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CLINICAL STUDY

Vitamin D status, bone metabolism and bone mass in patients with alcoholic liver cirrhosis

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Abstract: *Introduction:* Osteoporosis is seen in some 12–50 % patients with liver cirrhosis. Detrimental effects of alcohol are exerted directly on the bone cells and indirectly on hormones. Vitamin D is involved in osteoblast differentiation, bone matrix synthesis and bone mineralization, as well as in its decomposition. Vitamin D deficiency has been reported in about 2/3 patients with liver cirrhosis.
Objective: Determination of vitamin D status, bone metabolic activity and bone mass in patients with alcoholic liver cirrhosis (ALC).
Methods: Thirty male patients with ALC were investigated in the period October 2011– March 2012. Total vitamin D, parathormone, osteocalcin and CrossLaps were determined by the ECLIA method (*electrochemiluminiscence immunoassay*) using Elecsys 2010 analyzer. Bone mineral density was measured by means of dual-energy *x*-ray absorptiometry (DXA) using the Lunar Prodigy. Result analysis was performed using descriptive statistics and hypothesis testing, as well as nonparametric one-way analysis of variance, Kruskal-Wallis test, Mann-Whitney U-test, Pearson correlation coefficient.
Results: Deficiency in vitamin D (< 50 nmol/l) was noted in 66.66 % patients, with highest prevalence in Child-Pugh C class patients (chi-square = 5.878, $p < 0.05$). Osteocalcin levels were below the lower limit of normal in 86.7 % patients. CrossLaps was increased in only 20 % patients, but a significant increase was noted in Child-Pugh C class patients. Osteoporosis was diagnosed in 20 % of patients, with no correlation with disease severity and vitamin D status.
Conclusions: Vitamin D deficiency is present in patients with ALC. Decrease in bone formation and bone mass is most probably multicausal *(Tab. 2, Fig. 1, Ref. 30)*. Text in PDF *www.elis.sk.*
Key words: alcoholic liver cirrhosis, vitamin D, bone metabolism, bone mass.

Hepatic osteodystrophy includes metabolic bone diseases associated with chronic liver disease. Osteoporosis is usually dominant in patients with underlying chronic liver disease, occurring in some12–50 % of patients with liver cirrhosis (1, 2).

Osteoporosis results from an imbalance between bone formation and bone resorption causing reduction in bone mass (3–5). Assessment of bone metabolic activity is performed by laboratory analysis of blood and urine and by evaluating the markers for bone formation and resorption (6, 7).

Reduction in bone mass in patients with liver disease is determined by the aetiology, duration and severity of the disease as well as by numerous factors such as age, sex, genetic and immunological factors, dietary deficit and malnutrition, insufficient movement, hypogonadism, administration of corticosteroids and antiviral therapy, low calcium and vitamin D intake, impaired vitamin D metabolism in the liver, accumulation of iron and copper in the liver, cholestasis, loss of liver synthetic function etc. (8). The most abundant research was performed in the field of chronic cholestatic liver diseases and conditions pre and post liver transplantation, whereas viral hepatitis, haemochromatosis and alcohol liver disease were addressed more rarely.

Osteoporosis is diagnosed in 17–23 % patients with alcoholic liver disease. Alcohol directly affects bone cells, whereas the normal hormone balance and hormones that regulate mineral status, and foremostly the vitamin D are affected indirectly (9–11).

Vitamin D deficiency is reported in 2/3 of patients with liver cirrhosis, in 90–96 % patients waiting for a liver transplant and in 91–92 % patients with chronic non-cholestatic liver disease (12–16).

The spectrum of vitamin D actions includes genomic effects via vitamin D receptor (VDR) present in the cytoplasm, i.e. cell nucleus, and non-genomic effects via the membrane receptors and second messengers. Vitamin D carries out the vital biological functions affecting numerous health aspects (17–21).

