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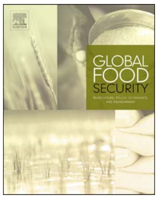

Approaches to reduce zinc and iron deficits in food systems

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ABSTRACT

There is a deficit of mineral micronutrients in global food systems, known as ‘hidden hunger’, especially in the global south. This review focuses on zinc (Zn) and iron (Fe), whose entry into food systems depends primarily on soil and crop factors. Approaches to increase dietary supplies of Zn and Fe include: (1) supplementation, (2) food fortification, (3) dietary diversification, and (4) crop biofortification, including breeding and fertilizer-based approaches. Supply-based estimates indicate that Zn deficiency might be more widespread than Fe deficiency in sub-Saharan Africa, although there are major knowledge gaps at an individual biomarker level. Recent analytical advances, including the use of stable isotopes of Zn and Fe, can play an increasing role in improving our understanding of the movement of micronutrients in food systems, and thereby help to reduce the immense human cost of ‘hidden hunger’.

1. Introduction

1.1. Scope of review

Micronutrient deficiencies (MNDs) can occur due to inadequate dietary intakes of vitamins and mineral elements, excessive losses, or malabsorption. Also known as ‘hidden hunger’, the consequences of MNDs are often less apparent than energy or protein deficiencies. However, their prevalence is likely to be more widespread than energy/protein malnutrition, with at least 1.5 billion (GBD, 2016), and potentially more than 3 billion (Kumssa et al., 2015a, 2015b), people likely to be affected by one or more MNDs. Micronutrients is a term often used to include any of the > 20 essential elements required by humans; the elements most commonly studied are calcium (Ca), copper (Cu), iron (Fe), iodine (I), magnesium (Mg), selenium (Se) and zinc (Zn) (Black et al., 2008; Broadley and White, 2010; Bouis et al., 2011; Muthayya et al., 2013). The greatest prevalence of most MNDs occurs in less developed countries, including in sub-Saharan Africa (Muthayya et al., 2013; Joy et al., 2014; Kumssa et al., 2015a, 2015b). However, estimating the prevalence of MNDs at national and sub-national scales remains a considerable challenge in terms of selecting appropriate biomarkers of nutritional status, measuring these in population-level surveys, and linking these with health outcomes. In turn, this constrains the development of policies to alleviate MNDs, including the application of innovations from the agriculture/nutrition research sectors.

The scope of this review is to provide an overview of dietary supplies of Zn and Fe in current global food systems. Dietary deficiencies of Zn and Fe have been estimated as the 40th and 16th leading risk factors, respectively, underlying global burden of disease (GBD, 2016). It has been estimated that Zn and Fe deficiency reduces the Gross Domestic Product (GDP) of developing countries by 2–5% (Stein, 2014). The potential to develop policies to address deficits of Zn and Fe in food systems are considered from an agriculture/nutrition perspective, including the potential to use micronutrient fertilization and crop breeding to benefit human health.

1.2. Functions of zinc and iron in humans

An adult human body contains ~2 g of Zn of which ~60% is found in skeletal muscle and 30% in bone mass (Saltzman et al., 1990). Zinc has many fundamental roles for all life forms (Broadley et al., 2007), and binds with > 900 proteins in the human body (Oliver and Gregory,

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2015). The World Health Organization and Food and Agriculture Organization (WHO and FAO, 2004) Reference Nutrient Intake (RNI) for Zn is 14 and 10 mg *capita*$^{-1}$ d^{-1} for adult males and females, respectively; the requirements for adolescents are greater. In children, Zn deficiency increases the incidence and severity of diarrhoea and increases the risk of stunting (Brown et al., 2009; Mayo-Wilson et al., 2014). There is mixed evidence to suggest an increase in mortality and morbidity due to lower respiratory tract infections and malaria (Bates et al., 1993; Salgueiro et al., 2002; Brown et al., 2009; Mayo-Wilson et al., 2014).

An adult human body contains ~4.0 g of Fe of which ~75% is in the oxygen-transporting proteins haemoglobin and myoglobin (Bothwell et al., 1979). The redox potential of Fe is critical in binding and releasing oxygen and for its functions in enzymes including energy, protein and nucleotide metabolism. The RNI for Fe is 13.7 mg *capita*$^{-1}$ d^{-1} for adult males (WHO and FAO, 2004). Dietary requirements are greater for women of reproductive age (up to 29.5 mg *capita*$^{-1}$ d^{-1} for adolescent females) due to increased blood losses, and during pregnancy. Recommended intakes of Fe are also greater in cereal-based diets that are low in animal products, due to the presence of inhibitors of Fe (and Zn, Ca, Mg etc.) absorption, such as phytate (Gibson et al., 2010; Kumssa et al., 2015a, 2015b). The consequences of dietary Fe deficiency include Fe-deficiency anaemia (Lynch, 2007), which is defined as low haemoglobin together with one or more indicators of Fe deficiency, e.g. low body Fe stores (Cook et al., 2003). Anaemia results in decreased physical capacity (Hass and Brownlie, 2001), and increased risk of low-birth weight, perinatal and neonatal mortality (Rasmussen, 2001; Kozuki et al., 2012; Rahman et al., 2016). In children, Fe deficiency impairs cognitive development and the immune system leading to increased susceptibility to infectious diseases (Oliver and Gregory, 2015).

