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The relationship of serum vitamin D and Zinc in a nationally representative sample of Iranian children and adolescents: The CASPIAN-III study

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Abstract

Background: Vitamin D (VitD) deficiency is a common worldwide problem. Some previous studies have shown that both Zinc (Zn) and VitD deficiency are prevalent in Iran. This study aimed to assess the relationship of serum Zn and vitamin D levels in a nationally representative sample of Iranian children and adolescents.

Methods: This case-control study was conducted as a sub-study of a school-based surveillance program entitled “the CASPIAN-III Study”. An equal number of individuals with and without hypovitaminosis D including 330 participants aged 10 to 18 years were selected. The correlation of serum 25 hydroxy vitamin D (25(OH) D), cardiometabolic factors and Zn concentrations was determined. Statistical analysis was done using one-way analysis of variance (ANOVA), Pearson's correlation, linear regression, and logistic regression.

Results: The mean age was not significantly different in participants with and without hypovitaminosis D (14.74±2.52 vs. 14.74±2.66 years, respectively, p>0.05). The mean 25(OH) D level was 6.34±1.47ng/ml in the group with hypovitaminosis D and 39.27±6.42ng/ml in controls. The mean Zn level was significantly lower in the hypovitaminosis D group than in controls (1.15±0.26 vs. 1.43±0.32µg/ml, respectively, p<0.001). The Pearson's analysis showed a positive and significant correlation between Zn and 25(OH) D serum levels (p<0.0001). Odds ratios analysis for VitD level between various quartiles of serum zinc concentration for all participants showed that the odds of higher levels of VitD increased by higher levels of Zn.

Conclusion: We found significant associations between low serum concentrations of zinc and 25(OH) D. Food fortification or mineral supplementation should be considered in future health programs.

Keywords: Vitamin D, Zinc, Adolescents, Iran.

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Introduction

Vitamin D deficiency is a global health problem even in sunny regions as the Middle Eastern countries (1).Vitamin D is a steroid hormone and plays a key role in minerals metabolism, specially calcium and phosphorus, as well as in bone strength (2). The active type of this vitamin is synthesized in the skin, liver and kidneys. In addition to its multi-functions in the body, vitamin D reinforces the immune system. Vitamin D metabolism activates macrophages

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and limits mycobacterium tuberculosis intracellular growth (3). Receptors for vitamin D exist in most organs including pancreas, stomach, genital system, skin, brain etc (3-8). 25-hydroxy vitamin D (25(OH) D) level is the best index to determine vitamin D status in the body, with a half-life of 2-3 weeks (9). Adequate exposure to sunlight and dietary intake of foods rich in vitamin D are necessary to satisfy the daily need of the body and prevent hypovitaminosis D (10,11).

Many studies have indicated the association of serum 25(OH) concentrations with serum levels of other vital elements. From the several elements found in the body, only a few number as zinc, copper, magnesium, iron and calcium play important roles in the body's chemical and physiological functions. Zinc has several important roles in the human body; for instance, it is used in the process of synthesizing insulin and some enzymes as superoxide dismutase. Zinc is a trace element, which after Iron, has the highest amount in the body. It is mainly accumulated in the muscles but can also be found in the blood cells, retina, bones, skin, kidneys, liver and the pancreas. Zinc is the second most vital element after Iron and its deficiency during pregnancy may cause serious feto-maternal complications (12) including impaired cognitive development in the infant during the first six months of life, immunological complication in fetus, low birth weight, prematurity, miscarriage, fetal or infant death, postdate pregnancy, premature rupture of membranes, cleft palate and neural tube defects in the fetus (13). A study on 150 Iranian pregnant women showed that 37% of them were vitamin D deficient and 23% were zinc deficient, with a statistically significant association between serum zinc and 25 (OH) D levels (14). Such experience is scarce in the pediatric age group.

Given the high prevalence of hypovitaminosis D and zinc deficiency, as well as their possible interactions, this study aimed to assess the relationship of serum zinc and 25 (OH)D levels in adolescents.

