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Review Article

The phenomenon of micronutrient deficiency among children in China: a systematic review of the literature

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Abstract
Objective: The present study aimed to review the literature on micronutrient deficiency and other factors influencing a deficiency status among children living in China.
Design: A systematic review was performed to analyse the literature.
Setting: Studies were identified through a search of PubMed and secondary references.
Subjects: Children living in China aged less than 18 years.
Results: Sixty-one articles were included. The prevalence of vitamin A deficiency decreased to approximately 10 % in 1995–2009. It increased with age but no significant difference was found between genders. The prevalence of thiamin and vitamin B_{12} deficiency was 10·5 % in Yunnan and 4·5 % in Chongqing provinces, respectively. Higher vitamin D deficiency rates were seen in spring and winter. The incidence of bleeding due to vitamin K deficiency was 3·3 % in 1998–2001 and more prevalent in rural areas. Both iodine deficiency and excess iodine intake were observed. Goitre rates were reported in Tibet, Jiangxi, Gansu and Hong Kong (3·5–46 %). Anaemia rates ranged from 20 % to 40 % in 2007–2011. High Se deficiency rates were found in Tibet, Shaanxi and Jiangsu. High Zn deficiency rates were also found (50–70 %) in 1995–2006. Few studies reported Ca deficiency rates (19·6–34·3 %). The degrees of deficiency for vitamin A, vitamin B_{12}, Fe and Zn were more substantial in rural areas compared with urban areas.
Conclusions: The prevalence of micronutrient deficiency rates varied. Socio-economic status, environmental factors and the Chinese diet may influence micronutrient deficiency. Public health policies should consider implementing programmes of supplementation, food fortification and nutrition education to address these deficiencies among Chinese children.

Keywords
Micronutrients
China
Hong Kong

Micronutrients are vitamins and minerals consumed in small quantities, but are essential for body biochemical processes[1]. They are critical in producing enzymes, hormones and metabolites that are essential for growth and development.

According to the WHO, micronutrient deficiencies of iodine, vitamin A and Fe are of the greatest concern worldwide[1]. Thirty-two countries reported a significant proportion of their population who were affected and classified as iodine-deficient in 2012[2]. Iodine-deficiency disorder (IDD) is characterised by a range of symptoms/diseases which includes thyroid function abnormalities, goitre, impaired brain development and brain damage[3,4]. However, excessive iodine intake was found in twenty-nine countries, potentially leading to iodine-induced thyroid dysfunction[5]. Vitamin A deficiency (VAD) is one of the important causes of blindness in children. Pre-school age children were affected in 122 countries from 1995 to 2005[6]. VAD was reported to account for 0·6 million deaths globally and constituted the largest disease burden (6 % of deaths in children under 5 years of age) among micronutrient deficiencies in 2004[7]. The prevalence of Fe-deficiency anaemia is usually indicated by the prevalence of anaemia[8]. Anaemia was known to affect

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about 47 % of pre-school age children globally during 1993–2005[8,9]. Fe deficiency can lead to premature death and impaired or delayed mental and physical development in children[10,11].

Vitamins B, D and K, Zn, Se and Ca are also considered vital for child health and development. Thiamin (vitamin B_1) assists in the metabolism of carbohydrates and branched-chain amino acids[12]. Beriberi is associated with those populations who have a low thiamin intake together with a low-fat but a high-carbohydrate diet[13]. Vitamin B_{12} is responsible for brain development during infancy and DNA synthesis[14]. One review demonstrated the existence of low vitamin B_{12} levels in specific populations of children and adolescents in five countries[15]. Vitamin D plays an important role in Ca uptake for bone growth, osteoporosis and rickets prevention[16]. Vitamin D deficiency was suggested to be common despite the lack of information on global prevalence[17]. Zn and vitamin K are essential for protein synthesis[18,19]. More than 25 % of the populations in Latin American, Asian and African countries were categorised as at high risk of Zn deficiency[20]. Vitamin K deficiency bleeding (VKDB) is commonly recognised in neonates with inadequate intake/levels of vitamin K[21]. Se acts as an antioxidant to help protect the body against free radicals[22]. Keshan disease, a congestive cardiomyopathy, is recognised to be associated with Se deficiency[23] and is endemic in China[24]. Se deficiency is also implicated in Kashin–Beck disease (osteochondropathy)[25] although iodine deficiency is considered common in this disease[26,27]. Ca is required to maintain the rigidity and strength of bones to prevent osteoporosis[28]. It was suggested that low Ca intake was commonly seen in developing countries[17].

In order to address micronutrient deficiency among children aged 6–59 months, UNICEF collaborated with the WHO to develop a daily multiple micronutrient formula for supplementation[29]. Further, the FAO and the WHO published guidelines for implementing the fortification of widely distributed and consumed foods such as wheat, maize and flour[30]. In 1995, China initiated universal salt iodisation (USI) to prevent and control IDD[31]. The effectiveness of food-based approaches has also been explored[32–34]. The objective of the present study was to review the literature on the deficiency status of micronutrients among children and the factors influencing various deficiency statuses in China. Information on deficiencies can guide policy makers to assess the potential long-term consequential impact on children and implement interventions accordingly.

Method

The systematic review was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) Statement, which was included to ensure the transparency and completeness of reporting systematic reviews and meta-analyses[35]. The search was performed in PubMed by using MeSH (Medical Subject Headings) terms and keywords. Search terms were used as follows: (Vitamin OR minerals OR nutrient) AND child AND (Hong Kong OR China) AND (deficiency OR malnutrition OR deficient). All databases were searched in June 2012. Titles, abstracts and the content of the articles were screened to determine the suitability for inclusion. Reference lists from retrieved studies were reviewed for the identification of potentially relevant studies.

