DIFFERENT TYPES OF COMPLICATIONS IN PATIENTS SUFFERING FROM B-THALASSEMIA (THALASSEMIA MAJOR)

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ABSTRACT

INTRODUCTION

Thalassemia is a heterogeneous group of gene disorders caused byan inherited mutation or deletion of genes at chromosome 16 & 11 resulting in decreased synthesis of adult hemoglobin. Its incidence is higher in people/children having a positive family history of Thalassemia Among its various types Beta Thalassemia major is the one which requires regular blood transfusions.

OBJECTIVES

The main objective of the study was to determine the frequency of different types of complications in patients suffering from B-Thalassemia.

METHODOLOGY

The study was conducted in two private originations in Peshawar i.e. Fatimid Foundation and Hamza Foundation.150 patients) were studied, the study was Cross-Sectional, descriptive type and sampling type was Non-Probability, convenience type sampling. All necessary data were obtained by using semi structured questionnaire, having both closed and open ended questions. Pilot Study was conducted on 15 patients (10%of target questionnaires). After completing the pilot study necessary changes were made in questionnaire and a well-informed, well-designed and organized questionnaire was finalized. An informed consent was taken from respondents and the responses were obtained each from the parents & from children themselves (in case of older children). Data was collected and results were presented in the form of tables and charts. Manual analysis of the data was carried out.

RESULTS

According to the study, among 150 patients, Splenectomy was done in about 86% patients. Consanguinity among the parents of these patients was about 76%, while awareness only 72% of patients. About 64% patients were having psychological problem. Among neurological problems 57% of patients had headache. Among complications, majority of patients had palpitations about 54% joint pains about 32% & history of bones fractures about 21%. Socioeconomic condition of majority of them was poor about 52%. All of them were taking primary treatment i.e. Blood transfusion &Chelating Therapy to prevent iron overload.

CONCLUSSIONS

Thalassemia major is a life threatening disease causing morbidity and mortality among those who are not treated properly. The incidence of the disease is high among those with a family history of Thalassemia.

***KEY WORDS**: Thalassemia major, inherited mutation, chelating therapy. Splenectomy*

INTRODUCTION

Thalassemia is the commonest inherited disorder present throughout world affecting approximately 5% of the world population. Beta-Thalassemia Major affects a significant segment of population in certain areas of the world. Alternation in migration patterns have changed the geographic distribution of this disease and have made it a worldwide disease health problem with a high frequency in Africa, India, Southeast Asia and Mediterranean area.[1] Thalassemia is a heterogeneous group of genetically determined hemolyticanemias due to an impaired synthesis of globins' chains which are an integral part of the hemoglobin molecule.[2] There are two types of Thalassemia: Alpha-Thalassemia and Beta-Thalassemia. Alpha-Thalassemia is a disorder in

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which there is defective synthesis of α-globins chains resulting in depressed production of hemoglobin that contain α-chains i.e. HbA_1, HbA_2 and HbF[3]. Beta-Thalassemia is a common autosomal recessive disorder generally caused by point mutations in β-globins gene that is located as a cluster on the short arm of chromosome 11.[4,5.] Beta-Thalassemia occurs worldwide, with a higher prevalence among Mediterranean population, in the Middle East, in parts of India, Pakistan, and South East Asia. It is also prevalent in southern parts of former USSR and People's Republic of China. It is seen in all racial groups, even in the homozygous states, in persons of pure Anglo0Saxon stock. In Pakistan, the disease is seen in almost all parts of the country. The estimated carrier status is around 5-7% meaning thereby that there are about 9.8 million carriers in the total population. Although no documented registry of Thalassemia patients exists in Pakistan, the estimate is that approximately 9000 Beta Thalassemia children are born every year. The average life expectancy in Pakistan is 10 years and at present the disease load is of 90000 to 100000 patients throughout the country. [5]

In Pakistan it is the β-Thalassemia which is the most prevalent; other forms of Thalassemia are uncommon. Gene frequency of β-Thalassemia in Pakistan stands at 6% with a population of 140 million; there are over 8 million carriers of β-Thalassemia. Inter-marriages and first cousin marriages has resulted in high incidence of homozygous β-Thalassemia (β-Thalassemia major). It is estimated that in Pakistan at present there are about 121,000 patients of β-Thalassemia major.[5] Over 5000 children are born with transfusion dependent Thalassemia annually in Pakistan and 65% of them belong to KPK.[6] The major life threatening complications of B-Thalassemia are due to Iron overload, Infections, and Transfusion reactions.[7] The management of Beta-Thalassemia includes: Conservative Management which includes Regular blood transfusion, Iron Chelating agents and Management of complications. In developing countries patients are not ideally managed on the conservative regiment due to a number of reasons. It is partially the unavailability of safe blood, lack of education and poverty. Curative Treatment: includes bone Marrow transplantation.[8] The basic aim of management of the disease is to alleviate the anemia by blood transfusion therapy, maintaining a mean Hb level of at least 10g/dl at different weekly intervals. In order to prevent accumulation of iron, iron-chelating agents are used as chelating therapy to reduce the resulting hemosidrosis and organ failure.[7]

