

# Vitamin D and iron deficiencies among Saudi children and adolescents: A persistent problem in the 21<sup>st</sup> century

Abdulrahman A. Al-Hussaini<sup>1,2,3</sup>, Zahir Alshehry<sup>4</sup>, Abdulwahid AlDehaimi<sup>5</sup>, Muhammed Salman Bashir<sup>6</sup>

<sup>1</sup>Division of Pediatric Gastroenterology, Children's Specialized Hospital, King Fahad Medical City, <sup>2</sup>College of Medicine, Alfaisal University, <sup>3</sup>Prince Abdullah bin Khalid Celiac Disease Research Chair, Department of Pediatrics, Faculty of Medicine, King Saud University, <sup>4</sup>The Department of Pathology and Laboratory Medicine, Division of Biochemistry, King Fahad Medical City, <sup>5</sup>Department of Pathology and Laboratory Medicine, Division of Toxicology, King Fahad Medical City, <sup>6</sup>Department of Biostatistics, Research Services Administration, Research center at King Fahad Medical City, Riyadh, Saudi Arabia

## Abstract

**Background:** Although several studies have reported on the prevalence of micronutrients in Saudi Arabia, most frequently vitamin D and iron, they are either old or hospital- or primary health care center-based. The objectives of our study were to provide more updated data on the prevalence rate of micronutrients deficiency among the Saudi general pediatric population and to determine if there is an association between micronutrients deficiency and undernutrition.

**Methods:** The present study is part of a cross-sectional mass screening study, "Exploring the Iceberg of Celiacs in Saudi Arabia" conducted among school-aged children (6–16 years) in 2014–2015. A sample of 7,931 children aged 6–16 years was randomly selected. We identified thin children [body mass index (BMI) z-score < -2 SD, for age and gender], using the WHO reference 2007. A case-control study was performed, where the sera of 182 thin children (cases) and 393 normal BMI children (controls) were tested for levels of iron, ferritin, vitamin D, zinc, selenium, and copper.

**Results:** The prevalence of thinness was 3.5%. The two most common micronutrients deficient among Saudi children with normal BMI were iron (20%) and vitamin D (78%). Vitamin D levels were significantly higher among boys as compared to girls (39.6 nmol/L vs. 31.15 nmol/L;  $P < 0.001$ ). Deficiency of copper, zinc, and selenium occurred in 0.25%, 1%, and 7.4% of the children with normal BMI. Comparisons between the cases and controls did not show statistically significant differences.

**Conclusion:** Vitamin D and iron deficiencies are still common forms of malnutrition in the Saudi community, that have remained unchanged over the past 20–30 years, while the intake of trace elements (zinc, copper, and selenium) is adequate as evident by normal serum levels in the vast majority of the investigated children. We could not observe a correlation between undernutrition and micronutrient deficiencies.

**Keywords:** Copper, iron deficiency, micronutrients, Riyadh, Saudi Arabia, selenium, thinness, undernutrition, vitamin D deficiency, zinc deficiency

**Address for correspondence:** Dr. Abdulrahman A. Al-Hussaini, Department of Pediatrics, Children's Specialized Hospital, King Fahad Medical City, Riyadh, Saudi Arabia.

E mail: aa\_alhussaini@yahoo.com

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## INTRODUCTION

The role of specific micronutrient deficiencies in the etiology of growth retardation has gained the attention of researchers. The essential role for several micronutrients in growth has been demonstrated by both animal- and clinical-based human trials of supplementation with single micronutrients.<sup>[1]</sup> Hundreds of enzymes in the human body require micronutrients as cofactors for different metabolic pathways, especially important for growth and development. However, it has been unclear as to which nutrient deficiencies contribute most often to faltering growth. Different hypotheses have been proposed for the effects of micronutrients on growth. Deficiencies of some micronutrients, such as iron, zinc, copper, selenium, manganese, vitamin D, and vitamin A, may contribute directly to growth retardation via their effects on the growth hormone and insulin-like growth factor I system,<sup>[2,3]</sup> bone development,<sup>[4]</sup> and impairment of collagen-cross linking,<sup>[1]</sup> or indirectly by reducing the appetite and subsequent poor energy intake.<sup>[5,5]</sup> Undernutrition during childhood is associated with adverse effects on school achievement, cognitive development, and general health.<sup>[6,7]</sup> Because of their public health importance, up-to-date information on micronutrient deficiencies and monitoring of trends is crucial for developing and evaluating success of interventional programs to promote good nutrition in any country.

