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Comparison of serum selenium concentration with ulcerative colitis flare up: A case control study

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Abstract

Background and Aims: Ulcerative colitis is a long-lasting inflammatory bowel disease that is caused by an abnormal immune response. Selenium concentrations may influence the development of some human disorders, such as the severity of inflammatory bowel disease and the likelihood of developing colon cancer. The present research sought to examine the correlation between blood Selenium concentrations and ulcerative colitis flare-ups.

Material and Methods: In 2019, we performed a prospective case-control research at Imam Khomeini Hospital of Ahvaz. The study included 56 patients with ulcerative colitis (29 in remission and 29 experiencing flare-ups) and 29 healthy volunteers. To measure serum Selenium concentrations, blood samples were obtained from both patients and healthy volunteers. The method used for this assessment was atomic absorption spectroscopy.

Results: The serum concentration of Selenium was 109.91 g/mL in the control Jundishapur University of Medical Sciences group, 112.40 g/mL in the remission group, and 98.40 g/mL in the flare-up group. Patients with ulcerative colitis experiencing a disease flare-up showed notably decreased levels of Selenium in their blood compared to both healthy individuals (P=0.0001) and patients in remission (P=0.0001). There was no notable disparity in serum Selenium concentrations (P=0.338) between patients in remission and controls

> Conclusions: Patients experiencing a flare-up of ulcerative colitis had decreased levels of Selenium in their blood serum compared to ulcerative colitis patients in remission and those in the control group. Additional research is required to ascertain if dietary supplements might enhance the clinical progression of ulcerative colitis.

> Keywords: Selenium, Inflammatory bowel disease, Ulcerative colitis. Remission, Flare-up.

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Introduction

Inflammatory bowel disease (IBD), which encompasses Crohn's disease (CD) and ulcerative colitis (UC), is a chronic, idiopathic inflammatory condition characterized by unpredictable patterns of exacerbation and remission. International research has shown a rise in the prevalence of IBD in the United States, Canada, and Europe from 2000 to 2010. Recent studies have further shown the fast occurrence of IBD throughout Asia [1].

The incidence rates for UC in Europe, Asia, the Middle East, and North America were 0.6-24.3, 0.1-6.3, and 0-19.2 per 100,000 persons respectively. For CD, the incidence rates were 0.3-12.7, 0.04-5.0, and 0-20.2 per 100,000 individuals in the same regions [2].

IBD leads to heightened intestinal permeability, which may serve as an indicator of the severity of the illness, the effectiveness of therapy, and the likelihood of recurrence [3-5].

IBD affects the structural integrity of the intestines and results in malnutrition. The occurrence of malnutrition in patients with IBD may be attributed to several underlying processes, including reduced food consumption, impaired nutrient absorption, heightened energy expenditure resulting from inflammation, nutritional depletion via ulcerated mucosa, and unfavorable responses to medications [6]. Individuals diagnosed with IBD have a higher probability of experiencing deficiencies in essential nutrients such as Iron, vitamin B12, vitamin D, vitamin K, Folic acid, Selenium (Se), and Zinc [7, 8].

CD and UC patients often have a prevalent occurrence of Se insufficiency. Recent research has shown that the blood Se level is notably reduced in individuals with pancolitis compared to those with proctitis [9, 10].

Se exists in two forms: organic and inorganic Se. Selenomethionine and Selenocysteine, both organic molecules, are taken up in the small intestine by a sodium-dependent transport mechanism [11, 12].

Regarding inorganic substances, Selenate is taken up by a Sodium-dependent transport pathway, while Selenite is transported via passive diffusion without relying on sodium [12, 13].

Se requires a transporter to reach its intended tissues. Selenoprotein P (SELENOP), synthesized mostly by hepatocytes and present in breast milk, is responsible for transportation [14]. The distribution of Se in the body is regulated by a tissue hierarchy. In the case of Se insufficiency, large levels of Se are stored in the brain and testis due to their vital role in their respective functions [12].

The majority of Se in the body is kept in the skeletal muscles [15].

Recent research has shown that the levels of Se in our diet may increase the production of selenoproteins in the body and influence several components of the immune system [16-18].

