Original Communication

# The Prevalence of Zinc Deficiency and its Correlation with Iron Status and Economical Living Area in 9 – 12-Year-Old Children

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**Abstract:** *Objective:* This study aimed firstly to assess zinc and iron status of 9 – 12-year-old children of Tehran and secondly to determine a cut-off for circulating biomarkers of iron status to identify children at increased risk of zinc deficiency. *Research methods & procedures:* In a cross-sectional study, demographic and anthropometric data from 505 boys and 467 girls aged 9 – 12 years from Tehran primary schools were obtained and their zinc and iron status was assessed. *Results:* The prevalence of zinc deficiency, anemia, and iron depletion was 12.4, 14.6, and 9.5%, respectively. Serum zinc con-centration was significantly lower in children with anemia than in their non-anemic peers ($p < 0.05$). There was no significant association between zinc and iron status and serum high sensitivity C-reactive protein. Zinc-deficient children, compared to those with normal serum zinc, had significantly shorter stature (139.7 (±6.9) vs 141.3 (±7.1) cm, CI: -2.97 – -0.2, $p = 0.029$). Serum zinc concentration was the predictor of height in the children ($p = 0.004$, CI: 0.01 – 0.054). A logistic regression model showed an increased risk of low serum zinc and ferritin in children who resided in economically poor regions (OR = 1.65, $p = 0.043$; OR = 1.92, $p = 0.016$, respectively). Using ROC curve and Youden index, the optimal cut-off value for serum ferritin to indicate zinc deficiency was 14.9 µg/L (sensitivity = 90%, specificity = 61%). *Conclusions:* Lowered zinc and iron status among the children in deprived regions is likely to be due to poor quality of diet. Moreover, children with serum ferritin lower than 14.9 µg/L must be carefully assessed for concomitant zinc deficiency.

**Keywords:** Iron, zinc, ferritin, school children

## Introduction

Zinc and iron deficiencies are among the prevalent nutritional problems in developing countries [1] and may bring about severe consequences in childhood and adolescence [2, 3]. Iron deficiency anemia (IDA) is the most common type of anemia globally, affecting more than 60% of children worldwide [4]. The outcomes of IDA are many, including weakness, cognitive and mood disorders, decreased work capacity and in-creased susceptibility to infections [5]. Zinc deficiency, a nutritional problem known in Iranian children for a long time [6], has been identified as one of the main causes for mortality in developing countries [7]. Zinc and iron share many dietary sources including meat and legumes, thus iron deficiency may be accompanied by various degrees of zinc deficiency [8].

Linkage between iron and zinc deficiencies has been described already in the late 1960s [9]. Later, high occurrence of concomitant micronutrient deficiencies, including iron, zinc and vitamin D was observed in Chinese school children [10]. Linear association between zinc and iron stores in non-anemic females has also been reported [11]. The latest national food consumption survey showed that the main dietary sources of both iron and zinc in Iran are bread and cereals [12], which are also rich in fiber and phytate, the main inhibitors of intestinal absorption of the two micronutrients [13, 14]. While there are precise methods to assess iron status, assessment of zinc status is still highly disputable.

This study aimed to determine a cut-off for circulating markers of iron status to identify children at increased risk of zinc deficiency. To do this, first the prevalence of poor

zinc and iron status in primary school children in Tehran was estimated using available sera and the databank of «Vitamin D Study in School Children of Tehran (VDST)» [15]. Then, the link between serum zinc concentration, indicators of iron status, and anthropometric parameters was evaluated. Finally, the optimal cutoff value for serum markers of iron status to indicate zinc deficiency was determined.

Subjects and methods

The detailed method of sampling has been described elsewhere [15]. Briefly, using a 2-stage sampling method, 60 primary schools were selected by systematic random sampling from all 19 districts of the Ministry of Education in Tehran. 16–20 children in grades 4 and 5 were recruited from each school. Finally, 1111 children (573 boys, 538 girls) were enrolled in VDST. Based on the prevalence of low serum ferritin in adolescents in the latest National Investigation on Micronutrient Status (NIMS) [16], which gave the largest sample size, 393 boys and 343 girls were needed to estimate the prevalence of both iron and zinc deficiency. We finally used data and sera from 505 boys and 467 girls to conduct the study. According to the Iranian Ministry of Education, districts 1 to 7, 8 to 14, and 15 to 19 were considered as economically prosperous, semi-deprived, and deprived regions, respectively.

## Anthropometrics

As described earlier [15], weight was measured using a digital scale to the nearest of 0.1 kg (model 840, Seca, Hamburg, Germany) with light clothes and no shoes. Height was measured using a measuring tape while the child was standing upright with shoulders and heels touching a wall. Body mass index (BMI) was calculated by dividing weight (kg) by square of height (m). Weight for age (W/A), height for age (H/A) and BMI for age (BMI/A) were used to evaluate the nutritional status using NCHS/CDC/WHO reference tables. Using Epi-info (Centers for Disease Control and Prevention, Atlanta, Georgia, US), Z-scores were calculated. In this study, Z-score of W/A ≤-2 and Z-score of H/A ≤-2 were considered as underweight and stunting, re-spectively. Similarly, BMI/A Z-scores ≤-2 and ≥+2 were considered as low weight and overweight/obesity, respectively.

