Global Micronutrient Deficiencies in Childhood and Impact on Growth and Survival: Challenges and Opportunities

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Abstract
Despite numerous advances and improvements in child health, malnutrition still remains as one of the main public health challenges of the 21st century, particularly in developing countries. It undermines the survival, growth and development of children, and is associated with almost 35% of all deaths in children under the age of 5 years worldwide. An estimated 178 million children are stunted globally, and an additional 19 million children have severe acute malnutrition (wasting). These conditions are very often associated with concomitant micronutrient deficiencies, and among these, vitamin A, iron, zinc and iodine deficiencies are the most prevalent in childhood. Vitamin A and zinc deficiency is associated with an estimated 1 million child deaths and 9% of global childhood disability-adjusted life years. Recent data on the timing of growth retardation and stunting in infants suggest that the onset is commensurate with inappropriate complementary feeding and potentially compounded by maternal undernutrition and intrauterine growth retardation, and that the first 24 months represent a critical window of opportunity for intervention. Given the wide prevalence of multiple micronutrient deficiencies in malnourished children in developing countries, the challenge is to implement intervention strategies that combine appropriate infant and young child feeding with micronutrient interventions at scale. Emerging data from community intervention trials now provide evidence that this is both tangible and can lead to alleviation of childhood undernutrition. Some of these recent findings will be discussed.

Introduction
Despite numerous advances and improvements in child health, malnutrition still remains as one of the main public health challenges of the 21st century, particularly in developing countries [1, 2]. It undermines the survival, growth
and development of children, and is associated with almost 35% of all deaths in children under the age of 5 years worldwide [3]. An estimated 178 million children are stunted globally and an additional 19 million children have severe acute malnutrition (wasting) [3]. Many of these conditions are associated with concomitant micronutrient deficiencies, and among these, vitamin A, iron, zinc and iodine deficiencies are the most prevalent in childhood. Vitamin A and zinc deficiency is associated with an estimated 1 million child deaths and 9% of global childhood disability-adjusted life years [3]. Recent data on the timing of growth retardation and stunting in infants suggest that the onset is commensurate with inappropriate complementary feeding and potentially compounded by maternal undernutrition and intrauterine growth retardation, and that the first 24 months represent a critical window of opportunity for intervention [4].

The relationship between micronutrient deficiencies and increased risk of infections and mortality is well established [5-7]. Several micronutrients play an important role in the immune system, and are critical in determining the outcome of host microbe interactions [8, 9]. Infections on the other hand are a risk factor for malnutrition as during an episode of infection, there is a general decrease in nutrient intake, increase in losses (e.g. GI losses, fluid losses, etc.) and altered metabolic pathways [9]. This condition is more prevalent among poor children whose micronutrient status is already marginal, and they also have a high frequency of infectious disease. This leads to a vicious cycle where malnutrition is a health outcome as well as a risk factor for disease and exacerbation of malnutrition [10]. The resulting complex and mutually adverse interactions with infections constitute the major determinants of childhood morbidity and mortality among the underprivileged preschool children in several developing countries [11].

Knowledge of prevalence of micronutrient deficiencies and their role in childhood morbidity and mortality is of great importance in planning comprehensive strategies to promote child health and survival in developing countries [5]. The purpose of this chapter was to summarize the current knowledge on micronutrient deficiencies and their role in reducing morbidity and mortality during childhood. A literature search was conducted on PubMed, Cochrane library and WHO and UNICEF databases. We discuss the epidemiology, effective intervention and challenges and opportunities for vitamin A, zinc, iodine, iron and other micronutrients.

