Echocardiographic Parameters of Left Ventricle Systolic and Diastolic Function in Patients with β-Thalassemia Major

Asaad Abdullah Abbas , Basil Najeb ,Alaa Abdulhussein , Jassim Hanoon Jassim , Majid Abdulmuhsin Falih, Hussein Jubiaer ,Qasim Mudalal Ubaid

ABSTRACT:

BACKGROUND:

Advances in the current treatment of β-thalassemia major have contributed to improve prognosis, and nowadays, an increasing number of patients do survive up to the third or fourth, decade. Cardiac complications are still the most common cause of death in patients with major thalassemia.

OBJECTIVE:

Assessment of Left ventricular systolic and diastolic parameters in β-Thalassemia Major patients and its relation to ferritin level and to spleen status.

PATIENT AND METHODS:

A Cross -sectional descriptive study done at Ibn Al- Albalady Hospital for Children and Maternity Baghdad city from beginning of January 2011-to the end of July 2011,(427) patients with β-thalassemia major were considered for analysis, all patients on regular blood transfusion & chelation therapy. M-mode, 2D and Doppler echocardiographic parameters were averaged over 3 cardiac cycles and all echocardiographic measurements were performed according to the guidelines for performance of a pediatric echocardiogram by American Society of Echocardiography

RESULTS:

LA, Aortic diameter ,LA/AO ratio, LV posterior wall thickness , interventricular wall thickness, Left Ventricular end systolic and diastolic diameter were larger in β-thalassemic patients. Peak E, peak A, isovolumic relaxation time were higher in thalassemic patient. There were no difference in E/A flow ratio and E deceleration time. Strok volume, LV mass index and MPI were higher in thalassemic patients. No change in Ejection Fraction and Fraction Shortening. No effect found in all mitral valve Doppler parameters in relation to ferritine level. LV mass index higher in splenctomized patients. No effect found in all mitral valve Doppler parameters in relation to spleen status.

CONCLUSION:

The findings of this study shows that in β-Thalassemic patients there is good systolic function but decrease in diastolic function and there was no correlation between ferritin level and LV systolic and diastolic function.

KEY WORDS: β-Thalassemia, Systolic and Diastolic function, Echocardiography

INTRODUCTION:

Advances in the current treatment of β-thalassemia major have contributed to improve prognosis, and nowadays, an increasing number of patients do survive up to the third or fourth, decade. Indeed, a long term Italian study recently reported that 68% of patients with thalassemia major were alive at age of 35 years.(1)

Cardiac complications are still the most common cause of death in patients with major thalassemia. Iron overload causes severe and permanent cardiac damage even more than untreated anemia. Cardiac complications due to iron overload are recurrent pericarditis, recurrent forms of heart block, ectopic ventricular beats, ventricular tachycardia, ventricular fibrillation, cardiomegaly, left ventricular (LV) dysfunction and finally heart failure resistant to any therapeutic measures (2)

Baghdad Medical City.

AIMS OF THE STUDY:

Assessment of Left ventricular systolic and diastolic parameter by echocardiography in β-Thalassemia Major patients, Assessment of Left ventricular systolic and diastolic parameter by echocardiography in β-Thalassemia Major patients according to ferritin level and Assessment of Left ventricular diastolic parameter by echocardiography in β-Thalassemia Major patients according to spleen status

PATIENTS & METHODS:

This is a prospective study,(427) patients with β-thalassemia major in thalassimic centre at Ibn Al- Albalady Hospital for Children and Maternity Baghdad city during the study period (from beginning of January 2011-end of July 2011) were considered for analysis, all patients on regular blood transfusion & chelation therapy.