## Laboratory analyses

Non-fasting blood samples were obtained in the morning and kept at RT for 1 h to clot. Sera were separated by centrifugation and stored at -80 °C until analysis. Clean, acid-washed tubes were used for trace element assays. Serum concentration of zinc was determined using a commercial kit (Elitech, Paris, France). In our hands, the intra- and inter-assay variations were 1.44 and 3.46%, respectively, and the recovery was 98–105%. We used two control sera (normal and high) for each batch of samples. The result was considered as the subject›s serum zinc concentration only when the results of both control sera were in the acceptable range presented by the manufacturer (Randox Laboratories Limited, County Antrim, UK). Concentrations of serum iron (Pars Azmoon, Tehran, Iran) were determined using a colorimetric method while transferrin and high sensitivity C-reactive protein (hs-CRP) were measured both by immunoturbidometric assay (Pars Azmoon, Tehran, Iran) with the aid of an auto-analyzer (Selectra E, Vitalab, Holliston, Netherlands). Serum ferritin was measured by immunoradiometric assay (IRMA) (Radim, Pomezia, Italy) using a gamma-counter system (Gamma I, Genesys, IL, USA). Hemoglobin (Hb) and hematocrit (Hct) had been determined earlier by an automatic cell counter (Mythic 18, Orphee, Geneva, Switzerland) [15]. The presumed cutoffs were: anemia based on hemoglobin <115 g/L [17], non-fasting serum zinc concentrations <10.7 (boys) and <10.0 µmol/L (girls), and desirable serum zinc 10.7–18 µmol/L (boys) and 10.0–18 µmol/L (girls), excess zinc >18 µmol/L (conversion factor for serum zinc concentration: µmol/L ÷ 0.153 = µg/dL) [18]. For serum iron: deficiency <3.9 µmol/L, desirable 3.9–32.9 µmol/L, excess >32.9 µmol/L (conversion factor for serum iron concentration: µmol/L ÷ 0.179 = µg/dL). For transferrin: deficiency <0.95 g/L, desirable 0.95–3.85 g/L, excess >3.85 g/L. Serum ferritin reference range for children in this age group was considered 7–140 µg/L [19]. However, serum ferritin <15 µg/L was actually regarded as iron stores being depleted [20]. In this study, children with normal hemoglobin but with ferritin <15 µg/L were considered as "at risk of IDA"; those with Hb <115g/L plus ferritin <15 µg/L were considered as affected by IDA [16].

## Statistical analyses

Quantitative and qualitative data were expressed as mean ± standard deviation (SD) or number (%), respectively. Correlations between variables were evaluated using Pearson's correlation. Qualitative data were compared by Chi square. A between groups comparison of was done by using Independent Samples t-Tests and ANOVA followed by Tukey's post hoc analysis for two and more than two groups, respectively. To eliminate the possible effect of a variable on comparison of two or more sets of variables, analysis of covariance (ANCOVA) was employed. Association of changes of the variables was evaluated by simple and multiple regression models. To determine a cutoff

point for iron status indices to indicate zinc deficiency, receiver operating characteristic (ROC) curve followed by Youden index was used and the most appropriate sensitivity and specificity were found. In this study p ≤0.05 was considered as the level of statistical significance. All analyses were performed using Statistical Package for Social Sciences (SPSS, 16.0, IBM, Chicago, IL).

## Ethical issues

The protocol of this study was approved by the Ethical Committee of the National Nutrition and Food Technology Research Institute (Code No. 04442).

# Results

The anthropometric and biochemical data are shown in Table I. The mean age of the children was 10.5±0.7 years. The occurrence of stunting (based on Z-score of H/A) and underweight (based on Z-score of W/A) was 1% for both. There was no significant association between gender and categories of Z-score for H/A, W/A or BMI/A.

Serum concentrations of zinc and indicators of iron status showed no significant difference between boys and girls with the exception of transferrin, which was slightly but significantly higher in girls than in boys (p<0.001; Table 1). All children with low serum iron had low serum ferritin as well (n=7). Serum hs-CRP did not differ significantly between boys and girls (p=0.517), between children with low and normal ferritin (0.33±0.51 vs 0.49±0.58 mg/L, p=0.310) or between children with low or normal serum zinc concentrations (0.34±0.52 vs 0.57±0.81 mg/L, respectively). Regression analysis revealed serum iron as the main predictor of hemoglobin (B=0.005, confidence interval (CI): 0.002–0.008, p<0.001). Serum zinc concentration in anemic children was significantly lower than in non-anemic children (13.8±3.2 vs 14.9±3.0 µmol/L, p<0.001). The prevalence of zinc deficiency among the children was 12.4%. Zinc status showed no significant difference between boys and girls (p=0.513).

In general, 14.6% of children were anemic, 16.1% had depleted iron stores (ferritin<15 µg/L), 9.5% had very low serum ferritin (<7 µg/L), 13% were at risk of IDA and 3.1% had actually IDA. Serum ferritin concentrations were below 7 µg/L in 7.3 and 2.5% in non-anemic and anemic children, respectively. There was no significant difference in indicators of iron status between the two genders (Table II).

