Original Research Article

Frequency of cardiomyopathy in children having Thalassemia major: A cross-sectional study

Abstract

Aim: To determine the frequency of cardiomyopathy in children having Thalassemia major diagnosed on the basis of Echocardiography

Study design: A cross-sectional study

Place and Duration: Paediatric department at PMCH hospital, Nawabshah from September 2019 to March 2020

Methodology: A total of 236 Thalessemic children visiting as outpatients or inpatients meeting inclusion criteria were enrolled. Informed consent was taken from the patients or their attendants. All demographic variables that included age, gender, address, educational status, family history, age of diagnosis of the disease, start of treatment and number of transfusions graded as none, occasional, were included. Echocardiography findings were performed and then recorded.

Results: Mean age of the patients was 10.60±4.064 (5-18) years, 118(49.1%) study subjects were female and 126(50.8%) were male patients. While 75(31.78%) study subjects have family history of thalassemia. A total of 87(36.9%) study subjects have left ventricular dysfunction, 13(5.5%) have global dysfunction, 11(4.7%) have isolated systolic dysfunction and 37(30.9%) have isolated diastolic dysfunction.

Conclusion: In -thalassemia, heart disease is the key determinant of prognosis and survival. In this study we found a significant number of thalassemia children having cardiac involvement and ventricular dysfunction

Key Words: cardiomyopathy, Thalassemia major, Echocardiography, Children, ventricular dysfunction

Introduction

Thalassemia is an autosomal recessive condition that affects about 15 million people globally [1]. The disease is notably prevalent among Mediterranean and Asian peoples, with the Maldives population having the highest rate of carrier state (18%) [2, 3]. In Pakistan, almost forty thousand children are infected by Thalassemia major, with an additional five thousand added each year. Thalassemia was diagnosed on electrophoresis in 61 percent of Pakistanis in 2013, with thalassemia significant occurring in 5.9% of the population [4].

Cardiomyopathies are cardiac muscle illnesses that cause heart failure, either as a result of a dilated left ventricle and decreased contractility [5]. The cause of cardiomyopathy in Thalassemia major is multifaceted, with iron overload playing a significant role. Despite breakthroughs in treatment, cardiac problems from iron overload remain the leading cause of morbidity and mortality [6]. Diastolic dysfunction precedes systolic dysfunction in Thalessemic cardiomyopathy, and early chelation treatment intervention is critical due to a poor prognosis.

Clinically there is a variable presentation of heart failure including exertional dyspnea, orthopnea and crackles on examination in case of left heart failure and for right heart failure increased jugular venous dilatation, hepatomegaly, peripheral edema, tender liver and ascites. Doppler

echocardiography is the imaging modality of choice for revealing progressive myocardial contractility [7].

According to Faruqi et al, 88.1 percent of Thalessemic patients had echocardiographic abnormalities. Cardiovascular problems include tachy-bradyarrythmia, conduction abnormalities, abrupt cardiac death, and heart failure, according to Faruqi et al in a 2014 research [8]. Another observational study published in 2009 by Arshad et al reported that 38 percent of thalassemic patients' not on chelation therapy or on irregular chelation had LV dysfunction, with systolic dysfunction (2%), diastolic dysfunction (30%), and global dysfunction (3%) cases 9. LV dimensions and stroke volume were also quite large [9].

The current study is planned to determine the frequency of clinical and radiological findings of cardiomyopathy in thalassemia major patients in order to help improve the quality of life of patients by regularly assessing cardiac function as poor compliance with chelation, chronic anemia and non-availability of cardiac monitoring is increasing cardiac morbidity in thalassemia major patients.

Methodology

This study was done at Paediatric department at PMCH hospital, Nawabshah from September 2019 to March 2020. Non-probability, convenient sampling technique was used. A sample of 236 patients as calculated by 95% confidence interval and prevalence of global dysfunction in Thalassemia major patients 4% at margin of error 2.5%. All known thalassemic children age between 5-18 years of both gender were included in the study. Thalessemic patients with mental retardation or suffering from some other chronic illness and patients taking oral iron chelators were excluded.

Data were collected from Thalessemic patients visiting as outpatients or inpatients in Department of Pediatrics in PMCH Hospital meeting inclusion criteria. Consent was taken parents were assured for confidentiality of information. Plain language was used between researcher and responders. Age, sex, address, educational status, family history, age of disease diagnosis, commencement of treatment, and number of transfusions rated as none, occasional (1-5 times/year), low (6-12 times/year), and high (13-22 times/year) were all included in the study. The results of the echocardiography were then documented.