Se, known for its capacity to protect against oxidative damage and inflammation, has been hypothesized to potentially benefit individuals with UC. Furthermore, a shortage in Se has been linked to the occurrence of flare-ups. The present research sought to examine the correlation between blood Se concentrations and the occurrence and severity of ulcerative colitis flare-ups.

Material and Methods

This research is an observational case-control study that was done on patients with UC who were hospitalized at Ahvaz Imam Khomeini Hospital in 2019. The inclusion criteria encompass the following: willingness to participate in the study, age range between 18 and 80 years, clinical diagnosis of UC based on clinical records, colonoscopy, and pathology according to Lennard-Jones criteria, absence of chronic diseases such as cancer, diabetes, and renal failure, and no history of major gastrointestinal surgery.

The exclusion criteria included individuals who had used Se supplements or multivitamins during the last six months, were using medications that might potentially disrupt Se absorption, and were either pregnant or lactating. Based on the research conducted by Sturniolo et al. [19], the control group had a median normal serum level of Se of 60, while the moderate ulcerative colitis group had a median normal serum level of Se of 43. The 10-point difference between the two groups is regarded as statistically significant. The sample size for each group was determined to be 29 individuals using NCSS software, with a significance level (α) of 0.05 and a power of 90%.

We conducted an assessment on two cohorts of UC patients and one cohort of healthy adults as a control group. The study recruited UC patients who were in a state of remission from the pool of individuals referred to the hospital's outpatient clinic for IBD. For the second group, we chose UC patients who were in the active or flare-up phase among those who were hospitalized in the gastrointestinal ward at Imam Khomeini Hospital. The control group was comprised of medically fit volunteers from the personnel of Imam Khomeini Hospital. Random sampling was conducted in all three groups.

The research protocol (AJUMS.rec.1397.908) has been approved by the Ethics Committee of Ahvaz Jundishapur University of Medical Sciences. The research adhered to the principles outlined in the Declaration of Helsinki, and before the commencement of data collection, all participants provided written informed permission.

Following an overnight fast of 10 to 12 hours, a blood sample was collected from the antecubital vein of each participant. The blood samples were centrifuged at 3000 g for 10 minutes after they spontaneously coagulated, to extract serum. The serum was subsequently cryopreserved at a temperature of -80°C until a Se determination could be conducted. Serum Se concentrations were measured using atomic absorption spectrophotometry. The absorbance of each sample was linked with its Se content using the addition-calibration technique. The analyses were performed in duplicate and random order.

The data was analyzed using SPSS version 22.0 (SPSS Inc., Chicago, IL). The significance threshold was established at a level of 0.05. Descriptive statistical methods were utilized to analyze the data. The data are reported as the mean value plus or minus the standard deviation (SD), or as a numerical value expressed as a percentage. The Chi-square test and ANOVA were employed to compare categorical variables. The Pearson correlation coefficient is employed to ascertain the correlation between numerical variables. P values less than 0.05 were considered statistically significant.

Results

Figure 1 depicts the flow chart outlining the design of the investigation. The present research included a cohort of 41 women and 46 males.



Statistical analysis revealed no significant disparity between the control and sick groups in terms of gender. The participants had a mean age of 37.18 years with a standard deviation of 8.13 years. The age range of the participants ranged from 22 to 59 years.

Table 1 displays the serum Se concentrations and the fundamental features of the subjects.

Table 1 indicates a statistically significant disparity in the ages of the participants across the three groups (p=0.025). Furthermore, there were notable disparities in the levels of selenium in the blood serum across the three groups (p=0.0001), with the flare-up group exhibiting the lowest concentration of Se in the blood serum (98.40 x 7.37 g/mL).

During the disease's flare-up stage, the levels of serum Se were considerably lower compared to both the control group (p=0.0001) and the remission group (p=0.0001). The blood Se concentrations did not show a significant difference between the control and remission groups (p=0.338).

Table 1. E	Basic charac	teristics of	participants
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Varia	ıbles	Control Group (n=29)	Remission Group (n=29)	Flare-up Group (n=29)	P-value
Gender, n (%)	Male	14 (48.28)	16 (55.17)	16 (55.17)	0.83
	Female	15 (51.72)	13 (44.83)	13 (44.83)	
Age, Year ± SD)	rs (mean	40.13±9 .37	34.41±7.08	37±6.92	0.025
Serum s concentra µg/mL	selenium ations,	109.91± 7.92	112.40±4.23	98.40±7.3 7	0.0001

Table 2 presents the average and variability of serum Se concentrations based on gender across the three groups.

