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ORIGINAL ARTICLE

Prevalence and Clinical Features of Thalassemia Minor Cases

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ABSTRACT

Background: Thalassemia, the most common heterogeneous single gene disorder causing sever genetic health problem in the world. In 1932 George and William gave it the name thalassemia derived from Greek words (“thallassa: mean sea) and (“aima: mean blood). The research was conducted on thalassemia minor patients in North Waziristan and some selected areas of Peshawar Khyber pakhtunkhwa.

Methods: During this survey 100 thalassemia minor patients were interviewed belonging to different castes. It was observed that majority of the patients were from the age group 1-10 years both in male asn females. Different ethnic groups were interviewed such as Yousafzai, Halimzai, Dawar, Wazir, Noor khel, Musazai, Saidan, Miserkhal, Afridi, Miagan, and Afghan.

Results: The most of the thalassemia minor patients belonged to rural area (62.4 %) while 36.6% patients were reported from urban area. The maximum number of thalassemia minor patients belonged to lower class which was reported 47% followed by middle class (35%) and rich people (18%). The parents of 64 patients were cousin while the parents of 36 patients had marriage out of the family. The birth abnormalities were also recorded and observed as abortion (30%), delay birth (23%), still birth (13%) and premature birth (17%). During this study it was observed that majority of the patients were of the moderate body status (54.5%) Interestingly the ratio of obese people was very low. While the ratio of thin people was 39.4%. The physical abnormalities found in thalassemia minor patients included eye, skin, ear, mental and bone and joint abnormalities. the people having the age from 1-10 have an average HB level of 9.45 g/dl while those having age of 41-60 have an average HB level of 11.58 g/dl. The physical infections also reported such as eye infection (39%), GIT infection (20%), Lung infection, Skin infection (16%), UTI (7%) and Ear infection (2%).

Conclusion: This study provides an insight in to the mechanism of transmission of thalassemia in the family and suggest social awareness about the disadvantages of the interfamilial marriages.

Keywords: Thalassemia, Consanguineous marriages, Hemoglobin, Birth Abnormalities, Infections.

INTRODUCTION

Thalassemia is the most prevalent heterogeneous single gene disorder in the world and a severe genetic health issue. There are over 40 million carriers of hemoglobinopathies all over the world[1]. α and β thalassemia are the two main types, based on which portion of the globin chain forms in lower amounts[2]. Usually, four genes (two from each parent) two on each strand of chromosome 16 made the alpha globin chain. A reduction in the production of alpha globin chains is the cause of alpha thalassemia due one or more of the four alpha globin genes on chromosome 16 are deleted or mutated[3]. Also called as mild alpha-thalassemia. Two alpha globin genes have been lost in these patients. Patients do not have obvious symptoms in this condition, although they have small red blood cells and a mild anemia. They appear and feel normal, but routine testing may discovered[4]. It is also called as hemoglobin H disease. Three alpha globin genes have been lost in these patient. Patients with this condition typically require blood transfusions to stay alive due to their severe anemia. Infants with alpha thalassemia intermedia seem normal at birth but frequently progress splenomegaly and anemia at the end of their 1st year. It is uncommon to detect hepatomegaly, and there may be some correlation with mental obstruction. The hemolytic nature of severe anemia may cause a rise in gallstones, leg ulcers, and respiratory infections. In the hemoglobin H disease skeletal changes are not commonly seen[5].

More than 200 mutations in the beta globin gene have been identified as causing beta thalassemia globally. beta thalassemia is caused by mutation on chromosome 11, Unlike the deletion that create most of the alpha thalassemia syndromes that affect all aspect of beta globin formation : stability of the beta globin production, transcription and translation[6]. Beta+ and beta0 thalassemia are the two types of beta thalassemia.in which there is a degradation in and complete absence of the beta chain formation respectively. Homozygous state for either beta+ or beta0 thalassemia results in beta thalassemia major, or rarely from the compound heterozygous condition for both beta+ and beta0 thalassemia. Homozygous beta0 thalassemia is correlated with, Hb F predominates, variable amount of Hb A2 and Hb A is absent. Homozygous beta+ thalassemia patients have varied Hb A, elevated and heterogeneously distributed Hb F among red cells and normal, lowered, or increasing Hb A2 level[7]. The production of beta chains is absent or decreased in beta thalassemia due to molecular abnormalities. Alpha chain production is unpretentious, hence there is an imbalance in the formation of globin chains, which results in an excess of alpha chains. In the absence of their companions, they are unstable and precipitate in red cell precursors, resulting in substantial intracellular attachments, which interfere in maturation of red cells. Hence, there is a variable degree of intramedullary devastation of red cell ancestors (i.e. ineffective erythropoiesis)[8].

