Foundation for Survival of Women and Children

Quintuply-fortified salt for the improvement of micronutrient status among women of reproductive age and preschool-aged children in Punjab, India: protocol for a randomized, controlled, community-based trial

The burden of iron, zinc, vitamin B12, and folate deficiencies among women of reproductive age (WRA) in India is high. India's 2016–2018 Comprehensive National Nutrition Survey (CNNS) found that while 31% of adolescents were deficient in zinc nationwide; in Punjab, this prevalence was 52%. Micronutrient deficiencies during the preconception and antenatal period increase the risk of adverse pregnancy and birth outcomes. Zinc is essential for immune health, reproductive function, growth, and development, and its deficiency during pregnancy has been associated with an increased risk of preterm birth. Vitamin B12 and folate are essential for DNA synthesis and neurological development, and deficiencies increase the risk of miscarriage and congenital abnormalities, including neural tube defects. Large-scale food fortification (LSFF) is an effective, low-cost, and safe strategy to address micronutrient deficiencies at the population level. Among the food vehicle options available in resource-poor settings, salt is considered effective because it is relatively inexpensive, consumed in fairly consistent amounts across population

Methodology:

- The study protocol was approved by the Institutional Review Board, University of California San Francisco, Institutional Ethics Committee, Post Graduate Institute of Medical Education and Research, and Health Ministry's Screening Committee (HMSC) of India.

- A formative cross-sectional study among NPWRA in Mohali district, Punjab, (December 2020 and February 2021) was conducted to assess: (1) the prevalence of inadequate micronutrient intake and micronutrient deficiencies, (2) average discretionary salt intake, and (3) the optimal levels of micronutrients to be added to the MFS. The current paper reports the results of these formative assessments, which informed the design of the MFS trial.

- Potentially eligible participants were NPWRA (18–49 years) living in the district. A census of all households (n = 2974) was carried out in a subset of 11 villages. Households that did not have a WRA and did not plan to stay in the area for at least one month were excluded from the sampling frame, reducing the number of potentially eligible households to 2614.

- On the screening day, potential study participants were excluded from the study if they (1) had experienced nausea or vomiting in the past three days (symptoms of early pregnancy), (2) had a hemoglobin concentration less than 8 g/dL as measured from a finger prick blood sample using the Hemocue® Hb 301 system (Angelholm, Sweden), (3) planned to leave the study area for one month or more in the next 12 months, (4) had any medical condition that required regular visits to a health facility or (5) did not use refined salt as the primary source of household discretionary salt.

- After screening, eligible NPWRA interested in participating in the study provided informed consent, including assent to undertake anthropometric assessments in their children under five years, and were enrolled in the study.

- Data were collected on household socio-demographic characteristics, salt procurement and utilization practices, and household food security after enrolment. Dietary intake was assessed in the home of all participants. One-day in-home weighed food records were collected from all 100 NPWRA participants and repeated on a non-consecutive day approximately one week later among a sub-sample of 40 NPWRA.

- On the dietary assessment day, for each food or beverage item, including discretionary salt and water consumed by the participant, the time, place, amount consumed, and the amount left over were recorded by field research assistants on paper forms.

- Detailed recipes of mixed dishes consumed by participants prepared during the dietary assessment period were collected in real-time. For any left-over mixed dishes prepared the previous day, the recipe was recalled or estimated using raw ingredients (including water) to represent the final dish.

- Women were asked to appear for the biochemical and anthropometric assessment in a fasted state (no food or beverages apart from water consumed within the past 8 h) between 6.30 am to 10.30 am at a central location in the village.

- All samples were placed in electronic portable coolers maintained at 4 _C and transported to the field laboratory for processing.

- Morning spot urine samples (50 mL) were collected from each participant woman at home and transported to the field laboratory for processing.

- A team of two trained individuals completed the anthropometric assessments of participant women and their children under five years of age following standard procedures.

- Processing and Analysis of Biological Specimens were done.

- To demonstrate the potential effect of salt fortification on inadequate and excessive intake in the current sample, a two-step model simulation referred to as the “shrink then add” approach was used. The first simulation step involved modeling the effect of the four nutrients consumed from the usual diet only. The second step modeled the effect of the four micronutrients from food sources plus the anticipated amount of each micronutrient that the MFS would contribute based on the estimated intake of discretionary salt obtained from the weighed food records.

- The prevalence estimates of inadequate and excessive intake were reported for each simulation to demonstrate how much the intake of the MFS will potentially affect the baseline prevalence estimates of inadequate intake.

- The MFS premix was manufactured before the modeling activity was conducted. Therefore, it was only possible to adjust the micronutrient content of the MFS by varying the premix: salt blending ratio. Our approach was to ensure that the simulated prevalence of excessive intake did not exceed >5% for any micronutrient.

- Given the micronutrient content of the women’s usual diet, iron was the key micronutrient that drove these analyses. The levels of iron in the MFS premix: salt blending ratio were varied from the maximum possible level (2.5 mg/g of salt) and in decreasing amounts to determine the fortification level that ensured the prevalence of excessive iron intake did not exceed 5%.

- The fortification level for iron dictated the corresponding fortification levels of zinc, vitamin B12, and folic acid.

Key Highlights

- On average, women were 35 years old, with the majority (98%) having at least a middle school education. Participants belonged to households with an average size of six persons and a monthly household income of INR 12,000.

- All participants were classified as food secure. More than half (55%) of the women were either overweight or obese (BMI _ 25 kg/m2). Women who were overweight or obese had a higher prevalence of elevated CRP (33%) and AGP (33%) compared to women of normal BMI with CRP (9%) and AGP (11%).

- About 59% of the children of participant women under five years of age were male.

- The prevalence of inadequate and excessive dietary intake of iron, zinc, vitamin B12, and folic acid in the usual diets including intake of micronutrient supplements and the projected changes after the introduction of MFS.

- The modeling results showed that, given the study population's discretionary salt intake, the introduction of MFS containing the optimized ratio of pre-mix to salt is expected to reduce the prevalence of inadequate intake of iron from 46% to 17%, zinc from 95% to 18%, vitamin B12 from 83% to 0%, and folate from 36% to 0%, while ensuring that less than 5% of NPWRA will have excessive intake of iron, zinc, and folic acid.

- The biochemical assessment revealed a high prevalence of micronutrient deficiencies. A total of 37%, 67%, and 35% of women had anemia, iron deficiency, and iron deficiency and anemia, respectively.

- Thirty-four percent of women had hypozincemia, and the prevalence of vitamin B12 deficiency and insufficiency combined was 60%. The composite indicator of vitamin B12 (cB12) also showed that 63% of women had low and possibly deficient levels of vitamin B12.

- The majority (70%) of women were folate insufficient (RBC folate < 748 nmol/L).

- None of the participants had urinary iodine levels < 100 _g/L.

- The current study confirms a high prevalence of inadequate micronutrient intake and micronutrient deficiency among NPWRA in the Mohali district, Punjab. These results highlight the urgent need for innovative, cost-effective strategies to improve micronutrient status among vulnerable populations in India. Large-scale food fortification is one such strategy and this current population is likely to benefit from MFS.