceclofenac which is a non-steroidal agent and 429 (99.8%) didn't. 1 (0.2%) patient taking Ondansetron which is a serotonin 5-HT3 receptor antagonists 429 (99.8%) didn't. 2 (0.5%) advised Hydroxyurea which is used in chronic myeloid leukemia (CML) and 428 (99.5%) didn't.

Table 4. Treatment pattern with differential diagnosis.

Medicines	β-thalassemia minor n(%)	β-thalassemia major n(%)	Homozygous β-thalassemia n(%)	Hemolytic anemia n(%)	Intermedia thalassemia n(%)	Total n(%)
Desferoxamine	4 (12.90)	25(8.10)	6(7.10)	0(0.00)	0(0.00)	35(8.1)
Deferasirox	9(29.00)	80(26.00)	29(34.10)	0(0.00)	0(0.00)	118(27.4)
Deferiprone	5(16.10)	9(2.90)	3(3.50)	0(0.00)	0(0.00)	17(4.00)
Supportive Therapy						
Folic acid	7(22.60)	52(16.90)	26(30.60)	0(0.00)	0(0.00)	85(19.80)
Calcium supplements	7(22.60)	48(15.60)	26(30.60)	0(0.00)	0(0.00)	81(18.80)
Vitamin supplements	1(3.20)	9(2.90)	0(0.00)	0(0.00)	0(0.00)	10(2.30)
Cefeclor	0(0.00)	2(0.60)	0(0.00)	0(0.00)	0(0.00)	2(0.50)
Hepa-Merz	0(0.00)	2(0.60)	0(0.00)	0(0.00)	0(0.00)	2(0.50)
Aceclofenac	0(0.00)	1(0.30)	0(0.00)	0(0.00)	0(0.00)	1(0.20)
Ondansetron	0(0.00)	0(0.00)	1(1.20)	0(0.00)	0(0.00)	1(0.20)
Hydroxyurea	2(6.50)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	2(0.50)

Table 4. Patient diagnosed with different types are treated with different treatment patterns. Patients diagnosed with β-thalassemia major are received 25% of Desferoxamine which is majority in their numbers.118 of total, Deferasirox given in which majority is given to β-thalassemia major 80. Deferiprone prescribed to 17 participants majority to β-thalassemia major 9. Other supportive therapy given in which folic acid is prescribed to 85 participants, Calcium supplement to 81 participants and vitamin supplement to 10 participants. Data shows that the computed spearman correlation value illustrates the statistical non-significant correlation of differential diagnosis with medications used for the treatment whose p value is >0.05.

Table 5. Correlation of age with Consanguinity, correlation of differential diagnosis with iron chelators, Correlation

	Characteristics	Categories	Spearman Correlation	p value
Correlation of age with Consanguinity	Consanguinity	First-cousin	.947	<0.001*
		Second-cousin		
		No relation		
Correlation of Differential diagnosis with Iron chelators	Iron Chelators	Deferasirox (DFX)	.487	<0.001*
		Deferiprone (DFP)	.053	<0.001*
		Deferoxamine (DFO)	.325	<0.001*
Correlation of Differential diagnosis with Concomitant therapy	Concomitant therapy	Folic acid	.091	<0.001*
		Calcium supplement	.061	<0.001*
		Vitamin supplement	.126	<0.001*
		Ceclor	.665	<0.001*
		Hepa-Merz	.665	<0.001*
		Aceclofenac	.760	<0.001*
		Ondansetron	.090	<0.001*
		Hydroxyurea	.004	<0.001*

