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Evaluation of the Level of Alkaline Phosphatase, Calcium, and Vitamin D3 in Patients with Celiac Disease

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ABSTRACT: Celiac disease, sometimes called wheat allergy, is multiple names for one disease. It is a long-term acquired autoimmune disease that primarily affects the small intestine, as individuals develop intolerance to gluten, which is found in foods such as wheat, rye, and barley. Our study aims to monitor biochemical parameters such as alkaline phosphatase, calcium, and vitamin D3 as an indicator to monitor the progress of bone health in the blood serum of patients with celiac disease in Wasit Governorate/Iraq. In this research, studied 80 samples, including 50 samples from patients with celiac disease of both sexes, 19 men and 31 women with 30 control samples for both sexes equally. used an Enzyme-linked immunosorbent assay (ELISA) kit to measure the concentrations of vitamin D3 and alkaline phosphatase, while a Cobas c111 device was used for calcium. The results showed that the level of alkaline phosphatase increased more in patients with celiac disease than in the control group at $p\leq (0.05)$, while the concentrations of calcium and vitamin D3 decreased more than in the control group at $p\leq (0.05)$. The studied criteria contribute as indicators of developing health risks to the body and bone health in patients with celiac disease.

Keywords: Alkaline Phosphatase; Calcium; Celiac Disease and Vitamin D3

1. INTRODUCTION

The research focuses on the issue of osteoporosis in patients with celiac disease, which is caused by poor absorption and metabolism of minerals and vitamins due to villous atrophy in the intestines, potentially leading to future problems that could affect bone health.

Celiac disease is a condition characterized by an inappropriate immune response that happens when gluten is consumed. This immune reaction leads to damage in the small intestine, which is characterized by the thinning of the finger-like projections called villi and an increase in the number of cells in the intestinal crypts (1, 2).

Celiac disease is a chronic condition that may manifest at any stage of life. This is a gender-biased autoimmune disorder that occurs twice as often in women compared to males (1).

A gluten-free diet is the primary therapy for celiac disease. Products with a gluten level over 1 mg per 100 grams are strictly forbidden (3).

In the management of celiac disease, pharmaceuticals such as enzymes, vitamins (B1, B6, nicotinic acid (administered subcutaneously), iron, calcium, and vitamin D (in tablet form) may be used. Additionally, treatments for symbiosis may also be prescribed (4).

In 2016 research, it was shown that 56.1% of individuals who were newly diagnosed with celiac disease had osteopenia, while 29.2% had osteoporosis (5). Another research indicated that those with osteoporosis are 17 times more likely to have celiac disease. The correlation was so significant that the project's main researcher, William Stenson, advised “all individuals with osteoporosis undergo screening (for celiac disease)” (6).

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2. MATERIALS AND METHODS

2.1 Study design

Samples were collected from Al-Zahraa Teaching Hospital in Wasit Governorate, Iraq, where we obtained official approvals for collection and work in the hospital's laboratories, along with ethical approvals from patients. Cases with concomitant diseases such as diabetes, blood pressure, and other chronic diseases were excluded.

Eighty samples were collected in this study, including 50 samples from patients with celiac disease as a patient's group and 30 samples as healthy people. The ages of the patients ranged from 24 to 42 years, while the gender distribution was 31 and 19 for each of women and men, respectively. Fifteen samples were collected for comparison for each of the males and females. The study period was from November 2023 to February 2024.

2.2: Methods

Blood samples—5 milliliters — were collected in a gel collection tube for both groups—patients and healthy people. After 20 minutes of coagulation at room temperature, the blood was centrifuged at 5000 rpm for 10 minutes. After obtaining the blood serum, the Enzyme-linked immunosorbent assay (ELISA) technique was used to measure the alkaline phosphatase and vitamin D3 levels, while Cobas c111 was used to measure the calcium level.

2.3 Statistical analysis

The present study's statistical analyses were executed using (SPSS 27) discovery version 2020. Data conveyed as (Mean ± Standard Deviation). Statistical data analysis of means between patients and control groups was done using an independent sample T-test at $P \leq 0.05$ value accepted as statistically significant between means.

3 RESULTS AND DISCUSSION

The results in Table 1 show the mean of Human Anti-Deamidated Gliadin Peptide IgG+ IgA (IU/ml), Calcium (mg/dl), Alkaline Phosphatase (U/L), and Vitamin D3 (ng/ml) concentration.

Table 1: Levels of the Parameters in Control and Celiac Disease Groups.

