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Echocardiographic status of cardiac left ventricular function in thalassemia intermedia patients

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Abstract

This study was conducted to assess the cardiac function by echocardiography in a group of thalassemia patients. Thirty thalassemia intermedia participants (mean age: 24.5±9.7years) were examined clinically and subjected to routine hematological investigations, serum ferritin level, chest radiography, ECG and Echocardiography. The findings of thalassemia intermedia participants were as follows: the mean ejection fraction (%) was 65.30±6.42, among 30 patients, 29(96.7%) showed normal and one (3.3%) showed mildly abnormal ejection fraction. The mean fractional shortening (%) was 36.20±4.93 and 30 patients (100%) showed normal fractional shortening. Furthermore, the mean myocardial performance index was 0.62±0.13 and one patient (3.3%) showed normal and 29(96.7%) showed abnormal myocardial performance index. The mean left ventricular post wall thickness was 0.84±0.11cm and 29(96.7%) patients showed normal and one (3.3%) showed mildly abnormal left ventricular post wall thickness. The mean septal thickness was 0.87±0.12cm and 27(90%) patients showed normal and 3 (10%) showed mildly abnormal septal thickness. The mean pulmonary arterial systolic pressure was 27.73±8.23 mm Hg and 20(66.7%) patients showed normal and 10(33.3%) showed abnormal pulmonary arterial systolic pressure. The mean isovolumic relaxation time was 81.33±16.23msec and 13(43.3%) patients showed normal and 17(56.7%) showed abnormal isovolumic relaxation time. The mean mitral inflow velocity in thalassemia intermedia was 1.66±0.76 and 17 (56.7%) patients showed normal, one (3.3%) showed mild and 12(40.0%) showed severe diastolic dysfunction. Finally, it can be said that the cardiac left ventricular systolic and diastolic function of thalassemia intermedia participants were affected in respect to investigations performed.

Introduction

ß-Thalassemia is considered as an inherited hemoglobin disorder due to chronic hemolytic anemia.1Depending on clinical severity, two forms of thalassemia such as thalassemia major and thalassemia intermedia have been identified as thalassemia major is a severe anemia that started at the first year of life and life-long blood transfusion therapy is needed for survival. On the other hand, thalassemia intermedia is measured as a milder anemia which permits patient survival without regular transfusions and a longer life expectancy.2Previous studies have anticipated that the patients who naturally maintain hemoglobin at or above 7g/dl, even with bone marrow hyperplasia are considered as thalassemia intermedia.3,4Chronic anemia due to thalassemia intermedia causes growth retardation,

extra medullary hematopoiesis, bone marrow expansion, splenomegaly, increased intestinal iron absorption, prone to infections, and hypercoagulability.1,5

Heart disease is not only a leading cause of mortality but also responsible for morbidity in ß-thalassemia.6Furthermore, without proper treatment of thalassemia intermedia, the diastolic function of the left ventricle can be maintained stable but the pressure of pulmonary arteries rises continuously that causes death of these patient.2Furthermore, it was reported that deposition of iron causes heart failure in thalassemia major patients whereas high cardiac output causes heart failure in thalassemia intermedia patients .7However iron induced cardiac dysfunction may also occur in thalassemia intermedia patients during exposure to non-transferrin bound iron.8, 9

Inappropriate erythropoiesis due to chronic hemolytic anaemia is considered as a symbol of all thalassemia syndromes.10However in thalassemia intermedia chronic anaemia may always not be severe and the hemoglobin usually maintained within 7-11g/dl. In normal individual with hemoglobin range between 8-10g/dl, the resting cardiac output is usually maintained within the normal limit.11The percentage of fetal hemoglobin is also important as it decrease the oxygen delivery to the tissue due to its high oxygen affinity. 12

Prolong tissue hypoxia causes reactionary expansion of the bone marrow, splenomegaly, extra medullary hematopoiesis, hepatomegaly and ultimately leads to high output state.13, 14-16It is also stated that, high cardiac output results from the combined action of intramedullary shunting and peripheral vasodilatation.15,16

Every year approximately 60,000-70,000 children are born around the world with severe form of thalassemia. Most of them are born in the countries with lower socioeconomic condition where child mortality from infection and malnutrition is more prioritized.17It isestimated that, each year, around six thousands children are born with thalassemia in Bangladesh.18In a study, Khan et al19 found that, there is about 1 lac thalassaemic patient prevailing in Bangladesh and it is assumed that each year approximately 1040 β-thalassaemia major and 6443 Hb-E β-thalassaemia are born in our country. Another study, that was performed at Department of Haematology, Bangabandhu Sheikh Mujib Medical University, showed that 61.8% of the HbE/β thalassemia patients were transfusion independent, indicating the higher incidence of thalassemia intermedia in Bangladesh20.

