ANAEMIA IN PREGNANCY

BACKGROUND INFORMATION

Anaemia in pregnancy is defined as an Hb <110 g/L in the first and last trimester, and a Hb <105 g/L in the second trimester. Women with anaemia in pregnancy may experience fatigue, reduced energy levels, reduced mental performances, and in cases of severe anaemia it is associated with preterm birth, low birth weights, and a small for gestational age fetus. In the postpartum period anaemia has been found to be linked to depression, emotional instability, stress and lower cognitive performance tests.

The most common causes of anaemia in pregnancy include iron deficiency, folate deficiency, vitamin B12 deficiency, haemolytic diseases, bone marrow suppression, chronic blood loss and underlying malignancies. 30-50% of women become anaemic during pregnancy, with iron deficiency being the most common form of anaemia in more than 90% of the cases.

The gastrointestinal tract increases iron absorption when the body's iron stores are low, and it reduces the absorption when there are sufficient stores. Requirement for absorbed iron ranges from 0.8mg/day in the first trimester to 7.5 mg/day in the second trimester, averaging approximately 4.4 mg/day in pregnancy. Iron requirements increase rapidly in the second and third trimester due to fetal growth, however iron absorption in the gut is not sufficient to meet this increased demand. Thus iron balance depends on maternal iron stores during this period.

A trial of oral iron should be considered as a diagnostic test for all pregnant women with suspected iron deficiency anaemia (IDA). The haemoglobin should increase within 2 weeks, otherwise further tests are required. Oral iron supplementation is the primary treatment option. A high iron diet should be recommended, including red meats (if possible), fortified cereals and drinks. Intravenous iron should only be used in severe cases of iron deficiency, if the woman is unresponsive to oral iron treatment, or when rapid repletion of iron is required.

KEY POINTS

1. All women should be offered screening for anaemia:
   - in first trimester (or at booking)
   - with the next screening bloods (usually performed between 24-28 weeks)
   - and at 36 weeks gestation
2. A FBP should be ordered within 2 - 8 weeks following initiation of treatment (dependent upon gestation) to assess response and compliance with oral iron treatments.
3. IDA in most circumstances is diagnosed by a full blood examination and serum ferritin levels. Do not use serum iron , or serum ferritin alone to diagnose IDA. Ferritin levels are elevated in active infection or inflammation and in these cases concurrent measurement of C-reactive protein (CRP) will support interpretation of ferritin levels.
4. Seek the advice of a Haematologist in diagnosing and treating IDA in women with known haemoglobinopathies. Serum ferritin should be checked prior to starting iron with known haemoglobinopathy.
5. Oral iron if taken at the appropriate dose, and for a sufficient time, is an effective first-line treatment for most women in pregnancy.  
6. If a woman fails to respond to iron therapy further investigation is indicated to assess for malabsorption problems, non-compliance with medications, co-existing disease, or an incorrect diagnosis.
7. Parenteral (intramuscular or intravenous) iron enhances haematological response compared to oral iron, but there is insufficient data on adverse effects e.g. severe allergic reactions or venous thrombosis.
8. Intravenous iron polymaltose therapy is an effective alternative to oral treatment during the second or third trimester only for treatment of IDA. Intravenous iron should only be used in women failing to respond to oral iron treatment with known IDA or in those whom a rapid repletion of iron stores is required.
9. The type, dosage, and frequency of iron supplements for treatment of IDA should be documented in MR 220 'Pregnancy Health Record'.
10. At each antenatal visit all women taking iron supplements should be monitored for medication compliance and side-effects.
11. Women with a normal Hb and ferritin levels < 30µg/L should be commenced on oral iron supplements in pregnancy to prevent development of anaemia. A dosage of 65mg elemental iron should be taken once daily.

**INTERPRETING SERUM BLOOD RESULTS FOR ANAEMIA IN PREGNANCY**

Please note that some Pathology Laboratories report results using non-pregnant adult reference ranges, when interpreting results. Use the reference ranges in the table below as a guide.