Micronutrient deficiencies are highly prevalent in developing countries, and the most probable cause is low content in the diet.<sup>[8]</sup> Several local studies have reported data on the prevalence of few micronutrients individually, most frequently vitamin D and iron.<sup>[9-23]</sup> Majority of these studies were hospital- or primary health care center-based, with very few community-based studies. There are several major limitations in these studies which are related to small sample size, mostly adult population, and non-random selection of the study population. These major limitations led to significant bias and limited the precision of the study results. None of these studies investigated the relationship between a specific vitamin or mineral deficiency and undernutrition.

These facts prompted us to 1) estimate the prevalence rates of micronutrients deficiency among Saudi children and adolescents and 2) determine whether there is an association between micronutrients deficiency and growth impairment.

## PATIENTS AND METHODS

### Study setting and design

The present study is part of a cross-sectional mass screening study, “Exploring the Iceberg of Celiacs in

Saudi Arabia” conducted among children aged 6–16 years in 2014–2015.<sup>[24]</sup> The present research project constituted two study designs: 1) an observational cross-sectional population-based study to determine the prevalence of thinness; 2) nested case-control study, where the sera of thin children (cases) and age and gender-matched, normal BMI children (controls) randomly selected at the rate of 2 controls per one case, were tested for levels of iron, ferritin, vitamin D, zinc, selenium, and copper.

Thinness/wasting was defined as z-score of low body mass index [BMI] for age and gender  $< -2$  SD. The World Health Organization (WHO) 2007 growth standards and references were used to calculate the estimates of thinness,<sup>[25]</sup> and Z-scores of weight, height, and BMI for students aged 5–18 years were determined using the WHO Anthroplus software.<sup>[26]</sup> To determine whether the socioeconomic status has an impact on micronutrients deficiency, we collected data on four main indicators, namely parents’ educational level, family income, habitation, and parents’ jobs, as we described in more detail previously.<sup>[27]</sup>

### Study population

*Source population:* The details of the methodology of the celiac mass screening study, from which the study population for the present study was recruited, has been described elsewhere.<sup>[24]</sup> In brief, a total of 104 schools (61 primary schools and 43 intermediate schools; 53 male schools and 51 female schools) were randomly selected from the five “administrative” geographic regions of Riyadh city (North, South, East, West, and Center) using probability proportionate sampling procedure. Parents of 10,046 children signed the informed consent and accepted to participate in the study, however, 7,931 students [mean age:  $11.22 \pm 2.62$  years; 4,988 females (63%)] accepted to participate in the study and provided complete data for the analysis. Riyadh city is considered the most representative of the whole Saudi population because of its high rate of migration from different parts of the country and the similar demographic, ethnic, genetic, and dietary characteristics of its inhabitants with the population in other regions of Saudi Arabia.

**Table 1: Prevalence of thinness based on age groups and gender**

Age Group (year)	Total (n=7931)	Thin (n=274)			P
		Total (n=274)	Males (n=140)	Females (n=134)	
6–16 years	2943 males 4988 females	3.45%	4.75%	2.68%	$\chi^2$ 0.048
6–9	2250	104 (4.6%)	60 (42.9%)	44 (32.8%)	$\chi^2$ 0.087
10–13	3885	119 (3.1%)	54 (38.6%)	65 (48.5%)	$\chi^2$ 0.097
>13	1796	51 (2.8%)	26 (18.6%)	25 (18.7%)	$\chi^2$ 0.986

$\chi^2$  Chi-square test of significance;  $P < 0.05$  was considered statistically significant

## Study procedures

### 1. Anthropometric measurements

The weight and height of the participants were measured in the school by a trained team of doctors and nurses. Weight was measured with the students wearing light clothing and no shoes, using an electronic scale to the nearest 100 grams. Height was measured using a wall-mounted stadiometer, with the children not wearing shoes. The measurements were recorded to the nearest 0.1 cm. BMI was calculated as the ratio of weight (kilograms) to the square of height (meters).

