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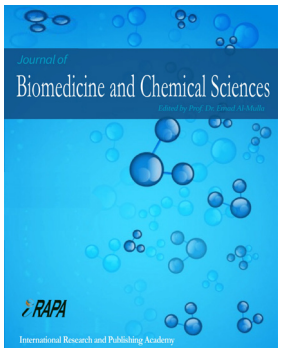

Effect of Vitamin D and Bone Density in Patients with Chronic Hepatitis C

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ABSTRACT

Hepatitis C virus (HBV) infection is a common health problem that has a worldwide distribution. Apart from the direct effect of the virus on the liver, there are many extrahepatic manifestations among which the probable effect on bone turnover associated with low bone mineral density (BMD) and deficiency of vitamin D. The aim of this study was to investigate the effects of bone mineral metabolism and vitamin D in patients with chronic hepatitis C. This study which included a total of 45 patients with chronic HBV (age range 25–50 years) and 50 healthy people were invited to participate in the present study. Attending Imam Hussein Medical City, Karbala. Biochemical tests included total serum calcium, phosphate, and creatinine and total alkaline phosphatase and vitamin D. Serum concentrations of biochemical bone markers were in the normal range for both CHC patients and controls did not differ significantly in results.

INTRODUCTION

The World Health Organization has estimated that about 3.2% of the world population has positive serology for hepatitis C virus (HCV) (Hu et al., 1991). Bone diseases are common complications of chronic hepatitis C (CHC), mainly related to the associated cirrhosis. Among the bone abnormalities reported, hepatitis C-associated osteosclerosis (HCAO) is a rare acquired condition characterized by generalized increase in bone mineral density (BMD), bone pain, elevated serum alkaline phosphatase, generalized cortical thickening and increased uptake on bone scan (Schwartz & Skinner, 2008; Khosla et al., 1998). Such effect of chronic HBV is not always recognized. That is because osteoporosis and low Bone mineral density (BMD) are associated with too many risk factors, such as aging, immobility, hypertension, hyperparathyroidism, use of antihypertensive agents, diabetes mellitus (DM), low calcium intake, Vitamin D deficiency, and genetic factors (Chen et al., 2015).

Natural sources of vitamin D in humans are mostly cholecalciferol (also called vitamin D3) which is synthesized in the skin from 7-dehydrocholesterol by sunlight exposure. Cholecalciferol is firstly converted by the 25-hydroxylase to 25-hydroxyvitamin D (25OHD) in the liver (Kitson & Roberts, 2012; Christakos et al., 2016). Vitamin D deficiency results in abnormalities in calcium, phosphorus, and bone metabolism. Also, it has been suggested to be involved in the pathogenesis of autoimmune disorders, type 2 diabetes, cancers and the course of several infectious diseases recently (Rosen 2011). Regarding liver diseases, clinical evidence has shown that patients with chronic liver diseases such as chronic hepatitis C (CHC) is at higher risk of vitamin D deficiency (Chen et al., 2014). Low serum levels of 25OHD were reported to be an independent factor of adverse outcomes in alcoholic liver diseases and

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impaired virological response to interferon-based therapy in CHC patients (Trépo et al., 2013; Petta et al., 2010; Mandorfer et al., 2013).

Vitamin D status also reportedly correlates with liver histology in CHC. Patients with vitamin D deficiency have a higher grade of hepatic necroinflammation (Bitetto et al., 2011). More advanced fibrosis stage and may possibly have more rapid fibrosis progression (Terrier et al., 2011; Baur et al., 2012; Lange et al., 2011). At a cellular level, vitamin D deficiency is associated with downregulation of the 25-hydroxylase enzyme CYP27A1 in liver tissue. This may have pathogenetic relevance, given the established inverse relationship between CYP27A1 expression and the severity of necro-inflammatory activity (Petta et al., 2010).

MATERIALS & METHODS

Subject

This study which included a total of 45 patients with chronic HBV (age range 25–50 years) and 50 healthy people were invited to participate in the present study. Attending Imam Hussein Medical City, Karbala, from March 2021 to July 2022. Patients with autoimmune liver disease, celiac disease, chronic kidney disease were excluded from the study as well as patients or healthy subjects who had a history of treatments that could affect bone mass (calcium, bisphosphonates, estrogens, diabetes mellitus, vitamin D supplements and with a history of hip or lumbar spine fracture were also excluded from this study.

Sample Collection

In this study About 5 ml of venous blood was collected from each participant. The sera were separated by centrifugation and kept at -20 temperature until be used. Biochemical tests included total serum calcium, phosphate, and creatinine and total alkaline phosphatase using standard methods. 25-hydroxy vitamin D (25OHD) (radioimmunoassay technique, DiaSorin, Stillwater, MN, USA.

Bone Mineral Density Measurements

Patients were offered DEXA as a follow-up for their condition. BMD was measured using DEXA scan (DEXXUM-3-OSTEOSYXS/ Korea) by a trained radiology technician on the anteroposterior lumbar spine (L1–L4 spine) views.

