PREVALENCE OF VITAMIN-D DEFICIENCY AMONG THE PATIENTS OF HBV AND HCV RELATEDCHRONIC LIVER DISEASE.

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ABSTRACT

INTRODUCTION: The viral infection by HBV & HCV are commonest cause leading to acute as well as chronic viral hepatitis. It is analysed in many studies from past era that levels of 25(OH) - D are decreased in subjects suffering from chronic hepatic disease due to HBV and particularly HCV in comparison to normal population. The occurrence of either insufficiency or deficiency of VD is more in subjects suffering from chronic hepatic disease secondary to HBV & HCV. The deficiency of VD is related with a large range of adverse effects in subjects with HBV and HCV. **OBJECTIVE:** research was aimed to see occurrence of deficiency of VDD in subjects with chronic hepatic illness with HBV and HCV. **METHODLOGY:** current research cross sectional type was done on blood samples of 300 subjects attending the laboratory at LUMHS Jamshoro Hyderabad, with acute or chronic HBV & HCV. According to our research, VD levels of >30 nm/ml are considered sufficient, 14-30 ng/ml are considered insufficient & VD levels lower 14 ng/ml are considered deficient. Hepatitis BV DNA & HBs surface antigen blood levels validate Hepatitis B diagnosis, whereas VIRAL HEPATITIS C RNA levels establish the diagnosis of Hepatitis C. **RESULT:** We received 60.3 percent men (n=181) and 39.7% females (n=119). After serological testing, 36.1 percent of patients (n=108) tested positive for HBV DNA, whereas 63.9 percent of patients (n=192) tested positive for VIRAL HEPATITIS CDNA. Hepatitis B and C infections were found in 22.3 percent (n=67) of the patients. A total of 57.3 percent of the 300 subjects were VD deficient, whereas 30.7 percent had adequate VD levels. **CONCLUSION:** The findings of our investigation indicated that more than half of the patients with HBV & VIRAL HEPATITIS C infection have VD insufficiency, which has been linked to negative clinical outcomes. Our findings show that VD supplementation is critical in the treatment of chronic liver disorders caused by HBC and HBV.

KEY WORDS: Chronic Liver Disease, VD deficiency, HBV infection, VIRAL HEPATITIS C infection.

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INTRODUCTION

VIT D is a vital micronutrient and a lipid-soluble VIT . VIT D is convoluted in a compound system which standardizes the mineral homeostasis, shelters skeletal reliability, and restrains cell growth and diversity so is also considered as hormone[1]. The two isoforms of VIT D are VIT D2 Ergocalciferol & VIT D3 cholecalciferol. VIT D2 is obtained from diet and only provides 10% of VIT D requirements while the greater proportion of VIT D, around 90%, is synthesized by exposure of skin to sunlight[2]. Both forms of this VIT (D2 and D3)share a parallel part in metabolism. After consumption or production from UV rays, VIT D2 and VIT D3 are hdroxylated in the liver to generate 25 hydroxy VIT D (25 (OH)

D or calcidiol). This 25 (OH) D or calcidiol is converted to 1,25 di-hydroxyl VIT D (1,25 (OH)2 D orcalcitriol)3 in the kidneys in reaction to parathyroid hormones (levels of PTH). Nearly in all cells a transcription factor the VIT D receptor (VDR) is present with variable levels. The chief facilitator of the actions of the biologically dynamic forms of VIT D (1,25D) or its synthetic derivatives is theVDR.