METHODOLOGY

This study was conducted to determine frequency of various complications of Beta-Thalassemia Major and its management and was carried out in Fatimid Foundation and Hamza Foundation Peshawar. Our study population included all Thalassemia patients suffering with B- thalassemia visiting Fatimid Foundation and Hamza Foundation, irrespective of their age and sex. This study was carried out from 1st November 2016 to 29thApril 2017.The sampling technique for our study was Non-Probability, Convenience Sampling. Sample of 150 respondents were included in the study.. The study design was Observational Cross-Sectional Study. Patients suffering from beta thalassemia of all ages were included in the study sample. Patients suffering from other types of thalassemia and receiving treatment outside of Peshawar were excluded from the study.

The questionnaire was designed to collect data from patients. Both open and close ended questions were included in questionnaire. The reason being to ensure objectivity as it was the only feasible method which could have help in getting the required information and to ensure statistical analysis. Firstly, Pilot Study was conducted on 15 patients (10% of target questionnaire). The purpose was to check the feasibility of questionnaire and to make necessary changes in required. In order to make it more informative and organized. After completing the pilot study necessary.

To study the complications of β-Thalassemia major & its management in (150) patient's changes were made in questionnaire and a well-informed, well-designed and organized questionnaire was finalized. An informed consent was taken from respondents and the responses were obtained each from the parents and from children themselves (in case of older children). Final data was collected and transferred to computer, compiled and processed and was presented on the master sheet, tables, bars and pie charts for analysis and statistical evaluation.

RESULTS

TABLE NO. 01

AGE OF THE REPONDENTS			
S. No	**DIAGNOSTIC AGE**	**OBSERVATION**	**PERCENTAGE**
1	BELOW 10 YEARS	77	51.33%
2	10 to 15 YEARS	54	36.00%
3	15 to 20 YEARS	14	9.33%
4	ABOVE 20 YEARS	05	3.34%
SS	**Total**	**150**	**100%**

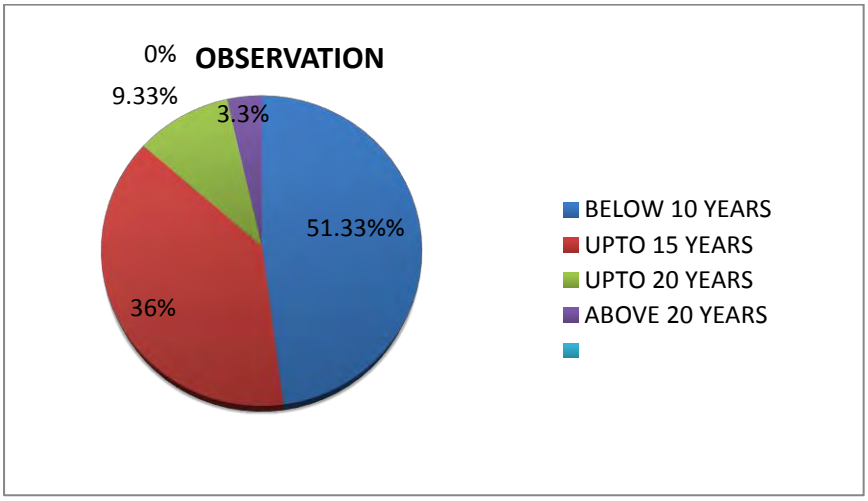


Table and fig no.1 shows different age groups of the respondents, showing that out of total150 respondents, most of the respondents are under the age of 10 years, i.e. 77(51%), 54 (36%) are upto 15 years of age, 14(9.3%) respondents are upto 20 years while on 05 (3.3%) are above 20 years of age.

Table No. 02

GENDER STATUS OF THE RESPONDENTS			
S. NO	**GENDER**	**OBSERVATION**	**PERCENTAGE**
1	MALE	88	58.66%
2	FEMALE	62	41.33%
	TOTAL	150	100%

Majority of the respondents are male, i.e. 88 (59%) while the remaining 62(41%) are female respondents, depicted in table and fig no. 2.

