Original Article

Thalassemia

Frequency of Cardiomyopathy in Beta Thalassemic Children

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ABSTRACT

Objective: To determine the frequency of cardiomyopathy in beta thalassemic children.
Study Design: Cross-sectional descriptive study
Place and Duration of Study: This study was carried out in the Pediatric department of Postgraduate Medical institute Lady Reading Hospital Peshawar from 1.1.2013 to 31.12.2013.
Materials and Methods: Total 334 Cases were collected by Consecutive (non probability) sampling technique using WHO sample size calculation soft ware. Patients collected according to fulfilling the inclusion/exclusion criteria. Beta thalassemic children with 10 or more blood transfusions, aged 2 to 15 years and both male and female children.
Results: In this study, 334 patients suffering from beta thalassemia were included. Male to female ratio was 1.62:1 and age ranged from 2 to 15 years. Average age was 7.57 years + 3.79SD. Dilated cardiomyopathy in beta thalassemic was observed in 13(3.9%), while restrictive cardiomyopathy was in 9(2.7%)patients.
Conclusion: The majority of patients with beta-thalassaemia demonstrated a unique hemodynamic pattern indicating cardiomyopathy.

Key Words: Frequency, Cardiomyopathy, Beta Thalassemia

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INTRODUCTION

Beta thalassemia is an inherited hemoglobin disease characterized by chronic hemolysis, which is due to impaired synthesis of β globin chains.[1] It is the commonest monogenic disorders in the world.[1] In Pakistan, beta thalassemia is seen in almost all parts of the country.[2] The estimated carrier rate is around 5-8% meaning that there are approximately 8-10 million traits (carrier) in the total population. In Pakistan about 5000 thalassemic children are born every year.[3]

Over the past three decades, the management of homozygous state by multiple transfusion therapy has greatly prolonged life expectancy and prognosis of patients with beta thalassemia.[4] On the other hand, the complications rate has been increased, mainly due to iron overload, both because of frequent blood transfusion and increased iron intestinal absorption.[4] Cardiac complications of iron overload represent the most common cause of death in beta-thalassemic patients.[5,6] In some studies 70-80% of deaths in beta thalassemic patients are due to heart failure[7]. The prevalence of cardiomyopathy in thalassemic patients is 4.4%.[8]More than half of deaths are due to left side heart failure and is the main determinant of survival.[9]In different 10 years follow up studies, 95% of all deaths in thalassemia occurred due to cardiomyopathy.[10]

A thalassemic child is a serious challenge to the public health services and resources of our country due to their continuous requirement of blood transfusions and high cost of iron chelating agents. Despite large number of deaths in thalassemia patients due to cardiomyopathy, no study is available regarding frequency of cardiomyopathy in thalassemic children in our country. The rationale of the current study is therefore, to determine the frequency of cardiomyopathy in beta thalassemic children. Based on the results of the study, regular screening of beta thalassemic children for cardiomyopathy by echocardiography and early treatment might prolong life expectancy; improve quality of life and prognosis of beta thalassemic children.

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MATERIALS AND METHODS

This descriptive cross sectional study was carried out in the department of Pediatric PGMI/Lady Reading Hospital Peshawar from11/1/2012 to 11/02/2013.Total 334 Cases were collected by Consecutive (non probability)sampling technique.

Inclusion criteria were beta thalassemic children with 10 or more blood transfusions,age 2 to 15 years and both male and female children while exclusion criteria were already diagnosed cases of cardiomyopathy in beta thalassemic children, beta thalassemic children with bone marrow transplant because not required blood transfusion and not exposed to iron overload

cardiomyopathy. Beta thalassemic children with other causes of cardiomyopathy like underlying congenital heart disease or rheumatic heart disease on echocardiography.

The ethical committee approved the study. All beta thalassemic children admitted in Pediatrics Department of Lady Reading Hospital Peshawar through casualty, out patients department, fulfilling the inclusion criteria were enrolled in the study. An informed written consent was taken from their parents or relatives. Diagnostic criteria were based on hemoglobin electrophoresis showing fetal hemoglobin more than 90% .

Detailed medical history including age, gender, address, number of blood transfusion was taken. All these children were screen for cardiomyopathy on same echocardiography machine using M-Mode & 2-Dimension by the same expert cardiologist of Lady Reading Hospital Peshawar.

