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3. Rossjohn RH. Tuberculosis meningitis in children in the third trimester. No beneficial effect on fetal birth weights was found on withholding of maternal iron supplementation. This study clearly demonstrated that white and urban black pregnant women require iron prophylaxis to maintain iron stores.

A prospective study of iron status in white and black pregnant women in an urban hospital
F. Guidozi, R. Patel, A. P. MacPhail

Evaluation of the iron status (haemoglobin and ferritin concentrations, and percentage transferrin saturation) in a prospective study of 65 pregnant women (55 white and 10 black) revealed that adequate maternal iron stores during pregnancy cannot be maintained with prevailing dietary patterns. Although 80.6% of the patients had normal indices in the first trimester, only 12.3% were normal in the third. Significant depletion of iron stores occurred in the second trimester, but significant iron-deficient erythropoiesis only occurred in the third trimester. Despite the decline in iron status, iron deficiency anaemia was only seen in 7 - 8% of the patients. Even after correction for the haemodilution and increased transferrin concentrations in pregnancy, over 70% of women had depleted iron stores in the third trimester. No beneficial effect on fetal birth weights was found on withholding of maternal iron supplementation. This study clearly demonstrated that white and urban black pregnant women require iron prophylaxis to maintain iron stores.

Since the 1940s it has been apparent that the amount of iron available from dietary sources during pregnancy may not meet the additional demands placed upon maternal iron stores by the fetus, placenta and the increased maternal red cell mass. As a consequence, iron supplements were widely prescribed to prevent the fall in haemoglobin concentrations, and percentage transferrin saturation) in a prospective study of 65 pregnant women (55 white and 10 black) revealed that adequate maternal iron stores during pregnancy cannot be maintained with prevailing dietary patterns. Although 80.6% of the patients had normal indices in the first trimester, only 12.3% were normal in the third. Significant depletion of iron stores occurred in the second trimester, but significant iron-deficient erythropoiesis only occurred in the third trimester. Despite the decline in iron status, iron deficiency anaemia was only seen in 7 - 8% of the patients. Even after correction for the haemodilution and increased transferrin concentrations in pregnancy, over 70% of women had depleted iron stores in the third trimester. No beneficial effect on fetal birth weights was found on withholding of maternal iron supplementation. This study clearly demonstrated that white and urban black pregnant women require iron prophylaxis to maintain iron stores.

Since the 1940s it has been apparent that the amount of iron available from dietary sources during pregnancy may not meet the additional demands placed upon maternal iron stores by the fetus, placenta and the increased maternal red cell mass. As a consequence, iron supplements were widely prescribed to prevent the fall in haemoglobin concentration known to occur in pregnancy, without any regard for the individual patient's needs. However, in 1978 Hemminki and Starfield questioned the value of this practice after having reviewed trials of iron prophylaxis which showed no evidence of benefit to either the mother or the fetus. Since then numerous arguments have been put forward, both in favour of and against this widely accepted essential component of good antenatal care. In South Africa, iron deficiency has been shown to occur commonly in pregnant Indian and coloured women, emphasising
the need for iron prophylaxis during pregnancy in these ethnic groups. Despite limited cross-sectional data that have shown that iron deficiency occurs less frequently in white and black women, it has been policy at Johannesburg Hospital to routinely supplement patients with iron from the 14th week of gestation. This prospective study was undertaken to delineate the prevalence of iron deficiency in an urbanised population of white and black pregnant women and to document the changes in iron status through pregnancy in women who received no iron supplements. In addition it was determined whether the withholding of iron supplements produced any clinical benefit for the neonate, as had been suggested previously.

Subjects and material

Eighty-six pregnant women presenting to Johannesburg Hospital with no adverse medical or obstetric history were recruited during their first antenatal visit and included in a prospective study. Thirty-six were in their first trimester and 50 in their second. None of these patients had received any iron supplementation. For the duration of their pregnancy iron supplements were withheld, but folic acid was given. Parity, age and social class of each patient were noted, and each patient confirmed at the interview that meat formed part of her dietary intake. Social class was determined as follows. Category A comprised single women earning less than R9 000 or with a family income less than R16 000 per annum. In category B, the amounts were less than R19 000 or less than R31 000 respectively per annum, and in category C, patients earned more than R19 000 or R31 000 respectively per annum. Baseline venous samples at first visit, 6-10 weeks later and in the third trimester were collected for measurement of haemoglobin concentration, serum iron level, total and unsaturated iron-binding capacity and serum ferritin concentration. Haemoglobin levels were determined on a model S-plus Coulter counter with standard calibration. Serum iron values, total and unsaturated iron-binding capacity were measured by the methods recommended by the Iron Panel of the International Committee for Standardisation in Haematology. Serum ferritin level was measured by an enzyme-linked immunosorbent assay. Placental iron content was also measured according to the method described by Torrance and Bothwell.