Inclusion and exclusion criteria

The inclusion criteria were published studies investigating the distribution of micronutrient deficiencies and factors influencing deficiency status. Subjects included should live in China. Articles written in both English and Chinese were included. Conference proceedings, animal studies, studies reporting interventions only and studies examining macronutrients in subjects aged >18 years were excluded.

Data extraction

Extracted data included study site (regions, cities, provinces of China), sample size, study duration and age of subjects. Statistical data such as prevalence and incidence; mean serum, urinary or hair levels of different micronutrient indicators; and odds ratios were also extracted.

Results

Figure 1 summarises the literature search and study selection process. The electronic database search yielded 335 studies. A total of 300 records were screened and full texts of eighty-seven studies were retrieved for in-depth evaluation. Of these, thirty-five studies were excluded as micronutrient deficiency was not reported. Nine additional publications were identified in the reference lists of retrieved studies. As a result, sixty-one articles were included in the current review. A summary of the included studies and the serum, urinary or hair levels of different micronutrient indicators are presented in Supplemental Table 1 and Supplemental Table 2, respectively (online supplementary material).

Vitamin A

The prevalence of subclinical VAD (serum retinol level ≤0·70 μmol/l or ≤20 μg/dl) decreased gradually from approximately 40 % to lower than 10 % from 1988 to 2009[36–46] (Table 1). However, there was little variation in the prevalence of marginal VAD (serum retinol level >0·70–1·05 μmol/l or 20–30 μg/dl), which ranged from 20 % to 45 % from 1989 to 2009[36–39,42,44–47].

Studies showed that the prevalence of VAD decreased with increasing age[36,38,39,43]. No significant difference was found in serum vitamin A level between genders in

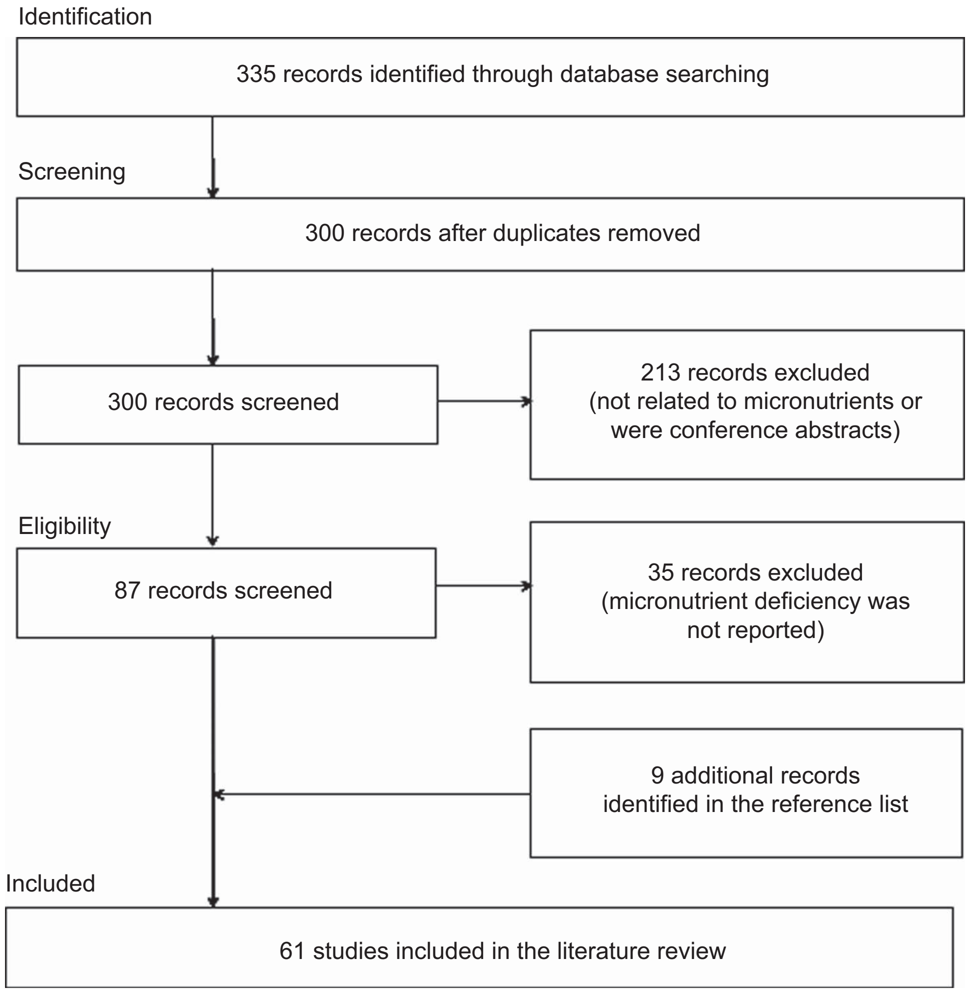

Fig. 1 Summary of the literature search and selection of studies for inclusion

all age groups(36,38,40,47). Vitamin A status was associated with growth rates among children(47). This implies that children with a high growth rate have high demand for vitamin A. However, a review suggested that children's diets generally contain small quantities of plant carotenoids(48). Four studies indicated that children living in rural areas had a higher risk of VAD than those in urban areas and over 50 % of vitamin A-related child deaths were in western provinces(36,37,40,44,49). A study showed that children with low socio-economic status had significantly lower mean serum retinol concentration than those with high socio-economic status in both urban (35·6 *v.* 37·5 μg/dl) and rural areas (26·5 *v.* 31·6 μg/dl)(42). A short duration of breast-feeding and low consumption of vitamin A-rich foods were suggested as reasons for low serum retinol concentration among children with low socio-economic status(42). However, breast-feeding was concluded to be a risk factor of subclinical VAD in Auhui since some lactating mothers might not provide adequate vitamin A in the breast milk(41). Children living in livestock farming counties had generally higher serum vitamin A concentration than those in other farming counties due to a common diet including milk and meat products in livestock farming counties in Tibet(38).