The development of new technologies such as cardiac magnetic resonance T2, Tissue Doppler, 3D detection of cardiac dysfunction helps in the early detection of cardiac iron overload and associated cardiac dysfunction in thalassemia.21 Moreover, the estimation of serum ferritin level along with echocardiogram might be more effective for the assessment of iron overload and cardiac function. However, few studies have been performed regarding this matter. From these discussions it is obvious that the abnormality in the cardiac function is the leading cause of death of these patients so the purpose of this study was to assess the cardiac functions of the thalassemia patients by means of

echocardiography, help in formulating an effective and better management plan to prevent chronic anemia, iron overload and its complication, other cardiac dysfunction in thalassemia patients and in this way the study may also help in improving survival.

Materials and Methods

This study was conducted on 30 thalassemia intermedia participants from January 2015 to December 2015 in the inpatient Department of Hematology. Patients with known case of thalassemia intermedia who don't have preexisting diseases that can affect the heart like rheumatic, congenital heart failure, systemic hypertension, endocrinopathy, renal diseases, anemic heart failure etc were randomly selected for this study. Other patients who are transfusion dependent or have those preexisting diseases were excluded.

At first, the investigations were performed for all participants that include complete blood count by using automated cell counter (Sysmex XT 2000i), serum ferritin level by chemiluminescent microparticle immunoassay (CMIA) using ARCHITECT ci 8200, Kit –ARCHITECT Ferritin 7K59 and standard 12-lead electrocardiography (ECG; FUKUDA M_E CARDISUNY)and heart rate was calculated by the standard method. After that, Echocardiography (2-D, M-mode and Doppler; General Electronics vivid-7 echocardiogram machine) was performed in thalassemia intermedia participants according to guideline of American Heart Association (AHA) of echocardiography. Echocardiographic assessment was performed using mechanical and phased array sector scanner with 2.5-3.5 MHz transducers. The examination was conducted with the patient lying in supine left lateral position. The left parasternal long axis and short axis and apical four chamber views were obtained in all thalassemia patients. The left ventricular systolic function such as fractional shortening, ejection fraction, left ventricular global function such as myocardial performance index, left ventricular diastolic function such as Mitral inflow velocity, intraventricular relaxation time, and other parameters such as left ventricular post wall thickness, septal thickness, pulmonary arterial systolic pressure and pulmonary arterial mean pressure were also measured. were also measured. Furthermore, all relevant hematological and biochemical tests were done at authentic laboratories. Statistical analysis was done by using SPSS software (version 22). The data were expressed as frequency, percentage and mean±SD

Results

Among 30 patients of thalassemia intermedia, 16 (53.3%) patients were male and 14 (46.7%) patients were female and male female ratio was 1.14: 1 (Table-1). The mean age of the participants was 24.5±9.67, among them 46.7% belonged to 19-29 years, 26.7% to 8-18 years and 26.7% to 30-40 years age group. The age range was 8-40 years (Table-2). Clinically all the study patients had anaemia (100%), 12(40.0%)

had jaundice and 29(96.7%) had splenomegaly. None of them had symptoms of heart failure or CVS abnormality (Table-3).