Serum zinc correlated with hemoglobin (r=0.161, p<0.001), serum iron (r=0.065, p=0.043) and ferritin (r=0.225, p<0.001), all remained significant and were even more strongly correlated after adjustment for BMI (r = 0.183, p< 0.001; r=0.086, p=0.009; and r=0.243, p< 0.001, respectively). When correlations were evaluated in zinc-deficient children, there was only a significant correlation between serum zinc and ferritin (r=0.205, p=0.027). Serum zinc concentration was the predictor of height in the studied children (p=0.004, CI: 0.01–0.054). Zinc-deficient children, compared to those with sufficient serum zinc, had significantly shorter stature (139.7±6.9 vs 141.3±7.1 cm, p=0.029). Concentrations of serum zinc showed a significant difference between different tertiles of height (p=0.001) being higher in the third than in the first (15.2±2.9 vs 14.3±3.3 µmol/L, p=0.001). Combined low serum zinc and ferritin was observed in 7.7% of children with no significant difference between boys and girls (p=0.539).

**Table I.** Comparison of anthropometric and biochemical variables between boys and girls*.

| | Boys (n1 = 505) | Girls (n2 = 467) | p-value** | Total (n = 972) |
|---|---|---|---|---|
| Weight (kg) | 38.0 ± 9.7 | 39.0 ± 10.5 | 0.140 | 38.5 ± 10.1 |
| Height (cm) | 140.5 ± 6.7 | 141.6 ± 7.4 | 0.018 | 141.1 ± 7.1 |
| BMI (kg/m2) | 19.1 ± 3.8 | 19.2 ± 3.9 | 0.534 | 19.1 ± 3.9 |
| Zinc (µmol/L) | 14.8 ± 3.2 | 14.9 ± 3.2 | 0.650 | 14.8 ± 3.2 |
| Iron (µmol/L) | 15.7 ± 4.6 | 16.1 ± 4.6 | 0.197 | 15.9 ± 4.4 |
| Transferrin (g/L) | 2.3 ± 0.4 | 2.4 ± 0.4 | < 0.001 | 2.4 ± 0.4 |
| Ferritin (µg/L) | 36.0 ± 23.5 | 36.8 ± 23.6 | 0.619 | 36.5 ± 23.7 |
| Hemoglobin (g/L) | 125 ± 11.0 | 126 ± 11.0 | 0.168 | 126 ± 11.0 |
| Hematocrit (%) | 37.5 ± 2.9 | 37.5 ± 2.9 | 0.636 | 37.5 ± 2.9 |

* Data are mean ± SD;
** Independent Samples t Test;
df = 970, two-sided

Anthropometric and biochemical indicators were compared among different economical regions (Table III). Serum zinc concentrations were higher in children of prosperous than in those of deprived regions (p=0.029). Hemoglobin (p<0.001, both) and hematocrit (p=0.003, p=0.001, respectively) were also both higher in prosperous regions as compared to semi-deprived and deprived regions. However, there were no significant differences between boys and girls in economically different regions. Low zinc, ferritin and hemoglobin were significantly more

 

**Table II.** Biochemical indicators in studied children.

| | | Zinc | Iron | Transferrin | Ferritin | Hemoglobin |
|---|---|---|---|---|---|---|
| | Low | 61 (12.4) | 5 (1.0) | 0 | 44 (9.1) | 88 (17.5) |
| Boys (n1 = 505) | Desirable | 430 (87.6) | 496 (99.0) | 495 (99.0) | 441 (90.9) | 414 (82.5) |
| | High | 0 (0) | 0 (0) | 5 (1.0) | 0 (0) | 0 (0) |
| | Low | 57 (12.3) | 2 (0.4) | 0 | 47 (10.6) | 53 (11.4) |
| Girls (n2 = 467) | Desirable | 407 (87.7) | 461 (99.6) | 458 (98.7) | 395 (89.4) | 411 (88.6) |
| | High | 0 (0) | 0 (0) | 6 (1.3) | 0 (0) | 0 (0) |
| p-value* | | 1.000 | 0.454 | 0.766 | 0.441 | 0.008 |
| | Low | 118 (12.4) | 7 (0.7) | 0 (0) | 91 (9.8) | 141 (14.6) |
| Total (n = 972) | Desirable | 837 (87.6) | 957 (99.3) | 953 (98.9) | 836 (90.2) | 825 (85.4) |
| | High | 0 (0) | 0 (0) | 11 (1.1) | 0 (0) | 0 (0) |

*P-values are for comparison of the variables between boys and girls by Chi square. Data are frequency (%).