Vitamin B

Two surveys conducted in Yunnan and Chongqing reported the prevalence of thiamin and vitamin B_{12} deficiency, respectively(50,51) (Table 2). In 2001, the prevalence of thiamin deficiency was 10·5 % in Yunnan(50). Vitamin B_{12} deficiency and marginal vitamin B_{12} deficiency respectively were present in 4·5 % (8/177) and 10·7 % (19/177) of children aged 2–7 years in Chongqing(51). The average serum vitamin B_{12} level was higher among urban children (615 pg/ml) than rural children (481 pg/ml)(51). There were no significant differences in serum vitamin B_{12} level between genders(51).

Vitamin D

Vitamin D deficiency rates were reported in different parts of China(52–56) (Table 3). The prevalence of severe vitamin D deficiency was found to be 45·2 % in winter and 6·7 % in summer among adolescents in Beijing(55). In

Table 1 Summary of the prevalence of VAD in different groups of Chinese children aged <18 years

Author/year	Study site	No. of subjects studied	Age (years)	Prevalence of marginal VAD* (%)	Prevalence of subclinical VAD† (%)
Tian (1988)[43]	Tianjin City	774	0·25–7	NA	0·25 year: 46·6 0·5 year: 55·9 1 year: 41·4 2 years: 29·5 3 years: 36·8 5 years: 21·0 0·25–7 years: 39·3
Wang (1989)[44]	Wuhan City	495	0·5–3	Urban Total: 23·5 0·5–1 year: 25·0 1–2 years: 26·6 2–3 years: 20·9 Rural Total: 37·5 0·5–1 year: 53·3 1–2 years 39·4 2–3 years: 22·7	Urban Total: 10·0 0·5–1 year: 12·5 1–2 years: 11·7 2–3 years: 8·2 Rural Total: 17·5 0·5–1 year: 15·6 1–2 years: 14·4 2–3 years: 22·1
Lin (2002)[36]	14 provinces	8669	0–5	Whole country Total: 39·2 0–0·5 year: 45·7 0·5–1 year: 45·9 1–2 years: 41·1 2–4 years: 37·5 4–5 years: 37·2 Area Rural: 44·5 Urban: 28·4 Coastal: 35·1 Inland: 39·0 Remote: 42·6	Whole country Total: 11·7 0–0·5 year: 33·4 0·5–1 year: 17·9 1–2 years: 12·7 2–4 years: 10·6 4–5 years: 8·0 Area Rural: 15·0 Urban: 5·2 Coastal: 5·8 Inland: 11·5 Remote: 16·8
Tan (2002)[37]	14 provinces	8669	0–5	39·2	11·7
Mi (2003)[38]	Tibet	1257	0–5	Total: 38·4 0–0·5 year: 54·2 0·5–1 year: 38·9 1–2 years: 35·6 2–3 years: 38·6 4–5 years: 36·9 Cities: 30·0 Livestock farming: 35·1 Farming: 43·2 Semi-farming: 45·1	Total: 8·4 0–0·5 year: 22·2 0·5–1 year: 13·3 1–2 years: 8·5 2–3 years: 5·4 4–5 years: 7·9 Cities: 5·4 Livestock farming: 4·7 Farming: 11·0 Semi-farming: 12·3
Jiang (2006)[39]	4–5 provinces	7826	0–6	40·1	Total: 12·2 0 year: 26·6 1 year: 14·1 2 years: 11·3 3 years: 10·1 4 years: 7·9 5 years: 8·4 6 years: 7·0 Western area: 17·4 Inland area: 11·8 Coastal area: 6·2
Li (2006)[45]	China	380	3–12	44·7	8·4
Yang (2007)[40]	Zhejiang Province	357	0–4	Total: 7·3 0–0·5 year: 2·6 0·5–1 year: 17·1 1–2 years: 12·9 2–3 years: 4·4 3–4 years: 4·2 4–5 years: 5·4	Total: 3·1 0–0·5 year: 15·8 0·5–1 year: 8·6 1–2 years: 2·9 2–3 years: 0 3–4 years: 0 4–5 years: 0
Zhang (2007)[41]	Anhui Province	1052	0–5	NA	Total: 6·9 0 year: 34·7 1 year: 26·4 2 years: 15·3 3 years: 6·9 4 years: 9·7 5 years: 6·9

Table 1 *Continued*

Author/year	Study site	No. of subjects studied	Age (years)	Prevalence of marginal VAD* (%)	Prevalence of subclinical VAD† (%)
Jiang (2008)[42]	Beijing City	1236	0–6	Total: 38·0 Urban 0–0·5 year: 41·2 1–2 years: 34·7 2–3 years: 33·3 3–6 years: 31·5 Rural 0–0·5 year: 59·5 1–2 years: 43·5 2–3 years: 40·2 3–6 years: 38·5	Total: 7·8 High SES groups in urban areas: 2·0 Low SES groups in urban areas: 1·4 High SES groups in rural areas: 6·3 Low SES groups in rural areas: 15·7
Chen (2009)[46]	Chongqing City	459	2–7	25·9	6·3

VAD, vitamin A deficiency; NA, not applicable; SES, socio-economic status.
*Marginal VAD defined as serum retinol level >0·70–1·05 μmol/l or 20–30 μg/dl.
†Subclinical VAD defined as serum retinol level ≤0·70 μmol/l or ≤20 μg/dl.