The echocardiographic findings showed that the mean ejection fraction (%) was 65.30±6.42, among 30 patients, 29(96.7%) showed normal and one (3.3%) showed mildly abnormal ejection fraction. The mean fractional shortening (%) was 36.20±4.93 and 30 patients (100%) showed normal fractional shortening .Furthermore, the mean myocardial performance index was 0.62±0.13 and one patient (3.3%) showed normal and 29(96.7%) showed abnormal myocardial performance index. The mean left ventricular post wall thickness was 0.84±0.11cm and 29(96.7%) patients showed normal and one (3.3%) showed mildly abnormal left ventricular post wall thickness. The mean septal thickness was 0.87±0.12cm and 27(90%) patients showed normal and 3 (10%) showed mildly abnormal septal thickness. The mean pulmonary arterial systolic pressure was 27.73±8.23 mm Hg and 20(66.7%) patients showed normal and 10(33.3%) showed abnormal pulmonary arterial systolic pressure. The mean isovolumic relaxation time was 81.33±16.23msec and 13(43.3%) patients showed normal and 17(56.7%) showed abnormal isovolumic relaxation time. The mean mitral inflow velocity in thalassemia intermedia was 1.66±0.76 and 17 (56.7%) patients showed normal, one (3.3%) showed mild and 12(40.0%) showed severe diastolic dysfunction (Table-4).

Gender	**Frequency**	**Percentage%**
Male	*16*	53.3
Female	*14*	46.7
Total	30	100.0

Table-1 Distribution of patients by gender (n=30)

Age Group (in years)	**Frequency**	**Percentage%**	
8-18 yrs	8	26.7	Mean±SD 24.5±9.67 Range (8 – 40)
19-29 yrs	14	46.7	
30-40 yrs	8	26.7	
Total	30	100.0	

Table-2 Distribution of patients by age group (n=30)

Clinical presentation	Frequency	Percentage%
Anaemia	30	100.0
Jaundice	12	40.0
Splenomegaly	29	96.7
Symptom of heart failure	0	0.0
CVS (any abnormality detected)	0	0.0

Table-3 Distribution of the patients by clinical presentation

Echo parameter	Frequency	Percentage%	Range	Mean±SD
Fractional shortening (FS) (%)				
Normal (Men: 25-43; Women: 27-45)	30	100.0		
Mildly abnormal (Men: 20-24; Women: 22-26)	0	0.0		
Moderately abnormal (Men: 15-19; Women: 17-21)	0	0.0	28 – 47 %	36.20±4.93
Severely abnormal (Men: ≤14; Women: ≤16)	0	0.0		
Ejection fraction (EF) (%)				
Normal (Men: ≥55; Women: ≥55)	29	96.7		
Mildly abnormal (Men:45-54; Women: 45-54)	1	3.3	53 – 79%	65.30±6.42
Moderately abnormal (Men: 30-44; Women: 30-44)	0	0.0		
Severely abnormal (Men: <30; Women: <30)	0	0.0		
Myocardial performance index (MPI)				
Normal (<0.40)	1	3.3	0.37-0.83	0.62±0.13
Abnormal (>0.40)	29	96.7		
Mitral inflow velocity (E/A)				
Normal (0.75-1.5)	17	56.7		
Mild diastolic dysfunction (impaired relaxation) (≤0.75)	1	3.3	0.69 -4.20	1.66±0.76
Moderate diastolic dysfunction (pseudo normal) (0.75 - 1.5)	0	0.0		
Severe diastolic dysfunction Restricted (≥1.5)	12	40.0		
Isovolumic relaxation time (IVRT)				
Normal (70±12 ms)	13	43.3		
Abnormal (< 58 ms)	6	20.0	39-111ms	81.33±16.23
Abnormal (> 82 ms)	11	36.7		
LV post wall thickness (cm)				

Normal Men: 0.6-1.0 cm Women: 0.6-0.9 cm	 16 13	 53.3 43.3	0.6-1.0cm	0.84±0.11
Mildly abnormal Men: 1.1-1.3 cm Women: 1.0-1.2 cm	 0 1	 0.0 3.3		
Septal thickness (cm)			0.6-1.1cm	0.87±0.12
Normal (Men: 0.6-1.0 cm) (Women: 0.6-0.9 cm)	 14 13	 46.7 43.3		
Mildly abnormal (Men: 1.1-1.3 cm) (Women: 1.0-1.2 cm)	 2 1	 6.7 3.3		
Pulmonary arterial systolic pressure (PASP)			12-46	27.73±8.23
Normal (15-30 mm Hg)	20	66.7		
Abnormal (>30 mm Hg)	10	33.3		
Pulmonary arterial mean pressure (PAMP)			4.0-25.0	13.48±4.78
Normal (upto 25 mmHg)	30	100.0		
Raised ((>25 mmHg)	0	0.0		

