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TO STUDY THE BONE MINERAL DENSITY IN NEWLY DIAGNOSED CHILDREN OF CELIAC DISEASE.

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ABSTRACT

Objective: To study the bone mineral density in newly diagnosed children of celiac disease. **Material and Method:** Osteoporosis is a common finding in adult celiac disease patients; however, there are still few data regarding children and adolescents. In the present study we measured the bone mineral density (BMD) in children and adolescents at diagnosis of celiac dis-ease. Study sample consist of thirty seven newly diagnosed pediatric patients 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 blood sugar, electrolytes and thyroid function tests were studied. Sera of all patients were tested for presence of IgA tissue transglutaminase (TTG) antibody by ELISA using commercially available kits and confirmed by UGI guided endoscopic biopsy. BMD of all these newly diagnosed patients of celiac disease was done with DXR and compared with age match appropriate control. **Results:** Lumbar spine and whole-body BMD values at diagnosis of celiac disease were significantly lower than in control subjects ($P = 0.013$ and $P = 0.0001$, respectively) after differences in age and anthropomorphic variables were con-trolled for. **Conclusion:** These results emphasize the need for an early diagnosis and treatment in patients with celiac disease to obtain an adequate peak bone mass appropriate for age.

KEYWORDS: Bone Mineral Density, Celiac Disease, Osteopenia.

INTRODUCTION

Bone density increases during childhood and adolescence to reach a peak value at the end of puberty[1-5]; it remains stable for some years and then decreases thereafter.[6-8] Besides race and heredity, multiple environmental and lifestyle factors con-tribute to the acquisition of peak bone mass. Among these, nutri-tional adequacy plays a crucial role; in particular, an ample cal-cium intake contributes to proper mineralization of bones.[9-11] Derangements of normal bone mineralization result in low bone density and consequently in increased bone fragility.

Celiac disease is a common cause of malabsorption in infancy and childhood. Loss of villous cells in the proximal intestine appears to be the cause of impaired absorption of nutrients. Particu-larly, decreased absorption of calcium results from both the loss of intestinal cells and the binding of calcium to unabsorbed fatty acids in the intestinal lumen.[12, 13] Adherence to a gluten-free diet reverses the histologic changes in the intestine and also the bio-chemical evidence of calcium malabsorption. Most studies on bone density of celiac disease patients have been performed in adults, and data on the effect of the disease on bone mineralization in children and adolescents are very scarce. A previous report did not show decreased forearm bone mineral content in children with celiac dis-ease diagnosed after the age of 3 y.[14] A more recent study, by contrast, showed that bone mineral content of the forearm was greatly reduced in young celiac disease patients.[15] A gluten-free diet has been shown to improve forearm bone mineralization after 1 y of dietary treatment[15] and to completely restore forearm bone mineral content in adolescents with celiac disease treated from childhood.[16] No data on bone mineralization of the axial or entire skeleton are currently available.

The prevalence of celiac disease is higher in type 1 diabetic patients than in the general population.[17–21] and several studies showed that reduced bone mineral density (BMD) is a frequent find-ing in type 1 diabetes.[22–27] The effect of the combination of the two diseases on bone mineralization has not been studied extensively.

BMD is easily assessed by dual-energy X-ray absorptiometry, which is an accurate method of obtaining measurements at different skeletal sites and of the whole skeleton. In the present study we measured bone density of the lumbar spine and of the whole skeleton in children at diagnosis of celiac disease. To study the influence of the coexistence of type 1 diabetes and celiac disease on bone density, we also compared the BMD values of diabetic patients with celiac disease and

those of patients with celiac disease alone.

SUBJECTS AND METHODS

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

INCLUSION CRITERIA

All children and adolescents, newly diagnosed as having celiac disease with diagnosis made by following the recommendations of the European Society of Paediatric Gastroenterology and Nutrition.[28]

EXCLUSION CRITERIA

Subjects who had been immobilized or hospitalized in the preceding 6 mo,
Those, who were taking medications known to affect bone metabolism,
Who had any chronic illness other than type 1 diabetes
Who had one or more nontraumatic fractures were excluded.

