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RESEARCH PAPER

Status of Vitamins D, C and Zinc Among Patients with Inflammatory Bowel Disease, Erbil Province

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A B S T R A C T:

Background and objectives: Inflammatory bowel diseases (IBD) are increasing worldwide and have become a global emergence disease, which includes Crohn's disease (CD), ulcerative colitis (UC) and indeterminate colitis. This study aimed to determine the status of vitamin D, C, zinc and oxidative stress among newly diagnosed IBD patients, in Erbil province for first time.

Materials and Methods: Sixty-six newly-diagnosed IBD patients and 80 healthy controls enrolled in this study. The serum concentration of vitamins (D and C), (Zinc) and plasma level of malondialdehyde (MDA) measured in both groups (patients and controls). The results compared statistically via SPSS version 25.

Results: High incidence rate of vitamin D and C deficiencies observed among patients with IBD. Significant difference reported among patients with IBD and controls in term of vitamins deficiencies, the p value was (p value 0.021) and (p value 0.001) for vitamin D and C, respectively. However, no significant difference identified for zinc deficiency. Statistically, higher level of MDA observed among patients with IBD compare to control, p value was (<0.001).

Conclusion: further studies are required to determine the status of vitamins, minerals and oxidative stress in IBD patients.

KEY WORDS: Crohn's disease, Erbil, Ulcerative colitis, Vitamins, Zinc.
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1.INTRODUCTION:

Inflammatory bowel disease (IBD) is a group of gastrointestinal disorders that clinically includes Crohn's disease (CD), ulcerative colitis (UC), and other indeterminate colitis (Guan, 2019). Over the past decade, IBD has emerged as a global public health challenge (Kaplan and hepatology, 2015). The incidence pattern of IBD has shifted during the past 20 years, increasing incidence in previously low incidence regions like Asia and the Middle East as well as continuing to rise in the West (Cosnes et al., 2011, Narula et al., 2021). The pathogenesis of IBD are not known however, it is considered to be multifactorial and a cure for IBD has yet to be discovered (Nishida et al., 2018, Ahlawat et al., 2021). Recent experimental and clinical studies agreed that genetics, environment, gut microbiota and immune response are responsible for the initiation and progression of IBD in susceptible host (Glassner et al., 2020).

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Additionally, it has been proposed that diet, lifestyle and pollutants and the deficiency of vitamins and minerals contribute to the severity or the development of (Lurz et al., 2020), (Celiberto et al., 2018), (Khalili et al., 2018) and (Altajar and Moss, 2020). Previously, the deficiency of micronutrients observed in IBD patients, such as, high prevalence of vitamin deficiency reported among patients with IBD including vitamins D, C, B12, folic acid and zinc (Ratajczak et al., 2020), (Park et al., 2021) and (Sakurai et al., 2022).

Experimental study revealed that reactive oxygen and nitrogen species (ROS and RNS) increase due to the invasion of muscular tissue, disruption of cellular homeostasis and inflammation (Tian et al., 2017), (Dudzińska et al., 2018) and (Krzystek-Korpacka et al., 2020). Thus, oxidative stress has been mentioned as a potential contributor to the etiology of IBD (Krzystek-Korpacka et al., 2020). The level oxidative stress can be evaluated indirectly by

assessing the quantities of DNA/RNA damage, lipid peroxidation, and protein oxidation/nitration (Katerji et al., 2019). Lipids are the most involved class of macromolecules among the numerous biological targets of oxidative stress (Del Rio et al., 2005). Malondialdehyde (MDA), is one of the final products of polyunsaturated fatty acids peroxidation which also well-known as an oxidative stress biomarker, it is overproductions related to increase of free radicals and decrease the levels of antioxidants (Morales and Munné-Bosch, 2019).

The present study aimed to determine the status of vitamins D, vitamins C, zinc and malondialdehyde (biomarker of oxidative stress) in newly diagnosed patient with IBD, to find the possible role of micronutrient deficiencies in the severity and the onset of disease. To the best of our knowledge, this is the first investigation on this topic in Kurdistan region of Iraq.