Around the world, there are at least 240 million people who are carriers of hemoglobinopathies[9]. In a growing state like Pakistan, where a large people living with beta-thalassemia major, the cost of implementing a chelation and hyper-transfusion programme on a nationwide level is excessive. Through prenatal screening and genetic counselling an alternative long term tactic would be to lowered the patients number[10]. Using oligonucleotides probes, B-thalassemia transporters were identified, and homozygous conception was prenatally diagnosed and Couples at risk will be able to prevent having children with B-thalassemia disease through restriction enzyme testing and pregnancy termination[11].

β-thalassemia is one of the most prevalent Hb disorders in Pakistan[12]. Over one-third of Pakistan's population is under 15 years old[13]. 5.4% is the carrier frequency (Hashmi and Farzana, 1976). β-thalassemia incidence varies from 1.4 to 8% . The disease extremely overcomes in areas along the Arabian Sea coast, in South and KPK province located near the Afghanistan border. Here, people from central Asia, the Middle East and Mediterranean settled as they attacked during several times in

history. Numerous factors like, preference to marry with their own ethnic groups and particularly cousin marriages, have significantly increased the prevalence of this disease in the Pakistani population[14].

Around 22,000 children with thalassemia have been recorded in Pakistan's various thalassemia centers. Whereas villages have a similar number of children, but none of them have been registered with a thalassemia center. In different racial groups, there are 7 to 10 million people, the occurrence of thalassemia carriers is 5-8%. In Pakistan the average life expectancy of β- thalassemia patients is ten years. Probable inhibition, which includes prenatal diagnosis, population education, genetic treatment, and screening of couples who are childbearing age, is an efficient method for controlling such disorder[15].

Studies have recommended that poverty, consanguinity and obliviousness about the disorder are the conspicuous factors in growing the incidence of this specific genetic ailment[16]. A patient with β -thalassemic disease has an average lifespan of ten years, and there are between 90,000 and 100,000 patients are recorded with this disorder throughout the country. Due to increasing disease load the number of younger patient is increasing day by day while the number of older patient is fewer due shorter life expectancy[17].

Some studies indicate that low poverty and lack of awareness also contribute to the disorder's rise in frequency[18]. Social factors like consanguineous marriages and marry within ethnic groups are also responsible for rising frequency of the disease[19]. In Punjab (60.7 %) B-thalassemia prevalent is highest followed by Sarikees (25.5 %). It was most common cast wise in Rajputs followed by, Arian, Jaats, Pathans and Sheiks[20].

Present study was carried out, to gather baseline data on various forms of -thalassemia in hospital population of Peshawar, KPK, Pakistan. This study is based on aspect like age at diagnosis of thalassemia and inbreeding effected regarding to various sur name. The aims and objectives of the study were to study the factors responsible for the prevalence of thalassemia of selected area of North Waziristan and Peshawar.

METHODS

Study Design and Setting: This descriptive cross-sectional study was carried out at North Waziristan and Peshawar. The study area was North Waziristan and Peshawar. Waziristan is famous throughout the Pakistan because it is full of alluring beauty, delightful scenes and elating climate. It is a part of Federally Administered Tribal Areas (FATA). It has two parts i.e. North and South Waziristan Agency. The North Waziristan agency is the second largest agency in FATA. The North Waziristan Agency was set up in 1895. It was in the year, 1910 when it was constituted as a full- fledged agency with its head- quarter “Miranshah” (Nawaz Khan, 2010). North Waziristan has been divided into three sub-divisions.

Participants Criteria: All the confirmed thalassemia minor patients was included in this study confirmed by Hb electrophoresis and other then thalassemia minor was excluded[21].

Data Collection Procedure: To collect information from Thalassemia minor patients, a questionnaire was designed, pre-tested and finalized before the actual survey was conducted. North Waziristan and some selected areas of Peshawar were visited. The research work on thalassemia minor patients was conducted in selected areas of Khyber pakhtunkhwa. The major aim of this research was to highlight the abnormalities and deficiencies which are present in the carriers of the thalassemia genes. The data was collected through a questionnaire.

Data Analysis Procedure: The collected data was entered in Microsoft Excel 2007 and further process through Statistical Package for Social Sciences version 22. Data were categorized and shown in table for better representation. Mean, Proportion and percentages were determined through SPSS-22.

