**Original article**

# A study of clinical, laboratory features and bone mineral density in newly diagnosed adult patients of celiac disease.

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**Abstract**

**Objective:** To study clinical, laboratory features, bone mineral density in newly diagnosed adult patients of celiac disease .

**Material and Method:** Study sample consist of eighty seven newly diagnosed adult patient of celiac disease. Detailed medical history, drug history, physical examination, complete blood count, erythrocyte sedimentation rate, calcium profile, liver and renal biochemistry, 25-OH-D, Blood sugar were performed. Other investigations like RA factor, CRP, electrolytes, thyroid function tests and anti CCP were performed wherever indicated. Sera of all patients were tested for presence of IgA tissue transglutaminase (TTG) antibody by ELISA using commercially available kits. Antibody titer >50 units was considered positive. BMD of all newly diagnosed patients of celiac disease was done with Pronosco X-posure V.2 based on DXR.

**Key words:** Bone Mineral Density, Celiac Disease, Osteopenia, Autoimmune

## Introduction

Celiac disease, gluten-sensitive enteropathy is a disease that results from permanent intolerance to wheat protein, gluten. Classically the patient manifests with diarrhoea. Such classical symptomatic patients represent the tip of the iceberg[1]. Majority of patients of Celiac disease manifest as anaemia, osteoporosis, convulsions, short stature, dental enamel defects, weight loss, fatigue, generalised weakness, cheliosis, glossitis, dry skin.

North India referred as a “celiac belt”, where a greater than average number of people exhibit symptoms of celiac disease.

This is partially because more wheat is consumed in this region, but also because the population possesses haplotypes necessary for celiac disease to develop[2]. The inflammatory process, mediated by T cells, leads to disruption of the structure and function of the small bowel's mucosal lining and causes malabsorption as it impairs the body's ability to absorb nutrients, minerals and fat-soluble vitamins A, D, E and K from food.Celiac disease is associated with a wide range of autoimmune diseases including insulin-dependent diabetes, dermatitis herpetiformis, autoimmune thyroid disease, autoimmune hepatitis and primary biliary cirrhosis. Celiac disease is strongly associated with osteomalacia and osteoporosis. Studies have suggested that treatment of malabsorption with a gluten-free diet reverses the loss of calcium in those with osteomalacia.

**Bone Mineral Density**

**Bone density** (or **bone mineral density**) is a medical term normally referring to the amount of mineral matter per square centimeter of bones[3].

Bone density (or **BMD**) is used in clinical medicine as an indirect indicator of osteoporosis and fracture risk.This medical bone density is not the true physical "density" of the bone, which would be computed as mass per volume. It is measured by a procedure called *densitometry*, often performed in the radiology or nuclear medicine departments of hospitals or clinics.

The measurement is painless and non-invasive and involves low radiation exposure. Measurements are most commonly made over the lumbar spine and over the upper part of the hip[4].

**Interpretation**

Results are generally scored by two measures, the T-score and the Z-score. Scores indicate the amount one's bone mineral density varies from the mean. Negative scores indicate lower bone density, and positive scores indicate higher.

**T-score**

The T-score is the relevant measure when screening for osteoporosis. It is the bone mineral density at the site when compared to the young normal reference mean. It is a comparison of a patient's BMD to that of a healthy thirty-year-old of the same sex and ethnicity. This value is used in post-menopausal women and men over age 50 because it better predicts risk of future fracture[5]. The criteria of the World Health Organization are[6]:

- Normal is a T-score of -1.0 or higher
- Osteopenia is defined as between -1.0 and -2.5
- Osteoporosis is defined as -2.5 or lower, meaning a bone density that is two and a half standard deviations below the mean of a thirty-year-old man/woman.

