

Assessment of different parameters of renal function in Egyptian patients with β -thalassemia major and β -thalassemia intermedia

Thesis submitted for partial fulfillment of Master Degree of Pediatrics

By

Karim Mahmoud Abo El Seoud

MB., B.Ch.

Faculty of Medicine – Cairo University

Under supervision of

Prof. Dr. Amira Abd El Moneam Adly

Assistant Professor of Pediatrics

Faculty of Medicine – Ain Shams University

Dr. Dalia Nabil Toaima

Lecturer of Pediatrics

Faculty of Medicine – Ain Sams University

Dr. Noha Refaat Mohamed

Lecturer of Clinical and Chemical Pathology

Faculty of Medicine – Ain Shams University

Faculty of Medicine

Ain Shams University

2013

"وَقُلْ رَبِّ زِدْنِي عِلْمًا"

سورة طه الآية (١١٤)



Acknowledgment

First of all, to **Allah** the most merciful for guiding me through and giving me the strength to complete this work the way it is.

I would like to express my deeply felt gratitude to **Prof. Dr. Amira Abd El Moneam Adly** assistant Professor of Pediatrics, faculty of Medicine, Ain Shams University for giving me the chance of working under her supervision. I appreciated her constant encouragement.

Great appreciation and gratitude to **Dr. Dalia Nabil toaima** lecturer of Pediatrics, faculty of Medicine, Ain Shams University for her great efforts. Valuable guidance, and great concern that really supported the work,

Many Thanks for **Dr. Noha Refaat Mohamed** lecturer of clinical and chemical pathology, faculty of Medicine, Ain Shams University, For her kind supervision, and great help throughout the practical part of this work,

Special thanks and respect to **Dr. Jonair Hussein Abd El Kafy**, lecturer of pediatrics, faculty of medicine, Ain shams university, for her invaluable help and assistance in the initial steps and the protocol of this work,

Finally, I would like to convey my gratitude to **my patients** and their families and to every person who helped me while performing this work,



 **To**

Family for their warm affection, patience,
encouragement, and for always being there
when I needed them

 **To**

My wife who always support me with
powerful spirit, my daughter **Lara** who fills my life
with joy.

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List of abbreviations

α	<i>Alpha</i>
β	<i>Beta</i>
ϵ	<i>Epsilon</i>
γ	<i>Gamma</i>
δ	<i>Delta</i>
ξ	<i>Zeta</i>
AG	<i>Arginine</i>
<i>AIDS</i>	<i>Acquired immunodeficiency syndrome</i>
<i>ALT</i>	<i>Alanine aminotransferase</i>
<i>CKD</i>	<i>Chronic kidney disease</i>
<i>CVS</i>	<i>Chorionic villus sampling</i>
<i>DFO</i>	<i>Desferrioxamine</i>
<i>DNA</i>	<i>Deoxy ribonucleic acid</i>
<i>ECG</i>	<i>Electrocardiogram</i>
<i>ELISA</i>	<i>Enzyme-linked immuno sorbent assay</i>
<i>FT4</i>	<i>Free thyroxine</i>
<i>GFR</i>	<i>Glomerular filtration rate</i>
<i>GT</i>	<i>Glutamine</i>
<i>GVHD</i>	<i>Graft Versus Host Disease</i>
<i>Hb</i>	<i>Hemoglobin</i>
<i>HBV</i>	<i>Hepatitis B virus</i>
<i>HCV</i>	<i>Hepatitis C virus</i>
<i>HIV</i>	<i>Human immunodeficiency virus</i>
<i>HLA</i>	<i>Human leukocyte antigen</i>
<i>HSCT</i>	<i>Hematopoietic stem cell transplantation</i>
<i>HU</i>	<i>Hydroxyurea</i>
<i>IGF-1</i>	<i>Insulin-like growth factor 1</i>
<i>IGFBP-3</i>	<i>Insulin-like growth factor binding protein</i>

