THE SERUM ERYTHROPOIETIN IN CHILDREN WITH β THALASSEMIA, SICKLE CELL ANEMIA AND APLASTIC ANEMIA

THESIS
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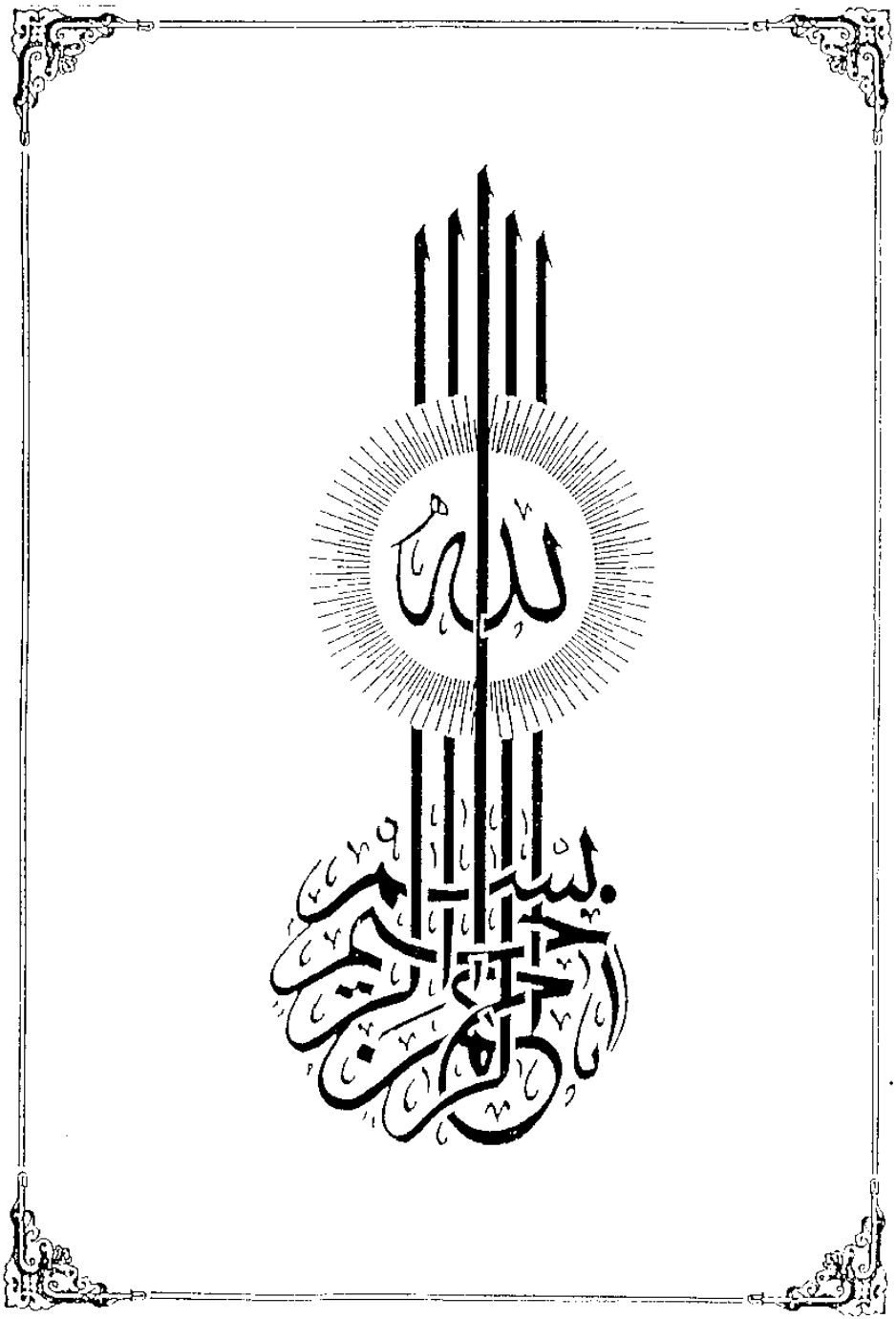

ABBREVIATION

AIDS	=	Acquired immune deficiency syndrome
ALG	=	Antilymphocytic globulin
ALG/ATG	=	Anti lymphocyte globulin/anti thymic globulin
ALT	=	Alanine transaminase
AST	=	Aspartate transaminase
BMT	=	Bone marrow transplantation
Cfu-E	=	Colony-forming units-erythroid
CPM	=	Counts per minute
CV	=	Coefficient of Variation
Df	=	Desferrioxamine
DNA	=	Deoxynuclic acid
Epo	=	Erythropoietin
F-reticulocytes	=	reticulocytes containing HbF
Hb	=	Hemoglobin
HbA	=	Adult hemoglobin
HbF	=	Fetal hemoglobin
HbS	=	Sickle hemoglobin
Hct	=	Hematocrit
HDMP	=	High dose methyl prednisolone
HLA	=	Human lymphocytic antigen
Hu	=	Hydroxy urea
MCHC	=	Mean corpuscular hemoglobin concentration
MCV	=	Mean corpuscular volume

O_2	=	Oxygen
PaO_2	=	Partial arterial oxygen pressure
RBCs	=	Red blood cells
RDW	=	Red cell distribution width
Retics	=	Reticulocytic count
rHG-CSF	=	Recombinant human granulocyte-colony stimulation factor.
r-Hu Epo	=	Recombinant human erythropoietin
RIA	=	Radioimmunoassay
S.C	=	Sub cutaneous
SHAM	=	Salicyl hydroxamic acid
TEC	=	Transient erythroblastopenia of children
NSB	=	Non specific binding tubes.

