International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 1 Jan-Feb 2024, pp: 977-984 www.ijprajournal.com ISSN: 2249-7781

Assesment and Analysis of Risk Factors Associated Withthalassemia in Pediatric Patients

Dr.Sravanthimuddada*, G.Pranathi, K. Rushali Reddy, N.Geethanjali
Department of pharmacy practice, Sri Venkateswara college of pharmacy, Etcherla, Andhra Pradesh, INDIA.

Submitted: 20-01-2024 Accepted: 30-01-2024

ABSTRACT:
Introduction: Thalassemia has inherited blood disorder. It makes fewer healthy red blood cells and less hemoglobin than normal. People who have thalassemia can have mild or severe anemia. HB is an iron-rich protein in RBC. Normal hemoglobin, also called hemoglobin A, has four protein chains - two alpha-globin and two beta-globin. Two major types of thalassemia alpha and betaare named after defects in these protein molecules. **Objectives:** To Assess the risk factors associated with thalassemia, to know the prevalence of thalassemia in pediatric patients and to know the complications associated with thalassemia. **Methods:** A prospective and cross-sectionalstudy was done in 55 patients and age group of 12 years were only included in this study. **Results and discussion:** From these male children are more in number compared to female children. Male children are 29 in number and the percentage was 52.72% and female children are 26 in number and the percentage was found to be 47.27% and 72.72% of marriages of patient's parents were consanguineous marriages and 15 cases i.e.27.27% of marriages of patient's parents were non- consanguineous marriages. The risk factor of grade 2 splenomegaly was 32.72%. The next highest was grade 3 and the percentage was 14.54%. The least cases are seen in grade 1 and the percentage was 7.27% **Conclusion:** Overall our study concluded that male children are more effected than the female children and the major risk factor for thalassemia was found to be the consanguineous marriage of patient's parents. Complications like splenomegaly and hepatomegaly were also observed, grade 2 splenomegaly was mostly observed than other grades.

Key words: Thalassemia, splenomegaly, consanguineous

I. INTRODUCTION

Thalassemia has inherited blood disorders. The word thalassemia derives from the Greek Thalassa means "sea" and New Latin -emia. It wascoined because the condition called "Mediterranean anemia" was first described in people of Mediterranean ethnicities. "Mediterranean anemia" was renamed thalassemia major once the genetics were better understood. The word thalassemia was first used in 1932. It makes fewer healthy red blood cells and less hemoglobin than normal. People who have thalassemia can have mild or severe anemia. HB is an iron-rich protein in RBC. Normal hemoglobin, also called hemoglobin A, has four protein chains - two alpha-globin and two beta-globin. Two major types of thalassemia alpha and beta are named after defects in these protein molecules.

TYPES:
α- THALASSEMIA
1. Hydrops fetalis
2. Hb – H disease
3. α- thalassemia trait
β- THALASSEMIA
1.β-thalassemia major
2. β- thalassemia intermedia
3. β- thalassemia minor

HYDROPS FOETALIS:

Hydrops fetalis is a rare but noble cause of perinatal morbidity and mortalitycaused by accumulation of interstitial fluid in fetus. Hematologicalcauses of thisinclude immuneand non-immune mediated mechanisms. α – thalassemia. Thethalassemia's are the most common monogenic diseases. The hallmark of this disease is an imbalancein globin-chain production in the adult α2β2-hemoglobin (Hb)molecule. In homozygousα-thalassemia, deletion of both copies of each of the two α-globin genes on chromosome 16 occurs, thus no α-globin is produced (α0) The tetramers that are made, Hb Bart's (γ4) and Hb H (β4), behave instead likemyoglobin in that they do not readily give up oxygen at physiologic tensionsleading to severe hypoxia. Typically, these new-borns die in uterus in the thirdtrimester or in the early postnatal period from severe hypoxia, and have congestive heart failure, ascites, edema, and hepato-splenomegaly.

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 1 Jan-Feb 2024, pp: 977-984 www.ijprajournal.com ISSN: 2249-7781

Hb- H DISEASE:

Hb H disease results from double heterozygosity for alpha (0)-thalassemia due to deletions that remove both linked alpha-globin genes on chromosome 16, and deletionalalpha (+)-thalassemia from single alpha-globin gene deletions (--/-alpha). However, Hb H disease may occur from interactions between alpha (0)-thalassemia with non-deletional mutations (alpha(T)alpha or alpha(T)) or withabnormal hemoglobin's.

