"Recognizing the complexity of anaemia in Bangladesh and developing effective strategies through National Consultation"

Webinar: 31 January 2017

Questions which were not able to be addressed in the time allowed:

1. **What is the best method that has been used to evaluate the content of iron in water?**

In Bangladesh two common portable field based devices were used to evaluate the content of iron in water; Colorimeter (HACH DR/890) and Test kit (HACH IR 18B) have been compared with the Atomic Absorption Spectrophotometry considered as the gold standard. Results suggests that the test kit delivers more accurate point -of –use results across a wide range of iron concentrations under challenging field conditions (R Merrill, JHPN 2009).

2. **You report fairly high levels of zinc deficiency in Bangladesh. Is the level of iron in groundwater water high enough to inhibit zinc absorption? Does the high content of iron in ground water interfere with absorption of any other nutrients from the diet? Similarly does arsenic affect the iron biochemistry?**

Theoretically iron and zinc interacts; in aqueous solution iron in high amount may inhibit zinc absorption through the gut lining. However, it is difficult to demonstrate this in a population based study. Some additional analyses were done (personal communication); and despite being a population based study, the NMS data indicated some inhibition of serum zinc by high iron in water; however, it was statistically non- significant. Reason for the non- significant observation perhaps was less number of study subjects who consumed surface water (i.e. proxy for iron- less water). High amount of iron is unlikely to inhibit micronutrients, e.g. zinc in food, because, zinc is laid in the food matrix. However, this may depend on digestion stage of the food. High amount of iron from water might compete with the zinc in aqueous solution (in intestines) to hinder its absorption.

3. **Why are you supporting MNP when the effectiveness of IFA is also good and cost effective?**

In Bangladesh, a number of studies reported multiple micronutrient deficiencies among women of reproductive age and also among pregnant women, specially vitamin B12, vitamin A, zinc and folate. Two study with adequate sample size reported benefits on birth outcomes after MM supplementation compared to IFA supplementation. Unfortunately no study examined the contribution of other haematopoietic micronutrients on anaemia prevalence but theoretically we know that vitamin B12, vitamin A, zinc also has role in erythropoiesis. To address the high prevalence of other micronutrient deficiencies that contribute to anaemia in the country, the Consultation recommended that the Government of Bangladesh consider giving a multiple micronutrient supplement (MMS) to pregnant women (instead of IFAS), still with 30 mg of iron, which also would also reduce adverse pregnancy and birth outcomes of preterm birth, small birth size and still birth as shown by research in Bangladesh. It was recognized that this supplement will cost more than IFAS (although delivery costs will be the same); therefore, the Consultation

recommended that cost-effectiveness be evaluated as a next step in guiding the possible adoption of MMS in Bangladesh.

4. **Is there any study to see the effect of 30 mg iron supplementation on the anaemia status of pregnant women in context of Bangladesh?**

   Until now no study has been conducted to see the effect of 30 mg iron supplementation on anaemia status of pregnant women in the context of Bangladesh. But there is a recommendation that research needs to be done before scale up of low dose iron in IFA supplementation.

5. **What evidence do we have about adverse perinatal outcomes from anaemia in pregnancy from other causes rather than iron deficiency?**

   We don't have evidence in the Bangladeshi population about adverse perinatal outcomes from anaemia in pregnancy from other causes rather than iron deficiency

6. **The NMS 2011-12 presents data on IDA in NPNL women. Do we have national level representative data on IDA among pregnant women in Bangladesh?**

   We don't have national level representative data on IDA among pregnancy. But other studies reported the following:

   - **UNICEF/INFS Study:** Prevalence of anaemia, iron deficiency and IDA in pregnant women living in areas of low iron in ground water were significantly higher compared with that in the pregnant women living in areas of high iron in ground water. Of all subjects, 34.7% had anaemia, 27% had iron deficiency and 13.4% had iron deficiency anaemia Prevalence of IDA among pregnant women living in low ground water iron area is 19.2% and in high ground water iron area is only 7.6%. (Report not published yet)

   - **Prevalence of anemia and micronutrient deficiencies in early pregnancy in rural Bangladesh, the MINIMat trial:** The study was conducted in rural sub-district which is identified as high groung water iron area. Anaemia was present in 28% and Iron deficiency anemia was present in only 2% among women with early pregnancy at around 14 weeks. But anaemia was found in over one-fourth of the women. Anemia with other coexisting micronutrient deficiencies was more prevalent; anemia and zinc deficiency was found in 16%, anemia and vitamin B-12 deficiency in 15% and anemia and folate deficiency in 6%. The most common combination of coexisting micronutrient deficiency was that of zinc and vitamin B-12 that affected 26% of the women with early pregnancy. http://onlinelibrary.wiley.com/doi/10.1111/j.1600-0412.2010.01014.x/epdf?r3_referer=wol&tracking_action=preview_click&show_checkout=1&purchase_referrer=www.google.com&purchase_site_license=LICENSE_DENIED

7. **The iron content in water varies according to the product used in the treatment of the water to make it drinkable. Has there been research that evaluates this?**