Table 2 Summary of the prevalence of vitamin B deficiency and insufficiency in different groups of Chinese children aged <18 years

Author/year	Study site	No. of subjects studied	Age (years)	Prevalence of vitamin B_{12} deficiency* (%)	Prevalence of marginal vitamin B_{12} deficiency† (%)
Gao (2006)[51]	Chongqing City	351	2–7	4·5	10·7
Author/year	**Study site**	**No. of subjects studied**	**Age (years)**	**Prevalence of thiamin deficiency‡ (%)**	**Insufficiency in thiamin supply§ (%)**
Li (2007)[50]	Yunnan Province	352	0–1·5	10·5	5·7

*Vitamin B_{12} deficiency defined as serum vitamin B_{12} level <200 pg/ml.
†Marginal vitamin B_{12} deficiency defined as serum vitamin B_{12} level of 200–300 pg/ml.
‡Thiamin deficiency defined as thiamin (μg)/creatinine (g) <120.
§Insufficiency in thiamin defined as thiamin (μg)/creatinine (g) between 85 and 120.

Table 3 Summary of the prevalence of vitamin D deficiency in different groups of Chinese children aged <18 years

Author/year	Study site	No. of subjects studied	Age (years)	Prevalence of severe vitamin D deficiency* (%)	% of children with 25(OH)D <25 nmol/l	% of children with 25(OH)D <50 nmol/l
Du (2001)[55]	Beijing City	787	12–14	Winter Total: 45·2 Rural: 45·1 Suburban: 49·6 Urban: 42·5 Summer Total: 6·7 Rural: 9·2 Suburban: 6·6 Urban: 5·1	NA	NA
Strand (2009)[53]	Yuci District	250	1–2	NA	Spring: 65·3† Fall: 2·8†	NA
Liang (2011)[56]	Nanjing City	142	0–10	Healthy children: 1·3 Sick children: 16·7	NA	Healthy children: 10·5 Sick children: 30·8
Zhu (2012)[52]	Hangzhou City, Zhejiang Province	6008	0–16	NA	0–1 year: 0·4 2–5 years: 1·1 6–11 years: 2·0 12–16 years: 3·3	0–1 year: 5·4 2–5 years: 21·9 6–11 years: 40·4 12–16 years: 46·4

25(OH)D, 25-hydroxyvitamin D; NA, not applicable.
*Severe vitamin D deficiency defined as 25(OH)D level <12·5 nmol/l.
†Children with 25(OH)D level <12 ng/ml.

Yuci, the percentage of children with 25-hydroxyvitamin D (25(OH)D) level <12 ng/ml was higher in spring (65·3 %) than in autumn (2·8 %) in 2003[53]. Another study showed that the percentage of children with 25(OH)D level <25 nmol/l and <50 nmol/l ranged from 0·4 to 3·3 % and from 5·4 to 46·4 %, respectively[52].

Table 4 Summary of the prevalence of vitamin K deficiency and incidence of VKDB in different groups of Chinese children aged <18 years

Author/year	Study site	No. of subjects studied	Age (years)	Prevalence/incidence (%)
Zhou (2002)[58]	Shangdong Province	28 156	0	Incidence of VKDB: 3·3 Rural: 5·0 Urban: 1·2
Wang (2009)[59]	Beijing Municipality	251	0–16	Among patients with haemorrhagic stroke, vitamin K deficiency: 76·6 (72/94) No vitamin K supplement after birth: 73·6

VKDB, vitamin K deficiency bleeding.

Age, gender and health status were the risk factors contributing to low serum 25(OH)D level. The mean serum 25(OH)D level decreased with age in 6000 children <16 years old in Zhejiang Province but no significant difference was found between genders[52]. Among them, adolescents aged 12–16 years had the highest prevalence of low serum 25(OH)D. In Anhui Province, a significant seasonal difference between genders was found and the serum 25(OH)D level among children at age 15 years was maximum in summer. In general, boys had higher levels of 25(OH)D than girls. In non-summer periods, boys' 25(OH)D level dropped with increasing age, but girls' 25(OH)D level increased gradually[57]. A study in Nanjing reported that the mean serum 25(OH)D level among sick children (65·7 nmol/l) was less than that of healthy children (80·5 nmol/l). There was no significant difference between age groups[56]. Furthermore, a seasonal pattern of vitamin D deficiency was observed from studies conducted in Yuci and Beijing[53–55]. Such patterns were also observed in Anqing[57] where vitamin D deficiency rates of nearly 50 % were found in spring and winter[53–55].

Vitamin K

One study reported the incidence of VKDB to be 3·3 % among 28 156 live newborns in Shandong from 1998 to 2001[58] (Table 4). VKDB was more prevalent in rural (5·0 %) than in urban areas (1·2 %). Further, preterm infants with diarrhoea, pneumonia and jaundice had a higher incidence of VKDB than full-term infants[58]. Infants who were breast-fed had higher risk of having VKDB[58]. Although one study proposed that vitamin K deficiency was the major cause of haemorrhagic stroke in young infants, 73·6 % of patients with VKDB did not receive vitamin K after birth in Beijing[59].

