

Parathyroid Hormone and Osteocalcin as Criteria for Osteoporosis in Patients with Celiac Disease

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KEYWORDS

Osteoporosis, Celiac Disease, Osteocalcin, Parathyroid Hormone, and Human Anti-Deamidated Gliadin Peptide IgG and IgA.

ABSTRACT

Background: Osteoporosis is a disease that affects the entire skeletal system. It is characterized by the deterioration of the fine structural structure of the bone and the decline in bone mass, which ultimately leads to an increase in the bone's susceptibility to fracture.

Celiac disease, often known as wheat allergy, is a single condition with numerous names. Celiac disease is a chronic autoimmune disorder that mostly affects the small intestine. It occurs when patients develop an intolerance to gluten, a protein found in foods including wheat, rye, and barley.

Aim of the study: The objective of our study is to track the levels of osteocalcin and parathyroid hormone in the blood serum of patients diagnosed with celiac disease in Wasit Governorate, Iraq. We will be using Human Anti-Deamidated Gliadin Peptide IgG and IgA to diagnose celiac disease and evaluate the progress of bone health. **Materials and methods:** This study examined a total of 80 samples, consisting of 50 samples from individuals with celiac disease. The sample group included 19 males and 31 women. There are 30 control samples, with an equal number of samples for each sexes. Utilized an Enzyme-linked immunosorbent assay (ELISA) kit to quantify the levels of osteocalcin, parathyroid hormone, and Human Anti-Deamidated Gliadin Peptide IgG and IgA. **Results:** The study revealed that individuals with celiac disease had significantly higher levels of osteocalcin, parathyroid hormone, and Human Anti-Deamidated Gliadin Peptide IgG and IgA compared to the control group, with a statistical significance of $p \leq (0.05)$.

Conclusion: The examined parameters serve as indicators of the development of health risks to the body and bone health in individuals with celiac disease.

1. Introduction

Osteoporosis (OP) is a disorder in the skeletal it has a systemic impact on the whole body. OP characterized by a reduction of bone mass, loss of microarchitectural integrity, diminished bone mineral density and diminished strength of bones, consequently of which fracture risk and bone fragility are raised up, mostly at the femur and spine levels (De Martinis et al., 2021). Osteoporosis is a major health problem for women who have gone through menopause (Marozik et al., 2019).

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 (Abadie et al., 2011; Green and Cellier, 2007).

2. Methodology

A total of eighty samples were gathered for this investigation, consisting of fifty samples from individuals diagnosed with celiac disease as the patient group, and thirty samples from healthy individuals. The patients' ages varied from 24 to 42 years, with 31 women and 19 men in the study. A total of fifteen samples were taken for comparison, with an equal number gathered from both males and females. The duration of the trial was from November 2023 to February 2024.

Both patients and healthy individuals had 5 milliliters of blood drawn using gel collection tubes. Following a 20-minute period of coagulation at ambient temperature, the blood was subjected to centrifugation at a speed of 5000 revolutions per minute for a duration of 10 minutes. The parathyroid hormone and osteocalcin levels were measured using the Enzyme-linked immunosorbent assay (ELISA) technique after obtaining the blood sample.

Statistical analysis

The statistical analyses for this study were conducted using the 2020 discovery version of SPSS 27. The data is presented as the mean value plus or minus the standard deviation. The statistical analysis involved

comparing the means of patients and control groups using an independent sample T-test. A significance level of $P < 0.05$ was used to determine if there was a statistically significant difference between the means.

3. Result and Discussion

The results in **Table 1** show the mean of Human Anti-Deamidated Gliadin Peptide IgG+ IgA (IU/ml), parathyroid hormone (pg/ml) and osteocalcin (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 $P \leq 0.05$
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.
Osteocalcin (ng/ml)	7.26 ± 1.42	10.64 ± 2.53	Sig.
Parathyroid Hormone (pg/ml)	44.95 ± 5.84	96.51 ± 12.76	Sig.

M.± S.D = Mean ± Standard Deviation Sig. = Significant Difference at $P \leq 0.05$

The results in **Table 1** showed that the average levels of the diagnostic parameter Human Anti-Deamidated Gliadin Peptide IgG were (5.71 ± 0.79 IU/ml) for the control group and (37.47 ± 5.72 IU/ml) for the group with celiac disease. It was also noted that there was a significant difference between the two groups at $p \leq 0.05$.

The average levels of the diagnostic parameter Human Anti-Deamidated Gliadin Peptide IgA were (8.09 ± 1.67 IU/ml) for the control group and (45.81 ± 10.22 IU/ml) for the group with celiac disease. It was also noted that there was a significant difference between the two groups at $p \leq 0.05$.

The mean of parathyroid hormone (pg/ml) concentration also showed a significant increase between the celiac disease group and the control group at ($P \leq 0.05$) where control (44.95 ± 5.84 pg/ml). In contrast, the celiac disease group is (96.95 ± 12.67 pg/ml).