Table 5. Illustrate correlation of age with Consanguinity. Data indicates that a total of 430 cases of β Thalassemia were identified, out of which the majority (221 cases, 51%) were found in individuals who had consanguineous relationships, such as first cousins. Specifically, the highest number of cases were found in individuals who had a first cousin relationship. The second-highest number of cases were found in individuals who had a relative relationship. The remaining 45 cases (15%) had no prior relation. Data shows that the computed spearman correlation value illustrates the statistical significant correlation of age with Consanguinity p value is <0.05. Correlation of differential diagnosis with treatment of iron chelators which are categorized into three classes; deferasirox (DFX), deferiprone (DFP), and deferoxamine (DFO). Data shows that the computed spearman correlation value illustrates the statistical significant correlation of differential diagnosis with iron chelators used for the treatment whose p value is <0.05. Correlation of differential diagnosis with concomitant treatment given to the thalassemic patients Data shows that the computed spearman correlation value illustrates the statistical significant correlation of differential diagnosis with concomitant therapy used for the treatment whose p value <0.05.

Discussion:

In current study, it was observed that registered thalassemia patients in hospitals of Government sector in were mainly diagnosed with β- thalassemia major rather α-thalassemia patients. Highest reported rate of thalassemia at 34.9% was found in age group 13-18yrs. While in another research thalassemia was reported in children ≤ 5 yr. with varying results regarding type of thalassemia and clinical diagnosis (Gafer et al., 2023). Similarly, in current study different type's thalassemia was mostly prevalent in children ≤ 3 years. According to (Barua et al., 2020) thalassemia was more prevalent in males than females while in current study it is noticed that participants have 1:1 ratio and belong to rural areas 74.9%. According to (Maatook et al., 2015) prevalence of the O+ blood group in Basrah (IRAQ) was mostly seen while in current study, blood group B^+ was prevalent in thalassemic patients.

According to findings of (Sattari et al., 2019) 61.3% patients had thalassemia without a family history while in our study, majority of the participants (70.6%) belong to consanguineous marriage which may pose a significant risk. Possible reasons behind this trend may be traditional practices in Pakistan. Pre-marital screening is not a well-known concept, especially in rural areas. Even though parental awareness of thalassemia carriers, screening, and prenatal diagnosis has increased in recent years, it is dire need of to raise public awareness to take preventive measures in order to reduce the disease's burden in Pakistan (Bennett et al., 1999).

According to (Jafroodi et al., 2015) only severely compromised β thalassemia major patients need blood transfusions, while in current study almost all types of thalassemia patients were transfused blood. Observations in current study can be justified by findings in another research by Hossain where he has found that β-thalassemia patients from South Asia require blood transfusions due to higher Hb levels (Hossain et al., 2017).

Many researchers confirmed that iron chelation therapy can manage early symptoms of thalassemia with appropriate treatment management (Olivieri & Brittenham, 1997),(Viprakasit et al., 2009). While in our study it was observed that almost all thalassemia patients in government hospitals of Pakistan received blood transfusions rather than iron chelation treatment

Though iron chelation therapy may be associated with complications due to uncontrolled overload and accumulation of iron in spleen and adipose tissues as it was seen in findings of (Moirangthem & Phadke, 2018) where among 39% of transfusion-dependent -thalassemia patients who received iron chelation therapy almost 28% suffered complications from uncontrolled iron. However, in current study among 34.9% patients who received iron chelation therapy no cases of complications have been reported. Different generics has been used for iron chelation therapy. Previously in a study by (Fibach & Rachmilewitz, 2008) 63 % patients were given desferoxamine however in current study only 8% patients were given desferoxamine. Other generics were also used in clinical settings in many researches (Olivieri et al., 1990) for iron chelation including deferasirox, deferiprone and found as

better option in ICT than desferoxamine. In current study deferasirox was found to be effective in (27.4%) patients and deferiprone was utilized in (4%) patients.

Limitations:

Holy Family Hospital Rawalpindi (HFH) is a well-established hospital where all thalassemic patients were registered. Each file has precise information and is organised properly. Due to the fact that our research was done using the medical reports of individuals registered in thalassemia centre and identified as having various forms of thalassemia, it has significant limitations. Any biasness in the data is possible. Patients with additional disorders like thrombocytopenia, anaemia, sickle cell anaemia were excluded from the study.

