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Original article:

Study of evaluation of carotid artery mechanics by duplex ultrasound in thalassemia syndrome cases

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Abstract

Introduction: Thalassemia syndromes are a heterogeneous group of single gene disorders, inherited in an autosomal recessive manner. Worldwide, 15 million people have clinically apparent thalassemic disorders. Reportedly, there are about 240 million carriers of β-thalassemia worldwide, and in India alone, the number is approximately 30 million with a mean prevalence of 3.3%.

Material and methods: This study was conducted in the Department of Pediatrics and Blood Bank of Nanavati Hospital and Research Centre. It is a tertiary care hospital where thalassemic patients receive regular transfusions. Patients aged 13-33 years coming for routine blood transfusions at the Nanavati hospital blood bank and also out-patients coming for regular follow up and receiving transfusions at other blood transfusion centres between November 2011 and November 2012 were included in the study. A detailed history and physical examination were completed for all cases and the findings recorded on a proforma.

Results : Right common carotid artery, left common carotid artery and mean of both common carotid artery CIMT values were significantly greater in cases as compared with controls (with p value, p=0.00495; p=0.00279; p=0.00032 respectively)Right, Left & mean YEM were higher in cases as compared with cases (with p value,p=0.00174; p=0.00012; 0.00014). Significant correlation between Mean Stiffness index and Cardiac T2* MRI found as cardiac iron overload increases carotid artery mean stiffness also increases.

Conclusion: We conclude that CIMT is increased in thalassemia patients as compared to age and sex matched controls indicating early atherosclerosis amongst the cases. We also observed that there is no direct or significant correlation between carotid artery intimo-medial thickness and cardiac iron overload and hepatic overload.

Keywords: Thalassemia syndrome , CIMT

Introduction:

Thalassemia syndromes are a heterogeneous group of single gene disorders, inherited in an autosomal recessive manner.[1] Worldwide, 15 million people have clinically apparent thalassemic disorders. Reportedly, there are about 240 million carriers of β-thalassemia worldwide, and in India alone, the number is

approximately 30 million with a mean prevalence of 3.3%. [2,3] These inherited anaemias are encountered among all ethnic groups and in almost every country around the world. Every year approximately 100,000 children with Thalassemia Major are born globally, of which 10,000 are Indian. It is estimated that there are about 65,000-67,000 β-thalassemia patients in our country with around 9,000-10,000 cases being added every year.[1-4] The carrier rate for the β-thalassemia gene varies from 1 to 3% in Southern India to 3% to 15% in Northern India. Certain communities in India, such as Sindhis and Punjabis from Northern India, Bhanushalis, Kutchis, Lohanas from Gujarat, Mahars, Neobuddhists, Kolis and Agris from Maharashtra, and Gowdas and Lingayats from Karnataka have a higher carrier rate.[3,4]

β-Thalassemia major is an anaemia characterized by both ineffective erythropoiesis and haemolysis. [5] The underlying mechanism is defective production of haemoglobin β- chains, resulting in excess of α-chains, which are unstable and precipitate to form intracellular inclusion bodies which lead to haemolysis.[6 7] Regular transfusion is required to keep the ineffective erythropoiesis under control and prevent anaemia-related complications. Increased gastrointestinal iron absorption along with excess iron released from haemolysed RBCs remains in the body and causes secondary hemosiderosis which is major cause of morbidity and mortality in thalassemic patients.[5] Excess iron is deposited in the reticuloendothelial system (bone marrow, spleen, liver) the cardiac myocytes, and the endocrine glands. [5, 8, 9]

Material and methods:

This study was conducted in the Department of Pediatrics and Blood Bank of Nanavati Hospital and Research Centre. It is a tertiary care hospital where thalassemic patients receive regular transfusions.

Patients aged 13-33 years coming for routine blood transfusions at the Nanavati hospital blood bank and also out-patients coming for regular follow up and receiving transfusions at other blood transfusion centres between November 2011 and November 2012 were included in the study. A detailed history and physical examination were completed for all cases and the findings recorded on a proforma.

Sample of cases was a period sample collected over a period of 1 year from November 2011 to 2012. It was a multicentre sampling and a total of 53 β-Thalassemia major patients fitting into inclusion and exclusion criteria were enrolled for the study (Group 1). A control group (Group 2) of 25 age matched subjects was selected from healthy volunteers from hospital. Thus, it was a comparative cross-sectional study.

Inclusion criteria

Patients diagnosed with thalassemia major who received regular blood transfusions and chelation therapy with one or more chelating agents and in whom serum ferritin was monitored were included.

Exclusion criteria

In both groups, children who had diabetes mellitus, hypertension, hyperlipidemia, smoking or obesity were excluded from the study.

