A Study of the Association of Serum Zinc and Selenium Levels with the Severity of Asthma in Iranian Children

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Abstract

Background: Asthma is the most common respiratory disease among children with a growing prevalence worldwide. In addition to their multiple roles in human body, zinc and selenium have anti-inflammatory properties which is due to their presence in the structure of antioxidant enzymes namely superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px). Lack of these elements in the body can cause airway inflammation in asthma patients.

Methods: In the present case-control study, 50 asthmatic and 50 non-asthmatic children aged 5-15 years were selected at Taleghani Hospital of Gorgan using convenience sampling. The levels of zinc and selenium were determined in blood samples by an atomic absorption spectrophotometer. T-test, Man-Whitney, ANOVA, Kruskal-Wallis test, and multiple regression were used in this study. Statistical analyses were performed using SPSS statistical software version 16 at a significance level of 0.05.

Results: The case and control groups were similar in terms of demographic variables. The mean±sd level of zinc was 46.78±8.93 in the case group, and 50±7.8 in the control group ($p = 0.07$). The mean±sd level of selenium was 62.78±11.46 in the case group, and 67.86±7.87 in the control group ($p = 0.038$). The comparison of individuals in the control group and those with different degrees of asthma revealed a significant difference in the mean levels of zinc ($p = 0.003$) and selenium ($p = 0.009$). According to the multiple regression analysis, individuals with severe asthma had lower levels of zinc and selenium than the control group.

Conclusions: The present study indicated that the levels of zinc and selenium were lower in individuals with asthma than in healthy individuals; and the mean levels of zinc and selenium sharply decreased with increase in the severity of asthma.

Introduction

Asthma is characterized by airway hypersensitivity, reversible episodes of airflow obstruction, and wheezing. It is the most common respiratory disease among children. Its prevalence has increased in recent years as about 235 million people suffer from asthma worldwide (1). The disease is the leading cause of emergency referrals to hospitals and the school absence of children under the age of 15 in developing countries (2). A number of studies have found that patients with bronchial asthma have a high level of oxidative stress (3–6). Oxidative stress is caused by a disturbance of the oxidant-antioxidant balance which leads to tissue damages. Oxidative enzymes such as GSH-Px and SOD prevent tissue damages by eliminating the oxidative stress (4, 6).

Zinc and selenium are essential elements for human body, especially at the age of growth. These elements are involved in various biological activities and act as cofactors of antioxidant enzymes and are essential parts of their molecular structure. Selenium is an essential part of GSH-Px and multiple metabolic pathways including thyroid hormone metabolism, antioxidant defense, and immune system (7,

uding SOD (4). Moreover, zinc has antioxidant, anti-inflammatory, and anti-apoptotic properties in the body (9–13). Given the presence of selenium in the structure of GSH-Px, and zinc in the structure of SOD, their insufficient dietary intake and low serum concentrations have been suggested as the reasons of antioxidant-antioxidant imbalance (3, 14–16).

There are controversial reports on the relationship of zinc and selenium status to asthma. Several studies have observed lower selenium status in asthma patients (17, 18). Whereas, some observational studies did not report any significant differences on plasma concentrations or daily intake of zinc and selenium between healthy participants and asthma patients (3, 19). However, there are two studies that have reported higher concentrations of zinc in asthma patients (20, 21). In addition, zinc and selenium supplementation has not demonstrated preventive or therapeutic modality for reducing asthma burden (22–24). Given the existing uncertainty, the present study aimed to investigate the relationship between the plasma concentrations of zinc and selenium, and the severity of asthma.

Methods

The present study was a case-control study conducted on children aged 5–15 years in 2019. Fifty asthmatic children diagnosed by asthma and allergy specialist or pulmonologist or the consumption of inhaled steroids without receiving zinc and selenium supplements were considered as the case group. Fifty children who visited the center for reasons other than respiratory problems and asthma were considered as the control group. Inclusion criteria for the control group included children aged 5–15 years with no history of allergy, chronic diseases (cardiovascular, pulmonary, renal, etc.), respiratory problems, and receiving zinc and selenium supplements. The subjects were selected by the convenience sampling among patients referred to Taleghani Children Hospital in Gorgan province, Iran.