Parameters	Control M.± S.D (No. 30) 15♀,15♂	Celiac disease M.± S.D (No. 50) 31♀,19♂	P-value P≤0.05
Human Anti-Deamidated Gliadin Peptide IgG (IU/ml)	**5.71 ± 0.79**	**37.47 ± 5.72**	***Sig.***
Human Anti-Deamidated Gliadin Peptide IgA (IU/ml)	**8.09 ± 1.67**	**45.81 ± 10.22**	***Sig.***
Calcium (mg/dl)	**10.52 ± 0.74**	**8.14 ± 1.26**	***Sig.***
Alkaline Phosphatase (U/L)	**117.76 ± 11.96**	**97.92 ± 20.16**	***Sig.***
Vitamin D3 (ng/ml)	**39.03 ± 6.18**	**18.14 ± 5.08**	***Sig.***

Determination of antibodies to synthetic deamidated gliadin peptides may work as an alternative or complement the commonly used test for tissue transglutaminase antibodies (TGA) in the diagnosis of celiac disease (7). Diagnosis is used by measuring the level of anti-gliadin antibodies in the early stages of the disease, especially in newborns and infants. Diagnosis using the tTg enzyme (tissue transglutaminase) is unclear and inaccurate at this age stage due to the absence of antibodies to the tTg enzyme in the early age of patients (8). Detection of IgG antibodies against deamidated gliadin peptides (DGP) is more sensitive and more specific for celiac disease than detection of IgG antibodies against native gliadin (9). The IgG anti-DGP option yields excellent results, with a low cost and independence from the observer (10).

A study in which they diagnosed celiac disease using Anti-Deamidated Gliadin Peptide IgG and IgA that it increased the level of immune antibodies IgG and IgA in patients with a significant difference from the level in healthy people (7). Celiac disease causes the destruction and disappearance of the villi in the duodenum, which play a crucial role in the absorption of calcium (11). A study published in 2022 studied the average of calcium (mg/dl) in the blood of healthy people and those with celiac disease patients for two groups: one group adhered to a gluten-free diet, and the other did not adhere to any diet for both males and females in all groups. The samples were analyzed at a significance level of $p \leq 0.05$, and show a significant decrease was observed between all groups (12). Our study agreed with (13) noted significant drops in levels of Ca+2 from 9.84 mg/dl, to 9.74 mg/dl, respectively, at p=0.03. Measurements of alkaline phosphatase, calcium, vitamin D3 are recommended by the celiac disease recommendations of the British Society of Gastroenterology (BSG). These measurements should be taken at the time of diagnosis as well as when it is necessary (14). In a cohort study based on the Copenhagen Primary Care Laboratory database over 15 years, 43.964 alkaline phosphatase (U/L) samples were analyzed and published in 2022. It was found that the rate for celiac disease in men is (113.3 U/L) and in healthy men (100.1 U/L), while in celiac disease women (87.2 U/L) and healthy women (74.1 U/L) (15). A study was conducted on 120 people, including 60 patients diagnosed with celiac disease and 60 healthy people of the same age. The results showed that there were statistically significant increases in the alkaline phosphatase value (U/L) between celiac disease patients and the control group (16). Although it is expected that the results of our study are consistent with the sources mentioned, our results were not identical, perhaps because there are reasons that we did not discover in patients that caused basal phosphatase to decrease, such as: Zinc deficiency (17), an underactive thyroid, or hypothyroidism (18), ALP may be decreased by fasting, Pernicious anemia (19), congenital hypophosphatasia, fulminant Wilson disease (20), malnutrition (21), in addition, some medications, such as birth control pills, can lower ALP levels (22). In a study conducted based on a huge database that includes 28.599 vitamin3 D tests (nmol/L) during the period 2000-2015, they found that the values of vitamin D3 in men with a positive test for celiac disease are (66.8 nmol/L) and in men with a negative test for celiac disease (55.1 nmol/L), while in women with a positive test for celiac disease (60.3 nmol/L) and women with a negative test for celiac disease (58.9 nmol/L) (15). In a meta-analysis, the vitamin D3 status of celiac disease patients was studied. It was found that the vitamin D3 level in patients who were not on a gluten-free diet was lower than the normal level, with an average of 8.36 nmol/L. In contrast, after treating the patients and subjecting them to a gluten-free diet, the average vitamin D3 level of untreated patients was higher by 15.6 nmol/L (23). The level of vitamin D3 for celiac disease patients was measured, and the readings for both men and women were 11.17 (ng/mL) and 11.37(ng/mL), respectively, which is much lower than the average percentage for healthy people (24).

Untreated celiac disease can result in vitamin D3 insufficiency due to impaired absorption of fat. Secondary lactose intolerance can also decrease the consumption of milk, which is one of the limited food sources that contain Vitamin D3. Vitamin D3 levels may return to normal after 1-2 years of following a gluten-free diet, although the use of supplements may still be necessary (25). Therefore, calcium and vitamin D3 should be supplemented in celiac disease patients with documented low serum levels, those with loss of BMD, or those who cannot achieve adequate intake via diet to prevent osteoporosis and fractures (26).

4 CONCLUSION

Our research summarized that the levels of alkaline phosphatase, calcium, and vitamin D3 changed significantly from the average. Both calcium and vitamin D3 decreased in patients with disorders, while the level of alkaline phosphatase increased above the normal limit.

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