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Research Article
Effect of Dietary Habits on Serum Zinc Level in Patients with Inflammatory Bowel Disease During Remission Phase

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Abstract

Background and Objective: In ulcerative colitis and Crohn's disease, low zinc levels can worsen gastrointestinal symptoms. However, there is ongoing debate regarding zinc levels in individuals with Inflammatory Bowel Disease (IBD). The aim of this study was to investigate the relationship between dietary habits and serum zinc levels in patients with Inflammatory Bowel Disease (IBD) during remission and to identify potential factors contributing to zinc deficiency in this population. **Materials and Methods:** A retrospective cohort study was conducted at two hospitals, including 60 patients with IBD and 30 healthy controls. All participants completed a dietary questionnaire and serum zinc levels were measured. **Results:** Patients with Crohn's disease and ulcerative colitis had significantly lower serum zinc levels compared to the control group. Regression analysis identified two significant determinants of lower zinc levels: being female and having any form of IBD. **Conclusion:** The study found that female sex and the presence of any form of IBD were associated with lower serum zinc levels. Dietary intake did not significantly influence zinc levels. It may be crucial to monitor zinc levels in IBD patients, particularly women, for proper management.

Key words: Crohn's disease, dietary pattern, diet, ulcerative colitis, zinc

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INTRODUCTION

Inflammatory Bowel Disease (IBD) is a chronic immunological disorder characterized by relapse and remission, whose etiology remains unknown. The disorder affects millions around the world. The rising incidence of IBD in countries where it was previously rare, specifically in recently industrialized areas, suggests a strong environmental contribution to its pathogenesis[1]. Of these many environmental factors, diet seems to play a vital role and malnutrition is the common problem of the patients suffering from IBD.

Zinc deficiency has been often noticed in patients with chronic diarrhea, malnutrition and different catabolic states. Like copper, zinc deficiency is a common occurrence in IBD patients during the active phase of the disease and in remission[2-4]. In ulcerative colitis, zinc deficiency is caused by mucosal damage, malabsorption and poor nutritional support[5].

Hence, in the case of Crohn's disease, low levels of zinc might further deteriorate GI symptoms, which involve diarrhea and gut motility and provoke appetite and food choice disturbances. Besides, zinc deficiency delays intestinal healing and exacerbates the complications of the disease. In addition, growth retardation is also seen in young patients with low levels of zinc[6,7].

The body relies heavily on zinc occupancy to maintain structural and functional integrity[6,8-10]. Zinc acts either as an activator or cofactor for many enzymes involved in growth, cell signaling, cellular functions, immune responses and tissue repair[11].

Under conditions of intestinal inflammation and chronic malabsorption, deficiency in zinc probably caused by micronutrient leakage starting at the beginning of the disease[12,13]. Reports indicated that, in such patients, even subclinical zinc deficiencies can induce mucosal inflammation, which may further aggravate colitis and increase proinflammatory cytokines[14].

Several factors can account for low zinc levels in individuals with IBD. These factors include malabsorption and possibly altered zinc transporters in the inflammatory intestinal mucosa, enhanced losses due to inflammation and diarrhea[15], reduced dietary intake related to symptoms of IBD such as anorexia and dietary avoidance and lastly, oxidative stress, which impacts zinc metabolism and utilization[16-18]. The issue of zinc levels in patients with IBD is still debatable and some studies revealed that the level was normal, while others showed a low serum level of zinc[19-23]. This study was designed to examine the relation between dietary pattern and serum zinc levels among Iraqi IBD patients during remission.

MATERIALS AND METHODS

This retrospective cohort study was conducted in two Iraqi hospitals, the Gastrointestinal Tract Teaching Hospital and the Baghdad Teaching Hospital, from July to September 2023. A total of ninety men and women, aged from 18-56 years, were enrolled in this study. Sixty patients were in the remission phase from IBD (30 patients with CD and 30 patients with UC) and 30 healthy-matched participants were in a control group.