**Table III.** Comparison of anthropometric and biochemical indicators among 9 – 12-year-old children residing in economically different regions of Tehran.

| | Prosperous (n = 415) | Semi-deprived (n = 317) | Deprived (n = 220) | p1 | p2 | p3 |
|---|---|---|---|---|---|---|
| Weight (kg) | 38.9 ± 10.6 | 38.5 ± 9.9 | 37.8 ± 9.4 | 0.840 | 0.386 | 0.707 |
| Height (cm) | 141.1 ± 6.9 | 141.0 ± 7.6 | 141.0 ± 6.5 | 0.982 | 0.983 | 1.00 |
| BMI (kg/m2) | 19.3 ± 4.0 | 19.1 ± 3.7 | 18.8 ± 3.7 | 0.828 | 0.300 | 0.619 |
| Serum zinc (μmol/L) | 15.0 ± 3.0 | 14.9 ± 3.1 | 14.4 ± 3.6 | 0.776 | 0.029 | 0.140 |
| Serum iron (μmol/L) | 16.0 ± 4.5 | 15.7 ± 4.3 | 16.1 ± 4.6 | 0.471 | 0.933 | 0.796 |
| Transferrin (g/L) | 2.4 ± 0.4 | 2.3 ± 0.37 | 2.36 ± 0.38 | 0.002 | 0.488 | 0.165 |
| Ferritin (μg/L) | 35.2 ± 22.5 | 38.4 ± 24.7 | 35.5 ± 23.9 | 0.163 | 0.996 | 0.336 |
| Hemoglobin (g/L) | 129 ± 10.0 | 124 ± 9.0 | 124 ± 10.0 | < 0.001 | < 0.001 | 0.958 |
| Hematocrit (%) | 38.0 ± 3.0 | 37.2 ± 3.0 | 37.0 ± 2.6 | 0.003 | 0.001 | 0.679 |

Data are mean ± SD.
p1: Comparison between prosperous and semi-deprived (one-factor ANOVA followed by Tukey's post hoc analysis).
p2: Comparison between prosperous and deprived (one-factor ANOVA followed by Tukey's post hoc analysis).
p3: Comparison between semi-deprived and deprived (one-factor ANOVA followed by Tukey's post hoc analysis).

prevalent in deprived districts than in prosperous ones (p = 0.014, p < 0.001 and p = 0.019, respectively). Also, in semi-deprived regions, as compared to the prosperous ones, the occurrence of very low serum ferritin (<7 μg/L) and anemia (hemoglobin < 115 g/L) was significantly higher (p = 0.018 and p = 0.019, respectively; Table IV). Logistic regression analysis revealed that residing in deprived regions was accompanied by a 65% higher risk of being affected by zinc deficiency (OR = 1.65, B = 0.500, p = 0.043) and a 92% higher risk of having very low serum ferritin (OR = 1.92, B = 0.654, p = 0.016).

In ROC analysis, ferritin showed the biggest area under the curve (AUC), as compared to hemoglobin and serum iron (AUC = 0.800, CI = 0.765–0.847, p < 0.001), suggesting a high validity of serum ferritin as an alternative indicator of zinc deficiency. Using Youden index, the best cutoff for ferritin concentration to indicate zinc deficiency was 14.9 μg/L (sensitivity = 90%; specificity = 61%; Figure 1).

## Discussion

Our findings showed various degrees of zinc and iron deficiencies and a link between these two micronutrients among 9–12-year-old children in Tehran. In this investiga-

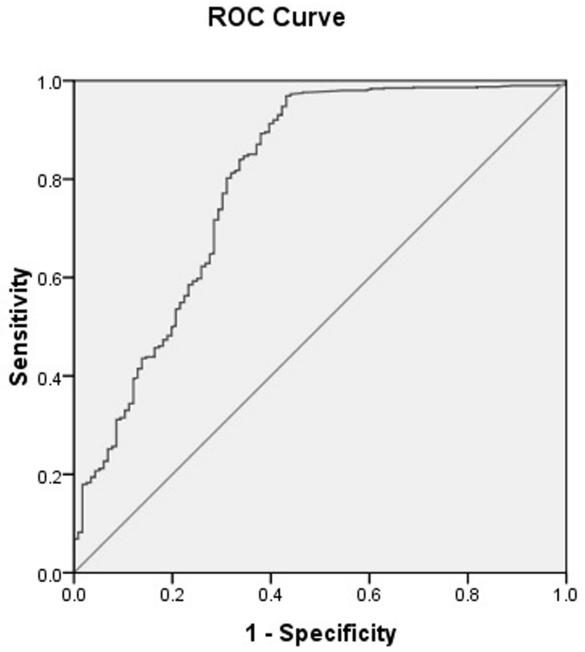


**Figure 1.** ROC curve for serum ferritin as an indicator of zinc deficiency

tion, serum zinc concentration was used as an indicator of zinc status. It is believed that serum zinc does not necessarily reflect zinc status of an individual and hence is not recommended for diagnostic and therapeutic purposes [21]. However, it is recognized as the most appropriate criterion for assessment of zinc status of a population [22, 23] as it reflects dietary intake, is responsive to interventions and since finally there are reference ranges defined for most age and sex subgroups [21].

Our data showed that more than 16% of the children were iron depleted, 14.6% were anemic and more than 3% were affected by IDA. Though only about 30% of anemic children had iron deficiency, regression analysis revealed iron status as the main predictor of hemoglobin status in these children. It has been estimated that some 1.6 billion people around the world are affected by anemia [24]. However, the prevalence of anemia and contribution of iron deficiency to anemia may differ in various populations. IDA is accompanied by impaired development in children, impaired mental and physical functions in adults and poor pregnancy outcomes (for both mother and child) [25]. Iron deficiency has been associated with dental caries [26] and poor educational progress in children [27, 28]. Nevertheless, the possible beneficial effects of improvement of iron status in children need more elucidation. For instance, in a study on 401 iron-deficient children aged 6–15 years, daily consumption of NaFeEDTA-fortified bread with lunch for 7 months resulted in significant improvement of iron status. Nevertheless, cognitive performance of the children who received iron-fortified bread, compared to the control group, was not significantly affected [29].

