Effect Of moderate and Severe Maternal Iron Deficiency Anemia On Fetal Outcome And Neonatal Hemoglobin(Cord Blood Sample)

Thesis Submitted For Fulfillment

Of Master Degree In Obstetrics and Gynecology

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List of Abbreviations

ATP	: Adenosine Triphoshate
CBC	: Complete blood count
CRP	: C-reactive protein
CS	: Cesarean section
DMT١	: Divalent metal transporter ١
EPO	: Erythropoietin
FeOOH	: Ferric oxyhydroxide
FEP	: Free erythrocyte protoporphyrin
Hb	: Hemoglobin
Hb A٢	: A variant of adult Hemoglobin
Hb F	: Fetal Hemoglobin
Hct	: Hematocrit
HLA	: Human leukocyte antigen
IDA	: iron deficiency anemia
IRE-BP	: Iron responsive element- binding protein
IRF	: Iron regulatory factor
K٢-EDTA	: Potassium-ethylene diamine tetra acetic acid
Kd	: Kilo daltons
MCA-PSV	: middle cerebral artery peak systolic velocity
MAO	: Monoamine oxidase
MCH	: Mean corpuscular hemoglobin
MCV	: Mean corpuscular volume
NESP	: Novel erythropoiesis stimulating protein
NSAIDs	: Non steroidal anti inflammatory drugs
NVD	:Normal vaginal delivery
PB	: Peripheral blood
RBCs	: Red blood cells

RC : Reticulocytic count

RDA : Recommended daily allowance

RDW : Red cell distribution width

Retics % : Reticulocytic count

RNA : Ribonucleic acid

RPI : Reticulocyte production index

SPSS : Statistical Package for Social Science

T_3 : Tri-iodo-thyronine

T_4 : Thyroxin

TFRs : Transferrin Receptors

TIBC : Total iron binding capacity

TS% : Transferrin saturation percentage

UIBC : Unsaturated iron binding capacity

WHO : World Health Organization

X ٢ : Chi-square test

٣q٢١-qter : Long arm of chromosome no. ٣ segment ٢ band ١ terminal portion of long arm.

٣q٢٦-٢qter : Long arm of chromosome no.٣ segment ٢ band ٦ sub-band ٢ terminal portion of long arm.

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Abstract

Anemia is a widespread public health problem associated with an increased risk of morbidity and mortality, especially in pregnant women Globally almost half of pregnant women and close to one third of non pregnant women suffer from anemia.

The aim of this study is to evaluate the effect of moderate and severe maternal iron deficiency anemia on neonatal hemoglobin (through sampling of cord blood) and fetal outcome (neonatal weight , apgar score and neonatal asphyxia).

The present study shows that maternal iron deficiency anemia affect neonatal hemoglobin and neonatal outcome (neonatal weight, Apgar score and neonatal hypoxia) .

The study also shows that the severity of maternal iron deficiency anemia correlate with neonatal hemoglobin and neonatal outcome.

Key words
Anemia - neonatal hemoglobin fetal outcome

Aim of Work

The aim of this study is to evaluate the effect of moderate and severe maternal iron deficiency anemia on neonatal hemoglobin (through sampling of cord blood) and fetal outcome (neonatal weight and apgar score).

Chapter One
Anemia

Definition:

Anemia is defined as a reduction of the red blood cell volume or hemoglobin concentration below the range of values occurring in healthy persons to meet the tissue demands for oxygen delivery ***(Glader, ٢٠٠٧).***

ERYTHROPOIESIS:

Red blood cells (RBCs), also known as erythrocytes (Fig. ١) carry oxygen throughout the body to nourish tissues and sustain life. Red blood cells are the most abundant cells in our bodies. Newborns have about ٤,٧ million red blood cells per cubic millimeter of blood and women have about ٤,٧ million per cubic millimeter of blood ***(Karine, ٢٠٠٧).***