Table No. 03

FAMILY'S SOCIOECONOMIC CONDITION			
S. NO	**SOCIOECONOMIC CONDITION**	**OBSERVATION**	**PERCENTAGE**
1	POOR	78	52.00%
2	SATISFACTORY	56	37.34%
3	GOOD	16	10.66%
	TOTAL	150	100%

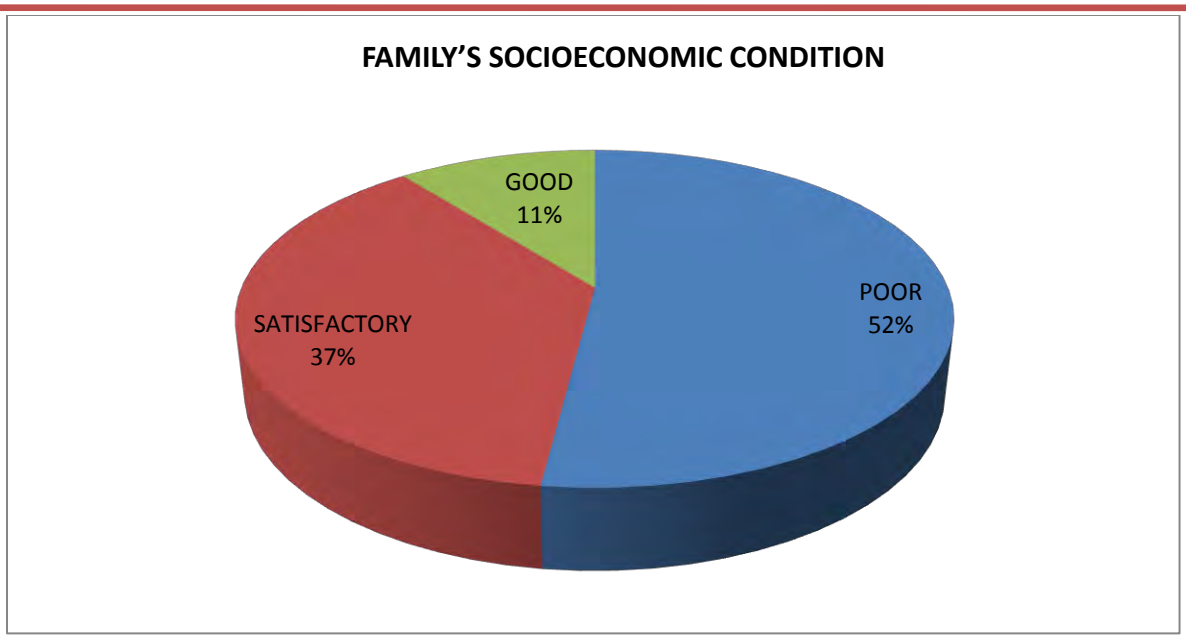


Table and fig no. 3 is showing the socioeconomic condition of the patient's family. In this result we found that majority of the respondents i.e.78 (52%), belongs to poor families, few of them i.e. 56(37%) had satisfactory socioeconomic condition while very few i.e. only 16 (11%) are in a good socioeconomic condition.
During our survey, we found that 55% of respondent's siblings were also having Thalassemia while the remaining 45% were free of this disease. These results are shown in table and fig no. 6

Table No. 04

FAMILY HISTORY OF THALASSEMIA			
S . NO	**FAMILY HISTORY**	**OBSERVATION**	**PERCENTAGE**
1	YES	53	35.34%
2	NO	97	64.66%
	TOTAL	150	100%

