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Thalassemia Phenotypes and Associated Mortality among Yemeni Patients: A Single-Center Retrospective Analysis

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ABSTRACT

Objective: To retrospectively analyze thalassemia phenotypes and associated mortality among Yemeni patients seeking healthcare in Sana'a city, Yemen.

Methods: This retrospective, cross-sectional study was conducted in the medical center of Yemen Society for Thalassemia and Genetic Blood Disorders (YSTGBD) in Sana'a city from January 2010 to December 2016. Data about gender, age, governorate of origin, type of thalassemia and thalassemia-related mortality were retrieved from the records of 496 thalassemia patients. Data were then entered into an Excel spreadsheet, cross-checked for accuracy and presented as frequencies and proportions. Factors associated with deaths among thalassemia patients were analyzed using chi-square or Fisher's exact tests.

Results: A total number of 496 patients attended the medical center of YSTGBD in Sana'a city in the period from January 2010 to December 2016. The majority of thalassemia patients were males (57.9%), and approximately half of the patients were aged 10 years or younger with a comparable proportion to those older than 10 years. Most thalassemia patients had β-thalassemia (92.7%), while 7.3% had α-thalassemia. The majority of patients were from Hajjah governorate (16.5%) followed by those from Sana'a (13.1%) and Amran (11.9%), while lower proportions ranging from 0.2% to 8.1% were recorded for patients from other governorates. Thirty out of the total attending thalassemia patients died, and mortality was significantly associated with recurrent transfusions of whole blood but not with the gender and age of the patients or thalassemia phenotype.

Conclusions: The majority of thalassemia patients seeking healthcare in Sana'a city suffer from thalassemia, where males represent more than half of them and the patients are almost equally distributed in relation to the cut-off age of 10 years. The mortality incidence among Yemeni thalassemia patients seeking healthcare is lower than that reported elsewhere in the world, and mortality was significantly associated with recurrent blood transfusions. Further studies to identify the genetic abnormalities associated with thalassemia are recommended together with the need for the launch of a national center for counseling, research and supervision of voluntary activities related to thalassemia and genetic blood disorders in Yemen.

Keywords: Thalassemia, Phenotype, Mortality, Yemen

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1. Introduction

Thalassemia is an inherited autosomal recessive disorder. Its most common type is α-thalassemia major, also called hemoglobin (Hb) Bart's disease, which was an invariably fatal disease in the past but is now salvageable.[1] Thalassemia is classified into two types according to the affected globin: α-thalassemia and β-thalassemia. The former is characterized by deletion or mutation in one or more α-globin genes located on the short arm of chromosome 16.[2] However, the latter is caused by a mutation in the β-globin gene located on chromosome 11, affecting all aspects of transcription, translation and stability of the gene product.[3, 4]

The high incidence of thalassemia occurs in the Mediterranean region, parts of Africa, the Middle East, the Indian subcontinent, Southeast Asia and the Pacific islands.[5–6] In α-thalassemia, HbA2 level is normal or slightly reduced.[7] HbH patients are anemic with variable amounts of HbH (0.8–40%), and Hb Bart's hydrops fetalis is the most severe form of α-thalassemia with the absence of HbF.[8] Abnormal hemoglobinopathies, including thalassemia, affect about 280 million people in the world. Of whom, 80 million are carriers of β-thalassemia.[9–11] Recent surveys suggest that between 300–400 thousand babies are born with serious hemoglobinopathies each year, with 23,000 having β-thalassemia major and up to 90% of them occur in low- or middle-income countries.[9] Approximately, 439,000 thalassemia patients have severe disease with almost similar rates among males and females, most commonly in Italy, Greece, Middle East, South Asia and Africa.[9] Thalassemia occurs in 4.4 per 10,000 live births, and the majority of patients die before the age of 20 years in the developing world.[12] However, the number of deaths declined from 36,000 deaths in 1990 to 16,800 deaths in 2015.[10]

The prevalence rate of α-thalassemia has been found to be 40.0% in Jeddah, indicating that the Saudi population in this area is at increased risk of having hemoglobinopathies [13] On the other hand, a prevalence of 2.1% was documented for β-thalassemia in Turkey, where about 1.6 million people have thalassemia trait and about 5,500 patients have homozygous thalassemia and other hemoglobinopathies.[14] In Arab countries, carrier rates of thalassemia range from 1.0% to 11.0%.[15] In Egypt, approximately 1,000 babies out of 1.5 million live births are born with β-thalassemia major annually.[16] In Iran, about one-fifth of blood donations are transfused to thalassemia patients.[17] The incidence of β-Thalassemia major is about 2.0–3.0% in Lebanon and represents more than two-thirds of all types of thalassemia in Iraq.[12, 18] Patients with β-thalassemia major often die from cardiac complications of iron overload by the age of 30 years.[19]

