Iron status, and factors affecting iron status during the third trimester of pregnancy in Sudanese
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ABSTRACT
Objective: Pregnant women worldwide are frequently prone to iron deficiency due to increased demand for fetal and maternal development. The objective of this study was to investigate the iron status, and factors affecting iron status in Sudanese pregnant women during the third trimester. Materials and methods: This study was conducted between November 2009 and February 2010 at Wad Medani Teaching Hospital of Obstetrics and Gynaecology. Pregnant women in the late third trimester attending the hospital for antenatal care were recruited. Serum iron, total iron binding capacity (TIBC), and ferritin were assessed; data on maternal characteristics and supplement use were recorded. Results: Of the 600, 525 (87.5%) were multigravida, and 395 (65.8%) were not treated with iron. A high percentage (84.2%) had a serum ferritin less than 50μg/l. Gravidity and gestational age are negatively associated with serum iron and transferrin saturation; birth space and iron supplementation are positively associated with serum iron, transferrin saturation, and ferritin. Conclusion: Gravidity, gestational age, close birth spacing, and lack of iron supplementation are risk factors for iron deficiency during pregnancy. Key words: Iron status, pregnancy, Sudanese.

INTRODUCTION
Anaemia during pregnancy continues to be a common clinical problem with high rates of prevalence (35 to 75%) in many developing countries 1. Iron deficiency (ID) is the most common cause of nutritional anaemia, it ranks 9th among 26 diseases with highest burden 2. During pregnancy there is a high risk of developing it, due to the increase of iron requirements for fetal and maternal tissues growth 3. ID during pregnancy has been associated with multiple adverse outcomes for both mother and fetus, including an increased risk of haemorrhage, sepsis, maternal mortality, prenatal mortality and low birth weight 4-6. Mounting evidence indicates that anaemia during pregnancy is a risk factor for ID anaemia in infants 7, 8. Anaemic infants failed specifically in language capabilities and body balance-coordination skills 9. The generally accepted
cut-off level for haemoglobin and serum ferritin, below which iron stores are considered to be depleted, are, 11.0g/dl and, 15ng/ml, respectively. The increased risk of mortality would also be more plausible and predictable if the mechanisms involved are understood. ID was associated with lower lymphocyte stimulation indexes; it diminishes the number of T-cells and the production of antibodies. The CD3+ and CD8+ cells were found to be correlated positively with maternal serum transferrin saturation. Consistently, significant lower levels of T lymphocytes as well as CD4+ cells were observed in the iron deficient children and iron supplementation improved the CD4+ counts significantly. In fact, iron excess and deficiency are situations where free radical damage has been observed and can lead to functional disturbances and foster genetic alterations. In animal studies, iron-deficient rats have higher levels of oxidative stress markers in liver and kidney, defective liver mitochondrial functions and mitochondrial DNA damage. Untreated ID, as well as excessive iron supplementation, are deleterious and emphasize the importance of maintaining optimal iron intake. Thus, in this study we investigated the iron status, and factors affecting iron status in Sudanese pregnant women in order to alleviate the ID-associated complications earlier.
SUBJECTS AND METHODS

This study was conducted between November 2009 and February 2010 in Gezira State, Central Sudan. Six hundred pregnant women in late third trimester, attending Wad Medani Teaching Hospital of Obstetrics and Gynaecology for antenatal care were enrolled as cases. Women with chronic disease, overt infection, febrile illness, high WBC count, ante-partum haemorrhage or who had received blood transfusion were excluded. The study was approved by the ethics committee of the University of Gezira and the Faculty of Medicine, Sudan. Written informed consent was obtained from participants. Participants are informed that they can withdraw from the study at any time point, without giving a reason for withdrawal. Participants who withdraw will receive regular health care according to the local protocols. Pregnant women had a detailed medical examination performed before collecting a sample of venous blood. A structured questionnaire was filled; information of gravidity, gestational age, birth space, and iron supplementation were recorded. On recruitment, serum iron, total iron binding capacity (TIBC), and ferritin, were assayed. The TIBC and iron were used to calculate the transferrin saturation (i.e serum iron/TIBC). Descriptive statistics and bivariate correlations were performed using SPSS version 12.

