Research Article

Comparison of changes in Bi-ventricular function through pulsed and tissue doppler echocardiography in children with thalassemia Major with varying degree of iron overload

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Abstract

Background: Ventricular dysfunction appears due to frequent transfusions in children with Beta-thalassemia major. The objective was to evaluate the changes of bi-ventricular function through Pulse waves and Tissue Doppler with serum iron overload in children.

Material and Methods: Cross sectional observational study was conducted at Cardiology department in the Children's Hospital, Lahore. Bi-ventricular functional assessment evaluated by pulse-wave and tissue Doppler and co-related which ventricular function effected earlier with different level of serum iron load. The data collected through performa. The data was enter in SPSS version 16 and then analyzed.

Results: 86 children with Beta-thalassemia major showed 56 male, 30 female with mean age of 9.2 years. 32 patients received blood transfusion routinely after 30 days, 45patients after 60 days and 9 after 180 days respectively.18 children has mild serum iron load, 12 has moderate and 58 has severe serum iron over load. The mean serum ferritin was 4538ml.

E' of LV and RV free wall were slightly decreased .Deceleration Time of LV showed 53 children has abnormal value while deceleration Time of RV showed 55 has abnormal value . Right ventricular A wave velocity, E' of RV with lateral wall and E' of LV with lateral wall were the early soft markers of ventricular dysfunction.

Conclusion: P/W and TDI echocardiographic study for evaluating bi-ventricular dysfunction in the patients with thalassemia major was simple tool. Similarly, the effect of iron load on RV appeared earlier even with low serum iron load than LV.

Keywords: Echocardiography, Beta-Thalassemia major, Left ventricular dysfunction, Iron load.

Abbreviation: LV=Left ventricle,RV= Right ventricle,P/W=pulse waves dppler,TDI=Tissue doppler imaging, DT=De-acceleration Time, E'=E-Prime , A' = A-Prime , E'-fw =E-Prime free wall ,A'-fw =A-Prime free wall.

Introduction

Beta-thalassemia major is a genetic disorder. Such children usually dependent on regular blood transfusion [1]. Repeated transfusion are source of excess serum iron and cause harmfulness effect in various body system along with the cardiac system[2]. Timely recognition of cardial dysfunction helps to protect heart failure [3]. By time several imaging modalities develope for the independent evaluation of total and focal both ventricular function [4]. Echocardiography is an important imaging test for reviewing of bi-ventricular function [5]. In thalassemic patients ,abnormal wall motion predicted to be an early signal of myocardial dysfunction. The changes of segmental wall motion may be acute. Optical evaluation by individual for ventricular function some time misguide [6]. Pulsed tissue doppler imaging is an authentic method for evaluating cardiac function and veloscity [7].

Cardiac failure presents as one of the major complication of repeated transfusions in-patient with thalassemia major. These patients initially presented with diastolic dysfunction earlier followed by systolic dysfunction and then causes severe heart failure. Very less literature showed which ventricle effected earlier with varying degree of iron load. Similarly, the right ventricular dysfunction appeared as a result of pulmonary hypertension also .In this study,the aim was to find out through pulsed wave tissue Doppler imaging based criteria that which ventricle effected earlier with different levels of serum iron load.

Materials and Methods

Cross sectional observational consecutive study was done at Thalassemia Centre and Cardiology department of university of child health, Lahore science October 2019 onward for 6 months after the approval from ethical committee. The patients of age 6month to 16 years were select in the sample groups after taking parents' consent. Patients excluded if they developed renal disease, liver disease or diabetes mellitus and age above 16 years and documented pulmonary hypertension.

In order to gather the data for this study, a performa was designed .The performa consisted of almost 18 questions, involved in the study to meet the requirement of the study. The reliability of performa was verify by using the Cronbach's Alpha instrument.

Patient included after careful history taking along with proper physical examination .Routine laboratory test taken including CBC, serum ferritin, RFTs , LFTs, electrolytes .

Echocardiography analysis:

Wall motion was judged visually in 2-D mode as per guidline of the American Society of Echocardiography (ASE) [8].