α – THALASSEMIA TRAIT:

There are two types of alpha thalassemia traits.

- The first type has one alpha gene missing on each chromosome. This is called the transform of alpha thalassemia trait.
- The second type has two missing alpha genes on the same chromosome. This iscalled the cis form of alpha thalassemia trait.

β –THALASSEMIA MAJOR:

This is the most severe type of beta thalassemia. It is often found during the first 2 years of life.Children often need frequent blood transfusions. This can cause serious problems with ironoverloads are common. Severe anemia develops and is associated with fatigue, weakness,shortness of breath, dizziness, headaches, and yellowing of the skin, mucous membranes, andwhites of the eyes (jaundice). Affected infants often fail to grow and gain weight as expected.based upon age and gender. Feeding problems, diarrhea, irritability or fussiness, recurrent fevers, abnormal enlargement of the liver (hepatomegaly), and abnormal enlargement of the spleen(splenomegaly) may also occur.

β-THALASSEMIA INTERMEDIA:

Individuals diagnosed with beta thalassemia intermedia have a widely varied expression of thedisorder. Moderately severe anemia is common and affected individuals may require periodicblood transfusions.

β-THALASSEMIA MINOR:Carriers of thalassemia minor are usually clinically asymptomatic but sometimes have mildanemia. When both parents are carriers there is a 25% risk at each pregnancy of having childrenwith homozygous thalassemia.

CAUSES:

- Thalassemia is caused by mutations in the DNA of cells that make hemoglobin.
- If only one of your parents has a carrier for thalassemia, you may develop a form of thedisease known as thalassemia minor.

RISK FACTORS:

- Family history: The genes for the disorder are passed from the parents to their children.
- Ancestry: Thalassemia most often occurs in the people of Greek, Italian, Middle Eastern,Southern Asian, and African descent.

COMPLICATIONS:

- Heart and liver diseases: regular blood transfusions are the standard treatmentfor thalassemia. Transfusions can cause iron to build up in the blood (iron overload). This candamage organs and tissues, especially the heart. Heart disease includes heart failure,arrhythmias, and heart failure and it is the main cause of deaths in people withthalassemia.
- Infections: Infections are the key cause of illness and the second most common cause ofdeath in patients of thalassemia's. People who have had their spleen removed are at evenhigher risk because they no longer have their infection-fighting organ.
- Osteoporosis:Many people who have thalassemia have bone problems osteoporosis.This is a condition in which bones are weak and brittle.

SIGNS AND SYMPTOMS:

- No symptoms – in alpha thalassemia they are silent carriers.
- Mild anemia – people who have an alpha or beta thalassemia trait.
- Mild to moderate anemia – people who have beta-thalassemia intermedia.

METHODOLOGY

STUDY DESIGN: It is a prospective and cross-sectional study.

STUDY DURATION: It is a 6 months' study conducted after approval of ethical committee.

SAMPLE SIZE:fifty-five patients

STUDY APPROVAL: The institutional ethical committee of government medical college and general hospital Srikakulam approved the study.

STUDY LOCATION: Government general hospital Srikakulam. Itis a1000 bedded general district hospital which is being runned by

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 1 Jan-Feb 2024, pp: 977-984 www.ijprajournal.com ISSN: 2249-7781

government of Andhra Pradesh. It is one of the premierinstitutes in A.P. with around 12 specialtiesserving the huge number of populations who are inneed of medical care.

STUDY CRITERIA:

Inclusion criteria:

- Age (below 12 yrs)
- Gender
- Percentage of hemoglobin
- Socio economic status
- Type of marriage
- Family history
- Aetiology
- Average number of transfusions
- Transfusion related problems
- Complications

Exclusion criteria:

- Age above 13 years

STUDY PROCEDURE:

- Approaching the pediatric ward
- Observing the thalassemia case

Approaching the patient's representative, talking about the project, and taking theconsent of the representative

- taking the information about the patient in detail
- filling the patient consent form

STUDY SETTING: The study was based on the patients who are affected by thalassemia whoare admitted to the government general hospital. The data is collected by approaching the patientadmitted in pediatric ward.

SOURCE OF DATA: The data was collected by approaching the pediatric ward, approaching the representative of patient,and observing the case sheet which is written by the physician.