Samples were obtained from healthy individuals and patients with IBD. Approximately 5 mL of blood was collected from each participant. Subsequently, the serum was isolated through centrifugation and stored at -40°C. Zinc was quantified using atomic absorption spectroscopy (novAA 300 by Analytik, Jena, Germany). Flame atomic absorption spectroscopy was employed for elemental analysis, utilising acetylene air as the flame source and hollow cathode lamps as the radiation source. A slit width of 0.7 nm was used to isolate the specific wavelength and the absorbance was at 213.9 nm. A questionnaire was designed by the research team. The researchers completed this questionnaire through in-person interviews with the participants. The questionnaire assessed demographic information, details regarding the disease (including type, disease duration, treatment duration and remission period) and food frequency, which was calculated using a zinc-specific food frequency calculation[12].

The data were imported from Microsoft Excel (Microsoft Corporation, Redmond, WA, USA) to SPSS version 26.0 (IBM Corporation, Armonk, NY, USA) where they were sorted and analysed. Categorical variables were presented as counts and percentages and their association with the study groups was tested using Pearson's chi-square test or the exact test accordingly (if >25% of the cells were <5). The numerical parameters were checked for normality using the Shapiro-Wilk test. Participants' age and zinc levels, which were found to be normally distributed variables, were presented as mean and standard deviation. The differences between the study groups were tested using two-group or analysis of variance (>two groups) parametric tests. All other numerical variables that were not normally distributed were presented as median and range. The differences according to study groups were tested using the Mann-Whitney U (two groups) or Kruskal-Wallis

(>two groups) nonparametric test. Spearman's nonparametric correlation was used to test the relationship between the zinc levels and participants' age, years since diagnosis, remission, treatment and weekly servings of food items. A multivariate linear regression model was used to find the real determinants of zinc levels among the study participants. The alpha level for significance was set at $p<0.05$.

Before commencing this study, approval from the Supervising Committee of the Arab Board of Medical Specialization was granted. An informed consent for inclusion was obtained from the study participants.

RESULTS

The results showed that approximately half of the study sample (47.8%) were unemployed (housewives, students and job-seeking individuals), while 31.1% were employed. Two-thirds of the control group were employed, compared with 13.3% in each diseased group, indicating a significant association between occupation and IBD ($p<0.001$). The income of the participants also showed a significant difference across the study groups ($p = 0.004$), as no participant in the control group reported low income compared with 20% in the UC group and 6.7% in the CD group (Table 1).

In the groups with CD and UC, median years since diagnosis, remission and treatment were not significantly different ($p = 0.051$, $p = 0.782$ and $p = 0.302$, respectively).

The median years since diagnosis were 5.5 and ranged from 1–25 years; the median number of years since diagnosis for patients with UC was 6.5 years (range: 1.5-25), compared with 5 years (range: 1-14) for patients with CD.

The median years since remission of IBD were 1 year and ranged from 0-8 years, while the median number of years since remission of patients with UC was 1.5 years (range: 1 month to 8 years) compared with 1 year in patients with CD (range: 1 month to 8 years); and one patient did not begin the remission phase.

The overall median years of treatment were 4.5 years and ranged from 10 months to 15 years; the median years of treatment in the CD group were 4 years (ranging from 10 months to 13 years), while it was 4.5 years and ranged from 1-15 years in the UC group (Fig. 1).

The researchers asked the participants about each food item usually consumed and to provide details about their weekly consumption. The results showed that the weekly median consumption of egg servings in the control group (4, range: 0-14) was significantly lower ($p = 0.024$) than that in the diseased groups [CD (7, range: 0-35) and UC group (6, range: 0-28), respectively]. The weekly median number of legume servings was significantly lower ($p = 0.002$) in the UC group (1, range: 0–2) compared with the CD (2, range: 0-7) and the control groups (2, range: 0-6). None of the other food items showed significant differences in median weekly consumption across the study groups (Table 2).