Iodine

According to the WHO, median urinary iodine concentration <0·79 μmol/l or <99 μg/l indicates mild iodine deficiency[60]. Table 5 illustrates the prevalence of goitre and percentages of subjects with different urinary iodine concentrations. A review indicated that Hong Kong children had optimal iodine nutrition levels in 1995–1997 in two surveys but elevated cord blood thyroid-stimulating hormone (>10 mU/l), indicating iodine insufficiency, among 22 % of neonates in 1984[61]. In contrast, another cross-sectional study conducted in Hong Kong reported that 45·3 % of 104 children aged 5–16 years had iodine deficiency[62]. There was an increase in the proportion of children with iodine deficiency from 11·4 % in 1999 (1476/12 984) to 15·6 % in 2005 (1707/10 939)[63]. A mean urinary iodine level of 100·7–110·0 μg/l was found in children aged 7–14 years in Guizhou Province[64] and only 29·9 % of 448 urinary samples in Zhejiang Province reached the normal urinary iodine level[65]. In addition, 353 children aged 5–14 years from three areas with endemic Kashin–Beck disease and one non-endemic area in Yulin had mean urinary iodine values in the range of 43–89 μg/l[66]. A study conducted in Tibet with 557 children aged 5–15 years reported that 66 % had urinary iodine level <20 μg/l[67]. However, some studies reported that about 80 % of the children reached normal urinary iodine level in Gansu[31,68]. A median urinary iodine level of 209·8–223·7 μg/l among forty children aged 8–10 years was observed[69]. In contrast, excessive iodine levels were observed in various parts of China including Anhui, Shandong, Shanxi and Jiangsu[70]. In provinces with median drinking-water iodine levels of 150 to ≥500 μg/l, the median urinary iodine level varied from 357·7 to 1150·4 μg/l in children aged 8–10 years[70]. In Shangdong Province, the mean urinary iodine levels of children aged 6–12 years were 427·0–1194·5 μg/l before the termination of iodised salt supply[71]. One study also reported a higher median urinary iodine level in rural areas (456–519 μg/l) compared with urban areas (231–354 μg/l)[72].

Goitre rates varied in different parts of China. In Hong Kong, 3·5 % of 2439 adolescents aged 12–18 years had goitre[73]. The goitre rate was much higher in Jiangxi Province (7·6 % in 1991)[74], Tibet (46 % in 1995)[26] and Gansu Province (13·5 % in 2005)[31] and the rate increased with age[31].

Iron

The prevalence of anaemia ranged from 8 % to 40 % in different regions[51,75–78] (Table 6). A survey reported the variation in the prevalence of anaemia to be 7·5–32·9 % among students aged 9–11 years in Shaanxi Province[79]. The Fe deficiency rate in 540 children aged 6–14 years was reported to be even higher (55·7 %) in Jiangxi Province[80] and a rate of 24·3 % was found in Jintan among 1656 children aged 3–5 years[81].

Table 5 Summary of the prevalence of goitre and the percentage of subjects with different UIC in different groups of Chinese children aged <18 years

Author/year	Study site	No. of subjects studied	Age (years)	Prevalence of goitre (%)	% of children with different UIC
Yan (1994)[74]	Jiangxi Province	NA	7–14	Before intervention* 1983: 7·4 1987: 21·0 After intervention 1993: 7·6	NA
Kung (1996)[62]	Hong Kong SAR	104	5–16	NA	UIC < 0·79 μmol/l†: 45·3
Moreno-Reyes (1998)[67]	Lhasa Prefecture, Tibet	575	5–15	46·0	UIC < 20 μg/l: 65·5 (365/557)
Wong (1998)[73]	Hong Kong SAR	2439	12–18	3·5	NA
Wang (1998)[65]	Zhejiang Province	6869	8–10	10·0	UIC ≤ 50 μg/l: 31·9
Shi (2002)[68]	Linxia Region, Gansu Province	151	0, 3–5	NA	UIC < 100 μg/l 0 year: 6·8 3–5 years: 21·7
Guo (2007)[71]	Gaoqing County, Shangdong Province	NA	6–12	15·2 (61/401)	NA
Wang (2009)[31]	Gansu Province	1241	8–10	1995: 38·7 2005: 13·5	NA
Liu (2010)[63]	China	NA	8–10	1999: 5·9–8·9 2002: 4·1–7·0 2005: 4·3–5·7	UIC < 100 μg/l 1999: 11·4 2002: 14·1 2005: 15·6
Shen (2011)[70]	Anhui, Beijing, Fujian, Hebei, Henan, Jiangsu, Inner Mongolia, Shandong, Shanxi, Tianjin and Xinjiang Provinces	56 751	8–10	1·2–14·4	NA

UIC, urinary iodine concentration; SAR, Special Administrative Region; NA, not applicable.
*Iodised salt, surgery and injection of iodine supplement.
†UIC < 0·79 μmol/l = mild iodine deficiency (WHO)[60].