Vitamin D interacts with vitamin D receptor (VDR) in osteoblasts regulating the gene expression which positively affects their differentiation, bone matrix formation and bone mineralization. Vitamin D supports RANKL (*receptor activator of NF kappa beta ligand*)-mediated osteoclastogenesis, and stimulates RANK (*receptor activator of NF kappa beta*) and osteoprotegerin (OPG)

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production. Produced multinuclear osteoclasts dissolve bone mineral substance and bone matrix (18, 19, 22).

Osteoblast dysfunction may play an important role in the pathogenesis of metabolic bone diseases associated with chronic liver disease, which can partly be attributed to disorders of vitamin D metabolism (19, 23).

The objective of this research was to investigate vitamin D status, bone metabolic activity and bone mass in patients with alcoholic liver cirrhosis (ALC).

Methods

The research encompassed 30 male patients with alcoholic liver cirrhosis, who were treated at the Clinic for Gastroenterology and Hepatology in Novi Sad or in outpatient facilities in the period October 2011 – March 2012. The severity of the disease was graded according to the Child-Pugh classification (24).

Quantification of vitamin D (total) was performed by ECLIA method *(electrochemiluminiscence immunoassay)* on automated analyzer *Elecsys 2010*, using the commercial kits manufactured by *COBAS-Roche Diagnostics*.

Vitamin D status is defined as its serum concentration described as adequacy (> 80 nmol/l) and inadequacy (< 80 nmo/l). Different degrees of vitamin D inadequacy are classified as follows: insufficiency (50–79 nmol/l), deficiency (< 50 nmol/l), mild deficiency (25–50 nmol/l), moderate deficiency (12.5–24 nmol/l), severe deficiency (< 12.5 nmol/l) (13, 16).

Quantification of parathormone (PTH), osteocalcin - bone synthesis marker and CrossLaps *(Cross-linking telopeptide of type 1 collagen)* -bone resorption marker, was performed by the same method.

The analyzer *Architect c8000* (manufacturer: *Abbott*) and original reagents from the same manufacturer were used for determining serum concentrations of alkaline phosphatase (ALP), total bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transpeptidase (GGT), urea and creatinine, albumin, total proteins, calcium (Ca), magnesium (Mg), phosphorus (P), potassium (K), sodium (Na), chlorine (Cl), and glycaemia.

Ionized calcium concentration was quantified using *iLyte* analyzer by the indirect method of ion-selective electrode.

The 24-hour urinary calcium excretion was not done because of secondary hyperaldosteronismus in these patients, and due to the use of furosemid medications in some cases.

Quantification of sex hormones was performed via the immunometric assay, i.e. chemiluminescent microparticle immunoassay (*CMIA*), whereas IGF-1concentration was determined by an enzyme immunoassay (EIA).

Prothrombin time *(*PT*)* was measured on an automated coagulometer *ACL9000* (manufacturer: Instrumentation laboratory) using original reagent kit from the same manufacturer. The INR (International Normalised Ratio) corresponds with the obtained ratio (R) of PT, while considering an International Sensitivity Index = 1 assigned to *ACL9000*.

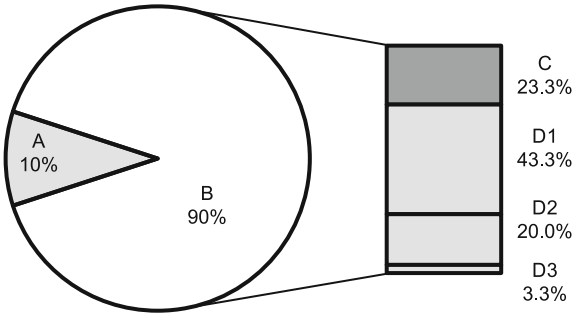
Bone mineral density (BMD) was assessed by the method of dual X-ray absorptiometry (DXA) using Lunar Prodigy bone densitometer. Results were interpreted in g/cm^2. In patients under the age of 50, osteoporosis was defined also on the basis of Z-score (≤ 2 SD), and in patients older then 50 according to T-score (≤ 2.5 SD) (2, 4, 5).

