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Comparison of Cardiac Function in Young Patients with Thalassemia Intermedia and Healthy Individuals Using Echocardiography Method

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Abstract

Background: Cardiac dysfunction due to chronic anemia and hemosiderosis are the major causes of death among patients with thalassemia intermedia. This study was performed to compare the cardiac function in thalassemia intermedia patients with normal subjects by means of echocardiography.

Materials and Methods: This was a case-control study performed on 22 patients affected by thalassemia intermedia in the age range of 8 to 25 years treated in pediatric ward of Ali Ibn-e Abi Talib teaching hospital, Zahedan, , South East of Iran, from January 2007 until July 2008. There was no sign of cardiac involvement by physical examination, chest x-ray and ECG in these patients. The control group was selected from normal individuals and was matched by sex and age (66 healthy individuals). Echocardiographic parameters were measured in patient and control groups.

Results: Findings of this study showed that the mean age of patients was years and the mean age of the control group was years (p=0.6). The mean left ventricular myocardial performance index (p=0.001), left ventricular mass index (p=0.0001) interventricular septal dimension in diastole (p=0.002), left ventricular posterior wall thickness in diastole (p=0.001), interventricular septal dimension in systole (p=0.01), left ventricular posterior wall dimension in systole (p=0.003), aortic pre-ejection period/ejection time (p=0.009), ejection fraction (p=0.019), fractional shortening (p=0.04), left ventricular isovolumetric contraction time (p=0.0001), left ventricular isovolumetric relaxation time (p=0.0001), right ventricular myocardial performance index (p=0.0001), and isovolumetric relaxation time (p=0.0001) were statistically significantly different between patients and controls. Other echocardiographic parameters did not show a statistically significant difference between patients and controls.

Conclusion: The results of the present study show that cardiac systolic and diastolic function in patients with thalassemia intermedia is compromised in comparison with the control group.

Keywords: Thalassemia intermedia, echocardiography, cardiac function

Introduction

Thalassemia is one of the most common hematologic disorders in human beings. This disease is prevalent in Mediterranean region, India, Burma, north of China, up to regions in Pacific Islands. Thalassemia is of two major types namely Alpha and Beta in which the alpha and beta globin chains are involved. The main feature of this anemia syndrome is the deficiency or the lack of one or more globin chains [1]. Beta thalassemia intermedia is a kind of beta thalassemia which shows clinical symptoms somewhere between asymptomatic carriers and thalassemia major [1].

The main cause of early death in such patients is the cardiac complications such as systolic and diastolic disorders caused by hemosiderosis [2,3]. The studies conducted so far indicate that the end-systolic and the end-diastolic dimension index and also the whole heart index and the systolic

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dimension among thalassemia intermedia patients show a significant increase compared with the control group. It happens while the patients do not receive blood transfusion and do not show any clinical symptoms of cardiac disorder [4].

Aessopos et al. study showed that two factors have a major role in the cardiac failure among thalassemia intermedia patients namely the increase in cardiac output, which is the result of chronic tissue hypoxia, and the vascular complications which increase pulmonary vascular resistance and systemic vascular rigidity [5]. Another study showed that in the absence of regular treatment for thalassemia intermedia the diastolic performance of the left ventricle is maintained, while the pressure of pulmonary arteries continues to rise which is the main cause of death among these patients [6].

In another research performed by Mavrogeni et al, they found that although, iron plays a significant

Table1: Echocardiographic parameters of the left ventricle among patients and the control group.

*Parameter	Thalassemia Intermedia group (n=22)	Control group (n=66)	p-value
MPI	0.14±0.61	0.06±0.4	0.0001
LVMI	110.5.40.86±	32.60±76.53	0.0001
PEP	9.90±93.31	9.46±90.85	0.19
ET	25.45±250.8	20.76±07/262	0.034
PEP/ET	0.03±0.36	0.04±0.34	0.009
(IVSD (mm	1.76±7.29	1.02±6.44	0.002
(LVPWD (mm	1.4±4.61	0.49±3.99	0.001
(IVSD (mm	2.52±10.84	1.32±9.84	0.01
(LVPWS (mm	1.50±4.72	0.48±4.13	0.003
(LVEDD (mm	6.93±48.72	5.98±48.31	0.78
(LVESD (mm	5.36±31.78	7.6±32.93	0.49
(%) EF	7.12±61.56	6.63±65.46	0.019
(%) SF	5.26±33.68	4.94±36.17	0.041
(AO(mm	4.08±24.26	2.95±23.63	0.42
(LA (mm	3.81±29.45	3.81±27.89	0.09
(AO/LA (mm	0.17±1.22	0.17±1.18	0.32
(ICT (m/sec	18.78±43.68	11.13±28.10	0.0001
(IRT (m/sec	16.64±110.09	15.34±96.25	0.0001
(AT (m/sec	16.33±61.86	9.67±78.10	0.43
(DS (m/sec	31.79±122.31	35/23±118.56	0.54
(DT (m/sec	18.78±126.09	18.69±125.43	0.88
(Peak E (m/sec	16.76±102.04	24.61±103.85	0.44
(Peak A (m/sec	12.70±46.65	15.19±61.31	0.34
(E/A (m/sec	0.23±1.59	0.73±1.94	0.34