RESULTS: The presence of a chronic disease like thalassemia has a tremendous impact on patients and their families. The present study was designated to identify the risk factors of thalassemia on patients. Thalassemia patients required regular attention throughout their life. It is a lifelong illness and has a devastating impact on the patients and their family life. In our study period of 6 months, we have observed fifty-five cases of thalassemia.

Figure-1and Table-1shows demographic characters of patients.In a 6 month of the study period, 55 cases of thalassemia are noted, among them, female children were 26(47.27%) and male children were 29(52.72%). The patients age group is 0-12. among them patients who were of 0-3 age are 20 members of them females were 8(30.76%) and males were 12 (41.37%), 4-6 age group members counted 9 and of them, females were 5(19.23%) and males 4(13.79%), children of age 7-9 are 15 in which females are 10(38.46%)and males are 5(17.24%), children of age group 10-12 are 11 and of them, female was 3 (11.53%) and males are 8(27.58%).

Figure-1: Bar graph showing different age groups of children effected with thalassemia.

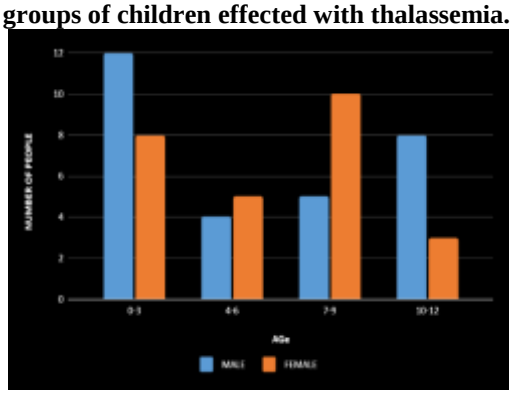
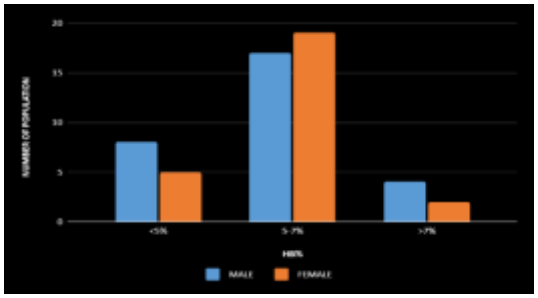


Table-1: Table showing statistical analysis of Different age groups of children affected with Thalassemia.

Age group	Mean Standard Deviation	P - Value
0-3	10± 2.83	0.195059
4-6	4.5 ± 0.71	
7-9	7.5 ± 3.54	
10-12	5.5 ± 3.54	

Figure-2 and Table-2 shows the hemoglobin percentage of the children areconsidered between7%. Female children who have 7% Hb values are 2 (7.69%) and coming to males the number is 4(13.79%).

Figure-2: Bar graph shows the percentage of hemoglobin present in male and female children.



International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 1 Jan-Feb 2024, pp: 977-984 www.ijprajournal.com ISSN: 2249-7781

Table-2: The Statistical analysis of percentage of the hemoglobin present in male and female children.

Hb%	Mean Standard Deviation	P - Value
<5%	6.5 ± 2.12	0.519352
5-7%	18 ± 1.41	
>7%	3 ± 1.41	

Figure-3 and Figure-4 show consanguineous marriagesfemale patient's parents is 19(73.07%) and male is 21(72.41%) and non-consanguineous of female patient's parent is 7(26.92%) and male is 8(27.58%).

Figure-3: The bar graph showing the type of marriage of patients and the number of people affected.

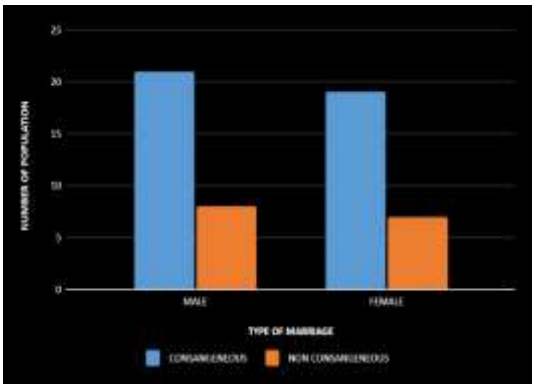


Figure-4: The bar graph shows the standard deviation of the consanguineous marriage.

