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Original Article

Blood levels related to the Z-score of bone mineral density in young males and females

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Abstract. [Purpose] The purpose of this study was to investigate the blood levels related to the bone mineral density by using the dual energy X-ray absorption for females before menopause and males younger than 50 years old. [Subjects and Methods] Between August 1, and September 15, 2013, the Z-score was measured in females before menopause and males younger than 50 years old using a bone mineral density measuring instrument. After the measurement, the subjects were classified into two groups, that is, the below expectations and within expectations groups. Next, we analyzed and compared the differences in age, body mass index, and blood levels between the 2 groups. [Results] The results showed a correlation of 0.212 for total protein, −0.317 for alanine aminotransferase, −0.199 for gamma-glutamyl transferase, −0.358 for alkaline phosphatase, 0.266 for uric acid, −0.313 for lactate dehydrogenase, 0.244 for creatinine, −0.234 for the red blood cell count, and −0.230 for the red cell distribution width in patients with less than expected level for their age. [Conclusion] In conclusion, osteoporosis may occur in females before menopause and males younger than 50 years old, and aggressive attention is required for prevention and treatment.
Key words: Z-score, Blood levels, Bone mineral density

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INTRODUCTION

Bone mineral density has decreased and fracture risk has increased in conjunction with aging of the world population[1)]. Recently, it was reported that the morbidity rates of osteoporosis reached 10% (4.5 million) and that that for osteopenia reached 49% (22.7 million). Osteoporosis has shown high morbidity rates in the US and Europe, but the rates have recently increased in Asia and Africa also. In the Republic of Korea, the number of femur fracture cases has increased for women older than 50 years, as has the treatment costs[2–4)]. The quantitative bone mineral density measurement methods used in the Republic of Korea include dual energy radiation absorption, quantitative ultrasound, quantitative CT scan, and peripheral quantitative CT scan[5, 6)]. Among the methods, positive energy x-ray absorption (DXA) is the most widely known. Interpretation of bone mineral density is based on the normal average values for age, gender, and race. The T-value is defined as (the measurement of the patient-average value of a young group) / standard deviation, and the Z-value is defined as (the measurement of the patient-average value in the same age group) / standard deviation[7–9)]. The bone densities of the terminal bones including the forearm and the calcaneus or ultrasonic measurement of the terminal bones well reflect the risk of the fracture but show a low rate of precision compared with bone mineral density measurement of the lumbar spine and femur (DXA). Improvement of the precision is required to use these methods for monitoring changes in bone density. The Z-value not the T-value, is used for children, adolescents, females before menopause, and males younger than 50 years old. The level is considered to be below the expected range if the Z-value is less than −2.0. Most studies related to bone mineral density focus on females, females after menopause, or the old, and there are just a handful of studies which cover young adults. The purpose of the present study was to investigate the blood levels related to bone mineral density by using dual energy X-ray absorption (DXA) for females before menopause and males younger than 50 years old.

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SUBJECTS AND METHODS

This study investigated the correlation of body and blood measurements with bone mineral density for subjects receiving medical checkups. The Z-score was applied on a random basis for the males younger than 50 years old and the females before menopause to those who performed a bone mineral density and blood test under diagnosis from August 1 to September 15, 2013. The total number of subjects was 104, with 62 males and 42 females assigned to two groups, that is, the below expectations and within expectation groups, in terms of age. The average age and height were 35.87±4.93 years and 174.67±4.80 cm for the male subjects. The average age and height were 34.28±5.45 years and 160.28±5.18 cm for the female subjects. All participants signed a written informed consent form approved by the Institutional Review Board at Soonchunhyang University Hospital. Bone mineral density was measured at the lumber spine (L1–L4), the major indicator of bone mineral density, using the DXA (Lunar Prodigy and Lunar Prodigy Advance). The average bone mineral density for L1 to L4 was used to improve the precision of the test, and the left femoral region was excluded due to poor test precision. Below expectation was defined as a lumbar Z-score of less than −2.0, and within expectation was defined as a lumbar Z-score larger than 2.0; this was, based on the classification of the International Society for Clinical Densitometry (ISCD). Height and weight were measured by an automatic measuring instrument during physical measurements, and BMI was calculated as weight (kg) / square of the height (m^2). The blood levels for the subjects were measured by performing blood and urine tests after fasting for at least 12 hours. The number of measured elements collected as research variables was 35 including the maximum blood pressure, minimum blood pressure, total protein, albumin, globulin, AG ratio, T/D, AST, ALT, GGT, ALT, uric acid, lactate dehydrogenase, cholesterol, neutral acid, blood glucose in fasting, amylase, urea nitrogen, creatinine, BUNCR ratio, iron, number of red blood corpuscles, hemoglobin, red blood corpuscle volume, average red blood corpuscle volume, average amount of the red blood corpuscle hemoglobin, average concentration of red blood corpuscle hemoglobin, red blood corpuscle size distribution (RDW), number of platelets, average platelet volume, platelet distribution coefficient, and percentages of, neutrophils, lymphocytes, monocytes, and eosinocytes. The features in the 2 groups, that is, the below and within expectation groups, were compared depending on the lumbar bone mineral density. First, the independent T-test was used to verify the difference in ages, BMI, and blood levels between the 2 groups. The subjects with a history of glycosuria were excluded from the blood sugar analysis. Then, a single variance analysis was performed to assess the factors with significant correlation. The statistical analysis was performed with the PASW Statistics software (ver. 18.0, SPSS Inc., Chicago, IL, USA), and the significance level was set at less than 0.05.

