

The Level of Vitamin D in NAFLD and Other Metabolic Diseases in Nepal

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Abstract:-

➤ Background and aims

Serum vitamin D level is deficient in many metabolic diseases and NAFLD. To discern the level of vitamin D among the patients with Obesity, Diabetes mellitus, Hypothyroidism, Dyslipidemia, Metabolic syndrome and NAFLD.

➤ Methods

A prospective hospital based observational study conducted from May 2019 for twelve months period in Medicine department, Bir hospital, NAMS, Nepal. Seventy patients with known fatty liver and its severity as assessed by Ultrasonogram after sorting out the exclusion criteria were enrolled. Patients were evaluated for Vitamin D level and its effects on obesity, diabetes mellitus, thyroid related disease, NAFLD and dyslipidemias. The level of vitamin D is correlated with the grade of the fatty liver and fibrotic stages of liver assessed by 2 d shear wave elastography.

➤ Results

Baseline Characteristics among seventy patients, male were 39(55.7%) and female were 31(44.3%) with mean age of the patients being 44.3 years. Among them, overweight with mean BMI of 28.2, kg/m^2 and most of them were of more than 25 kg/m^2 being 51(72.9%). Diabetes mellitus was 41.4%, hypertension in 77.1%, hypothyroidism in 30% and metabolic syndrome in 25.9%. More than 90% of vitamin D level is insufficient in all Metabolic diseases. The grade of fatty liver by ultrasound were mild in 64.28%, moderate in 25.72% and severe in only 10%. The mean fibrosis of 7.07 kpa was noted in Mild grade fatty liver, similarly mean fibrosis of 8.22 kpa in Moderate grade and 18.16 kpa in severe grade of fatty liver. The mean value of vitamin d for Mild grade were 22.61iu/ml, Moderate grade 24.89 iu/ml and for severe 17.4 iu/ml.

➤ Conclusion

The high prevalence of Vitamin D insufficiency is noted in individuals with obesity, Diabetes mellitus, Metabolic syndrome, Hypothyroidism, Dyslipidemia and NAFLD. The level of vitamin D is directly associated with the grade of fatty liver and the stages of fibrosis.

I. INTRODUCTION

In developed countries almost half of the healthy population are Vitamin D insufficient and deficient¹. About one billion people are suffering from deficiency or insufficiency of vitamin D.² Vitamin D 25(OH)D insufficiency defined as a level below 30 ng/mL and deficiency as levels below 20 ng/mL as defined by most experts.

Vitamin D deficiency is well known risk for osteoporosis, osteomalacia and increased fracture risk.^{3,4} Many reports have shown the association between vitamin D deficiency and the development of cardiovascular, degenerative, autoimmune diseases and infections, several types of cancer (prostate, colon, and breast cancer)⁵. Vitamin D deficiency is extremely common in patients with chronic liver disease. Some degree of vitamin D insufficiency is noted in Up to 93% of these patients^{6,7}. Several studies reported that the risk of mortality from all causes, including cardiovascular diseases are significantly increases in general populations with the low levels of vitamin 25(OH) D⁸. Low level of vitamin D has been associated with increase mortality among patients with chronic liver disease of different etiologies,^{9,10} such as bacterial infections, portal hypertension and its related complications¹¹ and fibrosis severity¹².

The prevalence of NAFLD associated chronic liver disease is increasing in both developing and developed countries and is considered as a leading cause of morbidity and mortality.¹³ Vitamin D has been implicated as the important factor for the progression of the fibrosis and its related complication. So vitamin D level need to be assessed in every patients of NAFLD with timely institution of vitamin D is important to prevent fibrosis and its related complication.

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 |

II. METHODS

The study was conducted from May 2019 till April 2020 for twelve months period in the Medicine department of Bir hospital NAMS, Nepal.

A prospective observational study was conducted in the hospital. Seventy patients with ultrasonography findings of fatty liver were enrolled in this study. The patients without consumption of alcohol beverages for more than 30 g/day for men and 20 g/day for women, not taking of hepatotoxic medication, and negative of HBsAG and HCV antibody tests were enrolled. Each patient was evaluated for general, systemic examination and anthropometry. Routine laboratory investigations were done.

Fatty liver and its severity was assessed by ultrasonography (USG) and fibrosis by 2d Shear wave elastography. The grade of fatty liver was categorized as Saadeh et al by ultrasonography which was defined as grade 1 (mild) grade- increase in liver echogenicity , grade 2 (moderate)- diffuse increase in liver echogenicity and blurring of diaphragm and hepatic vessels , grade 3(severe)-marked increase in hepatic echogenicity diaphragm and posterior liver not being visible. ¹⁴

Mean values of vitamin D was compared with grade of fatty liver and its severity of fibrosis 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 with NAFLD was correlated with the mean value of serum vitamin D level.