Materials and Methods

This study conducted in Erbil province - Kurdistan region of Iraq, from July 2021 to July 2022. Sixty-six newly-diagnosed patients with inflammatory bowel disease of which 58 with (UC) and 8 with (CD) and eighty matched healthy adult volunteers participated in this study. Sociodemographic variable including (age and gender) with the type of disease were collected from private clinic data-base. The diagnosis based on confirmation of clinical, radiographic or endoscopic, and histopathological characteristics of the diseases. All conscripts who were not given an IBD diagnosis were considered as control population. However, patients with indeterminate colitis, pregnant female, nursing mothers, a history of total colectomy, significant acute or chronic coexisting illness, treatment with experimental drugs, malignant or any concomitant end-stage organ disease, addicts, and severe malnutrition or impaired absorption were excluded.

Vitamins measurements were under taken directly a day after diagnosis. Briefly, after an overnight fast, blood samples were obtained, EDTA vacutainer was used for the separation of plasma while serum obtained by using serum separation tube. 25(OH) serum vitamin D deficiency is defined as Vitamin D <20 ng/ml, whereas 20–29 ng/ml indicated insufficiency and concentrations >29 ng/ml were considered to be normal (Holick, 2007) and (Kabbani et al., 2016). Vitamin C deficiency is defined as Vitamin C ≤0.4 mg/dL (reference range 0.5–2.0 mg/dL) (Aditi et al., 2012), and Zinc deficiency is defined as a concentration of <70 µg/dL (reference range 70-120 µg/dL) (Alkhouri et al., 2013). The methods used for vitamin analysis were taken from previous studies (Zhao et al., 2019). The concentration of MDA determined by enzyme linked immunosorbent assay (ELISA) kit (Melsin China), the results expressed as µmol/L.

All of the statistical analyses were performed in SPSS version 25 (IBM Corp., Armonk, NY, USA) and p-values of < 0.05 were considered to indicate statistical significance. There was no imputation of missing values. The relative risk determined through odds ratio (OR 95% CI) and Medcalc online website was used to confirm the odds ratio.

Results

The present study included 66 patients with IBD, (58 with UC and 8 with CD) and 80 healthy controls. Among patients with UC, 34 were males and 24 were females, their mean age was (32 ± 10) while among patients with CD, 5 were males and 3 were females, their mean age was (33± 10). The mean age of 80 healthy controls (51 males and 29 females) was (32± 11). No significant difference was identified among patients with IBD and controls in terms of gender and age (P>.05), as shown in Table (1).

The mean level of serum vitamin D, vitamin C and Zinc were lower in patients with IBD than in the controls while the level of oxidative stress was higher in IBD patients as shown in Table (2). The prevalence of vitamin D deficiency in IBD patients were 50%, (in patients with UC were 44.8% and in patients with CD were 87.5%) while the prevalence of vitamin D deficiency in healthy control were lower (42.5%). Highest percentage of vitamin C deficiency reported among patients with UC that was 36.2% compare to the patients with CD (12.5%) and controls (7.5%). The differences for both vitamin D and C deficiencies between patients with IBD and controls, were statistically significant (P>.05) as shown in Table (3). The prevalence of Zinc deficiency was 26.3%, 25%, and 24.1% for control, CD, and UC, respectively. We found no significant difference statistically. Significantly (P>0.001), higher level of MDA observed in IBD patients compared to their matched controls as shown in Figure (1).

The level of vitamins, zinc and MDA presented according to the severity of the disease

(IBD), Table (4). The lowest mean of vitamin D and C observed among sever cases of IBD that was (17.23±7.23), and (0.40±0.19), respectively. Lowest mean of zinc status observed among moderate cases of IBD which was (75.45±18.33).

According to the results of the Table (4), the level of the oxidative stress increases with the severity of the cases comparing mild to sever.

Table 1: Baseline characteristics

Characteristic		IBD or Case (n 66) and %	UC (n 58) and %	CD (n 8) and %	Control (n 80) and %	P-value Case vs Control
Gender	Male	39 59.1%	34 58.6%	5 62.5%	51 63.7%	0.564
	Female	27 40.9%	24 41.4%	3 37.5%	29 36.3%	
Age	Mean ± SD*	32.84 ± 9.94	32.93 ± 10	33.25± 10.13	31.80± 10.52	0.086

Table 2: Vitamin, mineral status and level of oxidative stress in patients with IBD compared with controls*

Micro-nutrients	IBD N=66	UC N=58	CD N=8	Control N=80
Vitamin D	19.74±8.25	20.78±8.09	12.14±4.93	22.74±7.31
Vitamin C	0.71±0.57	0.69±0.577	0.81±0.54	1.20±1.10
Zinc	78.69±22.47	78.25±22.39	81.88±24.29	79.53±21.39
MDA, nmol/mL	4.55±1.65	4.68±1.61	3.61±1.76	1.97±0.30

*Values are expressed as mean ± SD.