Conclusion:

Regular examination and follow-up examination are advised as a top priority to increase patient compliance, life expectancy, treatment of problems, and quality of life. It is advised that patients with thalassemia take advantage of the newly authorised treatment alternatives, such as gene therapy and hematopoietic stem cell transplant, in order to improve their long-term conditions, reduce their need on transfusions, and increase their life expectancy and quality of life. Most thalassemia patients experience a considerably diminished quality of life. In addition to traditional therapy, programmes for psychological support should be created to enhance the quality of life for thalassemia patients. Due of its accessibility to an average person, government sector hospitals need money and blood donations.

Each patient should have a medical file with precise documentation of blood transfusion requirements, iron chelation therapy requirements and CBC, haemophilia, electrophoresis monitoring, and transfusion reactions. Patients and relatives should be informed about thalassemia.

Don't use iron supplements.

To address this issue and lessen the impact of this disease, it is strongly advised that effective and well-organized nationwide screening and preventive programmes be launched.

Before getting married, couples should do a quick blood test to check for thalassemia to see if they are carriers or not.

It is recommended to avoid tablet dosage form in children’s which are less than 9 years.

Abbreviations:

According to WHO: Full form

Abbreviations	Full Form
Hb	Haemoglobin
β	Beta
HFH	Holy Family Hospital
DFO	Desferoxamine
DFP	Deferiprone
DFX	Desferasirox

Supporting information:

Patients Medical Reports

Patients consent forms

Permission was obtained from the appropriate authorities of institute.

Ethical Approval (IRB letter)

Acknowledgment:

I thank the Hospital Authority and people that contributed to this study. Without their collaboration, it could not have been done.

Dr. Muhammad Aslam (Head of department of thalassemia Centre of HFH)

Dr. Javeria (Hematologist in Hospital)

Author contributions:
Conceptualization:
Data curation:
Formal analysis:
Supervision:
Funding acquisition:
Methodology:
Project administration:
Validation:
Writing – original draft:
Writing :

Reference:

1. Agarwal, M. (2009). Advances in management of thalassemia. *The Indian Journal of Pediatrics*, *76*, 177-184.
2. Ansari, S. H., Shamsi, T. S., Ashraf, M., Bohray, M., Farzana, T., Khan, M. T., Perveen, K., Erum, S., Ansari, I., Nadeem, M., Ahmed, M., & Raza, F. (2011). Molecular epidemiology of β-thalassemia in Pakistan: far reaching implications. *Int J Mol Epidemiol Genet*, *2*(4), 403-408.
3. Asif, N., & Hassan, K. (2014). Prevention of beta thalassemia in Pakistan. *J Islam Med Dent Coll*, *3*(2), 46-47.
4. Bajwa, H., & Basit, H. (2019). Thalassemia.
5. Black, M. L., Sinha, S., Agarwal, S., Colah, R., Das, R., Bellgard, M., & Bittles, A. H. (2010). A descriptive profile of β-thalassaemia mutations in India, Pakistan and Sri Lanka. *Journal of Community Genetics*, *1*(3), 149-157. https://doi.org/10.1007/s12687-010-0026-9
6. Cappellini, M.-D., Cohen, A., Porter, J., Taher, A., & Viprakasit, V. (2014). *Guidelines for the management of transfusion dependent thalassaemia (TDT)*. Thalassaemia International Federation Nicosia, Cyprus.
7. Cappellini, M. D., Cohen, A., Piga, A., Bejaoui, M., Perrotta, S., Agaoglu, L., Aydinok, Y., Kattamis, A., Kilinc, Y., & Porter, J. (2006). A phase 3 study of deferasirox (ICL670), a once-daily oral iron chelator, in patients with β-thalassemia. *Blood*, *107*(9), 3455-3462.
8. Chatterjee, R., & Bajoria, R. (2010). Critical appraisal of growth retardation and pubertal disturbances in thalassemia. *Annals of the New York Academy of Sciences*, *1202*(1), 100-114.
9. Davis, B. A., & Porter, J. B. (2002). Results of long term iron chelation treatment with deferoxamine. *Iron Chelation Therapy*, 91-125.
10. Fica, S., Albu, A., Vladareanu, F., Barbu, C., Bunghez, R., Nitu, L., & Marinescu, D. (2005). Endocrine disorders in beta-thalassemia major: cross-sectional data. *ACTA ENDOCRINOLOGICA-BUCHAREST-*, *1*(2), 201.
11. Forget, B. G., & Bunn, H. F. (2013). Classification of the disorders of hemoglobin. *Cold Spring Harbor perspectives in medicine*, *3*(2), a011684.
12. Galanello, R., & Origa, R. (2010). Beta-thalassemia. *Orphanet Journal of Rare Diseases*, *5*(1), 11. https://doi.org/10.1186/1750-1172-5-11
13. Haddad, A., Tyan, P., Radwan, A., Mallat, N., & Taher, A. (2014). β-thalassemia intermedia: a bird's-eye view. *Turkish Journal of Hematology*, *31*(1), 5.
14. Kadhim, K. A., Baldawi, K. H., & Lami, F. H. (2017). Prevalence, incidence, trend, and complications of thalassemia in Iraq. *Hemoglobin*, *41*(3), 164-168.
15. Khalid, N., Noreen, K., Qureshi, F., & Mahesar, M. (2019). Knowledge of thalassemia and consanguinity: A multicenter hospital based retrospective cohort study from metropolitan city of Karachi, Pakistan. *The Professional Medical Journal*, *26*, 1580-1586. https://doi.org/ 10.29309/TPMJ/2019.26.09.168

