Modifiers of the effect of maternal multiple micronutrient supplementation on stillbirth, birth outcomes, and infant mortality: a meta-analysis of individual patient data from 17 randomised trials in low-income and middle-income countries


Summary

Background Micronutrient deficiencies are common among women in low-income and middle-income countries. Data from randomised trials suggest that maternal multiple micronutrient supplementation decreases the risk of low birthweight and potentially improves other infant health outcomes. However, heterogeneity across studies suggests influence from effect modifiers. We aimed to identify individual-level modifiers of the effect of multiple micronutrient supplements on stillbirth, birth outcomes, and infant mortality in low-income and middle-income countries.

Methods This two-stage meta-analysis of individual patient included data from 17 randomised controlled trials done in 14 low-income and middle-income countries, which compared multiple micronutrient supplements containing iron-folic acid versus iron-folic acid alone in 112,953 pregnant women. We generated study-specific estimates and pooled subgroup estimates using fixed-effects models and assessed heterogeneity between subgroups with the $\chi^2$ test for heterogeneity. We did sensitivity analyses using random-effects models, stratifying by iron-folic acid dose, and exploring individual study effect.

Findings Multiple micronutrient supplements containing iron-folic acid provided significantly greater reductions in neonatal mortality for female neonates compared with male neonates than did iron-folic acid supplementation alone (RR 0.85, 95% CI 0.75–0.96 vs 1.06, 0.95–1.17; p value for interaction 0.007). Multiple micronutrient supplements resulted in greater reductions in low birthweight (RR 0.81, 95% CI 0.74–0.89; p value for interaction 0.049), small-for-gestational-age births (0.92, 0.87–0.97; p=0.03), and 6-month mortality (0.71, 0.60–0.86; p=0.04) in anaemic-pregnant women (haemoglobin <110g/L) as compared with non-anaemic pregnant women. Multiple micronutrient supplements also had a greater effect on preterm births among underweight pregnant women (BMI <18·5 kg/m²; RR 0.84, 95% CI 0.78–0.91; p=0.01). Initiation of multiple micronutrient supplements before 20 weeks gestation provided greater reductions in preterm birth (RR 0.89, 95% CI 0.85–0.93; p=0.03). Generally, the survival and birth outcome effects of multiple micronutrient supplementation were greater with high adherence (≥95%) to supplementation. Multiple micronutrient supplements did not significantly increase the risk of stillbirth or neonatal 6-month, or infant mortality, neither overall or in any of the 26 examined subgroups.

Interpretation Antenatal multiple micronutrient supplements improved survival for female neonates and provided greater birth-outcome benefits for infants born to undernourished and anaemic pregnant women. Early initiation in pregnancy and high adherence to multiple micronutrient supplements also provided greater overall benefits. Studies should now aim to elucidate the mechanisms accounting for differences in the effect of antenatal multiple micronutrient supplements on infant health by maternal nutritional status and sex.

Funding None.

Copyright © The Author(s). Published by Elsevier Ltd. This is an Open Access article under the CC BY 4.0 license.

Introduction Micronutrient deficiencies are common among women in low-income and middle-income countries mainly due to inadequate dietary intake and limited diversity of fruits, vegetables, animal protein, and fortified foods. The burden and severity of micronutrient deficiencies are exacerbated during pregnancy because of increased demands of both the mother and the growing fetus. It is
Articles

Pediatrics, University College of Health, International Maternal and Child Health, Department of Global Health, Muhimbili University of Health and Allied Sciences, Tanzania

Evidence before this study

Micronutrient deficiencies are common in pregnant women in low-income and middle-income countries. However, debate persists regarding the current WHO recommendation to provide pregnant women with iron-folic acid supplementation alone, rather than multiple micronutrient supplements containing other essential micronutrients in addition to iron-folic acid during routine antenatal care. In the past two decades, more than 20 randomised trials have examined the effect of multiple micronutrient supplements during pregnancy, compared with iron-folic acid alone, on maternal and child health outcomes. The 2017 Cochrane review and meta-analysis established that provision of daily oral multiple micronutrient supplements reduced the risk of low birthweight (<2500 g) and small-for-gestational-age births, but had no overall effect on perinatal and neonatal mortality as compared with iron-folic acid alone.

The recently updated 2016 WHO antenatal care recommendations acknowledged that policy makers in populations with a high prevalence of maternal nutritional deficiencies might wish to provide multiple micronutrient supplements. However, WHO does not universally recommend multiple micronutrient supplements. This novel analysis identified subgroups of mothers and infants that might benefit the most from multiple micronutrient supplements. This new evidence suggests that WHO might wish to re-evaluate the balance of benefits and harms of universal multiple micronutrient supplementation in their antenatal care recommendations.

Research in context

Evidence before this study

Micronutrient deficiencies are common in pregnant women in low-income and middle-income countries. However, debate persists regarding the current WHO recommendation to provide pregnant women with iron-folic acid supplementation alone, rather than multiple micronutrient supplements containing other essential micronutrients in addition to iron-folic acid during routine antenatal care. In the past two decades, more than 20 randomised trials have examined the effect of multiple micronutrient supplements during pregnancy, compared with iron-folic acid alone, on maternal and child health outcomes. The 2017 Cochrane review and meta-analysis established that provision of daily oral multiple micronutrient supplements reduced the risk of low birthweight (<2500 g) and small-for-gestational-age births, but had no overall effect on perinatal and neonatal mortality as compared with iron-folic acid alone.

The recently updated 2016 WHO antenatal care recommendations acknowledged that policy makers in populations with a high prevalence of maternal nutritional deficiencies might wish to provide multiple micronutrient supplements. However, WHO does not universally recommend multiple micronutrient supplements. This novel analysis identified subgroups of mothers and infants that might benefit the most from multiple micronutrient supplements. This new evidence suggests that WHO might wish to re-evaluate the balance of benefits and harms of universal multiple micronutrient supplementation in their antenatal care recommendations.

Added value of this study

This study uses the most detailed approach to analysing existing trial data on multiple micronutrient supplements. Previous meta-analyses identified overall benefits of multiple micronutrient supplements in terms of birth size, but our findings show that specific subgroups experience mortality benefits, notably female neonates. Women with indicators of malnutrition during pregnancy who took multiple micronutrient supplements also had greater reductions in low birthweight, preterm, and small-for-gestational-age births. We found no evidence that multiple micronutrient supplements significantly increased the risk of stillbirth or neonatal, 6-month, or infant mortality, neither overall or in any of the 26 examined subgroups.

Implications of the available evidence

This novel analysis identified subgroups of mothers and infants that might benefit the most from multiple micronutrient supplements. This new evidence suggests that WHO might wish to re-evaluate the balance of benefits and harms of universal multiple micronutrient supplementation in their antenatal care recommendations.

Methods

In this two-stage meta-analysis of individual patient data, we identified potential studies for inclusion
دریافت فوری متن کامل مقاله

امکان دانلود نسخه تمام متن مقالات انگلیسی
امکان دانلود نسخه ترجمه شده مقالات
پذیرش سفارش ترجمه تخصصی
امکان جستجو در آرشیو جامعی از صدها موضوع و هزاران مقاله
امکان دانلود رایگان ۲ صفحه اول هر مقاله
امکان پرداخت اینترنتی با کلیه کارت های عضو شتاب
دانلود فوری مقاله پس از پرداخت آنلاین
پشتیبانی کامل خرید با بهره مندی از سیستم هوشمند رهگیری سفارشات