<table>
<thead>
<tr>
<th>BLOOD RESULT</th>
<th>INTERPRETATION</th>
<th>ADDITIONAL INFORMATION</th>
</tr>
</thead>
</table>
| Hb: < 110 g/L (1st & 3rd trimester) | Anaemia in pregnancy. | The CDC definition of anaemia is:
| | | - Hb <110 g/L in the first and last trimester |
| | | - Hb <105 g/L in the second trimester. |
| Hb<105g/L (2nd trimester) | Anaemia in pregnancy. | |
| Hb: ≤ 110g/L (postpartum) | Anaemia in the post-partum period. | |
| Ferritin levels²: | Indicates a low iron status – i.e. small or no iron reserves. | Elevated ferritin levels also occur with inflammation, infection, liver disease, malignancy, and lead poisoning. |
| - < 30µg/L | Indicates depletion of iron stores. |
| - < 15µg/L | |
| Mean corpuscular volume (MCV). | Low MCV indicates small cells(microcytosis) and associated with IDA. High MCV is associated with folate and B12 deficiency. | Haemoglobinopathy risk should be assessed and excluded. MCV can be normal in early IDA, or with coexisting vitamin B12 or folate deficiency. |
| Transferrin, or total iron binding capacity. | High levels are associated with IDA. Levels are normal with thalassaemia | Levels can be normal in early IDA. |
Transferrin saturation
Low levels are associated with IDA. Normal or elevated levels are associated with thalassaemia minor.\(^9\)

Serum iron
Low levels are associated with IDA. Levels are normal in thalassaemia minor.\(^9\)

Serum B\(_{12}\)
Levels below 200pmol/L indicate B\(_{12}\) deficiency.\(^{11}\)

Serum folate
Levels < 7 nmol/L indicate folate deficiency.\(^{12}\)

Severe folate deficiency in pregnancy can result in megaloblastic anaemia.\(^{10}\) Multiple pregnancy increases the demand for folate. Alcohol and some drugs may interfere with absorption e.g. anticonvulsants and sulphonamides.\(^{13}\)

**IRON DEFICIENCY ANAEMIA IN PREGNANCY**

**DEFINITION USED FOR DIAGNOSIS AT KEMH**

For management purposes at KEMH iron deficiency anaemia in pregnancy is diagnosed when the:

- Hb <110 g/L in the first and last trimester\(^1\)
- Hb <105 g/L in the second trimester\(^1\).

Mild iron deficiency anaemia results in a Hb between 90-105 g/L in 2\(^{nd}\) trimester, 90-109g/dL in 1\(^{st}\) and 3\(^{rd}\) trimester.\(^{14}\)

More severe iron deficiency may result in a more significant anaemia with a Hb < 90g/dL.\(^{2,14}\)
## MANAGEMENT IN PREGNANCY

<table>
<thead>
<tr>
<th>Level of Anaemia</th>
<th>Treatment</th>
<th>Duration of Treatment</th>
<th>Follow-up of Treatment</th>
<th>Additional Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Hb</td>
<td>Daily oral elemental iron treatment 65mg mg e.g. FGF or equivalent medication. Consider a higher dose supplement (100mg) in the third trimester for cases of poor compliance, poor dietary habits, or when the expected date of delivery (EDD) is near.</td>
<td>Throughout pregnancy until levels are within normal range postpartum.</td>
<td>FBP and ferritin levels to be checked at 28 weeks gestation. Perform FBP at 36 weeks gestation.</td>
<td>With this result the woman is not anaemic, however she has low iron stores, and as requirements increase in pregnancy this may lead to anaemia. Ferritin levels to be checked by the GP 6 weeks postpartum.²</td>
</tr>
<tr>
<td>Ferritin &lt; 30</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hb 95 -110 g/L</td>
<td>Daily oral elemental iron treatment 100-200mg daily e.g. Fefol, FGF or Ferrogradumet.</td>
<td>Throughout the pregnancy and until the GP assesses the FBP and Ferritin levels at the 6 week postnatal check.</td>
<td>Check the FBP within 2 - 4 weeks of initiating treatment, at 28 weeks gestation, and at 36 weeks gestation.</td>
<td>A higher dosage of the recommended iron supplementation would be beneficial later in the third trimester to allow IDA to be corrected prior to delivery.</td>
</tr>
<tr>
<td>Ferritin &lt; 15</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hb &lt; 95 g/L</td>
<td>Oral iron supplementation can be used (200mg elemental iron daily). In cases of poor compliance, gestation near term, particularly in patients at high risk of iron depletion or in whom tolerance levels for anaemia should be raised including: twin pregnancy, refusal of blood, teenagers, co morbid conditions, history of anaemia, planned home birth or major placenta praevia, intravenous iron should be considered.</td>
<td>Review by obstetric team for ongoing management. Individualised management according to the gestation and the clinical situation.</td>
<td>Women attending a low risk midwives clinic should be referred to her medical obstetric team for review at their next clinic, or if symptomatic, discuss management with the obstetric team the same day during her visit. Discussion with the obstetric consultant should always take place before a decision for intravenous iron therapy is made.</td>
<td></td>
</tr>
</tbody>
</table>

² Ferritin levels to be checked by the GP 6 weeks postpartum.
### Level of Anaemia