This cross sectional study was conducted on patients of thalassemia taking regular blood transfusion and chelation therapy**.**

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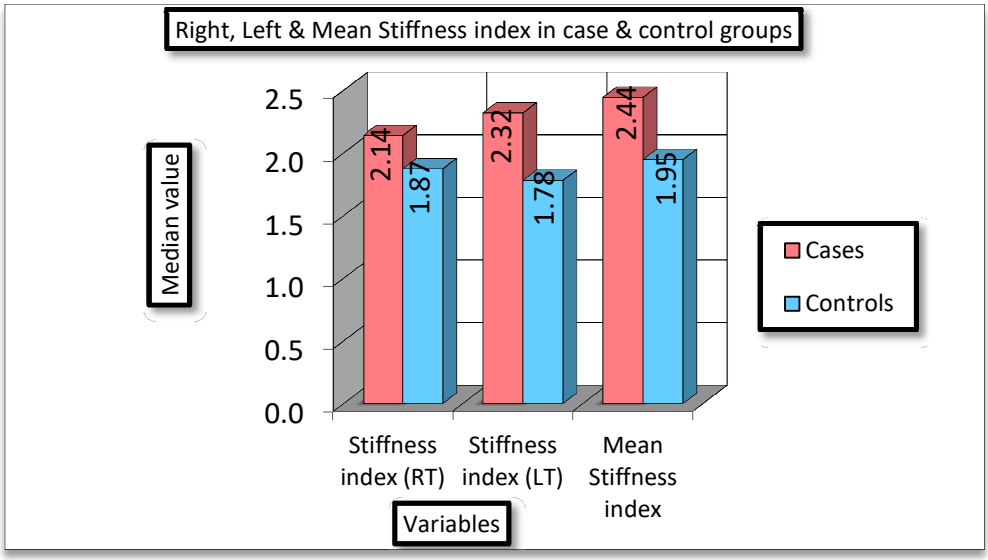
Results:

A total of 78 subjects were included in the study comprising of two comparison groups: Group 1 consisting of 53 cases of thalassemia on regular transfusion and chelation therapy, and Group 2, consisting of 25 healthy volunteers from the hospital environment as controls. The patients were between 13 years and 33 years with 37.7% (20 cases) below 20 years, 45.3% (24 cases) between 21 to 25 years & 17% (9 cases) above 25 years. Controls were equally distributed in the age groups defined above. The mean ages were 21.85±4.58 years and 23.08±4.46 years in cases and controls respectively.

Right common carotid artery, left common carotid artery and mean of both common carotid artery CIMT values were significantly greater in cases as compared with controls (with p value, p=0.00495; p=0.00279; p=0.00032 respectively)

Graph 1: Comparison of Mean Stiffness Index between Case and Control Groups

Right, left and Mean Stiffness index values were higher in cases as compared with cases (with p value, p=0.02559; p=0.00892; 0.00985)



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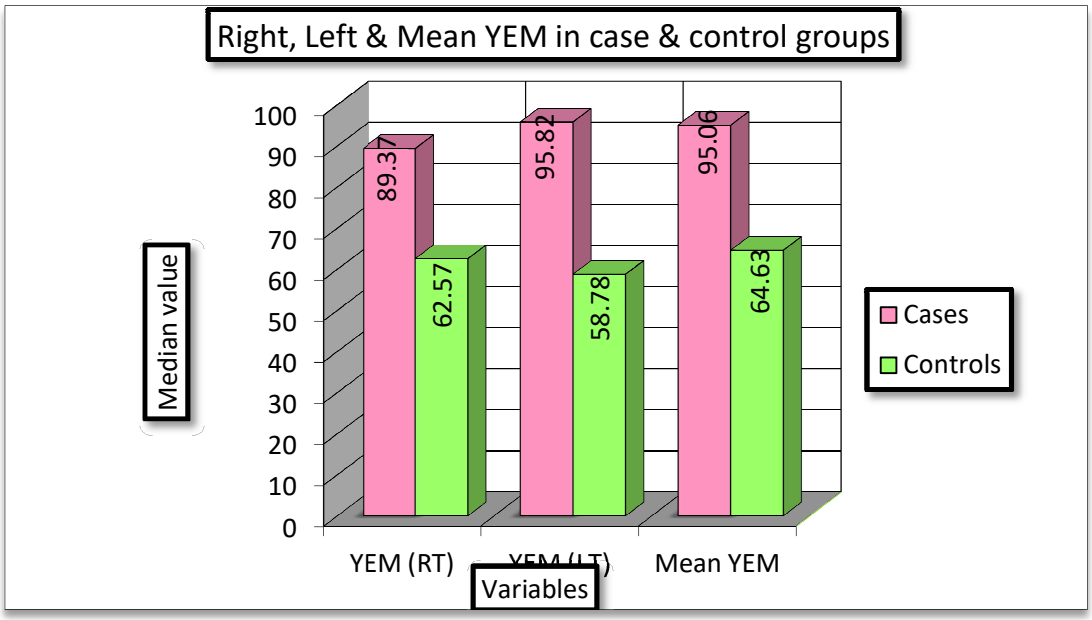
Graph 2: comparison of mean YEM between cases & control

Right, Left & mean YEM were higher in cases as compared with cases (with p value,p=0.00174; p=0.00012; 0.00014)



Significant correlation between Mean Stiffness index and Cardiac T2* MRI found as cardiac iron overload increases carotid artery mean stiffness also increases.