### 2. Laboratory testing

The blood collected during a school day was centrifuged at 2000 RPM for 10 minutes and plasma was separated and stored at  $-80^{\circ}\text{C}$  until analysis. The sera of the selected cases and controls were tested for levels of iron, ferritin, vitamin D, zinc, selenium, and copper, as described below:

- Serum iron was measured using a Roche Cobas c701 automated analyzer (Abbott, Chicago, Illinois, IL, United States). Normal reference value is as follows: male = 11–28  $\mu\text{mol/L}$ , female = 6.6–26  $\mu\text{mol/L}$ .
- Serum ferritin was measured using a Cobas e602 automated analyzer (Abbott, Chicago, Illinois, IL, United States). Normal reference value is as follows: serum ferritin, male = 30–400  $\text{ug/L}$ , female = 13–150  $\text{ug/L}$ .
- Serum 25-OH vitamin D was measured using a Cobas e602 automated analyzer (Abbott, Chicago, Illinois, IL, United States). Normal reference value is 50–250  $\text{nmol/L}$ . We adopted the Institute of Medicine cutoff points for vitamin D levels<sup>[28]</sup> classifying serum levels into sufficient (50–75  $\text{nmol/L}$ ), desirable ( $>75$   $\text{nmol/L}$ ), vitamin D insufficient (VDI) [25–50  $\text{nmol/L}$ ], vitamin D deficient (VDD) [ $<25$   $\text{nmol/L}$ ].
- Sera of copper, selenium, and zinc were measured using Agilent technology in a 7500ce series automated analyzer using inductively coupled plasma mass spectrometry (Santa Clara, CA, United States). Normal reference values are as follows: zinc = 9.7–18.9  $\mu\text{mol/L}$ ; selenium = 0.8–1.9  $\mu\text{mol/L}$ ; copper = 12.6–23.5  $\mu\text{mol/L}$ .

## Ethical considerations

This study was approved by the institutional review board (number: 11-066) and the Ministry of Education in Saudi Arabia. All study participants, or their legal guardians, provided informed written consent prior to study enrollment.

## Statistical analysis

All Categorical variables such as gender and age group are presented as numbers and percentages. Continuous variables, age, z-scores and serum iron, serum ferritin, etc., are expressed as mean  $\pm$  standard deviation (SD) and median interquartile range, (IQR). Nonparametric tests were used when data were skewed. Kolmogorov–Smirnov test was used to check the assumption of normal distribution. Independent sample t-test/Mann–Whitney U test was applied to find the significant differences between groups. Furthermore, ANOVA/Kruskal–Wallis was used to determine the significant differences between groups. Chi-square/Fisher's exact test was used accordingly where the cell expected frequency was smaller than 5, and it was applied to determine the significant association between categorical variables. Multivariate logistic regression analysis by backward elimination method was applied to determine the most significant risk factors/predictors by using a specified reference level. A two-tailed *P* value of  $<0.05$  was considered as statistically significant. All data were entered and analyzed through statistical package SPSS 25 (SPSS Inc., Chicago, IL, USA).

## RESULTS

Out of 7,931 participants in the celiac mass screening study, a total of 274 children and adolescents were thin (3.5%). Stratification of thinness prevalence rate according to age group is presented in Table 1 and indicates a progressive decrease in the prevalence of thinness with advancing age, without significant differences between girls and boys. Out of 274 sera for thin children and adolescents, 182 sera were sufficient to undergo laboratory testing.

