Original Article

Iron overload and pregnancy outcome among Sudanese women

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Abstract:

Dispensing iron tablets to pregnant women at antenatal clinics is a common practice in Sudan. Iron overload and, consequently, oxidative stress is a possible risk.

Objective: In this study, we examined the iron status in pregnant women in correlation to pregnancy outcome.

Subjects and methods: The study was conducted in Khartoum state, Sudan in the period December 2007 – February 2009. Venous blood samples were obtained from 123 women at delivery. Undesirable pregnancy outcomes as preeclampsia, low birth weight, caesarean sections and preterm delivery, if any, were recorded. Serum iron and hematological parameters were determined.

Results: Mothers were grouped, according to their serum iron levels, as low serum iron (LSI: < 50 µg/dl, *n=14*), normal serum iron (NSI: 50 - 170 µg/dl, *n=98*) and iron overload (IOL: >170 µg/dl, *n=11*) groups. The incidence of preeclampsia was highest among the IOL group (72.7%), followed by the LSI group (35.7%) and lowest among the NSI (19.4%) group, p=. The mean babies' birth weights were comparable among the IOL and the LSI groups but both were significantly lower than that among the NSI group.

Conclusion: Iron supplementation to pregnant women must be rationalized so that women will benefit without developing undesirable effects.

Key words: iron, oxidative stress, preeclampsia.

Hypertensive disorders complicating pregnancy are common and form one of the deadly traits, along with haemorrhage and infection that results in much of the maternal morbidity and mortality related to pregnancy. Pregnancy induced hypertension is a potential precursor of preeclampsia or eclampsia, which require the presence of proteinuria for diagnosis[1]. The combination of proteinuria and hypertension during pregnancy markedly increases the risk of prenatal mortality and morbidity[2]. The maternal preeclampsia occurs mostly in multiparous patients with known risk factors of preeclampsia such as insulin resistance, diabetes mellitus, obesity and chronic hypertension[3].

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Other risk factors associated with preeclampsia include African American ethnicity[4, 5]. It has been proposed that maternal endothelial cell dysfunction is the key event resulting in the diverse clinical manifestations of preeclampsia. Current concepts of the genesis of preeclampsia include endothelial dysfunction and oxidative stress[6-9]. The factors that lead to endothelial cell dysfunction have not been determined with certainty, but the evidence points to poor placentation[10-12]. The effect of poor placentation is to leave the spiral arteries smaller than normal for the second half of pregnancy. The obstructive lesion of the spiral arteries, called acute atherosis, leads to placental ischaemia and the malperfused placenta is a likely site for the production of reactive oxygen species such as superoxide and hydrogen peroxide[13,14]. But neither of these is reactive enough to initiate cellular damage directly. One hypothesis receiving increased attention is that placental and maternal free radical reactions promote a cycle of events that compromise the defensive

functioning of the vascular endothelium in preeclampsia. Since the time that data relevant to this hypothesis were initially reviewed[15]; a significant body of new information has been generated. It has been suggested that reduced antioxidants and increased oxidative stress leading to impaired essential polyunsaturated fatty acid levels may be a key factor in the development of pre-eclampsia[16]. Antioxidant vitamins directly scavenge reactive oxygen species and up regulate the activities of antioxidant enzymes. Among them, vitamin E and carotenoids have attracted most attention as antioxidants important in human diseases including preeclampsia[17,18]. Thus, variations in these antioxidants in patients with preeclampsia may be of considerable clinical importance. In the presence of catalytic amounts of transition metal ions, particularly iron and copper, the reactive oxygen species can generate the highly reactive hydroxyl radical by Fenton chemistry. This radical can initiate the process of lipid peroxidation, which if uncontrolled, may result in endothelial cell damage[18,19]. Some studies demonstrate that serum iron[20-23] levels are elevated in preeclampsia. An iron supplement during pregnancy is a common practice in Sudan because of the high prevalence of anaemia among pregnant women[24]. However, the possible burden and impact of iron status on pregnancy outcome has not been studied. This is a cross – sectional study aiming to present preliminary data on the effect of serum iron level on the development of preeclampsia among Sudanese pregnant women.

Methods:

The study was ethically approved by the committee of the college of applied and industrial sciences, university of Juba, Sudan. It was carried out in Khartoum state- Sudan, in the period December 2007 till February 2009. Participants were recruited from Rabat, Bashaer, Omudurman, Alsaudi and Khartoum Teaching Hospitals. One hundred and twenty three women were included, mothers of >35 years age and those with glucosuria were excluded. A questionnaire form including personal data was completed for each participant. A five ml venous blood sample was obtained at delivery after taking the consent of participant. Samples were divided into 2 aliquots, 2.5 ml in plain tubes to obtain serum for iron determination and 2.5 ml in EDTA tubes for haematological determinations.