The mean of osteocalcin (ng/ml) concentration also showed a significant increase between the celiac disease group and the control group at ($P \leq 0.05$) where control (7.26 ± 1.42 ng/ml). In contrast, the celiac disease group is (10.64 ± 2.53 ng/ml).

Discussion

Assessing the presence of antibodies to synthetic deamidated gliadin peptides might serve as a substitute or supplement to the routinely used tissue transglutaminase antibody (TGA) test for diagnosing celiac disease. (Lammi *et al.*, 2015,). 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 (Ciccocioppo *et al.*, 2003). The detection of IgG antibodies against deamidated gliadin peptides (DGP) is both more sensitive and more selective for diagnosing celiac disease compared to the detection of IgG antibodies against natural gliadin (Vermeersch *et al.*, 2010). The IgG anti-DGP option yields excellent results, with a low cost and independence from the observer (Ortiz *et al.*, 2019). 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 (Lammi *et al.*, 2015).

Celiac Disease is often linked to indications of vitamin D insufficiency and impaired calcium

absorption, which are both factors contributing to secondary hyperparathyroidism. While it is anticipated that there is a connection between celiac disease and increased levels of parathyroid hormone (PTH), the link between celiac disease and high levels of calcium in the blood (hypercalcemia) leading to a diagnosis of primary hyperparathyroidism is unexpected (Ludvigsson et al., 2012).

Zylberberg et al., (2018) studied the level of parathyroid hormone and other parameters in celiac disease patients at Columbia University (Celiac Disease Center) who were diagnosed with osteoporosis via DXA scan and found that the level of parathyroid hormone (pg/ml) in celiac disease patients is 50.38 pg/ml, while the normal range is 10-65 pg/ml.

In a study conducted in Italy, which gathered data from 105 celiac disease patients for laboratory tests, it was discovered that participants with untreated celiac disease had a serum parathyroid hormone level that was 42.5% greater than normal people at $p < 0.001$ (Ciacci et al., 2020).

A cohort study was conducted on patients with recent clinical fractures in (VieCuri Medical Centre, Venlo, The Netherlands), aged 50-90, and the number of subjects was 1042. The study found that the average parathyroid hormone (PTH) was 5.3 pmol/L = pg/mL = 49.979 (reference range: 2.2-10.0 pmol/L = 20.74-94.3 pg/mL) (de Bruin et al., 2020).

72 out of 193 individuals with celiac disease, or 27.2%, had elevated levels of PTH. There was a notable disparity in PTH levels among individuals with osteopenia, osteoporosis, and normal BMD ($P = 0.0001$). Those diagnosed with celiac disease and low bone mineral density (BMD) had substantially elevated levels of parathyroid hormone (PTH) as compared to those with normal bone density. Hyperparathyroidism, characterized by elevated levels of parathyroid hormone (PTH), may contribute to bone loss in individuals with celiac disease due to an autoimmune origin (Ganji et al., 2022).

Elevated concentrations of parathyroid hormone and osteocalcin, have been suggested as indicators of bone disease and inadequate response to a gluten-free diet during follow-up (Gonzalez et al., 1995).

A study published in La Tunisie Medicale magazine included 30 patients diagnosed with celiac disease, including three men and 27 women, with an average age of 30.4, and 30 healthy people as a control group, osteocalcin levels were higher in satisfaction than healthy subjects at a level that did not record significant differences at $p \leq 0.05$ (Younes et al., 2012, Ahmed et al., 2020).

Szymczak et al., (2012) studied the level of osteocalcin (ng/ml) in both healthy people and Celiac disease patients in two subgroups: the first subject to a gluten-free diet with supplements for both calcium and vitamin D3, and the second not subject to a gluten-free diet, and their results concluded that there was a significant increase at $p < 0.05$ between negative GFD group with the control group, while the positive GFD group did not notice any significant difference with the control group.

In a study conducted in Colombia on 66 samples from women, 33 were newly diagnosed with celiac disease, 33 were control samples, and all were in the premenopausal stage. However, 36% and 67% of women took calcium and vitamin D3 supplements respectively. The study found that the rate of osteocalcin (ng/ml) in patients was 17.0 ng/ml, while in healthy people, it was 19.4 ng/ml (Stein et al., 2015). This is explained by women's supplements from calcium and vitamin D3, which ensure bone safety during the disease stage.

In a study that included 8 positive samples for the IgA antitissue transglutaminase test and those suffering from type 1 diabetes and 12 control samples, the aim of the study was to evaluate bone density in patients with type 1 diabetes and the rates of osteocalcin (ng/ml) were very close between patients and healthy people. At a significant level, $p = 0.37$ (Diniz-Santos et al., 2008).

In a study that included a case study of 10 males and 11 females with celiac disease and was compared with 30 healthy controls, conducted in Egypt by Abd ElBaky et al., (2009), it was found that there was a significant decrease in calcium and osteocalcin ($p = 0.0002, 0.0001$), respectively

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