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

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"وَقُل رَّبِّ زِدْنِي عِلْمًا" ۝

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List of abbreviations

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

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

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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-thalasemia 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).***

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 etal., 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 β2 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.