Relationship between Nonalcoholic Fatty Liver Disease and Vitamin D in Nepal

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ABSTRACT

BACKGROUND AND AIMS

Vitamin D deficiency has been frequently reported in many causes of chronic liver disease and has been associated with the development and evolution of non-alcoholic fatty liver disease (NAFLD).The study was done to explore associations between serum vitamin D concentrations among obesity, diabetes mellitus, hypothyroidism, and metabolic syndrome and its effects on liver fibrosis by ultra-sonogram and 2 d shear wave elastography in patients with nonalcoholic fatty liver disease (NAFLD).

METHODS

A hospital based prospective observational study was conducted from May 2019 for twelve months period in Gastroenterology Unit, NAMS, Nepal. Seventy patients with known fatty liver identified by Ultrasonogram criteria were enrolled. All patients were evaluated by different fibrosis scores (NAFLD Fibrosis, FIB4, APRI, AST/ALT ratio) and 2d shear wave score. Patients were evaluated for Vitamin D level and its effects on obesity, diabetes mellitus, thyroid related disease, dyslipidemias and NAFLD.

RESULTS

Among 70 patients, 39 (55.7%) were male and 31 (44.3%) were female with mean age of 44.3 years. Most of the patients were overweight with mean BMI of 28.2 kg/m^2;among them 51 (72.9%) were more than 25.kg/m^2. About 41.4% had diabetes mellitus, 77.1% had hypertension, 30% had hypothyroidism and 25.9% had metabolic syndrome. Majority of patients on ultrasound grading were mild with 64.28%; 25.72% were moderate and only 10 % were in severe groups. A study of 2 d shear wave elastography showed mean fibrosis of 7.07 kpa for mild grade, 8.22 kpa for moderate grade and 18.16 kpa for severe grade. The mean value of vitamin D was 22.61iu/ml for mild grade, 24.89 iu/ml for moderate grade and 17.4 iu/ml for severe grade.

CONCLUSION

The results of this study showed high prevalence of serum 25(OH) vitamin D inadequacy in individuals with obesity, diabetes mellitus, hypothyroidism and metabolic syndrome which worsens as the stage of liver disease progresses.

INTRODUCTION

Vitamin D insufficiency and deficiency are prevalent in almost half the healthy population of developed countries[1]. Most experts define vitamin D insufficiency as a 25(OH) D level below 30 ng/mL and deficiency as levels below 20 ng/mL. It is estimated that one billion people suffer from deficiency or insufficiency of vitamin D[2].

The outcome of vitamin D deficiency in terms of osteoporosis, osteomalacia and increased fracture risk is well known[3,4] . Furthermore, the association between vitamin D deficiency and the development of infections, cardiovascular, autoimmune and degenerative diseases and several types of cancer (colon, prostate and breast cancer) has also been reported[5]. Vitamin D deficiency is extremely common in chronic liver disease patients. Up to 93% of these patients have some degree of vitamin insufficiency[6,7]. Several studies in general populations have shown that low levels of 25(OH)D significantly increase the risk of mortality from all causes, including cardiovascular diseases[8]. Regarding patients with chronic liver disease of varying etiologies, vitamin D deficiency has been associated with increased mortality [9,10], bacterial infections, portal hypertension complications[11]and fibrosis severity[12].

NAFLD is the most common form of liver disease and a leading cause of morbidity and mortality in both developed and developing countries.[13] NAFLD progresses to liver fibrosis and ultimately cirrhosis and its complication.

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So early diagnosis and timely treatment with vitamin D is important to prevent cirrhosis related complications, mortality and healthcare cost.

Table : 1

Base line Characteristics	Total (n=70)
Male	39(55.7%)
Female	31(44.3%)
Age	44.3±12.1
HDL.	45±12.3
LDL	96.±35.2
TG	213.3±146
AST	64.5±117.1
ALT	63.3±80.3
GGT	70±75
Platelets	231.4±91.5
AST/ALT ratio	32(45.7%)
Serum vitamin D mean level	23.02±17.24

METHODS

The study was conducted from May 2019 for twelve months period in the Gastroenterology, NAMS, Nepal. The study was designed as a hospital based prospective observational study. Seventy patients with fatty liver in ultrasonography were enrolled in the study. The criteria of inclusion consisted of no consumption of alcoholic beverages for more than 20 g/day for women and 30 g/day for men, no chronic use of hepatotoxic medication, and negative HBsAG and HCV antibody tests. Complete general and systemic examination including anthropometry was done. Routine blood investigations were done.

