

Full Length Research Paper

Iron deficiency anaemia in pregnancy and the new born child

Sana E. Abdalla^{1*}, Enaam A. Abdelgader¹, Tayseer A. Diab², Ilham M. Omer³ and Anwar A. Kordofani⁴

Abstract

¹AL-Neelain University, Faculty of Medicine, Khartoum, Sudan. Pathology department

²AL-Neelain University, Faculty of Medicine, Khartoum Sudan. Obstetrics and gynecology department.

³Khartoum University, Faculty of Medicine, Khartoum Sudan. Pediatrics department.

⁴Khartoum University, Faculty of Medicine, Khartoum Sudan .Pathology department.

*Corresponding Author's E-mail: sanaseed@hotmail.com; Tel 00249912359969; Fax 00249 183 797002

Iron is an important element for all living cells and plays an important role in many metabolic pathways. Iron deficiency is by far the most common causes of anaemia in general and microcytic anaemia in particular. Iron deficiency anaemia develops as the end result of a series of steps that begin by depletion of iron stores. Pregnant women and infants are recognized as the groups most vulnerable to iron deficiency anaemia. The aims of this study were to measure Hb, RBCs indices, serum iron, serum ferritin and total iron binding capacity in mothers and their newborns at the time of delivery. Eighty blood samples were collected from pregnant ladies during the first stage of labour and after delivery cord blood samples were taken from the babies. Complete blood count was measure using automatic blood counter (Sysmex Kx-21), Serum iron and total iron binding capacity (TIBC) were measured by an automatic instrument (BTS-370 Plus), and Serum Ferritin was estimated by ELIZA technique. Results showed that eight mothers had low Hb level and their haematological indices as follows: 4 (50%) had normal MCV and 4 (50%) had low MCV, 4 (50%) had normal MCH, while 4 (50%) had low MCH, 6 (75%) had normal MCHC, while 2 (25%) had low MCHC. Two (25%) had normal S. ferritin, while 6 (75%) had low serum ferritin, 5 (62.5%) had normal serum iron, while 3(37.5%) had low serum iron. 4(50%) had normal TIBC, while 4(50%) had low TIBC. New born Hb showed 18 (22.5%) babies had low Hb level (< 14 g/dl). All of the anaemic babies had normal MCV, MCH and MCHC. One (5.6%) baby showed low serum ferritin while 16 (88.9%) showed normal level and one baby (5.6%) showed high level of serum ferritin. 13 (72%) babies showed normal serum iron while 5 (27.8%) showed high serum iron. All anaemic babies showed normal TIBC. Babies born to anaemic mothers showed normal Hb, blood indices and normal serum iron while 3 (37.5%) showed low serum ferritin and one (12.5%) showed high TIBC. This study concluded that Anaemia in the mother does not affect the newborn and anaemia in the babies born to non - anaemic mothers is not uncommon. Low serum ferritin in mother significantly affects the baby's iron stores.

Keywords: Serum iron, iron stores, pregnancy, newborn.

INTRODUCTION

Iron deficiency anaemia is the most common nutritional deficiency in the world; estimates suggest that 2billion

persons worldwide are iron deficient (Allen LH, 200). Because of the increased iron requirements of pregnancy

and growth, pregnant women and infants are recognized as the groups most vulnerable to iron deficiency anaemia. It occurs during pregnancy in 23% of pregnant women in developed countries and 52% of pregnant women in developing countries (WHO Scientific Group, 1968).

Symptomatic iron deficiency during pregnancy has delirious effects on maternal and perinatal health (Scholl TO and Reilly T, 2000). Iron deficiency anaemia during pregnancy is associated with higher rates of premature birth and low birth weight (Viteri FE, 1994).

Iron deficiency in infants may also adversely influence cognitive development and may have long-term consequences (Lozoff B et al., 2000). Severe iron deficiency anaemia in infants has been associated with impaired psychomotor development and developmental delays >10 y after the treatment of iron deficiency during infancy (Harthoorn EJ and Langenhuijsen, MM 2001).

The overall iron requirement during pregnancy is significantly greater than that in the non-pregnant state despite the temporary respite from iron losses incurred during menstruation. Iron requirement increase notably during the second half of pregnancy because of the expansion of the red blood cell mass and the transfer of increasing amount of iron to both the growing fetus and the placental structures. Patients at particular risk include those with poor nutrition and those with frequent pregnancies without an interval to replenish iron stores. The incidence of anaemia during pregnancy changes with epidemiological differences in the population studied, so it is difficult to determine the true incidence (Cunningham F, 2001).

