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THE CORRELATION OF RELATIVE WALL THICKNESS, LV MASS/LV MASS INDEX, CARDIAC INDEX AND PCWP IN RELATION TO SERUM FERRITIN IN TRANSFUSION DEPENDENT BETA THALASSMEIC CHILDREN IN NORTH WEST RAJASTHAN

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Abstract

Objective: Regular blood transfusions used for long term survival in ß-thalassemia major patients cause a secondary state of tissue iron overload. Myocardial iron deposition can result in cardiomyopathy, and heart failure remains the leading cause of death. This study was planned to see the correlation of Relative Wall Thickness (RWT), LV Mass, Cardiac Index(CI) and pulmonary capillary wedge pressure(PCWP) in relation to Serum Ferritin in transfusion dependent Beta Thalassemia children.

Methods: Patients of ß thalassemia major above 2 years of age received regular blood transfusions at least for 1 year duration, attending OPD in the Department of Pediatrics, S.P. Medical College, Bikaner were enrolled. Echo findings of 50 cases were correlated with serum ferritin level(SFL).

Result: Mean RWT in SFL group <2500ng/ml was 0.40±0.09, in SFL group 2500-5000 ng/ml, it was 0.41±0.08 and in SFL group >5000 ng/ml, it was 0.49±0.09; p value>0.05. Mean LV mass in SFL group <2500 was 68.76±24.32, in SFL group 2500-5000, it was 90.07±24.18 and in SFL group >5000, it was 123.06±42.42. The difference was found statistically highly significant (p<0.001). Mean PCWP in SFL group <2500 was 11.55±1.53, in SFL group 2500-5000, it was 12.02±2.06 and in SFL group >5000, mean PCWP was 13.31±2.09;p value>0.05. Mean CI in SFL group <2500 was 5.24±0.99, in 2500-5000 group was 5.79±1.07 and in SFL group >5000, it was 5.91±1.26 ; p value>0.05.

Conclusion: There was significant positive correlation of serum ferritin level only with LV Mass.Relative Wall thickness, PCWP and cardiac index were insignificantly correlated. .

Keywords: ß-thalassemia major; Relative wall thickness, LV mass/ LV mass index, cardiac index, PCWP, Echocardiogram; Tissue Doppler Imaging

Introduction

Globally, there are at least 60,000 individuals born with ß-thalassemia major (TM) each year[1]. Regular blood transfusions are mandatory for long term survival, but over a period of years these cause a secondary state of tissue iron overload. Myocardial iron deposition can result in cardiomyopathy, and heart failure remains the leading cause of death[2-4] The introduction of the iron chelator deferoxamine greatly ameliorates the effects of iron toxicity, but long-term cardiac mortality has been very disappointing[3,5]. The ongoing deaths from cardiac iron loading may relate to inadequate compliance or genetic factors related to metal transporters not yet fully elucidated[6-8], but whatever the cause, there is strong evidence that long-term deferoxamine chelation does not effectively prevent myocardial siderosis in a majority of patients[9,10].Deferiprone, the first approved oral chelator, has been shown in randomized controlled trials to be effective monotherapy at 100 mg/kg/day dose in treating mild to moderately severe myocardial iron loading (myocardial T2* 8–20 ms), significantly improving both myocardial iron and ejection fraction[11], and the combination of deferiprone at 75 mg/kg/day with deferoxamine is likewise effective[12]. However greater total iron clearance is seen with combined treatment[13-15] which suggests that it might be useful for severe myocardial siderosis (T2* < 10 ms). Cardiac iron overload or the iron overload cardiomyopathy is regarded as the most serious condition and is the leading cause of morbidity and

mortality (63.6%-71%)[17].The reported incidence of iron overload cardiomyopathy ranges from 11.4% to 15.1% in thalassemia major[17].Iron deposition in myocardium mainly results in decreased left ventricular function[17]. Although systolic dysfunction becomes obvious during the late stage .Left sided heart failure is clinically more common than right sided heart failure. However it has been shown that right ventricular dysfunction develops earlier in asymptomatic patien