RESULTS

In this analysis among different age groups the frequency of thalassemia minor patient in both the males and females was high in the age group between 1-10 years, out of 51 males 16 (31.37%) and 18 (36.73%) females out of 49 were found in this range (Table 1).

Table 1: Frequency of thalassemia minor patients among different age group.

S#	Age	No. Males	%age	No. Females	%age
1	1-10	16	31.37	18	36.73
2	11-20	9	17.64	10	20.41
3	21-30	7	13.72	10	20.41
4	31-40	13	25.49	9	18.37
5	41-60	6	11.76	2	4.08
Total		51	100	49	100

During this research I interviewed 100 patients of thalassemia minor in Waziristan and other different areas of Khyber pakhtunkhwa, which belongs from different ethnic groups. Among them the maximum thalassemia minor patients were interviewed from Yousafzai which is reported 24 followed by 21 patients reported from Dawar ethnic group (Table 2).

Table 2: List of ethnic group of the thalassemia minor patients

Ethnic group	Number
Yousafzai	24
Halimzai	19
Dawar	21
Wazir	7
Noor khel	4
Musazai	5
Saidan	4
Miserkhal	3
Afridi	5
Afghan	5
Miagan	3
Total	100

During this survey it was observed that most of the thalassemia minor patients belonged to Rural area (62.4 %) while 36.6% patients were belonging to Urban area (Table 3).

Table 3: Thalassemia minor patients in case of Rural and Urban area

Area	Frequency	Percent	Valid Percent	Cumulative Percent
Rural	63	62.4	63.0	63.0
Urban	37	36.6	37.0	100.0
Total	100	99.0	100.0	

During this survey the carrier were classified according to the economic condition, it was found that the maximum number of thalassemia minor patients belonged to lower class which was reported 47% followed by middle class (35%) and rich people(18%) (Table 4).

Table 4: Economic status of thalassemia minor patient.

Status	Frequency	Percent	Valid Percent	Cumulative Percent
Poor	47	47.0	47.0	47.0
Middle	35	35.0	35.0	82.0
Rich	18	18.0	18.0	100.0
Total	100	100.0	100.0	

Table 5: Family relation between parents of thalassemia minor patients

Parent Marriage	Frequency	Percent	Valid Percent	Cumulative Percent	Thalassemia major
First cousin marriage	38	38	38	38	60 46 40
Second cousin marriage	26	26	26	64.	
No relation	36	36	36	100.0	
Total	100	100.0	100.0		

In this study a total of 100 thalassemia minor cases were interviewed. The parents of 64 patients were cousin while the parents of 36 patients had marriage out of the family. During this study it was identified that 38% of thalassemia minor patients were first cousin resulting in the Thalassemia major cases are 60, 26%

were second cousin and 36% of thalassemia minor patients were having no family relations (Table 5).

During this study which conducted on the thalassemia minor people, it was found that among the birth abnormalities the abortion is maximally reported (30%) followed by 23% delay birth. Similarly still birth reported (13%) while premature birth as well as died after birth reported (17%) (Table 6).

Table 6: Prevalence of birth abnormalities in the married thalassemia minor people

Birth abnormalities	Frequency	Percent	Valid Percent	Cumulative Percent
Abortion	30	30.0	30.0	30.0
Pre Mature Birth	17	17.0	17.0	47.0
No Of Delayed Birth	23	23.0	23.0	70.0
No Of Still Birth	13	13.0	13.0	83.0
No Of Deaths After Birth	17	17.0	17.0	100.0
Total	100	100.0	100.0	

A survey was carried out in various areas of North Waziristan and Thalassemia Frontier Hospital of Peshawar. During this study data was collected from 100 people to find out the health status of thalassemia minor patients. During this study it was observed that majority of the patients were of the moderate body status (54.5%). Interestingly the ratio of obese people was very low during this study. While the ratio of thin people was 39.4 %(Table 7).

Table 7: List of physical status of thalassemia minor patients

Physical Status	Frequency	Percent	Valid Percent	Cumulative Percent
Thin	39	39.4	39.4	39.4
Moderate	54	54.5	54.5	93.9
Obese	7	6.1	6.1	100.0
Total	99	100.0	100.0	

According to this research work different physical abnormalities were found in the evaluated patients and it was observed that eye abnormality was the most (35%) followed by skin abnormality (17%), bone and joint abnormality (13%), ear abnormality (08%) and mental abnormality (02%) while 25% of evaluated member of the population were normal with no visible physical abnormality (Table 8).