16. Lasco, A., Morabito, N., Gaudio, A., Buemi, M., Wasniewska, M., & Frisina, N. (2001). Effects of hormonal replacement therapy on bone metabolism in young adults with beta-thalassemia major. *Osteoporosis International*, *12*, 570-575.
17. Lucarelli, G., & Gaziev, J. (2015). Hematopoietic cell transplantation for thalassemia. *Thomas' Hematopoietic Cell Transplantation: Stem Cell Transplantation*, *1*, 842-854.
18. Olivieri, N., Freedman, M., Koren, G., Hermann, C., Bentur, Y., Chung, D., Klein, J., Louis, P. S., Templeton, D., & McClelland, R. (1990). Comparison of oral iron chelator L1 and desferrioxamine in iron-loaded patients. *The Lancet*, *336*(8726), 1275-1279.
19. Origa, R., Galanello, R., Ganz, T., Giagu, N., Maccioni, L., Faa, G., & Nemeth, E. (2007). Liver iron concentrations and urinary hepcidin in β-thalassemia. *Haematologica*, *92*(5), 583-588.
20. Pennell, D. J., Berdoukas, V., Karagiorga, M., Ladis, V., Piga, A., Aessopos, A., Gotsis, E. D., Tanner, M. A., Smith, G. C., & Westwood, M. A. (2006). Randomized controlled trial of deferiprone or deferoxamine in beta-thalassemia major patients with asymptomatic myocardial siderosis. *Blood*, *107*(9), 3738-3744.
21. Piga, A. (2017). Impact of bone disease and pain in thalassemia. *Hematology 2014, the American Society of Hematology Education Program Book*, *2017*(1), 272-277.
22. Rachmilewitz, E. A., & Giardina, P. J. (2011). How I treat thalassemia. *Blood, The Journal of the American Society of Hematology*, *118*(13), 3479-3488.
23. Rund, D., & Rachmilewitz, E. (2005). β-Thalassemia. *New England Journal of Medicine*, *353*(11), 1135-1146.
24. Shahid, S., Nadeem, M., Zahid, D., Hassan, J., Ansari, S., & Shamsi, T. (2017). Alpha thalassemia deletions found in suspected cases of beta thalassemia major in Pakistani population. *Pakistan journal of medical sciences*, *33*(2), 411.
25. Unissa, R., Monica, B., Konakanchi, S., Darak, R., Keerthana, S. L., & Kumar, S. A. (2018). Thalassemia: a review. *Asian Journal of Pharmaceutical Research*, *8*(3), 195-202.
26. Weatherall, D., & Clegg, J. B. (2001). Inherited haemoglobin disorders: an increasing global health problem. *Bulletin of the World Health Organization*, *79*(8), 704-712.
27. Barua, T., Das, A. K., Sultana, R., Das, D., & Arju, M. A. C. (2020). Socio-demographic profile of patients admitted in Thalassemia care center of Chattogram Maa Shishu-O-General Hospital. *Chattagram Maa-O-Shishu Hospital Medical College Journal*, *19*(1), 33-37.