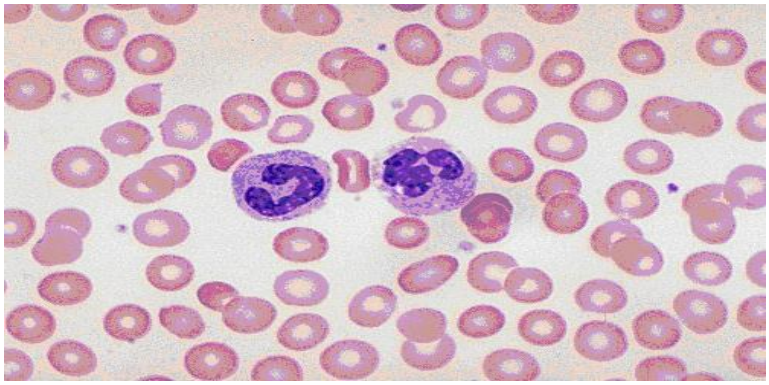
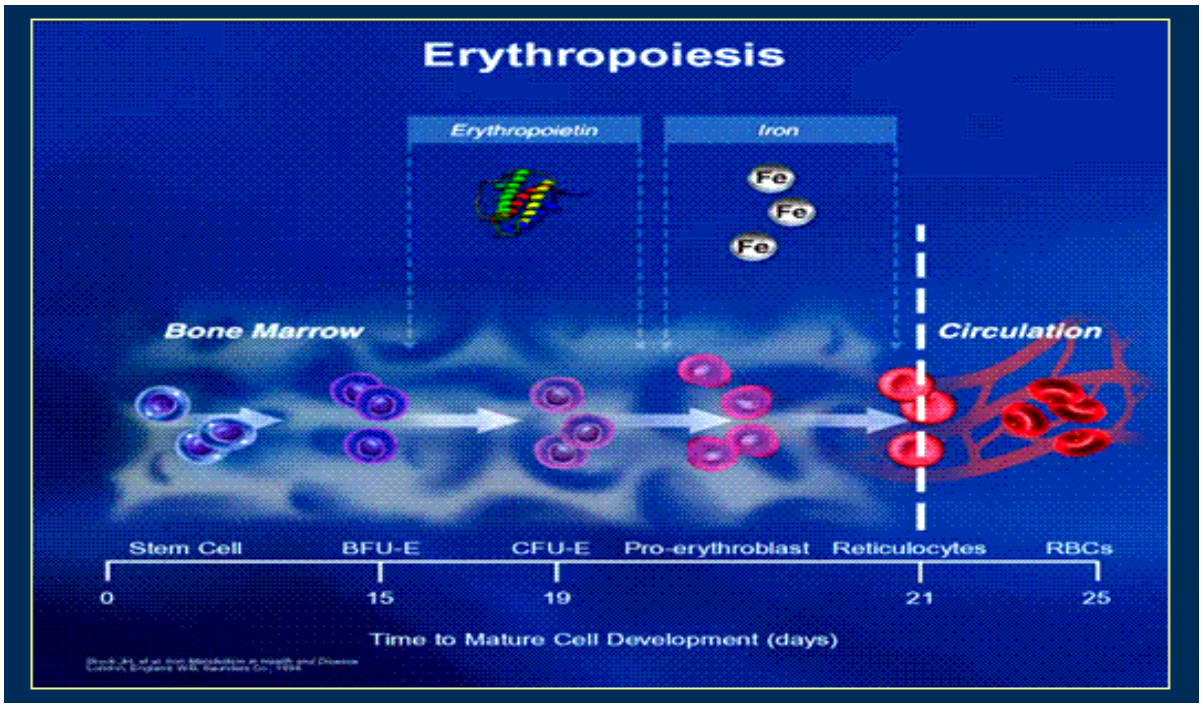


Figure (١): Photomicrograph of a peripheral blood smear showing the normal red blood cells ***(Karine, ٢٠٠٧)***

The actual process of making red blood cells is called erythropoiesis. In Greek, erythro means "red," and poiesis means "the making of things." So Erythropoiesis is the process of manufacturing, recycling, and regulating the number of red blood cells ***(Van Meter, ٢٠٠٨).***

Most of the work of erythropoiesis occurs in the bone marrow it takes about ٢٥ days (Fig. ٢). In children younger than ٥ years old, the marrow of all the bones of the body is enlisted for producing red blood cells. As a person ages, red blood cells are eventually produced only in the marrow of the spine, ribs, and pelvis ***(Kalantar et al., ٢٠٠٠).***



BFU-E (Burst forming unit erythroid) CFU-C(colony forming unit erythroid)

Figure (٢): Erythropoiesis ***(Kalantar et al., ٢٠٠٤)***

The body carefully regulates its production of red blood cells so that enough are manufactured to carry oxygen but not so many that the blood becomes thick or sticky (viscous) ***(Glader, ٢٠٠٦).***