Methods

This study was conducted as a sub-study of "The National Survey of School Students' High Risk Behaviors", which was performed as the third survey of the school-based surveillance system entitled: "Childhood and Adolescence Surveillance and Prevention of Adult Non-communicable Disease Study (CASPIAN-III)". CASPIAN-III is a school-based nationwide health survey that includes 5,528 students aged 10-18 years from 27 provinces in Iran.

In this case-control study, as a sub-study of the CASPIAN III study, 165 students with hypovitaminosis D as the case group and 165 normal students without Hypovitaminosis D as the control group were randomly selected from the sample of frozen sera (−70°C) of the participants in which 25-hydroxy vitamin D (25(OH) D) was checked (15). Serum concentration of 25(OH) D was analyzed quantitatively by direct competitive immunoassay chemiluminescene method applying LIASON 25 OH vitamin D assay TOTAL (DiaSorin, Inc.), with a coefficient of variation of 9.8%.25 (OH) D levels of less than 10ng/ml as vitamin D deficiency and levels between 10 and 30ng/ml as vitamin D insufficiency (16). Sera of the two groups of participants with or without vitamin D deficiency were randomly selected. Zinc level of the samples was determined by atomic absorption spectrophotometer using hollow cathode lamps of Zn.

Data were obtained using the questionnaires completed by students and their parents. A trained team of health professionals conducted physical examination and blood sampling. Blood samples were taken after twelve hours of fasting. Sera were analyzed for glucose and lipid profile including total cholesterol, high-density lipoprotein cholesterol (HDL-C), LDL cholesterol (LDL-C) and triglycerides (TG), as well as liver function tests including Serum Glutamate Oxaloacetate Transaminase (SGOT) and Serum Glutamate Pyruvate Transaminase (SGPT) using Pars Azmoon reagent kits (Tehran, Iran).

The Research and Ethics Committee of Isfahan University of Medical Sciences, Isfahan, Iran, approved this study.

Statistical Analysis: The relationship between serum vitamin D and Zn levels was measured through linear regression analysis considering Zn as an independent variable and 25(OH) D as a dependent variable. Data analysis was conducted using SPSS (version 22.0; SPSS Inc. Chicago, IL, USA) by applying t test, one-way analysis of variance (ANOVA), and Pearson's correlation tests. To assess the relationship between serum Zn concentration and Vitamin D level, logistic regression was used to calculate odds ratios (OR) for VitD level between various quartiles of serum Zn concentration; the lowest quartile of serum Zn concentration was used as the reference category. A p value of less than 0.05 was set as statistically significant.

Results

The mean age of the participants was not significantly different among groups with and without hypovitaminosis D (14.74± 2.52 vs.14.74 ± 2.66 years, respectively, p>0.05). No significant difference was observed in the baseline characteristics of the participants of the two groups (Table 1).

The serum mean±SD level of 25(OH) D was 6.34±1.47ng/ml in the group with hypovitaminosis D and 39.27±6.42ng/ml in the control group (p<0.001). The mean±Zn level in hypovitaminosis D group was significantly lower than in controls (1.15± 0.26 vs. 1.43±0.32µg/ml, respectively, p<0.0001).

The Pearson correlation of serum Zn concentration and Vit D with metabolic factors and existence of metabolic disease showed that Zn levels had a significant positive correlation (p<0.001) with Vit D level.

As demonstrated in Table 2, the OR of higher levels of Vit D levels was higher in the second (Q2) and fourth (Q4) quartiles significantly as compared to the reference quartile (Q1).

Discussion

The main aim of this study was to determine the relationship between serum vitamin D and serum Zn levels in children and adolescents. We found a positive correlation between serum Zn and serum vitamin D levels, and this finding was consistent with a previous study conducted on children (14). This might have been caused by

Table 1. Baseline Characteristics of the Adolescents with and without Hypovitaminosis D: The CASPIAN-III Study

Variables	Hypovitaminosis D group (N=165)	Normal group (N=165)
Age (year)	14.74±2.25	14.74±2.66
BMI	19.64±5.41	19.58±4.56
SBP (mmHg)	102.55±14.47	102.33±12.55
DBP (mmHg)	65.37±9.90	63.87±9.52
HDL-C (mg/dL)	48.69±14.10	48.55±14.95
LDL-C (mg/dL)	80.81±29.47	82.34±26.49
Total cholesterol (mg/dL)	147.15±30.685	148.19±32.22
TG (mg/dL)	95.07±40.20	97.46±44.81
FBG (mg/dL)	87.93±12.09	87.85±12.26
SGOT (U/L)	23.49±10.39	24.51±9.48
SGPT(U/L)	17.82±9.20	18.21±14.10