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INTRODUCTION

The role of erythropoietin is very essential for the normal erythropoiesis.

Thalassemia is the commonest chronic hemolytic anemia in Egypt, the relative frequency is 52.7/100,000 attendants of the out-patient clinic in the children Hematology/Oncology Clinic, Ain Shams University, it constitutes 47.7% of the hemolytic anemia patients in the same hospital. Previous controlled studies were done and the results proved that there was a statistically significant increase in serum level of erythropoietin in thalassemic patients ***(Politis et al., 1992).***

Sickle cell anemia is the second common type of chronic hemolytic anemia in the hematology/oncology clinic of children's hospital of ain shams university. These patients have lower endogenous serum erythropoietin concentration than those with other comparable anemias. This may be related to the right shifted oxygen dissociation curve which also favours deoxygenation and polymerization of sickle haemoglobin ***(Pippard et al., 1992).***

Aplastic anemia is not uncommon in Egypt. Recently some studies were done to measure the serum erythropoietin level in aplastic anemia in order to explore the clinical significance of this parameter, the serum

erythropoietin level was the highest in aplastic anemia patients among all types of anemia, also these was a difference in its level in severe cases than in moderate and in mild cases. So, it was suggested that erythropoietin level could correlate with the severity of the aplastic anemia ***(Hesegawa et al., 1992)***.

Serum erythropoietin level varies markedly in different types of anemia and the significance of such variation has to be clarified.

AIM OF THE WORK

The aim of the present study is to clarify the significance of the measurement of erythropoietin level in some types of anemia as ß thalassemia, sickle cell anemia and aplastic anemia.

Review of Literature

THALASSEMIA

Definition:

Thalassemias are heterogenous group of heritable hypochromic anemias of varying degrees of severity. They are characterized by a decrease or total suppression of hemoglobin polypeptide chain synthesis ***(Behrman et al., 1991)***.

Classification:

The alpha and Beta chains of hemoglobin are synthesized independently and are under separate genetic control. Thus, there are two groups of thalassemias; one affecting the synthesis of α - chains and the other affecting the synthesis of ß - chains. These are called α - thalassemia and Beta thalassemia respectively ***(De-Gruchy, 1976)***.

Alpha Thalassemia:

Four α-globin genes are present in normal individuals. Two α-chain genes are inherited from each parent. Thus four distinct forms of α-thalassemia have been identified corresponding to deletion of one, two, three or all of the four genes ***(Behrman et al., 1991)***.

Beta Thalassemia:

Since individuals inherit only one ß-chain gene from each parent, affected individuals are either homozygotes or heterozygotes ***(Wilson et al., 1991)***.

If the two genes are completely absent, ß-homozygous state will result. If the two genes are partially reduced, ß-heterozygous state will occur ***(Bollekens and Benze, 1990)***.

Clinically ß thalassemia is divided into three traits. The first is thalassemia major. This is the most common type of chronic hemolytic anemia ***(Thaman, 1984)***. It is the homozygous state of ß-globin chain synthesis ***(Pearson and Benz, 1984)***.

The second trait is thalassemia intermedia. It occurs in a number of patients with homozygous ß thalassemia who do not require regular blood transfusion ***(Bollekens and Benz, 1990)***.

The third trait is thalassemia minor. This is the heterozygous state for the ß thalassemia gene.

In Egypt, ß thalassemia was reported as early as 1944 by Diwani, Sabry (1973) reported that ß thalassemia is the most common chronic

hemolytic anemia in Egypt. He reported an incidence of 0.3% homozygous ß thalassemia and 1.3% heterozygous ß thalassemia .

Hashem (1982) reported an incidence of 0.13% homozygous ß thalassemia and 2-23% heterozygous ß thalassemia.

El-Shinawy (1990) reported that the incidence of hemoglobin (Hb)-Barts positive cases was about 10%. The rate of positive cases was higher in lower Egypt than in upper Egypt. This may be due to the proximity to the mediterranean area. Also he found that the overall carrier frequency of beta-thalassemia is about 4.2%. The author concluded that there are about 4 million alpha-thalassemia carriers and 2 million beta thalassemia carriers.

Khalifa (1992) reported that a relative frequency of 52.7/100,000 of the out patient attendants. It was considered by far the commonest chronic hemolytic anemia, attending the Hematology/Oncology Clinic, Children's Hospital, Ain Shams University.

Pathogenesis of Beta thalassemia major:

Normal hemoglobin:

Hemoglobin is a conjugated protein, consisting of two pairs of polypeptide chains, to each a hem is attached. Human hemoglobin exists