Methods

This hospital based cross sectional study Done on 50 Cases Was conducted in HRMC PBM HOSPITAL SPMC Bikaner Rajasthan Over a period of 1 Year 2016-2017. Patients of ß thalassemia major above 2 years of age receiving regular blood transfusions at least for 1 year duration with exclusion of Patients of ß-thalassemia with Congenital Heart Disease ,Ex-thalassemic patients undergone bone marrow transplant ,Thalassemia intermedia ,Patients on cardio toxic drugs . All subjects Serum Ferritin level was detected and also underwent 2D and doppler transthoracic echocardiography for evaluation of the correlation of the relative wall thickness, LV mass and PCWP in relation to serum ferritin in transfusion dependant beta Thalassemia children at Sardar Patel Medical College, Bikaner.

Statistics

Required information from eligible patients were collected in a pre-structured pre-tested Proforma. For data analysis statistical software SPSS was used and data were analyzed with the help of frequencies, figures, proportions, measures of central tendency, appropriate statistical test.

Results

Table 1: Distribution of Cases according to age group (years) in relation to serum ferritin level

Age Group (Years)	Serum Ferritin Level						Total	
	<2500		2500-5000		>5000			
	No.	%	No.	%	No.	%	No.	%
3-8	19	70.4	7	38.9	1	20.0	27	54.0
9-12	5	18.5	8	44.4	1	20.0	14	28.0
>12	3	11.1	3	16.7	3	60.0	9	18.0
Total	27		18		5		50	

Table 2: Distribution of cases according to LV Mass in relation to serum ferritin level

Percentile (gms)	Serum Ferritin Level						Total	
	<2500		2500-5000		>5000			
	No.	%	No.	%	No.	%	No.	%
<3	1	3.7	0	0	0	0	1	2.0
3-97	22	81.5	10	55.6	1	20.0	33	66.0
>97	4	14.8	8	44.4	4	80.0	16	32.0
Total	27		18		5		50	
Mean	68.76		90.07		123.06			
SD	24.32		24.18		42.42			
F	10.362							
P	<0.001							

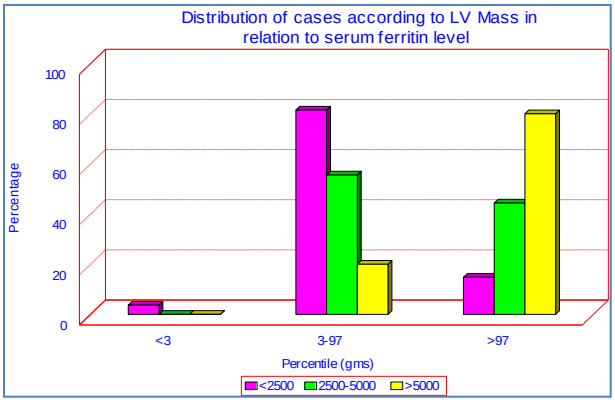

Figure 1:

Table 3: Distribution of cases according to LV Mass Index in relation to serum ferritin level

Percentile (gm/m^2)	Serum Ferritin Level						Total	
	<2500		2500-5000		>5000			
	No.	%	No.	%	No.	%	No.	%
<3	1	3.7	0	0	0	0	1	2.0
3-97	22	81.5	12	66.7	1	20.0	35	70.0
>97	4	14.8	6	33.3	4	80.0	14	28.0
Total	27	100	18	100	5	100	50	100
Mean	85.11		100.98		121.05			
SD	20.09		17.08		21.78			
F	9.014							
P	<0.001							

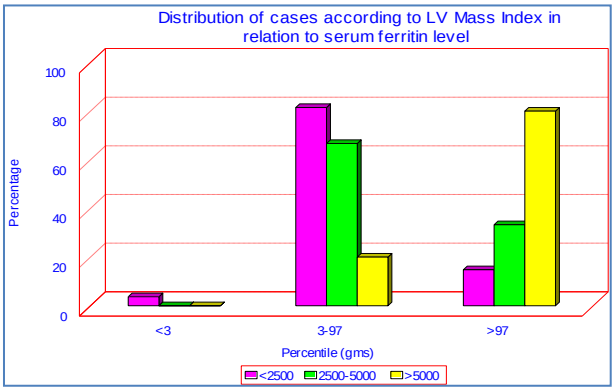

Figure 2:

Table 4: Distribution of cases according to pulmonary capillary wedge pressure (PCWP) grade in relation to serum ferritin level

PCWP Grade (mmHg)	Serum Ferritin Level						Total	
	<2500		2500-5000		>5000			
	No.	%	No.	%	No.	%	No.	%
High (>12)	7	25.9	9	50.0	4	80.0	20	40.0
Normal (4-12)	20	74.1	9	50.0	1	20.0	30	60.0
Total	27	100	18	100	5	100	50	100
Mean	11.55		12.02		13.31			
SD	1.53		2.06		2.09			
F	2.104							
P	0.133							

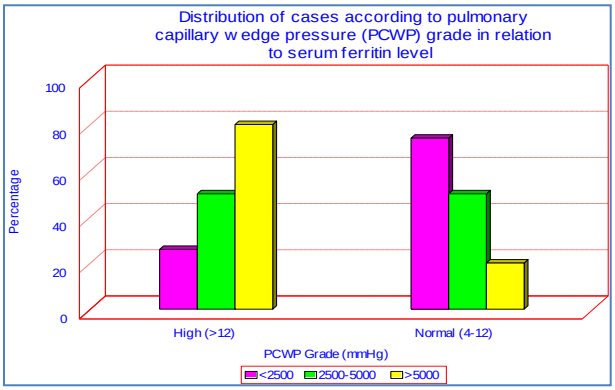

Figure 3:

Table 5: Distribution of Cases according to type of Relative Wall Thickness (RWT) in relation to serum ferritin level

RWT Type (mm)	Serum Ferritin Level						Total	
	<2500		2500-5000		>5000			
	No.	%	No.	%	No.	%	No.	%
CH	0	0	0	0	5	100	5	10.0
EH	3	11.1	8	44.4	0	0	11	22.0
CR	9	33.3	6	33.3	0	0	15	30.0
NG	15	55.6	4	22.2	0	0	19	38.0
Total	27		18		5		50	
Mean	0.40		0.41		0.49			
SD	0.09		0.08		0.09			
F	2.390							
P	0.103 NS							

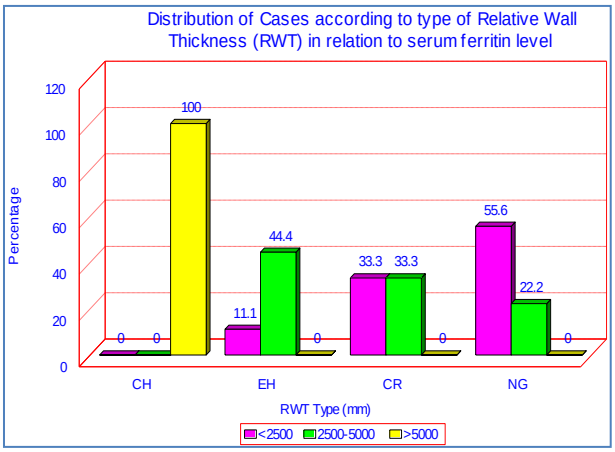

Figure 4

Table 6: Distribution of cases according to Cardiac Index in relation to serum ferritin level

Grade (l/min/m^2)	Serum Ferritin Level						Total	
	<2500		2500-5000		>5000			
	No.	%	No.	%	No.	%	No.	%
>2SD	8	29.6	10	55.6	3	60.0	21	42.0
Normal	19	70.4	8	44.4	2	40.0	29	58.0
Total	27	100	18	100	5	100	50	100
Mean	5.24		5.79		5.91			
SD	0.99		1.07		1.26			
F	1.879							
P	0.164							