**Table 2: Micronutrients serum levels among normal and thin children**

Variables	Thin children (n=182)	Normal BMI children (n=393)	OR [95% C.I.]	P
Age (yrs)	11.01 $\pm$ 2.65	10.66 $\pm$ 2.48	1.031 [0.907–1.173]	‡ 0.639
Gender M/F	105 (57.7%)/77 (42.3%)	210 (53.4%)/183 (46.6%)	0.96 [0.941–1.03]	‡ 0.681
Mean z-score BMI for height	-2.17 $\pm$ 0.55	-0.26 $\pm$ 0.76	0.03 [0.001–0.222]	‡ $<0.001$
Mean z-score height for age	-1.74 $\pm$ 0.95	-0.66 $\pm$ 0.79	0.006 [0.0003–0.111]	‡ $<0.001$
Serum iron (9.0 – 30.4 $\mu\text{mol/L}$ )	16.6 $\pm$ 6.5	16.14 $\pm$ 6.3	0.997 [0.955–1.041]	‡ 0.899
Serum ferritin (22–275 $\text{ug/L}$ )	47 $\pm$ 71.6	54 $\pm$ 119	0.998 [0.992–1.004]	‡ 0.471
Serum vitamin D (50–350 $\text{nmol/L}$ )	33 $\pm$ 10	40.6 $\pm$ 12.6	1.006 [0.984–1.029]	‡ 0.590
Serum copper (13.2 – 21.4 $\mu\text{mol/L}$ )	32 $\pm$ 12.2	32.6 $\pm$ 11.4	1.012 [0.983–1.043]	‡ 0.418
Serum zinc (9.7 – 18.9 $\mu\text{mol/L}$ )	22.2 $\pm$ 8.2	22.8 $\pm$ 9.1	0.995 [0.961–1.03]	‡ 0.773
Serum selenium (0.8 – 1.9 $\mu\text{mol/L}$ )	1.32 $\pm$ 0.48	1.4 $\pm$ 0.56	1.628 [0.933–2.84]	‡ 0.086

Data presented as mean  $\pm$  standard deviation, or *n* (%) as appropriate. ‡ Chi-square test of significance; † Independent sample t-test; *P* < 0.05 was considered statistically significant

**Table 3: Micronutrients serum levels among normal BMI children according to gender**

Variables	Males	Females	OR [95% C.I.]	P
Serum iron (9.0 – 30.4 umol/L)	18.5 [22.575–13.725]	17.3 [21.3–13.8]	0.997 [1.039–0.956]	° 0.874
Serum ferritin (22–275 ug/L)	34.2 [48.75–23]	28.65 [43.525–17.25]	0.989 [1.003–0.975]	° 0.134
Serum vitamin D (50–350 nmol/L)	39.6 [51.8–31.35]	31.15 [41.575–25.15]	0.949 [0.972–0.927]	° <0.001
Serum copper (13.2 – 21.4 µmol/L)	30.75 [38.65–23.575]	35.15 [42.175–26.4]	1.042 [1.07–1.014]	° 0.003
Serum zinc (9.7 – 18.9 µmol/L)	21.05 [26.35–17.025]	22.35 [28.525–17.925]	0.998 [1.03–0.967]	° 0.920
Serum selenium (0.8 – 1.9 umol/L)	1.3 [1.7–1]	1.3 [1.65–0.9]	1.448 [2.413–0.869]	° 0.155

° Mann–Whitney U test;  $P < 0.05$  was considered statistically significant

### Micronutrients among normal growth children and adolescents

We analyzed the sera of 393 healthy normal growing children and adolescents [Tables 2–4]. The majority of the group fell within the vitamin D deficiency/insufficiency range (78%) [VDD = 46 (12%), VDI = 252 (65.8%)]; the remaining had sufficient ( $n = 83$ ; 21.7%) and desirable ( $n = 2$ ; 0.5%) 25-OH vitamin D levels. Deficiency of iron, ferritin, copper, zinc, and selenium occurred in 20%, 24%, 0.25%, 1%, and 7.4%, respectively, of the normal growing children and adolescents.

Comparative analysis of the median serum levels of the micronutrients by gender [Table 3] delineated 25-OH vitamin D concentrations as significantly higher among boys as compared to girls (39.6 nmol/L [IQR: 51.8–31.35] versus 31.15 nmol/L [IQR: 41.575–25.15];  $P < 0.001$ ), while copper concentration was significantly higher among girls as compared to boys (35.15 µmol/L [IQR: 42.175–26.4] versus 30.75 µmol/L [IQR: 38.65–23.575];  $P = 0.003$ ). Stratification by age group [Table 4] showed a progressive decline in median concentrations of 25-OH vitamin D and copper with advancing age, with adolescents consistently having lower concentrations than younger children. However, the median iron concentration in adolescents was significantly higher than in children.