Echocardiographic assessment

Echocardiac study done at least 48 hours after last transfusion Echocardiography was performed with a Philips Envisor Ultrasound Machain, with a 3.5/5 and 2.5/3.5 MHZ transducer. Patient's recordings were taken while patients were in supine position without breath holding. M-mode, 2D and Doppler echocardiographic parameters were averaged over 3 cardiac cycles and all echocardiographic measurements were performed according to the guidelines for performance of a pediatric echocardiogram by American Society of Echocardiography

M-mode views were obtained from a parasternal position at mitral and tricuspid valves level. Systolic and diastolic interventricular septum diameter, LV end-diastolic diameter, LV endsystolic diameter, LV posterior wall thickness in diastole and systole, and ejection fraction were calculated by M-mode echocardiography. Pulsed Doppler method was used for blood flow measurements from cardiac valves (mitral, aortic, tricuspid and pulmonary): flow velocity during early filling (E), flow velocity during atrial contraction (A) and ejection time (ET), then E/A was calculated. Isovolumic relaxation time was obtained from the apical five- chamber view and MPI was measured according to the formula: MPI=(IRT+ICT/ET). Doppler and M-mode views were recorded at 50 mm/s velocity *(5,6,7)*

Because Echocardiographic measurements were obtained according to the recommendation of the American Society of Echocardiography, LV mass was calculated using this formula:

Mass (g) =0.8×1.04× [(LV end-diastolic diameter +IVS thickness +posterior wall thickness) ^{3}-(LV end diastolic diameter) ^{3}] +0.6

LV mass index was calculated by the formula:

LV mass index (g/m^2) =Mass/Body surface area

To record LV inflow velocities, the apical four chamber view was used, &the wave Doppler sample volume was placed at the level of the leaflets tips of the MV, where the highest peak velocity was recorded. Peak flow velocity of the LV inflow in early diastole (E) & late diastole with atrial contraction (A) were measured from the base line to the maximum flow velocity,Valsalva maneuver used to differentiate normal from pseudonormal pattern of LV inflow. An E/A velocity ratio was calculated for each cardiac cycle .E wave deceleration time(EDT)was measured as the distance between the projection of the E velocity on the base line &the point where the ejection fraction slope encounters the base line. Isovolumic relaxation time (IVRT) was measured as the time from the end of aortic flow to the beginning of mitral inflow *(6,7,8,9)*

Statistical analysis:

All data were coded and entered to computer by using statistical package for social sciences (SPSS14) association between variables measured by Chi- Square test, difference between variables measured by t- test. P< 0.05 consider as level of significant.

RESULT :

A tota l of 427 patients with β-Thalassemia Major were included in this study, compared to 100 healthy population.

Comparison of demographic characteristics between patients group and control group. Studying age and gender shows matching between both groups. No significant difference in Body surface area and heart rate between patients and control groups

Data shows that echocardiography the LA, Aortic diameter and LA/AO ratio were larger in β-thalassemic patients than healthy population. This difference proved to be of statistical significance (P<0.05), LV posterior wall thickness and interventricular wall thickness found to be larger in thalassemic patient that control group. (P<0.05). Left Ventricular end systolic and diastolic diameter were more in thalassemic patients in comparison to control group as shown in table (1)

Table 1: Conventional 2-dimensional, M-mode echocardiography measurement in patients with β-thalassemia and control subjects (mean ± SD).

Parameter	Thalassemia N= 421 Mean ±SD	Control N=100 Mean ±SD	P value
Left atrium (cm)	2.42± 0.33	1.97±0.34	0.0001
Aortic diameter (cm)	1.90± 0.44	1.63± 0.31	0.001
LA/AO ratio	1.27± 0.3	1.04± 0.2	0.01
LV posterior wall thickness (cm)	0.90± 0.20	0.65± 0.15	0.0001
Interventricular wall thickness (cm)	0.93± 0.22	0.67± 0.11	0.001
LV end diastolic diameter (cm)	4.00± 0.97	3.35± 0.61	0.001
LV end systolic diameter (cm)	2.62± 0.68	2.22± 0.27	0.005

Table (2) shows a that strok volume was larger in thalassemic patient than control group (P=0.03). While Ejection fraction and fraction shortening were lower in thalassemic group but this finding did not reach a statistical significances (P =0.06). Left ventricular mass was larger in first group in comparison to control group (P=0.04). while myocardial performance index (MPI) or tie index was more among thalassemic patients and this difference proved to be of statistical significant. (P=0.03)

Table 2: Left Ventricular function between thalassemic patients and control group

Parameter	Thalassemia N= 421 Mean ±SD	Control N=100 Mean ±SD	P value
Stork volume (ml)	22.4± 802	16.3± 8.2	0.032
Ejection fraction (%)	60.70± 8.94	64.6± 6.23	0.06
Fractional shortening (%)	34.66± 6.0	36.84± 4.82	0.06
LV mass index (g/m²)	159.62± 79.58	95.03± 19.79	0.04
MPI (Tei Index)	0.42±0.06	0.38±0.02	0.03

