Early Detection of Premature Atherosclerosis in β-Thalassemia Patients by Measuring Carotid Intima-Media Thickness

Thesis

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List of Abbreviations

Abb.	Full term

µg..... Microgram
µl..... Microliter
ACA.....Anticardiolipin Antibody
aPL .....Anti-Phospholipid Antibodies
BMI..... Body Mass Index
BP .....Blood Pressure
CACS .....Coronary Artery Calcification Score
CAD .....Coronary Artery Diseases
CB .....Carotid Bulb or Bifurcation
CBC.....Complete Blood Picture
CCA .....Common Carotid Artery
CIMT .....Carotid Intima–Media Thickness
CT CT .....Computed Tomography
CV .....Cardiovascular
CVD .....Cardiovascular Disease
DFO .....Desferoxamine
DFP.....Defriprone
DFX.....Defrasirox
DVT .....Deep Venous Thrombosis
EC .....Endothelial Cells
ECA.....External Carotid Artery
EPO .....Erythropoietin
ERFE .....Erythroferrone
GDF15 .....Growth Differentiation Factor 15
GVHD .....Graft Versus Host Disease
HB .....Hemoglobin
HCT .....Hematocrit
HCV .....Hepatitis C Virus

List of Abbreviations (Cont...)

Abb.	Full term
HDL-C	High- Density Lipoprotein Cholesterol
Hg A	Hemoglobin A
Hg A2	Hemoglobin A2
Hg F	Hemoglobin F
HPFH	Heridetery Persistence of Fetal Hemoglobin
HR	Heart Rate
HS	Highly significant
ICA	Internal Carotid Artery
ICAM-1	Intercellular Adhesion Molecule-1
IDDM	Insulin-Dependent Diabetes Mellitus
IE	Ineffective Erythropoiesis
IL- 1, 2, and 6	Interleukins 1, 2, and 6 ()
IMT	Intima–Media Thickness
IVUS	Intravascular Ultrasonography
LA	Lupus Anticoagulant
LDL	Low-Density Lipoprotein
LDL-C	Low Density Lipoprotein Cholesterol
LIC	Liver Iron Concentration
LPI	Labile Plasma Iron
MCV	Mean Corpuscular Volume
MDA	Malondialdehyde
mg/dl	Mille gram per deciliters
mg/g	Mille gram per gram
mg/kg/day	Mille gram per kilogram per day
ml/min	Mille liter per minute
mm	Milli meter per Liter
MRI	Magnetic Resonance Imaging
ng/ml	Nanogram per mille litter

List of Abbreviations (Cont...)

Abb.	Full term

nm ..... Nanometer
NO.....Nitric Oxide
NS .....Non Significant
NTBI .....Non-Transferrin-Bound Iron
NTDT .....Non-Transfusion Dependent Thalassemia
^{o}C ..... Centigrade
OxLDL .....Oxidized LDL
PLT ..... Platelet
PON .....Paraoxonase
PRBCs.....Packed Red Blood Cells
RBC .....Red Blood Cell
ROS .....Reactive Oxygen Species
S .....Significant
SCT .....Stem Cell Transplantation
SD .....Standard Deviation
SDS .....Standard Deviation Score
TC .....Total-Cholesterol
TF .....Tissue Factor
TGF-beta1 .....Transforming Growth Factor Beta1
TI.....Thalassemia Intermedia
TLC .....Total Leucocytic Count
TM.....Thalassemia Major
TMB .....Tetramethylbenzidine
TNF-α ..... Tumor Necrosis Factor α
TWSG1 .....Twisted-Gastrulation 1
UCB .....Umbilical Cord Blood
VCAM-1 .....Vascular Cell Adhesion Molecule-1
VWF .....von Willebrand factor

List of Abbreviations (Cont...)

Abb.	Full term

α ..... Alpha
β-Thal ..... Beta Thalassemia
β-tI ..... βeta-Thalassemia Intermedia
β-tM ..... βeta-Thalassemia Major
β-TM ..... β-thalassemia major
γ ..... Gamma

ABSTRACT

Background: Beta-thalassemia patients still suffer from many complications. Transfused patients may develop complications related to iron overload including growth retardation and failure or delay of sexual maturation, cardiac involvement (dilated cardiomyopathy or rarely arrhythmia), liver (fibrosis and cirrhosis), endocrine glands (diabetes mellitus, hypogonadism, insufficiency of parathyroid, thyroid, pituitary and less commonly, adrenal glands).

Purpose: The present study was undertaken to evaluate the role of Carotid artery intima media thickness (CIMT) measurement as an early detector of premature atherosclerosis in beta-thalassemia children and early adolescents and its relation to biochemical risk factors as iron overload and lipid profile.

Patients and Method: Twenty-two β-thalassemia major (TM), 8 β-thalassemia intermedia (TI) with confirmed diagnosis of beta-thalassemia (major and intermedia) proved by clinical and laboratory investigations, frequent blood transfusion, chelation therapy with their age ranging from 10 to18 years old and 30 age-and sex matched healthy controls were included. Lipid profile (by colorimetric assay), serum ferritin, and CIMT measurements using high-resolution B-mode ultrasonography were estimated.

Results: CIMT of thalassemic patients (major and intermedia) was highly significantly increased compared to controls with no significant difference between β-thalassemia major and β thalassemia intermedia groups could be detected. CIMT was positively correlated with serum ferritin, TG, Total cholesterol level in both diseased groups and LDL level in B-TM group only. This provides a good evidence of the presence of premature atherosclerosis in vascular-free TM and TI patients and its relation to increased body iron and dyslipidemia.

Conclusion: Carotid artery intima media thickness represented a simple, accurate and non-invasive method for early detection of premature atherosclerosis which started early in β- thalassemia patients This study identified a relationship between body iron status, dyslipidemia and increased carotid IMT.

Keywords: Beta-thalassemia, Carotid artery intima media thickness, premature atherosclerosis.

INTRODUCTION

Beta-thalassemia syndromes are a group of hereditary disorders characterized by a genetic deficiency in the synthesis of beta-globin chains. In the homozygous state, beta - thalassemia (ie, thalassemia major) causes severe, transfusion-dependent anemia. In the heterozygous state, the beta thalassemia trait (ie, thalassemia minor) causes mild to moderate microcytic anemia ***(Rachmilewitz et al., 2011).***

Individuals with thalassemia major usually come to medical attention within the first two years of life and require regular RBC transfusions to survive. Thalassemia intermedia includes patients who present later and don't require regular transfusion ***(Galanello et al., 2010).***

However, beta-thalassemia patients still suffer from many complications. Transfused patients may develop complications related to iron overload including growth retardation and failure or delay of sexual maturation, cardiac involvement (dilated cardiomyopathy or rarely arrhythmia), liver (fibrosis and cirrhosis), endocrine glands (diabetes mellitus, hypogonadism, insufficiency of parathyroid, thyroid, pituitary and less commonly, adrenal glands) ***(Borgna-Pignatti et al., 2004).***

Cardiac disease caused by myocardial siderosis is the most important life- limiting complication of iron overload and it is the cause of death in 71% of patients of beta-thalassemia ***(Borgna-Pignatti et al., 2004).***