<table>
<thead>
<tr>
<th>Level of Anaemia</th>
<th>Treatment</th>
<th>Duration of Treatment</th>
<th>Follow-up of treatment</th>
<th>Additional Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb &lt; 85</td>
<td>In cases of acute blood loss, immediate cardiac compromise or symptoms requiring immediate attention, transfusion may be appropriate.</td>
<td>Individualised management according to the gestation and the clinical situation.</td>
<td>Maternal blood transfusions may be indicated for maternal and fetal reasons associated with severe anaemia.</td>
<td></td>
</tr>
<tr>
<td>Postpartum Hb &lt; 70 g/L</td>
<td>Urgent Consultant Obstetrician/Haematology review as blood transfusion indicated unless the woman has expressed a preference for no blood</td>
<td>Individualised management.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Note

Lower dosage iron supplements can be effective for treatment of IDA, and are associated with less gastrointestinal side-effects. However it is recommended in confirmed iron deficiency states, that treatment with oral ferrous iron (100 – 200mg daily) is required to correct the deficiency. Clinical staff should be familiar with the iron content of freely available supplements women take in pregnancy, as many contain insufficient elemental iron to be therapeutic.

### Prescribing Iron Supplements and Follow-up

All women with IDA should be advised:
- the type, frequency, and duration of the treatment or medication
- side-effects of the medication which can exacerbate the symptoms of pregnancy including heartburn, nausea, vomiting and constipation
- management of side-effects
- how and when to take the medications
- of medications or food that may inhibit iron absorption
- dietary information to increase oral iron intake

Provide written instructions to the woman about iron supplementation - [KEMH brochure – Iron Supplements](#).

At each antenatal visit:
- assess and document the woman for compliance with taking the medication
- assess and document side-effects from the medication. Provide advice for management of any side-effects
- assess compliance to dietary recommendations
**Dietary Information**

Sources of dietary iron include meat, poultry and fish which are two to three times more absorbable than plant-based iron foods and iron-fortified foods. Meat, poultry and fish increase absorption of iron, and ascorbic acid provides an enhancing effect on absorption. Orange juice is often recommended in pregnancy, although some iron supplement contain Vitamin C. Vegetarians should be encouraged to eat foods high in iron, such as, tofu, beans, lentils, spinach, whole wheat breads, peas, dried apricots, prunes and raisins. Foods or medications that interact or inhibit iron absorption include:

- anticonvulsants
- sulphonamides
- medications that raise gastric pH e.g. antacids (avoid where possible)
- Dietary inhibitors may include:
  - calcium in dairy products e.g. cheese
  - tea and coffee
  - chocolate
  - spinach and beetroot
  - soy products
  - phytates (salts found in plants capable of forming insoluble complexes with iron) e.g. bran, cereal.

Non-haem iron requires an acidic pH to be reduced to ferrous for gut absorption. A gap of 2 hours from dietary or medication inhibitors of iron absorption appears to be sufficient to avoid the problem.

**Side-effects of oral medications and management**

When oral liquid iron is used it should be diluted with water and a straw used to prevent discolouration of the teeth. However, liquid iron supplements should be checked for the content of elemental iron. Side-effects of oral iron supplements include nausea, epigastric pain, constipation and black discolouration of the faeces. Management for side effects include:

- nausea and epigastric discomfort – take iron tablets on an empty stomach 1 hour prior to or 2 hours after a meal, commence tablets on a low dosage and then gradually increase the amount or iron, or take small doses more frequently.
- constipation – see Clinical Guideline Minor symptoms or disorders in pregnancy.

**ANAEMIA AND HAEMOGLOBINOPATHIES**

See Clinical Guideline Haemoglobinopathies Screening and Referral

**ANAEMIA AND VITAMIN B₁₂ DEFICIENCY**

Vitamin B₁₂ deficiency is uncommon in pregnancy as it is often associated with infertility. As it is required for synthesis of new DNA the demand in pregnancy increases by up to ten times. It is generally only found in foods of animal origin, therefore deficiency is more likely to occur in women who are vegetarians’ or vegans. These women are recommended to take supplementation during pregnancy. If deficiency is not treated in pregnancy it can lead to neurological sequelae in exclusively breastfed infants. Management:

1. Women who follow a vegetarian diet should have their vitamin B₁₂ levels checked in early pregnancy.
2. Women who are vegetarians are recommended to have vitamin B₁₂ supplements during pregnancy and lactation. Malabsorption problems can also lead to deficiency in vitamin B₁₂.
3. Treatment for vitamin B₁₂ deficiency is intramuscular Cobalamin 1000mcg daily for 1 week followed by Cobalamin 1000mcg of monthly injections. In strict vegans, it is recommended 3 monthly injections of Cobalamin 1000 mcg be administered.¹¹

4. Neonatal review should be arranged prior to discharge if a mother is diagnosed with Vitamin B₁₂ deficiency in pregnancy.

