

The Prevalence of Zinc Deficiency in Crohn's Disease Patients

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ABSTRACT

Objectives: Zinc is a trace element, which has been related to inflammatory diseases such as inflammatory bowel disease (IBD). We aimed to evaluate the serum zinc levels in Iranian patients with Crohn's disease (CD).

Materials and methods: The present study was conducted on 65 CD patients and 65 healthy controls. Serum zinc levels were measured in both patients and controls and compared by age, sex, and site of inflammation between groups.

Results: Mean serum zinc level in the study population was 86.2 ± 17.0 ng/dL. The serum zinc level was 88.1 ± 16.7 ng/dL in CD patients and 86.2 ± 17.0 ng/dL in the control group. The difference between groups was not statistically significant ($P=0.191$). No significant differences were observed in serum zinc levels of males and females ($P=0.087$). Zinc deficiency was observed in 21.5% and 7.7% of cases and controls, respectively. Compared to the control group, low serum zinc levels were significantly higher in CD patients ($P=0.025$). Regarding the site of inflammation, neither the concentration of serum zinc ($P=0.058$) nor zinc deficiency prevalence ($P=0.864$) were significantly different in cases compared to controls.

Conclusions: The prevalence of zinc deficiency was higher in CD patients compared to controls. However, serum zinc concentrations were not significantly different between groups. Age, sex, and site of inflammation were not found to be predictors of zinc deficiency. Evaluating the zinc status of CD patients for possible supplementation in cases of deficiency is recommended

Keywords: zinc deficiency, Crohn's disease, inflammatory bowel disease.

INTRODUCTION

The category of diseases commonly known as inflammatory bowel disease (IBD) includes Crohn's disease (CD) and ulcerative colitis (UC), which are characterized by chronic inflammation of the gastrointestinal (GI) tract. These conditions appear to be caused by some combination of he-

reditary, genetic, and/or environmental factors. The main symptoms of IBD are persistent diarrhea, abdominal pain, bloody stools, weight loss, and fatigue. A systematic review of population-based studies demonstrated that the prevalence of this disease in Westernized countries has increased in the 21st century (1).

It appears that nutrition is important in both the prevention and treatment of IBD. Abundant

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evidence shows high prevalence of malnutrition (deficiency of macro- and micronutrients) in patients with IBD, especially in CD patients, due to the greater extent of gastrointestinal involvement (2). Although micronutrient deficiencies are seen in patients with mild IBD, they are less likely to be considered by clinicians (3). Micronutrients are involved in the pathogenesis of CD through affecting the immune responses, their involvement in the identification of and response to pathogens and maintenance of the integrity of the GI tract (4).

Zinc is an essential micronutrient that appears to play a role in CD pathogenesis. This trace element is a cofactor for a number of enzymes, which is involved in the development of innate immunity, and has anti-inflammatory effects (5). Zinc deficiency has been associated with diarrhea and risk of GI infectious diseases (6). Low serum zinc levels have been reported in nearly one third of CD patients (7). There are several reasons for zinc deficiency in CD including low GI absorption, increased loss (8), and reduced intake due to anorexia (9). On the other hand, zinc deficiency results in mucosal permeability with consequent neutrophil transmigration and luminal antigen permeation. The combination of these factors affects the activity of CD and the probability of relapse (10-12). Therefore, it is necessary to determine the zinc status of CD patients for possible supplementation in cases of deficiency. In this study, we aimed to evaluate the serum levels of zinc in Iranian patients with CD. □

MATERIALS AND METHODS

Patients

The present study consisted of 65 CD patients and 65 healthy controls. Patients admitted to private offices and clinics, aged 1 to 18 years from January 2018 to April 2019, were enrolled in the study. Eligible cases were patients with a confirmed diagnosis of CD. The diagnosis of CD was based on clinical, radiological, and histological criteria by gastroenterologists. Controls were recruited from the same clinics in which cases were enrolled, and were considered eligible if they did not have a clinical diagnosis of CD, diarrhea or vomiting and had not used dietary supplements or followed a diet during the past month. The study protocol was in accordance

with the Helsinki Declaration principles and ethical approval was obtained from the Ethics Committee of the Najafabad Islamic Azad University. Written informed consent was obtained from all participants.