In children with β-thalassemia, symptoms appear in the first two years of life and include paleness, headache, fatigue, irritability, failure to grow, and pulmonary dysfunction.[20–22] The most common symptoms are jaundice, enlarged spleen or liver, or deformed bones.[17, 23–25] The natural course of thalassemia major is modified by iron chelation therapy (ICT) with desferrioxamine to avoid death from cardiomyopathy.[26] Treatment strategies are also unique and include blood transfusion in addition to ICT.[11] β-thalassemia intermedia is less severe than β-thalassemia major and may require episodic blood transfusions. Transfusion-dependent patients may develop iron overload and require ICT to remove excess iron. Bone marrow transplants can be curative for some children with β-thalassemia major.[21]

The prevalence of thalassemia trait in Yemen is 13.3%; 4.4% for β-thalassemia and 8.9% for α-thalassemia.[27] This study aimed to retrospectively analyze thalassemia phenotypes and associated mortality among Yemeni patients seeking healthcare in Sana'a city.

2. Methods

2.1. Study design and setting

A retrospective, cross-sectional study was conducted in the medical center of YSTGBD in Sana'a city from January 2010 to December 2016.

2.2. Data collection and analysis

Data about gender, age, governorate of origin, phenotype of thalassemia and mortality were retrieved from the records of 496 patients. Data were then entered into an Excel spreadsheet and cross-checked for accuracy and presented as frequencies and proportions. Factors associated with mortality among thalassemia patients were analyzed using chi-square or Fisher's exact test, whichever appropriate, using IBM SPSS Statistics, version 22 (IBM Corp., Armonk, NY, USA). Statistical significance was considered at *P*-values <0.05.

3. Results

3.1. Characteristics of thalassemia patients

Table (1) shows that the majority of thalassemia patients were males (57.9%), and approximately half of the patients were aged 10 years or younger with a comparable proportion to those older than 10 years. Most thalassemia patients had β-thalassemia (92.7%), while 7.3% had α-thalassemia. The majority of patients were from Hajjah governorate (16.5%) followed by Sana'a (13.1%) and Amran (11.9 %), while lower proportions ranging from 0.2% to 8.1% were from other governates as shown in Table (1). Out of 496 cases, 30 deaths were documented thalassemia patients over the study period (data not shown).

3.2. Factors associated with mortality among thalassemia patients

Table (2) shows that mortality among thalassemia patients was significantly associated with the type of the transfused blood product, being higher among those who had received recurrent transfusiond of whole blood compared to those receiving packed red blood cells (RBCs). In contrast, mortality was not significantly associated with the gender and age of the patients or thalassemia phenotypes.

Table 1. Characteristics of thalassemia patients attending the medical center of Yemen Society for Thalassemia and Genetic Blood Disorders in Sana'a city, Yemen (2010–2016)*

Characteristics		*n* (%)
Gender		
	Male	287 (**57.9**)
	Female	209 (**42.1**)
Age (years)		
	≤10	250 (**50.4**)
	>10	246 (**49.6**)
Thalassemia phenotype		
	Alpha	36 (**7.3**)
	Beta	460 (**92.7**)
Governorate of origin		
	Hajjah	82 (**16.5**)
	Sana'a	65 (**13.1**)
	Amran	59 (**11.9**)
	Taiz	40 (**8.1**)
	Ibb	38 (**7.7**)
	Dhamar	37 (**7.5**)
	Al-Amanah	30 (**6.0**)
	Hodeidah	27 (**5.4**)
	Al-Mahweet	26 (**5.2**)
	Abyan	20 (**4.0**)
	Al-Dhalae	15 (**3.0**)
	Shabwah	14 (**2.8**)
	Al-Baydha	13 (**2.6**)
	Rayemah	11 (**2.2**)
	Hadhramout	7 (**1.4**)
	Lahj	6 (**1.2**)
	Aden	3 (**0.6**)
	Mareb	2 (**0.4**)
	Sa'adah	1 (**0.2**)

* Total number of patients was 496.

