PATTERN AND CLINICO-LABORATORY PROFILE IN THALASSEMIC CHILDREN IN SOHAG CITY

By

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ABSTRACT

Background: *Thalassemia is one of the most common autosomal recessive disorders worldwide. It is a genetic disorder of hemoglobin synthesis. Beta-thalassemia has a particularly high prevalence in populations in the Mediterranean, Middle East, and India. Long-term blood transfusion, splenectomy, and iron chelation therapy- these interventions play a crucial role in the management of thalassemia patients.*

Objective: *This is a demographic study aimed to determine the age and sex distribution, clinic-laboratory profile, investigation, complications to management of transfusion-dependent B-thalassemia major in children at El-Helal hospital in Sohag city.*

Patients and Method: *This study was carried out prospectively from 1st April 2019 to the 31st December 2021, the study included total of 166 children aged between 6 months to 12 years, clinically diagnosed with transfusion-dependent β-thalassemia major attending hematology clinic at Sohag El-Helal Hospital for Health Insurance.*

Studied children were subjected to complete history, clinical examination and laboratory evaluation.

Results: *A total of 166 children that age range from 6 months to 12 years, with a mean age of 9.2±4.4 years, most of them were male 122 (73.5%) and female 44 (26.5%). There was a significant statistical attachment between both sex and the Consanguinity, 151 (91%). Allergic reactions were developed in 12 (7.2 %) patients during blood transfusion. Splenomegaly was reported to be a major complication among study patients.*

Conclusion: *Severe anemia is present in nearly all patients; Serum ferritin concentration accurately reflects high body iron stores. liver, kidney, bone, and endocrine functions significantly deteriorate in almost all studied patients.*

Keywords: *Beta-thalassemia, Hemoglobinopathies, transfusion, iron overload.*

INTRODUCTION

Beta-thalassemia is the most common inherited monogenic disorders worldwide (known as Mediterranean anemia, Cooley's anemia) characterized by quantitative defects in globin chain synthesis, a major component of adult hemoglobin A (HbA, α2β2), that disserve hemoglobin synthesis and creates an imbalance with the other normally produced globin chains leading to variable degree of microcytic anemia and lifelong blood transfusions **(Settin AA., et al., 2006)**.

Beta thalassemia clinical and hematological picture ranges from mild to clinically overt, including transfusion dependent beta-thalassemia major and non-transfusion dependent beta-thalassemia intermedia or thalassemia minor **(El Beshlawy A., et al., 2014)**.

Globally, there are 270 million carriers with abnormal hemoglobin and thalassemias, an estimated 80 million of them are carriers of β-thalassemia. Recently between 300 000 and 400 000 babies are born with a severe hemoglobin disorder each year and nearly 90% of these births occur in developing countries or low-income **(Williams TN, Weatherall DJ.7, 2012)**. Thalassemia is prevalent in the Mediterranean, Africa and Southeast Asia **(Ladis V., et al., 2013)**.

In Egypt, thalassemia is the most common genetically-determined, chronic, hemolytic anemia **(Ilham et al., 2018)**, in different governorates (85.1%) **(Shawky and Kamal, 2012)**. It is a significant public health problem in Egypt and the incidence varies from region to another, the carrier rate varies between 5.5% to ≥ 9% or more; Estimates indicate that there are 1000/1.5 million per year live births born with β-thalassemia **(El-Beshlawy A, Youssry., 2009)**. Higher rate of consanguineous marriage aid to pile up deleterious genes in families, reaching 35.3%.

Individuals with thalassemia major usually come into attention in initial two years of life where they present with severe anemia requiring regular blood transfusions for their survival. Thalassemia major affected infant's failure to thrive and gradually become pale, problems of feeding, diarrhea, irritability, bouts of fever, and enlargement of the abdomen, caused by splenomegaly. In the last few decades, the life expectancy of thalassemic patients has progressively increased, as reported by several studies in

different countries. The improvement can be attributed to several factors, including availability of sufficient blood donated by volunteer donors; screening of blood for the most frequent viral agents; aggressive treatment of infection and improved treatment of cardiac complications **(C. Borgna-pignatti, 2009)**.

Aim of work

To determine the demographic pattern, clinico-laboratory profile, complications of transfusion-dependent β-thalassemia major in children., at El-Helal hospital in Sohag city.

Ethical consideration:

1. A written informed consent was obtained from parents or the legal guardians before the study.

2. The approval of the local ethical committee was obtained before the study.

3. The authors have declared that there were no potential conflicts of interest regarding the research, authorship, and/or publication of this article.