Trans-valvular filling velocities assessed by Pulse wave doppler. The peak diastolic (E), and the atrial flow velocities (A), alogwith the E/A ratio and the deceleration time (DT) were evaluated [9].Tissue Doppler Imaging of both ventricular were evaluated both in contraction and relaxation. The measurement takenat apical 4 chamber view by palcing curser at the lateral margin of the mitral annulus and tricuspid annulus and at interventricular septal annulus.TDI included systolic myocardial velocity (S), early diastolic myocardial velocity (E'), late diastolic myocardial velocity (A') measurement.Three cardiac cycles used for measurements of all parameters.

Statistical analysis:

All the data entered in SPSS version 16 and then analyzed for statistically significant outcomes. Descriptive analysis with Pearson correlation used together with simple graphical analysis, it formed the basic virtual of any quantitative analysis of data. The ANOVA (F) obtained by dividing one variance by the other.

Results

86 patients of thalassemia major were included in the study. Echocardiography data was collected prospectively on a pre-designed performa. Variables like frequency of blood transfusion, serum ferritin, A-waves, E-waves, A', E', '-free wall, A' free wall, DT of RV and LV were noted on the performa of each patient.

Figure-1

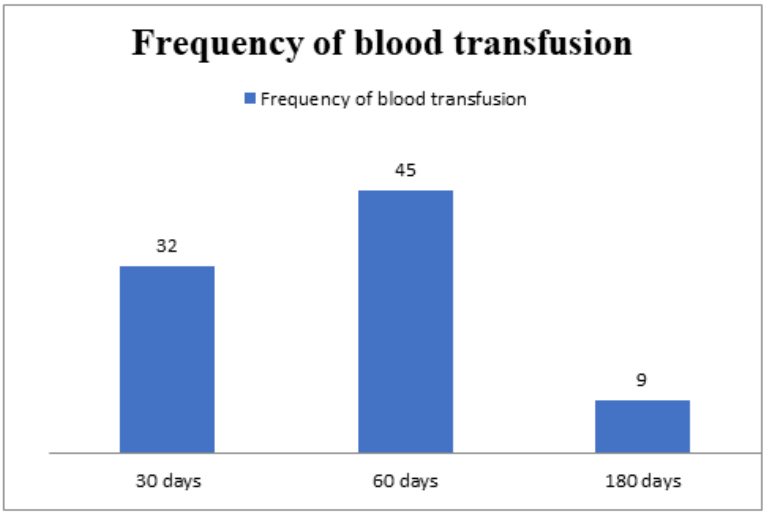
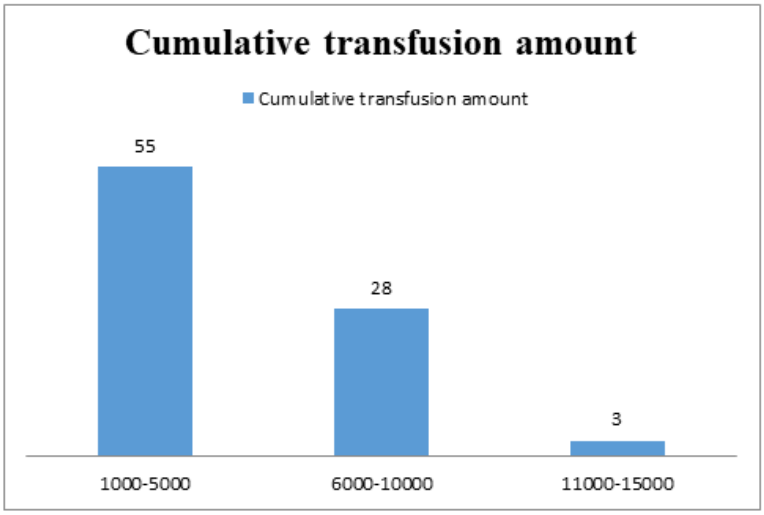