SPSS version 23.0 was used for data handling. Statistical analysis was expressed as frequencies and percentages for qualitative variables gender, family history of thalassemia, Left ventricular dysfunction, isolated systolic & diastolic dysfunction and global dysfunction. Mean and standard deviation of patient's age, number of transfusions, and age at diagnosis were measured, Effect modifiers age, gender, age at diagnosis, family history of thalassemia were controlled through stratification chi square test was applied. P-value less than 0.05 was kept significant.

Results

A total of 236 patients were included in the study. In table 1 descriptive statistics of all quantitative variables was calculated in term of mean and standard deviation. Mean age of the patients was 10.60±4.064 (5-18) years. Mean number of transfusion was 12.6±4.7 (2-26). Mean age at diagnosis of thalassemia was 4.3±1.8 (3-7) years. In table 2, 118(49.1%) study subjects were female and 126(50.8%) were male patients. While 75(31.78%) study subjects have family history of thalassemia.

In table 3 echocardiographic finding of cardiomyopathy were stated, 87(36.9%) study subjects have left ventricular dysfunction, 13(5.5%) have global dysfunction, 11(4.7%) have isolated

systolic dysfunction and 37(30.9%) have isolated diastolic dysfunction. In table 4 - 7 stratification for echocardiographic finding were stated with respect to age, gender, family history of thalassemia, age at diagnosis and number of blood transfusions. P-values were significant with p-value=<0.05.

Table: 1 Descriptive statistics of study participants (n=236)

Variables	**n**	**Mean**	**Std. Deviation**
Age (Years)	236	10.60	4.064
No. of transfusions	236	12.6	4.7
Age at diagnosis	236	4.3	1.8

Table: 2 Characteristics of study participants (n=236)

Variables	**Frequency(n)**	**Percentages**
Gender		
Female	110	49.1
Male	126	50.8
Family H/o thalassemia		
Yes	75	31.78

No	161	68.22

Table: 3 Distribution of cardiomyopathy (n=236)

Cardiomyopathy (Echocardiographic finding)	**Frequency**	**Percentages**
Left ventricular dysfunction	87	36.9
Global dysfunction	13	5.5
Isolates systolic dysfunction	11	4.7
Isolated diastolic dysfunction	73	30.9

Table: 4 Stratification of left ventricular dysfunction with respect to effect modifiers (n=236)

Effect modifiers	**Left ventricular dysfunction**		**Total**	**P-value**
	Yes	**No**		
Age				0.23

<10 years	38(33.3%)	76(66.7%)	114(100%)	
≥10 years	49(39.8%)	74(60.2%)	122(100%)	
Gender				
Female	41(37.3%)	69(62.7%)	110(100%)	
Male	46(36.5%)	80(63.5%)	126(100%)	0.90
Family H/o thalassemia				0.29
Yes	24(32%)	51(68%)	75(100%)	
No	63(39.1%)	98(60.9%)	161(100%)	
No. of transfusions				
<10	29(30.9%)	65(69.1%)	94(100%)	0.12
≥10	58(40.8%)	84(59.2%)	142(100%)	
Age at diagnosis				
<5 years	51(32.3%)	107(67.7%)	158(100%)	0.03
≥5 years	36(46.2%)	42(53.8%)	78(100%)	

Table: 5 Stratification of Isolated systolic dysfunction with respect to effect modifiers (n=236)

Effect modifiers	**Isolated systolic dysfunction**		**Total**	**P-value**
	Yes	**No**		
Age				
<10 years	5(4.4%)	109(95.6%)	114(100%)	
≥10 years	6(4.9%)	116(95.1%)	122(100%)	0.8
Gender				
Female	4(3.6%)	106(96.4%)	110(100%)	
Male	7(5.6%)	119(94.4%)	126(100%)	0.5
Family H/o thalassemia				0.02
Yes	7(9.3%)	68(90.7%)	75(100%)	
No	4(2.5%)	157(97.5%)	161(100%)	
No. of transfusions				
<10	4(4.3%)	90(95.7%)	94(100%)	0.8
≥10	7(4.9%)	135(95.1%)	142(100%)	
Age at diagnosis				0.12

<5 years	5(3.2%)	153(96.8%)	158(100%)	
≥5 years	6(7.7%)	72(92.3%)	78(100%)	

Table: 6

Stratification of Isolated diastolic dysfunction with respect to effect modifiers (n=236)

Effect modifiers	**Isolated diastolic dysfunction**		**Total**	**P-value**
	Yes	**No**		
Age				0.16