RESULTS

The total protein level was to 7.31±11.38 g/dl in the below expectations group and 11.38±15.90 g/dl in the within expectations group, meaning that the latter group showed a higher total protein level ($p<0.05$). The AST level was 24.25±16.81 u/L in the below expectations group and 11.38±15.90 u/L in the within expectations group, meaning that the latter group showed a lower AST level ($p<0.05$). The ALT level was 32.25±22.11 u/L in the below expectations group and 18.25±14.98 u/L in the within expectations group, meaning that the latter group showed a lower ALT level ($p<0.05$). The ALP level was 70.05±18.15 u/L in the below expectations group and 55.43±16.88 u/L for the within expectation, meaning that the latter group showed a lower ALP level ($p<0.05$). The uric acid level was measured 5.13±1.30 mg/dl in the below expectations group and 6.07±1.70 mg/dl in the within expectations group, meaning that the latter group showed a higher uric acid level ($p<0.05$). The LDH level was measured 191.50±30.26 u/L in the below expectations group and 171.37±23.87 u/L in the within expectations group, meaning that the latter group showed a lower LDH level ($p<0.05$). The creatinine level was 0.80±0.13 mg/dl in the below expectations group and 0.87±0.14 mg/dl in the within expectations group, meaning that the latter group showed a higher creatinine level ($p<0.05$) (Table 1). Then, the single variance analysis was performed to assess the factors with significant correlation. The related elements included total protein, AST, ALT, GGT, ALP, uric acid, LDH, creatinine, red blood cell count, and RDW ($p<0.05$). For the patients in the below expectations group, the correlation was 0.212 for total protein, −0.317 for AST, −0.307 for ALT, −0.199 for GGT, −0.358 for ALP, +0.266 for the urine acid, −0.313 for the LDH, +0.244 for creatinine, −0.234 for the red blood corpuscle count, and −0.230 for the RDW (Table 2).

DISCUSSION

Most of the studies related to bone mineral density focus on females, females after menopause, or the old, and there are just a handful of studies covering young adults[10–13]. The purpose of this study was to investigate the blood levels related to the bone mineral density by using dual energy X-ray absorptiometry (DXA) in males and females. The related elements included total protein, AST, ALT, GGT, ALP, uric acid, LDH, creatinine, red blood cell count, and RDW. The total protein level was higher in the patients in the below the expectations group. Protein is an important factor in forming and maintaining the maximum bone mass for skeletal health, and it is said that the protein insufficiency causes osteoporosis[14]. As a result, it was considered that bone mass would be higher with a higher protein level. The biochemical skeletal indicator is the product of the bone formation and absorption extricated into the circulation system of the human body, reflects the dynamic process of the bone metabolism and the bone formation indicators including the bone specific ALP and osteocalcine[14]. A study in the Republic of Korea showed a negative correlation between ALP and bone mineral density[15]. We found the same result in the present study. Creatinine and uric acid were low in the patients in the below expectations group. Kim et al.[16] reported that in their study, the group with the minimum lumbar bone mineral density showed low levels of uric acid