Table-4. Echocardiographic findings:

Discussion:

In echocardiography among 30 patients with thalassemia intermedia, 29(96.7%) showed higher myocardial performance index and 29(96.7%) patients showed normal and one (3.3%) showed mildly abnormal left ventricular post wall thickness. Regarding mean septal thickness, 27(90%) patients showed normal and 3 (10%) showed mildly abnormal septal thickness. The ejection fraction (%) was normal in 29(96.7%) and mildly abnormal in one (3.3%) patient and the fractional shortening (%) was normal in 30(100%) patients. The pulmonary arterial systolic pressure was normal in 20(66.7%) and abnormal in 10(33.3%) patients and the isovolumic relaxation time was normal in 13(43.3%) and abnormal in 17(56.7%) patients. The mitral inflow velocity was normal in 17 (56.7%) patients and mild diastolic dysfunction in one (3.3%) and severe diastolic dysfunction in 12(40.0%) patients.

Bosi et al.22 reported an increased in myocardial performance index in thalassemia group which is similar to our findings. An increased in left ventricular posterior wall thickness in the study patient was reported by Stakos et al.23 and Aessopos et. al.24 but our result showed 29(96.7%) patients with normal and one (3.3%) with mildly abnormal left ventricular post wall thickness. In our study 27(90%) patients showed normal and 3 (10%) showed mildly abnormal septal thickness but the study of Stakoset al.23 and Nouri et al.25 reported significant difference in the mean septal thickness between thalassemia intermedia and healthy group, but Karimi study26 showed a decreased in both the parameters. In our

study the ejection fraction (%) was normal in 29(96.7%) and mildly abnormal in one (3.3%) patient and the fractional shortening (%) was normal in 30(100%) patients but both the parameters were lower in thalassemia group in a study of Nouri et al.25. Other study showed a decrease in fractional shortening of these patients that was a sign of left ventricular dysfunction.22,27

The pulmonary arterial systolic pressure was normal in 20(66.7%) and abnormal in 10(33.3%) patients. Aessopos et. al.13 reported pulmonary hypertension in a small sample of 7 patients with thalassemia intermedia and that was the main cardiac finding in the other systematic study.28 Furthermore, tissue hypoxia, inevitable in patients who undergo delayed or infrequent blood transfusions, seems to play the central role in the development of pulmonary hypertension in thalassemia intermedia.13 The isovolumic relaxation time was normal in 13(43.3%) and abnormal in 17(56.7%) patients in the present study. Furthermore, a higher isovolumic relaxation time of the left ventricle is a diastolic performance index showed in many studies and it may due to deposition of iron during the resting time of the ventricles. It is considered as the gradual cause for restrictive cardiomyopathy which is the earliest symptom of diastolic performance disorder of left ventricle.29,30,31The mitral inflow velocity was normal in 17 (56.7%) patients and mild diastolic dysfunction was found in one (3.3%) and severe diastolic dysfunction in 12(40.0%) patients.

Vaccari M et. al.27 also concluded an increased mitral inflow velocity in thalassemia patients which is comparable with this study. But Iarussi32 showed a decrease in mitral inflow velocity in thalassemia patients.

In a study Amoozegar33showed that, in thalassemia patients, pulsed Doppler and pulsed tissue Doppler imaging were better than M-mode and 2D echocardiography in assessing cardiac dysfunction. But Bilge et al.34showed, for detection of early LV dysfunction, tissue Doppler imaging was more helpful. However, from this study it is obvious that, in Bangladesh perspective, 2D and Doppler echocardiography has significant importance in the assessment of cardiac function in thalassemia intermedia patients.

Conclusion

Finally it can be concluded that both the systolic and diastolic performance of the left ventricle in thalassemia intermedia patients were affected due to the parameters used in this study that includes ejection fraction, fractional shortening, myocardial performance index, left ventricular post wall thickness, septal thickness, mitral inflow velocity and isovolumic relaxation time.

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