<10 years	41(36%)	73(64%)	114(100%)	
≥10 years	32(26.2%)	90(73.8%)	122(100%)	
Gender				
Female	31(28.2%)	79(71.8%)	110(100%)	
Male	42(33.3%)	84(66.7%)	126(100%)	0.39
Family H/o thalassemia				0.39
Yes	26(34.7%)	49(65.3%)	75(100%)	
No	47(29.2%)	114(70.8%)	161(100%)	
No. of transfusions				
<10	33(35.1%)	61(64.9%)	94(100%)	0.25
≥10	40(28.2%)	102(71.8%)	142(100%)	
Age at diagnosis				
<5 years	45(28.5%)	113(71.5%)	158(100%)	0.24
≥5 years	28(35.9%)	50(64.1%)	78(100%)	

Table: 7 Stratification of global dysfunction with respect to effect modifiers (n=236)

Effect modifiers	Global dysfunction		Total	P-value
	Yes	No		
Age				
<10 years	4(3.5%)	110(96.5%)	114(100%)	
≥10 years	9(7.4%)	113(92.6%)	122(100%)	0.19
Gender				
Female	5(4.5%)	105(95.5%)	110(100%)	
Male	8(6.3%)	118(93.7%)	126(100%)	0.54
Family H/o thalassemia				0.25
Yes	6(8%)	69(92%)	75(100%)	
No	7(4.3%)	154(95.7%)	161(100%)	
No. of transfusions				
<10	3(3.2%)	91(96.8%)	94(100%)	0.25
≥10	10(7%)	132(93%)	142(100%)	
Age at diagnosis				0.02
<5 years	5(3.2%)	153(96.8%)	158(100%)	

≥5 years	8(10.3%)	70(89.7%)	78(100%)	

Discussion

Higher LV early diastolic filling and a high E/A ratio in this case study indicated a restricted diastolic pattern and, as a result, a stiff LV wall. Yaprak et al. [10] found that -TM patients (n = 63) exhibited significantly larger E wave, E/A ratio, and lower A wave velocity, indicating restrictive pattern in 54 percent of the study group. In a similar study, Doppler measurements of trans-mitral diastolic filling in individuals with -TM (n = 32, none of whom had heart failure) revealed a restrictive pattern. [11] This was also in line with a prior analysis that stated that the most common finding in individuals with TM is a high E/A ratio [12].

The TDI peak systolic velocity (Sm) and diastolic parameter (E/Em ratio) in our instance were both abnormally high. Marci et al. found a link between baseline systolic velocity (Sm) of less than 7.9 cm/s and cardiac problems (P 0.05). They also discovered that systolic velocity is inversely associated to plasmatic levels of NT-proBNP (P 0.001) [13].

The current study found that 40 women vs 19 males had normal LV systolic function, with a significant difference (P=0.024), despite the fact that both groups received the same treatment. These results are comparable to those reported by Hahallis et al [14]. For example, Bosi et al. [15] found that serum ferritin levels >2,500 ng/mL were associated with lower LV systolic performance than levels 1,000 ng/mL. When serum ferritin levels were less than 2,500 ng/mL,

Silvilairat et al. [16] discovered that cardiac systolic function was normal. Shahmohammadi et al. [17,] Finazzo et al. [18], and Yapark et al. [19] conducted research that were similar to ours. The disparity across the studies could be due to differing time intervals between the onset of cardiac siderosis and the onset of cardiac dysfunction.

Previous research compared thalassemia major patients' cardiac function to that of a healthy control group, ignoring the separate effects of anaemia on the heart. This is the only study that we are aware of that compares thalassemia major patients to groups of healthy controls or anaemic patients. Anemia has been linked to changes in cardiovascular structure and function.

In comparison to healthy controls, people with thalassemia major had decreased haemoglobin levels at the time of the echocardiographic exam (at least 4 hours following blood transfusion). Patients with thalassemia major had higher haemoglobin levels than those with anaemia.

We also found that the amount of thalassemia major haemoglobin before blood transfusion on the day of echocardiographic evaluation did not differ substantially from the Anemia group (data not shown). As a result, we may conclude from our research that the cardiac changes observed in the Thalassemia group versus the Anemia group are due to iron overload rather than anaemia. A large observational research of 6,657 people found that a left atrium volume/body surface area ratio of > 34 ml/m2 is an independent risk factor for heart failure [20].

Limitations

Our study has some limitations, such as the small number of participants and the lack tissue Doppler that can detect left ventricular diastolic abnormalities more better.

Conclusion: Heart disease is the primary determinant of prognosis and survival in β-thalassemia. In this study we found a significant number of thalassemia children having cardiac involvement and ventricular dysfunction

Permission

It was taken from the ethical review committee of the institute

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