Table 1: General characteristics of the study groups

	Type of disease								
	Crohn		Ulcerative Colitis		Control		Total		
Variables	Mean	SD	Mean	SD	Mean	SD	Mean	SD	p-value [a]
Age (years)	29.2	8.9	32.2	9.8	33.5	9.7	31.6	9.5	0.197
	No.	%	No.	%	No.	%	No.	%	p-value[b]
Sex									
Male	15	50.0	14	46.7	14	46.7	43	47.8	0.956
Female	15	50.0	16	53.3	16	53.3	47	52.2	
Education level									
Primary or less	2	6.7	4	13.3	3	10.0	9	10.0	0.776
Intermediate/secondary school	17	56.7	13	43.3	13	43.3	43	47.8	
College or higher	11	36.7	13	43.3	14	46.7	38	42.2	
Marital status									
Never married	13	43.3	11	36.7	12	40.0	36	40.0	0.87
Ever married	17	56.7	19	63.3	18	60.0	54	60.0	
Occupation									
Unemployed	14	46.7	19	63.3	10	33.3	43	47.8	<0.001**
Self-employed	12	40.0	7	23.3	0	0.0	19	21.1	
Employed	4	13.3	4	13.3	20	66.7	28	31.1	
Income									
Low	2	6.7	6	20.0	0	0.0	8	8.9	0.004**
Medium	25	83.3	17	56.7	29	96.7	71	78.9	
Good	3	10.0	7	23.3	1	3.3	11	12.2	

**Significant at 0.01 level by exact test, [a] ANOVA test, [b] Chi-square and exact test accordingly and SD: Standard deviation

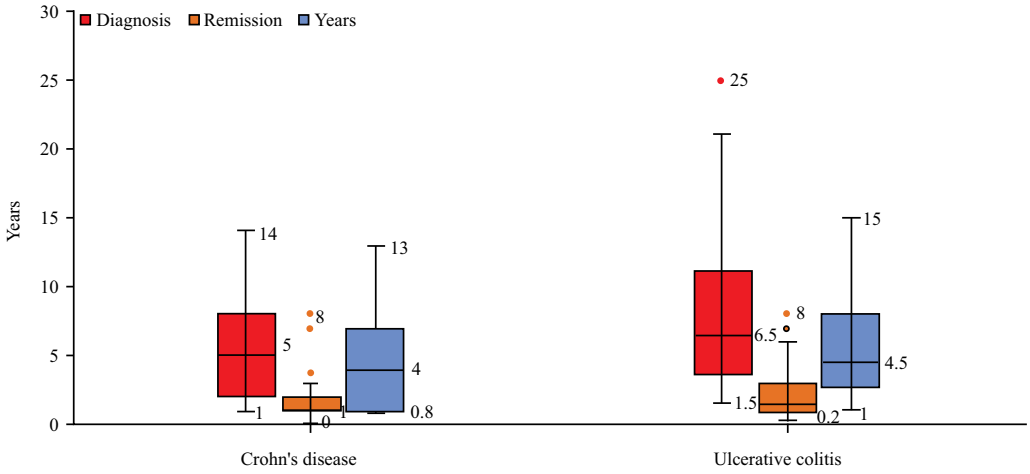

Fig. 1: Comparison of years since diagnosis, remission and treatment between patients with Crohn's disease and ulcerative colitis

Table 2: Weekly servings of each food item across study groups

	Study groups								
	Crohn		Ulcerative colitis		Control		Total		
Servings per week	Median	Range	Median	Range	Median	Range	Median	Range	p-value
Meat	2	0-35	2	0-21	2	0-14	2	0-35	0.833
Chicken	3	0-70	4	0-7	3	0-7	3	0-70	0.412
Fish	1	0-5	1	0-2	1	0-3	1	0-5	0.789
Egg	7	0-35	6	0-28	4	0-14	6	0-35	0.024*
Milk	3	0-14	3	0-14	6	0-10	3	0-14	0.202
Cheese	2	0-21	3	0-21	5	0-14	3	0-21	0.175
Bread	42	0-168	28	1-112	42	0-84	42	0-168	0.878
Rice	14	0-56	14	0-28	14	0-84	14	0-84	0.280
Vegetables	14	0-21	7	0-21	14	3-28	14	0-28	0.185
Fruit	7	0-21	7	0-28	14	0-21	7	0-28	0.486
Legume	2	0-7	1	0-3	2	0-6	2	0-7	0.002*
Nuts	2	0-14	2	0-14	2	0-14	2	0-14	0.318
Chocolate	1	0-21	2	0-21	4	0-21	2	0-21	0.183

IQR: inter-quartile range, *Significant at 0.05 level by Kruskal Wallis test for median

The average zinc level of the participants was 77.6±16.9 µg/dL. The results revealed that the mean zinc level in women was significantly lower than those of the men (73.6 µg/dL vs 82.1 µg/dL, p = 0.016). The zinc level also showed a significant difference based on the participants' occupation, as the mean level in self-employed participants was 67.8±8.5 µg/dL and significantly lower (p = 0.001) than that of the unemployed (76.9±12.5 µg/dL) and employed participants (85.4±22.7 µg/dL).