In the present study, 12% of the children had zinc deficiency and serum zinc concentrations significantly correlated with serum ferritin and iron. As both serum zinc and ferritin can be affected by inflammation, we measured serum hs-CRP as an indicator of inflammatory status. Absence of any significant association between serum hs-CRP with zinc and ferritin in our study population lessens the possibility of confounding effects of subclinical inflammation on our findings.

**Table IV.** Comparison of the biochemical indicators of zinc and iron status in 9 – 12-year-old children residing in economically different regions of Tehran.

| | | Serum zinc | Serum iron | Transferrin | Ferritin | Hemoglobin |
|---|---|---|---|---|---|---|
| Prosperous | Low | 41 (10.1) | 3 (0.7) | 0 (0) | 28 (6.9) | 45 (10.9) |
| | Normal | 366 (89.9) | 410 (99.3) | 405 (98.3) | 378 (93.1) | 367 (89.1) |
| | High | 0 (0) | 0 (0) | 7 (1.7) | 0 (0) | 0 (0) |
| Semi-deprived | Low | 39 (11.6) | 2 (0.6) | 0 (0) | 31 (9.4) | 57 (16.9) |
| | Normal | 296 (88.4) | 333 (99.4) | 334 (99.1) | 298 (90.6) | 280 (83.1) |
| | High | 0 (0) | 0 (0) | 3 (0.9) | 0 (0) | 0 (0) |
| Deprived | Low | 38 (17.8) | 2 (0.9) | 0 | 32 (16.7) | 39 (18.0) |
| | Normal | 175 (82.2) | 214 (99.1) | 214 (99.5) | 160 (83.3) | 178 (82.0) |
| | High | 0 (0) | 0 (0) | 3 (0.5) | 0 (0) | 0 (0) |
| p-value | | 0.061* | 0.906 | 0.334 | 0.001 | 0.019 |

Data are frequency (%).
* The occurrence of zinc deficiency in deprived regions was significantly higher than in prosperous regions (p = 0.014).

 

Zinc deficiency is associated with higher morbidity and mortality in children [30]. Severe zinc deficiency was first described in Iranians [6] and later in Egyptians [31]. It was then known that zinc and iron have almost the same dietary sources and inhibitors of intestinal absorption [32]. Parasitic infections, especially giardiasis, may have contributed to zinc deficiency in developing countries [33]. Concomitant deficiency of iron and zinc has been recently reported from Thailand [34], India [35] and Sri Lanka [36]. In the Sri Lanka study, adolescents with relatively poor iron stores (serum ferritin <30.0 µg/L), compared to those with normal iron stores, had a significantly increased risk (1.7) of being zinc-deficient (serum zinc<9.95 µmol/L) [36]. Concomitant zinc and iron deficiencies may not be confined to children and may be encountered in adults and elders. In a study on 33 apparently healthy premenopausal women, there was a significant correlation between zinc pool and iron stores, serum ferritin concentration<20 µg/L was proposed as a cutoff for increased probability of poor zinc status in this gender and age group [11]. A few years later, a significant correlation between serum zinc and hemoglobin in African-American and Hispanic children of low-income households living in Atlanta, USA, was reported [37]. An experimental study revealed that iron deficiency for 30–40 days in rats results in altered zinc and copper metabolism [38]. Our findings show for the first time that a significant link exists between serum concentrations of ferritin and zinc among primary school children, and that with serum ferritin concentrations<14.9 µg/L there is an increased likelihood of poor zinc status in this age group.

Lower zinc status in anemic children compared to non-anemic is another important finding. Zinc deficiency-associated anemia was defined nearly 57 years ago in Iran [39]. This situation might be due to low intake of common dietary sources and/or high intake of common inhibitors of intestinal absorption of both elements [39, 40]. Direct effect of zinc on hematopoiesis has also been proposed to be mediated by insulin-like growth factor (IGF)-1 [41]. Zinc supplementation in anemic hemodialysis patients has been shown as a beneficial and safe adjunct treatment of anemia [42, 43]. Nevertheless, in a large trial on 459 Guatemalan women, addition of either weekly 30 mg or daily 15 mg zinc to iron-folate supplements did not significantly improve the efficacy of the supplementation [44].

Desirable zinc status is essential for normal growth and immunity against infections in children. In the present study, zinc-deficient children had relatively shorter stature. Direct association of serum zinc level with height has already been reported [20, 45]. Despite 12% occurrence of poor zinc status and its correlation with height, the occurrence of stunting in our study population was low. In a study on 812 adolescent children aged 12–16 years, the efficacy of iron (50 mg), zinc (14 mg), and a combination of both against placebo for 5 days a week for 24 weeks was evaluated. In that study, though iron and/or zinc status was improved in the related groups as compared to the placebo group, no significant change was observed in the growth trend of the children [36]. Functional effects of zinc status improvement in children need further elucidation.

We found low occurrence of underweight among the school children. It is likely that energy intake was fairly adequate whereas higher occurrence of zinc and iron deficiency was probably due to poor diet quality in terms of micronutrients. Nevertheless, we did not perform dietary assessment.