Table 2. Factors associated with mortality among thalassemia patients attending the medical center of Yemen Society for Thalassemia and Genetic Blood Disorders in Sana'a city, Yemen (2010–2016)*

Variable		*N*	*n* (%)	*P*-value
Gender				
	Male	287	17 (**5.9**)	
	Female	209	13 (**6.2**)	0.891
Age (years)				
	≤10	250	1 (**0.4**)	
	>30	246	1 (**0.4**)	1.000
Thalassemia phenotype				
	Alpha	36	2 (**5.6**)	1.000
	Beta	460	28 (**6.1**)	
Region of residence				
	Azal region	191	14 (**7.3**)	
	Tehama region	146	6 (**4.1**)	
	Aden region	44	5 (**11.4**)	
	Al-Janad region	78	4 (**5.1**)	0.376
	Hadhramout region	21	0 (**0.0**)	
	Shiba region	13	1 (**7.7**)	
Type of recurrently transfused blood product				
	Whole blood	47	22 (**46.8**)	<0.001
	Packed RBCs	449	8 (**1.8**)	

* Total number of patients was 496; *N*, number of thalassemia patients; *n*, number of deaths; RBCs, red blood cells.

4. Discussion

Over the seven years spanning the period of this study, 496 thalassemia cases on treatment and 30 thalassemia-related deaths were recorded in the medical center of the YSTGBD in Sana'a. Comparable proportions of patients were observed for both genders and age groups in relation to a cut-off age of 10 years. However, β-thalassemia was the most predominant thalassemia type among more than 90.0% of patients. The majority of cases seeking healthcare in the medical center of the YSTGBD were from the northern governorates of Yemen (Hajjah, Sana'a and Amran), which could be attributed to the close location of such governorates to the medical center in Sana'a city but does not necessarily reflect the highest burden of this disorder in these governorates. Moreover, there are other centers offering healthcare for thalassemia patients in Taiz, Hodeidah, Aden and Hadhramout.

The finding of this study is consistent with the fact that up to 90% of thalassemia patients in low- and middle-income countries have β-thalassemia major.[9] The high proportion of β-thalassemia patients in this single-center study is comparable to that (447 patients) reported from a single Egyptian center over a ten-year period.[28] In Iraq, β-thalassemia represented 73.9% of all types of thalassemia,[12] while the overall incidence of β-thalassemia trait in Turkey was reported to be 2.1%.[14] In Iran, 19.2% of the total number of blood donations were reported to be allocated to the treatment of thalassemia.[17] In Lebanon, an incidence of 2-3% was estimated for β-thalassemia carriage.[18]

Out of 496 thalassemia patients attending the medical center in the present study, 30 died over the study period, with a significant association with the transfusion of whole blood compared to packed RBCs. This study revealed no significant association with age considering 10 years as a cut-off. Nevertheless, there is evidence that most thalassemia major patients cannot survive beyond the second decade of life without ICT.[29] In the United Kingdom, about half of thalassemia patients were reported to die before the age of 35 years,[30] while 68.0% of Italian patients were reported to remain alive at this age.[31] Treatment of thalassemia mostly depends on life-long blood transfusions and the removal of excess iron from the bloodstream.[32] In the present study, a higher proportion of deaths occurred among patients receiving recurrent whole blood transfusions. This could be attributed to the iron overload as well as the lack of ICT because of the armed conflict in Yemen. Mortality of thalassemia patients in other countries have been attributed to several complications such as endocrinopathy, infections, heart diseases and heart failure as well as hepatic complications.[18, 29, 31–33]

5. Conclusions

The majority of thalassemia patients seeking healthcare in Sana'a city suffered from β-thalassemia, where males represent more than half of them and the patients are almost equally distributed in relation to the cut-off age of 10 years. The mortality incidence among Yemeni thalassemia patients seeking healthcare is lower than that reported elsewhere in the world, and mortality was significantly associated with recurrent blood transfusions. Further studies to identify the genetic abnormalities associated with thalassemia are recommended together with the need for the launch of a national center for counseling, research and supervision of voluntary activities related to thalassemia and genetic blood disorders in Yemen.

Ethical considerations

Neither ethical approval nor informed consent were required for the retrospective analysis of the anonymous data in this study, which are routinely collected for the sake of improving the quality of healthcare services. However, inistitutional permission was obtained before data collection

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Authors' contributions

TAAA and AA design the study MEMS, TAAA collected data, TAAA analyzed and interpreted data, TAAA and AA drafted the manuscript, and all authors revised the manuscript and approved the final submission.

Competing interests

The authors declare that they have no competing interests associated with this article.

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