The research was approved by the Ethics Committee of the Institution, Decision No 00-01/559, and the written informed

Tab. 1. Clinical features, bone metabolism and bone mass parameters in patients with ALC (whole group and categorization of patients according to Child–Pugh classification).

	Patients with ALC (n=30)				Child A (n=13)	Child B (n=9)	Child C (n=8)	difference Child A, B, C
	$\bar{x}$	SD	Min	Max	$\bar{x}$	$\bar{x}$	$\bar{x}$	
Age	59.10	5.91	48.3	70.0	57.69	60.06	60.33	NS
Duration of ALC (years)	5.20	5.20	0	20.0	6.31	5.33	3.25	NS
Duration of alcohol intake (years)	22.30	10.26	10	48	21.08	19.67	27.25	NS
Amount of alcohol taken g/day	162.33	108.46	80	440	132.31	205.56	162.50	NS
Abstinence (years)	2.30	3.22	0	14	3.00	1.89	1.63	NS
Vitamin D 30–150 nmol/l	44.80	27.50	8	113	56.54	42.11	28.75	p<0.05
Osteocalcin 21–41 ng/ml	13.48	6.48	3.4	27.1	14.48	12.99	12.44	NS
CrossLaps 160–504 pg/ml	437.4	358.01	72	1679	262.8	396.3	767.5	p<0.05
Parathormone 15–65 pg/ml	42.01	14.20	20.9	84.3	45.90	38.60	39.54	NS
Ionized Ca 0.85–1.20 mmol/l	1.02	0.06	0.96	1.10	1.02	1.00	1.04	NS
Phosphorus 0.81–1.45 mmol/l	1.02	0.18	0.71	1.34	1.05	1.08	0.91	NS
Magnesium 0.73–1.06 mmol/l	0.78	0.10	0.58	1.04	0.80	0.78	0.73	NS
BMD L1–L4 (g/cm^2)	1.135	0.212	0.743	1.559	1.175	1.131	1.074	NS
BMD femur neck (g/cm^2)	0.971	0.167	0.728	1.300	0.907	1.033	1.005	NS
Total hip BMD (g/cm^2)	1.041	0.157	0.810	1.400	0.987	1.088	1.077	NS
IGF-135–210 mg/l	29.78	16.20	12	64	39.00	25.22	19.94	NS
Testosterone 5.76–28.14 nmol/l	13.29	11.00	1.79	46.36	18.80	13.65	3.96	p<0.01
Estradiol 11.0–44.0 pg/ml	79.07	54.55	25	227	41.54	87.02	131.13	p<0.01

NS – not significant



A - adequacy >80 nmol/l (3)
B - inadequacy <80 nmol/l (27)
C - insufficiency 50-79 nmol/l (7)
D - deficiency <50 nmol/l (20)
D1 - mild deficiency 25-49 nmol/l (13)
D2 - moderate deficiency 12.5-24 nmol/l (6)
D3 - severe deficiency <12.5 nmol/l (1)

Fig. 1. Adequacy of vitamin D in only three patients (10 %), inadequacy in 90 % (27/30) patients, while insufficiency and deficiency were observed in 23.33 % (7/30) and 66.66 % (20/30) patients, respectively. Mild deficiency in 43.33 % (13/30) patients, moderate in 20 % (6/30) and severe in 3.33 % (1/30) patients.

consent was obtained from all patients before they were included in the research.

The following statistical methods have been used in this research: Descriptive statistics: arithmetic mean, standard deviation; Statistical methods of hypothesis testing: methods comparing metric variables (t-test) and methods comparing categorical variables (χ^2 test), special, non parametric tests for ordinal variables. Significance level 95%, with marginal p value = 5 % (< 0.05) and 95 % Confidence Interval. Analysis of variance, single-factorial (one-way), nonparametric; Kruskal-Wallis test for evaluating difference significance in medians among three or more independent groups; Mann-Whitney U-test, nonparametric rank-sum test; Pearson correlation coefficient test.