Table 7: Frequency of ECG Findings

ECG Findings	No. of Cases	Percentage
LVH	6	12.0
RVH	1	2.0
BVH	1	2.0
Sinus Tachycardia (ST)	9	18.0
RBBB	3	6.0
Normal	30	60.0
Total	50	100

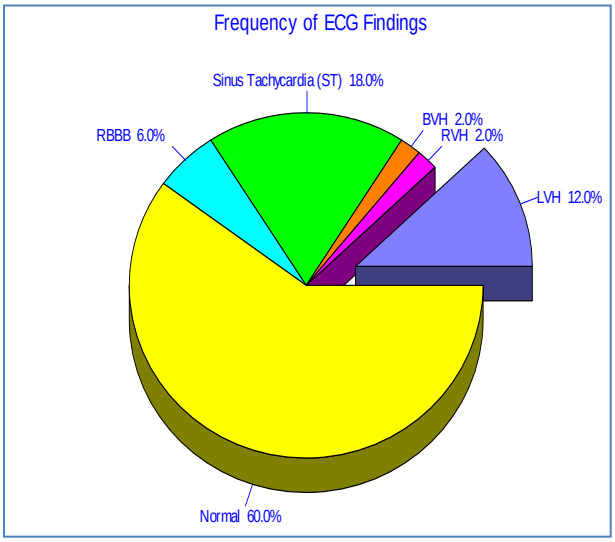

Figure 5:

TABLE 1 shows maximum 27 cases were from age group 3-8 years followed by 14 patients age group 9-12 years and minimum 9 patients were from age group >12 years .Majority of patients were males 31(62%) while only 19(38%) were females.

TABLE 2 & Figure 1 shows Mean LV mass in SFL group <2500 was 68.76±24.32, in SFL group 2500-5000, it was 90.07±24.18 and in SFL group >5000, it was 123.06±42.42. On applying ANOVA test, the difference was found statistically highly significant (p<0.001).

TABLE 3 & Figure 2 shows Mean LV mass index in SFL group <2500 was 85.11±20.09, in SFL group 2500-5000, it was 100.98±17.08 and in SFL group >5000, it was 121.05±2178. On applying ANOVA test, the difference was found statistically highly significant (p<0.001).

TABLE 4 & Figure 3 shows PCWP grade, in SFL group <2500, only 7(25.9%) patients had high grade of PCWP, in SFL group 2500-5000, 9(50%) patients had high grade of PCWP while in SFL group >5000, 4(80%) patients had high PCWP grade. Mean PCWP in SFL group <2500 was 11.55±1.53, in SFL group 2500-5000, it was 12.02±2.06 and in SFL group >5000, mean PCWP was 13.31±2.09 and the difference was found statistically insignificant (p>0.05).

TABLE 5 & Figure 4 Mean relative wall thickness in SFL group <2500 was 0.40±0.09, in SFL group 2500-5000, it was 0.41±0.08 and in SFL group >5000, it was 0.49±0.09. On applying ANOVA test, the difference was found statistically insignificant.

Table 6 shows Mean cardiac index in SFL group <2500 was 5.24±0.99, in 2500-5000 group was 5.79±1.07 and in SFL group >5000, it was 5.91±1.26 and this difference was found statistically insignificant (p>0.05).

Table 7 & Figure 5 shows Majority of patients (60%) had their ECG findings within normal limit while 40% patients had abnormal ECG. Out of them 9(18%) patients had sinus tachycardia, 6(12%) patients had LVH followed by 3(6%) patients had RBBB while 1(2%) each patient had RVH and BVH in ECG.

Discussion

The present study was undertaken to evaluate the cardiac functions of ß-thalassemia major patients, in the Department of Pediatric Medicine, Sardar Patel Medical College, Bikaner. A total of 50 ß-thalassemia major Children on regular blood transfusions were taken and assessed for their cardiac functions. All children were evaluated for cardiac functions using 2D-Echocardiography with Tissue Doppler Imaging (TDI) and a 12 lead ECG. Mean serum ferritin and mean annual hemoglobin level of preceding 1 year was calculated. The following parameters were assessed LV mass,LV mass index ,PCWP and RWT . All parameters were correlated with serum ferritin.

