STUDY OF GROWTH DIFFERENTIATION FACTOR 15 EXPRESSION IN PATIENTS WITH BETA THALASSEMIA INTERMEDIA

Thesis

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Presented By

Rania Mohamed Wagdy Salah El-Deen

(M.B,Bch.)

Faculty of Medicine- Cairo University

Supervised

Prof. Dr.Mona Hassan El-Tagy

Professor of Pediatrics

Cairo University

Dr. Dalia Said Mossalam

Assistant Professor of Pediatrics

Cairo University

Dr. Nadia Ibrahim Sewelam

Lecturer of Clinical Pathology

Cairo University

Faculty of Medicine

Cairo University

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Abstract

Background: The thalassemia syndromes represent the most common causes of ineffective erythropoiesis . The increased but ineffective erythropoiesis resulting in tissue iron overload induces numerous endocrine diseases, hepatic cirrhosis, cardiac failure and even death .

Objectives: we aim to study GDF15 levels in β- thalassemia intermedia patients and to correlate its level to their iron status and different clinical and laboratory disease parameters.

Method: This is case control study conducted on 25 pediatric patients under 18 years with beta thalassemia intermedia and 30 healthy children taken as control group . GDF 15 level was performed using (ELISA) kit in serum samples that obtained from children of both groups . Abdominal examination , frequency of blood transfusion , Complete blood picture , Reticulocytic count , liver function tests , serum ferritin were done in case group to assess severity of beta thalassemia intermedia .

Result: . Our results showed that GDF 15 levels were statistically higher in cases compared to control (P Value < 0.05).

Conclusion:GDF15 level in our study represent a first step for its use as biomarker in thalassemia patients although future studies may be needed before its routine use**.**

Key words: Thalassemia intermedia (TI), Growth Differentiation Factor 15 (GDF 15),Ferritin

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List of Abbreviations

3'UTR	3' untranslated region
AFSC	Control sample containing A, F, S, and C hemoglobins
ALT	Alanine transaminase
AST	Aspartate transaminase
ATO	Arsenic trioxide
BM	Bone marrow
BMPRs	Bone morphogenic protein receptors
BMPs	Bone morphogenic proteins
CBC	Complete blood count
CT scanning	Computerised tomography
d	Day
DFO	Desferoaxamine
DFP	Deferiprone
DNA	Deoxyribonucleic acids
DVT	Deep vein thrombosis
ECG	Electrocardiogram
EDTA	Ethylene diamine tetra-acetic acid
EMH	Extramedullary hematopoiesis
EPO	Erythropoietin
ESR	Erythrocyte sedimentation rate
g	Gram

GDF15	Growth differentiation factor 15
Hb	Hemoglobin
Hb A	Adult hemoglobin
Hb F	Fetal hemoglobin
HbE	Hemoglobin lepore
Hct	Hematocrit
HFE	HFE gene product
HJV	Haemojuvelin
HPFH	Hereditary persistence of fetal hemoglobin
HPLC	High-performance Liquid chromatography
HSCT	Hematopoietic stem cell transplantation
HSM	Hepatosplenomegaly
HU	Hydroxyurea
ICL 670	Iron chelator 670 (Deferasirox)
IL-1	interleukin -1
IL6R	IL-6 receptor
IVS	Intervening sequence
Kg	Kilogram
L	Liter
L 1	Deferiprone
LIC	liver iron concentrations
m	Millimeter
MCH	Mean corpuscular hemoglobin

MCHC	Mean corpuscular hemoglobin concentration
MCV	Mean corpuscular volume
mg	Milligram
MIC-1	Macrophage inhibitory cytokine – 1
min	Minute
mmHg	Millimeter mercury
MMP	Mitochondrial membrane potential
mo	Month
Mr	Monomer molecular mass
MRI	Magnetic résonance imaging
mRNA	Messenger ribonucleic acid
NAG-1	Nonsteroidal anti-inflammatory drug activated gene
ng	Nanogram
nt	Nucleotide
PB	Peripheral blood
PCR	Polymerase chain reaction
PDF	Prostate derived factor
pg	Pico gram
PHT	pulmonary hypertension
PLT	Platelets
PTGFb	Placental transforming growth factor-b
RBC	Red blood cell
RE	Reticuloendothelial

SCF	Stem cell factor
sec	Second
sHJV	Soluble form of Haemojuevelin
Smad	Small molecules against decapentaplegic proteins
TF	Transcription factor
Tf	Transferrin
TGF-β	Transforming growth factor-β
TI	β-thalassemia intermedia
TLC	Total leucocytic count
TM	Thalassemia major
TWSG1	Twisted gastrulation
Tx	Thromboxne
U	Unite
USA	United States of America
WBC	White blood cells
WHO	World Health Organization
yrs	Years

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Introduction

and

Aim of the Work

Introduction

The thalassemia syndromes (**alpha and beta thalassemia**) represent the most common causes of ineffective erythropoiesis (**Tanno et al., 2010**). The increased but ineffective erythropoiesis resulting in tissue iron overload (**Casanovas et al., 2011**) induces numerous endocrine diseases, hepatic cirrhosis, cardiac failure and even death (**Weatherall and Clegg, 2001**).

Hepcidin regulated intestinal iron absorption represents a principal mechanism for iron homeostasis in humans (Donovan et al., 2006). It is commonly believed that ineffective erythropoiesis inhibits expression of hepcidin, a hepatic peptide hormone secreted from liver that regulates the release of iron into the blood stream from duodenal enterocytes, hepatocytes and macrophages (**Ramey et al., 2010**). It was shown that hepcidin levels are decreased in individuals with beta thalassemia syndromes (**Kattamis et al., 2006**).

It's hypothesized that the erythroid expansion could influence the regulation of hepcidin expression through systemic release of transforming growth factor β (TGF-β)