A STUDY OF MATERNAL AND FETAL BLOOD HEMOGLOBIN

THESIS

SUBMITTED FOR PARTIAL FULFILLMENT

OF THE REQUIREMENT

OF THE MASTER DEGREE

OF OBSTETRICS AND GYNECOLOGY

By

Ahmed Abd El Bary Ibrahim

SUPERVISED By :

Prof. MAHER MAHRAN

Dr. ABBAS GHAZI

AIN SHAMS UNIVERSITY

FACULTY OF MEDICINE

CAIRO

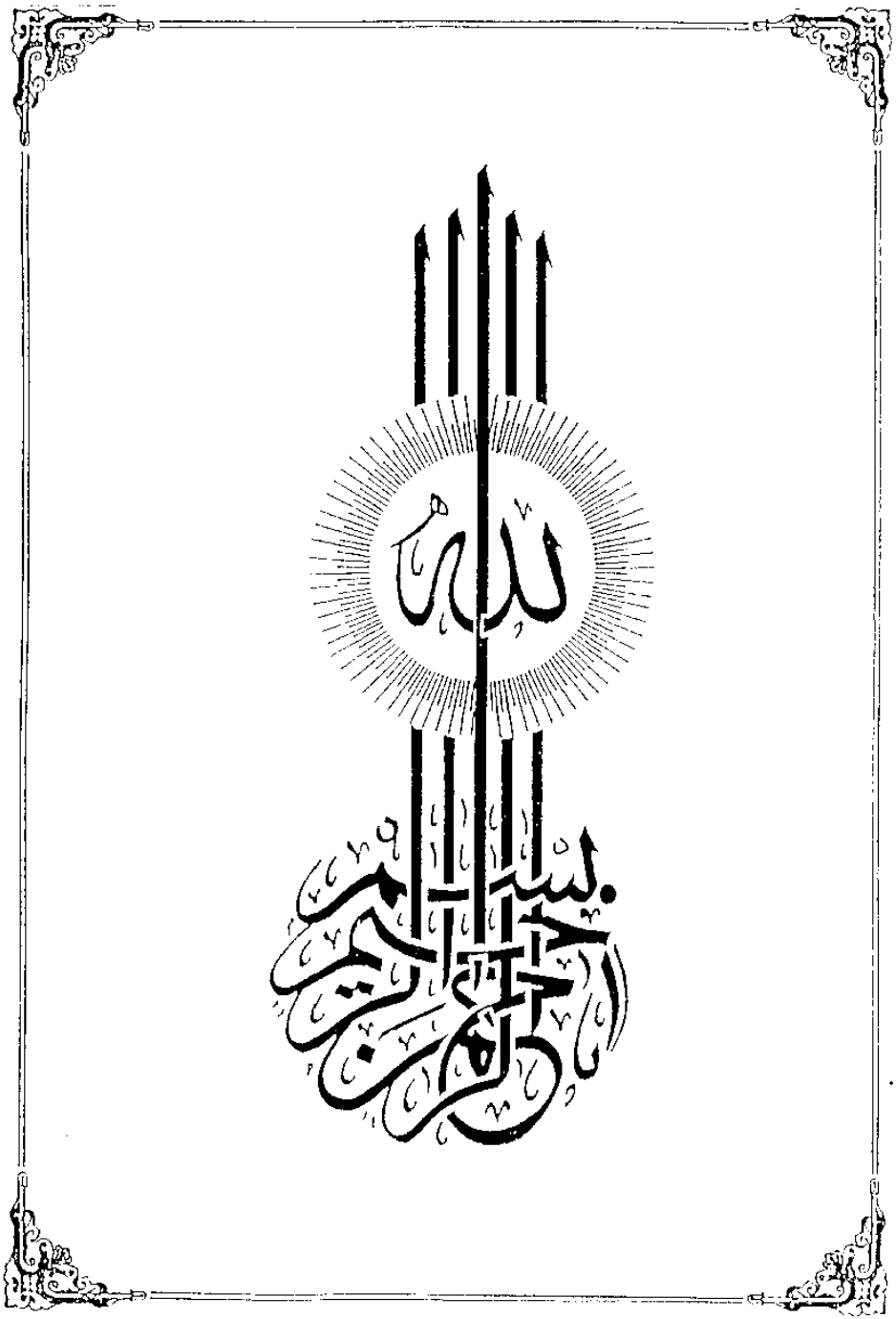
1984

ACKNOWLEDGEMENT

I would like to thank very much deeply Professor Maher Mahran because he,kindly and generously,provided me with a great and invaluable help in this work.

I find no thankful words enough to say to Doctor Abbas Ghazi;he was very patient with me and he helped me to be in the right way in every step in this work.

I would like also to thank the technicians in the outpatient laboratory of the Ain Shams University hospital for medical diseases,and also all the workers in the department of obstetrics and gynecology for their kind helps.