Data collection

Data regarding age, sex, and site of inflammation were gathered. Blood samples were obtained after an overnight fasting for the determination of serum zinc levels. The samples were centrifuged at 5,000 rpm for 10 minutes to obtain serum. Analysis was performed by a Spectra AA240Z (Varian®) atomic absorption spectrometer with wave length (λ), 213.9 nm; gap, 0.7 nm; and flame, acetylene oxidant/air.

Statistical analysis

The Statistical Software Package for Social Science (SPSS) (2013 IBM SPSS Statistics for Windows, v. 22.0) was used for analysis. Categorical data are presented as percentage of the group total. Continuous data are depicted as mean \pm standard deviation (SD). χ^2 and Student's t test were used to compare categorical and quantitative continuous data, respectively. Non-parametric tests were used if data were not normally distributed. A P-value of < 0.05 was considered statistically significant. □

RESULTS

Table 1 shows the characteristics of participants. Subjects had a mean age of 40.6 ± 14.9 years (39.2 ± 13.4 years in cases and 42.0 ± 16.2 years in controls). Ninety-three participants were females (71.5%), with 49 female participants among cases (75.4%) and 44 among controls (67.7%). The most common sites of inflammation in CD patients were colon and ileum, respectively.

The mean serum zinc level in the study population was 86.2 ± 17.0 ng/dL. The mean serum zinc level was 88.1 ± 16.7 ng/dL in CD patients and 86.2 ± 17.0 ng/dL in the control group (Table 1). The difference between groups was not statistically significant ($P=0.191$). Zinc deficiency was observed in 21.5% and 7.7% of cases and controls, respectively (Figure 1). Compared to the control group, low serum zinc levels were significantly higher in CD patients ($P=0.025$).

Variable		CD patients (n=65)	Controls (n=65)	P-value
Sex	Male	16 (24.6)	21 (32.3)	0.331
	Female	49 (75.4)	44 (67.7)	
Site of inflammation	Ileitis	29 (44.6)	-	-
	Colitis	32 (49.2)	-	
	Ileocolitis	4 (6.2)	-	
Age (years)		39.2±13.4	42.0±16.2	0.284
Serum zinc (ng/dL)		84.2±17.2	88.1±16.7	0.191

TABLE 1. Characteristics of participants

TABLE 2. Proportion of Crohn's disease patients with zinc deficiency according to sex, site of inflammation, and age group

Variable		N (%)	P-value
Sex	Male	4(25.0)	0.144
	Female	10(20.4)	
Site of inflammation	Ileitis	7(24.1)	0.864
	Colitis	6(18.8)	
	Ileocolitis	1(25.0)	
Age group	<30 years	1(6.7)	0.110
	30-60 years	12(26.1)	
	>60 years	1(25.0)	

levels of males and females (P=0.087). Regarding the site of inflammation, both concentration of serum zinc levels (P=0.058) and prevalence of zinc deficiency (P=0.864) were not significantly different in the two groups. Zinc deficiency was not different among age groups (P=0.110). □

DISCUSSION

To date, available data regarding zinc deficiency in patients with CD is scarce. The present study confirmed the significantly higher prevalence of zinc deficiency in CD patients.

Conflicting data exist on the effect of sex and age on serum zinc levels. An analysis of data from the second National Health and Nutrition Examination Survey showed that zinc concentrations were higher in males compared to females between the ages of 10 and 40 years, with this difference decreasing between the ages of 40 and 60 years, and almost disappearing after the age of 60 (13). In another study, men had higher zinc levels than women, but age did not affect zinc concentration (14). Schuhmacher *et al.* revealed higher serum zinc levels in women (15). In accordance with our study, Romero *et al.* found no age- and sex-differences in the serum zinc concentration of a representative sample of the Canarian population (16). Confounding factors such as stool frequency, diagnostic delay, and immunosuppressive therapy may affect the impact of age and sex on zinc concentration.

