Maternal iron supplementation: one size does not fit all

Anaemia is the most common nutritional deficiency worldwide. The prevalence of anaemia in non-pregnant and pregnant African women (47.5% versus 57.1%) and Southeast Asian women (45.7% versus 48.2%) suggests that majority of reproductive age women at risk for anaemia reside in these countries. Anaemia in pregnant women from developing countries remains as a major public health concern despite a few decades of efforts through special policies and national programmes.

In developing countries, anaemia is attributed primarily to iron deficiency (~50%); however, other concurrent micronutrient deficiencies of vitamin A, folic acid, vitamin B12, copper, and riboflavin can increase the risk of anaemia. Diets of pregnant women in these countries are less diverse with poor access to animal sources of food to meet the increased nutrient requirements of growing maternal and foetal tissues. Further, parasitic infections, acute and chronic infections, diseases that influence the absorption and metabolism of nutrients, and haemoglobinopathies can cause low haemoglobin status (i.e., haemoglobin concentration <110, <105 and <110 g/l in the first, second and third trimesters of pregnancy respectively) or anaemia. The dual burden of undernourished and overweight/obese women adds a different dimension to the challenge of managing anaemia in these countries.

Given the multifactorial etiology of anaemia, to diagnose iron deficiency anaemia (IDA), pregnant women should be screened using a combination of hematological indices such as haemoglobin and serum ferritin. In certain developing countries, often due to lack of resources and local laboratory facilities, women are less routinely screened for anaemia, or not at all. In areas where laboratory facilities are available, women are screened for any anaemia using only haemoglobin
as a marker. A low haemoglobin status is commonly attributed to IDA without further biochemical evaluations in these settings. On the contrary, haemoglobin is a less specific marker of IDA because iron deficiency can exist in women without overt anaemia and a low haemoglobin status together with low serum ferritin (<15 µg/l) is indicative of IDA.\(^2\)

Supplementation of pregnant women with daily iron and folic acid (IFA) tablets is the most common and cost-effective strategy implemented to combat anaemia in developing countries. Certainly, the use of supplements benefits women with iron deficiency, especially those with less access to animal sources of food or women who are less likely to use animal foods. Because anaemia can occur in pregnant women due to reasons other than iron deficiency, it is important to consider whether women without anaemia, even more specifically IDA, need daily high-dose IFA (i.e. elemental iron ≥60 mg and ≥500 µg folic acid) supplementation. Instead, it might be more prudent to have intermittent use of IFA tablets for pregnant women as a prophylactic measure from likely subclinical iron deficiency as this approach is better tolerated and accepted with less adverse effects.\(^3\) Furthermore, daily high-dose IFA supplementation should be restricted only to pregnant women diagnosed with IDA for a specific period followed by periodic evaluation.

Intake of iron >45 mg/day in adults, the tolerable upper intake limit, has been reported to cause gastrointestinal disturbances such as constipation, diarrhoea, nausea and vomiting.\(^4\) Studies indicate that excess iron intakes in pregnant women adversely influence maternal and infant outcomes. Implications of excess maternal supplemental iron intake include a higher risk for gestational hypertension in women supplemented with 50 mg iron compared to non-iron-supplemented women,\(^5\) and increased risk for gestational diabetes;\(^6\) both these conditions increase the risk of complications in pregnancy. On the other hand, excess maternal iron intakes influence foetal and infant growth and health. In Indian non-anæmic women, >39.2 mg/day of supplemental iron intake was associated with higher risk for low birth weight at the term (adjusted risk ratio: 1.89; 95% confidence interval: 1.26, 2.83) compared to intakes ≤36.6 mg/day. Further, Shastri et al.\(^7\) reported inverse correlations between supplemental iron intakes and gestational age \((r = -0.20, \ P < 0.001)\) and birth weight \((r = -0.07, \ P = 0.011)\). In another study,\(^7\) infants of Finnish mothers who were supplemented with 100 mg/day of iron had a higher frequency of hospitalization due to convulsions compared to infants of mothers who were supplemented with iron if the hematocrit was <30%. Ziaei et al.\(^3\) also reported that non-anæmic women (haemoglobin concentration ≥132 g/l) who were supplemented with 50 mg/day supplemental iron compared to non-iron supplemented group had a higher risk of having small for gestational age babies. Collectively, the above studies suggest the deleterious effects of excess iron intakes during pregnancy, predominantly from supplements. More studies are needed to develop evidence-based guidelines to reconsider the existing policy of universal IFA supplementation of pregnant women in developing countries and to identify a safe dose of supplemental iron intake for optimum gestational outcomes.

Given the risk of excess iron intakes in pregnancy on maternal and infant outcomes, the following scenarios need special attention: first, in countries where pregnant women are exposed to multiple micronutrient-enriched or fortified foods, including iron; secondly, when pregnant women use daily high-dose IFA supplements without frequent screening and evaluations and finally, when pregnant women use multiple iron-containing supplements from national programmes as well as those purchased from local pharmacies or other outlets. Before private practitioners prescribe dietary or medicinal supplements, they should verify if pregnant women are using the supplements distributed through national anaemia control programmes as a part of their antenatal care.

In conclusion, emerging evidence emphasizes the need to personalize IFA supplementation of pregnant women based on their iron status. In developing countries where national programmes distribute IFA tablets as a part of their routine antenatal care with higher than the WHO recommended dose of iron (i.e. >60 mg/day), there should be options of low-dose supplements for pregnant women. Above all, adequate counselling to educate women and health professionals about the appropriate use of gestational supplements dispensed during antenatal care in terms of the frequency of use, dose and adverse effects would be useful to prevent excess iron intake.


KAVITHA C. S. MENON\(^3\)*
SHEILA A. SKEAFF\(^1\)
SANJAY ZODPEY\(^2\)

\(^3\)Department of Human Nutrition, University of Otago, Dunedin, New Zealand
\(^4\)Public Health Foundation of India, Gurgaon 122 002, India
\(*\)e-mail: kavitha.menon3@gmail.com