III. RESULTS

Among the enrolled patients, male were 39(55.7%) and female were 31(44.3%) with mean age of the patients were 44.3 years. The mean value of serum vitamin D level was 22.38 iu/ml in male and 23.61 iu/ml in female. Among all NAFLD patients overweight with mean BMI of 28.2, kg/m² was seen in most of the patients, among them 51(72.9%) patients were more than 25. kg/m² The prevalence in NAFLD with DM was seen in 41.4%, hypertension in 77.1%, hypothyroidism in 30% and metabolic syndrome in 25.9% as defined by Adult Treatment Panel III clinical definition of Mets. Other variables are given in table 1.

More than 90% of NAFLD and Metabolic diseases (Diabetes, Metabolic syndrome, Obesity, Hypothyroidism, and Dyslipidemia) have insufficient serum vitamin D level. In overweight patients mean value of serum vitamin D level was 23.39±25.74, in grade 1 obesity 26.11±27.93, in grade 2 obesity 16.63±16.3, in grade 3 obesity serum vitamin D level was 9.35.

Majority of patients have mild (64.28%), (25.72%) have moderate and only (10 %) have severe fatty liver. Among them in mild fibrosis, serum vitamin D level was 22.61±28.07, in moderate fibrosis was 24.89±26.45, in severe fibrosis 17.4±6.4.

Similarly among all NAFLD patients, the mean value of serum vitamin D level was 23.02±28.07. In NAFLD patients with Obesity was 19.10±25.74, with Diabetes Mellitus was 25.27±26.45, with Hypertension 31.68±28.07, with Hypothyroidism 18.29±17.52, with Metabolic syndrome 22.65±26.45, with Dyslipidemia 24.01±29.95.

Table: 2 Mean Vitamin D level among BMI grade:

| WHO Grade | BMI | Mean Serum vitamin D level |
|---------------|-----------------------------|----------------------------|
| Normal range | 18.5-24.9 kg/m ² | 24.98±29.6 |
| Overweight | 25-29.9 kg/m ² | 23.39±25.74 |
| Obese grade 1 | 30-34.9 kg/m ² | 26.11±27.93 |
| Obese grade 2 | 35-39.9 kg/m ² | 16.63±16.3 |
| Obese grade 3 | ->40 kg/m ² | 9.35 |

Patients with higher grade of obesity have lower mean vitamin D level and among morbid obese have deficient level of serum vitamin D level.

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

| Grading fibrosis of liver disease | USG grading 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 |

There were deficient level of Vitamin D level among the severe grade of fibrosis than mild and moderate grade of liver fibrosis.

Table: 4 Vitamin D level on other metabolic diseases:

| Metabolic diseases | Total number of 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 |

There were significant deficient and insufficient mean vitamin D level among NAFLD, and other metabolic diseases. In hypertensive patients, there were normal level of vitamin D level.

IV. DISCUSSION

The level of vitamin D is low in chronic liver disease and NAFLD, as shown in many previous studies. Evidences have shown that the liver cirrhosis have very low level of vitamin D in comparison to mild liver disease.⁷ In one study from Nepal, low serum vitamin D level was observed in patients with chronic liver disease especially liver cirrhosis.¹⁵ However, the data in NAFLD patients are scanty.¹⁶

In our study, the level of serum vitamin D is more deficient in patients with higher body weight, severe fatty liver and higher grade of fibrosis which is similar to the study done by Cordeiro A, et al.¹⁶ Similarly serum vitamin D level deficient in patients with Hypothyroidism and NAFLD which resembles the study done by Mackawy MH et al.¹⁷ Karau PB et al in their study found that the level of vitamin D is high among Diabetic patients which is similar to our study showing more than 90% of patients with diabetes with NAFLD.¹⁸ A study done by Alquaiz AM in their study found the association of vitamin D level and dyslipidemia which is similar to our study.¹⁹ On contrary to study done by Vatakencherry R J. et al showing high prevalence of vitamin D among hypertensive patients, our study showed no association of serum vitamin D level in hypertensive patients with NAFLD.²⁰ However our study was done to see the association of serum vitamin D level with obesity, hypothyroidism, Diabetes mellitus, dyslipidemia in NAFLD patients but the studies coded over here were done in isolated metabolic diseases without NAFLD.

In my study more than 90% of vitamin D level is insufficient in all Metabolic diseases including NAFLD. Pacifico and colleagues in their systemic review of 45 studies had explored the association between NAFLD and vitamin D.²¹ 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 NASH and fibrosis score among patients with NAFLD.²²

V. CONCLUSION

The high prevalence of Vitamin D insufficiency is noted in individuals with obesity, Diabetes mellitus, Metabolic syndrome, Hypothyroidism, Dyslipidemia and NAFLD. The level of vitamin D is directly associated with the grade of fatty liver and the stages of fibrosis.

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