Discussion

This study shows the Carotid intimo-medial thickness (CIMT) of Right Common carotid artery (CAA), Left CCA and mean of right as well as left common carotid artery of cases was significantly greater than controls with p value (p=0.00495, P=0.00279, P=0.00032) respectively. The distribution of CIMT of Right CCA, Left CCA and mean CIMT among cases as mean ±SD (0.48±0.06mm; 0.47±0.04mm; 0.48±0.04mm) respectively. Similarly in controls CIMT of Right CCA, Left CCA & mean CIMT as mean+ SD (0.44±0.03mm; 0.44±0.04mm; 0.44±0.02mm).

Carotid IMT is considered an early marker of atherosclerotic process and is currently used to assess the presence and the progression of atherosclerosis. Common carotid intima-media thickness (IMT) and distensibility are markers of structural and functional vessel wall properties. Several cross-sectional community-based studies consistently showed that increased IMT of the carotid artery is associated with atherosclerosis. Moreover, follow-up studies have shown a strong and graded association between increased IMT and increased incidence of myocardial infarction and stroke. Results of these studies support the view that increased IMT is an indicator of extent of generalized atherosclerosis. Distensibility is the ability of the artery to expand as a response to pulse pressure, i.e. the change in arterial diameter during the cardiac cycle.

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Distensibility decreases with age. Cross-sectional studies showed associations between decreased distensibility and cardiovascular risk factors, i.e., hypertension, diabetes mellitus, hypercholesterolemia, and myocardial infarction. [10]

Our study shows that the CIMT is increasing as the age of thalassemia patients increases. The thalassemia patients were divided in <20 years, 21 to 25 years and >25 years age groups and the mean CIMT were 0.47 mm, 0.48 mm and 0.49 mm in the age groups mentioned respectively. The other studies also show that CIMT increases as the age of thalassemia patient increases. Ismail & El-sheriff et al[11] show that there was significant difference of CIMT in relation to patient's age. Tantawy et al 2009, concluded that in thalassemic patients, CIMT was positively correlated with age. The Akhlaghpoor et al.[12] divided the thalassemia patients in different age group such as 10-19 year, 20-29 year, 30-39 year and 40-50 year and found at the age group of 10-19 years, no significant differences are seen in mean carotid IMT based on the severity of iron loading. This finding could be resulting from this fact that, atherogenesis is a prolonged process and should not be expected in such young patients.

In our study of Right, Left and mean stiffness index in Thalassemia patients as mean ±SD (2.51±1.12; 2.38±0.70; 2.45±0.79) and in controls (2.02±0.74; 1.94±0.61; 1.98±0.58) respectively found. While comparing stiffness index between cases and control, cases have significantly higher stiffness index than controls with p value (p=0.02559; p=0.00892; 0.00985). Same thing proved by Cheung et al (2006) arterial stiffness index (4.8 ± 1.7 vs. 3.7 ± 0.7, P = 0.009). It suggests that the carotid artery wall is stiffened and there is an increased risk of atherosclerosis. Similarly Right, Left and mean Young's elastic modulus (YEM) in cases as mean ±SD (100.19; 92.06; 96.12) and in controls (70.51; 58.78; 64.63) respectively found. While comparing YEM between cases and controls, cases have significantly higher YEM than controls with p value (p=0.00174; p=0.00012; 0.00014) respectively. It also suggests an increase in the stiffness of the carotid artery in cases compared to controls. Cheung et al (2006) study shows that compared with controls, patients had significantly greater YEM (180 ± 60 mmHg mm vs. 135 ± 34 mmHg mm, P = 0.005). Furthermore, this study extends their previous observation (Cheung et al, 2002) by demonstrating a correlation between arterial stiffening and atherosclerotic changes. [13]

Alterations of arterial structures with disruption of elastic tissue and calcification, on the other hand, have been demonstrated in patients with β-thalassemia major. These structural changes may translate functionally into alteration of arterial stiffness in vivo. Arterial stiffness and Young's elastic modulus are important mechanical properties, because they are related to vascular impedance and in turn to the after load that is presented to the left ventricle Duffy et al have recently shown that iron chelation with desferrioxamine in adults with coronary artery disease improves endothelium dependent vasodilatation. Their findings suggest that iron contributes to impaired nitric oxide function in atherosclerosis. In patients with β-thalassemia major, despite desferrioxamine therapy, their body iron load remains significantly higher than normal. Indeed, in vitro studies have shown disturbances of human vascular endothelial cell function when the cell culture is incubated with thalassemic serum.[14]

A potential limitation of this study is the cross-sectional and observational nature of our study. This type of study cannot identify a cause-and-effect relationship, but associations can be examine. Another limitation is the relative low sample size, especially at the high age groups.

Conclusion:

We conclude that CIMT is increased in thalassemia patients as compared to age and sex matched controls indicating early atherosclerosis amongst the cases. We also observed that there is no direct or significant correlation between carotid artery intimo-medial thickness and cardiac iron overload and hepatic overload.

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