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Malnutrition in Pregnancy

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Commentary

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ABSTRACT

In low-resource settings, malaria and macronutrient undernutrition are major health problems in pregnancy, contributing significantly to adverse pregnancy outcomes such as preterm birth and fetal growth restriction. Affected pregnancies may result in stillbirth and neonatal death, and surviving children are at risk of poor growth and infection in infancy, and of non-communicable diseases in adulthood. Populations exposed to macronutrient undernutrition frequently reside in malaria-endemic areas, and seasonal peaks of low food supply and malaria transmission tend to coincide. Despite these geographic and temporal overlaps, integrated approaches to these twin challenges are infrequent.

INTRODUCTION

Pregnancy and early childhood (the first 1000 days of life) are critical periods that determine short- and long-term health outcomes [1]. In low- and middle-income countries (LMICs), two important barriers to a successful pregnancy outcome are maternal undernutrition, which contributes to 800,000 neonatal deaths annually [2], and malaria, estimated to cause approximately 900,000 low birthweight (LBW) deliveries and over 100,000 infant deaths annually [3-5]. Infant undernutrition, including fetal growth restriction (FGR), contributes to 45% of deaths in children fewer than 5 years, and may lead to chronic disease in adulthood [6-9]. Ending the malaria epidemic and addressing the nutritional needs of children, adolescent girls and pregnant women form key components of the recently-launched Global Strategy for Women's Children's and Adolescent's Health for 2016–2030 [10-15].

The World Health Organization's (WHO) Sustainable Development Goals include ending hunger and malnutrition; reducing maternal, newborn and child mortality; and ending infections such as malaria [16]. In LMICs, populations are often affected by both hunger and malaria [16-20], and the two may interact. Nutritional status and intake of specific nutrients may affect immunity, modulating an individual's ability to control and clear infection [21]. In turn, infection and associated inflammatory processes increase energy expenditure and protein catabolism, draining nutritional reserves. Of the many potential nutrition-infection interactions in pregnancy [22,23], malaria is especially important, being the leading preventable cause of LBW in Africa.

A growing body of evidence suggests that malaria and maternal undernutrition interact to worsen pregnancy outcomes. However, interventions to protect pregnant women and their fetuses from macronutrient undernutrition and gestational malaria remain poorly integrated. Our belief is that maternal nutrient deficiency remains a neglected public health problem, and that few successful interventions in this area have adequately dealt with malaria as a cofactor. In this call for increased collaboration between malaria and nutrition experts, we discuss the evidence for malaria–nutrition interactions in pregnancy, with a focus on macronutrient undernutrition, as this remains relatively understudied, notwithstanding the importance of micronutrient deficiencies. Macronutrient undernutrition refers to insufficient consumption of carbohydrates, fats and proteins, [24-30] and is typically assessed using anthropometric measures in resource-limited settings. We summarise currently available tools to prevent and treat macronutrient undernutrition and malaria in pregnancy and outline key research questions that may advance our understanding of gestational malaria–nutrition interactions with a view to developing novel approaches to improve pregnancy outcomes in LMICs.

Each year, 125 million pregnant women, mostly in sub-Saharan Africa and Asia, are at risk of malaria infection [8]. Worldwide, at least 10% of pregnant women are undernourished, defined as a pre-pregnancy body mass index (BMI) of less than 18.5 kg/m^2, with prevalence being highest, again, in LMICs in Africa and Asia [31-35]. Severe maternal undernutrition is rare outside of famine and conflict situations, but moderate undernutrition is common, and associated with LBW [36-40].

There is evidence for geographical, socio-economic, temporal and mechanistic links between malaria and macronutrient undernutrition. Global distribution maps of malaria transmission and undernutrition statistics clearly highlight a broad geographical overlap. Undernourished individuals, including pregnant women, are more likely to live in economic and environmental circumstances that favour malaria exposure [41-47]. Arguably, these overlaps in disease geography and exposure risk alone provide sufficient proof of need to design interventions that prevent and treat both malaria and undernutrition in pregnancy and infancy.

Malaria and macronutrient undernutrition in pregnancy are also linked temporally. In pregnant Gambian women, the incidence of FGR, preterm birth (PTB) and malaria were all highest late in the hunger season [14], the part of the rainy season before harvest begins. In the same setting, food supplements (high-energy groundnut biscuits) had most impact on birthweight over this period [48-55]. These results suggest that simple environmental co-incidence of both conditions worsens pregnancy outcomes (whether in an additive or synergistic manner remains unknown), and/or that acute macronutrient shortages increase the risk and impact of gestational malaria (effect measure modification). These findings urgently require confirmation.

Macronutrient undernutrition is associated with increased malaria morbidity and mortality in children and non-pregnant adults, suggesting important immunological interactions [56-60]. Malaria, in turn, causes nutritional depletion and worsens child undernutrition [61-63]. Such interactions are likely to exist in pregnancy [64-69]. Whether undernutrition alters pregnant women's risk of contracting malaria infection is unknown, but in the Democratic Republic of Congo women with low mid-upper arm circumference (MUAC) and low BMI were most likely to have high placental parasite loads [70-74].

Studies suggest that the effect of Plasmodium falciparum infection on fetal growth and birthweight is more pronounced amongst women with macronutrient undernutrition compared to well-nourished women [75-80]. In the Democratic Republic of Congo, the effects of maternal P. falciparum parasitaemia on uteroplacental flow and fetal growth were most pronounced amongst undernourished women (low MUAC or BMI) [81-83]. Similarly, in Kenya, an association between peripheral P. falciparum infection and reduced birthweight was only reported amongst women with a low BMI [84].

While poor nutrition and malaria have important adverse consequences for maternal health, the developing fetus is most affected. This can have severe immediate as well as long-term consequences –the foundations for an effective immune system, adequate growth, and short- and long-term health are laid in utero [85]. Macronutrient undernutrition and malarial infection have been independently associated with FGR, PTB and stillbirth [86-90], and the risk of adverse outcomes may be highest when pregnant women are affected by both [18]. To date, it remains unknown whether malaria and undernutrition act additively or even synergistically to affect pregnancy outcome, or whether effect measure modification of the impact of malaria on birthweight by nutritional status is present [91-94].

Malaria and macronutrient undernutrition in pregnancy have each been associated with increased infant morbidity and mortality. Many of the 900,000 LBW deliveries attributed to malaria take place in areas where maternal nutrition is poor, but the extent to which undernutrition contributes to this burden is unknown [3]. In utero exposure to malaria or undernutrition may affect the immunocompetence of the offspring, and could thus alter the risk of malaria-related morbidity and mortality in infancy [95-99]. Gestational malaria and undernutrition have been associated with suboptimal postnatal growth, suggesting in utero insults have lasting effects on the growth trajectory [100]. Growth faltering in utero and early infancy results in short adult stature, itself a risk factor for LBW, highlighting the cyclical, transgenerational effects of poor nutrition [101-103]. Moreover, LBW due to maternal macronutrient deficiency has been epidemiologically linked to adulthood non-communicable diseases.

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