Original Article

Vitamin D Deficiency

Frequency of Vitamin D Deficiency and its Severity Grades Among Cirrhotic Patients Due to Hepatitis C

Momin Khan, Abdul Jabbar and Bacha Amin Khan

ABSTRACT

Objective: To determine the frequency of vitamin D deficiency and its severity grades among cirrhotic patients due to hepatitis C.

Study Design: Descriptive / cross-sectional study.

Place and Duration of Study: This study was conducted at the Department of Medicine, Saidu Teaching Hospital Swat from 01-01-2016 to 30-12-2016.

Materials and Methods: In this study a total of 210 patients were observed. Patients with history of osteomalacia, primary hyperparathyroidism, malignancy or bone metastatic diseases, patients on drugs like vitamin D replacement therapy, phenytoin, thiazide diuretics, Calcium containing antacids and glucocorticoids were excluded. They were admitted in Medical Department of Saidu Teaching Hospital Swat for further evaluation. Patients who were fulfilling the inclusion criteria had included in the study. From all patients, included in the study, blood were obtained and was sent to laboratory for detection of serum 25-hydroxyvitamin D (25OHD) deficiency and once detected was categorized as mild, moderate and severe. All the laboratory investigations were done in the same hospital under the supervision of a pathologist having at least 5 years of experience.

Results: In this study mean age was 50 years with standard deviation ± 1.33. Fifty eight percent patients were male, 42% patients were female. Vitamin D deficiency was found in 92% patients while 8% patients had normal vitamin D level.

Conclusion: We conclude that frequency of vitamin D deficiency was 92% patients presenting with hepatitis C.

Key Words: Vitamin D deficiency, cirrhotic, hepatitis.

Citation of articles: Khan M, Jabbar A, Khan BA. Frequency of Vitamin D Deficiency and its Severity Grades Among Cirrhotic Patients Due to Hepatitis C. Med Forum 2017;28(12):6-9.

INTRODUCTION

Cirrhosis is a scarring of the liver that lead to the formation of fibrous (scar) tissue associated with diffuse destruction of the normal liver architecture. As a consequence this will lead to derangement of the liver functions in a progressive fashion. Cirrhosis occurs due to any long standing injury to the liver. Liver plays a vital role in the metabolism of vitamin D as Vitamin D3 is hydroxylated by hepatic 25 hydroxylase to convert it into 25-hydroxyvitamin D3, the major circulating form of vitamin D3.As liver functions are impaired in cirrhosis, this will results in disturbance of the hydroxylation step of vitamin D metabolism leading to vitamin D deficiency in cirrhosis.

Vitamin D is important in calcium and phosphorus homeostasis and promoting bone mineralization[1]. Recently vitamin D3 deficiency is significantly recognized in chronic liver disease and cirrhotic patients[2,3].

Department of Medicine, Saidu Teaching Hospital Swat

Correspondence: Dr. Momin Khan, Assistant Professor, Department of Medicine, Saidu Teaching Hospital Swat
Contact No: 0345-2176667
Email: Mominkhanm1970@gmail.com

Received: August 17, 2017; Accepted: October 23, 2017

According to one study published in the United States, up to 92% chronic liver disease and cirrhotic patients have some degree of vitamin D deficiency[4]. In the hepatitis C cirrhosis group, 16.3% (7/43) had mild, 48.8% (21/43) had moderate, and 30.2% (13/43) had severe vitamin D deficiency[4]. It is now proved by one study that vitamin D deficiency is related with the degree of liver dysfunction rather than etiology[5]. One study conducted on HCV-HIV co-infected patients shows that low serum 25(OH) D3 correlates with the severity of liver fibrosis rather virological response to therapy or severity of immunodeficiency[3]. Low vitamin D is linked with severe fibrosis and low sustained virological response (SVR) in genotype 1 chronic hepatitis C patients[6].

Vitamin D deficiency is implicated in the pathogenesis of Osteopenia and Osteoporosis. There is one study published about frequencies of Osteoporosis in cirrhotic patients due to Hepatitis B and C in Peshawar tertiary care hospital[7]. Osteoporosis was found in 26% of subjects and Osteopenia in 42%, While 32% of subjects had BMD in normal age[7].

As vitamin D deficiency is increasingly identified in chronic liver disease and cirrhosis, I choose this topic for my research work because by this I will establish burden of severity of vitamin D deficiency problem in

local cirrhotic patients due to hepatitis C in our set of population and the result of the study can be used to recommend future guidelines for planning supplements of active form of vitamin D3 therapy (1, 25(OH) Vitamin D3) in this group of patients.