Haematological changes during pregnancy

The maternal blood volume increases markedly during pregnancy. The blood volumes at or very near term averaged about 40 to 45 percent above their non-pregnant levels⁽⁶⁵⁾. The degree of expansion varies considerably, in some women there is only modest increase, while in others the blood volume nearly doubles (Hallberg L and Hulten L, 1996).

In spite of erythropoiesis, haemoglobin concentration and the haematocrit decrease slightly during pregnancy, so Hb concentration at term averages 12.5mg/dl thus in most women a Hb concentration below 11.0 g/dl, should be considered abnormal and usually due to iron deficiency rather than to hypervolaemia of pregnancy. The world health organization (WHO) defines anaemia as an Hb level less than 11g/dl throughout pregnancy (this is the most widely used definition worldwide). The American Centres for Disease Control and Prevention modified this by trimester of pregnancy: First-trimester Hb level less than 11g/dl, second –trimester Hb level less than 10.5g/dl and third-trimester Hb level less than 11g/dl.

Iron stores

Approximately 65% of stored iron in the circulating red cells in the adult women, additional iron stores located in the bone marrow, liver and spleen in the form of ferritin. The first pathologic changes to occur in iron-deficiency anaemia is the depletion of iron stores in the bone marrow, liver and spleen, resulting in a depressed serum ferritin level, the serum iron level falls, as the percentage saturation of transferrin. The total iron binding capacity rises, as this is a reflection of the amount of unbound transferrin. A fall in the haematocrit follows microcytic hypochromic red cells are released into the circulation (Hallberg L and Hulten L, 1996).

Assessment of iron status in pregnancy

During pregnancy, haemodilution leads to reduced haemoglobin concentration, whereas both serum iron and ferritin concentration decrease and total iron-binding capacity increases.^(80,81) The relative contributions of pregnancy per se and a pregnancy induced negative iron balance in bringing about these changes can be assessed by measuring the changes in haemoglobin, serum iron, serum ferritin, and total iron binding capacity that occur during pregnancy in women rendered iron replete after adequate iron supplementation during pregnancy (Carriaga MT et al., 2001).

Neonatal erythropoiesis

The mean Hb level in cord blood at term is 16.8g/dl, with 95% of the values falling between 13.7 and 20.1g/dl. More extreme ranges (12 to 25g/dl) are thought to depend on large fetomaternal or materno-fetal transfusion. This variation reflects perinatal events, particularly asphyxia and also the amount of blood transferred from the placenta to the infant after delivery. Delay of cord clamping may increase the blood volume and red cell mass of infant by as much as 55 %. The mean total blood volume after birth is 86.3 ml/Kg for the term infant. The blood volume per kilogram decreases over the ensuing weeks, to reach a mean value of about 65ml/Kg by 3 or 4 months of age (Beutler E et al., 2001). Normally the Hb and Haematocrit values rise in the first several hours after birth because of the movement of plasma from the intravascular to the extravascular space. A venous Hb concentration of less than 14g/dl in a term infant or a fall in haematocrit in the first day of life is abnormal (Beutler E, 2001). The RBCs, Hb and haematocrit values decrease only slightly during the first week, but decline more rapidly in the following 5 to 8 weeks, producing the physiologic anaemia of the newborn, and this occur by two months of age, when Hb concentration falls below 11 g/dl (Rennie.J and

Robertson.N, 2001).

Pathological anaemia in the newborn

It can result from haemorrhage, haemolysis or failure of red cell production. Anaemia at birth is usually due to severe immune haemolysis or haemorrhage. Infants with impaired red cell production do not usually develop anaemia until after 3 months, like congenital red cell aplasia and congenital dyserythropoietic anaemia (McArdle HJ et al., 2003).

During pregnancy, iron is transferred from the mother to the fetus across the placenta. Many studies have found that the fetus can accumulate sufficient iron even in the face of mild or moderate maternal iron deficiency (Wong CT and Saha N, 1990). By contrast, other findings indicate that maternal iron deficiency anaemia during pregnancy compromises fetal iron reserve. To pursue maternal-iron transfer, recent studies have focused on characterizing the physiologic adaptations that occur at the level of the placenta to support fetal iron demand in both iron-replete women and in women with dietary intakes or medical situations that increase the risk of iron deficiency (CookJD, Reddy MB, 1995).

Objectives

The main objectives of this study are to measure the Hb level and RBCs indices in mothers and their newborns at the time of delivery. To determine iron status of mothers and their newborns at time of delivery by measuring serum iron, total iron binding capacity, and serum ferritin and to see the effect of iron deficiency in mothers on their newborn iron stores.

METHODS

This is a prospective comparative hospital based study was conducted in Khartoum State. Eighty deliveries were attended, of which 64 were normal vaginal delivery, and 16 were elective caesarean sections. All pregnant females with singleton pregnancy at term, in labor, irrespective of gravity, iron supplements, having systemic disease or not and mode of delivery were included in this study. Twenty healthy women, apparently healthy not on any tablets or tonics, and not having chronic illnesses, were taken as controls group.

