

Prevalence of cardiac complications among patients with β -Thalassemia major in Erbil city, Iraq

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Abstract

The cardiac complications are the most common leading cause of morbidity and mortality in β -thalassemia major patients due to iron overload secondary to frequent blood transfusions. This study aims to estimate the prevalence of cardiac complications in the patients with transfusion-dependent thalassemia and associated factors. The present study is a cross-sectional study conducted in the Erbil Thalassemia Centre, Erbil, Kurdistan Region, Iraq. A total of 200 patients with β -thalassemia major recruited to participate. The patients were assessed with echocardiography to check for possible cardiac complications. Data were analyzed using SPSS, with the chi-square test and the t-test used for statistical analysis. A total of 200 patients with transfusion-dependent thalassemia participated. The prevalence of cardiac complications is 16.5%, in which 7%, 4.5% and 5% had diastolic dysfunction, pulmonary hypertension, and heart failure, respectively. The mean age was 23.65 ($\pm$ 12.39) years, and the mean duration of blood transfusion was 19.69 ($\pm$ 12.5) years. The occurrence of complications had a significant correlation to mean age (P value = 0.005) and blood transfusion duration (P value = 0.003). It also has a significant correlation with gender (P value < 0.0001). However, there is no significant correlation with either a specific diet pattern (P value = 0.531), smoking (P value = 0.085), or alcohol (P value = 0.493). The prevalence of cardiac complications among patients with Transfusion-Dependent Thalassemia (TDT) was high and had a significant correlation with age, gender, and transfusion duration. We recommend early screening for detection and treatment of iron overload to minimize the cardiac complications.

Keywords: Blood transfusion, Cardiac complications, Thalassemia, Transfusion-Dependent thalassemia, And β -Thalassemia major

Introduction

Thalassemia is a group of quantitative hematological disorders characterized by reduced or absent globin chain production. The inherent pattern of thalassemia is mostly autosomal recessive. Based on clinical severity and transfusion requirement, they are classified into two main groups: Transfusion-Dependent Thalassemia (TDT) and Non-Transfusion-Dependent Thalassemia (NTDT).¹ Without adequate transfusion support, the TDT would suffer various complications and have a short life span; they require regular blood transfusions to survive. One of the TDT is β -thalassemia major.¹ The prevalence of thalassemia in Iraq is about 37.1/100,000.²

One unit of transfused blood contains around 200-250 mg of iron. Patients who receive more than 10 to 20 units of blood transfusions run a high risk of developing iron overload. Some patients require multiple transfusions, and excess iron accumulates in the liver, endocrine organs, heart, and other tissues, leading to significant morbidity and mortality.³ The most common cause of mortality in Transfusion-Dependent Thalassemia (TDT) is cardiomyopathy

due to iron overload, where iron overload plays a significant role in heart failure pathophysiology in early life, whereas hypoxia and chronic hemolysis play the main role in cardiac diseases in later life.^{4, 5} Serum ferritin level is commonly used to monitor iron overload, and serum ferritin of more than 2500 ng/Dl in TDT carries a high risk for cardiac-related mortality.⁶ Despite advancements in iron monitoring and iron chelators, comorbidities in β -thalassemia patients continue to manifest at an advanced age.^{7, 8}

Nameq et al. conducted a study at the Erbil Thalassemia Center and found that the prevalence of cardiac complications was 18.6% among the Transfusion-Dependent Thalassemia (TDT) patients.⁹ While other studies from different centers and countries show different prevalence of cardiac diseases, a study from Pakistan shows the prevalence of 60.6%,¹⁰ and a study from Iran demonstrates the prevalence of 62.8%.¹¹ The variation may be due to different management strategies.

Several studies have been done in the region to evaluate the prevalence of cardiac complications among patients with Transfusion-Dependent

Thalassemia (TDT), but most of them were based on a variable and relatively small sample size. Therefore, the present study was undertaken to better estimate the prevalence of cardiac complications among TDT patients using a larger sample size. Furthermore, this study intends to evaluate and determine the most common demographic and clinical factors related to the emergence and development of cardiac complications in this group of patients.

Methods and Material

This is a hospital-based, observational, cross-sectional study conducted in the Erbil Thalassemia Center, Erbil City, Kurdistan Region, Iraq, which serves as the primary referral center for patients with thalassemia in Erbil and the surrounding areas. This study was submitted to the Ethics and Scientific Committee of the Kurdistan Higher Council of Medical Specialities for scientific and ethical approval. The researchers obtained informed consent from the participants. The researchers informed the participants about the study's aims, and participation was voluntary.