*** MPI**: Myocardial performance index; LVMI: Left ventricular mass index; PEP: Pre-ejection period; ET: Ejection time; PEP/ET: Pre-ejection period/ejection time; IVSD: Interventricular septal dimension in diastole; LVPWD: Left ventricular posterior wall dimension in diastole; IVSS: Interventricular septal dimension in systole; LVPWS: Left ventricular posterior wall dimension in systole; LVEDD: Left ventricular end-diastolic dimension; LVESD: Left ventricular end-systolic dimension; EF: Ejection fraction; SF: Shortening fraction; AO: Aorta diameter; LA: Left atrium diameter; AO/LA: Aorta/Left atrium diameter; ICT: Isovolumic contraction time; IRT: Isovolumic relaxation time; AT: Acceleration time; DS: Deceleration slope; DT: Deceleration time; Peak E: Peak E velocity; Peak A: Peak A velocity; E/A: E/A velocity ratio.

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role in pathophysiology of cardiac failure in thalassemia major, but it seems that in thalassemia intermedia, the cardiac output is the major cause of cardiac failure [7]. Since there has been no study on the cardiac problems of such patients in Iran, and the studies in other parts of the world are not plenty, the present study compares the heart performance of these patients by means of echocardiography with normal subjects.

Materials and Methods

This was a case-control study performed on 22 patients affected by thalassemia intermedia in the age range of 8 to 25 years treated in pediatric ward of Ali Ibn-e Abi Talib teaching hospital, Zahedan, South East of Iran, from January 2007 until July 2008. The patients were initially interviewed, clinically examined, and the chest radiography and electrocardiogram was taken.

Those participants who suffered from high blood pressure, metabolic, endocrine , kidney disorders or used to take heart drugs or had a Hb<8g/dl were excluded from the study.

At the end, 22 patients (group A) were selected for the experiment. Sixty six children at the same age and gender and without any cardiac or other problems were selected as the control group (group B). Both groups underwent echocardiography test using 2D, M-mode, and Doppler methods and parameters such as aorta/left atrium diameter, shortening fraction, ejection fraction, left ventricular end-systolic dimension, left ventricular end-diastolic dimension, left ventricular posterior wall dimension in systole, interventricular septal dimension in systole, left ventricular posterior wall dimension in diastole, interventricular septal dimension in diastole, pre-ejection period/ejection time, ejection time, pre-ejection period, left ventricular mass index, myocardial performance index , E/A velocity ratio , peak A velocity , peak E velocity , deceleration time , deceleration slope, acceleration time , isovolumetric relaxation time, and isovolumic contraction time were measured in both groups.

Data analysis was performed using statistical software SPSS (version 18) and Student's t- test, $\chi 2$ (Chi-square), and also Fisher's exact tests were used to perform the statistical analysis. Also Pearson correlation coefficient was used to determine the correlation between quantitative variables. The values $p<0.05$ were considered statistically significant.

Results

The mean age in group A was 16.5±5.8 while in group B it was 16.07± 2.9 (P=0.6). The mean weight was 35.65 ± 11.36 kg in group A and 54.01± 5.84 kg in group B(P=0.01). The mean height in group A was 137.8 ± 17.86 and in group B was 152.± 13.52 cm (P= 0.0001).

Table 2 summarizes the echocardiographic findings of the left ventricle and table 3 summarizes the echocardiographic findings of the right ventricle among thalassemia intermedia patients and controls. The mean left ventricular myocardial performance index (p=0.001), left ventricular mass index (p=0.0001) interventricular septal dimension in diastole (p=0.002), left ventricular posterior wall thickness in diastole (p=0.001), interventricular septal dimension in systole (p=0.01), left ventricular posterior wall dimension in systole (p=0.003) aortic pre-ejection period/ejection time (p=0.009), ejection fraction (p=0.019), fractional shortening (p=0.04), left ventricular isovolumetric contraction time (p=0.0001), left ventricular isovolumetric relaxation time (p=0.0001), right ventricular myocardial performance index (p=0.0001), and isovolumetric relaxation time (p=0.0001) were statistically significantly different between patients and control groups. Others echocardiographic parameters between patients and the control group did not show a statistically significant difference.

Discussion

Beta-thalassemia intermedia, is a subcategory of beta thalassemia, and its clinical symptoms varies from thalassemia major to asymptomatic carrier. The patients with hemoglobin over 10gr/dl require no blood transfusion and since they show no clinical traits, they may go undetected up to adulthood. Another group of patients with hemoglobin level of 6 gr/dl need blood transfusion and they may display clinical features such as bone deformity, arthritis, bone pain, progressive splenomegaly, growth failure, ankle ulcers, and cardiovascular disorders, which sometimes require blood transfusion. Cardiomyopathy is regarded as the main cause of mortality among these patients [1, 5].