Vitamin A

Vitamin A has been termed an anti-infectious agent [12, 13], and it plays an important role in the visual system [14]. Vitamin A deficiency (VAD) impairs numerous body functions, and can lead to many adverse health consequences including xerophthalmia (dry eyes), infectious morbidity, mortality, suboptimal
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physical growth and anemia [12, 15]. VAD is a major nutritional public health problem in the developing world. According to the latest report of the WHO, globally about 190 million preschool-aged children and 19.1 million pregnant women are vitamin A deficient (i.e. serum retinol <0.70 µmol/l) [16]. This corresponds to 33.3% of preschool-aged children and 15.3% of pregnant women in populations at risk of VAD. According to current estimates, 122 countries are classified as having a moderate to severe public health problem based on biochemical VAD in preschool-aged children, and 88 countries based on biochemical VAD in pregnant women [16]. Xerophthalmia, resulting from VAD, is the primary preventable cause of blindness, and of the world’s children with xerophthalmia, nearly half reside in South or South-East Asia, of whom more than 85% live in India [17]. About 5.2 million preschool-aged children and 9.8 million pregnant women suffer from night blindness, which represents 0.9 and 7.8% of the population at risk of VAD, respectively. The estimates show that Africa and South-East Asia contain the highest proportions of preschool-aged children and pregnant females with biochemical VAD and night blindness [16]. Evidence from community trials has shown that vitamin A supplementation (VAS) reduces all-cause mortality and diarrhea- and measles-specific mortality [18–21]. It also reduces incidence of measles and diarrhea infection [21]. VAS has also been shown to reduce prevalence of xerophthalmia (RR 0.31, 95% CI 0.22–0.45) and night blindness (RR 0.32, 95% CI 0.21–0.50) [21]. VAS as an adjunct in the treatment of measles has been shown to reduce mortality (RR 0.18; 95% CI 0.03–0.61), pneumonia-specific mortality (RR 0.33; 95% CI 0.08–0.92) and incidence of croup (RR 0.53; 95% CI 0.29–0.89) [22].

World Health Organization recommends two annual high-dose supplements of vitamin A for every child at risk of VAD [23]. Administering vitamin A is a simple act that can be performed by a trained health worker, community worker or volunteer. It is one of the most cost-effective large-scale child survival interventions [24]. VAS is inexpensive on a per-child basis, with the cost of single capsule approximately USD 0.02 [25]. The total cost of two annual doses varies according to the region, and it has been estimated that supplementing each child with two doses per year, it costs USD 1.20 per child per year for South Asia and sub-Saharan Africa, with relatively higher costs for Central Asia and Latin America [26].

Since 1998, large VAS programs are in place in about 193 UNICEF-targeted countries to deliver the required dose of vitamin A [27]. Figure 1 shows the progress of increase in VAS from 1999–2007. It can be noted that in 1999, just 16% of children in these countries received full VAS, while in 2005 this number increased to 72% [28]. In 2007, the rate of coverage dropped to 62% partly because India increased its target group from 3 to 5 years of age [28]. An important point to note is that least developed countries showed the most impressive progress in achieving two-dose coverage [29] (fig. 2). While these figures are encouraging, significant gaps in VAS coverage remain and continue to
undermine children’s health [30] (fig. 3). An effort should be made to improve the current strategies of vitamin A delivery to achieve at least 80% coverage on persistent basis. Special efforts should be made to cover the hard-to-reach children through complementary strategies, such as special outreach programs, to reach the final 20% who have not been reached through regular programs. To maintain the sustainability, resources should be mobilized in national budgets, and VAS programs should be made part of integrated delivery strategies, with continuous monitoring and tracking of progress.

**Zinc**

Zinc is the second most abundant transition metal in humans after iron. It is an essential part of about 100 specific enzymes and also serves as structural ions in transcription factors [31]. The association of zinc deficiency in children with
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Growth retardation and hypogonadism was first described in 1963 in a study from Iran [32], and it is now well established based on animal and human studies demonstrating that zinc plays a critical role in cellular growth, cellular differentiation and metabolism [33], and in turn promotes immunity, resistance to infection, and the growth and development of the nervous system [31]. Although zinc deficiency is increasingly being recognized as a widespread problem, there is very limited nationally representative data on the magnitude and severity of this deficiency [34]. Some of this is due in part to the lack of reliable biomarkers of zinc status. Recently, Wuehler et al. [35], using data from national food balance sheets compiled by the Food and Agricultural Organization, estimated that 20% of the world's population is at risk of low zinc intakes. The global prevalence of low intakes by region indicates that 26% of population in South Asia and 28% in Sub-Saharan Africa are at risk of deficiency [35].