Figure-2

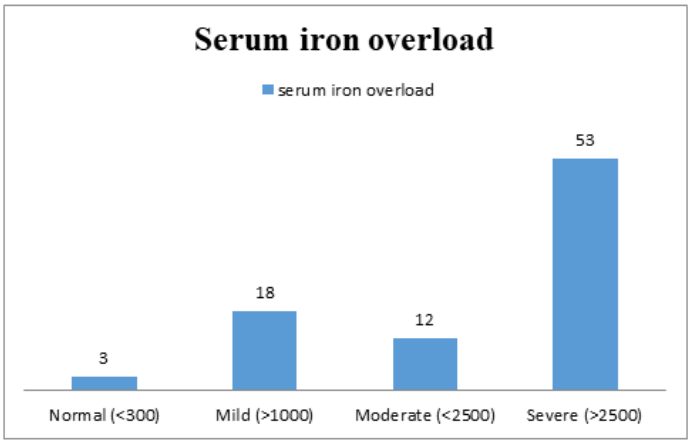


There were 56 males and 30 females. Among 86 patients of thalassemia Major, 32 patients received blood transfusion after 30 days, 45patients received after 60 days and 9 patients received after 180 days (Figure-1). 55 patients received transfusion amount between 1000 ml to 5000 ml, 28 received between 6000 to 10,000 and 3 patients received 11,000 ml to 15,000 ml.(Table-2). Among 86 patients who were receiving blood transfusion, 3 were normal, 18 has mild serum iron overload, 12 has moderate serum iron overload and 53 has severe iron overload (Figure-3).

Echocardiographic parameters for assessment of bi-ventricular diastolic function showed marked abnormal values that indicated both ventricular function effected by iron load in thalassemia major patients. Deceleration Time of LV showed that 61.6% (n=53) patients have abnormal DT along with other echocardiographic

parameters (Table-1). Deceleration Time of RV showed that 64% (n=55) patients have abnormal value of DT along with other echocardiographic parameters. (Table-2).

Figure-3



One-way Analysis of Variance (ANOVA) used to assess the groups. Patients were categorized into four groups (Normal, Mild, Moderate and Severe) based on serum overload. In this study A wave velocity of RV, E' of LV with free wall and E' of RV with free wall were slightly decreased which reflected significant association with iron load (p=>.05) (Table-3) .LV function with different levels of iron loads have demonstrated that LV was well tolerated even with high level of serum iron load (Table-4). It seen that RV function with iron load is more badly effected than LV .Similarly RV function effected earlier with even low level of iron load. The effect of iron load to RV showed that with even less than 300ng/ml serum iron load RV diastolic dysfunction noted in some patients. While with severe iron load all patients of thalassemia major were noted RV dysfunction (E-Prime, A' , E'-fw , A'-fw) (Table-5).

Table-1

Descriptive analysis of LV echocardiographic parameters					
	Mean	Std. Error of Mean	SD	Skewness	Range
DT of mitral valve	136.14	3.97055	36.8214	-0.198	145
E wave	0.9605	0.02638	0.2446	0.631	1.1
A wave	0.7616	0.05694	0.52807	3.02	2.6
E' septal	0.3258	0.11777	1.09215	5.062	5.95
A' septal	0.0669	0.00971	0.09008	3.938	0.49
E' free wall	0.1129	0.00896	0.0831	4.832	0.59
A' free wall	0.0713	0.01153	0.10692	4.31	0.59

DT=De-acceleration Time, E'=E-Prime , A' = A-Prime , E'-fw =E-Prime free wall ,A'-fw =A-Prime free wall.

Discussion

Ehocardiography is still non-invasive good and cheap tool for assessment of bi-ventricular function in thalassemia major. It is not time consuming and has not highly technical dependency as required in case of MRI. In thalassemia , early appreciation of iron-load cardiomyopathy is important for earlier chelation therapy to prevent and improve cardiac function[10]. The major reason of mortality in thalassemia is Iron-induced cardiac

disease[11]. Iron load in cardiac tissue as detected by biopsy or through serum never predict cardiac functional status, and normal echocardiographic parameters only detect cardiac dysfunction at advance stage [12,13].

Table-2

Descriptive analysis of RV echocardiographic parameters					
	Mean	Std. Error of Mean	SD	Skewness	Range
DT of tricuspid valve	142.116	5.64197	52.3215	0.49	215
E wave	0.75	0.02236	0.20736	1.272	1
A wave	0.697	0.09079	0.84194	4.795	4.93
E 'septal	0.1059	0.00376	0.03482	1.795	0.17
A' septal	0.0706	0.00955	0.08855	4.043	0.49
E' free wall	0.0969	0.00245	0.02271	0.733	0.18
A' free wall	0.0828	0.01357	0.12583	4.234	0.69

DT=De-acceleration Time, E'=E-Prime , A' = A-Prime , E'-fw =E-Prime free wall ,A'-fw =A-Prime free wall.