Statistical Analysis

All statistical analyses were performed by SPSS version 13 (SPSS, Inc., Chicago, IL, USA). Continuous variables were expressed as mean ± SD and analysed with analysis of variance. Dichotomous variables were expressed as numbers and frequency and analysed with Chi-square test. A $P \leq 0.05$ was considered statistically significant.

RESULTS

In this study, we found that Spine and femoral neck BMD did not differ significantly between HCV patients and healthy control, as shown Table 1. Total femur and trochanter BMD values were significantly lower in CHC men as compared to healthy controls, even after adjustments for body weight (p,0.05).

Table 1
Bone mass measurements in CHC patients and healthy controls

Bone mineral density (g/cm2)	CHC (N = 45)	Controls (N = 50)	p*
Spine (L1–L4)	1.154±0.13	1.151±0.11	0.92
Femoral neck	1.037±0.19	1.059±0.16	0.46
Trochanter	0.750±0.15	0.832±0.14	0.04
Total Hip	1.043±0.18	1.113±0.13	0.06

Serum concentrations of biochemical bone markers were in the normal range for both CHC patients and controls as shown in Table 2. Total calcium, phosphate, alkaline phosphatase and vitamin D did not differ significantly between HCV patients and controls. The mean serum Creatinine was no significant difference between HCV patients and controls.

Table 2
Biochemical bone markers of bone and mineral metabolism in CHC patients and healthy controls.

Parameters	CHC (N = 45)	Controls (N = 50)	p*
Total calcium (mg/dL)	8.17±0.43	8.16±0.44	0.74
Phosphate (mg/dL)	3.23±0.37	3.06±0.35	0.34
Creatinine (mg/dL)	0.78±0.12	0.80±0.12	0.45
Alkaline phosphatase (UI/dL)	88.34±63.06	75.70±17.22	0.42
25 OHD (ng/mL)	35.40±10.07	26.61±6.18	0.15

25 OHD status was classified in patients and controls as follows: sufficiency (>30 ng/mL), insufficiency (11–29 ng/mL) and deficiency (< 10 ng/mL). no statistically significant difference was observed between the groups in terms of 25OHD status (Table 3).

Table 3
Classification of vitamin D status in CHC men and healthy controls.

25 OHD (ng/mL)	CHC (N = 45)	Controls (N = 50)
Sufficiency (>30)	29 (64%)	13 (26%)
Insufficiency (11–29)	14 (31%)	36 (72%)
Deficiency (<10)	2 (5%)	1 (2%)

Discussion

In our study the results shown that Spine and femoral neck BMD did not differ significantly between HCV patients and healthy control. It is also important to note that both CHC patients and healthy controls exhibited high prevalence of overweight and that is well recognized as having a protective effect on bone density (Tanaka et al., 2001; Høiberg et al., 2007). The lower values for total hip BMD observed among CHC patients may be explained by the significantly lower BMD measurements at the trochanter in these patients. In agreement with this study, which included that have also observed a significant decrease in trochanter BMD in CHC patients, regardless of the liver function (Duarte et al., 2001).

Only a few studies had evaluated BMD measurements in non-cirrhotic CHC patients and their results in our study, we were able to demonstrate that HCV infection affects BMD at the proximal femur independently of liver function (Necati et al., 2006; Schiefke et al., 2005). Serum concentrations of biochemical bone markers were in the normal range for both CHC patients and controls as shown in Table 2. Total calcium, phosphate, alkaline phosphatase and vitamin D did not differ significantly between HCV patients and controls. Corroborating previous findings (Hofmann et al., 2008). To our knowledge this is the first study to classify non-cirrhotic CHC patients according to vitamin D status. No significant difference was observed in 25OHD status between CHC patients and healthy controls.

25 OHD status was classified in patients and controls as follows: sufficiency, insufficiency and deficiency (Table 3). Hepatic dysfunction with the intervenient vitamin D deficiency has been associated with low bone density. Therefore, there have been many studies on whether vitamin D supplementation positively affects treatment response in patients with CHC (Bitetto et al., 2011; Yokoyama et al., 2014). levels of vitamin D in HIV/HCV coinfected patients should be monitored according to the reference range for the sample setting (El-Maouche et al., 2013; Cosman et al., 1997; Taksler et al., 2015). As observed earlier, the high prevalence of overweight in our population might also have influenced our results and could have positively impacted on BMD measurements in both groups, this study is the first to evaluate BMD, bone metabolism and the prevalence of morphometric vertebral fracture in a significant number of men with CHC, without the classic confounding factors for low bone density as well as that was no significant abnormalities in bone and mineral metabolism and a vitamin D status similar to that seen for healthy (Trépo et al., 2013; Huang et al., 2017).

CONCLUSION

In this report we founded no differ significantly between HCV patients and healthy control as well as no different significant in biochemical bone markers for both groups.

Competing Interest

The authors had no competing interests.

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