### Comparison of micronutrients among thin and normal growing children and adolescents

As shown in Table 2, comparison between the two groups did not show statistically significant differences, although thin children had a tendency to have lower serum levels of selenium than normally growing children. Similar to the normal BMI children, 25-OH vitamin D in thin children was significantly more deficient in girls

than in boys (median 40.2 nmol/L in boys versus 31.4 nmol/L in girls;  $P = 0.003$ ) [Table 5]. Stratification by age group [Table 6] showed a significant progressive decline in median concentrations of 25-OH vitamin D and copper with advancing age among the thin group ( $P = 0.001$  and 0.014, respectively), similar to the observation among the normally growing children, but younger age group (6–9 years) were significantly more deficient in selenium than older children and adolescents ( $P = 0.036$ ). No significant association was observed between iron and vitamin D deficiencies and socioeconomic status.

### DISCUSSION

Our study presents a snapshot of the current undernutrition status of school-aged children and adolescents in a representative sample of Riyadh city and highlights several important observations. First, the prevalence of thinness among Saudi children and adolescents (3.6%) is comparable to that in developed countries (3%–6%).<sup>[29,30]</sup> Second, the two most common micronutrients deficiencies seen in Saudi children and adolescents, who are growing normally, are iron and vitamin D. Third, despite the extensive literature showing the importance of micronutrients for growth, no significant association was observed between undernutrition and micronutrients levels.

Over the past 40 years, Saudi Arabia has witnessed significant economic prosperity, leading to changes in diet, lifestyle, and health patterns. Concurrent with these changes, the prevalence rates of overweight and obesity are rising alarmingly among Saudi children. In a previous report, on the same population of the present study, we have shown that the prevalence rate of obesity in Riyadh city increased from 12.7% in 2006<sup>[29]</sup> to 18.2%

**Table 4: Micronutrients serum levels among normal BMI children according to age group**

Variables	6–9 years	10–13 years	>13 years	P
Serum iron (9.0–30.4 umol/L)	17.7 [21.88–13.4]	17.9 [22.15–13.7]	20.3 [23.83–15.98]	* 0.039
Serum ferritin (22275 ug/L)	33.9 [49.15–22.1]	32.6 [44.65–23.8]	26.9 [49.73–18.68]	* 0.439
Serum vitamin D (50–350 nmol/L)	46.3 [55.3–35.4]	37.05 [46.78–28.98]	29.6 [35–24.58]	* <0.001
Serum copper (13.2–21.4 µmol/L)	36.1 [43.9–28.1]	30.5 [37.18–23.9]	25.8 [34.85–18.4]	* <0.001
Serum zinc (9.7–18.9 µmol/L)	21.2 [27.9–17.4]	21.5 [26.93–16.48]	22.6 [27.4–18.2]	* 0.560
Serum selenium (0.8–1.9 umol/L)	1.25 [1.6–0.9]	1.4 [1.7–1]	1.2 [1.6–0.9]	* 0.093

\* Kruskal- Wallis;  $P < 0.05$  was considered statistically significant



**Table 5: Micronutrients serum levels among thin children according to gender**

Variables	Males	Females	OR [95% C.I.]	P
Serum iron (9.0–30.4 $\mu\text{mol/L}$ )	18.5 [22.3–13.6]	17.65 [22.8–13.03]	1.025 [1.088–0.965]	<sup>o</sup> 0.426
Serum ferritin (22–275 $\mu\text{g/L}$ )	34 [49.7–22.38]	28 [40.7–18.1]	0.999 [1.005–0.993]	<sup>o</sup> 0.698
Serum vitamin D (50–350 $\text{nmol/L}$ )	40.2 [51.75–31.98]	31.4 [39.75–25]	0.938 [0.978–0.9]	<sup>o</sup> 0.003
Serum copper (13.2–21.4 $\mu\text{mol/L}$ )	30.9 [38.7–24]	31.85 [41.25–24.7]	1.01 [1.055–0.967]	<sup>o</sup> 0.650
Serum zinc (9.7–18.9 $\mu\text{mol/L}$ )	21.1 [26–17]	21.95 [27.5–17.1]	0.959 [1.019–0.903]	<sup>o</sup> 0.177
Serum selenium (0.8–1.9 $\mu\text{mol/L}$ )	1.3 [1.7–0.9]	1.3 [1.7–1]	2.581 [7.598–0.877]	<sup>o</sup> 0.085

