



Association of Vitamin D Deficiency with Hepatitis B and C Virus Infection

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Authors' contributions

This work was carried out in collaboration among all authors. Authors DK and MUK were involved in conception of idea and study design. Author SMK did the data collection and performed bench work. Author US performed the statistical analysis. Authors MAS and ZN managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Objective: To evaluate the association of vitamin D deficiency with hepatitis B and C virus Infection.

Study Design: This is a prospective study.

Setting: Study carried out at Medicine department Civil Hospital Karachi, from March, 2018 to December, 2019.

Materials and Methods: 266 Participants of the study included patients with active hepatitis B or hepatitis C infection visiting OPD of the hospital. Vitamin D levels of 14-30 ng/ml have been described as insufficient and levels <14 ng/ml are labelled as deficient. Vitamin D level of >30 nm/ml have been defined as sufficient according to our study. Diagnosis of Hepatitis B is confirmed by HBV DNA and HBsAg serum levels and of Hepatitis C by HCV RNA levels.

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Results: We received 70.6% (n=266) males and 29.3% females. After serological tests 34.9% (n=93) patients were positive for HBV DNA whereas 47.7% (n=127) patients were positive for HCV DNA. Coinfection with hepatitis B and C was present in 17.2% (n=46) of patients. Amongst total 266 participants 54.31% patients have been vitamin D deficient and 32.7% have insufficient vitamin D levels.

Conclusion: Genetic and metabolic factors linked to hepatitis B and C with vitamin D deficiency should be studied on large scale. In our study patients infected with HBV and HCV have been vitamin D deficient, supplementation needs to be added to the treatment regimen.

Keywords: Vitamin D deficiency; hepatitis B; hepatitis C.

1. INTRODUCTION

Globally viral hepatitis B (Hep B) and C (Hep C) are a common healthcare problem and has infected more than 130 million individuals [1]. Hepatitis C current treatment guidelines include PEGylated interferon (PEG-IFN) and ribavirin (RBV) for 24 week duration as for genotypes 2 and 3. HCV genotype 1 treatment regimen is carried out for 48 weeks to obtain sustained virological response (SVR). SVR is defined as undetectable serum HCV RNA after completing 24 weeks on anti-HCV therapy [2]. The association of liver cirrhosis and vitamin D levels in the body has been studied by researchers. A lot of studies have been conducted on frequency of vitamin D deficiency and infection with HBV and HCV. It has been suggested in various studies that patients with HBV infection have greater vitamin D deficiency than HCV infection [3]. The treatment goal for HBV infection is decided on the basis of HBV DNA level and alanine aminotransferase levels. The viral load of patients coinfecting (HBV and HCV) should be monitored by HBV and HCV DNA levels in the blood. Reducing the progress to cirrhosis and monitoring viral levels during treatment is crucial because the treatment of one virus affects serum levels of another virus [4]. Pathophysiology of metabolic and genetic predisposition has been analyzed by the scientific community. One specific review by Cholangitis E *et al.* 2012 showed a correlation that vitamin D can affect HCV treatment and its progress. Currently a review study found a correlation that vitamin D levels can affect HCV treatment and its progress [5]. Vitamin D itself is a biologically inactive molecule and is activated by hydroxylation from liver and kidney. The final active form of vitamin D is 1, 25(OH)₂D which regulates calcium absorption and excretion [6]. Vitamin D deficiency has been linked to higher risk of cancer, cardiovascular and autoimmune diseases [7]. Few studies have shown that adequate levels of vitamin D help in achieving

sustained virological response independent of other factors. It was reported by Lange CM *et al.* 2011, that lower vitamin D levels are associated with low chances of achieving SVR only in HCV genotypes 2 and 3. While in HCV genotype 1 no such association was found during treatment [8]. As HBV infection is treated by potent nucleotide or nucleoside inhibitors, they are efficacious antivirals with genetic barrier to its resistance. It leads to suppression in viral replication but doesn't destroy HBV infected hepatocytes [9]. Active vitamin D metabolite 1, 25(OH)₂D₃ induces a number of genes and suppresses others regulating immunomodulatory activity to both adaptive and innate immunity. It has been found in various reviews that the degree of vitamin D deficiency correlates to liver fibrosis as compared to control groups with adequate vitamin D levels [10]. The aim of our study is to determine the prevalence of vitamin D deficiency in HBV and HCV infected patients.