If the body needs more oxygen, the kidney triggers the release of the hormone erythropoietin (EPO), a hormone that acts in the bone marrow to increase the production of red blood cells ***(Glader, ٢٠٠٦).***

EPO is a ٣٠-٣٩ kd glycoprotein that binds to specific receptors on the surface of erythroid precursors and stimulates their differentiation and clonal maturation into mature erythrocytes. The regulation of EPO gene

expression involves an oxygen sensing mechanism, and both hypoxia and anemia stimulate erythropoiesis by stimulating mRNA transcription and EPO production ***(Glader, ٢٠٠٧).***

In pregnancy, erythropoietin levels increase two to three fold, starting at ١٦ weeks and may be responsible for the moderate erythroid hyperplasia found in the bone marrow, and mild elevations in the reticulocyte count. The increased blood volume is protective given the possibility of hemorrhage during pregnancy or at delivery. The larger blood volume also helps fill the expanded vascular system created by vasodilatation and the large low-resistance vascular pool within the uteroplacental unit preventing hypotension ***(Steven Gabbe et al, ٢٠٠٧).***

Erythropoiesis in utero is controlled by erythroid growth factors produced solely by the fetus. Erythropoietin (EPO) does not cross the placenta in humans; therefore, stimulation of maternal EPO production does not result in stimulation of fetal red cell production. Moreover, suppression of maternal erythropoiesis by hypertransfusion does not suppress fetal erythropoiesis ***(Glader, ٢٠٠٧).***

The average life span of the neonatal red blood cell is ٦٠ - ٩٠ days while that of adults is ٩٠-١٢٠ days, this can be explained by some of the characteristics specific to newborn cells: a rapid decline in intracellular enzyme activity and ATP, loss of membrane surface area by internalization of membrane lipids, decreased levels of intracellular carnitine, increased susceptibility of membrane lipids and proteins to membrane deformability ***(Glader, ٢٠٠٧).***

The old red blood cells are removed from the blood by the liver and spleen. Once old red blood cells are broken down for removal, iron is returned to the bone marrow to make new cells ***(Van Meter, ٢٠٠٨).***

HEMOGLOBIN:

Each red blood cell contains ٢٠٠ - ٣٠٠ hemoglobin molecules. Hemoglobin is a complex molecule, and it is the most important component of red blood cells ***(Stamatoya et al., ٢٠٠٠).***

Hemoglobin is a complex protein consisting of iron-containing heme groups and the protein moiety, globin (Fig. ٣). A dynamic interaction between heme and globin gives hemoglobin its unique properties in the reversible transport of oxygen ***(Glader, ٢٠٠٧).***

The hemoglobin molecule is a tetramer made up of two pairs of polypeptide chains, with each chain having a heme group attached. The polypeptide chains of various hemoglobins are of chemical different types ***(Glader, ٢٠٠٧).***

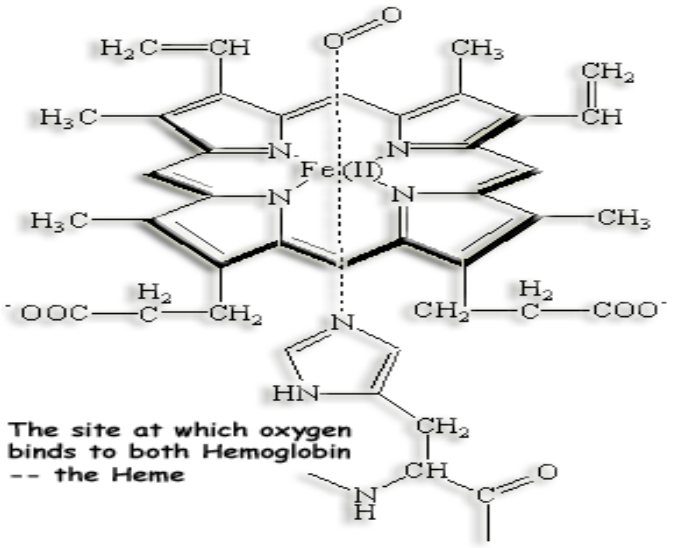


Figure (٣): Hemoglobin molecule ***(Stamatoya et al., ٢٠٠٠)***

The major hemoglobin of a normal adult (Hb A) is made up of one pair of alpha (α) and one pair of beta (β) polypeptide chains, represented as $\alpha_2\beta_2$. The major hemoglobin in the fetus (Hb F), which is made up of two alpha and two gamma globin chains, is represented by $\alpha_2\gamma_2$ ***(Glader, ٢٠٠٧).***

