Anaemia in Pregnancy

Introduction

The normal physiological change of an increase in plasma volume causes haemodilution in a pregnant woman. Although the red cell mass increases, plasma volume increases disproportionately, resulting in a lowering of the haemoglobin (Hb) to approximately 115 g/L.

The National Institute for Health and Care Excellence (NICE) advises that women should be offered screening for anaemia at booking and at 28 weeks of gestation.\(^1\) Anaemia is defined as an Hb level <110 g/L at booking; haemodilution will result in further drops during pregnancy and subsequent reduction in oxygen-carrying capacity. In the second and third trimesters the diagnostic level for anaemia is an Hb level of <105 g/L. Postpartum the diagnostic level is 100 g/L.\(^2\)

Aetiology

**Iron-deficiency anaemia** accounts for the majority of cases of anaemia that are identified and is characterised by low mean cell volume (MCV). It is usually caused by nutritional deficiency or low iron stores resulting from previous pregnancy or previous heavy menstrual blood loss. Physiological requirements for iron in pregnancy are three times higher than in non-pregnant menstruating women and iron requirement increases as pregnancy advances.

**Less common causes**

- Folic acid deficiency.
- Sickle cell disease.
- Haemoglobin sickle-C (HbSC).
- Beta thalassaemia (more common in patients from Southeast Asia, Southern Europe and Africa).
- Vitamin B12 deficiency.
- Chronic haemolysis (hereditary spherocytosis).
- Paroxysmal nocturnal haemoglobinuria.
- Leukaemia.
- Gastrointestinal bleeding.
- Coeliac disease.
- Parasitic diseases (e.g., hookworm, schistosomiasis).

Epidemiology

Anaemia in pregnancy is a common problem. In the UK, prevalence is estimated to be 24.4% antenatally.\(^3\) Nearly a third of women are anaemic postpartum. Worldwide prevalence of anaemia in pregnancy is estimated to be around 38% (compared to 29% of non-pregnant women).\(^4\)

Presentation

Anaemia in pregnancy may be asymptomatic. However, the following symptoms are most common:

- Fatigue
- Dyspnœa
- Dizziness

The patient may appear pale.
Investigations

- Hb.
- MCV: if ≤76 fl then the probable cause is iron deficiency but, if lower than concomitant with other signs of anaemia and a raised red blood cell count, this suggests possible B2-thalassaemia (estimate HbA2 and use Hb electrophoresis).
- Normal MCV (76-96 fl) with low Hb is typical of pregnancy.
- Ferritin is not required as a routine test. A two-week trial of oral iron with a subsequent improvement in Hb level confirms the diagnosis of iron deficiency. However, it should be checked in women with haemoglobinopathy or where the cause is in doubt.

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Management\[2\]

Routine iron replacement in pregnancy is not recommended in the UK.

- Women with known haemoglobinopathy should have serum ferritin checked and be offered oral supplements if their ferritin level is low (<30 μg/L).
- Women with unknown haemoglobinopathy status with a normocytic or microcytic anaemia, should start a trial of oral iron and haemoglobinopathy screening should be offered.
- Non-anaemic women at increased risk of iron deficiency should have a serum ferritin checked early in pregnancy and be offered oral supplements if ferritin is low.
- Women with established iron-deficiency anaemia should be given 100-200 mg elemental iron daily. They should be advised on correct administration to optimise absorption. (Avoid taking iron tablets or iron-rich food with substances which inhibit its absorption, such as tea, coffee, and foods rich in calcium. Vitamin C enhances absorption.) Supplementation should continue for at least three months and at least six weeks postpartum and should aim to restore iron stores.
- The Cochrane review comments that although iron therapy restores indices to normal, data on outcomes are scarce and gastrointestinal side-effects are common. [5]
- Referral to a haematologist should be considered if there are significant symptoms and/or severe anaemia (Hb<70 g/L) or late gestation (>34 weeks) or if there is failure to respond to a trial of oral iron.