INDEX

INTRODUCTION

Iron deficiency is probably the most common form of nutritional deficiency,in both developing and developed countries (WHO 1975 ; McFee 1979). It is reported to be the most common cause of anemia,both in general medical practice (Fry 1961) and in the practice of clinical hematology (Prager 1972) and is even alleged to be the most common organic disorder seen in clinical medicine (Fairbanks et al,1971).

Despite these assertions,there are relatively few adequate studies of the prevalence of iron deficiency in various populations.

The most commonly employed screening procedure has been a simple blood hemoglobin determination. As measured by this test,anemia has been defined by the World Health Organization as a value below 14 g/dl in men;12 g/dl in nonpregnant females and 11 g/dl in pregnant women (WHO 1968). Such a screening method cannot by definition detect latent iron deficiency (Foreman 1981 ; Taylor 1981). Furthermore,inaccuracies are introduced by anemias due to causes other than iron deficiency (Cook et al,1971).

Screening by determination of plasma iron and iron binding capacity obviates some of these inaccuracies,but the

procedure is more cumbersome and consequently has been performed less frequently (Wintrobe 1977).

Still less suited for the study of large groups is the determination of the reticuloendothelial iron stores by bone marrow aspiration (Scott et al 1967).

Probably the most important source of error in population surveys is the selection of samples. Most reported series are heavily weighted with representatives of low economic groups,a bias which may increase the apparent prevalence (Wintrobe et al 1977).

REVIEW

OF THE LITERATURE

Hematological Changes During Pregnancy

Pregnancy produces major hematological changes aiming at satisfying the increased circulation needed to sustain the fetoplacental unit as well as certain maternal organs, including the growing breast mass whose function increases during pregnancy. At the same time,they provide a safety valve in the face of blood lost at the time of delivary, thereby rendering the pregnant woman much more able to withstand significant hemorrhage than a nonpregnant individual (Levin 1982;Moghissi 1981).

Quantitative Changes:

The first of these pregnancy induced changes is the marked increase in blood volume;it is augmented by an average of 40 to 50 (ranging from 20 to 100) per cent by the 36th week of gestation over the nonpregnant state (Willoughby 1977;Messer 1974). Most of this increase occurs during the second trimester;during the last several weeks of pregnancy this volume either increases slightly or remains stable;it does not decrease. Most of the increase in blood volume reflects plasma volume expansion (Pitkin 1977;Willoughby 1977).

Secondly,the bone marrow becomes hyperplastic with accelerated erythropoiesis,which results in increasing the number of circulating red blood cells. Thus,the red cell volume is also augmented but by only 20 to 33 per cent,and this is a gradual rise up to term (Moghissi 1981).

The stimulus for the increase in plasma volume may be placental lactogen which causes increased aldosterone secretion (Kitay 1969). On the other hand,the stimulus for bone marrow erythroid hyperplasia in pregnancy is not fully understood, but control is through erythropoietin (Zivny et al 1982). There are several possible stimuli to erythropoietin production in pregnancy,including the placenta acting as an arteriovenous fistula,increased renin and decreased blood flow to the kidneys in later pregnancy (Lange and Dynesius 1973;Willoughby 1979).

The red cell survival does not change during pregnancy (Pritchard and Adams 1960),and the red cell mass declines immediately at delivary as a result of blood loss,and this is followed by a temporary erythroid hypoplasia until nonpregnant blood volume is reached around three weeks after delivary (Taylor & Lind 1981).

Since there is an expansion of plasma volume greater than that of the red cell volume,the red cell count,hematocrit and hemoglobin concentration decline during pregnancy;the lowest hemoglobin is observed at round 34 weeks of gestation, after which there is a rise of about 0.5 g/dl at term (Pitkin 1977;Willoughby 1979).

Owing to the wide range of variation of the increase of blood volume during pregnancy,it is not easy to arrive at a precise hemoglobin level at that time that can be called "anemia" (Messer 1974;Lind et al 1975;Taylor 1980;Foreman 1981)

The lowest normal hemoglobin level in adult nonpregnant women is 12 g/dl (WHO 1972,1979) and it may be deduced from the figures of plasma and red cell volume expansion in iron sufficient subjects that the lowest hemoglobin in normal pregnancy should be 10.6 g/dl (McFee 1973;Messer 1974). This theoretical figure is in close agreement to the lowest hemoglobin (10.4 g/dl) observed in the iron sufficient group of DeLeeuw et al (1966) and the agreed figure of 11 g/dl (WHO 1972,1979).

Clinical experience,however,shows that many apparently healthy women are able to proceed through pregnancy with hemoglobin lower than 11 g/dl without complications (McFee 1973,1979).

Pritchard(1965) showed in an evaluation of a large number of patients who were medically normal and whose bone marrows were positive for iron,that anemia may result from plasma volume expansion. 4 per cent of those in midpregnancy and 1 per cent in late pregnancy had hemoglobin levels less than 10 g/dl. Similarly,Lawrence(1962) observed that some supplemented patients who were otherwise normal ran lower hemoglobin levels than others. Red cell volumes were the same in both groups but plasma volumes were markedly increased in patients with the low hemoglobin levels. He has called this "iron sufficient hydremia" and he believed that the lowest hemoglobin concentration due to this hydremia may be about 10 g/dl.