<sup>o</sup> Mann–Whitney U test;  $P < 0.05$  was considered statistically significant

in 2015 (combined overweight and obesity = 31.6%),<sup>[30]</sup> a rate that is similar to the obesity rate in the pediatric population in the United States.<sup>[31]</sup> In 2017, Alshammari *et al.*<sup>[32]</sup> reported a prevalence rate of thinness in 6.9%, short stature in 5.7%, and overweight and obesity in 32% of 1107 children and adolescents (age: 5–18 years), from Hail region. The low prevalence rate of thinness (3.6% and 6.9%) and high prevalence rate of overweight and obesity (>30%) from two major cities (Riyadh and Hail) indicate that there is a rightward shift in the right tail of the BMI distribution associated with the obesity epidemic in Saudi Arabia, similar to developed countries.

Although undernutrition is low in Saudi Arabia by anthropometric measures, vitamin D and iron deficiencies, which are forms of malnutrition, are still common (78% and 20%, respectively). The deficiencies of vitamin D and iron in Saudi Arabia have remained at high rates [vitamin D: 50%–100%; Iron: 20%–40%] in the old and most recent reports,<sup>[9–23]</sup> which indicate lack of or ineffective intervention strategies during the past years. Similar to previous reports among Saudi children and adolescents, our data showed that adolescent girls are the most vulnerable group to develop vitamin D deficiency, likely related to two main reasons: lack of sunlight exposure and reduced vitamin D intake.<sup>[10,11,13,19–21]</sup> Majority of Saudi adolescent girls are veiled by pubertal age, which potentially reduces sun exposure, in addition to the very hot climate throughout most of the year, which restricts outdoor activities.<sup>[11,21]</sup> Inadequate exposure to sunlight in Saudi Arabia, which is likely to persist because of the difficult hot weather, necessitates attention to additional dietary sources of vitamin D. The Saudi diet is traditionally based on foods such as milk, wheat, rice, vegetables, lamb, chicken, and dates and other local fruits, which are poor

sources of vitamin D. The best sources of vitamin D are fish, such as salmon, tuna, and fish liver oils, but seafood, in general, is an uncommon dietary staple in Saudi Arabia. The American Academy of Pediatrics recommends a daily intake of 400 IU/day of vitamin D for infants and 600 IU/day for children.<sup>[33]</sup> However, natural milk and various dairy products contain only negligible amounts of vitamin D and hence are fortified voluntarily by manufacturers in Western countries, following the Food and Agriculture Organization guidelines.<sup>[34]</sup> Reports from Saudi Arabia showed that vitamin D deficiency is common even in individuals taking adequate amounts of dairy products because of the low vitamin D contents in the dairy products from different manufacturers.<sup>[13,35]</sup> Thus, it is less likely that children in Saudi Arabia will obtain sufficient vitamin D from dietary sources alone. Lack or inadequate vitamin D fortification of dairy products and other food products in Saudi Arabia<sup>[13,35]</sup> may be one of the major reasons for widespread deficient levels of vitamin D as compared to that in Western countries.

Vitamin D deficiency is a serious health threat in Saudi Arabia. Apart from its major role in bone metabolism by enhancing calcium absorption, receptors of vitamin D are expressed in several extra, skeletal tissues through which it regulates many physiologic functions. Besides adverse effects on bone growth, vitamin D deficiency has been linked to development of autoimmune diseases (such as type 1 diabetes, thyroid disease, and multiple sclerosis), cardiovascular disease, and cancer.<sup>[36]</sup> Our data showed that vitamin D deficiency was common early in childhood, a period of vigorous growth and development, and increased with age. Like an iceberg, the majority of the children with vitamin D deficiency are “asymptomatic” and unaware of their nutritional problem<sup>[9]</sup> (i.e. representing the invisible part of the iceberg under the water line). Initial