28. Bennett, R. L., Hudgins, L., Smith, C. O., & Motulsky, A. G. (1999). Inconsistencies in genetic counseling and screening for consanguineous couples and their offspring: the need for practice guidelines. *Genetics in Medicine*, *1*(6), 286-292.
29. Fibach, E., & Rachmilewitz, E. (2008). The role of oxidative stress in hemolytic anemia. *Current molecular medicine*, *8*(7), 609-619.
30. Gafer, A., Alrabeei, N. A., Al-Awar, M. S., Edrees, W. H., & Alyafrosi, O. A. H. (2023). Socio-demographic Profile of Patients Admitted in Thalassemia Center, Sana, a, Yemen. *Al-Razi University Journal for Medical Sciences*, *7*(1).
31. Hossain, M. S., Raheem, E., Sultana, T. A., Ferdous, S., Nahar, N., Islam, S., Arifuzzaman, M., Razzaque, M. A., Alam, R., & Aziz, S. (2017). Thalassemias in South Asia: clinical lessons learnt from Bangladesh. *Orphanet journal of rare diseases*, *12*(1), 1-9.
32. Jafroodi, M., Davoudi-Kiakalayeh, A., Mohtasham-Amiri, Z., Pourfathollah, A. A., & Haghbin, A. (2015). Trend in prevalence of hepatitis C virus infection among β-thalassemia major patients: 10 years of experience in Iran. *International journal of preventive medicine*, *6*.
33. Maatook, M. A., Mohammed, K. A., & Afat, A. M. (2015). The socio-demographic profile of thalassemia in Basrah. *Med J Babylon*, *3*, 670â.
34. Moirangthem, A., & Phadke, S. R. (2018). Socio-demographic profile and economic burden of treatment of transfusion dependent thalassemia. *The Indian Journal of Pediatrics*, *85*, 102-107.
35. Olivieri, N., Freedman, M., Koren, G., Hermann, C., Bentur, Y., Chung, D., Klein, J., Louis, P. S., Templeton, D., & McClelland, R. (1990). Comparison of oral iron chelator L1 and desferrioxamine in iron-loaded patients. *The Lancet*, *336*(8726), 1275-1279.

36. Olivieri, N. F., & Brittenham, G. M. (1997). Iron-chelating therapy and the treatment of thalassemia. *Blood, The Journal of the American Society of Hematology*, *89*(3), 739-761.
37. Sattari, M., Sheykhi, D., Nikanfar, A., Pourfeizi, A. H., Nazari, M., Dolatkhah, R., & Mashayekhi, S. (2019). The financial and social impact of thalassemia and its treatment in Iran. *Pharmaceutical sciences*, *18*(3), 171-176.
38. Viprakasit, V., Lee-Lee, C., Chong, Q. T., Lin, K.-H., & Khuhapinant, A. (2009). Iron chelation therapy in the management of thalassemia: the Asian perspectives. *International journal of hematology*, *90*, 435-445.