This study included a total of 200 transfusion-dependent β -thalassemia major patients, who had a confirmed diagnosis of thalassemia, were on regular blood transfusion, and had regular follow-up at the Erbil Thalassemia Center; those with non-transfusion-dependent thalassemia, known congenital structural heart disease unrelated to thalassemia, and cases with incomplete clinical or echocardiographic data were excluded from the study.

All patients had standard two-dimensional, M-mode, and Doppler echocardiography done by an experienced cardiologist to check for possible cardiac complications, including left ventricular systolic function (using Simpson's method, systolic dysfunction was defined as $EF < 55\%$), left ventricular diastolic function (E/A ratio and other diastolic indices; dysfunction was categorized according to standard guidelines), chamber dimensions and volumes (left ventricle internal dimensions, left ventricle mass, and left atrial size); valvular function (presence and degree of Mitral Regurgitation (MR), Tricuspid Regurgitation (TR),

and Aortic Insufficiency (AI)), and right heart and pulmonary pressure (right ventricular size, tricuspid regurgitation gradient, and pulmonary hypertension were defined by an estimated Pulmonary Artery Systolic Pressure (PASP) greater than 35 mmHg).

The sample size for this study was estimated using the Open Epi calculator and the single population proportion formula to determine the prevalence of cardiac complications among patients with transfusion-dependent thalassemia. Considering previous studies reporting an estimated prevalence of 18.6% with a confidence level of 95% and a 5% margin of error, the minimum required sample size was calculated to be about 206 participants. The calculated sample size was sufficient to produce reliable estimates of the prevalence of cardiac complications and to evaluate the demographic and clinical correlates associated with the study population.

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 25 (IBM, New York, USA). We described categorical variables using frequency and percent and numerical data using mean and standard deviation. The relation between cardiac complications and other variables was tested using the chi-square test; if this method was inappropriate (due to low cell frequency), Fisher's exact test was used. The data were examined for normality using the Shapiro-Wilk and Kolmogorov-Smirnov tests, and the homogeneity of variance was examined using Levene's test for comparing the mean of two independent groups, a sample t-test is used. A p-value of less than 0.05 is considered significant.

Result

The sociodemographic data of the participants are listed in Table 1. The mean age of the participants was 23.65 years (± 12.39 SD), and the mean duration of blood transfusion was 19.69 years (± 12.5 SD). 50% of participants were male and 50% were female. 34% of participants receive blood monthly, 33% every 2 months, and 33% every 3 months. 95% were on iron chelating medication, and 5% were not. 51% were on a specific diet pattern. 7% were smokers. 9% were using alcohol. 67% were doing regular physical activity.

Table 1: Sociodemographic characteristics

		Frequency	Percentage
Age (year)	0-16	60	30%
	>17	140	70%
Gender	Male	100	50%
	Female	100	50%
Transfusion frequency	Monthly	68	34%
	Every 2 months	66	33%
	Every 3 months	66	33%
Use Iron chelation	Yes	190	95%
	No	10	5%
Specific diet pattern	None	98	49%
	Low iron	20	10%
	Cardiac diet	20	10%
	Renal diet	22	11%
	Low fat	22	11%
	Low salt	18	9%
Smoke	Yes	14	7%
	No	186	93%
Alcohol	Yes	18	9%
	No	182	91%
Regular physical activity	Yes	134	67%
	No	66	33%

Table 2: The prevalence of cardiac complications

	Frequency	Percentage (%)
Normal	167	83.5%
Diastolic dysfunction	14	7%
Pulmonary hypertension	9	4.5%
Heart failure	10	5%

Based on the echocardiography results, 83.5% of participants had no complications. 7% had diastolic dysfunction, 4.5% had pulmonary hypertension, and

5% had heart failure (Table 2). So the prevalence of cardiac complications among transfusion-dependent thalassemia patients was 16.5%.

Table 3 and Table 4 show the association between the occurrence of cardiac complications and other variables, in which the complications have a significant correlation with gender (more among females, P value < 0.0001), age (P value = 0.005), and blood transfusion duration (P value = 0.003). While the complications have no significant correlation with transfusion frequency (P value = 0.996), use iron chelation (P value = 0.149), a specific diet pattern (P value = 0.531), smoking (P value = 0.085), alcohol (P value = 0.493), and regular physical activity (P value = 1.000).