RESULTS

The descriptive and investigated data of the 600 pregnant women are shown in Table 1. All the 600 were in the last trimester, 525 (87.5%) were multigravida, and 395 (65.8%) were not treated with iron.

Table 1 The age, gravidity, gestational age, birth space, and iron profile in 600 Sudanese pregnant women

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean±SD</th>
</tr>
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<tbody>
<tr>
<td>Age in years</td>
<td>27.78±3.55</td>
</tr>
<tr>
<td>Gravidity</td>
<td>4.74±1.94</td>
</tr>
<tr>
<td>Gestational age in weeks</td>
<td>38.22±1.53</td>
</tr>
<tr>
<td>Birth space in months</td>
<td>15.13±3.91</td>
</tr>
<tr>
<td>Serum iron (μg/dl)</td>
<td>80.77±36.09</td>
</tr>
<tr>
<td>Transferrin saturation (%)</td>
<td>21.13±10.98</td>
</tr>
<tr>
<td>Serum ferritin (μg/l)</td>
<td>40.88±6.85</td>
</tr>
</tbody>
</table>
Based on the iron status parameters, significant negative correlations were observed between increased gravidity and serum iron ($r = -0.105, p = 0.01$), and transferrin saturation ($r = -0.088, p = 0.032$). The birth space showed high positive correlations with serum iron ($r = 0.634, p < 0.001$), transferrin saturation ($r = 0.757, p < 0.001$), and ferritin ($r = 0.674, p < 0.001$). A perceptible effect of iron supplementation was seen on serum iron ($r = 0.329, p < 0.001$), transferrin saturation ($r = 0.326, p < 0.001$), and ferritin ($r = 0.308, p < 0.001$).

The distribution of pregnant women according to concentrations of iron, transferrin saturation, and ferritin is illustrated in figure 1. Although, ID results in a reduction in serum iron levels, a reduction in transferrin saturation; the serum ferritin level is the most specific biochemical test that correlates with relative total body iron stores. A low serum ferritin level reflects depleted iron stores and hence is a precondition for ID. In consistency, 84.20% of the 600 pregnant women had a serum ferritin less than 50 μg/l.

### Table 2 Correlation of iron profile with the gravidity, gestational age, birth space, and iron supplementation

<table>
<thead>
<tr>
<th></th>
<th>S. iron</th>
<th>TS</th>
<th>Ferritin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gravidity</td>
<td>-0.105*</td>
<td>-0.088*</td>
<td>-0.048</td>
</tr>
<tr>
<td>Gestational age</td>
<td>-0.055</td>
<td>-0.022</td>
<td>0.008</td>
</tr>
<tr>
<td>Birth space</td>
<td>0.634*</td>
<td>0.757*</td>
<td>0.674*</td>
</tr>
<tr>
<td>Iron suppl.</td>
<td>0.329*</td>
<td>0.326*</td>
<td>0.308*</td>
</tr>
</tbody>
</table>

*indicates significant value, S.iron for serum iron, iron suppl. for iron supplementation, gestational age in weeks and birth space in months.

### DISCUSSION

Pregnant women are particularly vulnerable to ID as a result of the increased demand for iron. We examined the iron status in Sudanese pregnant women during their last trimester, assessing the pregnancy-related factors e.g. gravidity, gestational age, birth space, and iron supplementation for ID. Serum iron, transferrin saturation, and ferritin are the conventional markers of iron status in the population; these are needed to determine the magnitude of deficiency and to monitor the effect of various programs aimed at controlling ID. In screening for ID, the WHO reported that individuals with more marked anaemia usually have ferritin ≤60μg/l, and transferrin saturation <16%.

In this study, a low serum ferritin was suggested as a potential predictor of low iron status compared with the other parameters of serum iron and transferrin saturation (Figure 1).
Figure 1: The distribution of pregnant women according to concentrations of iron (a), transferrin saturation (b), and ferritin (c) in the third trimester.