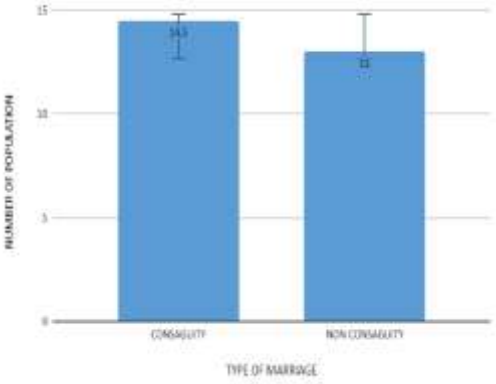


Table-3 and Figure-5 noticed about family history and found 3(11.53%) of the female children have a family history and 2(6.89%) of male children have a family history of thalassemia. female children who do not have family history 23 and male are 27 in number.

Table-3: Statistical analysis of the standard deviation of family history.

Family History	Mean Standard Deviation	P - Value
Present	2.5 ± 0.7.71	0.549939
Absent	25± 2.8284	

Figure-5: Statistical analysis of the standard deviation of family history.

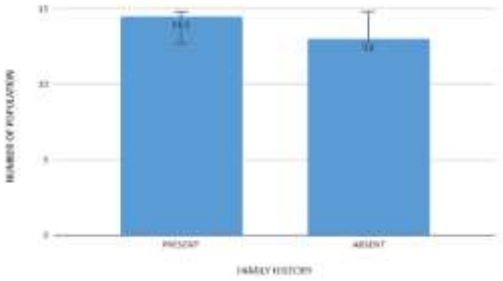


Figure-6 shows the financial condition of the parents of the affected child 2 (6.89%)of the male and 2 (7.6%)of the female children's parents are in good condition and 27 (93.10%)of male children and 24(92.30%) of female children are in poor condition.

Figure-6: The bar graph shows the financial condition of the patient's parents.

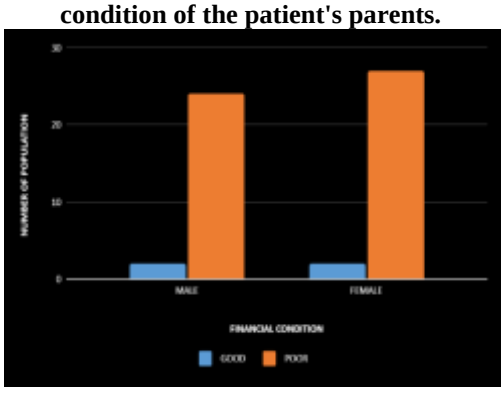


Figure-7 and Figure-8 shows the grades of splenomegaly were also observed and there are 5 grades of splenomegaly of the female children who don't have splenomegaly which means grade 0, 10(38.46%) and male children are 9(31.03%). Female children who have grade 1 splenomegaly are 4(15.38%) and males are 0. Female children who have grade 2 splenomegaly are 7(26.92%) and males are 11(37.93%). Grade 3 splenomegaly female children are 3(11.53%) in number and

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 1 Jan-Feb 2024, pp: 977-984 www.ijprajournal.com ISSN: 2249-7781

males are 5(17.24%). Female children who have grade 4 splenomegaly are 1(3.84%) in number and male children are 4(13.79%) in number. Grade 5 splenomegaly was not observed, and one female child's spleen was removed.

Figure-7: The bar graph representing the grades of splenomegaly and the number of the population affected.

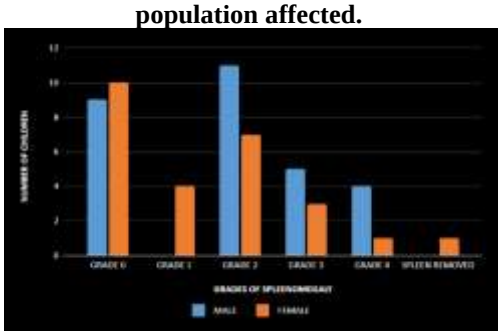
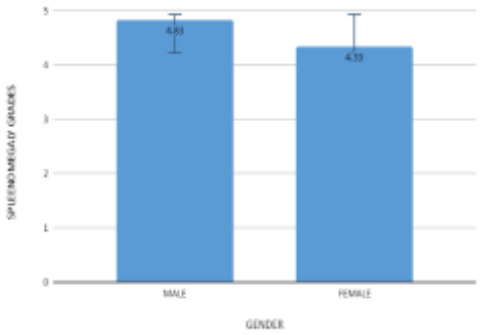


Figure-8: The bar graphs showing the standard deviation of splenomegaly grades.