**Z-score**

The Z-score is the comparison to the age-matched normal and is usually used in cases of severe osteoporosis. This is the number of standard deviations a patient's BMD differs from the average BMD of their age, sex, and ethnicity. This value is used in premenopausal women, men under the age of 50, and in children.[5] It is most useful when the score is less than 2 standard deviations below this normal. In this setting, it is helpful to scrutinize for coexisting illnesses that may contribute to osteoporosis such as glucocorticoid therapy, hyperparathyroidism, or alcoholism.

**Material And Methods**

Eighty-seven newly diagnosed adult patients of celiac disease from medical OPD and ward between January 2011 – September 2012 were included in the study.

**Inclusion Criteria :**

1. Newly diagnosed patients of celiac disease;
2. Patient age <55 years;
3. Patient age >20 years.

**Exclusion Criteria**

1. Patients with age > 55 years with osteoporosis;
2. Women, post-menopausal for > 10 years;
3. Patients on drugs causing osteoporosis like steroid, phenytoin, aromatase inhibitors etc;
4. Known case of celiac disease.

Detailed medical history, drug history, physical examination, complete blood count, erythrocyte sedimentation rate, calcium profile, liver and renal biochemistry, 25-OH-D, Blood sugar were performed. Other investigations like RA factor, CRP, electrolytes, thyroid function tests and anti CCP were performed wherever indicated. Sera of all



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patients were tested for presence of IgA tissue transglutaminase (tTG) antibody by ELISA using commercially available kits. Antibody titer >50 units was considered positive. Three to four intestinal mucosal biopsies will be obtained with GI endoscopy from the second part of duodenum in patients with presence of tTG antibodies. Longitudinally oriented biopsies, with muscularis mucosa seen in section were only included. Biopsies will be reported by pathologist, who will blinded for tTG antibody report.Biopsies with lesion i.e. total or subtotal villous atrophy in addition to crypt hyperplesia and intraepithelial and lamina propria infiltration with mucosal cell, will be considered to be consistent with the diagnosis of CD.

BMD of all newly diagnosed patients of celiac disease will be done with Pronosco X-posure V.2 based on DXR. BMD estimate is obtained through a combined computerized radiogrammetric analysis and textural analysis of a digitised radiograph of the hand. . Hand bone density will be measured on the plain radiographs of the hand using digital x-ray radiogrammetry (Pronosco Xposure System 2.0) a computerized version of the traditional technique of radiogrammetry. A standard x ray image of the hand is scanned by an x ray scanner into a PC.In order to estimate the BMD value, the digitized image is analysed via PRONOSCO SOFTWARE. mean surrogate bone density value will be calculated from cortical thickness from regions of interest measured at the center of the second, third, and fourth metacarpals. This surrogate bone density measurement (expressed as grams per square centimeter) is based on measurement of the outer and inner diameter, measuring combined cortical thickness Information from the middle three metacarpals is used by system to generate a BMD estimate. This is referred to as digital X-ray radiogrammetry BMD (DXR-BMD). The Pronosco X-posure which will be used in study will provides results for patients with age between 21 to 80 years only.The ethical committee of our hospital approved the protocol and informed consent will be obtained from all patients.

**Results**

In present study, out of total 87 patients, 46(52.87%) were from serum TTG group 50-200 and 41(47.12%) from serum TTG group >200. Out of total 87 patients 54(62.06%) were females and 33(37.93%) were males and out of 54 females 30 were from serum TTG group 50-200 and 24 were from serum TTG group >200, while out of total 33 males 16 were from serum TTG group 50-200 and 17 were from serum TTG group >200.

In our study, most common presenting complaint of patients was weakness which was found in 80(92%) of patients. Second most common complaint was easy fatiguability in 69(79.3%) of patients, diarrhoea was present in 28(32.25) patients, weight loss was present in 17(19.5%) patients, sensory loss was present in 8(9.2%) patients and malena was present in 7(8.0%) patients. ( Table I )In our study, severe anemia (Hb <7gm%) was found in 40(46.0%) patients. MCV <70 was found in 24 (27.6%) patients MCV >100 was found in 10(11.5%) patients. In PBF, most common type of anemia was microcytic found in 33(37.95) patients while 29(33.3%) patients having normocytic, 17(19.5%) patients having macrocytic and 8(9.2%) patients having dimorphic anemia.