A difference of up to 10 % in Fe deficiency rates was reported between urban and rural areas in 1992–2005[76] but another study reported similar deficiency rates in these areas[78]. A cross-sectional study reported that the incidence of Fe deficiency in 1012 children was 26·5 % in rural Beijing[82]. In Beijing, the highest anaemia rate (48·8 %) was found among the 211 exclusively breast-fed infant boys at 4 months in 2003–2004[83]. Another study also reported lower blood Hb levels among infants when compared with other age groups[84]. A study suggested that possible reasons to explain the high rate of anaemia among children in China[76] was that mothers lacked Fe during pregnancy. Moreover, Chinese infants and children mainly consumed vegetables, which have low Fe content, in their diets[76].

Zinc

Seven studies reported Zn deficiency rates[81,84–90] (Table 7). A study involving 13 929 children showed that the prevalence of Zn deficiency in Beijing was 13·7 % in 2007 and these rates decreased with age[84]. A study conducted in Jintan reported the Zn deficiency rate among children aged 3–5 years to be 38·4 %[81]. Other studies showed even higher Zn deficiency rates which were over 50 % in the age of 0–8 years[85–89]. However, two studies showed that Zn deficiency rates increased with age[85,89].

Selenium

Table 8 illustrates the prevalence and incidence of Se deficiency. A cross-sectional study showed that the blood Se level was lower than the normal reference value in 84·7 % of 532 subjects in Qinghai Province[91]. A study mentioned the increase in blood Se levels among patients with Keshan disease aged <18 years living in rural areas from 1995 to 2005[92]. The mean serum Se level increased steadily to a non-endemic level in 2000 and attained the highest level in 2005. Two studies conducted in Lhasa Prefecture, an Se- and iodine-deficient area in Tibet, reported that 49 % of 280 subjects had Kashin–Beck disease[67] and all had severe Se deficiency[27]. There was also high Se deficiency rate (83 %) in 120 children aged 6–14 years in Shaanxi Province[93]. Low hair Se concentration was found to be associated with an increased risk of Kashin–Beck disease in a study conducted in Shaanxi Province[66]. Another study conducted in Shaanxi also showed that the Se levels in hair samples of children living in a Kashin–Beck disease-endemic area were lower than the normal range[94].

Calcium

Table 9 demonstrates the prevalence of Ca deficiency. The prevalence of coexisting Ca and vitamin D deficiency was reported to be 9·4 % in winter in 1995–1996 among 1248 adolescent girls[55] in Beijing. In 2000, 116 children (19·6 %) had decreasing Ca level in hair with age in Jiangxi Province[85]. Another study also reported similar

Table 6 Summary of the prevalence of anaemia in different groups of Chinese children aged <18 years

Author/year	Study site	No. of subjects studied	Age (years)	Prevalence of anaemia* (%)
Leung (2001)[75]	Hong Kong SAR	51	4–14	8·5
Gao (2006)[51]	Chongqing City	351	2–7	8·3
Chang (2007)[76]	China	2416	0–5	In 2005 Total: 19·3 Urban: 11·3 Rural: 21·9
Ma (2008)[78]	31 provinces	NA	0–2	Total: 31·1 Urban: 29·3 Rural: 31·6
Chen (2009)[46]	Chongqing City	459	2–7	23·5
Willows (2011)[77]	Heqing County, Yunnan Province	172	1–5	Hb < 110 g/l Total: 36·3 1–2 years: 55·3 2–3 years: 26·3 3–4 years: 32·5 4–5 years: 32·7 Hb < 100 g/l Total: 10·5 1–2 years: 21·1 2–3 years: 5·3 3–4 years: 10·0 4–5 years: 7·3

SAR, Special Administrative Region.
*Anaemia defined as serum Hb level <110 g/l for children aged 3–6 years, serum Hb level <120 g/l for children aged 7–12 years, serum Hb level <130 g/l for males aged 13 years or more and serum Hb level <120 g/l for females aged 13 years or more.

findings[84]. Ca deficiency was also profound in Jintan (34·3 %) among children aged 3–5 years[81].

Discussion

This is the first systematic review summarising the available literature regarding micronutrient deficiency status and factors influencing micronutrient status among children in China. All studied micronutrients of interest (except iodine) were deficient among some children in China.

Public health implications of vitamin A, vitamin D, iron and iodine deficiencies

The WHO has established certain criteria for assessment of the severity of micronutrient deficiency. The prevalence of subclinical VAD among children aged <6 years in 1995–2009 indicated that VAD was a moderate public health problem in many parts of China[95]. However, the trend of VAD appeared to decrease throughout the study years. This may be due to administration of vitamin A in deficient areas which is based on the national programme of action for child development in China during 2001–2010[96]. With respect to Fe-deficiency anaemia, China could also be classified as a country in which this is of moderate public health significance as the reported prevalence ranged from 20 % to 40 % in 2007–2011[97]. For iodine, IDD in Hong Kong may be considered to be less severe than in Gansu Province, Jiangxi Province and Tibet as the total goitre rate in school-aged children was below 5 %[60,73]. According to a consensus statement of an Expert Panel Group in 2003, 35·8 % of pregnant women may have mild iodine deficiency[98,99]. Since iodised salt was not widely available in Hong Kong[100], IDD is still a concern. In contrast, some provinces had excess iodine supply after the implementation of USI including Shandong. Hence, termination of the iodised salt supply was considered. In addition to vitamin A, Fe and iodine, vitamin D deficiency was also a public health concern among adolescents in China especially in spring and winter. Further research should be conducted to monitor the latest deficiency prevalences of these micronutrients.