Results

In patients with ALC, average values of vitamin D were 44.80 nmol/l, parathormone 42.01 pg/ml, osteokalcin 13.48 ng/ml, Crosslaps 437.4 pg/ml, ionized Ca 1.02 mmol/l, Mg 0.78 mmol/l, phosphorus 1.02 mmol/l.

Patients with Child-Pugh class C revealed the lowest serum concentration of vitamin D (28.75 nmol/l), highest CrossLaps values (767.5 pg/ml) and lowest serum-osteocalcin levels (12.44 ng/ml). Decrease in vitamin D values and osteocalcin level, and increase in CrossLaps value associated with the severity of the disease was apparent (Tab. 1).

Adequacy of vitamin D was observed in only three patients (10 %), inadequacy in 90 % (27/30) patients, while insufficiency and deficiency were observed in 23.33 % (7/30) and 66.66 % (20/30) patients, respectively. Mild deficiency was established in 43.33 % (13/30) patients, moderate in 20 % (6/30) and severe in 3.33 % (1/30) patients (Fig. 1).

Tab. 2. BMD in the investigated regions in ALC patients with and without osteoporosis and clinical characteristics and laboratory findings in both groups of patients.

	Patients with ALC n=30 (100 %)	Patients without osteoporosis, n=24 (80 %)				Patients with osteoporosis, n=6 (20 %)				p
	$\bar{x}$	$\bar{x}$	SD	Min	Max	$\bar{x}$	SD	Min	Max	
BMD L1–L4 (g/cm^2)	1.135	1.194	0.189	0.940	1.559	0.898	0.112	0.743	1.043	p<0.01
BMD femur neck (g/cm^2)	0.971	1.011	0.158	0.766	1.300	0.809	0.083	0.728	0.928	p<0.01
Total hip BMD (g/cm^2)	1.041	1.076	0.154	0.810	1.400	0.901	0.071	0.827	1.020	p<0.05
Age	59.10	59.15	5.109	49.9	65.9	58.90	9.073	48.3	70.0	NS
Duration of alc. liver cirrhosis	5.20	5.04	5.385	0	20	5.83	4.73	1	15	NS
Duration of alcohol intake – years	22.30	21.33	10.20	10	48	26.17	10.46	13	44	NS
Amount of alcohol taken g/day	162.33	145.42	96.86	80	440	230.0	134.9	120	400	p<0.05
Vitamin D (30–150 nmol/l)	44.80	48.96	29.23	8	113	28.17	6.43	17	34	NS
Osteocalcin (21–41 ng/ml)	13.48	12.67	5.983	3.4	26.6	16.77	7.92	6.8	27.1	NS
CrossLaps (160–504 pg/ml)	437.4	391.3	301.6	101	1679	622.0	523.2	72	1467	NS
Parathormone (15–65 pg/ml)	42.01	42.44	15.15	20.9	84.3	40.30	10.44	28.8	57.1	NS
Ionized Ca (0.85–1.20 mmol/l)	1.02	1.02	0.06	0.90	1.11	1.00	0.03	0.96	1.02	NS
Magnesium (0.73–1.06 mmol/l)	0.78	0.77	0.19	0.6	1.04	0.86	0.16	0.76	1.04	NS
Phosphorus (0.81–1.45 mmol/l)	1.02	1.03	0.19	0.71	1.34	0.99	0.16	0.72	1.14	NS
Bilirubin (mmol/l)	39.84	38.90	27.62	10	93	43.62	30.53	15	90	NS
Albumins (g/l)	32.12	32.92	7.56	22	47	29.08	6.76	20	37	NS
IGF-1 (35–210 mg/l)	29.78	29.42	15.41	13	64	20.67	20.67	12	64	NS
Testosterone (5.76–28.14 nmol/l)	13.29	14.95	11.48	2.10	46.36	6.68	5.55	1.79	14.37	NS
Estradiol (11.0–44.0 pg/ml)	79.07	70.18	46.69	25	227	114.7	73.03	30	225	NS
FSH (1.37–13.58 IU/l)	5.41	5.83	4.23	0.37	18.09	3.75	2.69	0.40	7.74	NS
LH (1.14–8.75 IU)	4.33	4.72	2.64	0.11	10.23	2.75	2.37	0.25	5.90	NS