Before collecting samples, the participants responded to the "International Study of Asthma and Allergies in Childhood" questionnaire that was translated into Persian (25). In addition, the questions about socioeconomic status and tobacco smoke exposure were included in the questionnaire. The venous blood (3 ml) was taken from the participants and serum levels of zinc and selenium were measured using a standard kit and the atomic absorption spectrophotometry. The parents of the participants signed informed consent form to participate in the research. The parents were assured there would be no negative consequences of refusing to take part in the study and their children's information will be kept strictly confidential.

Patients were divided into three groups with mild, moderate, and severe asthma based on the Expert Panel Report 2 method (26). In addition, zinc and selenium deficiencies were determined according to age-gender related specific zinc and selenium levels (27, 28).

Table 1
Comparison of asthmatic and non-asthmatic group regarding demographic variable

	Case (n = 50)	Control (n = 50)	*p-value*
Gender, no (%)	25 (50)	24 (48)	0.84
Male	25 (50)	26 (52)	
Female			
Location, no (%)	26 (52)	22 (44)	0.42
Rural	24 (48)	28 (56)	
Urban			
Home, no (%)	23 (46)	14 (44)	0.84
Apartment	27 (54)	19 (56)	
Villa			
Smoking status, no (%)	22 (44)	13(26)	0.059
Yes	28 (56)	37 (74)	
No			
Selenium efficiency, no (%)	37 (74)	43 (86)	0.13
Yes	13 (26)	7 (14)	
No			
Zinc efficiency, no (%)	32(64)	42(84)	0.023
Yes	18(36)	8(16)	
No			
Age, mean(SD)	8.4(2.54)	9.06(2.66)	0.2

The Chi-square test was used to compare the groups on demographic variables. The comparison of mean levels of zinc and selenium was performed in various subgroups of demographic variables, asthmatics and non-asthmatics, and individuals with different severities of asthma using the two-sample t-test, Mann- Whitney, ANOVA, and Kruskal-Wallis tests. Finally, the comparison of zinc and selenium levels in the subgroups of individuals with different severities/types of asthma was performed by modifying the effects of other variables using multiple regression analysis. The Shapiro-Wilk test was used to test the normality of quantitative variables. The statistical analyses were performed using SPSS statistical software version 16 at a significance level of 0.05.

Results

The mean age of individuals was 8.4 ± 2.54 years in the case group, and 2.66 ± 9.06 in the control group ($p = 0.2$). As presented in Table 1, 50% of individuals in the control group and 48% in the case group were male ($p = 0.84$), 48% individuals in the case group and 56% of individuals in the control group lived in cities ($p = 0.42$), and 46% of individuals in the case group and 44% of individuals in the control group lived in apartments ($p = 0.84$). In the case group, 44% of individuals exposed to second-hand smoke and in the control group, 26% of individuals experienced the exposure. There was no significant difference between the groups ($p = 0.059$) on Smoking status.

Table 2
The comparison of Zinc and Selenium concentration in different subgroups

	Count	Zinc*	*p-value*	Selenium*	*p-value*
Gender	49	48.86(7.59)	0.93	64.94(9.57)	0.52
Male	51	47.94(9.34)		65.69(10.68)	
Female					
Location	48	48.75(7.72)	0.8	63.67(10.92)	0.078
Rural	52	48.06(9.18)		66.85(9.14)	
Urban					
Home	45	48.53(8.95)	0.75	67.84(8.76)	0.3
Apartment	55	48.27(8.19)		63.25(10.74)	
Villa					
Smoking status	35	48.37(7.67)	0.81	62.97(11.63)	0.17
Yes	65	48.4(8.97)		66.58(9.04)	
No					
Asthma	50	50(7.8)	0.038	62.78(11.46)	0.07
Yes	50	46.78(8.93)		67.86(7.87)	
No					
Asthma severity	50	50(7.8)	0.003	67.86(7.87)	0.009
Control	18	51.39(8.22)		68(7.12)	
Mild	17	45.59(8.38)		63.76(9.87)	
Moderate	15	42.6(8.3)		55.4(13.87)	
Severe					
Age, mean(SD)		r = 0.25	0.012	r = 0.252	0.011