Table 8: List of physical abnormalities found in thalassemia minor patients

Physical Abnormalities	Frequency	Percent	Valid Percent	Cumulative Percent
Eye abnormality	35	35.0	35.0	35.0
Mental abnormality	2	2.0	2.0	37.0
Ear abnormality	8	8.0	8.0	45.0
Bone and joint abnormality	13	13.0	13.0	58.0
Skin abnormality	17	17.0	17.0	75.0
Normal	25	25.0	25.0	100.0
Total	100	100.0	100.0	

During this research it was identified that Hb level found in thalassemia minor patient increases as the age increases. The people having the age from 1-10 have an average Hb level of 9.45 g/dl while those having age of 41-60 have an average Hb level of 11.58 g/dl (Table 9).

Table 9: Age wise Hb level in thalassemia minor patients.

Age(years)	Average of Hb level
1-10	9.45g/dl
11-20	10.6g/dl
21-30	11.21g/dl
31-40	11.4g/dl
41-60	11.58g/dl

During this survey 100 thalassemia minor patients from selected areas of Khyber pakhtunkhwa were interviewed, they were infected from different infections in which the most reported one in these people were eye infection which was 39% followed by Gastrointestinal Tract Infection (20%), Lung infection as well as Skin infection (16%) similarly Urinary Tract Infection and Ear infection were reported 7% and 2% respectively (Table 10).

Table 10: List of parasitic infection found in thalassemia minor patients

Infection	Frequency	Percent	Valid Percent	Cumulative Percent
Eye infection	39	39.0	39.0	39.0
Lung infection	16	16.0	16.0	55.0
UTI infection	7	7.0	7.0	62.0
GIT infection	20	20.0	20.0	82.0
Skin infection	16	16.0	16.0	98.0
Ear infection	2	2.0	2.0	100.0
Total	100	100.0	100.0	

DISCUSSION

α and β thalassemia are two main types of thalassemia, depends upon on whichpart of globin chain is formed in lower quantities[22]. Alpha Thalassemia The alpha thalassemia is initiated by a reduction in production of alpha globins chains due to one or more of the four alpha globin genes located on chromosome 16 being deleted or mutated[3]. There are two alpha thalassemia sub-types, Alpha Thalassemia Trait Also called as mild alpha-thalassemia. In these patient, two alpha globin genes have been losted[23]. Alpha Thalassemia Intermedia It is also called as hemoglobin H disease. Three alpha globin genes have lost in these patients. Patients with this disorder typically require blood transfusions to stay alive due to their severe anemia. Alpha thalassemia intermedia infants are born normal at birth but frequently progress anemia and splenomegaly by the end of their 1st year. It is uncommon to find hepatomegaly, and there may be some correlation with mental impairment. Due to the hemolytic nature of severe anemia may cause a rise in gallstones, leg ulcers, and respiratory infections. In hemoglobin H disease skeletal changes are not commonly seen[24]. Beta Thalassemia more than 200 mutations in the beta globin gene have been identified as producing beta thalassemia worldwide. beta thalassemia is caused by mutation on chromosome 11, Unlike the deletion that create most of the alpha thalassemia syndromes that affect all aspect of beta globin formation : stability of the beta globin production, transcription and translation[25].

The present study indicates that the frequency of thalassemia minor patient in both the males and females was high in the age group between 1-10 years, out of 51 males 16 (31.37%) and 18 (36.73%) females out of 49 were found in this range. The present study has somesimilarity with the study performed by Reza et al., (2012) in Iran[26]. They conducted a study on 100 patients of thalassemia in which 43 were females and 57 were males. Middle ages of females and males subjects were 18.5±14.9 and 13.3±6.9 years, respectively.

According to the present study different abnormalities were found in the evaluated patients and it was observed that eye abnormalities were found with high frequency of 35% followed by skin abnormality 17%, bone and joint abnormality13 %, ear abnormality 8% and mental abnormality 02 % while 25 % of evaluated member of the population were normal with no visible physical abnormality. The present study has some similarities with the study performed by Erickson et al, (1980)[27]. According to their study 15% of patients were having Superficial skin infections (tinea versicolor, other scabies, mycosis and pediculosis), 10% with psychiatric problems, 8% were having Otorhinological problems (deafness, otitis media, chronic sinusitis), and 6% were having opthalmological problems (conjunctivitis, cataract)[28].