During the first stage of labor the samples were taken from the mother. And after delivery cord blood samples were taken from the babies. Samples collected were 2.5 ml venous blood in EDTA was collected for measurement of hematological values. 4 ml venous blood collected as clotted blood to obtain serum.

For the target population and controls the following

tests were done: Haemoglobin (Hb), Haematocrit (Hct), red cell indices (MCV, MCH, and MCHC), using automatic blood counter (Sysmex Kx-21) and peripheral blood films were done. Serum iron and total iron binding capacity (TIBC) were measured by an automatic instrument (BTS- 370 Plus), and Serum Ferritin was estimated by ELIZA technique.

RESULTS

Age of the studied mothers showed minimum of 18 years and maximum of 42 years. (Figure 1), 64 (80%) of them by normal vaginal delivery, while 16 (20%) by caesarean section. Gestational age of the studied mothers was between 36 - 42 weeks, gravity of the pregnant women was between gravida I to gravida X. (Figure 2). All babies were term, their weights between 2.5 and 4.5 kg. (Figure 3) and their gender showed 33 (41.3%) males and 47(58.7%) females.

Haematological findings in the studied anaemia mothers

Eight mothers had low Hb level as seen in Figure (4) and their haematological indices as follows: 4 (50%) had normal MCV and 4 (50%) had low MCV, 4 (50%) had normal MCH, while 4 (50%) had low MCH while 6 (75%) had normal MCHC, while 2 (25%) had low MCHC see Figure (5)

Of these 8 mothers, 4 mothers had normal Haematological indices, while 2 mothers had combination of 2 Haematological indices (both low MCV and MCH), 2 mothers had low MCV, MCH, and MCHC. Those mothers who had combination of low Haematological indices had very low S. ferritin.

Biochemical findings in the studied anaemic mothers

Two (25%) had normal S. ferritin, while 6 (75%) had low serum ferritin, 5 (62.5%) had normal serum iron, while 3(37.5%) had low serum iron. 4(50%) had normal TIBC, while 4(50%) had low TIBC. Figure (6)

Haematological findings in the studied anaemic babies

Hb results showed 18 (22.5%) babies had low Hb level (< 14 g/dl) Figure (7). All of the anaemic babies had normal MCV, MCH and MCHC. Figure (8)

Biochemical findings in the studied anaemic babies

One (5.6%) baby showed low serum ferritin while 16

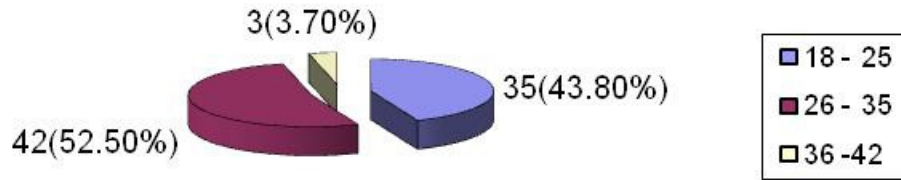


Figure 1. Distribution of age (in year) of studied mothers

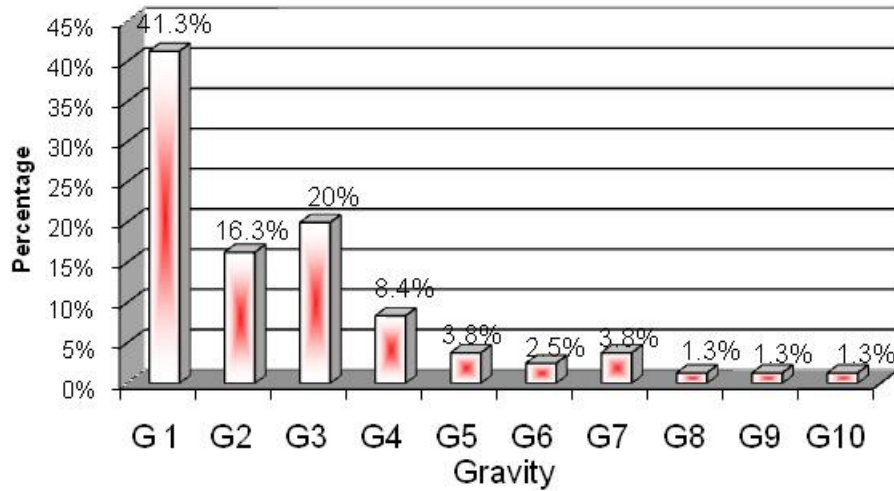


Figure 2. Distribution of gravity of the studied mothers

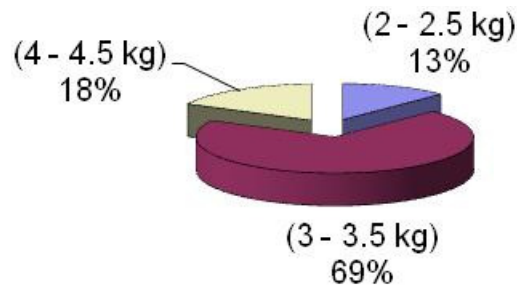


Figure 3. Distribution of the weight of the studied babies (in kg)