$^{*}\mu g/l$

Among asthmatic individuals, 18 (36%) had mild asthma, 17 (34%) had moderate asthma, and 15 (30%) had severe asthma. Table 2 presents the comparison of zinc and selenium levels in different subgroups of demographic variables. As shown, there was no significant difference between the mean levels of selenium and zinc in men and women, and also between those living in apartments and villas, and smokers and non-smokers. There was also no significant difference between rural and urban individuals on zinc and selenium levels, however, the serum level of selenium in individuals living in villages was lower than those living in cities (p = 0.078).

In the case group, the mean serum level of zinc was 46.78 ± 8.93 $\mu g/l$ which was significantly lower than that of the control group (50 ± 7.8 $\mu g/l$; p = 0.038). In addition, in another comparison, 36% of individuals in the case group and 16% of individuals in the control group had zinc deficiency (p = 0.023).

Table 3
Comparison of zinc and selenium levels in different asthmatic groups based on the severity after considering other covariates.

	Zinc			**Selenium**		
	Beta	**Std.Error**	**Sig**	**Beta**	**Std.Error**	**Sig**
Total mean	65.67	7.07	0.00	50.01	6.26	< 0.001
Age	0.63	0.37	0.09	.77	.33	.01
Gender Male	-0.59	1.90	0.76	-1.07	1.68	.52
Female						
Environment Urban	2.74	1.87	0.15	− .55	1.65	.74
Rural						
Location Apartment	-3.64	1.93	0.06	− .09	1.70	.96
Villa						
Smocking Yes	-0.68	2.08	0.74	-2.53	1.84	.17
No						
Asthma Control	− .060	2.49	.98	1.08	2.21	.62
Severity Mild	-3.46	2.57	.18	-4.14	2.28	.07
Moderate	-11.51	2.74	< .001	-7.38	2.43	.003
Severe						

There was no significant difference between the case (62.78 ± 11.46 $\mu g/l$) and the control group (67.86 ± 7.87 $\mu g/l$)(p = 0.07) on the mean level of selenium. In addition, 26% of individuals in the case group and 14% of individuals in the control group had selenium deficiency (p = 0.13).

Based on the severity of asthma, the asthmatic individuals were divided into three groups: mild, moderate, and severe asthma. The comparison of zinc and selenium levels of these groups with the control group showed that the control group had the highest mean levels of zinc and selenium, but the mean levels of zinc and selenium decreased significantly with increase in the severity of asthma as est levels of zinc (p = 0.009), and selenium (p = 0.003).

There was a positive correlation between the individuals' age and serum levels of zinc ($r = 0.25$, $p = 0.012$) and selenium ($r = 0.252$, $p = 0.011$). There was also a positive and significant correlation between the serum levels of zinc and selenium ($r = 0.54$, $p < 0.001$).

Table 3 presents a comparison between the serum levels of zinc and selenium in the case and control groups after adjusting the effects of other variables. As shown, the concentration of selenium significantly increased with age ($p = 0.01$). There was no significant difference between zinc and selenium concentrations in patients with mild and moderate asthma with those in the control group, but the level of zinc in individuals with severe asthma was 11.51 $\mu g/l$ lower than that of those without asthma ($p < 0.001$). The level of selenium in individuals with severe asthma was 7.38 $\mu g/l$ lower than that of those without asthma ($p = 0.003$).

Discussion

The present study aimed to investigate the relationship between the levels of zinc and selenium and the severity of asthma in children. The study indicated that zinc and selenium levels were lower in individuals with asthma than healthy individuals. According to the comparison between the mean levels of zinc and selenium in healthy individuals and those with different severities of asthma, the mean levels of zinc and selenium in individuals with severe asthma were significantly lower than that of those in the control group, but no significant difference was observed between the levels of zinc in individuals with mild or moderate asthma and the control group. The differences between groups remained unchanged after considering confounders.