All information were recorded into a self structured Proforma

All the study variables of these patients were analyzed for descriptive statistics like mean ± standard deviation for numerical variables like age, weight, number of blood transfusions and values of echocardiography finding while frequency/ percentage were calculated for categorical variable like sex. All the data were analyzed on computer using SPSS version 17.0 and were presented in the form of graphs and tables.

RESULTS

Total 334 beta thalassemic children were included in the study. There were 201 (60.18%) male patients and 133(39.82%) were females. Male to female ratio was 1.62:1(Figure 1).

The average age of the patients was 7.57 years ±3.79SD which ranged 2-15 years. Age wise patients were divided in four groups, the most common age group for beta thalassemia was less than or equal to 5 years,123(36.8%) patients. One hundred and two (30.5%) patients were in the age range of 6-9 years, 73 (21.9%) were of age range 10-13 years, 36(10.8%) presented at age more than 13 years of age. (Table 1).

Average blood transfusion was 121±20.3SD ml/year. Dilated cardiomyopathy was observed in 13(3.9%) patients, restrictive cardiomyopathy was in 9(2.7%) patients while 312(93.41%) patients show no cardiomyopathy. (Table 2)

Age wise distribution of cardiomyopathy shows that cardiomyopathy in above 14 years of age was little bit high as that of younger age. The patients having age less than or equal to 5 years of age have dilated cardiomyopathy 1.6%, restrictive cardiomyopathy was 4.1% , age group 6-9 years had dilated cardiomyopathy 3.9%, restrictive cardiomyopathy was 2%, in 10-13 years age group dilated cardiomyopathy was noted in 6.8% of cases, and patients having more than 13 years of age have dilated cardiomyopathy 5.6%, restrictive cardiomyopathy was 5.6% .(Table 3)

Tabl:No:1: Age Distribution

Age	Frequency	Percent	Cumulative percent
<= 5.00	123	36.8	36.8
6.00 - 9.00	102	30.5	67.4
10.00 - 13.00	73	21.9	89.2
14.00+	36	10.8	100.0
Total	**334**	**100.0**	

Table No. 2: Cardiomyopathy in Patients with Beta Thalassemic

	Frequency	Percent
No	312	93.4
Dilated	13	3.9
Restrictive	9	2.7
Total	**334**	**100.0**

Table No. 3: Age Wise Distribution of Cardiomyopathy

		Cardiomyopathy			Total
		No	Dilated	Restricive	
age ()	<= 5.00	116	2	5	123
		94.3%	1.6%	4.1%	100.0%
	6.00 - 9.00	96	4	2	102
		94.1%	3.9%	2.0%	100.0%
	10.00 - 13.00	68	5	0	73
		93.2%	6.8%	.0%	100.0%
	14.00+	32	2	2	36
		88.9%	5.6%	5.6%	100.0%
Total		312	13	9	334
		93.4%	3.9%	2.7%	100.0%

Table No. 4. Gender Wise Distribution of Cardiomyopathy

		Gender		Total
		Male	Female	
Cardiomyo-pathy	No	191	121	312
		95.0%	91.0%	93.4%
	Dilated	5	8	13
		2.5%	6.0%	3.9%
	Restrictive	5	4	9
		2.5%	3.0%	2.7%
Total		**201**	**133**	**334**
		100.0%	**100.0%**	**100.0%**

Gender wise cardiomyopathy in beta thalassemic shows that sex have minor role. In males dilated cardiomyopathy was 2.5%, restrictive 2.5% and 95% had no cardiomyopathy. On other hand 6% of female patients shows dilated cardiomyopathy 3%, restrictive while 91% were normal. (Table 4).

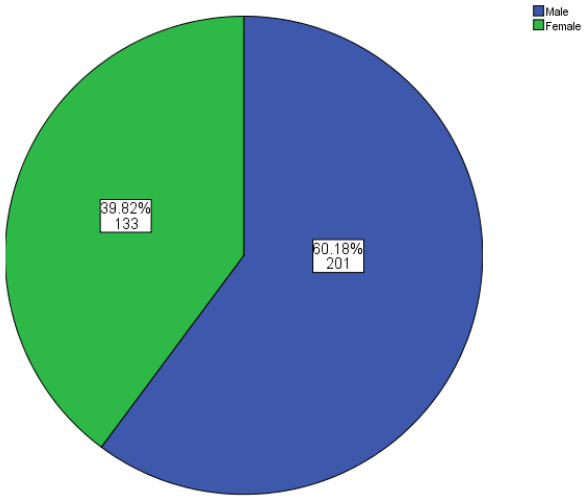

Figure No. 1: Sex Wise Distribution of The Patients

DISCUSSION

The controlled regimen of blood transfusion and iron chelation treatment has greatly improved the life expectancy of beta-thalassemia major patients, as it delay the hemosiderosis effects in the heart. Still, cardiac complications are the most common cause of death among these patients (63%) and the early mortality remains high, even in patients treated with desferrioxamine (DFO)[11]