Table 3: Relation between sociodemographic characteristics and cardiac complications

		Cardiac complications		
		Normal	Complication	P-value
Gender	Male	93 (93%)	7 (7%)	< 0.0001

	Female	74 (74%)	26 (26%)	
Transfusion frequency	Monthly	57 (83.8%)	11 (16.2%)	0.996
	Every 2 months	55 (83.3%)	11 (16.7%)	
	Every 3 months	55 (83.3%)	11 (16.7%)	
Use Iron chelation	Yes	157 (82.6%)	33 (17.4%)	0.149
	No	10 (100%)	0 (0%)	
Specific diet pattern	None	83 (84.7%)	15 (15.3%)	0.531
	Low iron	18 (90%)	2 (10%)	
	Cardiac diet	15 (75%)	5 (25%)	
	Renal diet	16 (72.7%)	6 (27.3%)	
	Low fat	19 (86.4%)	3 (13.6%)	
	Low salt	16 (88.9%)	2 (11.1%)	
Smoke	Yes	14 (100%)	0 (0%)	0.085
	No	153 (82.3%)	33 (17.7%)	
Alcohol	Yes	14 (77.8%)	4 (22.2%)	0.493
	No	153 (84.1%)	29 (15.9%)	
Regular physical activity	Yes	112 (83.6%)	22 (16.4%)	1.000
	No	55 (83.3%)	11 (16.7%)	

Table 4: Relationship between age, blood transfusion duration and cardiac complication

	Mean (SD)		
	Normal (N=167)	Complications (N=33)	P-value
Age	22.57 ($\pm$ 12.26)	29.12 ($\pm$ 11.73)	0.005
Blood transfusion duration	18.51 ($\pm$ 12.32)	25.64 ($\pm$ 11.83)	0.003

Discussion

The patients with Transfusion-Dependent B-Thalassemia (TDT) face many complications due to iron overload from frequent blood transfusions, and one of the most common complications is related to the cardiovascular system, including heart failure, diastolic dysfunction, Mitral Regurgitation (MR), Tricuspid Regurgitation (TR), and pulmonary hypertension. With advancements in the management of iron overload, the complications

become fewer. We found that the prevalence of cardiac complications among transfusion-dependent thalassemia patients is 16.5%. And 7% had diastolic dysfunction, 4.5% had pulmonary hypertension, and 5% had heart failure. A study was conducted at the same center in 2020 and found that the prevalence of cardiac complications is 18.6%.⁹ While other studies from different countries have reported a higher prevalence of cardiac complications, two studies from Pakistan show the prevalence of 60.6% and 54.8%.^{10, 12} Two studies from Iran demonstrate the

prevalence of 62.8% and 12.3%.^{11, 13} Also, a systematic review by Koochi et al. in 2019 found that the prevalence of cardiac complications is 42% in transfusion-dependent β -thalassaemia.¹⁴ Several factors may contribute to the variability in the prevalence of cardiac complications in patients with transfusion-dependent thalassemia among studies. Variations in patient demographics, duration and severity of disease and access to healthcare services can have a major impact on the reported prevalence rates. Other important factors are the changes in transfusion practices and compliance to iron chelation therapy. Suboptimal chelation may lead to iron overload and increased cardiac involvement. In addition, differences in socioeconomic status, the availability of specialized thalassemia centers, and the use of different diagnostic methods or criteria to define cardiac complications may also contribute to the inconsistency among studies performed in different countries and regions. Disease severity and susceptibility to cardiac complications in thalassemia patients may also be influenced by genetic and environmental factors.

We found that there is a significant association between the occurrence of cardiac complications and the age of the patient and the duration of frequent blood transfusions. Older patients and those with longer transfusion durations have a higher prevalence of cardiac complications. This phenomenon is most probably due to more blood transfusions, which lead to more iron overload and then more deposition in different tissues, including the myocardium. Others, like Khalid et al. and Hussein et al. found that age and duration of blood transfusion significantly correlated with the occurrence of cardiac complications.^{10, 12}

The study has some limitations. It is cross-sectional and cannot establish causality. Echocardiography was limited to conventional parameters in many patients, and cardiac MRI T2* was not routinely available to directly quantify myocardial iron. In addition, some clinical data (e.g., exact transfusion volume per year, detailed adherence to chelation) may be incomplete or based on records that vary in quality. Despite these limitations, the study provides valuable, real-world insight into the cardiac burden among TDT patients in Erbil City.

Conclusion

We concluded the prevalence of the cardiac complications among patients with β -thalassemia major is 16.5%. The study found that the condition predominantly affects females, older age groups, and those with long transfusion durations. The study points out the necessity of early screening for patients who have been on transfusions for a long time. Routine screening in patients with Transfusion-Dependent Thalassemia (TDT) for the cardiac complications is essential for early detection of iron overload and myocardial deposition. This is for early treatment and management to minimize cardiac complications and optimize outcomes.

Conflict of interest

No conflict of interest.

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