**Table 6: Micronutrients serum levels among thin children according to age group**

Variables	6–9 years	10–13 years	>13 years	P
Serum iron (9.0–30.4 $\mu\text{mol/L}$ )	16.4 [22.23–12.63]	18.8 [23.5–12.8]	17.1 [23.7–11.35]	* 0.394
Serum ferritin (22–275 $\mu\text{g/L}$ )	28.85 [48.95–16.05]	30.4 [48.9–19.9]	27.5 [54.25–17.1]	* 0.726
Serum vitamin D (50–350 $\text{nmol/L}$ )	42.5 [48.53–33.58]	37.4 [48.7–29.2]	29.5 [40.2–23.05]	* 0.001
Serum copper (13.2–21.4 $\mu\text{mol/L}$ )	34.45 [44.73–26.98]	29.3 [36.2–22.35]	25.3 [33.6–15.9]	* 0.014
Serum zinc (9.7–18.9 $\mu\text{mol/L}$ )	22 [27.23–16.48]	20.9 [23.83–16.63]	20.5 [27.3–15.8]	* 0.354
Serum selenium (0.8–1.9 $\mu\text{mol/L}$ )	1 [1.6–0.7]	1.4 [1.7–1.1]	1.35 [1.8–1.03]	* 0.036

\*Kruskal- Wallis;  $P < 0.05$  was considered statistically significant

symptoms of vitamin D deficiency are subtle and can go unrecognized, including body, muscle aches, and fatigue, or could be misdiagnosed as fibromyalgia, chronic fatigue syndrome, or depression.<sup>[37]</sup> The overt manifestation of vitamin D deficiency, such as rickets, osteomalacia, and bone fracture (visible tip of the iceberg), occurs with advanced persistent deficiency. This calls for the implementation of a multifaceted policy in facing the threat of vitamin D deficiency; this policy should constitute 1) campaigns of medical education to increase awareness of children, adults, and physicians of benefits of vitamin D, dietary sources rich in vitamin D, early symptoms of vitamin D deficiency, and importance of sun exposure; 2) screening of high-risk groups for vitamin D deficiency and provide vitamin D supplements; and 3) fortification of common Saudi food staples with vitamin D. What serum level of 25-OH vitamin D should be targeted to avoid consequences of vitamin D deficiency has been a controversial issue. However, the Pediatric Endocrine Society targeted a serum 25-OH vitamin D level of at least 50 nmol/L as meeting the needs of nearly all children and adults.<sup>[38]</sup>

The second most common micronutrients deficiency in Saudi Arabia is iron deficiency. Reports from 1999 until 2015 revealed that iron deficiency anemia (hemoglobin <12 g/dl) ranged between 10% and 30% among Saudi children and adolescents, with adolescent girls most affected.<sup>[14-17]</sup> The presence of iron deficiency/depletion in 20%–25% of Saudi children and adolescents in our study indicates that the prevalence of iron deficiency has remained the same over the past two decades. There is substantial evidence in the literature that iron has beneficial effects on the normal growth and psychomotor and mental development of children. Deficiency of iron in the body of a child might impair learning abilities, cognition, school performance, and behavior, negatively affect the immune system, and can be a risk factor for attention-deficit/hyperactivity disorder and cerebral vein thrombosis.<sup>[15,39-41]</sup> Depletion of iron stores, even without hemoglobin drop, might impair exercise tolerance.<sup>[42]</sup> Early recognition of iron deficiency, even before the development of anemia, is very crucial in preventing these complications. If not treated early, these complications could be irreversible.<sup>[42]</sup> Foods rich in iron include red meat, liver, legumes, foods like spinach and broccoli, and fish, are not common food staples on Saudis' tables. In addition, some dietary habits might impair iron absorption like ingestion of carbonated beverages and high phytate-containing items (grains, beans, nuts) while or immediately after eating iron-containing food. Hence, health education is very critical to raise awareness of the public on dietary choices rich in iron and the practice of healthy dietary habits.