MATERIALS AND METHODS

This study was conducted at Department of Medicine, Saidu Teaching Hospital Swat. Study design was descriptive, cross-sectional study and the duration of the study was one years, from 01-01-2016 to 30-12-2016. All patients with liver cirrhosis due to hepatitis C and male and female above 20 years were included while patient who are in hepatic encephalopathy on clinical assessment, patients who have systemic diseases e.g. multiple myeloma, sarcoidosis, Tuberculosis (Based on medical records) which can influence vitamin D levels in a patient. Patients with history of osteomalacia, primary hyperparathyroidism, malignancy or bone metastatic diseases, patients on drugs like vitamin D replacement therapy, phenytoin, thiazidediuretics, Calcium containing antacids and glucocorticoids were excluded from this study. They were admitted in Medical Department of Saidu Teaching Hospital Swat for further evaluation. Patients who were fulfilling the inclusion criteria had included in the study. An informed written consent was taken from patients or relatives of the patients. All the investigations were done in the same laboratory.

RESULTS

In this study age distribution among 210 patients was analyzed as 4(2%) patients were in age ranged < 30 years, 21(10%) patients were in age ranged 31-40 years, 88(42%) patients were in age ranged 41-50 years, 70(33%) patients were in age ranged 51-60 years and 27(13%) patients were < 60 years. Mean age was 50± 1.33 years . Gender distribution among 210 patients was analyzed as 122(58%) patients were male, 88(42%) patients were female. Vitamin D level among 210 patients was analyzed as the vitamin D level was normal in 17(8%) patients while vitamin D was low in 193(92%) patients. Vitamin D deficiency among 210 patients was analyzed as the vitamin D deficiency was found in 193(92%) patients while 17(8%) patients had normal vitamin D level. Severity of vitamin D deficiency among 193 patients was analyzed as 48(25%) patients had mild deficiency of vitamin D, 97(50%) patients had moderate deficiency of vitamin D and 48(25%) patients had severe deficiency of vitamin D (Table No.1).

Association of severity of vitamin D deficiency among age distribution was analyzed as among 193 cases of vitamin D deficiency 48 patients had mild deficiency of vitamin D, in which 4 patients were in age range 31-40 years, 19 patients were in age range 41-50 years, 18 patients were in age range 51-60 years and 7 patients were in age > 60 years. 97 patients had moderate deficiency of vitamin D in which 8 patients were in age range 31-40 years, 42 patients were in age range 41-50 years, 35 patients were in age range 51-60 years and 12 patients were in age > 60 years. 48 patients had severe deficiency of vitamin D in which 3 patients were in age range 31-40 years, 19 patients were in age range 41-50 years, 18 patients were in age range 51-60 years and 8 patients were in age > 60 years. (Table No 2). Association of severity of vitamin D deficiency among gender distribution was analyzed as among 193 cases of vitamin D deficiency 48 patients had mild deficiency of vitamin D, in which 27 patients were male and 21 patients were female. 97 patients had moderate deficiency of vitamin D in which 60 patients were male and 37 patients were female. 48 patients had severe deficiency of vitamin D in which 23 patients were male and 25 patients were female (Table No 3).

Table No.1. Demographic variable of patients

Variable	No.Patients	Percentage
Age Distribution		
• < 30 years	4	2%
• 31-40 years	21	10%
• 41-50 years	88	42%
• 51-60 years	70	33%
• > 60 years	27	13%
Gender Distribution		
• Male	122	58%
• Female	88	42%
Vitamin D Level		
• Normal	17	8%
• Low vit. D Level	193	92%
Vitamin D Deficiency		
• Yes	193	92%
• No	17	8%
Severity Of Vitamin D Deficiency		
• Mild	48	25%
• Moderate	97	50%
• Severe	48	25%

Table No. 2. Association of severity of vitamin d deficiency in age distribution (n=193)

Severity /Age	31-40 years	41-50 years	51-60 years	>60 years	Total
Mild	4	19	18	7	48
Moderate	8	42	35	12	97
Severe	3	19	18	8	48
Total	**15**	**80**	**71**	**27**	**193**

Chi square test was applied in which P value was 0.591

Table No. 3. Association of severity of vitamin d deficiency in gender distribution (n=193)

Severity /Gender	Male	Female	Total
Mild	27	21	48
Moderate	60	37	97
Severe	23	25	48

DISCUSSION

Cirrhosis is a scarring of the liver that lead to the formation of fibrous (scar) tissue associated with diffuse destruction of the normal liver architecture. As a consequence this will lead to derangement of the liver functions in a progressive fashion. Cirrhosis occurs due to any long standing injury to the liver. Liver plays a vital role in the metabolism of vitamin D as Vitamin D3 is hydroxylated by hepatic 25 hydroxylase to convert it into 25-hydroxyvitamin D3, the major circulating form of vitamin D3.As liver functions are impaired in cirrhosis, this will results in disturbance of the hydroxylation step of vitamin D metabolism leading to vitamin D deficiency in cirrhosis.