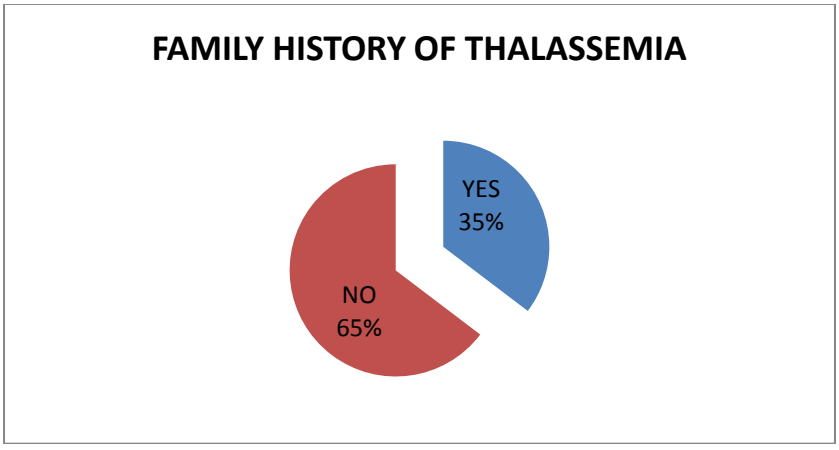
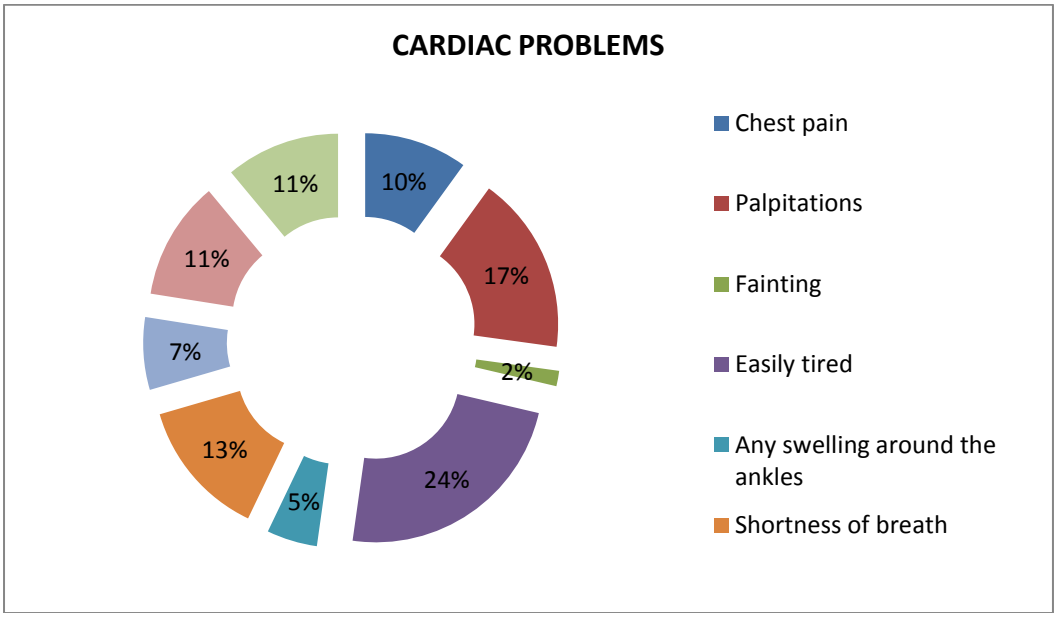


Table and fig no. 04 shows that majority of the respondents i.e. 97(65%) were not having any family history of Thalassemia while in 53 (35%) patients we saw that this disease was running in their families.

RELATED TO CARDIAC COMPLICATIONS

Table No. 05

CARDIAC PROBLEMS TO THE RESPONDENT			
S. No	**Cardiac problems**	**Observation**	**Percentage**
1	Chest pain	47	31.34%
2	Palpitations	81	54.00%
3	Fainting	07	04.66%
4	Easily tired	111	74.00%
5	Any swelling around the ankles	23	15.34
6	Shortness of breath	63	42.00
7	Disturbed sleep while lying flat	33	22.00%
8	Persistent coughing or wheezing	54	36.00%
9	Polyuria	52	34.66%



About cardiac complications, about 47 (31%) patients complained of chest pain,81 (54%) responded to palpitations, 07 (5%) responded to fainting,111 (74%) were complaining of easily tiredness, 23 (15%) complained about swelling around the ankles, 63(42%) were facing problem of shortness of breath, disturbed sleep while lying flat was answered by 33 (22%) of the respondents, persistent cough and wheezing was the problem of 54 (36%) patients while 52 (35%) patients were having polyuria. Fig 5shows the doughnut chart that represents the different responses of the people.

RELATED TO SPLENOMEGALY
Table No. 06

SPLENOMEGALY			
S. NO	**SYMPTOMS OF SPLENOMEGALY**	**OBSERVATION**	**PERCENTAGE**
1	Pain in left upper side of abdomen	55	36.66%
2	Pain in left shoulder	21	14.00%
3	Constant hiccups	34	22.66%
4	Anorexia & early fullness of stomach	57	38.00%
5	Frequent infections	64	42.66%
	Total	150	100%

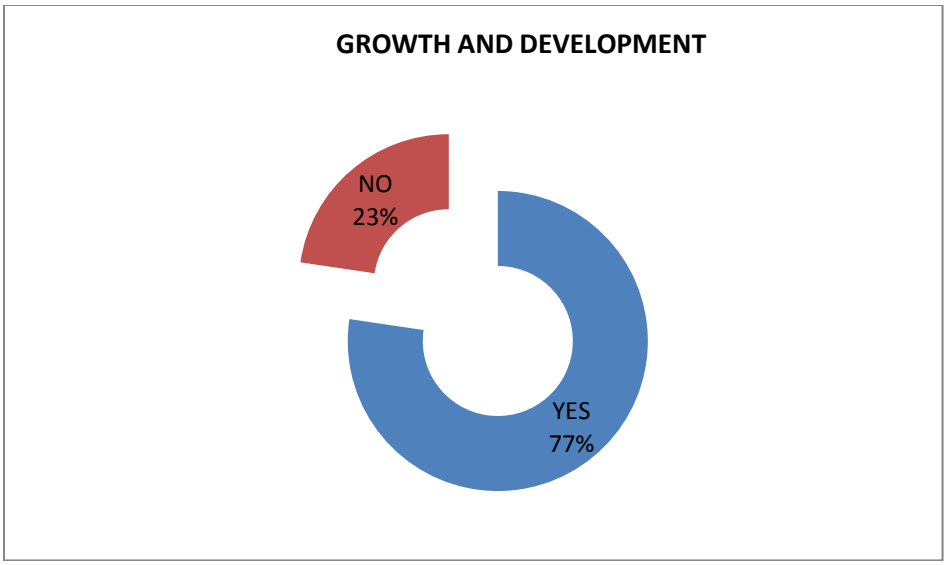
Table and fig06is showing the symptoms of splenomegaly. This shows that majority of the patients i.e. 64 (43%) are having frequent infections, anorexia and early fullness of stomach was seen 57 (38%) patients,