In our study, out of 87 total patients (54 females and 33 males) 67 patients had their BMD within normal range while 20 patients had osteopenia and they all were from serum TTG group >200 so the



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difference was statistically highly significant (p<0.001).(Table II)In present study out of total 87 patients, 2 patients had their TSH <0.270 and both were from serum TTG group 50-200 while 71 patients had their TSH between 0.270-4.20 and out of them 32 and 39 were from serum TTG group 50-200 and >200 respectively while remaining 14 patients had their TSH >4.2 and out of them 12 and 2 patients were from serum TTG group 50-200 and >200 respectively and the difference was also statistically significant (p<0.01). (Table III)Out of total 87 patients, 62 patients had their fasting blood sugar within normal range, while 15 patients were found in impaired glucose tolerance and out of them 11 and 4 were from serum TTG group 50-200 and >200 respectively. Only 10 patients had their fasting blood sugar >125 and out of them 9 and 1 were from serum TTG group 50-200 and >200 respectively and the difference was found significant (p<0.01). (Table IV)

**Table 1: Distribution of cases according to serum tTG in relation to presenting complaints**

| Presenting Complaints | | Serum tTG Group | | | | Total | | $\chi^2$ | P |
|---|---|---|---|---|---|---|---|---|---|
| | | 50-200 | | >200 | | | | | |
| | | No. | % | No. | % | No. | % | | |
| Diarrhoea | No | 28 | 60.9 | 31 | 75.6 | 59 | 67.8 | 2.158 | 0.142 |
| | Yes | 18 | 39.1 | 10 | 24.4 | 28 | 32.2 | | |
| Weight Loss | No | 41 | 89.1 | 29 | 70.7 | 70 | 80.5 | 4.668 | 0.029 |
| | Yes | 5 | 10.9 | 12 | 29.3 | 17 | 19.5 | | |
| Weakness | No | 7 | 15.2 | 0 | - | 7 | 8.0 | 6.785 | 0.009 |
| | Yes | 39 | 84.8 | 41 | 100.0 | 80 | 92.0 | | |
| Sensory Loss | No | 46 | 100 | 33 | 80.5 | 79 | 90.8 | 9.885 | 0.002 |
| | Yes | 0 | - | 8 | 19.5 | 8 | 9.2 | | |
| Fatigue | No | 8 | 17.4 | 10 | 24.4 | 18 | 20.7 | 0.647 | 0.295 |
| | Yes | 38 | 82.6 | 31 | 75.6 | 69 | 79.3 | | |
| Melena | No | 46 | 100 | 31 | 75.6 | 77 | 88.5 | 12.677 | 0.002 |
| | Yes | 0 | - | 7 | 17.1 | 7 | 8.0 | | |

**Table 2: Distribution of cases according to serum tTG in relation to Bone Mineral Density**

| BMD | Serum tTG group | | | | Total | |
|---|---|---|---|---|---|---|
| | 50-200 | | >200 | | | |
| | No. | % | No. | % | No. | % |
| Normal | 46 | 100 | 21 | 51.2 | 67 | 77.0 |
| Osteopenia | 0 | - | 20 | 48.8 | 20 | 23.0 |
| Total | 46 | 100 | 41 | 100 | 87 | 100 |
| $\chi^2$ | 29.137 | | | | | |
| P | <0.001 | | | | | |



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**Table 3: Distribution of cases according to serum tTG in relation to TSH Group**

| TSH Group | Serum tTG group | | | | Total | |
|---|---|---|---|---|---|---|
| | 50-200 | | >200 | | | |
| | No. | % | No. | % | No. | % |
| <0.270 | 2 | 2.3 | 0 | - | 2 | 2.3 |
| 0.270-4.2 | 32 | 36.8 | 39 | 44.8 | 71 | 81.6 |
| >4.2 | 12 | 13.8 | 2 | 2.3 | 14 | 16.1 |
| Total | 46 | 100 | 41 | 100 | 87 | 100 |
| $\chi^2$ | 9.577 | | | | | |
| P | 0.008 | | | | | |