Table 1. Values of the below and within expectations groups

Division		Mean	Division		Mean
BMI (kg/m)[a]	≤ −2.0	36.01±62.59	FPG (mg/dl)[g]	≤ −2.0	90.61±8.04
	> −2.0	22.47±3.38		> −2.0	95.13±21.47
Total protein (g/dl)	≤ −2.0	7.31±0.42	Amylase (mg/dl)	≤ −2.0	53.97±18.18
	> −2.0	11.39±15.90		> −2.0	57.13±17.80
Albumin (g/dl)	≤ −2.0	4.41±0.24	Blood urea nitrogen (mg/dl)	≤ −2.0	13.08±3.41
	> −2.0	4.41±0.17		> −2.0	11.75±3.06
Globulin (g/dl)	≤ −2.0	2.90±0.37	Creatinine (mg/dl)	≤ −2.0	0.80±0.13
	> −2.0	2.93±0.31		> −2.0	0.88±0.14
Albumin/globulin ratio (%)	≤ −2.0	1.56±0.26	BUN/Cr ratio (%)[h]	≤ −2.0	15.01±3.56
	> −2.0	1.53±0.21		> −2.0	14.67±2.69
Total bilirubin (mg/dl)	≤ −2.0	1.34±2.18	Fe (mg/dl)	≤ −2.0	112.58±44.53
	> −2.0	1.00±0.47		> −2.0	124.75±48.09
AST (u/L)[b]	≤ −2.0	24.25±11.96	Red blood cell count (10^6 /um)	≤ −2.0	4.89±0.44
	> −2.0	16.81±5.21		> −2.0	4.65±0.53
ALT (u/L)[c]	≤ −2.0	32.25±22.11	Hemoglobin (g/dl)	≤ −2.0	14.58±1.71
	> −2.0	18.25±14.99		> −2.0	13.95±1.70
GGT (u/L)[d]	≤ −2.0	46.83±35.64	Hematocrit (%)	≤ −2.0	53.45±64.40
	> −2.0	30.88±38.94		> −2.0	40.97±4.12
ALP (u/L)[e]	≤ −2.0	70.06±18.16	MCV (fl)[i]	≤ −2.0	87.21±3.83
	> −2.0	55.44±16.89		> −2.0	88.26±3.42
Uric acid (mg/dl)	≤ −2.0	5.13±1.30	MCH (uug)[j]	≤ −2.0	29.74±1.82
	> −2.0	6.07±1.70		> −2.0	29.99±1.37
LDH (u/L)[f]	≤ −2.0	191.50±30.27	MCHC (%)[k]	≤ −2.0	34.10±1.13
	> −2.0	171.38±23.88		> −2.0	33.99±1.13
Cholesterol (mg/dl)	≤ −2.0	183.92±34.22	RDW (%)[l]	≤ −2.0	13.05±1.15
	> −2.0	190.88±36.12		> −2.0	12.54±0.42
Triglyceride (mg/dl)	≤ −2.0	133.67±102.10	Platelet count (10^3/um)	≤ −2.0	250.33±53.51
	> −2.0	109.88±79.88		> −2.0	244.63±59.69
MPV (fl)[m]	≤ −2.0	10.31±0.78	Lymphocyte (%)	≤ −2.0	35.33±8.06
	> −2.0	10.35±0.66		> −2.0	32.44±6.97
PDW (%)[n]	≤ −2.0	12.08±1.78	Monocyte (%)	≤ −2.0	7.06±1.68
	> −2.0	11.79±1.23		> −2.0	7.19±1.84
Number of white blood cells (10^3/um)	≤ −2.0	6.31±1.99	Eosinocyte (%)	≤ −2.0	3.11±3.73
	> −2.0	6.24±1.55		> −2.0	3.25±4.38
Neutrophil (%)	≤ −2.0	54.42±8.13			
	> −2.0	56.69±6.73			

[a]Body mass index, [b]Aspartate aminotransferase, [c]Alanine aminotransferase, [d]Gamma-glutamyl transferase, [e]Alkaline phosphatase, [f]Lactate dehydrogenase, [g]Fasting plasma glucose, [h]Blood urea nitrogen/creatinine ratio, [i]Mean corpuscular volume, [j]Mean corpuscular hemoglobin, [k]Mean corpuscular hemoglobin concentration, [l]Red cell distribution width, [m]Mean platelet volume, [n]Platelet distribution width

and creatine compared with the maximum density group, and the present study showed the same results. Uric acid is the most abundant antioxidant in the human body and plays a role in removing 2/3 of the free radicals in the plasma[17]. Maggio et al.[18] reported that antioxidant intake increased the bone mineral density and that the bone mineral density was low for those who had low antioxidant concentrations, including uric acid. In addition, it has been hypothesized that the uric acid level may be low in females after menopause compared with females near menopause and that this would work as a mechanism in the osteoporosis[17]. Given this, the uric acid concentration in the blood would not play a role in protection from bone losses related to aging if the concentration is too low, which raises the possibility of a decrease in bone mineral density[18]. The limitations in the study are as follows: First, it was a single-sided study, resulting in difficulties in proposing correlation of the bone mineral density with various factors. Second, the research subjects were limited to those from a single university hospital, and this may have caused selection bias in the subjects. Third, the study failed to perform the radiological imaging to precisely diagnose the degenerative bone changes when selecting

Table 2. Factors showing significant correlations with the below and within expectations groups

Division		
BMI (kg/m)	Pearson correlation coefficient	−0.244
	p	0.016
Total bilirubin (mg/dl)	Pearson correlation coefficient	−0.318
	p	0.001
ALP	Pearson correlation coefficient	0.429
	p	0.000
FPG (mg/dl)	Pearson correlation coefficient	−0.201
	p	0.047
Fe (mg/dl)	Pearson correlation coefficient	−0.211
	p	0.037
Neutrophil (%)	Pearson correlation coefficient	0.199
	p	0.049
Monocyte (%)	Pearson correlation coefficient	−0.205
	p	0.043
Eosinocyte (%)	Pearson correlation coefficient	−0.227
	p	0.024

the subjects and assessed them with images from the bone mineral density test, raising the possibility of not being able to completely rule out degenerative changes. In conclusion, osteoporosis is the most frequently found disease in older females mainly due to aging and menopause but may also be found in women before menopause and men younger than 50 years old. More aggressive attention is required for the prevention and treatment. Large-scale progressive studies seem to be required because the present study failed to clarify the direct cause of the bone mineral density losses.

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