All variables were reported in mean±SD. BMI: Body Mass Index, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, HDL-C: High Density Lipoprotein-Cholesterol, LDL-C: Low Density Lipoprotein-Cholesterol, TG: Triglyceride, FBG: Fasting Blood Glucose, SGOT: Serum Glutamate Oxaloacetate Transaminase, SGPT: Serum Glutamate Pyruvate Transaminase, SD: Standard Deviation

Table 2. Odds Ratios for 25-Hydroxy Vitamin D Level across Various Quartiles of Serum Zinc of Adolescents: The CASPIAN-III Study

Quartile	OR	95% CI for OR	p*
Q1 (0.70-1.00 µg/ml)	Reference	Reference	-
Q2 (1.00-1.30 µg/ml)	2.603	1.710-3.851	0.002
Q3 (1.30-1.70 µg/ml)	1.561	0.824-3.745	0.219
Q4 (1.70-2.00 µg/ml)	24.646	20.120-26.682	<0.001

the prominent effects of lifestyle factors as inadequate exposure to sunlight, air pollution and poor nutrition. Aside from hazardous effects on the respiratory system and pollution caused diseases, living in populated cities means less sunlight for children, especially during cold seasons when there is higher air pollution and weaker sunlight intensity (16,17).

A nationwide study in Iranian adolescents demonstrated a high prevalence of hypovitaminosis D and an association of serum 25(OH) D levels with cardiometabolic risk factors. It showed an inverse association of 25(OH)D with systolic blood pressure, diastolic blood pressure, total cholesterol and low-density lipoprotein cholesterol. In contrast, this association was significantly positive with high-density lipoprotein cholesterol, but not with fasting plasma glucose and MetS (19).

Zn has several health effects (20). The first evidence of Zn deficiency in humans was reported from central part of Iran (21). Zn deficiency has several etiologies; one of them might be the consumption of white flour and white rice as the main dishes in Iran. The Zn intake from these diets is high at 15mg a day, but it is not available because of the high phytate content of this kind of diet. Phytate, the phosphorus storage compound of plant seeds, bind Zn and other bivalent ions in insoluble complexes, making them unavailable to human and other monogastric species (22).

Iron, when present in large amounts in the diet, also inhibits Zn absorption. Epidemiological studies in Iran showed a considerably high prevalence of Zn deficiency, as high as 31.1% among school students and 28.1% in children (23). The most important causes of Zn deficiency are soil content of Zn, dietary deficiency (phytate containing whole grains), malabsorption due to impaired transport across intestinal absorptive surface, damaged or absent intestinal absorptive surface, increased loss, increased utilization, and chronic disease (24). The vitamin D receptor (VDR) binds zinc, and the activity of vitamin D dependent genes in cells is influenced by intracellular zinc concentrations. Zinc help vitamin D to work inside the cells. It is also important to ensure that the calcium from foods or supplements is used in your bones. Hence, low level of both Zn and VitD can affect many important body functions (25). However, studies in animals have shown positive effects of VitD on zinc increases (26) the effects of Zinc and VitD on absorption-desorption and eventually the amount of each other, but their basic metabolic pathways in humans are not clear.

Our results revealed that hypovitaminosis D was accompanied with low serum Zn level. Comparing our results with those of other studies, it could be concluded that hypovitaminosis D is probably due to inadequate exposure to sunlight. In addition, it seems inappropriate diet and lack of absorbable Zn in our foods lead to Zn deficiency in our schoolchildren. Finally, conducting future studies to identify the factors affecting Vitamin D and Zinc deficiency in schoolchildren, their relationship and the real causes of simultaneous lack of VitD and Zinc is highly recommended.

Study Limitations and Strengths: The main limitation of this study was its cross-sectional nature. Moreover, we did not obtain the detailed dietary intake of the participants. The strengths of the study were its novelty in the pediatric age group and recruiting a nationally representative sample.

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