55(37%) responded to pain in left upper side of abdomen, 34 (23%) answered to constant hiccups while pain in left shoulder was seen in 21 (14%) respondents.

RELATED TO GROWTH AND DEVELOPMENT

TABLE NO.07

GROWTH AND DEVELOPMENT OF RESPONDENT			
S. No	**Normal growth & development**	**Observation**	**Percentage**
1	YES	116	77.34%
2	NO	34	22.66%
	Total	**150**	**100%**

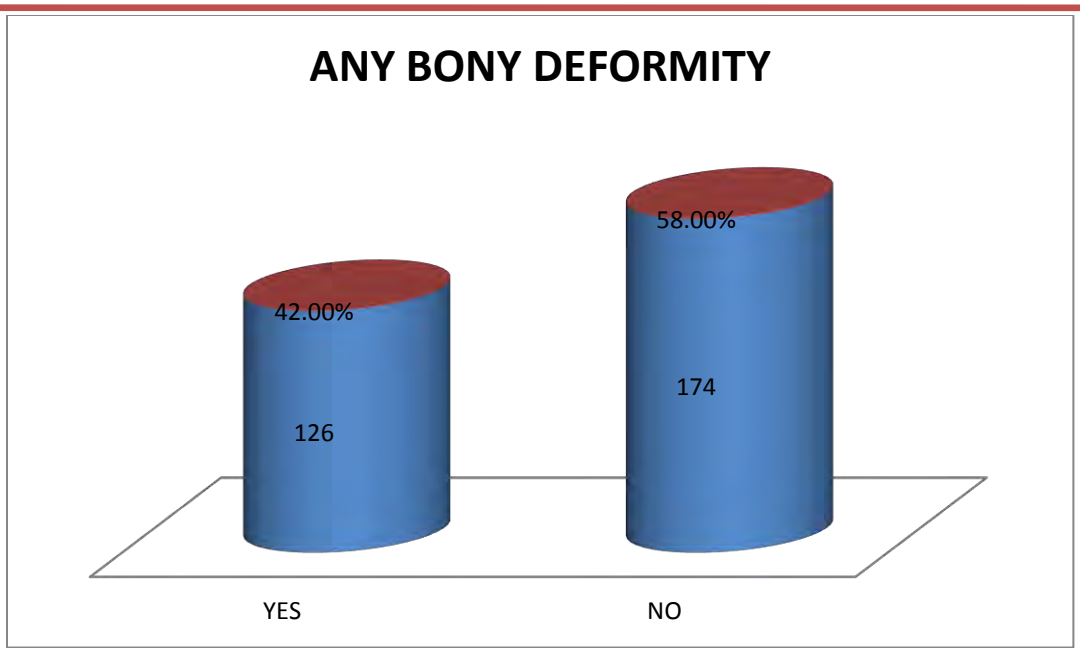


Out of150 respondents, growth and development was Normal in 116 (77%) respondents, which is the majority while only 34 (23%) complained of abnormal growth and development. These values are given in table and fig no. 07.

RELATED TO BONY DEFORMITIES

TABLE NO. 08

BONY DEFORMITIES REGARDING THALASSEMIA			
S. NO	**ANY BONY DEFORMITY**	**OBSERVATION**	**PERCENTAGE**
1	YES	63	42.00%
2	NO	87	58.00%
	Total	150	100%