2. MATERIALS AND METHODS

This is a prospective study carried out at Medicine department Civil Hospital Karachi after the ethical permission. It was done during the time period of March, 2018 to December, 2019. Participants of the study included patients with active hepatitis B or hepatitis C infection visiting OPD of the hospital. Age range of selected participants was 30-75 years of age. Patients with any autoimmune disease or ongoing cancer were excluded from the study. All sociodemographic and medical information was collected on a predesigned proforma. Vitamin D levels in the participants were assessed by measuring serum levels of 25(OH) D₃ by laboratory. Vitamin D levels of 14-30ng/ml have been described as insufficient and levels <14ng/ml are labelled as deficient. Vitamin D level of >30nm/ml have been defined as sufficient according to our study. Diagnosis of Hepatitis B was confirmed by HBV DNA and HBsAg serum levels and of Hepatitis C by HCV

RNA levels. Ultrasound abdomen was also performed in every participant to assess the degree of fibrosis. Analysis was done to determine prevalence of vitamin D deficient patients and their correlation to viral load using SPSS version 20.

3. RESULTS

During this 10 month time period, we received a total of 266 patients in the OPD having infection with hepatitis B and C. We received 70.6% (n=188) males and 29.3% (n=78) females. After serological tests 34.9% (n=93) patients were positive for HBV DNA whereas 47.7% (n=127) patients were positive for HCV DNA. Coinfection with hepatitis B and C was present in 17.2% (n=46) of patients as shown in Table 1.

Coinfection with hepatitis B and hepatitis C was found in 17.2% (n=46) patients. Vitamin D levels were measured as mean 25 (OH) D3 serum concentrations. The mean value of 25 (OH) D3 serum concentrations in HBV and HCV infections has been calculated in different way and is displayed in Table 2. Amongst the total 266 participants, 145 (54.3%) patients have been vitamin D deficient and 87 (32.7%) have insufficient vitamin D levels.

4. DISCUSSION

A meta-analysis of eleven studies showed positive correlation between Vitamin D supplementation and achievement of SVR in HCV infected patients. Vitamin D deficiency is also prevalent among candidates for liver transplantation; approximately 75% of patients have reported to be vitamin D deficient [11]. Vitamin D is metabolized into its active form 1,25-dihydroxyvitamin D₃ in healthy liver cells.

Patients with chronic liver disease have decreased rate of conversion of vitamin D to its active metabolite and there have been link between liver fibrosis and vitamin D deficiency [12]. In few studies, trials have been conducted for vitamin D supplementation in chronic liver disease patients [13-14]. Low levels of vitamin D are also independent predictors of hepatic decompensation and mortality in patients with liver failure [15]. Previous study by Gal-Tanamy et al in 2011 showed that vitamin D inhibits viral cell replication and decreases further expression of VDR [16]. It is also recommended by author Nimer A in 2012, increased sunlight exposure in patients with chronic hepatitis to increase vitamin D production [17]. Vitamin D supplementation increases the rate of achievement of SVR especially with the HCV genotype 1. Lack of proper data is due to conduction of studies on small scale, lost to follow up during treatment and lack of comparison to control groups infected with the same genotype [18]. In our study patients having co-infection with hepatitis B and C have the lowest levels of serum 25(OH)D3 followed by patients infected by HCV. A retrospective study was done to determine vitamin D levels after its supplementation in immunocompromised patients. Even after complete treatment these patients had low levels of vitamin D in 78% of cases [19]. Different methods of vitamin D levels determination also produce bias in clinical decision making and usage of a common method must be used to reduce variability. All the studies on this topic have been done on small scale and limited population samples; there is a dire need to conduct large scale studies in different populations. The exposure to sunlight and diet rich in vitamin D also differs with racial and social factors thus the prevalence of vitamin D deficiency in different populations is to be

Table 1. Frequency of viral infection in study participants

Viral Infection	Frequency (n)	Percentage (%)
Hepatitis B	93	34.9
Hepatitis C	127	47.7
Coinfection with hepatitis B and C	46	17.2

Table 2. Mean 25(OH) D3 concentrations of participants

Viral Infection Status	25 (OH) D3 Serum Concentration
Hepatitis B positive	24.31 ng/ml
Hepatitis C positive	13.42 ng/ml
Co infection with hepatitis B and C	9.86 ng/ml

known [20]. The response to vitamin D supplementation differs due to polymorphism in VDR and interleukin (IL)-28B gene, especially African and Hispanic origin patients are less likely to respond to standard vitamin D supplementation therapy [21]. Europeans and Caucasians have lesser exposure to sunlight and explain the overall vitamin D deficiency in this population [22]. The limitations of our study are that it is being conducted in a single center within limited groups. Meta-analysis are the best means to understand the prevalent trends of vitamin D deficiency in HBV and HCV infected groups and their correlation to liver fibrosis.

5. CONCLUSION

Genetic and metabolic factors linked to hepatitis B and C with vitamin D deficiency should be studied on large scale. In our study patients infected with HBV and HCV has been vitamin D deficient, so their supplementation needs to be added to the treatment regimen.

CONSENT AND ETHICAL APPROVAL

This study carried out at Medicine department Civil Hospital Karachi after the ethical permission. Written informed consent for the study was obtained from the every study participants.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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