During the inflammation of hepatocytes the levels of VDR are raised, thus giving a larger location for impending targets[4]. The protection of calcium homeostasis and promotion of bone mineralization are the main biological function of VIT D in human body. VIT D in the physique also achieves a number of other functions such as cell differentiation, apoptosis, anti- proliferation, immunosuppression and anti- inflammation[5]. The commonest causes of acute and chronic hepatitis are infection by Hepatitis B virus and Hepatitis C virus. It remains analysed in many studies from past era that levels of 25(OH) - D are decreased in subjects suffering from chronic hepatic disease due to VIRAL HEPATITIS B and particularly VIRAL HEPATITIS C in comparison to normal population[6]. The absorption, metabolism, and storage of fat- soluble VIT s (FSVs) are affected in chronic liver disease [7.] It plays essential part in different chronic ailments including; various infections, CVS illness, diabetes mellitus and few kinds of malignancies. Especially in Pakistan the pervasiveness of insufficiency and deficiency of VIT D are greater in subjects suffering from CLD secondary to VIRAL HEPATITIS B and VIRAL HEPATITIS C that is approximately 78.0%[8]. In many geographical areas of the globe the liver cirrhosis is ranked as the 4th leading cause of death. The large portion of this is related with hepatitis C virus. In subjects suffering from CLD most of them are found to have VIT D deficiency. Malfunctioning of endogenous VIT -D production as a consequence of decreased synthesis of 7- dehydrocholestrol is noted in subjects suffering from CLD because of severity and prognosis of VIRAL HEPATITIS C[9]. Hepatitis B Virus infection remains a liberated risk issue for VIT Ddeficiency. VIRAL HEPATITIS B infection appears to be a separate risk factor for VIT D insufficiency, which increases hazard of osteoporosis & other VIT D linked illnesses. It was significantly related with last phase cirrhosis of liver [10]. The regulation of cell proliferation,differentiation,
immunomodulation, anti- inflammatory, and antifibrotic characters are all related with 25-hydroxyVIT D. These effects are relevant in the pathogenesis and treatment of many causes of chronic liverdisease[11]. Studies has showed that VIT D also decreases viral replication[12]. Chronic liver disease due to hepatitis leads to low VIT D level in the blood which is further associated with the stage of hepatic fibrosis and cirrhosis[13]. Liver cirrhosis with extreme deficiency of VIT D is connected to advanced systemic inflammation and hepatocellular decompensation[14].

Current research is aimed to see frequency of deficiency and insufficiency of VIT Din the catchment population of Hyderabad, Sindh in subjects with chronic liver disease secondary to VIRAL HEPATITIS B and VIRAL HEPATITIS C.

METHODOLOGY:

The research was carried out at the LUMHS Diagnostic & Research Lab: in Jamshoro & Hyderabad. Subjects with active hepatitis B or C infection at the Diagnostic and Research Laboratory Liaquat University of medical and health sciences (LUMHS) Jamshoro and Hyderabad made up populace.

Design of Study: it is Descriptive cross-sectional research

Sample Duration: September 2018 to Number 2018

Sampling Technique: Sampling Technique was Non-Probability (purposive).

Sample Size: The size of sample for the current study was obtained by using online sample size calculator "OpenEpi. The confidence level was set at 95% limit with the margin of error of 0.05, based on estimation that approximately the occurrence of deficiency of VIT D in CLD subjects due to HBV & HCV is about 78%, so we obtained thesample size of n= 300.

Inclusion Criteria: We selected Subjects of both genders age ranging between the age of 1860 years who have hepatitis B and C related chronic liver disease.

Exclusion Criteria: We excluded the Liver cirrhosis due to any other cause such as:

Hepatocellular carcinoma, History of Diabetes mellitus or Hypertension, History of Ischemic heart disease, History of VIT D supplements, History of steroids, History of metabolic bone disease, chronic renal failure

Sample Size for Frequency in a Population	
Population size(for finite population correction factor or fpc)(*N*):	1000000
Hypothesized % frequency of outcome factor in the population (*p*):	78%+/-5
Confidence limits as % of 100(absolute +/- %)(*d*):	5%
Design effect (for cluster surveys-*DEFF*):	1
Sample Size(*n*) for Various Confidence Levels	

Confidence Level (%)	**Sample Size**
95%	**300**
80%	113
90%	186
97%	324
99%	456
99.9%	743
99.99%	1039

Equation
Sample size n = $[DEFF*Np(1-p)]/ [(d^2/Z^2_{1-\alpha/2}*(N-1)+p*(1-p)]$

Data collection procedure: Subsequent to the authorization by ethical committee of LUMHS Jamshoro the study will be directed and all the participants having fulfillment of inclusion criteria will be entered in this study after informed consent. The study Participants who satisfy the inclusion and exclusion criteria will be educated regarding the study, its aim and objectives. Indoor or outdoor Subjects diagnosed as case of chronic liver disease due to HBV & HCV in all 4 Medical units of LUH Hyderabad/Jamshoro will be taken as cases. Detailed questionnaires will be followed regarding demographic characteristics like sun exposure, weight, height, BMI, diet, supplements, clothing, history of smoking & co-morbidities including IHD, DM & HTN. 5cc blood sample will be collected from each individual and VIT D_3 test will be analysed using VIT D_3 kit running on Abbott ARCHITECT i2000SR. This method accomplishes chemiluminescent micro particle immunoassay (CMIA) for the quantitative determination of 25-hydroxyVIT D (25- OH VIT D) in serum and plasma. There will be no financial implication on the study participant. The data will becollected as per designed Performa "A". SPSS software package (SPSS version 22.0) was used for Analysis of statistical data. For quantitative variables Mean ± standard deviation (SD) were calculated. Frequency & percentage (%) were calculated for categorical variable. A statistically significant $P \leq 0.05$ was considered.