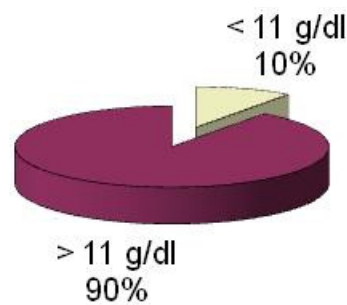


Figure 4. Hb level (g/dl) in studied mothers

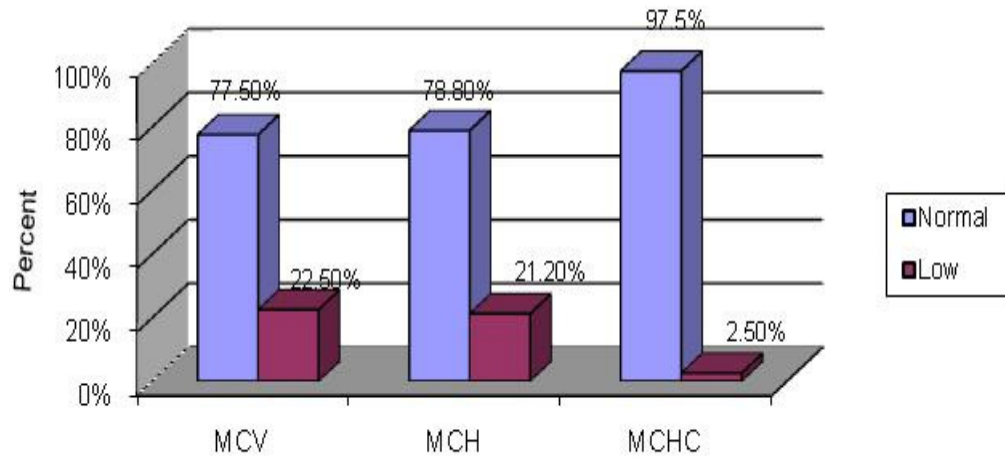


Figure 5. Red cell indices in the studied mothers

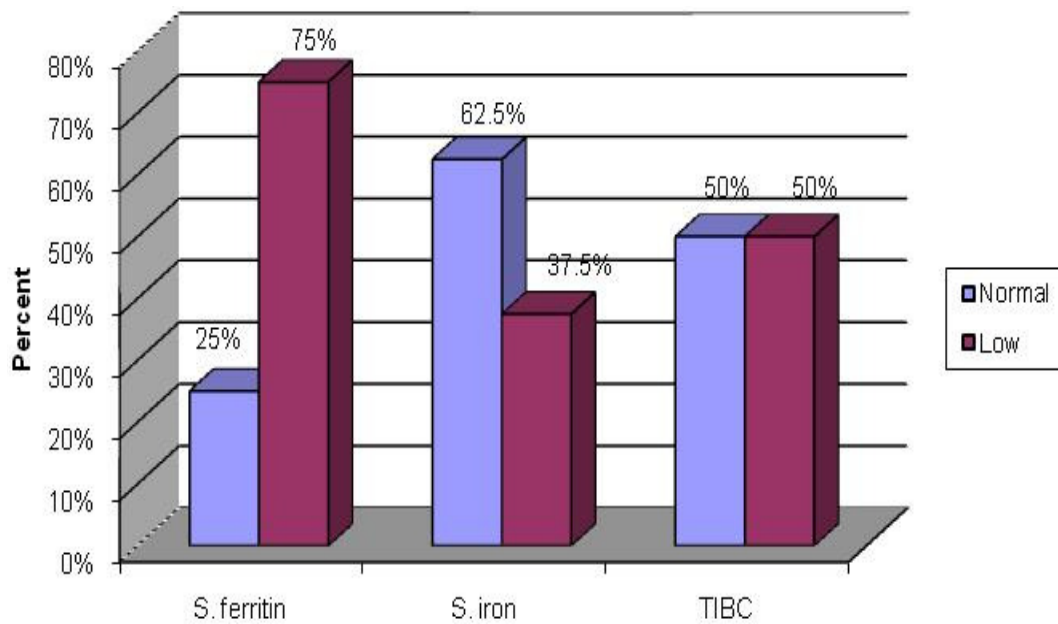


Figure 6. Biochemical findings of the studied anaemic mothers

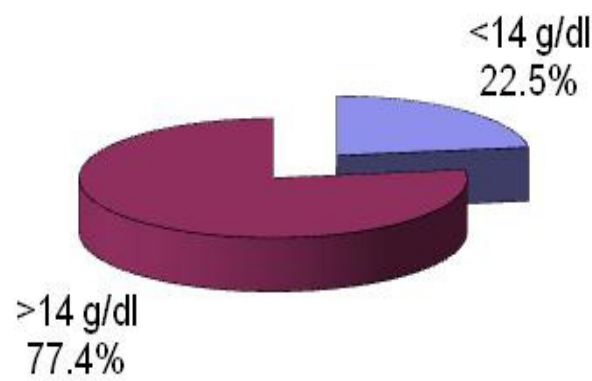


Figure 7. Hb level in the studied babies

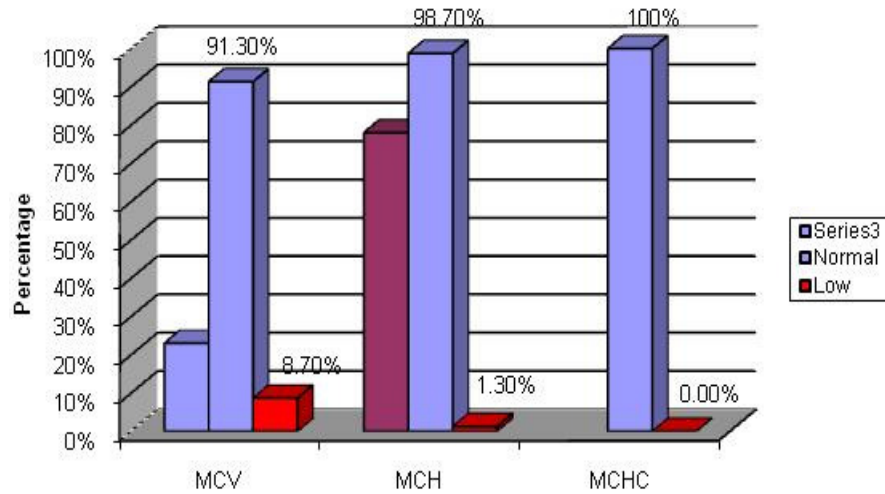


Figure 8. Red cell indices in the studied babies

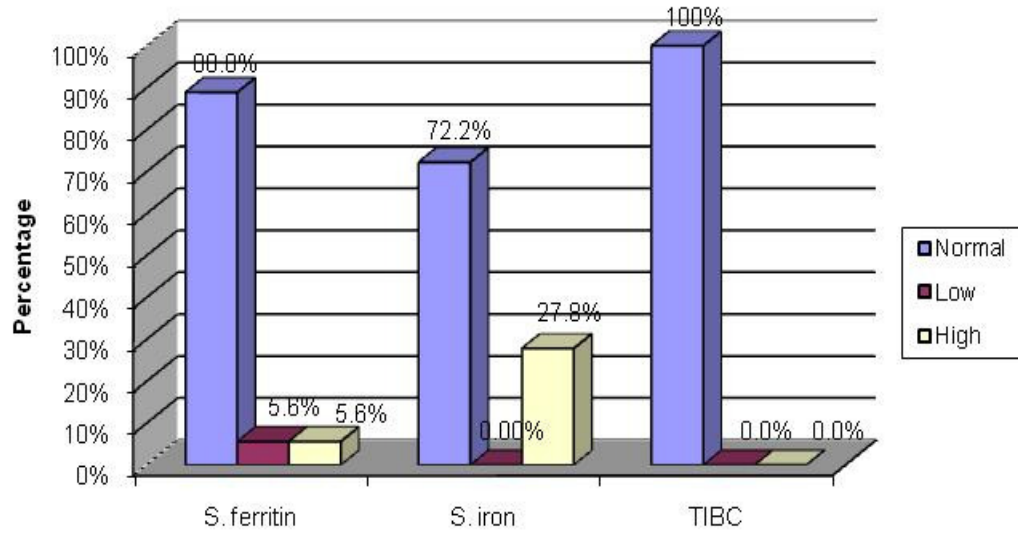


Figure 9. Biochemical findings of the studied anaemic babies

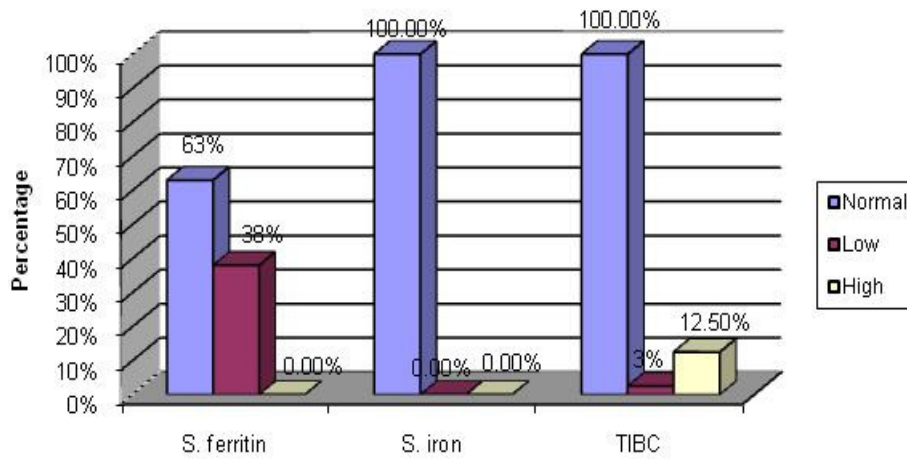


Figure 10. Biochemical findings of the studied babies born to anaemic mothers

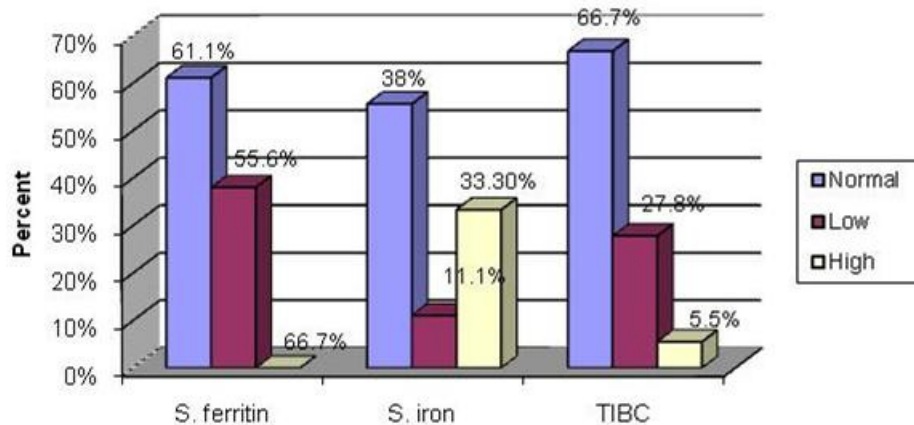


Figure 11. Biochemical findings of the studied mothers who gave birth to anaemic babies

(88.9%) showed normal level and one baby (5.6%) showed high level of serum ferritin. 13 (72%) babies showed normal serum iron while 5 (27.8%) showed high serum iron. All anaemic babies showed normal TIBC. Figure (9)

Haematological and Biochemical findings in babies born to anaemic mothers