Thirty-seven celiac disease patients were eligible for the study. Their ages ranged from 3.58 to 17.42 y. Seven patients had type 1 diabetes. The characteristics of the patients are summarized in

Table 1. Bone density was measured at diagnosis and before any treatment for celiac disease.

As a control group we measured the BMD of 37 healthy, volunteers aged 3.52–17.22 y. All subjects were in good health and appropriately physically active for their age; none was involved in competitive sports activities. Their weights and heights were within the third and 97th percentiles for age. Candidates were excluded if they had a history of chronic illness, if they had one or more fractures, and if they had taken any medication, hormone, vitamin preparation, or calcium supplement regularly. Informed consent was obtained from all the parents of the patients and volunteers.

Bone mineral measurements

BMD measurements were made with a dual-energy X-ray absorptiometer (DPX-L; Lunar Radiation Corp,). The instrument was calibrated daily according to the manufac-turer's instructions. Reproducibility was calculated as a CV obtained by weekly measurements of a standard phantom on the instrument, and by repeated measurements of children of different ages. The CV of our instrument is 0.5% with the stan-dard phantom; in vivo we calculated a CV of 1.5% for the lumbar spine and 1.5% for the whole skeleton. BMD was measured at the L2–L4 vertebrae level and in the whole skeleton as described pre-viously . The data were analyzed with a pediatric soft-ware program (version 1.5e; Lunar Radiation Corp). The effective radiation dose for each scan was <1 mSv for the lumbar spine and < 4 mSv for the whole-body scans.

BMD values are calculated by dividing the quantity of bone mineral within the scan area by the projected area within the region of interest and are given as g/cm^2. Because BMD values may be influenced by the size of the bones, we used a new variable referred to as bone mineral apparent density (BMAD, expressed as g/cm^3). The BMAD at each site was calculated as described previously by using the following formulas: spine BMAD = BMD/$A^{1/2}$ and whole-body BMAD = BMC/[A^2/ h], where A is the projected area of the bone and h is the height of the subject.

Statistics

Multiple regression analyses were used to compare the BMD and BMAD values of celiac disease and control subjects after confounding variables were controlled for. BMD and BMAD were the dependent variables. Sex, age, weight, height, and projected area were the confounding variables, and presence of celiac disease was the independent variable. Similar models were used to compare the bone density indexes of patients with celiac disease alone and patients with celiac disease and diabetes.

All significance tests were conducted at the = 0.05 level. Data are expressed as x ± SEM. The computer software program STATVIEW SE+ (Abacus Concepts) was used for the analyses.

RESULT

Mean lumbar spine BMD of all celiac disease patients at diag-nosis was 0.604 ± 0.038 g/cm ^{2}, and mean BMAD was 0.135 ± 0.004 g/cm^3. BMD was 0.040 ± 0.013 g/cm ^{2} and BMAD was 0.007 ± 0.003 g/cm ^{3} lower in celiac disease patients than in control subjects after confounding variables were controlled for. The differences were highly significant (P = 0.013 and P = 0.0066, respectively). Lumbar spine BMD and BMAD values of patients with celiac disease alone were 0.555 ± 0.034 g/cm ^{2} and 0.128 ± 0.004 g/cm^3, respectively. The differences of BMD (20.017 ± 0.034 g/cm^2) and BMAD (20.0002 ± 0.0005 g/cm ^{3}) between patients with celiac disease alone and patients with celiac dis-ease and diabetes were not significant. The mean whole-body BMD value of all celiac disease patients at diagnosis was 0.875 ± 0.020 g/cm ^{2}. The values were signify cantly lower than those of control subjects (20.045 ± 0.012 g/cm ^{2}, P = 0.0001). Whole-body BMAD at diagnosis

was 0.094 ± 0.002 g/cm^3. The difference between the values of celiac disease patients and control subjects was significant (20.004 ± 0.0001 g/cm ^{3}, P = 0.04). Patients with celiac disease alone had a mean whole-body BMD value of 0.833 ± 0.022 g/cm ^{2}, whereas the mean BMAD was 0.096 ± 0.002 g/cm ^{3}. After the confounding variables were controlled for, the difference in whole-skeleton BMD between patients with celiac disease alone and patients with celiac disease and diabetes was 20.047 ± 0.027 g/cm ^{2} and not significant. Sim-ilarly, the difference in BMAD values between the two groups was not significant (0.0004 ± 0.0002 g/cm ^{3}).