This is theoretically correct. In Bangladesh anecdotal experience suggests, in areas where iron in water is high, people are divided in their practice of water treatment. People of some areas use a homemade filtering device (a large earthen pot fitted with cloth on the top) to remove excess iron. Interestingly, people from other areas are habituated, and are just fine with excess iron and do not use filters. Since tube well water (i.e. groundwater) is assumed to be free from germs people do not boil it. Therefore, the temperature effect in relation to boiling (oxidizing ferrous iron to ferric form) is largely ruled out. However, another important factor to consider is how long people keep water to drink after pumping from the well. Here, lot of variations is expected. There is some research available on this. In the Jivita study representative of a district, it was observed that 60% people consumed within 5 minutes of pumping and 75% people drank within 30 minutes (R Merrill Int J Vit Min Res 2012); they adopted such practice in order to avoid metallic taste and smell from the water should they keep water for longer time. The recent INFS/UNICEF study (unpublished) representing 4 sub districts reported that mean concentration of iron in water at the time of pumping was ~3 times the concentration at the storage vessel; however still that lower concentration was many folds higher than the WHO aesthetic limit for iron in water (0.3 mg/l). We do not have a nationwide data on water drinking behavior and storage modalities of ground water; such data would provide better understanding of the issue at the country level. The issue of importance is proportion of ferrous iron at the time of drinking, which if present in a fair amount would likely to replete iron deficient population.

8. **Individuals with thalassemia absorb iron more efficiently than the general population. To what extent does thalassemia mitigate the risk of iron deficiency? Conversely, with iron fortification (or widespread supplementation), is there increased risk exposure of iron overload in the thalassemic subpopulation?**

Absolutely true. Even the minor form of thalassemia is associated with increased absorption of iron (due to imbalance with hepcidin mediated regulation) compared to normal population (Rivella et al, Blood 2007); and that's why we can speculate that in Bangladesh where mostly minor forms exist, thalassemia induced iron overload is highly likely. Iron supplementation/fortification in thalassemic people may worsen the iron overload. In Bangladesh to make it further complicated people in high iron areas are likely to get a good amount of iron from water. Hence, combination of thalassemia, high iron area and iron supplementation/fortification is understandable. We do not have nationally representative data on prevalence and area distribution of thalassemia rates. Two recent studies reported prevalence among women between 18-28% in Northern areas (R Merrill APJCN 2012, INFS/UNICEF study 2016, unpublished). This makes controlling population level anemia in the country complicated bearing in mind all those overlapping issues. This complexity may exist in many other countries in the world; Bangladesh is perhaps first in the world to explore anemia along with a new paradigm.

9. **What progress has been made in working with the government to implement these recommendations from the consultation?**

   It is still under discussion with the Government and development partners to design research with low iron containing IFA supplementation and MMS for pregnant women and scale up MNP supplementation for 6-23 months children.

10. **What recommendation has been made from this consultation to prevent other micronutrient deficiencies?**

    Recommendations includes improving dietary diversity through a multi sectoral approach, and also incorporating MNP supplementation for children age 6-23 months as well as exploring the opportunity for MMS for pregnant women

11. **Can you recommend to countries with high rates of anaemia what basic data they should invest in collecting to inform an appropriate anemia control strategy?**

    Bearing in mind the emerging complexities a country with high rates of anemia should invest in collecting data on – dietary intakes, especially the key micronutrient intakes (iron, vitamin A, zinc, folate, B12), animal source vs. plant source micronutrient intakes, status of iron, vitamin A, zinc supplementation/fortification, status of key micronutrient deficiencies (Hemoglobin, iron, vitamin A, zinc, folate, B12), source of drinking water, iron level in groundwater, water drinking habits, infections (worms, malaria, HIV), infection bio-markers, and of course prevalence of hemoglobin disorders (S Rahman, PHN 2016). These data at national level will provide the full picture explaining etiology of anemia and suggest specific interventions.

12. **What are the data gaps remaining? What would you like to still know that you don't know?**

    These are following,

    A) Iron concentration in tube well water is not consistent. It may vary even to the very next well. It might pose challenge in program setup if we decide to provide different doses of micronutrient/Fe preparations by high and low iron areas. However, in the defined "high" iron areas most of the well samples would likely to provide high concentration of iron; similarly in low iron areas most of the samples would likely to provide low concentration. Therefore, at population level unintended effect of different preparations is expected to be minimum if any. Since some mix up is inevitable; ideally it renders the need for the review of the groundwater iron mapping of the country. Having said that, it would be difficult to construct.

    B) Until now we do not know the efficacy of low dose iron/multiple micronutrient preparations in high iron areas in relation to anemia and iron associated adverse effects, e.g. gut microbiota.

C) As underscored earlier, we need a robust nationwide data on prevalence of hemoglobin disorders.

D) We need nationwide data on prevalence of anemia and iron deficiency in pregnant women. Pregnant women are more vulnerable to anemia for physiological reason (i.e. dilution anemia); and high iron level in water and hemoglobin disorder makes the physiology of iron regulation more complex in pregnancy.

13. We see in the 2007 anemia control guidelines, Bangladesh was forward thinking at the time to focus on biofortification efforts. What efforts were underway?

Bio fortification is one of the strategies being laid out in anemia control guidelines and the national micronutrient deficiency control strategy (2015-2023). There are some activities. Some international organizations/NGOs are promoting orange fleshed sweet potato in some parts of the country in order to increase intake of vitamin A. But, data is scarce or unavailable on systematic evaluation of these program activities. Likewise, a few national and international organizations have been working on zinc bio fortification of rice. Some new breeds of zinc bio fortified rice have been developed by national organizations. Others are trying to develop rice enriched with zinc in the kernel. However, data is still lacking on population level efficacy of improved zinc nutrition. The key challenges are acceptability, production, marketing, pricing, cost effectiveness, business management from farmers to consumers- all would determine effectiveness of the strategy.