Hb and Haematological indices of all babies (100%) were normal. Five babies (62.5%) had normal S. ferritin, while 3 (37.5%) had low serum ferritin while all babies (100%) had normal serum iron. 6 babies (75%) had normal TIBC, one (12.5%) had low TIBC and one (12.5%) had high TIBC. Figure (10)

DISCUSSION

The prevalence of overt anaemia in the studied mothers was found to be 10% as 8 mothers had low Hb level, (WHO criterion: Hb < 11g/dl). Among these 8 mothers, 2 mothers had normal iron status, while 6 showed evidence of iron deficiency anaemia, where all of them showed low levels of serum ferritin. This makes the prevalence of overt iron deficiency very low (7.5%) as compared to figures reported from developing countries (WHO Scientific group, 1968). 4 of these 6 mothers showed reduction in two or more of the haematological indices (MCV, MCH, and MCHC) while two had normal indices despite their low serum ferritin.

The results of serum iron and TIBC in these mothers were not in keeping with these findings, since low iron was found in only two of these mothers and TIBC was not raised in any of them.

This confirms the fact that the serum iron is very unreliable in assessment of iron status because it is affected by diurnal variation; ingestion of food rich in iron

or iron tablets and it is especially unreliable during pregnancy because most of the pregnant ladies will be taking oral iron supplementation. TIBC level is also affected very much by pregnancy. In 15% of pregnant ladies TIBC is reported to be elevated even without iron deficiency anaemia (Dale JC et al., 2002). In both serum iron and TIBC there is considerable overlap between iron deficient and normal people, so they are not usually necessary if ferritin is available. Serum ferritin measurement is a sensitive method to determine iron deficiency in pregnancy (Harthoorn-Lasthuizen, 2001; BYG, K and Milaman N, 1981). Also (Haram et al., 2001) have found that serum iron and TIBC have low sensitivity in the diagnosis of iron deficiency anaemia during pregnancy, in addition to that a normal range for pregnancy has not been firmly established (WHO, UN Children's fund, and UN University, 2001).

