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Commentary

Prevention & management of anaemia in pregnancy: Multi-pronged integrated interventions may pay rich dividends

Anaemia in pregnancy is a major public health problem across the globe[1,2]. India is the home of the largest number of anaemic pregnant women as well as mother-child dyads suffering from adverse health consequences of anaemia in pregnancy[3,4]. Anaemia is widely seen in India across all age groups because of inadequate iron and folate intake due to low vegetable consumption (not readily available, affordable and not tasty) and low flesh food consumption (cannot afford economically or ecologically); and poor bioavailability of dietary iron from the fibre, phytate rich Indian diets; but this should not be altered as plant-based diets are currently promoted as the sustainable diets which protect from cardiovascular diseases (CVD) and cancer.

Anaemia in pregnancy is associated with functional decompensations including immune depression, increased susceptibility to infections, low birth weight, high maternal morbidity and mortality[3]. It is estimated that in India, 20 per cent of maternal deaths are directly due to anaemia and in another 20 per cent anaemia was a contributory factor. Therefore, anaemia prevention and management has received high priority as a part of the antenatal care and ongoing national iron folic acid supplementation programmes[3].

Studies have reported that in Indian pregnant women prevalence of iron and folate deficiencies were high[5]. In 1973, India initiated the iron folic acid (IFA) supplementation (60 mg elemental iron and 500 µg of folic acid) to all pregnant women to combat these deficiencies[6]. Studies carried out in the 1970s showed that haemoglobin (Hb) response to supervised administration of iron at doses of 60, 120 and 240 mg daily to pregnant women was similar[7]. Increasing the dose of iron beyond 60 mg did not bring about commensurate increase in the amount of iron absorbed because higher iron doses resulted in increase in hepcidin and reduction in the absorption of iron[8,9].

One major reason for the suboptimal reduction in the prevalence of anaemia is the low compliance and continuation rates with IFA supplementation[3,4]. This is partly due to minor but troublesome gastrointestinal side effects associated with iron supplementation. Studies have shown that in the first fortnight of use 30 per cent of women taking 60 mg of iron and 40 per cent of those taking 120 mg of iron after a meal had side effects[10]. The small increase in side effects with 120 mg iron was not statistically significant; discontinuation rates were similar among those who took 60 or 120 mg daily[10]. In an effort to minimise side effects, obstetricians recommend that iron supplementation may be taken in two divided doses after two meals. The supplementation of 60 mg of iron twice daily resulted in a higher serum hepcidin concentration and reduction in iron absorption as compared to daily single supplementation of 120 mg of iron. It is therefore recommended that 120 mg of iron preparations for treatment of mild anaemia should be given as a single dose after a meal[11].

The study by Tekur *et al*[12] published in this issue reports the results of a randomized, parallel, open-label trial on the efficacy and safety of iron polymaltose complex (IPC), ferrous ascorbate (FeA) and FS for treatment of anaemia in pregnancy. Data from the study showed that the efficacy of ferrous sulphate (FS), IPC and FeA were comparable. The number of patients with side effects were 31 (62%), 23 (46%) and 21 (42%) from FS group, IPC group and FeA group, respectively. Gastrointestinal side effects were high with all the three preparations but side effects were marginally lower with IPC and FeA. In India, where 30 million pregnant women require IFA supplementation, any change over to a preparation with marginally lower side effects but which is ten times more costly cannot be recommended.

In view of the reported high prevalence of folate deficiency in anaemic pregnant women in the

seventies[5], it was recommended that along with 60 mg of elemental iron 500 µg of folic acid should be given to all pregnant women[6]. However, this recommendation was not always adhered to. Tekur *et al*[12] supplemented 550 µg, 1500 µg and 5000 µg of folic acid in the three study groups. In the last two decades, there have been Indian reports suggesting that prevalence of folate deficiency was relatively low and that vitamin B12 deficiency was high[13,14]. So, it is important to adhere to the recommendations regarding the dose of folic acid supplementation among pregnant women to prevent adverse health consequences associated with folate supplementation in women who are folate sufficient but vitamin B12 deficient.