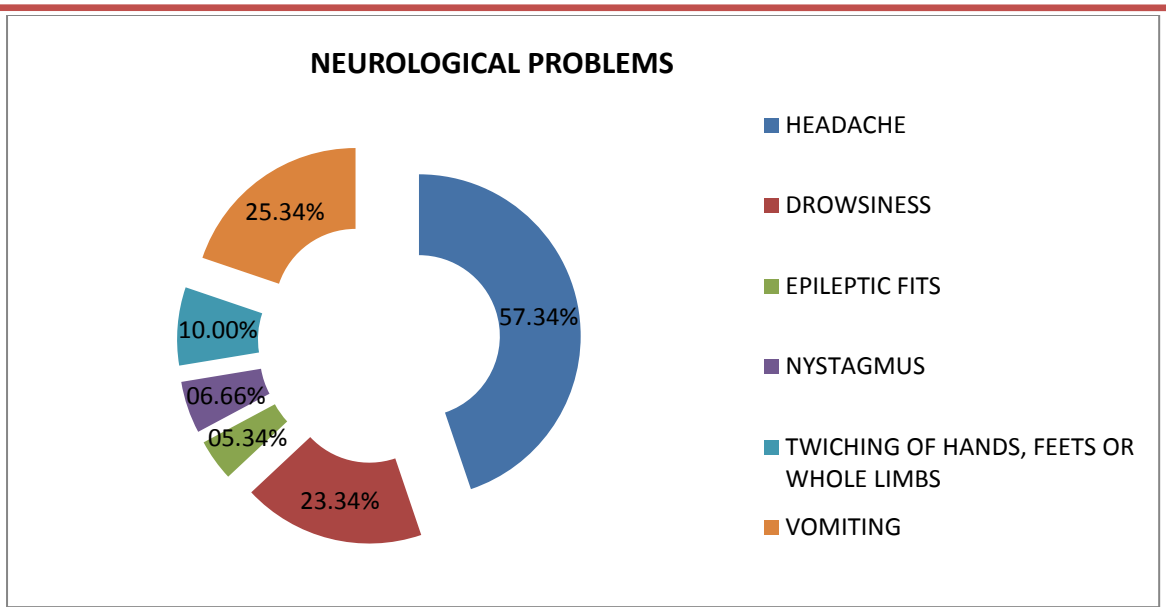


It was revealed by 42 % of the respondents that they were having bony deformities and 58% replied with no. (Table and fig. no 08).

RELATED TO NEUROLOGICAL PROBLEMS

TABLE NO. 09

NEUROLOGICAL PROBLEMS ASSOCIATED WITH THALASSEMIA			
S. NO	**NEUROLOGICAL PROBLEMS**	**OBSERVATION**	**PERCENTAGE**
1	HEADACHE	86	57.34%
2	DROWSINESS	35	23.34%
3	EPILEPTIC FITS	08	05.34%
4	NYSTAGMUS	10	06.66%
5	TWICHING OF HANDS, FEETS OR WHOLE LIMBS	15	10.00%
6	VOMITING	38	25.34%
	TOTAL	150	100%



Regarding Neurological Problems associated with Beta-thalaseemia major, we observed that headache was problem seen in 86 (57%) patients Drowsiness was problems of 35 (23%) respondents,08 (05%0 of patients were facing problem of epileptic fits, nytagmus was see in only 10 (07%) people, twitching of hands, feet of Whole limb was complain of about 15 (10%) respondents, while 38 (25%)patients were having vomit problem. (table and fig no.10)

RELATED TO PSYCHOLOGICAL PROBLEMS

Table No. 10

ANY PSYCHOLOGICAL PROBLEMS TO THE RESPONDENT			
S. NO	**ANY PSYCHOLOGICAL PROBLEMS**	**OBSERVATION**	**PERCENTAGE**
1	YES	97	64.66%
2	NO	53	35.34%
	Total	150	100%