Our study revealed that 61% has LV and 65% has RV dysfunction with various degree of serum iron load while one study revealed that in thalassemic patients 38% developed LV dysfunction, and out of witch 79% has isolated diastolic dysfunction [14]. Like our findings, other groups stated regional systolic dysfunction of lateral and septal walls of left ventricle, even if they did not have overt heart failure. Vogel et al assumed that iron deposited earlier at the interventricular septum[15], but our study reflected that RV function badly effected by even low level of serum iron load.

Table-3:

Association of serum iron with echo parameters by ONE WAY ANOVA variance

		Sum of Squares	Df	Mean Square	F	Sig.
	Between Groups	7.682	3	2.561	3.994	0.01
	Within Groups	52.571	82	0.641		
Av of RV	Total	60.253	85			
	Between Groups	0.08	3	0.027	4.286	0.007
	Within Groups	0.507	82	0.006		
E' of LVfw	Total	0.587	85			
E' of RVfw	Between Groups	.006	3	.002	4.090	.009
	Within Groups	.038	82	.000		
	Total	.044	85			

Echocardiography is usually easily available and cheap modality[16]. This is a simple available test to pick cardiac functional status and help in long –term assessment of cardiac function in thalassemia and also chelation effct[17], as reflected by our study also. Magnetic resonance imaging (MRI) is another good modality for assessment of cardiac function along with iron load but it is expensive, not available easily and expert dependent.

Our study revealed that RV function effected earlier by even little change in serum iron load in patients with thalassemia major as supported by G. Hahalis et al who predicted in his study that there was abnormal RV filling

pattern causing restricted relaxation which leaded pulmonary hypertension.On the contarary ,the LV filling is compatible in chronic anemia[18] which supported our study also. Suchaya Silvilairat et al revealed abnormal value of DT and other TDI values of tricuspid and mitral inflow carries important prognostic value[19] which was also supported by our study.

Table-4:

Echocardiographic Parameters of left Ventricle

LV IRON LOAD						
SF(ng/ml)		<300	>1000	<2500	>2500	Total
DT	Normal	0	11	2	20	33
	Abnormal	1	9	7	36	53
E -waves	Normal	0	3	0	8	11
	Abnormal	1	17	9	48	75
A-waves	Normal	1	9	5	31	46
	Abnormal	0	11	4	25	40
E'	Normal	1	16	8	43	68
	Abnormal	0	4	1	13	18
A'	Normal	0	4	3	16	23
	Abnormal	1	16	6	40	63
E'-fw	Normal	1	14	4	46	65
	Abnormal	0	6	5	10	21
A'-fw	Normal	0	4	2	14	20
	Abnormal	1	16	7	42	66

DT=De-acceleration Time, E'=E-Prime , A' = A-Prime , E'-fw =E-Prime free wall ,A'-fw =A-Prime free wall.

Conclusion

P/W and TDI echocardiographic study for evaluating LV and RV dysfunction in the thalassemia patients is non-invasive reliable tools. Similarly, the effect of iron load on RV appears earlier even with low serum iron load than LV.

Table-5: Echocardiographic Parameters of Right Ventricle.

RV IRON LOAD						
SF (ng/ml)		<300	>1000	<2500	>2500	Total
DT	Normal	0	11	4	16	31
	Abnormal	1	9	5	40	55
E-waves	Normal	0	7	3	13	23
	Abnormal	1	13	6	43	63
A-waves	Normal	0	10	3	31	44
	Abnormal	1	10	6	25	42
E'	Normal	0	0	0	0	0
	Abnormal	1	20	9	56	86
A'	Normal	0	0	0	0	0
	Abnormal	1	20	9	56	86
A'-fw	Normal	0	0	0	0	0
	Abnormal	1	20	9	56	86
E'-fw	Normal	0	0	0	0	0
	Abnormal	1	20	9	56	86

DT=De-acceleration Time, E'=E-Prime, A' = A-Prime, E'-fw =E-Prime free wall, A'-fw =A-Prime free wall.

Pit fall

This was one center study and did on limited patients. All parameters taken from stable patients and not co-related with patients with heart failure.

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