Table 3: Vitamin, mineral status and level of oxidative stress in IBD patients and controls

Micro-nutrients	Characteristics	IBD or Case (n 66) and %	UC (n 58) and %	CD (n 8) and %	Control (n 80) and %	P-value
Vitamin D	Deficient	33 50%	26 44.8%	7 87.5%	34 42.5%	0.021 (IBD vs CT) 0.142 (UC vs CT) <0.001 (CD vs CT)
	Insufficient	20 30%	19 32.8%	1 12.5%	24 30%	
	Sufficient	13 19.7%	13 22.4%	0 0%	22 27.5%	
Vitamin C	Deficient	22 33.3%	21 36.2%	1 12.5%	6 7.5%	0.001 0.002 0.332
	Normal	44 66.7%	37 63.8%	7 87.5%	74 92.5%	
Zinc	Deficient	16 24.2%	14 24.1%	2 25%	21 26.3%	0.817 0.734 0.770
	Normal	**50** **75.8%**	**44** **75.9%**	**6** **75%**	**59** **73.8%**	

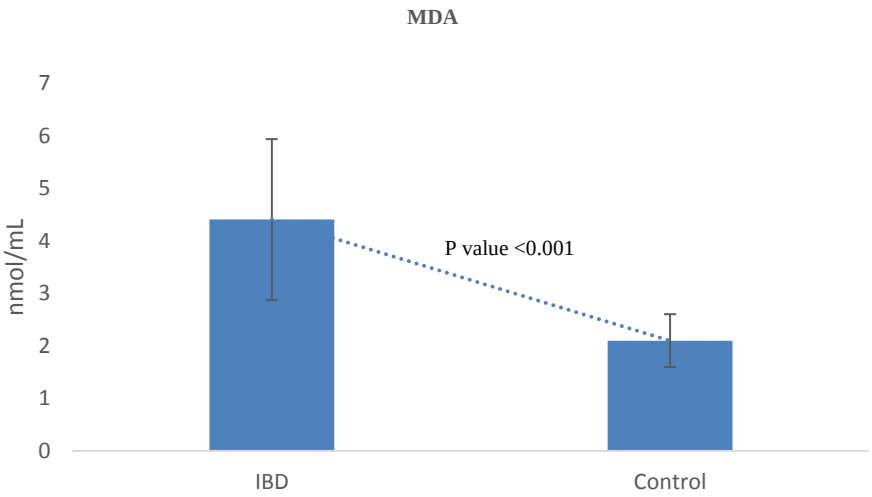

Figure 1: level of oxidative stress among patients of IBD and Controls

Table 4: Vitamin, mineral status and level of oxidative stress according to the severity of the disease (IBD).

Micro-nutrients	Mild (27)	Moderate (18)	Sever (21)	P-value
Vitamin D	18.86±9.16	24.13±6.33	17.23±7.23	0.0396 (Mi. vs Mo.) 0.5069 (Mi. vs Sv.) 0.0033 (Mo.vsSv.)
Vitamin C	0.87±0.49	0.82±0.81	0.40±0.19	0.7974 0.0001 0.0267
Zinc	81.59±19.73	75.45±18.33	77.74±28.76	0.2989 0.5853 0.7729
MDA, nmol/mL	4.41±1.68	4.32±1.47	4.92±1.77	0.8542 0.3134 0.2617

Discussion

This is the first study in Erbil province - Kurdistan region of Iraq that aimed to determine the level of vitamins (Vitamin D and C) and minerals (Zinc) in newly diagnosed patients with IBD. Previously, many studies reported that the deficiency of vitamins and minerals in IBD patients during different stages of the disease and determined their effects on the quality of life (Ratajczak et al., 2020). The present study

determined the deficiency of vitamin D, C with zinc and MDA in newly diagnosed IBD patients in order to determine their risks in the development and progression of IBD as causative agents.