In table (3) we can see that Peak E and peak A higher in thalassemic patients (130± 28 & 73± 17 respectively) in comparison to control group (104± 30 & 62± 15 respectively). There is no statistical significant difference between both group, in E/A flow ratio and E deceleration time. Regarding isovolumic relaxation time it was found that it higher in thalassemic patient in comparison to control group (73.52± 17.51 & 42.90± 15.38 respectively) this difference proved to be of statistical significance.

Table 3: Doppler LV diastolic parameters and time intervals in patients with thalassemia major and control subjects (Mean ±SD)

Parameter of Doppler study	Thalassemia N= 421 Mean ±SD	Control N=100 Mean ±SD	P value
Peak E (cm/sec))	130± 28	104± 30	0.01
Peak A (cm/sec))	73± 17	62± 15	0.04
E/A Ratio	1.80± 0.61	1.71± 0.43	0.27
E deceleration time (msec)	110.32± 39.36	105.70± 26.22	0.08
IVRT (msec)	73.52± 17.51	42.90± 15.38	0.04

In table (4) it was noticed that, in spite of the difference in ferritin level in both group, but there is no statistical in all mitral valve Doppler parameter.

Table 4: Doppler LV diastolic indexes and time intervals in patients with thalassemia major according to the ferritin level (mean ± SD).

Doppler index	Ferritin level <2000 (ng/ml)	Ferrilin level >2000 (ng/ml)	P-value
Peak E (cm/sec))	130±8	131±6	0.5
Peak A (cm/sec))	68±8	72±6	0.2
E/A Ratio	1.81±0.3	1.78±0.4	0.32
E deceleration time_(msec)	110±25	110±18	0.5
IVCT--ET—IVRT_(msec)	325±16	318±24	0.1
E T	228±14	220±18	0.08
IVRT (msec)	74±11	68±8	0.07
Tei index (MPI)	0.41±0.03	0.43±0.04	0.08

In table (5) It was found that LV mass was heavier in patients with history of splenoctomy (159.92± 11.78) in comparison to those patients with no history of splenctomy (137.81± 29.20) this difference has statistical significancy (P = 0.0 1). There was no significant difference in Doppler LV diastolic parameters and time intervals.

Table 5: Echocardiographic parameters of left ventricle in patient's group in splenctomizied and non splenctomized patients

Echocardiographic parameter	Splenectomized (N=102) Mean± SD	Non-splenectomized (N=325) Mean ±SD	P
LV mass index (g/m²)	159.92± 11.78	137.81± 29.20	0.01
Peak E (cm/sec))	130±3	130±4	0.22
Peak A (cm/sec))	69±8	71±5	0.52
E/A ratio	1.81± 0.67	1.80± 0.51	0.73
E.DEC.TIME (msec)	110.09± 37	109.86± 40.13	0.33
IVRT(msec)	74.67± 19.23	72.95± 15.40	0.08

DISCUSSION:

In our Study patient group match control group in their age and gender. No difference found between both group in their body surface area and hear rate.

Comparison of Conventional 2-dimensional, M-mode echocardiography measurement in both patients with β-thalassemia and control subjects shows that all these measurement were higher in thalassemic group. This is similar to that found by Arshad et al in Pakistan and Shahmohammadi et al and Noori et al in Iran [4,10,11]

Studying LV systolic function between both group shows that patient with thalassemia major had lower ejection fraction and Shortening Fraction but this difference not of statistical significance. The failure to detect impaired ventricular systolic function is not surprising since the haemodynamic effects associated with anemia helped to maintain normal ejection fraction and myocardial fibre shortening. Atiq M et al reported that 23% of their study patients had LV systolic while 29% had diastolic dysfunction.[12]

On echocardiography, β-thalassaemia patients had cardiac enlargement with high stroke volume. Bosi G et al, Chotivittayatarakorn et al, Kremastinos DT et al and Aessopos et al reported that the left ventricular diameter in the thalassaemic patients were significantly higher than in controls, which is in concordance with present study. [13,14,15,16]

Myocardial Performance Index (MPI) (Tie index) is a new Doppler–derived index of combined systolic and diastolic function which is independent of heart rate, blood pressure and severity of mitral valve regurgitation and is simple, reproducible and reliable and correlates well with invasive measurements of systolic and diastolic function. [8] It was found that MPI increased in our studied patients in comparison to control group, this suggests that MPI, are useful parameters in monitoring early ventricular dysfunction in young patients with thalassemia major while systolic parameters are preserved and not changed and patients are asymptomatic.