II. DISCUSSION:

In our study period of 6 months, we have observed 55 cases of thalassemia. In that male children are more in number compared to female children. Male children are 29 in number and the percentage was 52.72%.The majority of the parent's parents were illiterate and their monthly income was very low to bear the cost of the blood transfusion and medicines.Due to socio-cultural practices, marriages in India are usually among individuals of the same caste or ethnic group and this makes it important to know the prevalence of β-thalassemia in different ethnic groups. The cousin marriages of the parents are high and also it is the major risk factor for the thalassemia. 40 cases i.e 72.72% of marriages of patient's parents were consanguineous marriages and 15 cases i.e.27.27% of marriages of patient's parents were non-consanguineous marriages. Our study indicated that the major risk factor for thalassemia was consanguineous marriages of parents.Due to the regular blood transfusions the spleen and liver of children were damaged. Here we have taken the grades of splenomegaly and found grade 2 splenomegaly was more than 18 cases are observed the percentage was 32.72% among those 18 cases 11 are male and 7 are female. The next highest was grade 3 in that a total of 8 cases was observed and the percentage was 14.54% in which males are 5 in number and females are 3 in number. In grade 4 a total of 5 cases are seen i.e9.09% in that males are 4 in number and 1 female child was seen. The least cases are seen in grade 1 in which 4 cases are identified 7.27% was the percentage, in this males are nil and female are 4 in number. One case was identified in which the female child's spleen was removed. As Thalassemia is one of the forms of anemia's the percentage of hemoglobin is also noted in our study.

III. CONCLUSION:

In this study we conclude that the male children are more effected than the female children and the major risk factor for thalassemia was found to be the consanguineous marriage of patient's parents. The economic status of the parents is poor. Children come here monthly for regular blood transfusion. The children of age group 0-3 are more in number than other age groups. Complications like splenomegaly and hepatomegaly were also observed, grade 2 splenomegaly was mostly observed than other grades. The prevalence of thalassemia in the department of pediatrics in government general hospital Srikakulam was found to be 8.75%.

CONFLICT OF INTEREST: No conflicts of interest.

REFERENCES:

[1]. Bank,G.R.OVERVIEW ON THALASSEMIAS: A REVIEW ARTICLE.
[2]. Galanello, R., &Origa, R. (2010). Beta-thalassemia. Orphanet journal of rare diseases, 5(1),11.
[3]. Hossain, M. S., Raheem, E., Sultana, T. A., Ferdous, S., Nahar, N., Islam, S., ... &Khatun, H.(2017). Thalassemias in South Asia: clinical lessons learnt from Bangladesh. Orphanetjournal of rare diseases, 12(1), 93.
[4]. Innovare, I. BETA THALASSEMIA IN INDIA: CURRENT STATUS AND THE

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 1 Jan-Feb 2024, pp: 977-984 www.ijprajournal.com ISSN: 2249-7781

CHALLENGESAHEAD. technology, 15, 17.

[5]. Joshi, D. D., Nickerson, H. J., & McManus, M. J. (2004). Hydrops Fetalis Caused byHomozygous α-Thalassemia and Rh Antigen Alloimmunization Report of a Survivor andLiterature Review. Clinical medicine & research, 2(4), 228-232.

[6]. El Kamah, G., & Amr, K. (2015). Thalassemia-From Genotype toPhenotype. InheritedHemoglobinDisorders. AnjanaMunshi. Inde, 13-33.

[7]. Leecharoenkiat, K., Lithanatudom, P., Sornjai, W., & Smith, D. R. (2016). Iron dysregulationin beta-thalassemia. Asian Pacific journal of tropical medicine, 9(11), 1035-1043.

[8]. Chuncharunee, S., Teawtrakul, N., Siritanaratkul, N., &Chueamuangphan, N. (2019). Reviewof disease-related complications and management in adult patients with thalassemia: Amulti-center study in Thailand. PloS one, 14(3).

[9]. Nienhuis, A. W., & Nathan, D. G. (2012). Pathophysiology and clinical manifestations of β-thalassemias. Cold Spring Harbor perspectives in medicine, 2(12), a011726.

[10]. Fibach, E., &Rachmilewitz, E. A. (2017). Pathophysiology and treatment of patients withbeta-thalassemia.