**Table 4: Distribution of cases according to serum tTG in relation to Fasting Blood Sugar**

| FBS Group | Serum tTG group | | | | Total | |
|---|---|---|---|---|---|---|
| | 50-200 | | >200 | | | |
| | No. | % | No. | % | No. | % |
| <100 | 26 | 29.9 | 36 | 41.4 | 62 | 71.3 |
| 100-125 | 11 | 12.6 | 4 | 4.6 | 15 | 17.2 |
| >125 | 9 | 10.3 | 1 | 1.1 | 10 | 11.5 |
| Total | 46 | 100 | 41 | 100 | 87 | 100 |
| $\chi^2$ | 11.029 | | | | | |
| P | 0.004 | | | | | |

**Discussion**

In our study, most common presenting complaint of patients was weakness which was found in 80(92%) of patients. Second most common complaint was easy fatiguability in 69(79.3%) of patients, diarrhoea was present in 28(32.25) patients, weight loss was present in 17(19.5%) patients, sensory loss was present in 8(9.2%) patients and malena was present in 7(8.0%) patients.Scharla[7] in the year 2003 studied a case of 60 year old woman, she reported loss of weight, non specific GI symptoms and weakness.

Jones et al[8] in year 2006 studied that in recent years, there had been increasing recognition that the pattern of presentation of celiac disease may be changing. The classic sprue syndrome with diarrhoea and weight loss may be less common than the more subtle presentation of celiac disease such as anaemia.In present study, severe anemia (Hb <7gm%) was found in 40 (46.0%) patients. MCV <70 was found in 24 (27.6%) patients MCV >100 was found in 10 (11.5%) patients. In PBF, most common type of anemia was microcytic found in 33 (37.95) patients while 29 (33.3%) patients having normocytic, 17(19.5%) patients having macrocytic and 8(9.2%) patients having dimorphic anemia. In present study, out of 87 total patients (54 females and 33 males) 66 patients had their BMD within normal range while 20 patients had osteopenia and they all were from serum TTG group >200 so the difference was statistically highly significant ($p<0.001$).McFarlane et al[9] studied 45 women and 10 men with celiac disease diagnosed in adult life, who were already on a gluten free diet, had serial bone mineral density measurements at the lumbar spine and femoral neck over 12 months. Osteoporosis, defined as a bone mineral density (BMD) $\leq$2SD below the normal peak bone mass was found in 50% of male and 47% of female celiac patients.

In the year 2000, Vasquez et al[10] studied osteopenia and osteoporosis are well-recognized complications of celiac disease. They observed that among celiacs, 41 patients (25%) referred have had



