ANEMIA WITH PREGNANCY

Essay

Submitted for Partial Fulfillment of the Master Degree in Obstetrics & Gynecology

By

Mahmoud Hamed Hussein Ibrahim

M.B., B. Ch., Faculty of medicine, Ain Shams University (1999) Registrar of Obstetrics and Gynecology. Abou-korkas Hospital, Menya Governorate

Supervised by

Professor Ahmed Rashed Mohamed Rashed

Professor of Obstetrics and Gynecology Faculty of Medicine, Ain Shams University

Assistant Professor Abdel-Latif Galal El-Kholy

Assistant Professor of Obstetrics & Gynecology Faculty of Medicine, Ain Shams University

Dr. Wessam Magdy Abuelghar

Lecturer of Obstetrics & Gynecology Faculty of Medicine, Ain Shams University

> Faculty of Medicine Ain Shams University 2011

إِنَّ اللَّهَ عِنْدَهُ عَلَيْكُمُ السَّاعَةِ وَيُنَزِّلُ الْغَيْثَ وَيَعْلَمُ مَا فِي الأَرْحَام وَمَا تَدري نفس ماذا تكسب عداً وَما تَدْرِي نَفْسُ بِأَيِّ أَرْضٍ تَمُوتُ إِنَّ الله عَلِيمٌ خَبِيرٌ رازة العظمي

(سورة لقمان - الآية : 34)

ACKNOWLEDGEMENT

I am greatly thankful to my supervisors, Professor Ahmed Rashed Mohamed Rashed, Assistant Professor Abdel-Latif Galal El-Kholy and Dr. Wessam Magdy Abuel ghar, whose encouragement, guidance and support from the initial to the final level enabled me to develop an understanding of the study.

Moreover, I offer my regards and blessings to all of those who supported me in any respect during the completion of the study (particularly, my parents, my wife and my family).

Mahmoud Hamed

CONTENT

Item	Page
Tables	a
Boxes	b
Figures	c
List of Abbreviations	d
Protocol	1
Chapter One: Overview	3
Chapter Two: Etiology	72
Chapter Three: Treatment	86
Summary and Conclusion	121
Recommendations	130
References	132
Arabic summary	

Tables

Tables		pages	
Table 1	Cutoff Values for Anemia in Pregnant Women.		
Table 2	The prevalence of anemia in females in Egypt		
Table 3	Classification of anemias	10	
Table 4	Laboratory norms for the nonpregnant and pregnant patient	12	
Table 5	Nomenclature of normal and abnormal hemoglobins		
Table 6	Globin Chains		
Table 7	Iron losses and iron requirements in normal pregnancy and delivery		
Table 8	Clinical signs and symptoms of iron deficiency	35	
Table 9	The most important points in differential diagnosis of anemia	43	
Table 10	A comparison between B12 deficiency and folate deficiency		
Table 11	Pregnancy outcomes in patients with S/S anemia	57	
Table 12	Pregnancy outcomes reported since 1956 for women with sickle cell anemia and hemoglobin SC disease		
Table 13	Effects of alpha gene deletion		
Table 14	Iron balance in pregnancy	78	
Table 15	Oral iron versus placebo	89	
Table 16	Daily oral iron versus twice weekly	91	
Table 17	Daily oral iron versus once a week	92 95	
Table 18	IM sorbitol citric acid dose versus oral ferrous sulphate		
Table 19	IM iron sorbitol at four-weekly intervals versus 100 mg of elemental oral iron for at least 100 days	97	
Table 20	IM iron dextran versus 600 mg of oral ferrous sulphate plus vitamin C and folate.	98	
Table 21	IV iron sucrose given in six slow IV injections on days 1, 4, 8, 12, 15 and 21.	100	
Table 22	IV iron sucrose versus 300 mg of elemental iron	102	
Table 23	A comparison of oral ferrous fumarate 200 mg three times a day versus IV iron dextrin	104	
Table 24	IV iron sucrose (500 mg versus 200 mg) and IM iron sorbitol	106	
Table 25	IV administered iron sucrose with and without adjuvant recombinant human erythropoietin	108	