Birth weights of the neonates and placental weights were documented. These were then compared with the weights obtained from a control group of pregnant women who had received routine iron supplementation during their pregnancy. This control group was matched for race, age, parity, social class and gestational age at delivery.

The WHO criterion for the diagnosis of anaemia in pregnancy (haemoglobin < 11 g/dl) was used. Although this level was chosen as the dividing line between 'normal' and 'abnormal', it is acknowledged to be arbitrary, and there is likely to be an overlap between 'normal' and 'abnormal' distribution curves. Iron stores were considered absent if the serum ferritin level was less than 12 µg/l and the iron supply to the marrow was considered inadequate when transferrin percentage saturation was less than 16%. Previous studies have shown that no single measurement of iron status alone is a reliable indicator of iron deficiency and that if 2 or more indices are shown to be abnormal there is a much higher probability that the anaemia is in fact due to iron deficiency. The iron status of patients in this study was classified into 4 categories: (i) normal — normal haemoglobin level, normal ferritin level and normal percentage saturation; (ii) depleted iron stores — normal haemoglobin, low serum ferritin, normal percentage saturation; (iii) iron-deficient erythropoiesis — normal haemoglobin, low serum ferritin, low percentage saturation; and (iv) iron-deficiency anaemia — low haemoglobin, low serum ferritin, low percentage saturation.

The increased plasma volume of pregnancy may lead to overestimation of the prevalence of anaemia and iron deficiency. The measurements of iron status were therefore corrected for gestational age according to previously published criteria. In addition an index of total body iron stores (in mg) as described previously, was derived from the corrected measurements of iron status.

Statistical methods

The normality of distribution of the data was assessed by means of the univariate procedure of the Statistical Analysis System (SAS). The data on serum ferritin were positively skewed and normalised by logarithmic transformation. Comparisons between trimesters were made by analysis of variance, and the paired Student's t-test was used in the analysis of birth and placental weights.

In compliance with the Committee for Research on Human Subjects of the University of the Witwatersrand, the patients were only admitted to the study after one investigator (R.P.) had fully explained the purpose of the study and they had given written consent.

Results

Of the 86 patients who originally entered the study, 74 were white and 12 were black, and all had resided in an urban area for longer than 5 years. Thirty-six presented for their initial examination during the first trimester and 50 during the second trimester. Excluded from the final analysis of the study were 3 patients who aborted within 1 month of their first visit, 8 who delivered elsewhere and 10 who, because of logistic and administrative problems, did not have blood taken for measurement of iron status during the third trimester, although they did deliver at Johannesburg Hospital. The iron indices of 55 white and 10 black pregnant women were finally analysed.

Table I shows the mean haematological values of the patients according to the three trimesters. The mean haemoglobin, serum iron and serum ferritin concentrations, and percentage saturation all showed a significant decline as the pregnancy progressed from first to third trimester (P = 0.001). Equally significant was the increase in unsaturated iron-binding capacity (P = 0.001).
Categorisation of the patients according to iron status both before and after correction for the dilution of pregnancy in the three trimesters is shown in Table II. Although 80.5% were considered within a normal range of iron status during the first trimester, only 12.3% were in the normal range during their third trimester. Significantly depleted iron stores were noted in the second trimester (43.9%) while iron-deficient erythropoiesis only appeared significantly during the third trimester (33.8%). Only 8.2% of the patients had iron deficiency anaemia in the third trimester. As expected, the correction for the increased plasma volume of pregnancy reduced the prevalence of the more severe grades of iron deficiency, particularly in the third trimester. Nonetheless, 72.6% of the women had evidence of depleted stores in the third trimester.

<table>
<thead>
<tr>
<th>Trimester</th>
<th>Normal</th>
<th>Depleted iron stores</th>
<th>Iron-deficient anaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>80.5</td>
<td>9.1</td>
<td>2.8</td>
</tr>
<tr>
<td>2</td>
<td>45.5</td>
<td>48.3</td>
<td>0.9</td>
</tr>
<tr>
<td>3</td>
<td>12.3</td>
<td>73.5</td>
<td>31.2</td>
</tr>
</tbody>
</table>

Twenty-seven of the 36 patients who originally presented during the first trimester were followed up prospectively throughout their pregnancies. These were all white patients, as the black patients had presented for their initial visit only during the second trimester. The iron status of these 27 patients is shown in Table III. A similar significant decline in their iron status occurred, which was not associated with an increase in iron deficiency anaemia.