In Georgia, 200 pregnant women were studied for the level of iron and ferritin, the ID anaemia found in 22% especially in the third trimester, and quantity of ferritin was at the lower border of the normal \(^{19}\). In the line of this finding, a serum ferritin was used as index for iron supplementation in Danish pregnant women; recommended iron supplementation was proposed in women with ferritin \(\leq 70 \mu g/l\) \(^{20}\). A randomised study in prepartum and postpartum showed that ferritin concentration is the most reliable non-invasive marker of iron status \(^{21}\). Our findings (Table 1 and 2) can be summarized into the following points: serum ferritin is an expedient indicator used to
define iron depletion in pregnancy; gravidity and gestational age are negatively associated with serum iron and transferrin saturation; birth space and iron supplementation are positively associated with serum iron, transferrin saturation, and ferritin. A retrospective cohort study in Saudi Arabia demonstrated that ID was significantly associated with those who are in the third trimester, and non-compliance to iron supplementation. Similar study in Singapore confirms that ID anaemia is the most common cause of anaemia in pregnancy (81.3%), 15.3% of women who were anaemic at the time of delivery had a higher incidence of preterm delivery than did those who were not anaemic. However, in Nepal, anaemia with ID in the first or second trimester but not third trimester was associated with a 1.87-fold higher risk of preterm birth.

Shorter inter-pregnancy intervals have adverse effects on maternal and neonatal outcomes. In the United States, women with inter-pregnancy intervals of <8 months were more likely to have premature infants than were women with intervals of 18–59 months. Consistent reports showed that short interval between pregnancies are associated to a high score of prematurity. Conde-Agudelo and Belizan provided evidence that women with shorter inter-pregnancy intervals are at higher risk for maternal complications. The excess preterm birth rate and pregnancy complications among women with short pregnancy intervals may be due in part to poor maternal iron stores resulting from insufficient repletion after a previous pregnancy or to recent growth demands.

In the present study, gravidity also had a significant inverse association with iron (Table 2). In Malawi similar result has been claimed that 69% of pregnant women were multigravida, and 32% of them were classified with ID anaemia. This negative relationship has been attributed to the cumulative demands on iron stores of successive pregnancies and short inter-pregnancy intervals.

The effect of iron supplementation on serum iron, transferrin saturation, and ferritin has been observed. During pregnancy, oral iron therapy is given as first-line treatment. In cases with lack of efficacy, unwarranted side effects or very low haemoglobin values, intravenous iron treatment with iron carboxymaltose is a preferable alternative. Routine oral iron supplementation was used in our clinical settings. In the prevention of ID anaemia, suggested guidelines are (1) ferritin>70 µg/l: no iron supplements; (2) ferritin 30-70 µg/l: 40 mg ferrous iron daily; and (3) ferritin<30 µg/l: 80-100 mg ferrous iron daily.

The molecular basis of iron regulation in the body is critical for comprehensive understanding of susceptibility or resistance to the development of ID in humans. Iron homeostasis (availability, transport, and storage) is a complex trait and is influenced by multiple genes. Observations of genetic-based differences in TMPRSS6 (transmembrane protease, serine 6), ferritin and transferrin suggest that these variation play divergent role in the ability of individuals to maintain homeostasis in the face of fluctuations in dietary iron.

In conclusion, our data provide evidence that gravidity, gestational age, close birth spacing, and lack of iron supplementation are risk factors for ID during pregnancy. The use of iron profile in the routine tests of antenatal care during pregnancy should be included; strategies on family planning and reproductive health care services should be encouraged in Sudan.
future, more studies to highlight the adverse effects of ID on both the mother & fetus are needed.

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Disclosure of interests The authors have no conflicts of interest to state.

Contribution to authorship EM designed the study and carried out the laboratory work. The manuscript was written and revised by HY and BE. EME did a meticulous supervision to the work.

Details of ethics approval The study approval was obtained on 18.06.2009 by the ethics committee of the University of Gezira and the Faculty of Medicine, Sudan (Ref.app.ID.20090633).

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