Boxes

Boxes		Pages
Box 1	Body iron distribution	27
Box 2	Iron homeostasis	28
Box 3	The development of iron deficiency is a sequential Four-phase process	28
Box 4	Effects of iron overload	68
Box 5 Risks to women of thalassemia in pregnancy		70
Box 6	Box 6 Causes of iron deficiency anemia.	
Box7	Causes of Macrocytosis	80

Figures

Figures		Pages
Figure 1	Changes in blood volume (in milliliters) during antepartum, intrapartum, and postpartum portions of human pregnancy	
Figure 2	Erythropoiesis revealing metabolic determinants and cellular appearance at each stage	
Figure 3	Biosynthesis of hemoglobin	
Figure 4 Iron requirements during pregnancy and in the lactation period.		30
Figure 5 Marrow film, iron deficiency anemia.		37
Figure 6a Marrow film, Prussian blue reaction.		38
Figure 6b Marrow film, Prussian blue reaction.		38
Figure 7 Diagnosis of Iron Deficiency Anemia		41

List of Abbreviations

• ACE Angiotensin Converting Enzyme

• ACOG American College of Obstetrics and Gynecology

• CBC Complete Blood Count

CHr Reticulocyte Hemoglobin Content

• CRP C-reactive Protein

DMT Divalent Metal TransporterDNA Deoxyribonucleic Acid

• FAO Food and Agriculture Organization

• FBC Full Blood Count

• G6PD Glucose 6 Phosphate Dehydrogenase

GI Gastrointestinal
 Hb Hemoglobin
 HbA Adult Hemoglobin

Hb Bart's Hemoglobin Bart's
HbF Fetal Hemoglobin
HbH Hemoglobin H
Hct Hematocrit

HCYS

• HELLP Hemolysis Elevated Liver Enzymes Low Platelet Count

HFE Hemochromatosis gene

HIV Human Immunodeficiency Virus

Homocysteine

HPL Human Placental Lactogen

• HPLC High performance liquid Chromatography

• ID Iron Deficiency

IDA Iron Deficiency Anemia

IF Intrinsic Factor IM Intramuscular

• IUGR Intra Uterine Growth Restriction

IV Intravenous

LBW Low Birth Weight
 LFTS Liver Function Tests
 LMP Last Menstrual Period

• MCH Mean Corpuscular Hemoglobin

• MCHC Mean Corpuscular Hemoglobin Concentration

MCV Mean Corpuscular VolumeMRI Magnetic Resonance Imaging

N₂O Nitrous Oxide

NPW Non Pregnant Women

NSAID Non Steroidal Anti Inflammatory Drug

• NTDs Neural Tube Defects

PCR Polymerase Chain Reaction

PCV Packed Cell Volume

PIH Pregnancy Induced HypertensionPROM Premature Rupture Of Membrane

PV Plasma Volume
 PW Pregnant Women
 RBC Red Blood Cell

RCT Randomized Control Trials

• R/F Ratio Serum Transferrin to Serum Ferritin Ratio

RDW Red Cell distribution Width

SCD Sickle Cell Disease
 SF Serum Ferritin
 STRs Serum TRs

TBV Total Blood VolumeTCII Transcobalamin II

• TIBC Total Iron-Binding Capacity

• TRs Transferrin Receptors

• TSH Thyroid Stimulating Hormone

• UK United Kingdom

USPSTF United States Preventive Services Task Force

VOC Vaso-Occlusive CrisisWBC White Blood Cell

• WHO World Health Organization

• ZPP Zinc Protoporphyrin

Introduction & Aim of the work

Introduction

Anemia is a common medical disorder that contributes significantly to maternal morbidity and mortality, intrauterine growth retardation, preterm delivery and prenatal morbidity and mortality (**Diejomaeoh et al., 1999**).

Maternal mortality continues to be a major health problem in the developing world. In the year 1987, international agencies from 45 countries established the safe motherhood initiative with the goal of reducing maternal deaths. A key component of safe motherhood is the eradication of anemia during pregnancy, and an effective approach to curb the incidence of anemia in pregnancy would be to counter the underlying factors. In that vein, tackling iron deficiency in pregnancy comes first (Kumar et al., 2005).