Lower concentrations of zinc and hemoglobin in children of deprived districts, compared to prosperous ones, is noticeable. Several factors may have contributed to this finding, including higher prevalence of parasitic infections, lower micronutrient density of the diet and a combination of both. It has been suggested that serum ferritin, compared to hemoglobin, is a more sensitive indicator of parasitic infection-induced iron deficiency and is directly linked to intestinal worm load [46]. Though mean serum ferritin concentrations did not differ significantly among various economic regions, higher occurrence of low serum ferritin in children from deprived regions still brings forward the possibility of an effect of parasitoses on iron and zinc status. The prevalence of intestinal parasitoses in 19,209 school children in Tehran in 2008 was reported to be 18.4%. The prevalence of underweight and stunting in infected, compared to non-infected, children was significantly higher and although 9 parasitic species were identified, only giardia and enterobius infections showed significant associations with malnutrition [47]. However, it has been shown that only treatment of enterobiasis, but not giardiasis, may result in increment of serum zinc [48]. Notwithstanding, absence of significant differences in hs-CRP between children with normal and low serum ferritin further potentiates the possibility of nutritional inadequacy as the main factor of low zinc status.

This study has some limitations. The cross-sectional nature of the study hinders causal data interpretation. Serum zinc concentration, proposed as the most appropriate indicator of the population zinc status [21], has some limitations. Firstly, serum zinc is not a reliable indicator for mild and moderate zinc deficiency, as it is regulated in a rather narrow physiologic range via homeostatic mechanisms. Therefore it is affected only when depletion of the body zinc pool is prolonged and remarkable [18]. The necessity of description of cutoffs for biochemical indicators for risk of zinc deficiency in different sex and age subgroups has been emphasized [49]. The effect of intestinal parasitic infections on micronutrient status, which is demonstrated in several studies [24, 50], was not evaluated in the present study, which makes the etiology of poor iron and zinc status in the affected children debatable.

## Conclusions and key messages

In this study it was found that:

1. The prevalence of zinc and iron deficiency among 9–12-year-old children was noticeable, and there existed a link between iron and zinc status.
2. Children with serum ferritin <14.9 µg/L were at increased risk of zinc deficiency.
3. Deficiencies of both zinc and iron were more prevalent in deprived regions of Tehran, as compared to prosperous ones. This may have been due to the higher prevalence of intestinal parasites and/or poor quality of diet of children living in deprived regions. This issue needs to be addressed by further studies.

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## Authorship

T.R.N. designed the study, contributed to writing the preliminary manuscript, and supervised all laboratory bench work. B.N. made a remarkable contribution to the study design, performed all statistical analyses and also contributed to writing the preliminary manuscript. M.H. assisted in study design and sampling methodology. A.K. was actively involved in the field works and also performed all laboratory analyses.

## Conflict of Interest

Nothing to declare.

## References

1. Bhutta, Z.A. (2007) Iron and zinc deficiency in children in developing countries. Br. Med. J. 334, 104 – 105.
2. Moayeri, H., Bidad, K., Zadhoush, S., Gholami, N. and Anari, S. (2006) Increasing prevalence of iron deficiency in overweight and obese children and adolescents (Tehran Adolescent Obesity Study). Eur. J. Pediatr. 165, 813 – 814.
3. Halterman, J.S., Kaczorowski, J.M., Aligne, C.A., Auinger, P. and Szilagyi, P.G. (2001) Iron deficiency and cognitive achievement among school-aged children and adolescents in the United States. Pediatrics 107, 1381 – 1386.
4. Diaz, J.R., de las Cagigas, A. and Rodriguez, R. (2003) Micronutrient deficiencies in developing and affluent countries. Eur. J. Clin. Nutr. 57(Suppl 1), 70 – 72.
5. Grantham-McGregor, S. and Ani, C. (2001) A review of studies on the effect of iron deficiency on cognitive development in children. J. Nutr. 131, 649S – 666S; discussion 666S – 668S.
6. Prasad, A.S., Halsted, J.A. and Nadimi, M. (1961) Syndrome of iron deficiency anemia, hepatosplenomegaly, hypogonadism, dwarfism and geophagia. Am. J. Med. 31, 532 – 546.
7. De Benoist, B., Darnton-Hill, I., Davidsson, L., Fontaine, O., Hotz C. (2007) Conclusions of the Joint WHO/UNICEF/IAEA/IZiNCG Interagency Meeting on Zinc Status Indicators. Food Nutr. Bull. 28, 480S – 484S.
8. Brown, K.H., Rivera, J.A., Bhutta, Z., Gibson, R.S., King, J.C. et al. (2004) International Zinc Nutrition Consultative Group (IZiNCG) technical document #1. Assessment of the risk of zinc deficiency in populations and options for its control. Food Nutr. Bull. 25, S99 – 203.
9. Say, B., Ozsoylu, S. and Berkel, I. (1969) Geophagia associated with iron-deficiency anemia, hepatosplenomegaly, hypogonadism and dwarfism. A syndrome probably associated with zinc deficiency. Clin. Pediatr. (Phila.) 8, 661 – 668.
10. Chen, X.C., Wang, W.G., Yan, H.C., Yin, T.A. and Xu, Q.M. (1992) Studies on iron deficiency anemia, rickets and zinc deficiency and their prevention among Chinese preschool children. Prog. Food Nutr. Sci. 16, 263 – 277.
11. Yokoi, K., Sandstead, H.H., Egger, N.G., Alcock, N.W., Sadagopa Ramanujam, V.M. et al. (2007) Association between zinc pool sizes and iron stores in premenopausal women without anaemia. Br. J. Nutr. 98: 1214 – 1223.
12. Kalantari N GM (2005) National comprehensive study on household food consumption pattern and nutritional status, IR Iran, 2001 – 2003, National report. Nutrition and Food Science Institute. Tehran, Iran.
13. Brune, M., Rossander-Hulten, L., Hallberg, L., Gleerup, A. and Sandberg, A.S. (1992) Iron absorption from bread in humans: inhibiting effects of cereal fiber, phytate and inositol phosphates with different numbers of phosphate groups. J. Nutr. 122, 442 – 449.
14. Lonnerdal, B. (2000) Dietary factors influencing zinc absorption. J. Nutr. 130, 1378S – 1383S.
15. Neyestani T.R., Hajifaraji, M., Omidvar, N., Eshraghian, M.R., Shariatzadeh, N. et al. (2011) High prevalence of vitamin D deficiency in school-age children in Tehran, 2008: a red alert. Public Health Nutr. 15, 324 – 330.
16. National Investigation on Micronutrient Status (NIMS). (2005) 2001, Final report of a national survey. Ministry of Health, Treatment and Medical Education and National Nutrition and Food Technology Research Institute, Tehran, Iran.
17. WHO, Centers for Disease Control and Prevention. (2004) Assessing the iron status of populations: a report of a joint World Health Organization/Centers for Disease Control technical consultation on the assessment of iron status at the