Status of intake and its relationship to micronutrient deficiency

Apart from deficiency rates, insufficient micronutrient intake could be the proxy to indicate the severity of certain micronutrient deficiencies which were rarely reported in the available literature. The intakes of vitamin B, Zn, Se and Ca are discussed below to complement our findings. Most of the studies reported low intakes of these micronutrients, which supported our results showing the deficiency problems of these micronutrients. One study reported that vitamin B_{12} intake in 6·8 % of 177 children was lower than the recommendation from the WHO and the mean vitamin B_{12} intake was 5·1 μg/d[51]. For Zn, 150 children (87·2 %) did not meet the estimated average requirement in Yunnan Province[77]. A cross-sectional study reported that the mean Zn intake (8–10 mg/d) in thirty-one provinces in 2002 was lower than the recommended nutrient intake[101]. The inadequate Zn intake rate was shown to be higher in the rural area than in the urban area[78]. High prevalence of Se deficiency was found in our review. A study reported that 36·9 % of

Table 7 Summary of the prevalence of zinc deficiency in different groups of Chinese children aged <18 years

Author/year	Study site	No. of subjects studied	Age (years)	Prevalence (%)
Yang (1995)[89]	Zhejiang Province	NA	1–14	Zn deficiency*: 57·8
Lao (1999)[88]	Guangzhou Province	86	1–6	Serum Zn level lower than normal value: 57·0
Rao (2001)[85]	Jiangxi Province	826	NA	Hair Zn level below criterion†
				Total: 73·1
				0 year: 37·5
				0·5 year: 49·4
				1 year: 74·2
				2 years: 75·7
				3 years: 85·0
				4 years: 80·8
				5 years: 85·4
				6 years: 76·0
				7 years: 86·7
Ma (2003)[87]	Xi'an City, Shaanxi Province	98	0–15	Zn deficiency
				0–5 years: 47·3
				6–11 years: 68·4
				12–15 years: 49·0
Hu (2006)[86]	Guangzhou Province	632	NA	Zn deficiency
				Male
				Total: 45·6
				0–1 year: 78·9
				1–2 years: 41·8
				2–3 years: 48·5
				3–4 years: 45·0
				4–5 years: 47·0
				5–6 years: 56·0
				6–10 years: 38·0
				11–16 years: 30·0
				Female
				Total: 51·2
				0–1 year: 73·8
				1–2 years: 44·4
				2–3 years: 55·0
				3–4 years: 55·7
				4–5 years: 54·5
				5–6 years: 61·1
				6–10 years: 46·1
				11–16 years: 38·8
Song (2008)[84]	Beijing City	13 929	0–14	Zn deficiency‡: 13·7
Liu (2010)[81]	Jintan County, Jiangsu Province	1656	3–5	Zn deficiency: 38·1

NA, not applicable.
*Hair Zn level normal reference value: children aged 1–6 years, 100 μg/g; children aged 7–14 years, 135 μg/g.
†Hair Zn level criterion: age 0 years, 136 μg/g; children, 119 μg/g.
‡Peripheral blood Zn level normal reference range: children aged 0–1 year, 58–100 μmol/l; children aged 1–2 years, 62–110 μmol/l; children aged 2–3 years, 66–120 μmol/l; children aged 3–5 years, 66–130 μmol/l; children aged >5 years, 76·5–140 μmol/l.

Table 8 Summary of the prevalence and incidence of selenium deficiency, Kashin–Beck disease and Keshan disease in different groups of Chinese children aged <18 years

Author/year	Study site	No. of subjects studied	Age (years)	% of children with different blood or hair Se levels	Prevalence (%)/ incidence
Shu (1996)[91]	Qinghai Province	50	8–20	Blood Se ≤1·2 μmol/l: 84·7	NA
Moreno-Reyes (1998)[67] and Suetens (2001)[26]	Lhasa Prefecture, Tibet	575	5–15	Serum Se <5 ng/ml: 38·0	NA
Peng (2000)[93]	Shaanxi Province	NA	6–14	Hair Se <0·2 μg/g	NA
				Before Se supplementation: 83·0	
				After Se supplementation: 23·0	
Zhang (2001)[66]	Yulin City, Shaanxi Province	353	5–14	NA	Prevalence of Kashin–Beck disease: 33·7
Cai (2009)[92]	Sichuan Province	NA	0–18	NA	Incidence of Keshan disease: 1·7 in 100 000

NA, not applicable.

385 children aged 11–17 years in Jiangsu Province had insufficient Se intake in 2002 with a daily intake of <45–50 mg/d[101]. However, a national nutrition survey found that 80–90 % of the recommended daily intake was achieved in 1992[102]. In line with our findings, a low Ca intake was found among Chinese children, especially in rural areas, in many studies[77,102–104]. One study reported that all pre-school children (172/172) from Yunnan did not have adequate Ca intake in 2004[77]. This may be due to the lack of milk and dairy products intake in the traditional Chinese diet[48,102]. For vitamin K, incidence of VKDB could give some insights to assess vitamin K

Table 9 Summary of the prevalence of calcium deficiency in different groups of Chinese children aged <18 years

Author/year	Study site	No. of subjects studied	Age (years)	Prevalence (%)
Du (2001)[55]	Beijing City	1248	12–14	Clinical vitamin D and Ca deficiency in winter: 9·4
Rao (2001)[85]	Jiangxi Province	826	NA	Hair Ca level below criterion* Total: 19·6 0 year: 6·2 0·5 year: 1·3 1 year: 5·0 2 years: 11·4 3 years: 23·9 4 years: 11·5 5 years: 27·0 6 years: 20·0 7 years: 30·0
Liu (2010)[81]	Jintan County, Jiangsu Province	1656	3–5	Ca deficiency: 34·3

*Hair Ca level criterion: for age 0 years, 992 μg/g; children, 801 μg/g.

deficiency and our result showed that it was fairly common among newborns. Due to the limited information on the deficiency status of these micronutrients, an effective national surveillance system should be developed to assess micronutrient deficiency in China.