The cause of anaemia in the two mothers with normal serum ferritin could not be ascertained but it could be due to delusional effect of pregnancy or due to other causes of anaemia.

Serum ferritin was found to be low in 48 mothers (60%), including the 6 mothers who showed overt anaemia, that leaves us with 42 mothers (52.5%) with latent iron deficiency and this gives a prevalence of iron deficiency of 60% in the study group.

The true prevalence of iron deficiency anaemia in pregnancy is difficult to determine, and the prevalence will vary at different times over the 40 weeks of gestation, and it is different in developed countries from that of developing countries. The prevalence of iron deficiency anaemia in developing countries is 52% (WHO Scientific group, 1968). It has decreased in the developed countries over the past several decades and this has been variously attributed to iron fortification, prophylactic iron supplements, better health care and public health programs aimed at women and children (Scholl and Hediger, 1994). Prevalence of iron deficiency anaemia in Sudanese pregnant females has not been reported.

It is interesting that the babies born to the 8 anaemic mothers had normal Hb levels. However 3 of these babies had latent iron deficiency as shown by their low serum ferritin and when we looked at ferritin levels of the babies born to all mothers with low levels of ferritin seven of them (14.6%) showed low values. It is very important to note that mothers of these babies had the lowest ferritin values in our study ranging from 0-1.6 ng/ml except one whose ferritin level was 13ng/ml, which is still very low. This highlights the fact that very low maternal stores can jeopardize baby's iron stores. Mild to moderate reduction of ferritin in our studied mothers did not affect their babies' stores. Many studies have found that the fetus can accumulate sufficient iron even in the face of mild or moderate maternal iron deficiency. (Wong CT, 1990).

(Balai KS, in 1992) also found no correlation between serum ferritin of the mothers and babies. (Harthoorn L, 2001). found that serum ferritin was higher in cord serum than in respective maternal samples but he also stated that iron stores of newborns delivered by mothers with very low serum ferritin concentrations were lower than in newborns of mothers having normal ferritin levels ((Harthoorn-Lasthuizen, 2001).

Prevalence of anaemia in the studied newborns was found to be 22.5% as 18 babies had low Hb level (<14g/dl). This agrees with a study done in Sudanese newborn babies, which reported it to be 29.9% (Suaad El-Nour Mohamed, 1997). All of the anaemic babies in the present study had normal haematological indices and only one (5.6%) baby had low serum ferritin level. This baby's mother had very low serum ferritin. This confirms the finding that severely depleted maternal iron stores can affect the baby (Milman N, 1987; Fenton et al., 1997).

In this study 17 of the anaemic babies had normal serum ferritin and normal indices. Their anaemia can be due to undiscovered causes or probably due to early clamping of the umbilical cord, which can lead to anaemia (Blot and co workers, 1999). It is worth mentioning that none of these babies was clinically jaundiced which rules out haemolysis as a cause of their low Hb.

Interestingly all mothers of the anaemic babies had normal Hb and almost normal haematological indices, indicating that the cause of anaemia lies in the babies and not in their mothers. However 7 of those mothers had low serum ferritin, but we do not think that the cause of anaemia in their babies is due to iron deficiency anaemia since the babies serum ferritin was normal.

TIBC was found to be unexpectedly low in some babies and mothers in our study. Contrary to our findings it has been reported in the literature that 15% of pregnant ladies have high TIBC even without iron deficiency anaemia (Hallberg L and Hulten L, 1996). On the other hand it is also reported that TIBC is not elevated above reference limits in 30% -40% of patients with chronic iron

deficiency anaemia so normal but not low levels may be found (Ravel R, 1995). In another study however 69% of iron deficiency patients with low serum iron levels had an elevated TIBC, 11% had a TIBC within reference limits, and an additional 21% had decreased TIBC values ((Ravel R, 1995). Therefore the results in this study of low TIBC can be acceptable but they contradict with the claim that pregnancy raises the TIBC.

CONCLUSION

This study concluded that the prevalence of overt iron deficiency anaemia in the studied mothers is not high, but of latent anaemia is quite high. Anaemia in the mother does not affect the newborn and anaemia in the babies born to non - anaemic mothers is not uncommon, early cord clamping should always be taken in to consideration, if other causes could not be found.

Extremely low serum ferritin in mother significantly affects the baby's iron stores and ferritin level is the best parameter for assessment of iron status, while TIBC and serum iron are unreliable during pregnancy. Combined reduction of MCV, MCH is more sensitive to detect iron deficiency anaemia while MCHC reduction comes late.