Predominant right heart failure is caused by pulmonary hypertension, which was presumed to occur because of lung haemochromatosis in patients with high serum ferritin level[12]. Haemodynamic complication has been reported in few patients with thalassaemia intermedia[13]. We recently found that patients with thalassaemia major and normal left ventricular systolic function, showing an abnormal right ventricular relaxation pattern but normal left ventricular filling and the prognostic superiority of short tricuspid E deceleration time on the other clinical and echocardiographic parameters in these patients[14].

Most of the patients with thalassaemia major and heart failure represent abnormal haemodynamics, which is similar to right ventricular infarction[15] or that of sub acute tricuspid insufficiency[16]. These conditions are acute or sub acute, and there is right ventricular pattern in thalassaemia major patients which is not reported before. Patients with constrictive pericarditis and restrictive cardiomyopathy show a characteristic haemodynamic pattern similar to the profile of our patients, having non-dilated ventricles, usually with normal ventricular systolic function and raised pulmonary artery pressures[16].Currently, cardiomyopathy is the leading cause of morbidity and mortality in 63.6% to 71% of patients[17].

Studies on the cardiac implication of b-thalassemia patients who took chelation at the start of their disease are few and recent [18]. In these studies, it is found that life expectancy increases if chelation therapy started at proper time.

Despite of the advances in the treatment of thalassemia major and improvement in patients' survival, heart disease always remain the major cause of morbidity and mortility.[19]

In 1964, Engle et al,[19] studied a group of 41 patients and found that 63% of patients were in congestive heart failure and most of them died in a year from the onset of disease. In 1989, Zurlo et al [20] found that 64% of deaths were due to cardiac disease in a cohort of 1087 patients. Finally, in the Greek series of Ladis et al[21]it was reported that 71% of all deaths were due to cardiomyopathy.

Myocarditis is an important factor in the pathogenesis of cardiomyopathy. Thus, in a large cohort of 1048 patients with thalassemia major, 4.5% of patients developed signs/symptoms of acute myocarditis at a mean age of 15.3 years, and biopsy confirmed the diagnosis in more than half of the patients.[22] These patients were followed-up for 5 years,23.4% of patients had acute cardiac failure and most of them died within a year , whereas chronic cardiac failure developed in 27.6% of patients within a mean of 3 years, the rest of patients had a complete recovery.

In our study the mean value of body surface area was less in patients as compare to control without significant statistical difference. We also found cardiac enlargement in only 8% patients, and an abnormal ECG in 12%. The above results show that patients receiving chelation therapy have significant decrease in abnormal findings. In one study dilated cardiomyopathy was found in 4 out of the 76 patients aged 4 to 38 years and an increased LVDd in 8 out of the 76 patients. It was noted that some patients did not start iron chelation therapy in time.[24]

Valdez-Cruz, et al[18] followed 13 patients, aged 2 to 15 years, who were on chelation therapy at the start of their disease and they found that the left ventricular diastolic dysfunction(LVDd) and left ventricular systolic dysfunction(LVSd)increased but still its not significant statistically, as well as a there was a decrease of the Fraction shortening which is statistically significant . ($p<0.05$).

Favilli et al[14] compared twenty five b-thalassemia major patients (mean age of 15.8 ± 5.7 years, who were on regular blood transfusions and chelation therapy) to 25 healthy control subjects. In this study the mean value of LVDd and left ventricular MI was significantly higher as compared to controls ($p<0.001$ and $p<0.05$ respectively). The LVDd was significantly increased even in patients with normal systolic function.[14]. The higher mean value of LVDd in this study might be due to the greater age range of these patients.

CONCLUSION

In our study we found that most of the children having b-thalassemia and are on regular blood transfusions and chelation therapy have normal systolic and diastolic function of the left ventricle and normal ECG up to the age of fifteen years. It is established on the basis of this study that regular blood transfusions and chelation therapy can delay the development of cardiomyopathy and cardiac complications.

Conflict of Interest: The study has no conflict of interest to declare by any author.

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