TABLE: 1 Age, weight, and height of celiac disease patients at diagnosis

	Age *y*	**Weight** *kg*	**Age-adjusted weight**^{2} *%*	**Height** *cm*	**Age- justed height (SD)**^{3}
All (*n* = 37)	8.55± 0.58	22.4 ± 2.2	27.2± 2.6	117.9 ± 3.4	20.7± 0.2
Patients with celiac disease alone (*n* = 30)	866.± 0.67	24.4 ± 2.2	21.5± 3.0	117.4 ± 4.4	21.5± 3.0
Patients with celiac disease and diabetes (*n* = 7)	8.43± 1.3	29.1 ± 4.0	24.2 ± 2.3	118.5 ± 5.3	25.2 ± 2.3

DISCUSSION

The clinical features of celiac disease are extremely variable. The presentation can be overt, with diarrhea, weight loss, and generalized malnutrition, or subclinical, with isolated nutrient deficiencies but no gastrointestinal symptoms. Frequent complications of celiac disease include anemia, growth failure and reduced bone mineralization. Osteoporosis has been described as a frequent finding at diagnosis of celiac disease in adult patients regardless of clinical presentation.[13, 16,] The appen-dicular and the axial skeleton seem to be equally involved. Data on bone mineralization in children with celiac disease are scarce and still controversial. Although no alteration of forearm bone mineral content was observed in children older than 3 y with celiac disease.[14], a remarkable reduction of bone mineral con-tent of the forearm was reported in children with celiac disease at diagnosis.[15] In the present study we found significantly reduced bone density values at diagnosis of the disease in a group of children. The reduction was present both in the lumbar spine and in the whole skeleton. BMD values were obtained in the present study by using a bone absorptiometry technique. Absorptiometry is a projectional method and its measurements are based on two-dimensional projection of a three-dimensional structure. This process has been shown to lead to some size-dependent errors. Therefore, several correction methods have been proposed. Because short stature and low weight are clinically relevant features of celiac disease in children, even in patients with no gastrointestinal symptoms, we corrected the lumbar spine BMD values by the square root of the projected area of the vertebrae, on the assumption of the proportionality of the latter with the bone width. Furthermore, we corrected the whole-body BMD values by the height of the subject. The reduction of BMD was still present after the correction of BMD values, showing that reduced bone mineralization is not an artifact of differences in bone size. The prevalence of celiac disease is higher in type 1 diabetic patients than in the general population.[17–21] Furthermore, osteoporosis has been reported as a complication of diabetes mellitus.[22–27] Therefore, we expected to find lower BMD values in diabetic patients than in patients with celiac disease alone. Conversely, we found that the diabetic children with celiac disease had BMD and BMAD values comparable with those of patients with celiac disease alone.

The discrepancies observed may be explained by the physiologic changes of bone density occurring dur-ing a lifetime: bone density increases during childhood and adoles-cence until peak bone mass is reached (1, 2, 4, 5). Peak bone mass and subsequent bone loss are major determinants of osteoporosis during adulthood. Therefore, the achievement of an optimal peak bone mass during the first decades of life is of pivotal importance to minimize the risk of fracture later in life. In our study, we showed that bone mineral density was significantly reduced in children with celiac disease at time of diagnosis.

CONCLUSION

Our findings emphasize the need for early diagnosis of celiac disease, even in asymptomatic patients, to reverse osteopenia and to achieve normal mineralization.

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