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AMPATH LAB UPDATE

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Iron deficiency in pregnancy

SUMMARY

- An estimated 30% of women of reproductive age and 40% of pregnant women have anaemia, the major cause being iron deficiency due to low iron stores.
- Many women have iron deficiency (ID) without anaemia that may lead to iron deficiency anaemia (IDA) during pregnancy.
- No specific clinical characteristics can be used to distinguish between physiologic anaemia and IDA; the former is a diagnosis of exclusion and ID is common.
- All anaemic pregnant women should be evaluated for ID. For most of these women, iron status can be assessed with a serum ferritin level, with selected individuals requiring transferrin saturation (full iron studies).
- High-risk patients should be screened for ID regardless of the haemoglobin (Hb) level.
- All women with iron deficiency should be treated, regardless of the Hb level.
- Based on current available evidence, Ampath Laboratories will be implementing a ferritin level of < 30 ng/ml with a sensitivity of 90% and a specificity of 85% for defining ID in pregnant women.

The World Health Organization (WHO) and the American College of Obstetricians and Gynecologists (ACOG) define anaemia in pregnancy based on the haemoglobin (Hb) concentration as follows:

- First trimester: Hb < 11 g/dl
- Second trimester: Hb < 10.5 g/dl
- Third trimester: Hb < 10.5–11 g/dl
- Postpartum: Hb < 10 g/dl

It is estimated that 30% of women of reproductive age have anaemia. Among pregnant women, the prevalence is even higher with the WHO estimating that over 40% of pregnant women globally have anaemia. The major cause of anaemia in reproductive-age women is due to low or absent iron stores (i.e. micronutrient deficiency), making iron deficiency anaemia (IDA) the most common anaemia globally.

In addition to IDA, a large number of pregnant women have iron deficiency (ID) without anaemia (i.e. low iron stores that have not yet caused anaemia). Some studies estimate it to occur in 30–60% of these women. IDA is the second-most common cause of anaemia in pregnancy after physiological anaemia (which is not a pathological condition).

The factors that contribute to iron deficiency during pregnancy include:

- Insufficient dietary intake.
- Blood losses from previous pregnancies, menstruation or short inter-pregnancy intervals.
- Increased iron requirement during pregnancy due to expanding maternal blood volume, fetal red blood cell (RBC) production and fetal-placental growth.
- Underlying conditions precluding iron intake or absorption such as nausea and vomiting in pregnancy, and inflammatory bowel disease.

IDA in pregnancy is associated with a number of adverse health consequences for both women and their children:

- The maternal risk for mortality secondary to haemorrhage and sepsis is increased.
- Chronic fetal exposure to ID leads to low birth weight and doubles the risk of preterm delivery.
- Long-term impairment in cognitive development and growth in babies exposed to IDA in utero.

Screening for iron deficiency in pregnancy

Opinions vary between screening non-anaemic patients for ID versus testing for ID in anaemic patients. However, there is general consensus for screening all pregnant women who are at high risk for ID. This includes pregnant women who have one or more of the following conditions:

- Previous diagnosis of ID
- Diabetes mellitus (DM)
- Smoking
- HIV infection
- Inflammatory bowel disease
- Multiparity
- History of abnormal uterine bleeding
- Obesity or underweight
- Vegetarian diet

A serum ferritin level is generally sufficient for screening. Some women with ID may have a serum ferritin within the normal range, and may require testing of transferrin saturation to confirm ID. Therefore, it may be prudent to add iron studies to the ferritin test. This is especially true for patients with active inflammation, which can increase ferritin into the normal range, as it is an acute phase reactant.

Choosing a ferritin threshold based on consensus methods is challenging, as agreement between international experts on ID in pregnancy does not currently exist.

The most frequently cited study for a choice of a serum ferritin threshold in diagnosing ID in pregnancy, published in the *British Journal of Haematology* (Van den Broek et al., 1998), showed that, when bone marrow aspirate samples on 93 pregnant women were compared with serum ferritin levels, a ferritin level of <30 ng/ml had a sensitivity of 90% and a specificity of 85% in identifying individuals with absent iron stores on bone marrow staining.

This study continues to be referenced as a benchmark for defining ID, and is used as a method of justifying a serum ferritin threshold of <30 ng/ml for defining ID in studies of iron intervention and in national pregnancy guidelines. This ferritin threshold level is also widely used in practice by obstetricians and haematologists in the UK.

Other known markers of iron status, such as soluble transferrin receptor and hepcidin, are not routinely used.

Evaluation of iron status in anaemia in pregnancy

- Pregnant women presenting with anaemia should be investigated for the cause based on the clinical history, Red Blood Cell (RBC) indices and other findings on the full blood count. Physiological anaemia is a diagnosis of exclusion and other common causes like IDA should be eliminated first.

- All pregnant women with anaemia should be tested for ID as it is the most common cause. Microcytosis may be present, but is a late finding in ID and may also be found in thalassaemia. The absence of microcytosis does not eliminate the possibility of ID nor does the presence of microcytosis confirm it.

- When testing for ID, most women without comorbidities are initially investigated with a serum ferritin level alone. If it is low (<30 ng/ml), this is sufficient evidence to confirm ID; while levels >30 ng/ml are sufficient to eliminate the possibility of ID in the majority of cases.

  Borderline levels of serum ferritin may be in the range of 30–40 ng/ml with chronic illnesses such as DM, or up to 100 ng/ml with chronic kidney disease or active collagen vascular diseases such as systemic lupus erythematosus and rheumatoid arthritis (ferritin is an acute phase reactant). Some pregnancies will have evidence of an acute phase response, even in the absence of chronic illness.

- Borderline ferritin levels should prompt testing with a full iron profile (ferritin, serum iron, transferrin and transferrin saturation).

- A transferrin saturation <20% is considered evidence of ID irrespective of the ferritin concentration. This practice is consistent with other sources that cite values <16% without inflammation, and <20% with inflammation, as ID. The rationale is that a normal ferritin level may represent an elevation into the normal range due to inflammation.

- Iron supplements can falsely elevate transferrin saturation (making it appear within the normal range) by raising the serum iron level, an effect that peaks approximately four hours after an oral iron dose. This interference is best avoided by doing iron studies after an overnight fast or avoiding iron-containing foods or supplements before the test.

When requesting a serum ferritin or iron study on a pregnant patient, kindly ensure that the correct Ampath mnemonic is used as follows:

- **Ferritin (Pregnancy) – FERP**
- **Iron studies (Pregnancy profile) – FEPP**

References

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