NS – not significant

Increased PTH values were observed in only 7.4 % (2/27) of patients with vitamin D inadequacy D (< 80 nmol/l). One patient had vitamin D level of 75 nmol/l and PTH 70 pg/ml, whilst another patient revealed vitamin D concentration of 18 nmol/l, and PTH 84.3 pg/ml.

Statistically significant correlations between vitamin D and following parameters were not determined ($p > 0.05$): osteocalcin, CrossLaps, PTH, ionized Ca, phosphorus, Mg, bilirubin, INR, IGF-1, AST, ALT, ALP, thrombocyte, BMD L1-L4, BMD hip neck, total hip BMD.

Statistically significant correlations were determined between vitamin D and total calcium ($p < 0.01$), vitamin D and albumin ($p < 0.01$), and vitamin D and GGT ($p < 0.05$).

Out of the total number of 30 patients with ALC, 66.7 % (20/30) of patients had increased estradiol levels. Testosterone values were within the range of reference values in 60.0 % (18/30) patients, whereas 26.7 % (6/30) patients revealed decreased testosterone levels. In both hormones, highly statistically significant difference was established between patient groups with Child-Pugh classes A, B and C ($p < 0.01$). Normal levels of FSH (Follicle stimulating hormone) and LH (Luteinizing hormone) were determined in 83.3 % (25/30) and 86.7 % (26/30) of patients with ALC, respectively. Statistically significant decrease in gonadotropin levels was established that was proportional to the severity of the disease ($p < 0.05$). Average values of FSH, LH, estradiol and testosteron are given in Table 2.

Twenty-one patients (70 %) had IGF-1 (*insulin-like growth factor-1*) values below the lower limits of normal. Average value of IGF is given in Table 1.

Of the six patients with osteoporosis, 50% ($\bar{x} = 61.96$ years) had lowest BMD on femur neck with average BMD 0.738 g/cm^2. Another 50 % ($\bar{x} = 55.83$ years) had lowest BMD on L1–L4 region with average BMD 0.836 g/cm^2. Two of all were younger than 50 ($\bar{x} = 48.6$) with average Z-score –2.4 (BMD 0.853 g/cm^2) and four patients were older than 50 ($\bar{x} = 64$) with average T-score –3.175 (BMD 0.754 g/cm^2).

In patients with ALC and osteoporosis average values of ionized Ca were 1.00 mmol/l, Mg 0.86 mmol/l, phosphorus 0.99 mmol/l, parathormone 40.30 pg/ml, vitamin D 28.17 nmol/l, osteokalcin 16.77 ng/ml, Crosslaps 622 pg/ml (Tab. 2).

Average INR in these patients was 1.495, but in other patients INR was 2.085.

Two patients with osteoporosis were categorized into the Child–Pugh class A, one into class B and three patients into class C.

Statistically significant difference in vitamin D status and serum levels of bone metabolism markers between patients diagnosed with osteoporosis and those without the disease was not established, although the results clearly indicated an increase in CrossLaps and decrease in vitamin D level in patients with osteoporosis.

The only statistically significant difference between patients with and without osteoporosis was established with respect to the amount of daily alcohol intake (145.42 g/day: 230 g/day), $U = 32.500$, $p < 0.05$ (Tab. 2).

