HEALTHY MOTHERS HEALTHY BABIES

Coffee and Chai Chat
"Expert Insights and Country Perspectives on the Use of Multiple Micronutrient Supplementation (MMS) During Anemia Treatment in Pregnancy"

16 April 2025

Questions raised by the participants

Where can we obtain the MMS TAG guidance on use of MMS during anemia treatment in pregnancy?

The "Interim Guidance for Concurrent Antenatal Multiple Micronutrient Supplementation and Anemia Treatment in Pregnant Women", based on expert opinion of the MMS TAG guidance, can be found here. This guidance is expected to be updated as new evidence becomes available.

Are there any trials assessing the use of only iron (or IFA) supplementation compared to MMS + iron (or IFA) supplementation, in anemia treatment during pregnancy?

We are not aware of trials with this specific design. However, the recommendation for the continued use of MMS during treatment of gestational anemia is based on the fact that:

1. MMS reduces adverse birth outcomes for all pregnant women, with even greater benefits among anemic women (e.g. there is a 29 % risk reduction in 6-month infant mortality among anemic women who receive MMS, compared to anemic women who receive IFA).

2. MMS continues to provide iron (contributing for target level of iron for anemia treatment), while also providing adequate amounts of vitamins A, B2, B6, B9, B12, C, D and E, and the mineral copper, which are needed for synthesis of hemoglobin and/or erythrocyte production.

Other national guidelines recommend the continued use of MMS during anemia treatment. For example, the Clinical Management Guidelines from the American College of Obstetricians and Gynecologists state "Iron deficiency anemia during pregnancy (…) should be treated with iron supplementation in addition to prenatal vitamins".

Dose of iron: is 90 mg (30 from MMS + 60 mg from iron or IFA) enough for anemia treatment?

The WHO's target of 120 mg for anemia treatment is based on scant evidence, and other guidelines recommend less iron than 120mg/day for anemia treatment, such as the 2018 NATA consensus statement. This is a multidisciplinary consensus statement developed by the Network for the Advancement of Patient Blood Management, Haemostasis and Thrombosis (NATA) in collaboration with the International Federation of Gynaecology and Obstetrics (FIGO) and the European Board and College of Obstetrics and Gynaecology (EBCOG), and a co-author from WHO.

This document states that the recommendations are meant for clinicians managing the perinatal care of women in all settings and recommend 80-100 mg of iron/day + folic acid (400 mcg/day) to treat mild to moderate anemia (hemoglobin > 80 g/L). Ultimately, it all depends on the duration of supplementation, e.g. if the treatment to replenish iron stores in mild to moderate anemia requires 5000 mg of iron (500 mg absorbed elemental iron assuming 10% fractional absorption), this could be achieved with 120 mg/day over 42 days or 90 mg/day over 56 days.

In summary, 90 mg of iron is likely enough for the treatment of mild to moderate anemia. For severe anemia, local standard of care should be followed, which may include intravenous iron or blood transfusion.

Does the guidance on use of MMS during anemia treatment vary in the 1st, 2nd and 3rd trimester?

No, it doesn´t vary, in the same way that WHO recommends the same amount of iron for treatment of anemia independently of the trimester.

Inevitably, each clinical case requires the judgment of a qualified healthcare professional, e.g. if a woman is diagnosed for the first time with moderate anemia at 38 weeks of pregnancy, her physician may opt to provide intravenous iron (if available) instead or oral iron supplementation, given the limited time to replenish iron stores before giving birth.

Should MMS and IFA be administered together or separately?

While there is no clear guidance on this topic, we understand that both supplements can be taken together, although countries may decide to take a different approach.

The results from the few studies conducted in pregnant women do not discourage joint supplementation of iron and zinc, because of the lack of negative iron-zinc interaction when given at a ratio of 2:1 or 4:1. If MMS is administered with IFA (providing a total of 90 mg of iron and 15 mg of zinc, at a ratio of 6:1), it is possible that there is a small reduction in zinc absorption, but this is unlikely to be clinically significant given that zinc is being supplied in adequate amounts every day, through MMS. We could also expect an increased iron absorption from the vitamin C provided in MMS. As such, both MMS and IFA can be taken at the same time, if this is expected to be more convenient for the pregnant woman and consequently lead to increased adherence.

If the woman reports increased side effects by taking both supplements together, then she can be encouraged to take both supplements separately.

Are there any risks of taking MMS and IFA for anemia treatment, as both supplements provide a total of 800 mcg of folic acid per day?

Ideally, the additional elemental iron required for anemia treatment should come from iron supplements, instead of IFA. If only IFA is available, it can be used. Despite the increased dose of folic acid (400 mcg from IFA and 400 mcg from MMS), the total amount of this combination does not exceed the tolerable upper intake level of 1000 mcg/day.

Since the potential risks of long-term excessive intake of folic acid in pregnant women are not known, the combination of MMS and iron or IFA should be used until hemoglobin returns to normal levels (≥ 110 g/L), after which MMS only can be resumed.

How should MMS be used in areas with a high prevalence of anemia (over 40%)?