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from one to five fractures in the peripheral skeleton. On the contrary, only 14 (8%) control subjects experienced fractures. This difference was highly significant. Meyer et al[11] studied that osteoporosis, common in adults with celiac disease. They observed that osteoporosis (T score ≤ -2.5) was present in 34% of patients at lumbosacral spine, 27% at the femoral neck and 36 at the radius. So that they observed that routine screening for osteoporosis is indicated in patients with celiac disease.Stenson et al[12] in 2005 studied that there is increased prevalence of osteoporosis amongst patients with celiac disease. They concluded that the prevalence of celiac disease among osteoporotic individual 3.4% is much higher than that among non osteoporotic individuals (0.2%).Krzesiek and Iwanczak[13] studied to analyze BMD in children with celiac disease. They observed that the disturbances of BMD were observed in 15 out of 37 children with diagnosed celiac disease amounted 40.5%. Early screening of BMD was advised in children with celiac disease by this study.In present study out of total 87 patients, 2 patients had their TSH <0.270 and both were from serum TTG group 50-200 while 71 patients had their TSH between 0.270-4.20 and out of them 32 and 39 were from serum TTG group 50-200 and >200 respectively while remaining 14 patients had their TSH >4.2 and out of them 12 and 2 patients were from serum TTG group 50-200 and >200 respectively and the difference was also statistically significant (p<0.01).Out of total 87 patients, 62 patients had their fasting blood sugar within normal range, while 15 patients were found in impaired glucose tolerance and out of them 11 and 4 were from serum TTG group 50-200 and >200 respectively. Only 10 patients had their fasting blood sugar >125 and out of them 9 and 1 were from serum TTG group 50-200 and >200 respectively and the difference was found significant (p<0.01).Mehardad et al[14] in the year 2012 described that celiac disease (CD) is closely associated with other autoimmune endocrine disorders, particularly autoimmune thyroid disease. The aim of this study was to find the frequency of celiac disease in patients with hypothyroidism in Guilan province, north of Iran. A total of 454 consecutive patients with hypothyroidism underwent celiac serological tests Anti Gliadin Antibodies (AGA), antitissue transglutaminase antibodies (IgA-tTG) and antiendomysial antibodies (EMA-IgA). Small intestinal biopsy was performed when any of celiac serological tests was positive. Eleven (2.4%) patients were positive for celiac serology, and two patients with documented villous atrophy were diagnosed with classic CD (0.4%; 95%). Two patients with classic CD had Hashimoto's thyroiditis (HT) (0.6%; 95%). Six (54.5%) of 11 were suffering from overt hypothyroidism and 45.5% from subclinical hypothyroidism. Six (54.5%) had HT, and 45.5% had non autoimmune hypothyroidism.

In the year 2002, Collin et al[15] described that celiac disease is a permanent intolerance to dietary gluten. The risk of clinically silent celiac disease is increased in various autoimmune conditions. The endocrinologist, especially, should maintain high suspicion and alertness to celiac disease, which is to be found in 2–5% of patients with insulin-dependent diabetes mellitus or autoimmune thyroid disease. Patients with multiple endocrine disorders, Addison's disease, alopecia, or hypophysitis may also have concomitant celiac disease.

**Conclusion**

1. Celiac disease is a systemic autoimmune syndrome involving a gluten induced chronic inflammation of small bowel



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mucosa, with extensive short and long term negative health consequences if untreated including GI cancer.

2. Left untreated, people with celiac disease can develop further complications such as vitamin deficiencies, other auto immune disease, osteoporosis, thyroid disease and cancer.
3. Celiac disease is not age dependent and may become active at any age. It is often mis-diagnosed as IBS or stress.
4. In present study, weakness was present in 80(92%), easy fatiguability was present in 69(79.3%), diarrhoea was present in 28(32.2%) patients, weight loss was present in 17(19.5%), sensory loss was present in 8(9.2%), patients and melana was present in 7(8%) of patients.
5. In present study, severe anaemia (Hb <7.0gm%) was found in 40(465) patients of celiac disease at the time of diagnosis.
6. In present study microcytic anemia was found in 33(37.9%) patients, normocytic type of anemia was found in 29(33.3%) patients and macrocytic anemia was found in 17(19.5%) patients.
7. Association between patients of celiac disease and osteopenia was highly significant ($p<0.001$) as out of total 41 patients (TTG group >200) 20(48.78%) patients had osteopenia on BMD.
8. In present study, impaired glucose tolerance was found in 15 patients, out of them 11 and 4 were from serum TTG group 50-200 and >200 respectively and 10 patients had their fasting blood sugar >125 and out of them 9 and 1 were from serum TTG group 50-200 and >200 respectively and the difference was found significant ($p<0.01$).
9. In present study, 2 patients had their TSH <0.270 and 14 patients had their TSH level >4.2 (hypothyroidism required treatment).
10. Screening for celiac disease with serological testing is non invasive and should be considered in Indian patients with suggestive symptoms or refractory anemia or associated autoimmune conditions.

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