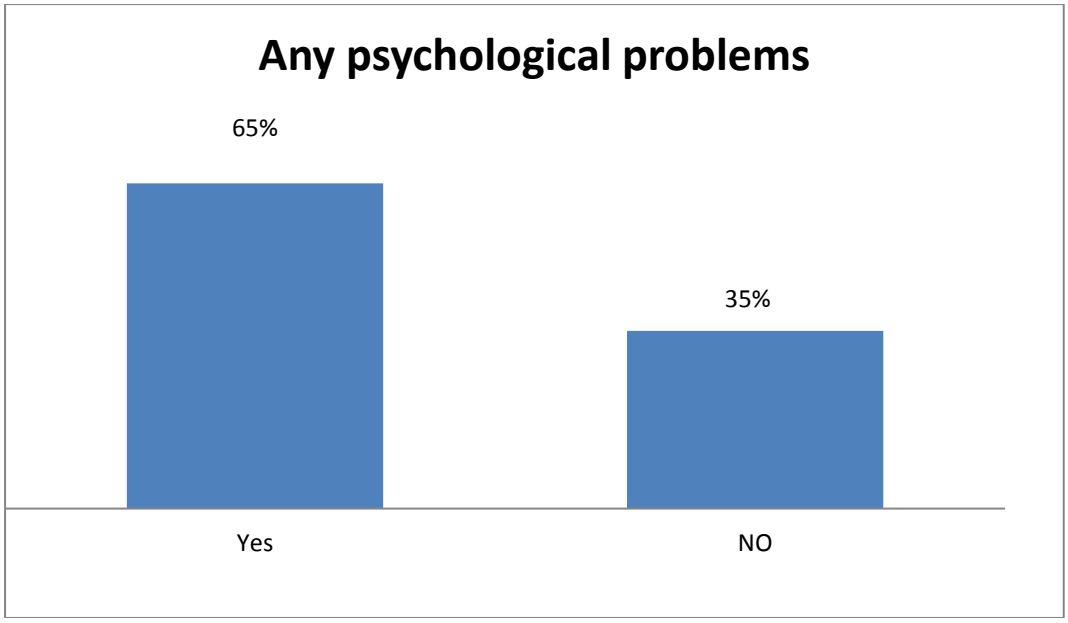


Table and fig no 10 indicates the frequency of psychological problems in Beta-thalaseemia patients. Out of 150 respondents, 97 (65%) answered yes while only 53 (35%) patients replied with No.

RELATED TO IRON OVERLOAD

Table No. 11

SYMPTOMS RELATED TO IRON OVERLOAD			
S. NO	**SYMPTOMS**	**OBSERVATION**	**PERCENTAGE**
1	JOINT PAINS	67	44.66%
2	ABDOMINAL CRAMPS	53	35.34%
3	WEAKNESS & LETHARGY	56	37.34%
4	DIABETES	06	04.00%
5	HYPOTHYROIDISM	02	02.66%
	TOTAL	150	100%

During our study, while asking about symptoms of iron overload we came to know that joint pain were present 67 (45%) patients, abdominal cramps in 53 (35%) respondents, Weakness and lethargy was replied by 56 (37%) patients,06 (04%) patients were diabetic while 02(03%) respondents were observed to have hypothyroidism. (table and fig no.11)

RELATED TO TREATMENT

Table No.12

TREATMENT FOR THALASSEMIA			
S. NO	**TREATMENT STARTED**	**OBSERVATION**	**PERCENTAGE**
1	YES	150	100%
2	NO	00	00.00%
	TOTAL	300	100%

On asking about the treatment for their disease from the respondents, we got yes answer from al of the 150 respondents and there was not a single patient who was not taking any treatment for the disease.

TABLE NO. 13

BLOOD TRANSFUSION PER MONTH			
S. NO	**NO. OF TRANSFUSION**	**OBSERVATION**	**PERCENTAGE**
1	1-2	91	60.66%
2	3-5	55	36.66%
3	6-10	2	01.34%
4	MORE THAN 10	2	01.34%
	TOTAL	150	100%

61% patients revealed that they were taking about 1-2 transfusion per month, 37% respondents were taking 3-5 transfusion, only 1 % patients were taking 6-10 transitions per month and also only 1% respondents were taking more than 10 transfusions per month. Table and fig no. 15.

Table No. 14

TRANSFUSION TRANSMITTED INFECTIONS				
S. NO	AGE GROUP IN YEARS	NO. OF PATIENTS POSITIVE FOR TTIS		
		HIV	HBV	HCV
1	1-10 YEARS	----	----	02
2	11-15 YEARS	----	1	05
3	16-20 YEARS	----	1	02
4	ABOVE 20 YEARS	----	----	02
	TOTAL	00	02	11

Table and fig no. 17 tell us about the Transfusion Transmitted Infections in different age groups, which shows that in a age group below 10 years, no cases of HIV and HBV was reported, while there were 2 cases of HCV. In age group 11-15 years, no HIV were seen, there was only 1 case of HBV and about 5 cases of HCV. In 16-20 years of patients, again no case of HIV, 1 case of HBV and 2 cases of HCV were there. No HIV case was found in age group above 20 years, no HBV was seen in this age group, but 2 HCV cases were seen in this age group. So total of 2 HBV and 11 HCV were seen among our 150 respondents, whereas no case of HIV was seen.

DISCUSSION

Thalassemia has forced an unbearable burden on the healthcare systems in developing countries. Thalassemia patients require lifelong medical care based on standards approved in developed countries which is extremely costly mokhtar 2011.[10] "β-Thalassemia major (β-TM) is an inherited Hb disorder characterized by chronic anemia and iron overload due to transfusion therapy and gastrointestinal absorption"(Mokhtar et al. 2011)[10].Iron overload is mostly responsible for the associated morbidity and mortality in these patients, affecting the endocrine glands resulting in growth retardation, failure of sexual maturation, diabetes mellitus, and insufficiency of the parathyroid, thyroid, pituitary, and less commonly, adrenal glands (Mokhtar et al. 2011; Cunningham et al. 2009).[10,11] Thalassemia major patients die during the first few years of life if remain untreated; patients may possibly survive until 4th-5th decades through regular transfusion programs, appropriate chelating therapy, and effective treatment of complications (Yaman et al. 2013)[12.]