Moreover, the zinc level in the control group was 91.9±20.7 µg/dL, which was significantly higher (p<0.001) than that of the CD and UC groups (71.2±8.2 and 69.9±8.0 µg/dL), respectively.

However, neither the education level nor the marital status showed a significant effect on zinc levels (Table 3).

The zinc levels of the participants did not correlate significantly with age, years since diagnosis and years of remission and treatment. In addition, the zinc level of the participants was significantly correlated with weekly servings of milk (r = 0.269, p = 0.01); however, this correlation was weak and milk servings affected the zinc level by 7% (r^2 = 0.072). A similar correlation was found between the zinc level and weekly servings of legumes (r = 0.221, p = 0.036) and the effect of legume consumption on the zinc level of the participants was approximately 5% (r^2 = 0.049). However, no other food items were significantly correlated with zinc levels (Table 4).

The regression model showed that the zinc level had only two determinants that interacted with each other significantly; Therefore, being a woman and having any type of IBD

Table 3: Zinc levels based on the characteristics of the participants

	Zinc level (µg/dL)		
Variables	Mean	Standard deviation	p-value
Sex			
Men	82.1	20.9	0.016*[t]
Women	73.6	10.8	
Education level			
Primary or less	79.3	18.6	0.885[a]
Intermediate/secondary school	76.8	15.8	
College or higher	78.2	18.0	
Marital status			
Never married	76.4	14.7	0.545[t]
Ever married	78.5	18.3	
Occupation			
Unemployed	76.9	12.5	0.001**[a]
Self-employed	67.8	8.5	
Employed	85.4	22.7	
Income			
Low	66.4	6.0	0.024*[a]
Medium	80.1	17.7	
Good	70.0	10.0	
Type of disease			
Crohn	71.2	8.2	<0.001**[a]
Ulcerative colitis	69.9	8.0	
Control	91.9	20.7	

*Significant at 0.05, **Significant at 0.01, [t]Student's t-test, [a]ANOVA

Table 4: Spearman's correlation between zinc levels and age, years since diagnosis, remission, treatment and weekly servings of food items

	Zinc level (µg/dL)		
Variables	Correlation Coefficient (r)	Coefficient of determination (r^2)	
Age (years)	0.083	0.007	0.435
Years since diagnosis	0.093	0.009	0.482
Years of remission	-0.086	0.007	0.512
Years of treatment	0.212	0.045	0.104
Servings per week			
Meat	0.197	0.039	0.062
Chicken	0.013	0.000	0.906
Fish	0.091	0.008	0.394
Egg	-0.04	0.002	0.710
Milk	0.269	0.072	0.01*
Cheese	0.191	0.036	0.071
Bread	0.119	0.014	0.264
Rice	0.077	0.006	0.471
Vegetables	0.105	0.011	0.323
Fruit	0.192	0.037	0.069
Legume	0.221	0.049	0.036*
Nuts	0.06	0.004	0.573
Chocolate	0.023	0.001	0.833

*Correlation is significant at the 0.05 level (2-tailed)

tremendously decreased the zinc level. The zinc levels in women were significantly lower than those of the men (B = -11.273, 95% confidence interval (CI): -17.046 to -5.5) and the zinc levels in patients with CD and UC were significantly lower than those of the control group (B = -18.26, 95% CI: -26.268 to -10.252) and (B = -18.26, 95% CI: -27.742 to -10.853). All the other variables were confounders (Table 5).