Iron deficiency anemia forms the commonest nutritional pathology in pregnant women. The prevalence of iron deficiency anemia in pregnancy in the developing world is 56% (range 35-75%), versus 18% in the developed world (**Perewusnyk et al., 2002**).

Anemia during pregnancy is a well known and considerable risk factor for both mother and fetus. Fetal consequences are an increased risk of growth retardation, prematurity, intrauterine death, amnion rupture and infection. Maternal consequences of anemia are also well known and include cardiovascular symptoms, reduced physical and mental performance, reduced immune function, tiredness, reduced peripartal blood reserves and finally increased risk for blood transfusion in the postpartum period. For clinical management, proper diagnosis and therapy are mandatory to reduce maternal and fetal risks and to enable optimal obstetrical outcome of both (Breymann, 2002).

Aim of the work

To review the etiological factors, prevalence and impact of anemia on pregnancy and fetus.

Chapter One

Overview of Anemia with Pregnancy

ANEMIA WITH PREGNANCY

Anemia is a reduction in the normal number of circulating red blood cells and in the quantity of hemoglobin in the blood. More than half a million maternal deaths occur each year, approximately 90% of which are in developing countries, making evident a large discrepancy between developed and developing countries (WHO, 2000).

The WHO defines anemia in pregnancy as an Hb levels of less that 11 g/dl, although a level of less than 10.5 g/dl is more widely adopted in the second trimester, when physiological hemodilution is at its greatest (Strong, 2005).

It also defined by the Centers for Disease Control and Prevention as hemoglobin (Hb) or hematocrit (Hct) value less than the fifth percentile of the distribution of Hb or Hct in a healthy reference population based on the stage of pregnancy. Classification derived from an iron-supplemented population lists the following levels as anemic:

- 1) In the first trimester Hb (g/dl) and Hct (percentage) levels below 11 g/dl and 33%, respectively,
 - 2) In the second trimester 10.5 g/dl and 32%, respectively,
- 3) In the third trimester 11 g/dl and 33%, respectively (ACOG, 2008).

Grades of anemias

Although anemia is frequently graded as "mild", "moderate", or "severe", the hemoglobin values at which the division into these three categories is made vary and are arbitrary. Standardized cut-off values are difficult to define because populations, geographic settings and needs are different according to specific areas (WHO, 1999).

Some authors suggest that hemoglobin values at sea level should be categorized as follows (WHO, 1999):

- (1) Mild anemia (Hb 10 to 10.9 g/dl);
- (2) Moderate anemia (Hb 7 to 9.9 g/dl);
- (3) Severe anemia (Hb less than 7 g/dl).

However, other criteria have been widely used to define anemia cut-off values:

- (1) Mild (Hb 9 to 10.9 g/dl),
- (2) Moderate (Hb 7 to 8.9g/dl) and
- (3) Severe (Hb below 7 g/dl) (Adam, 2005);

Or

- (1) Mild anemia (Hb 7 to 11 g/dl),
- (2) Moderate anemia (5 to 7 g/dl) and
- (3) Severe anemia (below 5 g/dl) (Brabin et al., 2001).

Table 1: Cutoff Values for Anemia in Pregnant Women (CDC, 2001).

	Hemoglobin (,g/dl)	Hematocrit (,%)
Trimester		
First	11.0	33.0
Second	10.5	32.0
Third	11.0	33.0
Adjustment for smoking		
0.5-,1.0 packs/day	10.3	11.0
1.0-,2.0 packs/day	10.5	11.5
.2.0 packs/day	10.7	11.5
Adjustment for altitude		
(feet)		
3,000–3,999	+0.2	+0.5
4,000–4,999	+0.3	+1.0
5,000-5,999	+0.5	+1.5
6,000–6,999	+0.7	+2.0
7,000–7,999	+1.0	+3.0
8,000-8,999	+1.3	+4.0