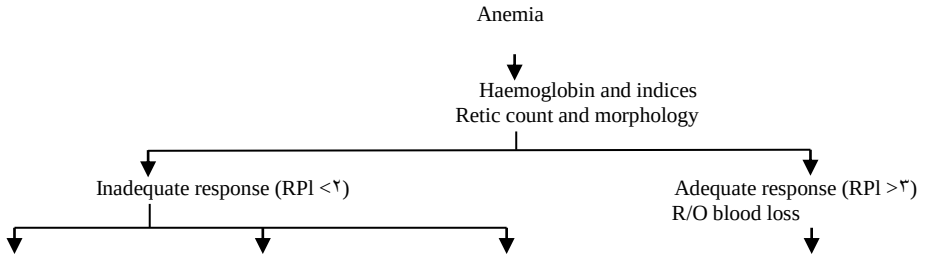
In the lungs, the heme component binds to oxygen in exchange for carbon dioxide. The oxygenated red blood cells are then transported to the body's tissues, where the hemoglobin releases the oxygen in exchange for carbon dioxide, and the cycle repeats ***(Karine, ٢٠٠٧).***

Neonatal red blood cells typically circulate for about ٦٠-٩٠ days before they are broken down in the spleen. Most of the iron used in hemoglobin can be recycled from there and reused ***(Karine, ٢٠٠٧).***

Types of anemia:

Anemia is a commonly encountered clinical condition caused by hereditary abnormalities of the RBCs as thalassemia , sickle cell anemia and spherocytosis or acquired condition as Iron-deficiency anemia, blood loss ,malignancies, inflammatory gastrointestinal disorder and drugs **(Ernest and Rosenbaum, ٢٠٠٧).**

Anemia is either **Microcytic hypochromic anemia** (Iron deficiency anemia, Thalassemia and Anemia of chronic disease) or **Normocytic nornochromic anemia** (Hemolytic anemia, acute post hemorrhagic anemia Aplastic anemia, Anemia of organ failure and Anemia of chronic disease) or **Macrocytic anemia** (Megaloblastic anemia) ***(William Ganon ١٩٩٥)*** .



Hypochromic Microcytic

Iron deficiency
- Chronic blood Loss
- Poor diet
- Cow's milk protein intolerance
- Menstruation

Thalassemia
- β major, minor
- α minor

Chronic inflammatory disease

Cooper deficiency

Sideroblastic anemia

Aluminum, lead toxicity

Hereditary pyropoikilocytose

Hemoglobin CC

Hemoglobin EE

Normochromic, Normocytic

Chronic inflammatory disease
- Infection.
- Collagen-vascular disease
- Inflammatory bowel disease

Recent blood loss

Malignancy/ marrow infiltration

Chronic renal failure

Transient erythroblastopenia of childhood

Marrow aplasia/hypoplasia

HIV infection

Hemophagoctic syndrome

Macrocytic

Vitamin B١٢ deficiency
- Pernicious anemia.
- Ileal resection
- Strict vegetation
- Abnormal intestinal transport
- Congenital intrinsic factor

Folate deficiency
- Malnutrition
- Malabsorption
- Antimetabolite
- Chronic hemolysis
- Phenytoin
- Trimethoprim/sulfa

Hypothyroidism
Orticaciduria
Chronic liver disease
Lesch-Nyhan syndrome
Down syndrome

Marrow failure
- Myelodysplasia
- Fanconi anemia
- Congenital dyserythropoietic anemia
- Aplastic anemia
- Pearson syndrome

Hemolytic Disorders

Hemoglobinopathy
- Hemoglobin SS, S-C
- S-β thalassemia

Enzymopathy
- G٦PD deficiency
- Pyruvate kinas deficiency

Membanopathy
- Hereditary spherocytosis
- Elliptocytos
- Ovalocytosis

Extrinsic factors
- DIC, HUS, TTP
- Abetalipoproteinemia
- Burns
- Wilson disease
- Vitamin E deficiency

Immuno hemolytic anemia
- Autoimmune
- Isoimmune
- Drug-induced

Figure (٤): Common causes of anemia ***(Glader, ٢٠٠٧)*** .