Data on trace elements' status in Saudi Arabia are very limited and old.<sup>[18,43-45]</sup> Two reports in the 1990s from the Western province of Saudi Arabia investigated serum zinc among children and adults and drew attention that zinc deficiency was common (serum zinc ranged between 0.50–13.90  $\mu\text{mol/L}$  versus the international established standard of 7.65–22.95  $\mu\text{mol/L}$ ).<sup>[43,44]</sup> In 2001, another study observed a negative effect of zinc deficiency on the growth of young children in Jeddah city.<sup>[46]</sup> Zinc is important in the production of growth hormones. Zinc deficiency is associated with various pathological conditions, including impaired immunity, delayed wound healing, retarded growth, neural development disorders, and degenerative diseases.<sup>[46]</sup> Results regarding the relationship between serum zinc levels and growth have been inconsistent.<sup>[1,47,48]</sup> Our data showed that zinc deficiency is rare among Saudi children and adolescents (1%). This suggests that the dietary intake of zinc has improved remarkably over the past two decades among Saudi children. Data on serum copper levels among Saudis are lacking. Copper is found in the body's connective tissues and participates in the metabolism of bone and cartilage. Copper can promote Ca and phosphorus deposits and collagen synthesis.<sup>[1]</sup> Our data are reassuring that deficiency of serum copper is very rare (<1%). In fact, the medians of serum copper concentrations (males = 30.75  $\mu\text{mol/L}$ , 38.65–23.57  $\mu\text{mol/L}$ ; females = 35.15  $\mu\text{mol/L}$ , 42.175–26.4  $\mu\text{mol/L}$ ) are above the internationally established standard (9–25  $\mu\text{mol/L}$ ), which indicate that the dietary intake of copper in Saudi children is sufficient. Our data is supported by Al-Daghri *et al.*<sup>[49]</sup>, who investigated the dietary intake of selected micronutrients among Saudi children and adults in Riyadh and found that the intake of copper is higher than the estimated average intake and adequate intake values, but far below their upper limit intake. Estrogens are reported to raise serum copper levels by increasing ceruloplasmin concentrations,<sup>[50]</sup> which might explain the higher levels among females in our study. Data on serum selenium levels among Saudis are lacking. The major sources of selenium in most diets are meat, poultry, fish, nuts, eggs, yogurt, cheese, and cereals. Meat, poultry, dairy products, eggs, and cereals are favorable diets among Saudis and seem to provide sufficient amounts of selenium as shown in a previous study.<sup>[49]</sup> Our data also supports this notion and shows that selenium deficiency is uncommon among normal growing children and adolescents (7.5% versus 22% among the low BMI group). There was a tendency toward lower selenium levels among low BMI group ( $1.32 \pm 0.48 \mu\text{mol/L}$ ) as compared to normal BMI group ( $1.4 \pm 0.56 \mu\text{mol/L}$ ,  $P = 0.086$ ).

Studies investigating the effects of micronutrients deficiency on growth have been inconsistent.<sup>[1]</sup> The

lack of association between any of the micronutrients and growth faltering in our study might be due to the low number of children and adolescents with low BMI. Our study could serve as a stimulus for investigators to carry out larger studies for proper evaluation of a relationship between micronutrients deficiency and growth impairment.

Our study has several limitations that need to be considered. The cross-sectional nature of our study precluded any inference on the causality between variables. The study sample was not a national sample; this makes it difficult to generalize the results to the whole country and does not necessarily represent the rural community in Saudi Arabia. However, this data from the largest Saudi city is representative of the Saudi urban setting and can be compared to prevalence data recorded in other urban cities in other countries. We strengthened the study by utilizing the random stratifying sampling methodology as an ideal source population pool from which our cases and controls were selected. The study has merits in providing updated data on the prevalence of micronutrients status among Saudi children and adolescents and in being the first to investigate the correlation between growth impairment and micronutrients deficiencies in Saudi Arabia.

In conclusion, despite the significant economic prosperity and high living standards in the Saudi community, vitamin D and iron deficiencies are still persistent in the 21<sup>st</sup> century, while the intake of trace elements (zinc, copper, and selenium) is adequate as evident by normal serum levels in the vast majority of the investigated children and adolescents. Despite the ample evidence on the importance of these micronutrients for growth, we could not observe a correlation between growth impairment and micronutrients deficiencies.

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### Conflicts of interest

There are no conflicts of interest.

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