Similar to our findings, Kuti et al. also reported lower levels of selenium in individuals with moderate to severe asthma than those with mild asthma in Nigeria. They also found that the levels of zinc and selenium were lower in asthmatics than in healthy individuals (29).

Several studies have reported the association of the level of selenium in serum, nails, and hair and asthma. Some studies have reported lower levels of selenium in asthma patients than in healthy individuals (17, 18, 30). A study in Brazil also showed that the prevalence of asthma was 5-fold lower among individuals in the highest quartile of selenium and zinc concentrations, whereas children in the lowest selenium quartile presented an almost 2.5-fold increase in the prevalence of asthma (6). Selenium deficiency during pregnancy was associated with lower levels of wheezing in children (31, 32). A negative correlation was also reported between the level of selenium and pulmonary function (30, 33).

Two pathways are considered to explain the role of selenium in asthma. The first pathway is the presence of selenium in the structure of selenoproteins. There are 25 selenoproteins in human body, the best known of which is GSH-Px (14). Numerous studies have found that selenium deficiency is associated with lower activity of *erythrocyte* GSH-Px in individuals with asthma (19, 30, 34–36). Another pathway is the effect of selenium in the immune system as selenium is involved in the regulation of the immune response of T-helper2 cells that lead to asthma symptoms (14, 15, 33, 37).

As a trace element, zinc plays a key role in many activities including building DNA and RNA, energy production, cell metabolism, and immune system regulation (3, 37, 38). Zinc is considered as an anti-inflammatory mediator in airway inflammation. Studies on mice indicate that its deficiency leads to an increase in eosinophils, neutrophils, monocytes, eotaxin and MCP, and reduction of IFN-γ mRNA expression (39).

There are different reports on the relationship between asthma and zinc. Many studies have reported lower levels of zinc in serum, nail, or hair of asthmatics compared to healthy individuals (17, 29, 30, 40–42). The effect of zinc deficiency on increasing the risk of asthma has been reported in children (6). However, there are studies that have not reported significant differences (3, 5, 19, 43, 44). Even in a number of studies, higher levels of zinc and SOD have been reported in asthmatics (20, 21, 34). However, in the current study, lower levels of zinc were observed in individuals with severe asthma.

In the present study, there was a significant correlation between zinc and selenium levels which is consistent with findings of Carneiro et al.(6). The mean levels of zinc and selenium in our population were lower compared to that of other studies in Iran (45, 46). Zinc deficiency is common in Iran (47). In the north of Iran, soils are poor in selenium (48).

Despite the strong evidence on the association of selenium and zinc with asthma, there is little evidence that zinc and selenium supplements reduce the symptoms of asthma (45). Several reasons have been reported for the discrepancy between research findings. Most of the studies have not considered atopic and non-atopic asthma. Due to the design of previous studies, the duration of exposure to allergen as well as fluctuations of selenium and zinc have not been considered over time. Even it has been hypothesized that lack of zinc and selenium may be the result of inflammation not the cause of inflammation (33).

Conclusions

According to the results of the present study, it seems that the levels of zinc and selenium are lower in individuals with asthma than in healthy individuals; and any increase in the severity of asthma decreases the mean levels of zinc and selenium. Given the prevalence of zinc and selenium deficiency among Iranian residents, prescribing these supplements might be beneficial to high-risk individuals including pregnant women.

Abbreviations

SOD= superoxide dismutase, GSH-Px= glutathione peroxidase , ANOVA= Analysis of Variances , *ug/l*=milligram / deci litter

Declarations

Ethical Approval and Consent to participate:The study was approved by the ethics committee of the Golestan University of Medical Sciences, Iran (IR.Goums.REC.1397.131).

Consent for publication: The parents of the participants signed informed consent form to participate in the research.

Availability of data and materials: The datasets gathered during the current study available from the corresponding author on reasonable request.

Competing interests: The authors declare that there is no conflict of interest.

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Authors' contributions: Mohsen Ebrahimi in Conceptualization, Project administration, Writing - review & editing. Majid siahpoor in Data curation, Writing - original draft. Mohammad Hassan Hamrah in Writing - review & editing and Bagher Pahlavanzade in Conceptualization, Statistical analysis, Methodology, Writing - original draft.

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