DISCUSSION

IBD is a chronic relapsing-remitting immunological condition of unknown cause where nutritional therapy is regarded as the supportive or primary treatment[24]. Our study reported a significant association between occupation and IBD in two-thirds of the control group, whereas only 13.3% of

Table 5: Multivariate linear regression model for the determinants of zinc level

	Coefficients of regression		95.0% confidence Interval for B	
Parameters	B	p-value	Lower boundary	Upper boundary
(Constant)	105.829	<0.001**	95.249	116.409
Sex				
Men	0			
Women	-11.273	<0.001**	-17.046	-5.5
Occupation				
Unemployed	2.839	0.441	-4.458	10.137
Self employed	-5.609	0.236	-14.963	3.745
Employed	0			
Study groups				
Crohn	-18.26	<0.001**	-26.268	-10.252
Ulcerative colitis	-19.298	<0.001**	-27.742	-10.853
Control	0			
Income				
Low income	-5.861	0.257	-16.085	4.364
Medium income	0			
Good income	-1.296	0.772	-10.15	7.559
Servings of milk per week	0.409	0.287	-0.351	1.168
Servings of legume per week	0.24	0.804	-1.682	2.161

[a]Dependent variable: Zinc level and **Significant at 0.01 level

the diseased group were employed. This result is consistent with previous studies[5,25]. This might be explained by the effect of IBD on productivity, as IBD may negatively affect work productivity and lead to higher unemployment and work disability rates than in the healthy population[11].

In addition to the association with occupation, IBD had a significant association with low income; this was in line with a previous study and again, this might be explained by the effect of IBD on work productivity[5]. The weekly median consumption of eggs was significantly higher in patients with IBD than in the control group. This might be because the Mediterranean diet is usually recommended for people with IBD. Fermented dairy products, eggs and white meat are the main sources of protein in the Mediterranean diet[26,27].

The weekly median number of legume servings was significantly lower in the UC group than that of the CD and control groups. However, previous studies have reported decreased legume intake in patients with both UC and CD, as patients believe that legume intake may exacerbate disease symptoms[8,17].

The zinc level in the CD group was 71.2±8.2 µg/dL and 69.9±8.0 µg/dL in the UC group. This was similar to previous studies that showed the median zinc level in patients with CD was 74.3±9.7 µg/dL and 72.6±15.2 µg/dL in those with UC[28,29]. The zinc level in the control group in our study was 91.9±20.7 µg/dL. This was in line with the Japanese Society of Clinical Nutrition, which showed normal serum zinc level as ≥80 µg/dL[18].

After adjustment with the regression model, the serum zinc level had only two determinants: being a woman and having any type of IBD. A significant decrease in serum zinc levels has been shown to be caused by these two factors. According to previous studies, the serum zinc levels of women are lower than those of men[7,30]. This difference in zinc levels between sexes could be because of the difference in muscle mass, as approximately 60% of the zinc in the body is present in muscles[15]. Previous studies have shown that serum zinc levels are higher in men with larger muscle mass[16,9].

In our study, zinc levels in patients with CD and UC were significantly lower than those of the control group. Previous studies reported low serum zinc levels in patients with IBD[13,31]. This result could be because the zinc transporter albumin might be affected by low albumin levels, which is more common in patients with IBD who are malnourished, have malabsorption, have a higher fractional catabolic rate of albumin and have higher albumin transfer out of the vascular system[32].

After adjustment with the regression model, serum zinc levels were unaffected by food consumption. Ruangritchankul *et al.*[28] showed no relationship between dietary zinc intake and serum zinc levels. Arnaud *et al.*[3] reported no association between dietary intake and serum zinc concentration[3]. However, a previous meta-analysis reported that zinc deficiency in patients with IBD may result from poor oral intake, especially because of the intrinsic malabsorptive nature of IBD[33]. Arnaud *et al.*[3] found that low serum albumin and depression were the main predictors of low serum zinc levels rather than low dietary intake[3].

CONCLUSION

Despite maintaining clinical remission, patients with IBD had lower serum zinc levels than the control group. The determinants of low serum zinc levels were being a woman and having any type of IBD. Dietary intake and food consumption were not determinants of serum zinc levels. Despite maintaining clinical remission, patients with IBD should undergo systematic laboratory tests for micronutrient deficiencies, including serum zinc levels. Further studies on the risk factors associated with low serum zinc levels are recommended. As patients with IBD experience reduced productivity, this implies that gastroenterologists should be more aware of the impact of IBD on patients' work lives and should raise the issue with patients and guide them with individually tailored action plans.

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