4. All the data of the patients and results of the study are confidential & the patients have the right to keep it.

5. The authors received no financial support for the research, authorship and/ or publications of this article.

Sample size:

The sample size was calculated using Power and Sample size software version 3 (epi info). The sample size was calculated using the following formula: **(Hoban et al., 2021)**.

$$n = 2\left[\frac{\left(Z_{\alpha/2} + Z_{\beta}\right) * \sigma}{\mu_1 - \mu_2}\right]^2$$

By calculation, the sample A total of 166 children aged between 6 months to 12 years was sufficient.

PATIENTS AND METHODS

Type of study: This is a descriptive prospective study, that was carried on the patient attending hematology clinic at Sohag El-Helal Hospital for Health Insurance during the period from 1st April 2019 to the 31st December 2021.

Study population: The included study population was children with β-thalassaemia major in El-Helal hospital Sohag city

Inclusion criteria:

All children aged between 6 months to 12 years who are transfusion dependent at the rate of once or twice monthly. Both genders will be included.

Exclusion criteria:

Age: less than 6 months and more than 12 years. Patients who had other chronic debilitating diseases not related to thalassemia. Children diagnosed with other heamoglobinobathes.

Method:

All children who fulfilled the inclusion criteria during the study period were included, the clinical data were evaluated as follow:

1. Clinical data:

Careful history was taken from patient's relatives including age at the time of diagnosis, consanguinity of parents, transfusion history, date of beginning of blood transfusion, treatment taken for iron overload, presence of complications or not.

Clinical examination including: (Pallor, Jaundice, Cyanosis, Body Built, Facial feature, Measurement of height and weight, Conscious level, General look).

Systemic examination of:

(Chest, heart and abdominal examination).

2. Laboratory investigation including:

- Complete blood count.
- Serum iron and serum ferritin and other iron profile.
- Blood sugar, Bl. urea, S. creatinine, liver function tests, S. calcium, thyroid profile, viral markers for hepatitis (B-C).

Statistical analysis of the data:

Data were fed to the computer and analyzed using the Statistical Package for the Social Science (SPSS) software (version 23.0; SPSS Inc., Chicago, IL, USA). Number and percentage were used to described qualitative data. Quantitative data were described using mean, standard deviation, median. Significance was judged at the 5% level for the obtained results.

Testing the correlation between continuous data was carried out using (Pearson’s correlation coefficients).

RESULTS

Our results will be demonstrated in the following tables:

Table (1): Demographic data of the studied patients

	Sex		Consanguinity		Age/In years	
	Male	Female	No	Yes	Mean	Std. D
No	122	44	15	151	8.95	4.39
Percent	73.5%	26.5%	9%	91%		

This table shows that the mean age of the study population was 9.2±4.4 years, with a very wide range from 8 months to 12 years. On the other hand, nearly three quarters of the study cases were males 122; (73.5%), while only 44(26.5%) were females. Additionally, the vast majority of cases had positive consanguinity of their parents 151 (91%) and the rest 15 (9 %) patients were born to non-relative parents.

Table (2): Patient's Height, Weight and body mass index

	Height	Weight	BMI
Mean	114.04	22.04	16.89
Std. Deviation	21.38	7.15	3.03

This table shows that the vast majority of the study population were underweight, reflecting the low mean BMI of only 16.9.

Table (3): Different laboratory parameters of the study population

	Mean	Median	Std. Deviation	Minimum	Maximum
HB	7.28	7.1	0.78	5.9	10
RDW	19.12	18.2	2.08	16.8	23
RBCs	3.22	3.2	0.41	2.4	4
WBCs	9.45	10	1.66	6.1	11.7
PLTs	355.4	357.5	82.53	128	480
Serum iron	240.55	205	96.95	100	500
Ferritin	973.23	1000	493.94	111.1	2000
Blood sugar	108.25	102	21.99	75.0	170
Blood urea	23.64	24	3.79	18	35
Creatinine	0.77	0.75	0.18	0.5	1.2
AST	64.69	47.5	46.83	18	200
ALT	87.33	70	54.89	20	255
TSH	3.66	2.51	2.44	0.5	8.7
T4	8.87	9	2.10	2.2	12
T3	101.99	100	36.44	24	250
HBV/ HCV	Negative for all cases				

Table (4): Regular medications in ß-thalassemia patients in the current study

		No	Percent
Regular medications	Folic acid	166	100%
	Calcium	122	73.5%
	Vitamin D	157	94.6%
	L. Carnitine	163	98.2%
	Vitamin B12	8	4.8%
	Penicillin	4	2.4%

Table (5): Complications in the ß-thalassemia patients in the current study

Iron overload		No	Percent
Complications	Non	94	56.6
	HSM	23	13.9
	Splenectomy	19	11.4
	Hepatomegaly	17	10.2
	Splenomegaly	13	7.8
	Total	166	100.0

DISCUSSION

Thalassemia is one of most common inherited autosomal recessive hematological disorders in the Mediterranean region due to defective formation of globin chain of the hemoglobin moiety of the RBC., resulting in asymptomatic to clinically severe hypochromic microcytic anemia **(Al-Kuraishy HM and Al-Gareeb AI., 2017)**.