A third of pregnant women taking IFA supplementation do experience side effects. Despite this, compliance and continuation rates with iron supplementation in pregnancy is higher as compared to the iron supplementation in non-pregnant women, school or pre-school children because pregnancy is a clearly defined short period and pregnant women know that maternal anaemia is associated with higher maternal morbidity, lower birth weight and higher infant mortality. Also, IFA supplementation has been an integral component of antenatal care; women do get reassured by medical and paramedical staff in the antenatal clinic as and when they had side effects, and lastly women will do whatever they can to improve the health of their offspring.

As a long-term strategy, the WHO had advocated IFA supplementation to women in reproductive age groups so that there is improvement in Hb status of women prior to pregnancy, however, the coverage and compliance with either of these two regimens of supplementation is low[15,16]. Also, the programme costs are high because such persons have to be traced and provided with the supplement and their response monitored[15].

India has periodically reviewed the data from programme evaluations and research studies to evolve and improve the national programme to combat anaemia in pregnancy[3,4]. India was the first developing country to initiate National Nutritional Anaemia Prophylaxis Programme in 1973, providing 60 mg of elemental iron and 500 µg of folic acid to all pregnant women[6]. In the initial decade, coverage and compliance of IFA supplements were low because of lack of healthcare infrastructure and low utilisation of available antenatal care services. Data from ICMR task force study showed that even those who consumed 90 tablets of IFA did not show an improvement in Hb status[17]. Assuming that this might be due to inadequate dosage associated with low bioavailability of iron, the dose of iron was increased to 100 mg[18]. In addition, the National Anaemia Control Programme added the test, detect and treat strategy for the management of anaemia in pregnant women in all settings[18,19]. The tenth five-year plan reiterated the importance of universal screening of pregnant women for anaemia and providing appropriate management depending on the severity of anaemia and time available for treatment[20]. This strategy has been reiterated in the National Iron Plus Initiative[21]. However even now, screening for anaemia has not been operationalized.

The Intensified National Iron Plus Initiative under POSHAN Abhiyyan[22] has recommended in addition to implementation of the NIPI guidelines, improving iron and folate intake by dietary diversification with increased vegetables intake and use of iron fortified iodised salt.

Low vegetable consumption resulting in low iron and folate intake is one of the major causes of anaemia[23].

The Indian estimated average requirement (EAR) for iron (ranging from 11 mg in men, to 21 mg in pregnant women) are high because it takes into account the low bioavailability of iron from Indian diets[24]. It is difficult to improve iron intake to meet the EAR through dietary diversification alone. The WHO had advocated food fortification with iron for sustained improvement in Hb levels in countries with low iron intake[25]. Given the widespread iron deficiency in Indians, food fortification offers a ready, relatively inexpensive and sustainable method of increasing the iron intake without altering dietary habits. The use of double fortified salt (DFS) in the daily diet increases iron intake by 10 mg/day; consistent use of DFS has been shown to improve Hb level by 0.5 g/year[26]. Dietary diversification with increased vegetable intake combined with use of iron fortified iodised salt can improve Hb levels by 0.5-0.7 g/yr. The Food Standards and Safety Authority of India has approved two formulations of iron fortified iodised salt (DFS) for use. Centralized production and pre-existing programmes for fortification of salt with iodine offer a ready platform to launch iron-fortified iodised salt. Once the production, distribution and sale of DFS have been scaled up, it might be possible to make DFS mandatory for human consumption, achieve sustained, population-wide increase in the intake

of iodine and iron, and thereby combat both iodine deficiency disorders and anaemia[27]. If this strategy is universalized and sustained for a decade, India can achieve the SDG target for reduction in anaemia in women during reproductive age by adopting the integrated three-pronged strategy of (*i*) increasing iron intake and Hb status of in all members of the family through dietary diversification and use of iron-fortified iodized salt; (*ii*) operationalizing Hb estimation by an accurate method in all pregnant women for early detection of anaemia; and (*iii*) providing IFA medication at appropriate dose to pregnant women and monitoring improvement following therapy.

This can pay rich dividends both in terms of accelerating the pace of reduction in the prevalence of iron-deficiency anaemia in pregnant women and reducing the adverse health consequences of anaemia in the mother child dyad.

***Conflicts of Interest**:* None.

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