In the present study, serum zinc levels did not differ between CD patients and controls. However, the number of individuals with low serum zinc levels was higher among CD patients compared to controls. There are conflicting findings about the relationship between zinc deficiency

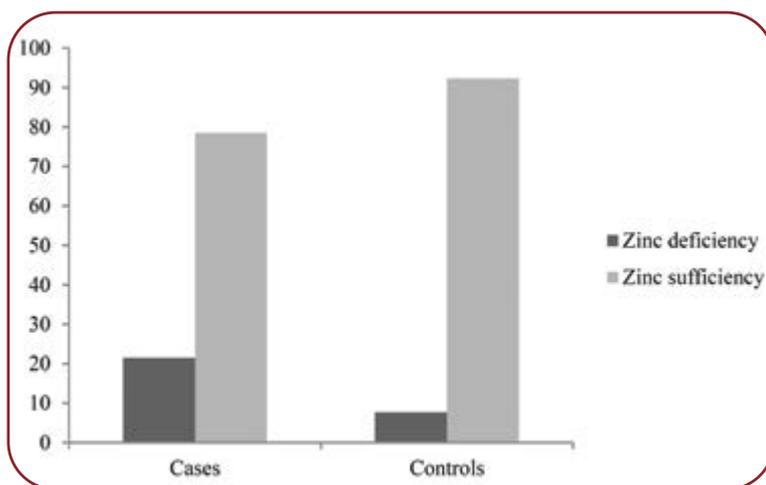


FIGURE 1. Prevalence of zinc deficiency among participants

Table 2 demonstrates the proportion of Crohn's disease patients with zinc deficiency based on sex, site of inflammation, and age group. No significant differences were observed in serum zinc

and Crohn's disease activity index (CDAI). Low-normal zinc concentration in CD patients has not been associated with complicated disease course in a three-year cohort study (5). In another retrospective cohort study, serum zinc had no relationship with clinical and deep remission of IBD patients (3). On the contrary, zinc deficiency was linked to higher risk of IBD clinical outcomes such as hospitalizations, surgeries, and disease-related complications in a three-year cohort (17). Although the prevalence of zinc deficiency was lower in studies with null results, compared to the third study, other factors, including history of GI surgery and disease activity, should be considered. As mentioned earlier, zinc deficiency in CD has several causes. Griffin *et al.* evaluated zinc metabolism in 15 CD children compared to 15 controls; zinc deficiency was the result of lower zinc intake and absorption as well as failure to compensate by reducing fecal zinc excretion (8). Among these factors, zinc absorption has been more extensively studied. Evaluating zinc absorption using short-lived isotopes of zinc in CD patients compared to normal individuals showed abnormal absorption (9). In addition, higher zinc intake was related to a reduced risk of CD in two large prospective cohorts (4). Being younger than 40 years was proposed as a risk factor for zinc deficiency in IBD patients by Han *et al.* (18). Previous studies have suggested that young patients suffer from a more severe form of IBD due to higher inflammation. However, our study did not confirm this finding. Daily supplementation with multivitamin-minerals containing 2.5 mg of zinc for five years resulted in replenishment of the zinc status of 63% of zinc-deficient CD patients, while 15% of patients who had normal serum zinc levels at baseline developed zinc deficiency. The authors su-

ggested that ongoing inflammation may be a cause for the continued deficiency. It was also suggested that the time of day in which the blood sample was collected might affect serum zinc levels (19). Even though serum zinc is affected by factors other than diurnal rhythm such as fasting, oral contraceptive use, and pregnancy (20, 21), studies have not found other methods for measuring zinc levels such as the determination of zinc in blood cells to be superior to the measurement of serum zinc (22)→.

Our study has some limitations, such as a relatively small sample size and our inability to evaluate the CDAI. Determining the relationship between zinc deficiency and CDAI can aid clinicians in correcting the deficiency and providing patients with appropriate treatment in order to reduce disease outcomes. □

CONCLUSION

Altogether, the prevalence of zinc deficiency was higher in CD patients compared to controls. However, there was no difference in serum zinc concentrations between the two groups. Age, sex, and site of inflammation were not found to be predictors of zinc deficiency. Assessment of zinc status in CD patients for possible supplementation in cases of deficiency is recommended. □

Conflicts of interests: none declared.

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