Evidence from community trials has shown that both therapeutic and preventive zinc supplementations are effective in reducing morbidity and mortality in children <5 years of age [36–40]. Therapeutic zinc supplementation as an adjunct in the treatment of diarrhea has been shown to reduce the duration of acute diarrhea by 0.5 days and that of persistent diarrhea by 0.68 days [37]. Preventive zinc supplementation reduces incidence of diarrhea by 20% (RR = 0.80; 95% CI, 0.71–0.90) and that of pneumonia by 15% (RR = 0.85; 95% CI, 0.75–0.97) [36]. Preventive zinc supplementation has been shown to reduce the rate of stunting as well [36, 41, 42].

Fig. 3. VAS coverage levels by country: two doses (2005). From UNICEF [30].
In 2004, the WHO and UNICEF formulated a new recommendation to administer zinc for 10–14 days as an adjunct treatment for diarrhea, along with low-osmolarity oral rehydration solutions and continuation of feeding [43]. Since then, the WHO and UNICEF in collaboration with USAID and Johns Hopkins University has worked to ensure the availability of zinc products [44], and about 91 million tablets had been provided in the year 2008 [45]. Despite all these efforts, zinc supplementation is not part of national programs around the globe. Figure 4 shows that only 46 countries have adopted zinc policy as part of their national child health policy [45]. It is therefore required to scale up the zinc supplementation, and it should be incorporated into national diarrhea management policy. Adequate funds with possible public and private partnerships should be sorted out, and general awareness about the effectiveness of zinc supplementations should be raised through media campaigns.

**Iodine**

Iodine is the key element required for thyroid hormone synthesis, and is also important for brain development during fetal and early years of life [46]. Iodine deficiency is the primary cause of preventable mental retardation and brain damage and also increases the chance of infant mortality, miscarriage and stillbirth.
Children born to iodine-deficient mothers may appear normal at birth, but might have suffered brain damage and loss in IQ points, affecting their ability to develop to their full potential. These seemingly normal children will later have difficulty learning in school and staying in school. It has been shown that in communities where iodine intake is sufficient, average IQ is on average 13 points higher than in iodine-deficient communities [46]. According to an estimate, about 2 billion people have insufficient iodine intake around the globe and about 31.5% of school-age children (266 million) have insufficient iodine intake (fig. 5) [47].

Salt iodization is one of the exemplary success stories of food fortification offering great benefits for the intellectual health of nations that have embraced it [48]. The number of countries where iodine deficiency disorders were a public health concern has been reduced by more than half from 1993 to 2007 [47]. Thirty-four developing countries have achieved the universal salt iodization goal, and an additional 38 countries are considered ‘on track’ for elimination of iodine deficiency disorders [48]. These are countries that have either shown increases in coverage of at least 20% over the previous decade or that have reached between 80 and 89% coverage with no indication of possible decline [48]. Despite this progress, many countries are lagging far behind. Twenty-four countries have experienced no growth in coverage rates or have even experienced a decline since the mid-1990s [48]. In 12 countries, less than 20% of the population are consuming adequately iodized salt [48].

Fig. 5. Prevalence of iodine deficiency in school-aged children [47].
In order to achieve universal salt iodization, country level legislation should be done, and adequate funds should be ensured to enforce it. At the same time, media campaigns should be launched for general awareness of the importance of salt iodization. Population monitoring systems should be strengthened so that program adjustments can be made as habits and diets change over time.

**Other Micronutrients**

Iron is an essential mineral for human development and function. It is required for hemoglobin and is critical for motor and cognitive development in childhood, and for physical activity in all humans [49]. Iron is also critical to the health of a pregnant mother and her unborn child. A woman needs more iron during pregnancy because the fetus and placenta both need additional iron. Iron supplementation during pregnancy lowers the risk of maternal mortality due to hemorrhage, the cause of more than 130,000 maternal deaths each year [27]. Supplementation also helps to lower the risks of premature birth and low birthweight. Studies have shown that infants with anemia caused by iron deficiency have lower mental scores and lower motor scores than infants without anemia [50]. Ensuring sufficient iron levels in the first months and years of life is, therefore, critical.

**Conclusions**

Micronutrients like vitamin A, zinc, iodine and iron are important for growth and survival of children. Given the wide prevalence of multiple micronutrient deficiencies in malnourished children in developing countries, the challenge is to implement intervention strategies that combine appropriate infant and young child feeding with micronutrient interventions at scale. Emerging data from community intervention trials now provide evidence that this is both tangible and can lead to alleviation of childhood undernutrition.

**References**


