Ferritin and Iron Deficiency in Pregnancy
Knowns and Unknowns

Fact Sheet.

There is a great deal of controversy about iron deficiency in the absence of anaemia during pregnancy. In this fact sheet we briefly summarise the evidence and highlight the considerable gaps in knowledge.
All diseases need a clear and consistent definition that is understood by clinicians. This enables the disease prevalence to be accurately measured, the load of disease calculated, and the success and safety of treatments studied.
Our PANDA prevention trial is testing the effect of oral iron in all women without anaemia (low haemoglobin). A different approach would be to use a ferritin cut-off. However, if is far from clear what threshold level of ferritin should be applied.

Iron Deficiency and use of Ferritin as a threshold.

Guidance from organisations around the world varies and many research studies have recommended a range of thresholds for ferritin, from 12μg/L, 15μg/L, 20μg/L, 25μg/L and 30μg/L. Because of the high level of uncertainty around serum ferritin, some studies have used multiples of biomarkers (Haemoglobin, TSAT, Hct, MCV and sTfR) in various combinations. In addition, and in recognition of the changing plasma volume during pregnancy, some these biomarkers, ferritin included, need to be adjusted for the period of gestation, which adds a further layer of complexity. This uncertainty means that there is no agreed way of defining iron deficiency using ferritin, and/or other biomarkers. Therefore, the evidence for recommending a threshold of ferritin carries a large potential for error.

What is the prevalence of ID in pregnancy?

The uncertainty and lack or precision around the definition of iron deficiency makes it very difficult to determine how many pregnant women are affected at any one time (the prevalence). A review of the literature found the quoted prevalences to range from 1.6% to 71.0% of pregnancies, with many estimates in between demonstrating a large degree of inconsistency.

Have researchers tried to measure the effect of ID on adverse perinatal outcomes?

The short answer is yes. But you will have worked out by now that this too, is difficult to answer. Overall, there is no evidence from prospective studies that pregnant women with "iron deficiency" fair worse than women who are iron replete. Adjusted odds ratios for preterm birth, stillbirth, and small for gestational age are shown below:

Preterm birth (<37 weeks gestation)	aOR 0.9 (ci 0.6-1.4)
Stillbirth	aOR 4.0 (ci 1.0–14.3)
Small for gestational age	aOR 0.8 (ci 0.5–1.2)

There are no statistically significant differences

What has been learned about the topic from the PANDA programme to date?

We examined iron biomarkers measured in our pilot trial (Workstream 2). The results showed that serum ferritin, along with haemoglobin fall across gestation. This fall is evident in the first trimester. We found that the only biomarker with potential to discriminate between iron deficiency and iron replete pregnant women is the soluble transferrin receptor (sTfR). But this test is not widely used and much more research is required before it can be recommended.

In the absence of clear evidence on iron deficiency what can be done?

We know that iron deficiency anaemia (IDA) is common in pregnancy and associated with adverse outcomes, stillbirth, preterm birth, fetal growth failure, and postpartum haemorrhage, to name a few. So, if we can prevent IDA in pregnancy, it might potentially reduce the disease burden for a great many mothers and babies. It is our view that rather than wait for more research on iron deficiency (ID) without anaemia, which will clearly take a long time, it is easier to discover, if by preventing anaemia we can improve outcomes for all pregnant women now. But this must be done safely, as giving iron to all pregnant women from the first trimester onwards, is a large under-taking. This is why we devised the PANDA programme, which as you know is now in the trial phase.

We hope that you found this information useful but if you have further questions, please contact the team. Thank you for participating in PANDA.

Bibliography

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