<table>
<thead>
<tr>
<th>Trimester</th>
<th>Normal</th>
<th>Depleted iron stores</th>
<th>Iron-deficient anaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>75.8</td>
<td>16.5</td>
<td>4.7</td>
</tr>
<tr>
<td>2</td>
<td>23.8</td>
<td>42.9</td>
<td>33.3</td>
</tr>
<tr>
<td>3</td>
<td>11.1</td>
<td>44.5</td>
<td>37.0</td>
</tr>
</tbody>
</table>

Correction for the increased plasma volume of pregnancy reduced the prevalence of iron-deficient erythropoiesis and anaemia. However, three-quarters of this group had no iron stores at the end of pregnancy. The mean fall in the calculated body iron levels in this group followed up throughout pregnancy was 456 (± 291) mg or about 1.6 mg per day. There was a significant positive correlation between the fall of calculated body iron and the level at the start of pregnancy (r = 0.84, P < 0.001).

Parity, age and social status had no effect on the indices of iron status at first visit (Table IV) or on the change in iron status as the pregnancy progressed. Although the mean values of the iron status indices of the 11 black patients were marginally lower, they did not differ significantly from those of the white patients during the second and third trimester. The placental weight and weight of the infant at delivery, born to mothers not receiving iron supplements, showed no significant differences when compared with the weights of the placenta (P = 0.12) and infants (P = 0.15) born to mothers on routine iron supplementation (Table V).

<table>
<thead>
<tr>
<th>Parity</th>
<th>No iron supplementation</th>
<th>Control (with iron supplementation)</th>
</tr>
</thead>
<tbody>
<tr>
<td>P0 G1</td>
<td>12.8 (1.0)</td>
<td>13.4 (0.9)</td>
</tr>
<tr>
<td>P1 G2</td>
<td>12.9 (0.9)</td>
<td>13.4 (0.9)</td>
</tr>
<tr>
<td>P2 G3</td>
<td>12.9 (0.9)</td>
<td>13.4 (0.9)</td>
</tr>
</tbody>
</table>

Despite the deterioration in serum iron status with the progression of pregnancy, analysis of 42 placentas revealed significant deposits of iron ranging from 50 to 147 μg/g wet weight with a mean of 83 μg/g wet weight. This represents a mean of 50 mg of iron per placenta. No correlation was found between the iron indices and the placental content of iron.

### Discussion

Although there is evidence that the iron requirements of pregnant women in the third trimester of pregnancy (5 - 6 mg per day) are unlikely to be met by any normal diet,' much debate has surrounded the routine supplementation of women with iron during pregnancy. Some workers have stated that the evidence that supplementation benefits the mother and her fetus remains unconvincing, while others feel that supplementation would appear to be non-
Physiological and suggest a failure of the pregnant woman to adapt to the pregnant state. Evaluation of iron status in the present study has clearly shown that adequate maternal iron stores during pregnancy cannot be maintained by prevailing dietary patterns in spite of the increased iron absorption that has been shown to occur in pregnancy. Only 12.9% of patients still had normal iron stores at the end of pregnancy. Correction for the increased plasma volume in pregnancy failed to improve the prevalence of depleted iron stores but did result in a reduction in the prevalence of the more severe grades of iron deficiency. Even so 74% had no iron stores at the end of pregnancy. In this regard the correlation between the fall in calculated body iron stores and the level at the start of pregnancy is of interest. Women with low stores at the start of pregnancy had the smallest fall in iron stores and thus required an even greater proportion of iron from the diet than women with normal stores. Most of the women in this study started pregnancy with normal stores and the mean cost of pregnancy in terms of the fall in calculated body iron stores was 456 μg.

It has been suggested that reversal of the normal fall in haemoglobin concentration and the normal size of red cells induced by iron may increase blood viscosity and result in impaired uteroplacental blood flow. However, there was no evidence that the withholding of maternal iron supplementation had any beneficial effect on fetal birth weight. There was no significant difference when the birth weights of the infants born to non-supplemented mothers were compared with those of a control group. In conclusion, this prospective study has shown that iron supplementation during pregnancy is necessary. Although only a small proportion of patients developed iron deficiency anaemia, the majority depleted their iron stores. Given that only about two-thirds of pregnant patients take their iron as prescribed because of the side-effects, and that the maximal iron demand is during the third trimester, iron supplementation should be given at least during the third trimester of pregnancy unless iron deficiency anaemia develops before this time. Women who have depleted iron stores at the beginning of pregnancy should receive supplementation throughout pregnancy.

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