Liley(1970) studied 114 pregnant patients with hemoglobins ranging from 8.6 to 14.2 g/dl,all of whom had normal bone marrow smears,normal iron studies,normal folate levels and no reticulocytosis. He compared plasma and red cell volumes with the hemoglobin levels and observed that 80 per cent of women in his clinic with hemoglobins 10-11 g/dl and 50 per cent with hemoglobins 9-10 g/dl were not anemic;he therefore put his conclusion that "in pregnant women with a reasonable diet and modest hematinic supplements,a low hemoglobin level more often indicates a high plasma volume than anemia".

Therefore,there is a difference of opinion as to how many low hematocrits and hemoglobins are due to hemodilution. Pritchard's figures are far lower than those of Liley.

In summary,differences between plasma and red cell volumes can result in some physiologic diminution of the hematological levels during pregnancy. While the lower limits of normal in the nonpregnant state have been placed at 12 g/dl hemoglobin and 36 per cent hematocrit,these levels drop during pregnancy to 11 g/dl hemoglobin and 33 per cent hematocrit (A.M.A.Council 1968;WHO 1975). In some cases of extremely large plasma volume expansion these levels may drop even lower. An absolute definition of anemia during pregnancy,utilising the hematocrit or hemoglobin is thus impossible. For practical purposes many authers define anemia in pregnancy as 10 g/dl hemoglobin (30 per cent hematocrit) or less (Hellman 1971),others use 11g/

hemoglobin (33 per cent hematocrit),(Hallberg 1969;McFee 1973). Thus,a hemoglobin of less than 11 g/dl or a hematocrit less than 33 per cent should be considered initially as due to a specific pathological cause for which adequate evaluation is mandatory (WHO 1979;Baker&DeMaeyer 1979).

Qualitative Changes:

The respiratory nervous centers are set from early pregnancy to maintain a low arterial PCO_2,which leads to decreased plasma bicarbonate (Robertson&Cheyne 1972);the resultant maternal alkalosis enables the fetus to off-load carbon dioxide,but it would also increase maternal hemoglobin oxygen affinity;this is counteracted by raised 2,3-diphosphoglycerate (DPG) in the maternal red cells,so enhancing oxygen release to the fetus and maternal tissues (Roth and Brahe 1971). Oxygen transfer is further helped by the fetal hemoglobin having a high affinity for oxygen and a low affinity for DPG (Willoughby 1977).

The decrease in serum colloid osmotic pressure is accompanied by a dilution of the red cell contents (Willoughby 1977),and hence increased red cell osmotic fragility. Robertson and Cheyne (1972) reported a mean of 50 per cent hemolysis in 4.58 g/l saline compared to 4.38 g/l in the nonpregnant,with a slight decrease in fragility near term, possibly due to a higher proportion of young red cells.

Another qualitative alteration in the red cells during pregnancy is a tendency to sphering which is accompanied by an increase of the mean cell volume in the latter half of pregnancy,coinciding with the rising of osmotic fragility. The mean cell hemoglobin does not alter significantly in normal pregnancy (Bolton & Marion 1982).

The activity of various red cell enzymes appear to be unchanged except for a tendency to a greater activity with a younger red cell population (Willoughby 1977).

Iron Metabolism

In The Nonpregnant State

Amount And Distribution:

The total body iron content of the normal adult varies from 3 to 5 g,depending on the sex and weight of the individual. It is greater in males than in females and it increases roughly in proportion to body weight. The iron is distributed in several physiologically and chemically distinct forms,as seen in table (1),(Gruchy 1970 ;McFee 1979;Williams 1981).

Hemoglobin Iron:

This constitutes approximately 60 to 70 per cent of the total body iron,and as a result any major blood loss will significantly lower the total iron content. The iron derived from the breakdown of hemoglobin released by the destruction of effete red cells is conserved by the body and is recycled for hemoglobin synthesis (Goodman & Gilman 1970;McFee 1979).

Storage Iron:

The stored iron forms a little less than one third of the total body iron and so it is sufficient to replace one third to one half of the circulating hemoglobin. Storage iron is less in the female and is slowly accumulated during childhood and adolescence due to the slight excess of absorption over excretion. It occurs in two forms-ferritin and hemosiderin,which are normally present in equal amounts. In the normal subject about one third of the storage iron is in the bone marrow,about one third in the liver and the last third in the spleen,muscle and other tissues (Gruchy 1970;McFee 1979).

Table (1)

Distribution Of Body Iron In Adults

(Gruchy 1970)

Hemoglobin	1.5-3 g
Storage(available)tissue iron (ferritin and hemosiderin)	0.6-1.5 g
Essential(nonavailable)tissue iron (myoglobin and cellular respiratory enzymes)	0.3 g
Plasma(transport)iron	3-4 mg
Total(varies with sex and size)	3-5 g