[11]. Ishfaq, K., Naeem, S. B., & Ali, J. (2013). SOCIO-ECONOMIC FACTORS OF THALASSEMIAMAJOR ON PATIENTS'FAMILIES: A CASE STUDY OF THE CHILDREN'S HOSPITAL AND THEINSTITUTE OF CHILD HEALTH MULTAN, PAKISTAN. Int. J. med. Appl. health. Vol, 1(1).

[12]. ISHFAQ, K., DIAH, N. M., ALI, J., Fayyaz, B., &Batool, I. (2018). Psychosocial Problems Facedby Thalassemia Major Patients of District Multan, Pakistan. Pak Pediatr J, 42(1), 22-26.

[13]. Saeed, U., &Piracha, Z. Z. (2016). Thalassemia: impact of consanguineous marriages on most prevalent monogenic disorders of humans. Asian Pacific Journal of Tropical Disease, 6(10),837-840.

[14]. Colah, R., Italia, K., &Gorakshakar, A. (2017). Burden of thalassemia in India: The road mapfor control. PediatricHematology Oncology Journal, 2(4), 79-84.

[15]. Sharma, D. C., Arya, A., Kishor, P., Woike, P., &Bindal, J. (2017). Overview on thalassemias: are review article. Med. Res. Chron, 4(3), 325337.

[16]. "What Are Thalassemia?" NHLBI. July 3, 2012. Retrieved 5 September 2016

[17]. What Causes Thalassemia's? NHLBI. July 3, 2012.Retrieved 5 September 2016. 6. John NL.The thalassemia and related disorders: Quantitative disorders of hemoglobin synthesis;Wintrobe's

[18]. Clinical Hematology, tenth edition, Vol. I, chapter 1999 53:1405–1448.

[19]. Global Burden of Disease Study 2013. Lancet (London England) 2013; 386(9995):743-899.

[20]. GBD 2013 Mortality and Causes of Death, Collaborations (17 December 2014). Globalregional and national agesex specific all cause and cause-specific mortality for 240 causes ofdeath,19902013: a systematic analysis for the Global Burden of Disease Study2013.Lancet.385:117-71

[21]. How Are Thalassemia Diagnosed? NHLBI.July 3, 2012.Retrieved 5 September 2016.

[22]. Thuret I (2000) Therapeutic management of patients with thalassemia major. BullSocPatholExot 94:95–97

[23]. Proter JB (1997) Practical management of iron overload. CurrOpinHematol 4:436–441

[24]. Graziano JH, Markenson A, Miller DR et al (1978) Chelation therapy in βthalassemia majorintravenousand subcutaneous desferoxime. J Paediatr 92:646–651

[25]. Cazzola M, Stefeno PD, Panchio L et al (1995) Relationship between transfusion regimenand suppression of erythropoiesis in β-thalassemia major. British J Hematology 89:473–478

[26]. Caro, JJ., A. Ward., T.C. Green., K. Huybrechts., A. Arana., S. Wait., and A.Eleftheriou, 2002. Impact of Thalassemia Major on Patients and theirFamilies.ActaHaematol., 107:150-157.

[27]. Hafeez, M., M. Aslam., A. Ali., Y. Rashid and H.Jafri, 2007. Regional and ethnic

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 1 Jan-Feb 2024, pp: 977-984 www.ijprajournal.com ISSN: 2249-7781

distributionof beta thalassemia mutations and effect of consanguinity in patients referred for prenataldiagnosis. J. Coll Physicians Surg Pak., 17(3): 144-147.

[28]. Najmabadi H, Karimi-Nejad R, Sahebjam S, Pourfarzad F, Teimourian S, Sahebjam F,Amirizadeh N, Karimi-Nejad MH. The beta-thalassemia mutation spectrum in the Iranianpopulation. Hemoglobin 2001; 25:285-96.

[29]. Merat A, Haghshenas M, Mostafavi Pour Z, Plonczynski MW, Harrel AN, Coleman MB,Steinberg MH. Beta-thalassemia in Southwestern Iran. Hemoglobin 1993; 17:427-37. 3.Thein SL. Beta-thalassemia. Bailliere'sClinHematol1998; 11:91-126.

[30]. Pippard MJ, Callender ST, Warner GT, Weatherall DJ. Iron absorption and loading in beta-thalassaemia intermedia. Lancet 1979; 2: 819-21.