LIC	<i>Liver iron concentration</i>
MCH	<i>Mean corpuscular hemoglobin</i>
MCV	<i>Mean corpuscular volume</i>
MDA	<i>Malondialdehyde</i>
mRNA	<i>messenger ribonucleic acid</i>
MRI	<i>Magnetic resonance imaging</i>
NESTROFT	<i>Naked Eye Single Tube Red Cell Osmotic Fragility test</i>
NTBI	<i>Non-transferrin-bound plasma iron</i>
OGTT	<i>Oral glucose tolerance test</i>
PCR	<i>Polymerase chain reaction</i>
RBCs	<i>Red blood cells</i>
rHUEPO	<i>Recombinant human erythropoietin</i>
SQUID	<i>Superconducting quantum interference device</i>
STFR	<i>Serum transferrin receptors</i>
TI	<i>Thalassemia intermedia</i>
TM	<i>Thalassemia major</i>
TRH	<i>Thyrotropin releasing hormone</i>
TSH	<i>Thyroid stimulating hormone</i>
U-NAG	<i>Urinary N-acetyl-Beta-D-glucosaminidase</i>

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Introduction

Beta thalassemia major is a type of chronic, inherited, microcytic anemia that is characterized by impaired biosynthesis of beta-globin leading to accumulation of unpaired alpha-globin chain (*Jalali et al., 2011*).

Patients with β -thalassemia major receive blood transfusion regularly. Repeated blood transfusions, however, do not come without their own side effects as iron overload inevitably manifests resulting in multiple organ damage, notably in the heart, liver and endocrine glands (*Taher et al., 2009*). Safe blood transfusion and iron chelation therapy is surely translated into prolonged survival and enhanced quality of life in patients with β -thalassemia major (*Borgna-Pigatti et al., 2004*).

β -thalassemia intermedia is a term used to define a group of patients with β -thalassemia in whom the clinical severity of the disease is somewhere between the mild symptoms of β -thalassemia trait and the severe manifestations of β -thalassemia major (*Cohen et al., 2004*). The diagnosis is a clinical one based on the patient maintaining a satisfactory hemoglobin level at least 6-7g/dl at time of diagnosis without the need for regular blood transfusion. Iron overload is a potential complication of β -thalassemia intermedia (*Smoklin et al., 2008*).

Limited data are available about renal involvement in thalassemic patients (*Oktenli and Bulueu, 2002*). Renal dysfunction in these patients is not known well and seems to be multifactorial; attributed mainly to long-standing anemia, chronic hypoxia, iron overload and toxicity of iron chelators (*Koliakos et al., 2003*).

Introduction & Aim of work

Anemia is associated with oxidative stress which contributes to lipid peroxidation and tubular cell dysfunction (*Nagababu et al., 2008*). Also there is evidence that anemia may cause hyperdynamic circulation, glomerular hyperperfusion and hyperfiltration which can lead to stretching of the glomerular capillary wall, resulting in endothelial and epithelial injury which by time may cause a marked decline in glomerular filtration rate (*Ponticelli et al., 2010*).

Hypoxia of the tubular cells secondary to anemia can cause apoptosis or epithelial-mesenchymal transdifferentiation leading to fibrosis of the kidney (*Nangaku et al., 2006*).

Iron overload may cause lipid peroxidation of the tubular cells and generation of oxygen free radicals which in term can lead to tubular cell injury or death (*Kassab-Chekir et al., 2003*).

Cases of acute renal failure requiring dialysis have been reported after deferoxamine overdose secondary to pump malfunction or inadequate dose monitoring during treatment (*Clajus et al., 2008*). Cases of acute kidney injury have also been reported in the post-markting surveillance of the novel oral chelator deferasirox (*Grange et al., 2010*).

There have been few published studies demonstrating proteinuria, aminoaciduria, low urine osmolarity and excess secretion of the proximal tubular damage markers such as N-acetyl β -D-glucosaminidase and β 2 microglobulin in such patients (*Aldudak et al., 2000*). In addition, serum sodium, potassium, phosphorus, uric acid and urinary protein to creatinine ratio were found to be significantly different from normal reference ranges (*Oktenli and Bulueu, 2002*).

Aim of the work

To assess renal functions in patients with β -thalassemia major and β -thalassemia intermedia in correlation with iron overload and type of chelator in order to detect early deterioration of renal functions.