1.3. *Prevalence of zinc and iron deficiencies*

Various types of data are used to estimate the prevalence of Zn and Fe deficiencies, including proxies based on (1) national food supply; (2) dietary intake surveys; (3) health data; and (4) biomarkers of status. Caution is needed when interpreting single sources of data and a combination of data sources and approaches is therefore generally considered to the most reliable method to assess MND prevalence (e.g. King et al., 2016). For example, food balance sheets (FBSs; FAO, 2016) represent net *per capita* food supply calculated from national production, trade, transport losses, storage, non-food uses, livestock feed, etc., but with no adjustment for household waste or inter- and intra-household variation in access to food (Joy et al., 2014; Kumssa et al., 2015a, 2015b). Household or individual-level consumption surveys can also be affected by behavioural factors and systematic misreporting (Rennie et al., 2007; Archer et al., 2013). Uncertainties about food supply or consumption can also be compounded by a lack of good quality data on the micronutrient composition of foods, which can be affected greatly by soil type and cultivation conditions (Joy et al., 2015a).

Tissue biomarkers and proxy health data for estimating Zn deficiency can be difficult to interpret. For example, King et al. (2016) concluded that the prevalence of Zn deficiency in a population was best achieved using a combination of intake data, plasma/serum Zn concentration, and height-to-weight ratios (stunting). However, data are often not available at appropriate scales. Using FBSs for 2011 and United States Department of Agriculture (USDA) food composition data, the prevalence of inadequate dietary Zn supplies was estimated to be 17% globally (Kumssa et al., 2015b; Fig. 1). The data are consistent with earlier studies (Wuehler et al., 2005; Wessells and Brown, 2012), including a study in Africa which used more regional food composition information (Joy et al., 2014), indicating that Zn deficiency is widespread in low-income countries. Recent studies of tissue biomarkers have shown that the prevalence of Zn deficiency appears to be higher than that of Fe deficiency in both Ethiopia (Gashu et al., 2016) and Malawi (Siyame et al., 2013; Gibson et al., 2015).

Quantifying the prevalence of Fe deficiency at wide scales can be particularly problematic. Currently, the prevalence of anaemia is used as a proxy for Fe deficiency with an assumption that half of all anaemia cases result from Fe deficiency (Stoltzfus et al., 2004; Lynch, 2007). However, the prevalence of dietary Fe deficiency estimated from food supply was lower than expected from anaemia rates in continental Africa (Joy et al., 2014; Fig. 2). Anaemia is also caused by other nutritional deficiencies (e.g. vitamin A and folic acid), impaired Fe absorption or increased Fe losses due to inflammatory and infectious diseases. The regulation of serum Fe is an important component of the immune system, starving pathogens of Fe (Ward et al., 2011; Guida et al., 2015); for example, anaemia offers children protection against *Plasmodium falciparum* malaria (Goheen et al., 2016). In a recent review, Petry et al. (2016) pooled data from 23 nationally-representative surveys of pre-school children and non-pregnant women, finding that the proportion of anaemia associated with Fe deficiency is typically much less than 50%, especially in countries with a high prevalence of anaemia, among rural populations and in countries with very high inflammation exposure. Progress is being made to define complementary markers of Fe status including serum ferritin, soluble transferrin receptor and hepcidin to quantify Fe stores and the adequacy of Fe supplies, although their application in developing countries has mainly been limited to small-scale studies (Lynch, 2012; Prentice et al., 2012).

2. Crop nutrition and Zn and Fe concentrations of edible plant parts

Zinc and Fe are both essential nutrients for plants, and in many low-income settings where consumption of animal-source foods is low, plant-based foods provide the majority of dietary Zn and Fe. The quantity of Zn and Fe contained in plant organs depends on several interacting factors including soil type, plant type and variety, and the growing environment and its management.

2.1. *Soil type*

Soil is the source of most Zn and Fe within plants, so soil type has a major role in determining the amounts contained in crops. Most soils used for agriculture contain 10–300 µg Zn g^{-1} soil with the concentration in soil solution ranging from 10^{-8} to 10^{-6} M (White and Greenwood, 2013). Concentrations of Fe in most agricultural soil solutions also range from 10^{-8} to 10^{-6} M but only 10^{-10} M in alkaline or calcareous soils (White and Greenwood, 2013). Table 1 summarises the major soil types and their association with both Zn and Fe deficiency and toxicity. Zinc deficiency in plants is often associated with alkaline and calcareous soils of high pH, and also with highly weathered soils, so occurs on a number of soil types. Iron deficiency in plants occurs on several soil types but is typically associated with low phytoavailability rather than low abundance per se (Fageria, 2009; White and Greenwood, 2013). The concentration of Fe in soil solution decreases as the redox potential and/or pH increases, with concentrations in calcareous and alkaline soils (such as the Aridisols and some Entisols and Inceptisols shown in Table 1) typically 100–1000 times lower than in soils with a pH of 6–7 (Fageria, 2009). It is estimated that up to one-third of the world's soils used for agriculture are calcareous with the plants grown on them susceptible to what is called ‘lime-induced Fe chlorosis’ (White and Greenwood, 2013; FAO, 2015). Toxicity of Fe occurs in soils with inherently high concentrations of Fe (such as some Oxisols) but more commonly on other soil types where flooding or waterlogging occurs resulting in the reduction of ferric Fe to ferrous Fe thereby increasing its bioavailability to plants. In contrast, Zn toxicity is rare but can occur on some acidic soils (especially in urban and peri-urban areas) enriched with sewage sludge or land contaminated by mining or smelting activities (White and Greenwood, 2013).