RESULTS

We assessed blood samples of 300 subjects in last six months period. We received overall 64.3 %(n=193) males and 35.6% (n=107) women. Afterward serum tests 36% (n=108) subjects were positive for VIRAL HEPATITIS B DNA whereas 64% (n=192) subjects were positive for VIRAL HEPATITIS C DNA. Confections with hepatitis B and C was present in 22.3% (n=67) of subjects, the bifurcation by gender is shown in Table 1.

The VIT D levels were calculated as mean 25 (OH) D3 serum concentrations. In VIRAL HEPATITIS B and VIRAL HEPATITIS C infections the mean levels of 25 (OH) D3 serum levels has been quantified. The average concentration for hepatitis B (VIRAL HEPATITIS B) positive cases remains 25.23 ng/ml, while for hepatitis C positive cases found to be 14.32 ng/ml, the co- infection with hepatitis B and C on average remains 10.96 ng/ml as presented in in Table 2.

The prevalence of VIT D among hepatitis B, hepatitis C and coinfected cases with HBV & HCV are categorized in table 3. The cases with confection show the peak occurrence of VIT D deficiency or insufficiency (81%) followed by hepatitis B subjects with 69% of cases either deficient or having insufficient quantity of VIT D. Amongst the total 300, 57.3% subjects have been VIT D

deficient and 31% have insufficient VIT D levels, while only 12% found to have insufficient serum VIT D level as shown in the figure 1.

Table 1. Frequency of VIRAL HEPATITIS B & H CV infection by Gender

infection Type	Male	Female
VIRAL HEPATITIS B	68 (63%)	40 (37%)
H CV	125 (65.1%)	67 (34.9%)
Total	193 (64.3%)	107 (35.6
VIRAL HEPATITIS B & H CV Confections	46 (69.2%)	21 (31.3%)

Table 2. Prevalence of mean D3 concentrations among

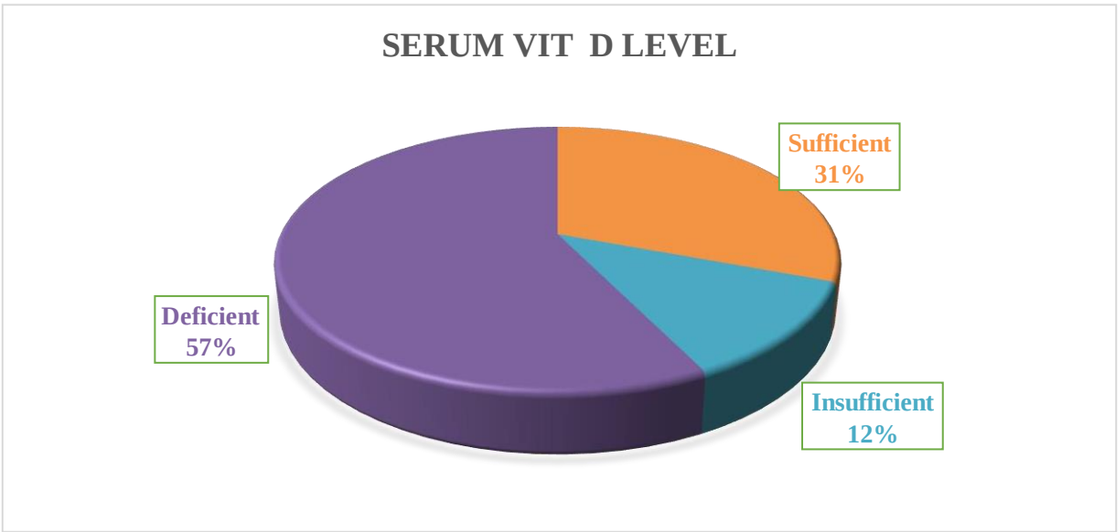
VIRAL HEPATITIS B & H CV status and Serum 25 (OH) D3 Concentration

Hepatitis B-positive 25.23 ng/ml
Hepatitis C-positive 14.32 ng/ml
Co infection with hepatitis B and C 10.96ng/ml

Table 3 Serum VIT D status in subjects infected with HepB Hep C& Confections.