[31]. Hershko C, Weatherall DJ. Iron-chelating therapy. Crit Rev Clin Lab Sci 1988; 26: 303-45

[32]. Hershko C, Konijn AM, Link G. Iron chelators for thalassaemia. Br J Haematol 1998; 101:399-406.

[33]. Risdon RA, Flynn DM, Barry M. The relation between liver iron concentration and liverdamage in transfusional iron overload in thalassaemia and the effect of chelation therapy.Gut 1973; 14: 421.

[34]. Vogiatzi MG, Macklin EA, Fung EB, et al. Bone disease in thalassemia: a frequent and stillunresolved problem. J Bone Miner Res 2009; 24:543-57.

[35]. Haidar R, Musallam KM, Taher AT. Bone disease and skeletal complications in patients withbeta thalassemia major. Bone 2011; 48:425-32.

[36]. Fung EB, Harmatz PR, Milet M, et al. Fracture prevalence and relationship toendocrinopathy in iron overloaded patients with sickle cell disease and thalassemia. Bone2008; 43:162-8

[37]. Wong P, Fuller PJ, Gillespie MT, et al. Thalassemia bone disease: a 19-year longitudinalanalysis. J Bone Miner Res 2014; 29:2468-73.

[38]. Rund D, Rachmilewitz E. Beta-thalassemia. N Engl J Med 2005; 353:1135-46.

[39]. Cappellini MD. The Thalassemias. In: Goldman L, Schafer AI, eds. Goldman-Cecil Medicine:Expert Consult - Online. 25 ed: Elsevier Health Sciences; 2015:1089-95.

[40]. Taher AT, Musallam KM, Inati A. Iron overload: consequences, assessment, and monitoring.Hemoglobin2009;33 Suppl1:S46-57.

[41]. Anand Kumar, K., Radhakrishna, N., &Sachdeva, A. (2014). Management of thalassemia inIndian perspective. Thalassemia: National Guidelines for anagement of transfusion-dependent thalassemia and non-transfusion dependent thalassemia, 296-302.

[42]. Aessopos A, Farmakis D, Deftereos S, Tsironi M, Tassiopoulos S, Moyssakis I, Karagiorga M.Thalassemia heart disease: a comparative evaluation of thalassemia major and thalassemiaintermedia. Chest. 2005 May 1;127(5):1523-30.

[43]. Borgna-Pignatti CA, Rugolotto SI, De Stefano P, Zhao HU, Cappellini MD, Del Vecchio GC,Romeo MA, Forni GL, Gamberini MR, Ghilardi R, Piga A. Survival and complications inpatients with thalassemia major treated with transfusion and deferoxamine. haematologica.2004 Jan 1;89(10):1187-93.

[44]. Pollak RD, Rachmilewitz E, Blumenfeld A, Idelson M, Goldfarb AW. Bone mineralmetabolism in adults with β-thalassaemia major and intermedia. British journal ofhaematology. 2000 Dec;111(3):902-7.

[45]. Borgna-Pignatti C, Gamberini MR. Complications of thalassemia major and their treatment.Expert review of hematology. 2011 Jun 1;4(3):353-66.

[46]. Pirastu M, Kan YW, Cao A, Conner BJ, Teplitz RL, Wallace RB. Prenatal diagnosis of β-thalassemia: detection of a single nucleotide mutation in DNA. New England Journal ofMedicine. 1983 Aug 4;309(5):284-7.

[47]. Cao A, Galanello R. Beta-thalassemia. Genetics in medicine. 2010 Feb;12(2):61-76.

[48]. Galanello R, Sollaino C, Paglietti E, Barella S, Perra C, Doneddu I, Pirroni MG, Maccioni L, CaoA. α-thalassemia carrier identification by DNA analysis in the screening for thalassemia.American journal of hematology. 1998 Dec;59(4):273-8.

[49]. Porter JB. Pathophysiology of transfusional iron overload: contrasting patterns inthalassemia major and sickle cell disease. Hemoglobin.2009Jan1;33(sup1):S37-45.
[50]. Giardini C, Galimbbrti M, Lucarelli G, Polchi P, Angelucci E, Baronciani D, Gaziev D, Erer B,Nasa GL, Barbanti I, Muretto P. Desferrioxamine therapy accelerates clearance of irondeposits after bone marrow transplantation for thalassaemia. British journal ofhaematology. 1995 Apr;89(4):868-73.