Published MMS TAG analyses showed that MMS with 30 mg of iron has comparable effects to IFA with 60 mg of iron, in terms of preventing third trimester maternal anemia, and this was demonstrated in settings with high baseline anemia (varying between 29 to 47% in 5 trials). Thus, MMS should also be used in settings with high prevalence of anemia, but coupled with strategies to identify and treat anemia, as would be done for preventive IFA programs.

During treatment of severe anemia with intravenous iron, should MMS be continued or discontinued?

MMS does not need to be discontinued in cases where intravenous iron is available and used for the treatment of severe anemia. MMS provides 15 micronutrients to support the health of the pregnant woman and the growth of her baby. MMS should be continued because of the well-known benefits in reducing adverse birth outcomes (such as low birthweight, preterm, small for gestational age births) and other micronutrient deficiencies beyond iron.

Should MMS be used during malaria treatment during pregnancy?

Despite the concern that iron supplementation could exacerbate malaria infection by providing additional iron for the parasites, a recent review describes that iron supplementation combined with malaria prevention and treatment has been shown to be beneficial in improving birth outcomes. In fact, WHO recommends that "In malaria-endemic areas, iron and folic acid supplementation programs should be implemented in conjunction with adequate measures to prevent, diagnose and treat malaria during pregnancy".

Thus, current guidance supports the use of MMS and other iron containing supplements in conjunction with malaria prevention and treatment measures, during pregnancy.

What would you recommend if a woman is receiving BEP supplements?

For anemia prevention:

If a woman is receiving a BEP supplement that is fortified with micronutrients, which already contains the same range and level of micronutrients provided by (UNIMMAP) MMS, there is no need to add MMS to BEP.

For anemia treatment:

Even if the BEP supplement is fortified with micronutrients, the amount of iron provided in BEP is unlikely enough and additional iron supplements are required to treat (iron deficiency) anemia. The total amount of supplemental iron could be in the range of 90 to 120 mg per day for mild to moderate anemia, similarly to what is being proposed to women receiving MMS.

Has any research been carried out after the guideline (on concurrent use of MMS during treatment of gestational anemia) was developed to check the acceptability, feasibility and implementation?

There are no published studies specifically assessing these points, but there is emerging evidence on acceptability and adherence of MMS (not necessarily during anemia treatment).

Could you share more about how health workers were trained on MMS in Indonesia? Was this incorporated into existing training programs or a supplemental training just on MMS? How has the online training experience been?

A dedicated online training module on MMS and anemia was developed and any healthcare worker can apply to do this training, at anytime. In a couple of months, more than 15,000 healthcare workers undertook this training. An improvement in their knowledge was also observed after taking the training.

What are the risks of repackaging a bottle of 180 tablets of MMS in sachets for a monthly supply of 30 tablets? Providing a small amount could be an incentive for women to return to ANC.

The practice of repackaging MMS, e.g. into plastic bags, is not recommended. This practice has adverse effects on the stability of the product (compromising the nutritional value of the product) and increasing the safety risks to the mother (by potentially exposing the product to harmful microorganisms) and their older children, who may have unintended access to MMS if put into plastic bags. In addition, there is no evidence that provision of smaller amounts of MMS tablets (compared to provision of 180 tablets in a single bottle) result in more ANC visits.

Are there any meta-analyses carried out on MMS and pregnancy?

Yes, several meta-analyses have assessed the effect of MMS in comparison to IFA in pregnant women. The two most relevant are a Cochrane review and an individual participant data meta-analysis, demonstrating that MMS reduces the risk of adverse birth outcomes such as preterm birth, stillbirth, low birth weight, and small-for-gestational-age birth.

Is there any evidence on the effect of MMS in maternal outcomes, including anemia rates?

Yes, as mentioned above, published MMS TAG analyses assessed the effect of iron doses in both MMS and IFA on third trimester maternal anemia, hemoglobin and iron deficiency anemia. These meta-analyses showed that, compared to IFA, MMS results in comparable hemoglobin concentration and protection against anemia during pregnancy, independently of iron dose (including the comparison of MMS with 30 mg of iron and IFA with double amount of iron).

Other studies (e.g. conducted in Nepal and Bangladesh) demonstrated that MMS improved maternal micronutrient status and ameliorated deficiencies, while others suggested improvements on maternal cognition.

MMS is a cost-effective intervention; is it affordable and accessible in LMICs?

Yes, MMS is now affordable and accessible in LMICs. It is now available at a similar price to IFA, a little over $0.01 per dose. The UNICEF supply catalogue shows a bottle with 180 MMS tablets costs USD 2.50. Countries can find more information about available funding mechanisms (e.g. Child Nutrition Fund) outlined in the Global Investment Roadmap for MMS.

Are there any MMS products registered by NAFDAC?

While we do not know if there are any MMS products registered in the National Agency for Food and Drug Administration and Control in Nigeria, MMS is included on the national Essential Medicines List of Nigeria. The most well-known and extensively studied MMS is the UNIMMAP formulation, also included in the World Health Organization's Model List of Essential Medicines since 2021.

How are programs ensuring equitable access to MMS for pregnant women who are most at risk of anemia, especially those in rural or low-resource settings?

In Indonesia, for example, the MMS program uses a blanket approach to reach all pregnant women through primary healthcare services. Other governments are exploring providing MMS as part of Essential Antenatal Care Package via the Universal Health Care platform.