The mean age of the participants in this study was lower compared with the patients who took

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part in Vaccari et al. [4] and Aessopos et al. [6] studies (the mean age in this study was 16.5 ± 5.8 while in the other two studies it was 29.5 ± 10 and 28.2± 7.4 respectively), and the mean weight of patients was 35.65 ± 11.36 kg while in Vaccari et al. [4] study it was 56.4± 10.6 kg. The mean height of the participants in this study was 138.78 ± 17.86 cm which was lower than the height of the patients who took part in Vaccari et al. study (the mean height 163 ± 19 cm) [4].

The myocardial performance index of the right and the left ventricles among our patients was higher compared to controls which is similar with Bosi et al. findings [8]. The increase of the left ventricular mass index in patients group was similar to results from Vaccari et al. study, which is regarded as the main factor in the cardiac compliance of these patients and can be one of the reasons for the high frequency diastolic dysfunction occurrence in such patients [4]. The increase of LVMI was also observed in Bosi et al. and Ocal et al. studies [8,9]. Pre-ejection period in the left side showed a significant increase. The increased PEP/ET indicates early changes of diastolic performance in ventricles. The mean IVSD in patients group was higher compared with the control group, which is in agreement with the findings of Bosi et al. [8].

The mean left ventricular end diastolic dimension among our patients was similar to Aessopos et al. [6] and Bosi et al. [8] studies but the left ventricular end systolic dimension did not show an increase which again agrees with Aessopos et al. [6] study. The mean left ventricular posterior wall dimension among patients increased which matches the findings in Aessopos et al. study [6]. Ejection fraction of the patients group compared with the control group was like Aessopos et al. study [6]. Like other studies, the fractional shortening among patients was decreased, which itself is a sign of the left ventricle dysfunction [4,6,8].

Increased isovolumetric relaxation time of the right ventricle is due to the disorder in the filling of the right ventricle in thalassemia patients. Increased isovolumetric relaxation time of the left ventricle which is a diastolic performance index has been reported in various studies on thalassemia patients, which is due to disorder during the resting time of the ventricle caused by iron deposits. It is considered as the gradual cause for the restrictive cardiomyopathy which is the earliest symptom of

Table2: Echocardiographic parameters of the right ventricle among patients and the control group.

p-value	Control group (n=66)	Thalassemia Intermedia group (n=22)	Parameter*
0.0001	0.52±0.08	0.13±0.63	MPI
0.0001	12.97±107.02	20.92±131.13	IRT (m/sec)
0.59	15.12±36.33	20.98±38.44	ICT (m/sec)
0.88	8.24±91.87	11.62±92.1	PEP(m/sec)
0.145	23.17±260.67	29.81±251.9	ET (m/sec)
0.086	0.03±0.34	0.06±0.36	PEP/ET
0.95	13.84±67.63	23.04±67.68	AT (m/sec)
0.85	36.86±120.36	27.90±121.95	DS (m/sec)
0.12	22.19±134.55	26.04±125.86	DT (m/sec)
0.56	15.29±61.27	15.90±63.44	Peak E (m/sec)
0.04	13.1±43.57	16.36±50.51	Peak A (m/sec)
0.12	0.29±1.44	0.37±1.33	E/A (m/sec)

*** MPI**: Myocardial performance index; IRT: Isovolumetric relaxation time; ICT: Isovolumetric contraction time; PEP: Pre-ejection period; ET: Ejection time; PEP/ET: Pre-ejection period/Ejection time; AT: Acceleration time; DS: Deceleration slope; DT: Deceleration time; Peak E: Peak E velocity; Peak A: Peak A velocity; E/A: E/A velocity ratio

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diastolic performance disorder of the left ventricle[10,11]. Low systolic and diastolic blood pressure and high heart rate of asymptomatic patients have also been mentioned in Vaccari et al. and Bosi et al. studies [4,8]. The cause of the low blood pressure in such patients can be attributed to the decrease of the systemic vascular resistance [4,6,8]. Increased volume load can also be attributed to Frank Starling mechanism which accelerates the heart rate [12]. In a study by Isma'eel et al. it was indicated that the evaluation of the right ventricle performance will be beneficial in future studies for the localization of pathologic findings in the cardiomyopathy among thalassemia intermedia patients [13].

Conclusion

It can be concluded that systolic and diastolic performance of the thalassemia intermedia patients is affected in comparison with the control group. The parameters of myocardial performance index, left ventricular mass index, isovolumetric relaxation time, ejection fraction, fractional shortening, interventricular septal dimension in diastole, and left ventricular posterior wall thickness in diastole are affected earlier in thalassemia intermedia patients.

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