REFERENCES

- Allen LH (2000). Anaemia and iron deficiency: effects on pregnancy outcome. *AM J Clin Nutr*; 71 (Suppl): 1280S-4S.
- Balai KS, Pendse V, Gupta S (1992). Effect of maternal anaemia on iron status of the newborn. PMID: 931424. *Indian J Matern Child Health*. Apr-Jun; 3(2): 54-6.
- Beutler E, Barrys C, Marshall A, Lich TM, Thommas JK (2001). *Williams's hematology*, 6th Edition.
- BYG KE, Milman N, Hansen S, Agger AO (1981). PMID: 11399631 (Pub Med- as supplied by publisher) *Scand J Haematol*. Oct; 27(4): 247-52.
- Carriaga MT, Skikne BS, Finely B, Cutler B, Cook JD (1991). Serum transferrin receptor for the detection of iron deficiency in pregnancy. *Am J Clin Nutr*; 54:1077-81.
- CookJD, Reddy MB (1995). Efficacy of weekly compared with daily iron supplementation. *Am J Clin Nutr*; 62:117-20.
- Cunningham F, Norman FG, Kenneth JL (2001). *Haematologic diseases of pregnancy*. William's Obstetrics 21st edition. USA. McGraw-Hill Company Page 177-179. And 1308-1310.
- Dale JC, Burritt MF, Zinsmeister AR (2002). Diurnal variation of serum iron, iron binding capacity, transferrin saturation and ferritin levels. *AMJ Clin Pathol*, 17:808.
- Fenton V, Cavill I, Fisher J (1977). Iron stores in pregnancy. *Br J Haematol*; 37:145-9.
- Hallberg L, Hulten L (1996). iron requirements, iron balance and iron deficiency in menstruating and pregnant women. In: Halberg L, Asp N-g, eds. *Iron nutrition in health and disease*. London: George Libby:165-82.
- Haram K, Nilsen,S.T, ULvik RJ (2001). iron supplementation in pregnancy- evidence and controversies. *Acta Obstetrica et Gynecologica Scandinavica* 80(8), 683-688.
- Harthoorn-Lasthuizen EJ Langenhuijsen MM (2001). Does iron deficient erythropoiesis in pregnancy influence fetal iron supply? *Acta Obstet Gynaecology Scand*; 80:392-6.
- Lozoff B, Jimenez E, Hagen J, Mollen E, Wolf AW (2000). Poorer behavioural and developmental outcome more than 10 years after treatment for iron deficiency in infancy. *Pediatrics*; 105:E51.

- McArdle HJ, Danzeisen R, Fosset C, Gambling L (2003). The role of the placenta in iron transfer from mother to fetus and the relationship between iron status and fetal outcome. PMID: 12219063, *Biometals*. Mar; 16(1): 161-7.
- Milman N, Ibsen KK, Christensen JM (1987). Serum ferritin and iron status in mother and newborn infants. *Acta Obstet Gynecol Scand* 66:205.
- Ravel R (1995). Factor deficiency anaemia. *Clinical laboratory medicine Mosby*. 6th edition: 22-34.
- Rennie J, Robertson N. (2001) Haematological values in newborn, *Textbook of neonatology*, 3rd edition. London, Churchill Living Stone, page 1399.
- Scholl TO, Hediger ML (1994). Anaemia and iron deficiency anaemia: compilation of data on pregnancy outcome. *Am J Clin Nutr*, 59, 482S-501S.
- Scholl TO, Reilly T (2000). Anaemia, iron and pregnancy outcome. *J NUTR*; 130:443S-7S.
- Suaad El-Nour Mohamed (1997) Anaemia at delivery. Prevalence, risk factors and consequence in the newborn. *Clinical MD. Obstetrics and Gynecology*. Research theses. The books of Abstracts by Asim Zaki, A/salam Gerais and Hisham Mirgani. University of Khartoum. Postgraduate medical studies board.
- Viteri FE (1994). The consequences of iron deficiency and anaemia in pregnancy. In: Allen L, King J, Lonnerdahl B, eds. *Nutrient regulation during pregnancy, lactation and growth*. New York: Plenum Press.
- WHO Scientific group (1968). *Nutritional Anaemias*. WHO Tech. Rept. Ser. No.405.
- WHO, UN Children's fund, and UN University (2001). *Iron deficiency anaemia: assessment, prevention, and control. A guide for programme managers*. WHO/NHD/01.3.
- Wong CT, Saha N (1990). Inter-relationships of storage iron in the mother, the placenta and the newborn. *Acta Obstet Gynecol Scand*; 69:613-6.