The appearance of complications in thalassemia patients are commonly observed after the first decade and rise with age (Olivieri and Brittenham 1997)[13]. In this study, the most common complications found in 97 respondents were psychological problems/psychiatric disorders (65%). According to a study conducted by Hoseini et al. (2007),[14] psychiatric disorders were found in 14 to 24 patients with thalassemia. While in other studies, approximately 80 % of young β-TM patients suffered from serious psychiatric disorders such as depression especially major depression disorder (MDD), obsessive-compulsive disorder (OCT), tic disorders, oppositional defiant disorders (ODD), psychosis, nocturnal enuresis nocturnal (Aydin et al. 1997; Messina et al. 2008)[15]. Similarly, a high rate of psychological problems has been reported in children with possible mental health disorders in a study by Aydinok et al. (2005)[16]. According to some studies psychological disorders are more prevalent in female thalassemia patients; however no such finding was observed in this study (Naderi et al. 2012).[17]

Among cardiac problems, chest pain was reported by 47 patients and 63 patients faced shortness of breath. Palpitations were a chief complaint in 81 respondents. Yemen retrospectively analyzed patients with thalassemia in Turkey where 22.4% patients suffered from cardiac complications. Iron overload is largely found to be the main cause of heart disease and about 71% of β-TM patients die due to cardiac complications (Borgna-Pignatti 2005; Mokhtar 2011).[10,18] The frequency and severity of iron overload-related complications is influenced by compliance with iron chelating therapy (Galanelloand Origa 2011).[19] Symptoms of iron-load such as joint pain, abdominal cramps and lethargy were seen in 67, 53 and 56 respondents respectively. Though, hypothyroidism as a result of iron overload was present in 2.6% of patients which makes its appearance in the second decade in the ratio of 6-24% (Borgna-Pignatti 2005).[18] Another study conducted by Adil et al. in Pakistan, 11.8% suffered from hypothyroidism. [20]

Patients in the study showed symptoms of splenomegaly which is documented to be one of complications of beta-thalassemia leading to Splenectomy (Mokhtar 2011).[10] Aessopos*et al.* (2004)[21] summarized that splenomegaly is a regular finding in β-TM patients which is mainly due to the development of extramedullary haematopoiesis, splenic pooling and chronic passive congestion of the spleen due to portal hypertension and/or heart failure. Increased transfusions or cellular components of the blood are needed in case of hypersplenism which is often associated with gradual splenic enlargement and ultimately leading to splenectomy (Aessopos*et al.* 2007)[22].On the other hand, splenectomy is an uncommon finding in β-TI patients and presented chiefly late in life(Mokhtar et al. 2011).[10]

Normal growth and development was present in 116 respondents (77.34%) which comprised of majority of the study sample. Growth retardation was found in 22.6 % similar to the studies conducted by yemen and Cario et al. 2000. Cario et al.[23] (2000) reported growth retardation in one third of 203 patients with mean age of 13.8 years. While, Yaman et al. (2013) [24]stated 19.4% of the patients in the study with growth retardation. Causes of growth retardation that usually becomes remarkable in puberty are chronic anemia-related chronic hypoxemia, increased calorie need due to increased erythropoietin, growth hormone deficiency that may develop as a result of toxicity on hypothalamo-hypophysial level caused by increased iron load, hypothyroidism, inability to make the growing spurt because of delayed puberty (Yaman et al. 2013).[23]

CONCLUSIONS

On the basis of results following conclusions are made:

1. 71% were diagnosed as Thalassemia at less than 6 months.
2. 45% of patients suffering from Thalassemia were under 10 years of age, more common in males.
3. 100% were complaining of cardiac problem and sign & symptoms of splenomegaly and iron overload.
4. 78% had retarded growth like short stature, delayed neck holding, late crawling, sitting and standing.
5. 100% of them are taking treatment for Thalassemia like blood transfusion & chelating therapy.
6. 77% patients had family history of Thalassemia.

RECOMMENDATION

Based on results following are the recommendations:

1. Provision of screening and counseling services for those genetically prone, to reduce chance of transmission of thalassemia to their offspring.
2. Provision of appropriate health care services and management for Thalassemia patients.
3. Patients should avoid food rich in iron to reduce problems caused due to iron overload like cardiac problem & hemosidrosis.
4. Always transfuse screened blood, never transfuse from addicts or person suffering from Hepatitis, AIDS or any other disease. .
5. Reduction of marriages between relatives who are suffering from Thalassemia or having history of familial Thalassemia. Make it possible to identify carriers of the disease and provide them with genetic counseling, marriage counseling sessions are appropriate information about Thalassemia.

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