Discussion

Our research revealed a vitamin D inadequacy in 90 % of patients with alcoholic liver cirrhosis. Vitamin D insufficiency and deficiency was established in 23.3 % and 66.7 % of patients, respectively. Patients with Child–Pugh class C had the lowest serum vitamin D levels. A correlation was established between decreased vitamin D levels and gamma-glutamyl transpeptidase, which is a highly sensitive indicator of hepatobiliary disease, and albumin, which are indicators of liver function impairment.

In patients with vitamin D inadequacy (< 80 nmol/l), elevated PTH values were observed in only 7.4 % (2/27) of patients. One patient had vitamin D level of 75 nmol/l and PTH 70 pg/ml, whilst another patient had vitamin D concentration of 18 nmol/l, and PTH 84.3 pg/ml. Statistically significant correlation between vitamin D and ionized calcium, phosphorus and parathormone levels has not been established. Average serum levels of magnesium and phosphorus were within the reference range, which corresponds with the reports of other authors (12, 13, 15, 25). The condition of normal to low PTH levels in presence of insufficiency or severe deficiency in vitamin D, designated as a "vitamin D-PTH paradox", was described also by other authors. All evidence suggests that multiple mechanisms, other than the vitamin D-PTH axis, might be involved in bone resorption in decreased vitamin D level (10, 12, 13).

The obtained results based on the evaluation of bone metabolism markers revealed a decreased bone formation. Osteocalcin level was below the lower limits of normal in 86.7 % of patients. CrossLaps values were within the range of reference values in 66.7 % of patients, whilst increased and decreased levels were observed in 20 % and 13.3 % of patients, respectively. Correlation of vitamin D was observed with neither bone synthesis markers nor bone resorption markers, which was addressed by other authors (1, 22, 23). It was established that severity of liver cirrhosis correlates with statistically significant increase in marker of bone resorption CrossLaps without impairment of serum parathormone level and no changes in bone mass.

Osteocalcin level is decreased in persons who consume 60–100 g alcohol per day, which is due to inhibition of proliferation and activation of osteoblasts (10). The average daily alcohol intake in our patients was 162.33 g/day.

Alcoholic liver disease is characterized by an increase in TNF-α (*Tumour necrosis factor alpha*) level, a potent pro-inflammatory cytokine that increases bone resorption either directly by osteoclast stimulation or indirectly, via the RANKL – OPG – RANK system. Serum concentrations of TNF receptor I (TNF-R1) correlate with the severity of liver disease. These might be the explanation for significant increase in CrossLaps in our patients with Child-Pugh class C. Incidence of osteoporosis observed in these patients did not significantly differ from classes A and B, most probably (though statistically insignificant) because in patients with most severe form of cirrhosis the disease itself had a shorter course as compared with milder forms.

Impaired liver cells produce cytokines that interfere with activation of osteoblasts leading to reduced bone formation. In liver disease, the activated stellate cells produce glycolized isoform of

plasma fibronectin, so-called oncofetal fibronectin, which negatively correlates with osteocalcin (8).

Chronic inflammation downregulates the 1-alpha hydroxilase by NF-κβ (*nuclear factor-kappa beta*) transcription, which may result in inflammation-mediated osteopenia / osteoporosis (20).

TGF-ß (*transforming growth factor-ß*), a growth factor secreted by osteoblasts, plays a major role in bone metabolism and growth. Vitamin D stimulates the expression of TGF-ß from human osteoblasts, and also has effects on other growth factors and molecules associated with osteoblasts, namely interleukins (IL-1, IL-6), PDGF (*platelet degradation growth factor*), OPG, and RANKL (22).

Considering a strong immunomodulatory effects of vitamin D, its deficiency may result in increased bone resorption through cytokines: interleukin (IL-2, IL-4, IL-5, IL-12), interferon-γ (IFN-γ); independently of PTH (20).