The classic function of vitamin D in maintaining bone mineral density is well-known (Hill and Aspray, 2017, Marozik et al., 2021). Vitamin D also affects the body's immune system in a significant "non-classical" way by influencing the innate and adaptive immune systems, affecting the generation of critical endogenous antimicrobial peptides like cathelicidin, and regulating the inflammatory cascade (Nobile et al., 2019). Additionally, there is evidence that vitamin D may modify the gut microbiota (Garg et al., 2018). Also it has been reported that vitamin D deficiency is associated with ulcerative colitis disease activity (Parizadeh et al., 2019). However, there is a little knowledge about vitamin C status in patients with IBDs. Vitamin C, also referred to

as L-ascorbic acid, is a water-soluble vitamin that is naturally present in some foods, fortified in others, and available as a dietary supplement alone or in multivitamins (Vinishdharma and Don, 2019) and (Patil and Patil). Many studies determined the important roles of Vitamin C in wound healing, skin disease, bacterial sepsis, viral infections, cardiovascular diseases (Carr and Rowe, 2020), (Moritz et al., 2020), (Villagran et al., 2021). Recently, epigenetic roles of vitamin C also observed by (Cimmino et al., 2018) and (Coker et al., 2022). Zinc is an important mineral that body cannot produce it on its own and most be obtained from animal sources (Beletate et al., 2007) and (Kanwar and Sharma, 2022). Zinc plays a key role in the synthesis of DNA, cell development, protein synthesis, wound healing, and immune system support (Palmieri et al., 2019).

This study confirmed that there are deficiencies of vitamins (D and C) and minerals (Zinc) among patients with IBD. Highest prevalence of vitamin D deficiency observed among patients with CD (87.5%) and followed by patients with UC and controls which was (44.8% and 42.5%), respectively. Notable, **30%** percentage of control group also showed insufficient concentration of vitamin D. The results showed that the prevalence of vitamin D deficiency is significantly higher in patients with IBD than healthy controls, p value was 0.021. This results are in line with the results of several studies (Zhao et al., 2019) and (Mohammed, 2019), while disagree with a study by (Veit et al., 2014).

The highest prevalence rate of vitamin C deficiency reported among patients with UC 36.2% followed by patients with CD 12.5%. The difference was significant for UC and not CD when compared to controls; p value was 0.002 and 0.332 for UC and CD, respectively. Same finding observed by (Ratajczak et al., 2020) and (Dunleavy et al., 2021). Also, the present study reported the decrease in the mean level of vitamin C according to the severity of the disease, for instance, the mean of vitamin C was (0.71±0.57), (0.69±0.577), and (0.81±0.54) in mild, moderate and sever cases, respectively. This finding agree with the findings of other studies which concluded that vitamin C seems to remain unchanged until the disease has severely progressed (Kuroki et al., 1993).

The prevalence rate of Zinc deficiency was 26.3%, 25% and 24.1% for control, patients with CD, and UC, respectively. However, no significant difference identified. This finding is not agree with previous findings which reported statistical significant difference in term of zinc deficiency between newly-diagnosed IBD group and control group (Alkhouri et al., 2013). This difference may due to the geographic location and number of the cases. Other studies concluded that concentration of serum zinc decreased with the progression of the disease which result from poor oral intake and decreased absorption (Siva et al., 2017) and (Ishihara et al., 2022), in the present study, we reported lowest mean of zinc level in moderate case which was (75.45±18.33) followed by sever and mild cases which was (77.74±28.76),and (81.59±19.73), respectively. Therefore, may be the pattern of the diagnosis, newly enrolled diagnosed patient, responsible for insignificant results in term of zinc deficiency.

The level of oxidative stress increased with the severity of the diseases. This finding is not agree with the findings of previous study which found no significant differences between the level of oxidative stress and the severity of IBD (Rezaie et al., 2007). While in line with the most recent studies (Tian et al., 2017) and (Wojcik-Grzybek et al., 2022).

Conclusions

To the best of our knowledge, this is the first study to determine the status of vitamins, mineral (zinc) and oxidative stress (MDA) among patients with UC and CD in Erbil province - Kurdistan region of Iraq. There were significant differences for both vitamin D and C deficiencies between patients with IBD and controls. No significant difference identified for Zinc deficiency between patients and controls. Significantly higher level of MDA observed among patients with IBD than their controls, also the level of oxidative stress increased with the severity of the disease.

Conflict of Interest

The authors have no conflicts of interest to declare.

Ethics

The corresponding author hereby confirms that ethics were considered for this research and that the article is original, and its contents are unpublished. The co-author has read and approved the manuscript for submission.

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