During the present study it was identified that 38% of thalassemia minor patients were first cousin resulting in the Thalassemia major cases which are 60, 26% were second cousin and 36% of thalassemia minor patients were having no family relations. So the first cousin marriages was correlated with the highest percentage of thalassemia cases.. The present study shows some similarities with the study conducted by Ain et al., in 2011. According to them, first cousin relationships rather than unique ones are associated with the highest percentage of -thalassemia in patients[29].

During this study it was found that among the birth abnormalities the abortion is maximally reported (30%) followed by 23% delay birth. Similarly still birth reported (13%) while premature birth as well as died after birth reported (17%). According to Ali et

al., (2009) The largest study performed thus far assessed 44 TI women who had 83 unexpected pregnancies, including 53 from Italy and 30 from Lebanon. 20.5% of these pregnancies resulted in abortions[29].

According present study the ethnic groups having thalassemia minor from different parts of North Waziristan and Peshawar included Yousafzai, Halimzai, Dawar, Wazir, Noor khel, Musazai, Saidan, Miser khel, Afridi, Afghan and Miagan. According to Kumar et al., (2015) that the majority of the cases are from Jharkhand, Bihar, Chhattisgarh Madhya Pradesh, Uttarakhand, and Uttar Pradesh and neighboring country Nepal. Similarly according to Hafeez et al., (2007) Punjabis had the highest prevalence of β-thalassemia (60.7%), followed by Saraikees (25.5%). Caste-wise, Rajputs, Pathans, Sheikhs, Jatts, and Arian was most likely to experience it[30].

In the this survey the carrier were classified according to the economic condition, it was found that the maximum number of thalassemia minor patients belonged to lower class which was reported 47% ,followed by middle class (35%) and rich people(18%). According to Sengupta M in 2008 found that recent studies have suggested that this disorder is becoming more frequent because of poor income levels and a lack of awareness[31].

CONCLUSION

This study will provide base line information of thalassemia and its types and also provide awareness about thalassemia disease and it associated clinical conditions. On large scale numbers of study will be more helpful in the prevalence of thalassemia.