 

population level. World Health Organization, Geneva, Switzerland.
18. Hotz, C., Peerson, J.M. and Brown, K.H. (2003) Suggested lower cutoffs of serum zinc concentrations for assessing zinc status: reanalysis of the second National Health and Nutrition Examination Survey data (1976 – 1980). Am. J. Clin. Nutr. 78, 756 – 764.
19. Imamoglu, S., Bereket, A., Turan, S., Taga, Y. and Haklar, G (2005) Effect of zinc supplementation on growth hormone secretion, IGF-I, IGFBP-3, somatomedin generation, alkaline phosphatase, osteocalcin and growth in prepubertal children with idiopathic short stature. J. Pediatr. Endocrinol. Metab. 18, 69 – 74.
20. Sayeg Porto, M.A., Oliveira, H.P., Cunha, A.J., Miranda, G., Guimaraes, M.M. et al. (2000) Linear growth and zinc supplementation in children with short stature. J. Pediatr. Endocrinol. Metab. 13: 1121 – 1128.
21. De Benoist, B., Darnton-Hill, I., Davidsson, L., Fontaine, O. and Hotz, C. (2007) Conclusions of the Joint WHO/UNICEF/IAEA/IZiNCG Interagency Meeting on Zinc Status Indicators. Food Nutr. Bull. 28, S480 – 484.
22. De Benoist, B., Darnton-Hill, I., Davidsson, L. and Fontaine, O. (2007) Report of a WHO/UNICEF/IAEA/IZiNCG Interagency Meeting on Zinc Status Indicators, held in IAEA Headquarters, Vienna, December 9, 2005. Food Nutr. Bull. 28, S399 – S400.
23. Hess, S.Y., Peerson, J.M., King, J.C. and Brown, K.H. (2007) Use of serum zinc concentration as an indicator of population zinc status. Food Nutr. Bull. 28, 403S – 429S.
24. McLean, E., Cogswell, M., Egli, I., Wojdyla, D. and De Benoist, B. (2009) Worldwide prevalence of anaemia, WHO vitamin and mineral nutrition information system, 1993 – 2005. Pub. Health Nutr. 12, 444 – 454.
25. Pasricha, S.R. (2012) Should we screen for iron deficiency anaemia? A review of the evidence and recent recommendations. Pathology 44, 139 – 147.
26. Shaoul, R., Gaitini, L., Kharouba, J., Darawshi, G., Maor, I. et al. (2012) The association of childhood iron deficiency anaemia with severe dental caries. Acta Paediatr. 101, e76 – 79.
27. Lozoff, B., Jimenez, E., Hagen, J., Mollen, E. and Wolf, A.W. (2000) Poorer behavioral and developmental outcome more than 10 years after treatment for iron deficiency in infancy. Pediatrics 105, E51.
28. Hurtado, E.K., Claussen, A.H. and Scott, K.G. (1999) Early childhood anemia and mild or moderate mental retardation. Am. J. Clin. Nutr. 69, 115 – 119.
29. Muthayya, S., Thankachan, P., Hirve, S., Amalrajan, V., Thomas, T. et al. (2012) Iron fortification of whole wheat flour reduces iron deficiency and iron deficiency anemia and increases body iron stores in Indian school-aged children. J. Nutr. 142, 1997 – 2003.
30. Fischer Walker, C.L., Ezzati, M. and Black, R.E. (2009) Global and regional child mortality and burden of disease attributable to zinc deficiency. Eur. J. Clin. Nutr. 63, 591 – 597.
31. Prasad, A.S., Miale, A., Jr., Farid, Z., Sandstead, H.H., Schulert, A.R. et al. (1963) Biochemical studies on dwarfism, hypogonadism, and anemia. Arch. Intern. Med. 111: 407 – 428.
32. Sandstead, H.H. (2000) Causes of iron and zinc deficiencies and their effects on brain. J. Nutr. 130, 347S – 349S.
33. Quihui, L., Morales, G.G., Mendez, R.O., Leyva, J.G., Esparza, J and Valencia, M.E. (2010) Could giardiasis be a risk factor for low zinc status in schoolchildren from northwestern Mexico? A cross-sectional study with longitudinal follow-up. BMC Public Health 10, 85.