Haematological parameters including haemoglobin (Hb), mean red cell volume (MCV) and packed cell volume (PCV) were determined using automated methods sysmex haemoglobin system, (Sysmex NE 8000). Iron ferrozine kits (REF 1135005, Linear Chemicals S.L., Spain) was used for determination of serum iron.

Results:

Mothers were grouped, according to their serum iron levels, as low serum iron (LSI: < 50 µg/dl), normal serum iron (NSI: 50 - 170 µg/dl) and iron overload (IOL: >170 µg/dl) groups. Age range was 15 – 35 years. All subjects were taking routine iron supplements of 150 mg/day ferrous sulphate sustained release capsules containing 500 micrograms folic acid. There were no significant differences between the three groups as far as age, parity, DBP, MCV (table 1) and frequencies of caesarean sections (C/S) and preterm deliveries (table 2) were considered. However, mean Hb and PCV were comparable among the NSI and the IOL and significantly higher than that of the LSI group (table 1). The incidence of preeclampsia was highest among the IOL group (72.7%), followed by the LSI group (35.7%) and lowest among the NSI (19.4%) group, p = 0.00. The mean babies' birth weights were comparable among the IOL and the LSI groups but both were significantly lower than that among the NSI group, p = 0.041 (tables 1 and 2).

Discussion and conclusion:

This cross – sectional study showed an evident association between iron status and pregnancy outcomes, namely development of preeclampsia and low birth weight among the study subjects. Both LSI and IOL groups showed higher frequencies of preeclampsia and LBW compared to the NSI group.

Table 1: Age, parity, diastolic blood pressure and haematological parameters among women with different serum iron levels.

Group (n)	LSI (< 50 µg/dl) (14)	NSI (50 - 170 µg/dl) (98)	IOL (>170 µg/dl) (11)	*P* - values
Age				
mean±SE	23.8±1.05	27.8±0.55	27.2±1.50	0.015
median	25.5	30	29	
Parity				
mean± SE	2.2±0.49	2.75±1.78	4.0±3.0	0.519
median	1.5	2.5	3	
DBP				
mean± SE	85.4±5.7	80.8±1.29	88.0±5.3	0.369
median	80	80	90	
Hb				
mean± SE	8.9±0.21	11.2±0.18	11.0±0.68	0.0000
median	9.3	11.8	11.6	
PCV				
mean± SE	27.6±0.74	32.61±0.59	33.95±2.18	0.00017
median	28.5	34.0	33.0	
MCV				
mean± SE	77.6±2.14	82.50±0.76	85.0±2.84	0.093
median	80.2	84.2	85.4	
Serum Iron				
mean± SE	39.2±1.96	100.5±3.37	193.8±7.71	0.000
median	40	94.5	190	

Table 2: Frequency of preeclampsia, C/S and preterm delivery among women with different serum iron levels.

Group	LSI (< 50 µg/dl) (14)	NSI (50 - 170 µg/dl) (98)	IOL (>170 µg/dl) (11)	*P - values
Preeclampsia	5 (35.7%)	19 (19.4%)	8 (72.7%)	0.00
**LBW babies	2/12 (16.7%)	2/85 (2.4%)	0/8 (0.0%)	0.041
C/S	7 (50%)	32 (32.6%)	4 (36.4%)	0.352
Preterm delivery	2 (14.3%)	3 (3.1%)	1 (9.1%)	0.095

*P- values were obtained by Fisher exact test.
**Some data on birth weight are not available.

Our results are in agreement with a previous observation that iron excess and deficiency are known conditions under which free radical damage has been observed[25]. This damage may be accompanied by high incidence of bad pregnancy outcomes such as preeclampsia[16]. On the other hand, according to our results, women with NSI or IOL were at a better status as far as Hb concentration, MCV and rate of caesarean section are concerned. Iron supplementation for pregnant women is a routine practice in Sudan. Benefits and risks of iron supplementation during pregnancy have been reviewed[26]. Contradicting results were

obtained concerning the benefits of iron supplementation on mother and foetus. Some studies have shown that iron supplementation during pregnancy improves maternal iron status as reflected by Hb level and MCV and reduces rate of caesarean section and improves foetal growth as shown by increased mean birth weight and higher mean gestational age at delivery[27-31]. However, iron supplementation, depending on the dose, has been shown to have a variety of outcomes. Doses of 36 – 100 mg/ day may exacerbate oxidative stress[32,33]. Sixty mg/ day increase Hb above 130 g/L leading to negative effects[34,35]. Supplements of more than 30 mg/day are also accompanied by gastrointestinal symptoms[27]. This study alarms antenatal care providers in Sudan to rationalize iron supplementation so that pregnant women would benefit without developing undesirable effects.

Acknowledgement:
We extend our sincere appreciation to Dr. Ayman Hussain, Institute of Endemic Diseases, University of Khartoum, Sudan for statistical analysis of data. This work is part of an M. Sc program at the college of Applied and Industrial Sciences, University of Juba, Sudan.

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