Other factors influencing micronutrient deficiencies

Factors that influenced vitamin A status such as poor family economic status and living in rural areas may be associated with a poor socio-economic status. Other micronutrients such as Fe and Zn also had higher deficiency rates in rural areas as compared with urban areas[76,78]. It is suggested that strong seasonal patterns may be observed with vitamin D deficiency. This may be due to the amount of sunlight exposure and lack of outdoor activities among Chinese children[53,57]. Few studies in the literature reported the impact of dietary intake on vitamin D deficiency, but one proposed that the amount of sunlight exposure was the main determinant of vitamin D status compared with dietary intake[54]. Furthermore, another study suggested that the lack of a formal recommendation on vitamin D daily requirement for children aged >2 years led to lower intakes of vitamin D supplements among this age group[52]. Infants with pre-existing disease or those from rural areas are at higher risk of developing VKDB. More attention should be focused on this vulnerable group in order to prevent vitamin K deficiency. Zn deficiency may also result from reduced Zn intake rates and the reduction in bioavailability of Zn. Consumption of foods with high phytate content (e.g. rice and wheat) in the rural population may result in low Zn absorption secondary to reduced bioavailability[105]. Low Ca intake rates were observed[102,106] and can result in Ca deficiency.

Interventions to tackle micronutrient deficiencies

Supplementation should be provided to those vulnerable groups on a short-term basis, while food fortification is recommended in a long-term strategy. A study showed that the cost of supplementation per disability-adjusted life year was higher than that of food fortification[78].

Previous studies have reported various interventions to control nutrient deficiencies. For vitamin A, supplementation was shown to be effective among children aged 2–7 years[107]. The daily administration of fortified biscuits is also suggested to be given to schoolchildren since it was shown to be effective in reducing VAD[108] and easily administered in schools. Other countries have used sugar and margarine as vehicles for vitamin A fortification[17,109]. Fortification vehicles should be carefully chosen based on their distribution and consumption patterns among the target group in China. Vitamin D supplements should be given to the adolescents, especially in winter. Milk powder can also be used to increase vitamin D and Ca intake[110]. However, Chinese children in general have low milk consumption, so nutrition education is needed to supplement the implementation of fortified milk. For iodine, there is evidence of an association between the 10-year implementation of USI and the reduction of iodine deficiency and goitre rate[59]. This finding is validated by other studies conducted in several countries[111–114]. However, in some places where the iodine concentration in water is high, the implementation of USI may result in excess iodine intake[71,115]. Further studies are required to determine the need for USI in these areas. For Fe deficiency, soya sauce fortified with NaFeEDTA was shown to be effective in Guizhou Province in reducing the anaemia rates in children[116]. In Venezuela, wheat and flour have been fortified with Fe but there are limited data demonstrating the efficacy and effectiveness of this addition[117]. For Zn, infant formula, milk and cereals could be considered as fortification vehicles but there is limited evidence of effectiveness[17]. For Se, supplements were introduced in Tibet and showed a reduction in incidence of Keshan disease[92]. More studies are needed to evaluate the effectiveness of these fortified vehicles on the nutritional status of Chinese children.

In contrast to supplementation and food fortification, increasing dietary diversity is a more sustainable option to control malnutrition[17]. However, regulatory policies and government support are needed for this type of intervention. Breast-feeding is recommended for infants to prevent micronutrient deficiencies, but supplementation of vitamins A, B and K and Fe should be given to improve the micronutrient intakes of lactating mothers before, during and after pregnancy as well as breast-fed neonates. A comprehensive review is strongly recommended to evaluate the cost-effectiveness and cost–benefit of the interventions specifically for the Chinese.

Limitations

There are several limitations with the current review. First, there is little published literature relating to some of the micronutrients, namely vitamin B, vitamin K and Ca. Second, a large range of micronutrient deficiency rates was observed in the included studies. This is likely due to a wide variation in sample sizes and different study locations, which makes the interpretation of results less applicable. Third, various blood sampling methods were used in the different studies – for example, samples collected from finger prick, an antecubital vein and the jugular vein – contributing to outcome measures that were not comparable. Fourth, subjects in some of the cross-sectional studies were recruited in hospitals or clinics resulting in higher deficiency rates that might result from selection bias. Moreover, most studies examined the deficiency rates in regions, provinces or counties, levels which covered only a small portion of the population in China. Hence generalisability is limited, especially considering the different cultures and food consumption habits in different regions of China.

Conclusion

The included studies reported that all micronutrients of interest were deficient among children in China to varying extents, except iodine. Poor socio-economic status, environmental factors and the Chinese diet inevitably contribute to micronutrient status. However, few studies relating to some micronutrients were found in the literature; therefore, it is hard to draw a conclusion of overall deficiency status for these micronutrients. Both supplementation and food fortification are effective ways to reduce the prevalence of deficiency, but even when supplements are given out free of charge, adoption would require a significant investment on attracting public engagement. Public health policies should consider implementing strategies such as increasing dietary diversity and fostering nutrition education to address these deficiencies among Chinese children.

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Supplementary material

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