It is a developing country of Pakistan, and the literacy rate is also low, which often raises information about pathogenicity, proper ways and diagnosis and treatment procedures. HCV infection is therefore an economic burden for Pakistani residents, and in particular for the KPK. Vitamin D deficiency is common (92%) among patients with chronic liver disease, with at least one third of them suffering from vitamin deficiency D. We found similar results in our study, which found a deficiency of vitamin D in 92% of patients.

As in our study 193(92%) patients in which 48(25%) patients had mild deficiency of vitamin D, 97(50%) patients had moderate deficiency of vitamin D and 48(25%) patients had severe deficiency of vitamin D. similar results were found in another study done by Arteh J et al[8] in which 109/118 (92.4%) had some degree of vitamin D deficiency. In the hepatitis C cirrhosis group associated with 16.3% mild, 48.8% moderate, and 30.2% (13/43) were severe vitamin D deficiency. Severe vitamin D deficiency (<7 ng/ml) was more common among patients with cirrhosis compared with non-cirrhotic (29.5% versus 14.1%, P value = 0.05). Female gender, African American race, and cirrhosis were independent predictors of severe vitamin D deficiency in chronic liver disease.

A lower serum 25 (OH) D level was previously reported in different populations in terms of the cause and severity of chronic liver disease [9,10]. We confirmed the reduction of 25 (OH) D to a homogeneous cohort for patients with G1 CHC, with low prevalence of Fibrosis F4. Although the significant trend in 25 (OH) D was found to be reduced with increased fibrosis levels, the subgroup of patients with light fibrosis (F1) also observed a significant reduction and it is unlikely that low levels of 25 (OH) D completely explained by decreased liver function.

Our study shows that a low level of 25 (OH) D is involved regardless of the gender of women and the intensity of necroinflammatory activity. Although the study did not confirm the correlation between the female sex and the lower level of 25 (OH) D, due to the decrease observed in women over 55 years, but not in men of the same age group, and due to the significant interaction between gender and age , we can imagine that hormonal changes in women after birth can modify the vitamin D status [11,12]. Our results highlight the inverse relationship between 25 (OH) D and the intensity of necroinflammatory activity. The lack of this relationship can be attributed to differences in middle age, alcohol consumption and the incidence of obesity and diabetes. In any case, we have declared a significant effect of metabolic changes on severe fibrosis of ferritin, a distance marker and metabolic syndrome[13].

It is possible that a reduced level of 25 (OH) D may promote the promotion of fibrosi itself. Experimentally different models show that vitamin D, through interaction with the vitamin D receptor, protects oxidative stress[14], can influence the migration, proliferation, and gene expression of fibroblasts,[15,16] and reduces the inflammatory and fibrogenic activity of liver stellate cells.[17,18] However, further potential cohort studies will be necessary to establish a link between the belief about vitamin D deficiency and fibrosis in patients with CHC.

Another interesting outcome of this study is the evidence that serum 25 (OH) D levels have a negative independent risk factor for SVR. Again, this observation will have to be needed in many different cohorts of patients, but it is supported by Experimental Data that contributes to the role of vitamin D in modifying the immune response,[17,18] and by recent clinical data[19] reporting higher early virological response rate in CHC treated with standard of care plus vitamin D, compared with those treated with standard of care only. Finally, in line with data from the literature, we found that steatosis[18] and lower cholesterol levels, a known surrogate marker of fibrosis severity,[13] were independently associated with lower SVR rate. We did not find any association between IR and SVR, in keeping the conflicting data reported in the literature on the role of IR as a predictor of SVR.

CONCLUSION

Our study concludes that the frequency of vitamin D deficiency was 92% patients presenting with hepatitis C.

Momin Khan, Abdul Jabbar and Bacha Amin Khan

Author's Contribution:

Concept & Design of Study:	Momin Khan, Abdul Jabbar
Drafting:	Abdul Jabbar, Bacha Amin Khan
Data Analysis:	Abdul Jabbar, Bacha Amin Khan
Revisiting Critically:	Momin Khan, Bacha Amin Khan
Final Approval of version:	Momin Khan

Conflict of Interest: The study has no conflict of interest to declare by any author.

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