In the present study, left ventricular mass and index was abnormal in one third of the patients (32% and 28%). Taksande et al in their study on 30 patients with ß-thalassemia major aged from 3 years to 15 years, observed cardiomegaly on chest X-ray in 60% of the patients and ECG changes of left ventricular hypertrophy in 23% of patients but not commented on left ventricular mass or left ventricular index[20]. Similar finding by Spirito et al in their study on 32 ß-thalassemia major patients age range from 12 years to 22 years, noted high left ventricular mass and left ventricular index[23].Chotivittayatarakorn et al in their study on 16 thalassemia major children also reported high left ventricular mass index in 88% of thalassemia major patients age group of 5 years to 14 years[22]. In the earlier study, Favilli et al commented, left ventricle end diastolic dimension is the first echocardiographic finding in

the thalassemia patients[24]. Kremastinos et al concluded that severe iron deposition leads to restrictive abnormalities of left ventricular filling[18]. Rodrigues et al in their study compared, 18 thalassemia major patients with anemic and healthy controls. Their finding reveal marginally higher left ventricular end diastolic values than controls but surprisingly they concluded no significant differences in left ventricle systolic indices[16.] Gharzuddine et al studied 50 thalassemia major patients with mean age of 16.9 years, suggested high left ventricular index in thalassemia patients as compared to control group and concluded earliest sign of diastolic dysfunction is an impairment in left ventricular relaxation manifested as a prolong isovolumetric relaxation time[21].

Relative wall thickness permits categorization of increase in LV mass as either concentric hypertrophy (RWT >0.42) or eccentric hypertrophy (RWT< 0.42) and allows identification of concentric remodeling (normal LV mass with increase >RWT). Calculation of relative wall thickness (RWT) by the formula[25], RWT= (2x PWTd)/LVIDd, where, PWTd= posterior wall thickness in diastole LVIDd= left ventricle inner diameter in diastole. In the present study, a total of 62% of the children noted to have abnormal relative wall thickness (Concentric hypertrophy (10%), Concentric remodeling (30%) and Eccentric hypertrophy (22%)). Eccentric hypertrophy shows normal periphery resistance but high cardiac index consist with excess circulating blood volume while concentric remodeling (normal LV mass with increased RWT) it characterized by high peripheral resistance, low cardiac index, and increase arterial stiffness

In the present study, pulmonary capillary wedge pressure (PCWP) was calculated by using mitral E velocity to early diastolic mitral annulus velocity (Em) ratio, with the formula[26]: PCWP=1.9+1.24(E/Em)

In the present study, only 40% (n=20) of children were noted to have high PCWP. Rodrigues et al, evaluated cardiac functions in 19 thalassemia patients with age group of 11 years to 25 years, observed higher mean PCWP in thalassemia major patients as compared to healthy and anemic controls[16].

The present study showed that, out of total serum ferritin >2500ng/ml patients, 52% and 43% of the patients had LV mass and LV mass index >97th centile. This is in agreement with the finding of Spirito et al(1990)[23], Kremastinos al[27], Gharzuddine et al[21], Bosi et al[19] and Sayed al[28]. Favilli et al suggested that LVEDV is the earliest change observed in asymptomatic Thalassemia major patients[24].

Conclusion

The present study was conducted on 50 children with ß-thalassemia major in the Department of Pediatric Medicine, Sardar Patel Medical College Bikaner, Rajasthan. Children in the age group of 3 year to 17 years were included in this study. All children were evaluated for cardiac functions by 2D Doppler Echocardiography with Tissue Doppler Imaging (TDI) and ECG. These examinations were done 1 hour after blood transfusion with Tissue Doppler Imaging (TDI) and 12 Lead ECG. Obtained parameters were correlated with serum Ferritin level. Serum ferritin level is Significantly correlated with LV Mass and Lv Mass Index and Insignficantly Correlated with PCWP and RWT

insignificant (p>0.05).

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