REFERENCES

1. Khan, J., et al., Haematological and Genetic Characterization of Thalassemia Intermedia in Tank and South Waziristan Agency of Khyber Pakhtun Khwa. Journal of Health Science, 2017. 7(3): p. 39-43.
2. Mankhemthong, K., et al., Molecular characteristics of thalassemia and hemoglobin variants in prenatal diagnosis program in northern Thailand. International Journal of Hematology, 2019. 110: p. 474-481.
3. Jasim, M.A. and A. Zgair, Hematological regulation using β-aminobutyric acid in staphylococcus aureus infected rats. Journal of Biotechnology Research Center, 2022. 16(02): p. 22-30.
4. RAHARJO, D.D.S., PREVALENSI TROMBOSITOPENIA PADA PASIEN KANKER PAYUDARA SETELAH KEMOTERAPI DI RSUD Dr. MOHAMMAD SOEWANDHIE SURABAYA PERIODE JANUARI–DESEMBER 2018. 2019, Universitas Airlangga.
5. Sylvester, R.J., et al., European Association of Urology (EAU) prognostic factor risk groups for non–muscle-invasive bladder cancer (NMIBC) incorporating the WHO 2004/2016 and WHO 1973 classification systems for grade: an update from the EAU NMIBC Guidelines Panel. European urology, 2021. 79(4): p. 480-488.
6. Batista, J.V., et al., Influence of UGT1A1 promoter polymorphism, α-thalassemia and β s haplotype in bilirubin levels and cholelithiasis in a large sickle cell anemia cohort. Annals of Hematology, 2021. 100: p. 903-911.
7. Li, J., et al., Prevalence, incidence, and outcome of non-alcoholic fatty liver disease in Asia, 1999–2019: a systematic review and meta-analysis. The lancet Gastroenterology & hepatology, 2019. 4(5): p. 389-398.
8. Yesilipek, M.A., et al., Thalassemia-free and graft-versus-host-free survival: outcomes of hematopoietic stem cell transplantation for thalassemia major, Turkish experience. Bone Marrow Transplantation, 2022. 57(5): p. 760-767.
9. Khan, H., et al., Exploration of solid waste materials for sustainable manufacturing of cementitious composites. Environmental Science and Pollution Research, 2022. 29(57): p. 86606-86615.
10. Ambaye, T.G., et al., Microbial electrochemical bioremediation of petroleum hydrocarbons (PHCs) pollution: Recent advances and outlook. Chemical Engineering Journal, 2022: p. 139372.
11. De Simone, G., et al., Thalassemias: From gene to therapy. Molecular Aspects of Medicine, 2022. 84: p. 101028.
12. Aziz, T., et al., A review on the modification of cellulose and its applications. Polymers, 2022. 14(15): p. 3206.
13. Nawab, T., et al., Multidimensional poverty index across districts in Punjab, Pakistan: estimation and rationale to consolidate with SDGs. Environment, Development and Sustainability, 2022: p. 1-25.
14. Khan, S.Y., et al., The role of FYCO1-dependent autophagy in lens fiber cell differentiation. Autophagy, 2022. 18(9): p. 2198-2215.
15. Singla, M., A. Chakrabarty, and S. Sengupta, Effect of multiple scattering on the Transmission spectra and the Polarization phase curves for Earth-like Exoplanets. arXiv preprint arXiv:2301.08487, 2023.
16. Khan, M.E., et al., Excellent visible-light photocatalytic activity towards the degradation of tetracycline antibiotic and electrochemical sensing of hydrazine by SnO2–CdS nanostructures. Journal of Cleaner Production, 2022. 349: p. 131249.
17. ul Ain, Q., M. Alam, and S. Anas, Response of two-way RCC slab with unconventionally placed reinforcements under contact blast loading, in Advances in Structural Mechanics and Applications: Proceedings of ASMA-2021 (Volume 3). 2022, Springer. p. 219-238.
18. Farooq, U., et al., EFFECT OF MORINGA OLEIFERA LEAVES ON HEMATOLOGICAL AND SERUM CHEMISTRY ATTRIBUTES OF APPARENTLY HEALTHY RABBIT DOES.
19. Menon, V., et al., Elevated p21 (CDKN1a) mediates β-thalassemia erythroid apoptosis but its loss does not improve β-thalassemic erythropoiesis. bioRxiv, 2022: p. 2022.03. 03.482874.
20. Kulkarni, H.V. and A. SenGupta, An Efficient Test for Homogeneity of Mean Directions on the Hyper-sphere. International Statistical Review, 2022. 90(1): p. 41-61.
21. Reis, F.M.P., et al., Discriminant indexes to simplify the differential diagnosis between iron deficiency anemia and thalassemia minor in individuals with microcytic anemia. Revista da Associação Médica Brasileira, 2020. 66: p. 1277-1282.
22. Victor, S., et al., System identification of MISO fractional systems: Parameter and differentiation order estimation. Automatica, 2022. 141: p. 110268.
23. Riquier, M.T., The ethics of genetic screening for beta thalassemia in Vietnam. Developing World Bioethics, 2022. 22(1): p. 44-52.
24. Cohen-Manheim, I., et al. Burns in Israel: Etiologic, Demographic, and Clinical trends—A 9-Year Updated Comprehensive Study, 2004–2010 versus 2011–2019. in Seminars in plastic surgery. 2022. Thieme Medical Publishers, Inc.
25. Steinberg, M.H., Targeting fetal hemoglobin expression to treat β hemoglobinopathies. Expert Opinion on Therapeutic Targets, 2022. 26(4): p. 347-359.
26. Dawood, K.A. and A.M. Jawad, Epidemiology of Thalassemia in Human of Babylon Iraq. Specialusis Ugdymas, 2022. 1(43): p. 6375-6380.
27. Hassan, S., et al., Next-Generation Sequencing (NGS) and Third-Generation Sequencing (TGS) for the Diagnosis of Thalassemia. Diagnostics, 2023. 13(3): p. 373.
28. Eini, M., M. Shoae, and E. Miri-moghaddam, Therapeutic approaches in patients with β-thalassemia. Iranian Journal of Pediatric Hematology and Oncology, 2022. 12(1): p. 55-67.
29. Jin, L.W., et al., The Impact of Chelation Compliance in Health Outcome and Health-Related Quality of Life in Thalassaemia Patients: A Systematic Review. 2022.
30. Panwar, N., et al., Pulmonary dysfunction in transfusion-dependent thalassemia and response to intensive chelation therapy. Indian Pediatrics, 2022. 59(6): p. 451-454.
31. Basu, T., et al., Clinico-Hematological Profile in Hemoglobin SE Disease: A Case Series from a Tertiary Care Centre. Indian Journal of Hematology and Blood Transfusion, 2022: p. 1-4.