34. Wasantwisut, E., Winichagoon, P., Chitchumroonchokchai, C., Yamborisut, U., Boonpraderm, A. et al. (2006) Iron and zinc supplementation improved iron and zinc status, but not physical growth, of apparently healthy, breast-fed infants in rural communities of northeast Thailand. J. Nutr. 136, 2405 – 2411.
35. Pathak, P., Kapil, U., Kapoor, S.K., Saxena, R., Kumar, A. et al. (2004) Prevalence of multiple micronutrient deficiencies amongst pregnant women in a rural area of Haryana. Indian J. Pediatr. 71, 1007 – 1014.
36. Hettiarachchi, M., Liyanage, C., Wickremasinghe, R., Hilmers, D.C. and Abrahams S.A. (2006) Prevalence and severity of micronutrient deficiency: a cross-sectional study among adolescents in Sri Lanka. Asia Pac. J. Clin. Nutr. 15, 56 – 63.
37. Cole, C.R., Grant, F.K., Swaby-Ellis, E.D., Smith, J.L., Jacques, A. et al. (2010) Zinc and iron deficiency and their interrelations in low-income African American and Hispanic children in Atlanta. Am. J. Clin. Nutr. 91, 1027 – 1034.
38. Rodriguez-Matas, M.C., Lisbona F., Gomez-Ayala A.E., Lopez-Aliaga I. and Campos M.S. (1998) Influence of nutritional iron deficiency development on some aspects of iron, copper and zinc metabolism. Lab. Anim. 32, 298 – 306.
39. Prasad, A.S. (2003) Zinc deficiency. Br. Med. J. 326, 409 – 410.
40. Hotz, C. (2007) Dietary indicators for assessing the adequacy of population zinc intakes. Food Nutr. Bull. 28, 430S – 453S.
41. Nishiyama, S., Kiwaki, K., Miyazaki, Y. and Hasuda, T. (1999) Zinc and IGF-I concentrations in pregnant women with anemia before and after supplementation with iron and/or zinc. J. Am. Coll. Nutr. 18, 261 – 267.
42. Fukushima, T., Horike, H., Fujiki, S., Kitada, S., Sasaki, T. et al. (2009) Zinc deficiency anemia and effects of zinc therapy in maintenance hemodialysis patients. Ther. Apher. Dial. 13, 213 – 219.
43. Kobayashi H., Abe, M., Okada, K., Tei, R., Maruyama, N. et al. (2015) Oral zinc supplementation reduces the erythropoietin responsiveness index in patients on hemodialysis. Nutrients 7, 3783 – 3795.
44. Nguyen, P., Grajeda, R., Melgar, P., Marcinkevage, J., Flores R. et al. (2012) Effect of zinc on efficacy of iron supplementation in improving iron and zinc status in women. J. Nutr. Metab. 2012, 216179.
45. Gibson, R.S., Vanderkooy, P.D., MacDonald, A.C., Goldman, A., Ryan, B.A. et al. (1989) A growth-limiting, mild zinc-deficiency syndrome in some southern Ontario boys with low height percentiles. Am. J. Clin. Nutr. 49, 1266 – 1273.
46. Osazuwa, F., Ayo O.M. and Imade P. (2011) A significant association between intestinal helminth infection and anaemia burden in children in rural communities of Edo state, Nigeria. North Am. J. Med. Sci. 3, 30 – 34.
47. Nematian, J., Gholamrezanezhad, A. and Nematian, E. (2008) Giardiasis and other intestinal parasitic infections in relation to anthropometric indicators of malnutrition: a large, population-based survey of schoolchildren in Tehran. Ann. Trop. Med. Parasitol. 102, 209 – 214.
48. Olivares, J.L., Fernandez, R., Fleta, J., Rodriguez, G. and Clavel, A. (2003) Serum mineral levels in children with intestinal parasitic infection. Dig. Dis. 21, 258 – 261.
49. Gibson, R.S., Bailey, K.B., Parnell, W.R., Wilson, N. and Ferguson, E.L. (2011) Higher risk of zinc deficiency in New Zealand Pacific school children compared with their Maori and European counterparts: a New Zealand national survey. Br. J. Nutr. 105, 436 – 446.
50. Hercberg, S., Chauliac, M., Galan, P., Devanlay, M., Zohoun, I. et al. (1986) Relationship between anaemia, iron and folacin deficiency, haemoglobinopathies and parasitic infection. Hum. Nutr. Clin. Nutr. 40, 371 – 379.

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