In the present study the total number of cases were 166; (73.5%) males, and 44(26.5%) were females. All children aged between 6 months to 12 years who are transfusion dependent at the rate of once or twice monthly. Similar age was reported in Tunisia with average of 10.7 years **(Bejaoui, M., and Guirat, N., 2012)**: in Pakistan it was12±8 years **(Adil, A., et al., 2012)**, and in Saudi Arabia the median age was 12.5 years.

Consanguineous marriage is still high in Egypt (35.3%), especially among first cousins (86%). However, the frequency varies by region. In Sohag represented by (42.2%) **(Rabah M. Shawky., et al., 2011)**.

In the present study, 12 (7.2 %) patients developed allergic reactions during blood transfusion process. In Egypt, previous studies reported that allergic reactions occurred in 72% of blood transfused thalassemic patients **(Lamis A. Ragab., et al., 2012)**.

In the current study, the average of serum ferritin level for patients was 973.2 ng/ml±493.93 and about half cases 84/166 (50.6 %) had SF ≥1000ng/ml. This is much higher than the cutoff point recommended for blood transfusion dependent patients ≤ 1000ng/ml **(Borgna-Pignatti, C. et al., 2004)**. The increase in serum ferritin level is known to put these patients at a great risk of developing cardiac injury **(Cario, H., Stahnke, K., and Kohen, E., 1999)**.

In the current study, splenomegaly was reported to be a major complication among thalassemic patients. Splenectomy was done for 38 patients with prevalence of 22.89%. Our finding in this respect is in agreement with most studies around the world indicating that splenomegaly is a major complication among thalassemic patients and is carried out aiming at reducing transfusion requirements **(Kurtoglu, A., Kurtoglu, E., and Temizkan, A., 2012)**.

Folic acid was prescribed to all patients; however, low compliance was reported. In addition to folic acid, calcium and alpha D3 were also prescribed to 122, 10 patients

with percent of 73.49 % - 6.02 % respectively. Vitamin alpha D3 is considered as the main support of hypoparathyroidism. Vitamin D status among our thalassemic children is poorly characterized as no regular evaluation for the level of this vitamin was conducted.

According to body mass index in our study population; underweight was reported in 133 (80.12%) patients, overweight in three (1.80%) patient and obese in one (0.60%) patient. Similar findings were shown by another study that reported low BMI in thalassemic patients which was attributed to low hemoglobin, high ferritin levels, and suboptimal iron chelation **(Saxena A., 2003)**. Hashemi et al., reported underweight in 45.71% compared to control and low BMI in 18.6% of their patients with BTM **(Asadi-Poyya, AA., Karamifar, H., 2004)**. Low BMI in beta thalassemia patients, especially who are older than 10 years old, has many etiologies. Multiple endocrinopathies especially hypogonadism seems to be the most important etiological factors. The findings regarding BMI among our study group is in agreement with such assumption.

Hypothyroidism cases were reported in 28.31 % of the tested patients in the present study. Similar incidence was reported among thalassemic patients from Oman **(Peacock, M., 2010)**. On the other hand, a higher percentage of primary hypothyroidism was reported among patients in Greece and Egypt **(Capellini, MD.et al., 2008)**.

In present study, elevated glucose levels were reported in 16 (9.63 %) cases. Similarly low rate of diabetes mellitus was previously reported in KSA and the researchers referred the role in delaying the onset of diabetes to the low BMI **(Mansi, K., and Aburaji, T., 2008)**. In contrast to our finding, high prevalence of diabetes mellitus as secondary complication of transfusion therapy is widely reported. In Morocco the prevalence was 7%, in China the prevalence was 21.7%, in France and North America the prevalence of diabetes mellitus was 6% and 10%, respectively **(Agouzal, M., et al., 2010)**.

CONCLUSION

Severe anemic presentation seen in the almost patients. Serum Ferritin were high reflecting high iron over load, where its complications are clear from frequency of splenectomy as well as deteriorated organ functions.

Low body mass Index reflecting underweight state in nearly half of the patients. Markedly deteriorated biochemical picture in almost studied patients for liver, kidney, bone and endocrine functions. Not all patients were subjected to regular check- ups.

RECOMMENDATION

1. Educational and awareness programs aiming to provide the population with information, regarding the risks for consanguineous marriages and disease complications are essential.
2. Suitable programs aiming to increase patient's adherence to the treatment are essential.
3. Modification of the care policy administrated to those patients to more strategic effective this in turn can improve their clinical situation.
4. There is a great need for assessment of transfusion frequency, use of chelators in relation to BMI and other indicators to limit further possible complications as this can lead to improvement of patient's clinical situation and better survival. It will also reduce cost which is a burden to country.

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