Fatty liver and its severity was assessed by ultrasonography (USG) and 2d Shear wave elastography. Mean values of vitamin D compared with grading of fatty liver and its severity by 2d shear wave elastography. Grading of obesity assessed by body mass index (BMI) which measured by weight divided by height meter2 and its severity assessed by mean value of serum vitamin D level. The effect of other metabolic diseases such as Diabetes mellitus (DM), Hypertension, Hypothyroidism, Dyslipidemia and Metabolic syndrome assessed with mean value of serum vitamin D level.

RESULTS

Among seventy patients 39(55.7%) were male and 31(44.3%) were female with mean age of the patients were 44.3. Most of the patients were overweight with mean BMI of 28.2, kg/m2among them 51(72.9%) patients were more than 25.kg/m2Most of the patients 41.4% were diabetes mellitus, 77.1% were hypertension, 30% were hypothyroidism and metabolic syndrome were 25.9% as defined by Adult Treatment Panel III clinical definition of Mets. Other variables are given in Table 1.

In the quantitative ultrasound classification system devised by Saadeh et al., steatosis can be categorized as follows : grade 1 (mild)—mild, diffuse increase in hepatic echogenicity, the hepatic vessels and diaphragm having a normal aspect; grade 2 (moderate)—moderate, diffuse increase in hepatic echogenicity, the hepatic vessels and diaphragm having a blurred aspect; grade 3 (marked)—marked increase in hepatic echogenicity, the hepatic vessels, diaphragm, and posterior liver not being visible.[14] Among 70 patients majority of patients were mild 64.28%, 25.72% were moderate and only 10 % were in severe groups.

Table: 2 Mean Vitamin D level among BMI grade:

WHO Grade	BMI	Mean Serum vitamin D level
Normalrange	18.5-24.9kg/m2	24.98±29.6
Overweight	25-29.9 kg/m2	23.39±25.74
Obesegrade1	30-34.9 kg/m2	26.11±27.93
Obesegrade2	35-39.9 kg/m2	16.63±16.3
Obesegrade3	->40 kg/m2	9.35

Table: 3 Vitamin D level on severity of liver diseases:

Gradingfibrosis of liver disease	USGgrading of fatty liver	2D Shear wave Elastography mean value	Serum vitamin D level
Mild	Grade 1	7.07	22.61±28.07
Moderate	Grade 2	8.22	24.89±26.45
Severe	Grade 3	18.16	17.4±6.4

Table: 4 Vitamin D level on other metabolic diseases:

Metabolic diseases	Totalnumberof patients	Mean vitamin D level
NAFLD	70(100%)	23.02±28.07
BMI >25	51(72.9%)	19.10±25.74
Diabetes mellitus	29(41.4%)	25.27±26.45
Hypertension	54(77.1%)	31.68±28.07
Hypothyroidism	21(30%)	18.29±17.52
Metabolic Syndrome	18(25.9%)	22.65±26.45
Dyslipidemia	17(24.28%)	24.01±29.95

DISCUSSION

Low vitamin D is prevalent in chronic liver disease patients. Even patients with mild liver disease are affected, although patients with liver cirrhosis are more commonly have severe deficiency[7]. Low serum levels of vitamin D have been observed in chronic liver diseases, especially with liver

cirrhosis[15], while in patients with NAFLD, the data are still scanty in Nepal. Our study demonstrates that the serum 25 (OH)D was significantly lower in the NAFLD was evaluated by 2 d shear wave elastography.[16] More than two thirds of NAFLD patients had vitamin D deficiency.

A systematic review of Pacifico and colleagues[17]included 45 studies exploring the association between vitamin D status and NAFLD/NASH. Of them, 29 studies reported an inverse association between vitamin D status and NAFLD, while 16 studies did not support this association. On the other hand, the meta-analysis on the relationship between serum vitamin D and NAFLD histologic severity found no association between serum vitamin D levels and disease severity as assessed by NAS and fibrosis score among patients with NAFLD[18].

In our study, the individuals with higher BMI and body weight were those who suffered NAFLD, and further studies highlight how there is a strong association between excessive adiposity and NAFLD. This association causes predisposition to systemic hypertension, dyslipidemia, and inflammation. Although Vitamin D deficiency (VDD) mechanisms that contribute to the deposition of fat in the liver are not yet well understood, studies show that VDD may be involved in the regulation of insulin action and could relate to a decrease in secretion of this hormone[19], Vitamin D also modulates the metabolism of free fatty acids (FFAs) acting on peroxisome proliferator-activated receptor (PPAR-), thereby relieving FFA-induced insulin resistance in vitro. Consequently the increased FFAs flowing in the bloodstream could promote fat deposition into the hepatocytes and the progression of NAFLD on condition of VDD20.

CONCLUSION

The results of this study showed high prevalence of serum 25(OH) vitamin D inadequacy in individuals with obesity, diabetes mellitus, hypothyroidism and metabolic syndrome which worsens as the stage of liver disease progresses.

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