VIT D status	VIRAL HEPATITS B n (%)	VIRAL HEPATITIS C n (%)	VIRAL HEPATITIS B+HBC(combined) n (%)
Sufficient	33 (31)	71(37)	13 (19)
Insufficient	12 (11)	29 (15)	9 (14)
Deficient	63 (58)	92 (48)	45 (67)

Figure 1: Prevalence of VIT -D deficiency in subjects with VIRAL HEPATITIS B+HBC disease.



DISCUSSION

A meta-analysis of eleven trials found a link between VIT D intake and the accomplishment of SVR in VIRAL HEPATITIS C-infected individuals. VIT D deficiency is very common amongst liver transplant contestants; nearly 70% of subjects have reported being VIT D deficient or having inadequate VIT D levels[11] In healthy liver cells, VIT D is converted to its active form1, 25-dihydroxyVIT D3. VIT D conversion to its active metabolite is reduced in CLD subjects, and there is a relationship between liver fibrosis and VIT D deficiency[12]. VIT D supplementation in CLD subjects has been studied in a few studies[13-14]. VIT D deficiency is also an independent predictor of hepatic decompensation and death in liver failure subjects[15]. VIT D suppresses viral cell multiplication and lowers subsequent development of VDR[16], according to a 2011 research by Gal-Tanamyet al. Increased sunshine contact in subjects with chronic hepatitis to boost VIT D production[17] was also advocated by author Nimer A in 2012. VIT D supplements improve the rate of SVR, notably in people with VIRAL HEPATITIS C genotype 1. Due to small-scale research, loss of continuation throughout management, & deficiency of evaluation to control sets diseased by similar genotype[18], there is a lack of reliable data. Individuals by hepatitis B & C co-infection had lowermost heights of serum 25(OH)D3, trailed by subjects diseased with VIRAL HEPATITIS C. VIT D levels were measured following supplementation in immunocompromised individuals in a retrospective investigation. In 78 percent of cases, these individuals still had low VIT D levels after completing treatment19. Different techniques for determining VIT D levels cause partiality in medical executive, hence single approach essential be adopted towards eliminate variability. Entirely of research scheduled these issues have been conducted on a trivial measure with small populace trials; large scale investigations in various communities are urgently needed. The amount of time spent in direct sunlight and eating a VIT D-rich diet varies depending on ethnic and social variables, hence the occurrence of VIT D deficiency in various groups is unknown18. Owing to polymorphisms in the VDR and interleukin (IL)- 28B genes, individuals of African and Hispanic ancestry remain less probable to react routine VIT D supplementation therapy[13]. Europeans & Caucasians receive less sunshine, which contributes to VIT D insufficiency in this population20. Our study is hampered by the fact that it is being undertaken at a single centre with a small number of participants. The greatest way to appreciate frequent patterns of VIT D insufficiency in VIRAL HEPATITIS B and VIRAL HEPATITIS C diseased populations & their relationship to fibrosis of liver is to use meta-analysis.

CONCLUSION

VIT D insufficiency was found in more than half of the participants with VIRAL HEPATITIS B, VIRAL HEPATITIS C infection, or who were co-infected with VIRAL HEPATITIS B and VIRAL HEPATITIS C, that has been connected to negative clinical outcomes. VIT D supplementation is critical in the therapy of CLD associated with HBC and VIRAL HEPATITIS B, according to our findings. Large-scale research on genetic and metabolic aspects associated to VIT D insufficiency in relation to hepatitis B and C is needed.

ETHICS APPROVAL: The ERC gave ethical review approval

CONSENT TO PARTICIPATE: written and verbal consent was taken from subjects and next of kin

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AUTHORS' CONTRIBUTIONS:

All individuals who meet criterion for authorship arelisted as authors. Hence it is certified by all authors that they have contributed in the work to yield communal concern of this document. All authors had read and sanctioned the final script.

CONFLICT OF INTEREST: No competing interest declared.

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