Thalassaemias

- Inherited blood disorders with reduced or absent production of alpha or beta chains of the globin content of haemoglobin (Hb).
- Women who are carriers of thalassaemia may be asymptomatic when not pregnant but more anaemic than usual during pregnancy.
- MCV ≤80 fl requires investigation, with an HbA2 ≥3.5% being positive for B2-thalassaemia.
- In these cases, the father of the child should be tested and the couple offered genetic counselling.
- Chorionic villus sampling in the first quarter of pregnancy and fetal cord blood sampling under ultrasound guidance in the second quarter can be used to detect B2-thalassaemia major, and termination of pregnancy offered.
- Women with known thalassaemia should have specialist antenatal care, high-dose folate (5 mg per day), frequent ultrasound scans, regular Hb monitoring and transfusions. [6]

See the separate Thalassaemia article for more detail.

Sickle cell anaemia\[7\]

- Genetic defect causes production of abnormal Hb with a red blood cell life of ≤15 days. In a sickle cell crisis, red blood cell destruction causes severe haemolytic anaemia and bone pain. The most common form is haemoglobin S but this mainly affects people from East and West Africa.
- Where suspected, women should receive folate supplementation of 5 mg per day. FBC should be routinely checked at 20, 28 and 32 weeks.
- Iron supplements are not needed unless serum iron and ferritin levels are reduced. If given routinely, iron supplementation causes iron overload leading to haemochromatosis.
- If Hb falls below 60 g/L, or there is a fall of 20 g/L from baseline, a transfusion is considered.
- Use of regular prophylactic transfusions is not recommended.
Give prophylactic antibiotics through pregnancy and afterwards. If a crisis occurs, heparin should be given. Measure Hb every two hours and, if it falls ≥20 g, give exchange transfusion. One study reported significant adverse effects of transfusion in pregnancy patients with multiple red cell antibodies and advised using such treatment with caution. Other measures tried in sickle crisis include steroids, fluid replacement therapy and oxygen but there is a lack of RCTs.

Complications of sickle cell anaemia in pregnancy

- Spontaneous abortion can occur in up to 25% of women affected by sickle cell anaemia with 15% approximate perinatal mortality also often associated with preterm delivery and low birth weight (30% ≤2500 g).
- Stillbirth rates of 8-10% have been seen and thorough antenatal fetal testing is required to assess growth, including ultrasound of the umbilical artery.
- Sickle cell crisis, stroke and pulmonary embolism are further complications which may occur.
- Frequent urinary tract infections are common and require prompt treatment.
- Pregnancy-associated hypertension is also thought to be more common.

Complications

Women with anaemia in pregnancy have been shown to have a higher risk of:

- Maternal death.
- Fetal death.
- Premature delivery.
- Low birth-weight babies.
- Cardiac failure.
- Their babies having subsequent developmental problems.
- Poor work capacity/performance.
- Susceptibility to infection.

However, the threshold at which these complications arise remains unclear.

Prevention

A number of studies have looked at the value of widespread routine use of prenatal iron. Some have found a positive effect on birth weight and other outcomes. Others point to the potential adverse effects of iron supplementation in women with normal levels (placental insufficiency, haemochromatosis, side-effects, accidental poisoning of children in the household, cost, etc). The most recent Cochrane review advises further work is needed regarding the safest dose and regimen before this can be recommended.

Further reading & references

1. Antenatal care - uncomplicated pregnancy; NICE CKS, March 2011 (UK access only)
2. UK Guidelines on the management of iron deficiency in pregnancy; British Committee for Standards in Haematology (July 2011)
6. Management of Beta Thalassaemia in Pregnancy; Royal College of Obstetricians and Gynaecologists (Mar 2014)
7. Management of Sickle Cell Disease in Pregnancy; Royal College of Obstetricians and Gynaecologists (August 2011)

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