The mean value of left ventricle mass index (MI) was greater in patients in comparison to control group. This is similar to studies done by Arshad et al (Pakistan), Papadopoulou et al (Greece) and Taksande et al (India). [3,11,17]

Assessment of LV diastolic function by Diastolic flow parameter shows that E, A and IVRT increased in patients group. Diastolic dysfunction affect the IVRT, but presence of increased IVRT is a strong and accurate variable in early stages of diastolic dysfunction that differentiates asymptomatic patients with early dysfunction from healthy subjects. [18]

Click et al. showed that in symptomatic patients with secondary hemochromatosis, restrictive diastolic dysfunction (stage III,IV) or decreased LV compliance pattern and markedly increased LA pressure results in shortened IVRT and greater initial transmitral gradient on high peak E velocity and increased E/A ratio and decreased E deceleration time. But in our study group, patients had no restrictive pattern and most of our patients were asymptomatic. [19]

Olson et al showed that iron is stored predominantly in the subepicardial layers,

causing abnormal subepicardial motion observed in this study by measurement of IVRT, while LV systolic function remains unchanged, unlike a later stage of disease as the subendocardial layer is spared. [20]

Shahmohammadi et al reported abnormalities of LV filling pattern associated with the relative degrees of abnormalities of myocardial relaxation and LV compliance [10]

Studying effect of ferrtin level on echocardiographic parameter of LV diastolic function.there are no difference in LV parameters between those patients whom their Ferritin level <2000 (ng/ml) and those with Ferritin level >=2000 (ng/ml). this is similar to that found by Shahmohammadi et al and Papadopoulou et al.*(10, 3)* Our data are in agreement with those reported by Vaccari et al, [21]

According to Aldouri et al., high ferritin levels do not reflect the degree of cardiac hemosiderosis, because patients with similar iron loads differ in the degree of cardiac dysfunction. [22].

Comparison of LV echocardiographic parameter in those splenctomized patients and those with non- splenctomized state. No difference found between both group except LV mass index (g/m^2) which found to be higher in splenctomized group. This is similar to that found by Al-Enbari in Iraq [23]

CONCLUSION:

LA, Aortic diameter ,LA/AO ratio, LV posterior wall thickness , interventricular wall thickness,

Left Ventricular end systolic and diastolic diameter were larger in β-thalassemic patients.,

Peak E, peak A, isovolumic relaxation time were higher in thalassemic patient there were no difference in E/A flow ratio and E deceleration time, Strock volume, LV mass index and MPI were higher in thalassemic patients. No change in Ejection Fraction and Fraction Shortening, No effect found in in all mitral valve Doppler parameter in comparison to ferritine level and

LV mass index higher in splenctomized patients. No effect found in in all mitral valve Doppler parameter in comparison to spleen status.

REFERENCES:

1. Derchi G et al, Clincical management of cardiovascular complications in patients with thalassemia major, a large observational multicenter study, European Journal of Echocardiograsphy, 2011;12:242-46.
2. Borga-Pignatti C, Rugolotto S, De Stefano P, Piga A, Di Gregorio F, Gamberini MR, et al. Survival and disease complications in thalassemiamajor. Ann NY Acad Sci 1998;850:227-31.
3. Papadopoulou-Legbelou1 K., Varlamis1 S.G., Athanassiou-Metaxa2 M., Karamperis1 S., Malaka-Zafiriou2 A. Full resting echocardiographic study of left ventricle in children with β-thalassemia major KAP¢IO§O°IA›· 2009;2-3:17-24.
4. Noori NM, Mehralizadeh S, Echocardiography and thalassemia major Ana do lu Kar di yol Derg 2010;10:150-3.
5. Khouri SJ, Malay GT, Suh DD, Walsh TE. A practical approach to the echocardiographic evaluation of diastolic function. J Am Soc Ecocardiogr 2004;17:290-97.
6. Harvey Feigenbaum, M.D. et al.Determination of LV mass.Feigenbaum's echocardiography, 6th edition, 2005; chapter 6:146-49.
7. .A.Rebecca Snider. Measurement of LV mass, Echocardiography in Pediatric Heart Disease, second edition 1997; chapter 5:151-53.
8. Tei C, Ling LH, Hodge DO, Bailey KR, Oh JK, Rodeheffer RJ, et al. New index of combined systolic and diastolic myocardial performance: asimple and reproducible measure of cardiac function -a study in normals and dilated cardiomyopathy. J Cardiol 1995;26:357-66.
9. Amoozgar, Hamid1; Farhani, Nahal; Karimi, Mehran, Early Echocardiographic Findings in β-Thalassemia Intermedia Patients Using Standard and Tissue Doppler Methods, Pediatric Cardiology, Volume 32, Number 2, February 2011:154-59.
10. Shahmohammadi A., Davari P. N., Aarabi Y., Meraji M., Tabib A. and Mortezaeian H. Echocardiographic Assessment of Cardiac Involvement in Patients with Thalassemia Major: Evidence of Abnormal Relaxation Pattern of the Left Ventricle in Children and Young Patients, Iranian Heart Journal 2006;7:31-36.
11. Arshad MS, Hyder SN, Evidence of abnormal left ventricular function in patients with thalassaemia major: an echocardiography based study, J Ayub Med Coll Abbottabad 2009;21.

12. Atiq M, Bana M, Ahmed US, Bano S, Yousuf M, Fadoo Z, et al. Cardiac disease in beta-thalassemia major: is it reversible? Singapore Med J 2006;47:693–96.

13. Bosi G, Crepaz R, Gamberini MR, Fortini M, Scarcia S,Bonsante E, et al. Left ventricular remodeling, and systolic and diastolic function in young adults with beta-thalassemia major: a Doppler echocradiographic assessment and correlation with hematological data. Heart 2003;89:762–66.

14. Aessopos A, Deftereos S, Tsironi M, Karabatsos F, Yousaf J,Fragodimitri C, et al. Predictive echo-Doppler indices of left ventricular impairment in B- thalassemic patients. Ann Hematol 2007;86:429–34.

15. Kremastinos DT. Heart failure in beta-thalassemia major. CHF 2001;7:312–4.

16. Chotivittayatarakorn P, Seksarl P, Pathmanand C,Thisyakorn, Sueblinvong V. Cardiac dysfunction in beta-Thalassemic children. J Med Assoc Thai 1993;76:591–96.

17. Taksande A, Vilhekar K, Chaturvedi P, Jain M, Bang A,Ganvir B. Cardiac changes in beta-thalassemia major children: assessment by echocardiography. J Mahatma Gandhi Inst Medl Sci 2006;11:45–51.

18. Angeja, BG, Grossman W. Diastolic dysfunction and congestive heart failure. Circulation; Feb 2003; 107:659-63.

19. Click R. Echocardiography and systemic diseases. J Am Soc Echo 1994; 7:201-16.

20. Olson LJ. Cardiac iron deposition in idiopathic hemochromatosis. J Am Coll Cardiology 1987; 10: 1239-43.

21. Vaccari M, Crepaz R, Fortini M, Gamberini R., Scarcia S, Pitscheider W and Bosi G , left ventricular remodeling, systolic function, and diastolic function in young adults with _-thalassemia intermedia a doppler echocardiography study, Chest 2002;121;506-12

22. Aldouri MA, Wonke B, Hoffbrand AV, Flynn DM, Ward SE, Agnew JE, et al. High incidence of cardiomyopathy in beta-thalassemia patients receiving regular transfusion and iron chelation: reversal by intensified chelation. Acta Haematol 1990;84:113-17.

23. Al-Enbari A, the effect of thalassemia major on left ventricle by echocardiography A thesis Submitted to the scientific council of Cardiology in partial fulfillment for the Degree of fellowship of the Iraqi Board For Medical Specialization in Pediatric Cardiology 2006**.**