Although the aforementioned has not been addressed in our study, it might theoretically support the facts observed in this research.

In the investigated patients, testosterone levels were within the limits of normal, but statistically significant lower values were obtained in patients with severe form of the disease. The same tendency was established for gonadotropine concentration, whilst estradiol levels progressively increased in parallel with disease severity. Thus, a relatively small number of patients with ALC diagnosed with osteoporosis could partly be explained by high estradiol levels.

IGF-1 values in the investigated patients were below the reference range. Low serum osteocalcin may be directly related with decreased IGF-1 levels in underlying liver cirrhosis (1, 26).

Our research revealed the presence of osteoporosis in 20 % (6/30) male patients with ALC. Difference in BMD decrease between patients with different degrees of cirrhosis severity was not statistically significant thus implying the necessity of early evaluation of bone mass. The obtained data are in accordance with the available literature (1, 2, 26–28).

Our research revealed no statistical significance for vitamin D insufficiency or deficiency related to BMD decrease at neither of measurement sites (lumbar spine, femur neck, total hip). Some authors reported that vitamin D contributed to low BMD in liver cirrhosis, as its deficiency associated with secondary hyperparathyroidism results in bone loss (predominantly cortical bone – hip). These authors consider vitamin D to be an independent predictor of BMD at cortical bone in patients with liver cirrhosis (12). This was not confirmed in our research. However, it was revealed that the lowest BMD measured in our patients with osteoporosis was that of the femoral neck (min 0.728 g/cm^2).

With respect to serum levels of bone metabolism markers, no statistical significant difference was established between patients diagnosed with osteoporosis and those without the disease. Evident decrease in osteocalcin level in patients with ALC, as well as increase in CrossLaps serum levels in patients with most severe disease strongly suggest an apparent impairment of bone metabolism in those patients, which could indicate potential loss of bone mass in the future.

Our research revealed that patients diagnosed with osteoporosis consumed higher daily amounts of alcohol than other patients did. Chakkalakal (29) reported that bone loss increases with the prolonged period of alcohol intake or with a higher abusus index. Other authors also pointed out the problem of excessive alcohol consumption as an independent risk factor for osteoporosis associated with 2.8-fold higher risk of hip fracture, as well as significance of inverse relationship between cumulative effects of alcohol intake and BMD. Alcohol decreases the level of vitamin D by dysregulating enzyme systems of its metabolism (1, 10, 11, 12, 26).

Since vitamin K mediates the carboxylation of glutamyl residues in bone protein such as osteocalcin, the vitamin K deficiency has been considered to be an ancillary factor in the pathogenesis of osteoporosis in liver disease (2).

In patients with ALC and osteoporosis, average INR was 1.495, but in other patients, INR was 2.085. Despite this, it is known that vitamin K may also play a role in osteoformation and osteoresorption. The mechanism by which vitamin K contributes to bone turnover is not clear. (30).

Our study has some limitations, mostly because of low number of patients and no control group included.

Conclusions

Considerable vitamin D deficiency is apparent in patients with alcoholic liver cirrhosis (ALC), which correlates with the disease severity categorized according to Child-Pugh classification.

Patients with ALC reveal reduced bone formation. In patients with ALC participating in this research, osteoporosis was diagnosed in 20 %, with no correlation with disease severity and vitamin D status.

The clinical implication of vitamin D insufficiency/deficiency in patients with ALC is not fully known. Considering the effects of vitamin D on bone and general health, and connection between its deficiency and severity of the liver disease, it is necessary to periodically determine the vitamin D status in these patients and perform supplementation.

Hence, evaluating the vitamin D status and markers of bone metabolism and bone mass is necessary at the moment of establishing the diagnosis of ALC. Strict abstinence of alcohol intake is necessary for preserving the bone mass. In the view of aforementioned as well as other well-established measures for preserving bone mass, a periodical monitoring of bone metabolism and bone mass is required.

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