No notable disparity in serum Se concentrations was detected based on gender across all three groups.

Table 2. Serum selenium concentrations (μ g/mL) by gender in the three groups studied

Variables	Male	Female	P-value
Control	111.73±8.75	107.96±6.68	0.206
Group (n=29)			
Remission	112.41±4.79	112.40±3.88	0.992
Group (n=29)			
Flare-up	101.04±8.65	96.25±5.54	0.081
Group (n=29)			

Discussion

The current investigation found that blood Se concentrations were considerably lower during the flare-up phase compared to both healthy controls and patients in the remission phase. However, there was no significant difference in Se concentrations between the remission stage and the control group. Consistent with our results, Sturniolo et al. investigated the correlation between serum Se levels and the stage of UC. The study revealed a significant decrease in blood Se levels in patients with active illness in comparison to those in remission and control groups [19].

Similarly, research conducted by Mortensen et al. [20] observed no notable difference between control groups consisting of healthy persons and patients with UC. However, it was shown that blood Se concentrations declined dramatically as the severity of the illness increased. The research done by Castro Aguilar-Tablada et al. [21] found that individuals with IBD had considerably decreased serum Se concentrations

compared to healthy controls. Based on this investigation, the levels of serum Se were significantly influenced by the severity of UC. Furthermore, the levels of serum Se in individuals with severe UC were considerably lower compared to those with moderate UC. Furthermore, according to our findings, the research conducted by Geerling et al. [22] showed a significant decrease in serum Se concentrations in UC patients compared to the control group.

The likely reason for the lower Se levels in those experiencing flare-ups might be a reduction in selenium absorption from the colon. The deficit of trace elements such as Se in UC patients might be caused by many mechanisms, including increased excretion and hypoalbuminemia [23].

It is important to highlight that two variables have a substantial impact on these processes: limited absorption of trace elements via the mucosal lining and a deficit of trace elements in the diet. Histological data suggests that the absorption of trace elements, such as Se, is reduced even in the normal mucosa of the jejunum [24].

It is important to acknowledge that the research has certain limitations, such as a limited sample size in each group, absence of matching patient ages, and lack of association between Se concentrations and demographic variables like body mass index (BMI), and illness duration. Ultimately, although the current research demonstrated a significant correlation between Se concentrations and UC flare-ups, it remains uncertain whether lower Se concentrations directly contribute to flare-ups.

This research suggests that individuals with UC should include selenium-rich foods in their diet or consider taking Se supplements, while also periodically monitoring their selenium levels. Future research should explore the impact of Se administration in preventing the recurrence of UC. Furthermore, it is necessary to investigate the correlation between inflammatory biomarkers such as CRP, TNF- α , and alpha-3-antitrypsin, and serum Se levels. Additionally, the potential of a Se-rich diet in reducing the risk of IBD and colon cancer should be explored. Moreover, the relationship between serum Se concentrations and variables such as disease duration, BMI, and treatment methods (surgical or pharmacological) in patients with UC should be examined. Moreover, it is worthwhile to examine the relationship between Se concentrations in various tissues and its ability to hinder pro-inflammatory cytokines, the impact of Se supplementation on the gut microbiome, and the clinical results of supplementation in patients with UC. Additionally, on the prolonged effects research of Se supplementation in UC patients is needed.

Conclusion

During the period of increased inflammation, patients with UC had notably reduced levels of Se in

their blood serum compared to both healthy individuals and patients in a state of remission. These data indicate a clear relationship between Se concentrations and UC flare-ups. However, further research is required to validate these findings, uncover potential causes, and determine whether or not to recommend supplements or introduce dietary modifications for these individuals.

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Contributorship Statement

A.P. conceived of the presented idea; E.H. and S.J.H. developed the theory and performed the computations; S.M. carried out the experiments with help from H.S.; A.P. verified the analytical methods and, S.M. and N.S. wrote the manuscript.

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