ANAEMIA AND FOLATE DEFICIENCY

Folate is required for DNA synthesis so demand increases by up to ten times in pregnancy. Deficiency can develop rapidly as stores are minimal.¹¹ Deficiency in folate can cause megaloblastic anaemia which is found in 5% of pregnancies. Anaemia is more likely to be found later in pregnancy due to the rapidly growing fetus, and primarily occurs as a result of reduced dietary intake or poor absorption.¹² ¹³ The recommended dietary allowance in pregnancy is 600µg/day, and most commonly prescribed prenatal vitamins contain 800µg which is more than the recommended dose. Meat is not a good source for folate, however folate can be found in green leafy vegetables, legumes and orange juice.¹¹

MANAGEMENT

Women at risk of folate deficiency (e.g. multiple pregnancy, haemolytic anaemia) should take 5 mg of folic acid throughout the pregnancy.²⁰

OTHER CAUSES OF ANAEMIA

Microangiopathic anaemia can be seen in pregnancy conditions such as preeclampsia, eclampsia, HELLP syndrome, and with thrombotic thrombocytopenia purpurae. Autoimmune haemolytic anaemia occurs up to four times more frequently in pregnancy.¹¹ Other causes of anaemia in pregnancy include malaria, hookworm infections and HIV.¹⁴

REFERENCES

4. Reveiz L, Gyte GMI, Cuervo LG. Treatments for iron-deficiency anaemia in pregnancy. The Cochrane Database of Systematic reviews. 2007(2).


Hb and ferritin levels | Immediate action | Review blood tests | Additional instructions
---|---|---|---
**1st Trimester**
Hb > 110 g/l & ferritin > 30 mcg/l | Continue iron rich diet | Routine follow up | Routine ANC
Hb > 110 g/l & ferritin ≤ 30 mcg/l | 65mg elemental iron O.D. Iron rich diet | Hb & ferritin 28/40 | Hb ↑ continue Fe. Hb ↔ review diet, Fe (type/dose). Recheck bloods 4/52 following review
Hb 70 and ≤ 110 g/l & ferritin ≤ 30 mcg/l | 100mg elemental iron O.D. Iron rich diet | Hb & ferritin 28/40 | Hb ↑ continue Fe. Hb ↔ review diet, Fe (type/dose), exclude/treat folate, B12 deficiency. Recheck bloods 4/52 following review
**2nd Trimester**
Hb > 110 g/l & ferritin > 30 mcg/l | Continue iron rich diet | Routine follow up | Routine ANC and follow up
Hb > 105 g/l & ferritin ≤ 30 mcg/l | 65mg elemental iron O.D. Iron rich diet | Hb & ferritin after 4/52 | Hb ↑ continue Fe. Hb ↔ review diet, Fe (type/dose), exclude/treat folate, B12 deficiency. Recheck 2/52 following review
Hb > 70 and ≤ 105 g/l & ferritin 30 ≤ mcg/l | 100mg elemental iron B.D. Iron rich diet | Hb & ferritin after 4/52 | Hb ↑ continue Fe. Hb ↔ review diet, Fe (type/ dose) and exclude/treat folate, B12 deficiency. Recheck 2/52. following review Refer to CNC PBM for IV Fe if no improvement
**3rd Trimester**
Hb > 110 g/l & ferritin > 30 mcg/l | Continue iron rich diet | Routine follow up | Routine ANC
Hb > 110 g/l & ferritin ≤ 30 mcg/l* | 65 -100mg elemental iron O.D.* Iron rich diet | Hb & ferritin after 2/52 | Hb ↑ continue Fe. Hb ↔ review diet, Fe (type/dose) exclude/treat folate, B12 deficiency. Recheck 2/52 following review.
Hb > 70 and ≤ 110 g/l & ferritin ≤ 30 mcg/l | 100mg elemental iron B.D. Iron rich diet | Hb & ferritin after 2/52 | Hb ↑ continue Fe. Hb ↔ review diet, Fe (type/dose), exclude folate, B12 deficiency (treat as required). Refer to CNC PBM for IV Fe if no improvement
**Any stage**
Hb ≤ 70 g/l | 100mg elemental iron O.D. Urgent referral to Haematologist KEMH | Ensure following blood tests undertaken prior to referral to Haematology Full blood picture, iron studies, coagulation screen, biochemical profile, folates and B12 levels. Haemoglobinopathy screen (high risk populations)

*Denotes patients considered high risk of iron depletion or in whom tolerance levels for anaemia should be raised and includes: Twin pregnancy, refusal blood components, teenage pregnancy, presence of co-morbidities, history of anaemia, bleeding disorders, planned home birth, poor compliance to ANC, malabsorption, thrombocytopenia