The Role Of Serum 25 Hydroxy Vitamin D Level, Lipid Profile And Blood Glucose Level In Diagnosed Case Of Osteoporosis

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ABSTRACT

Background and Objectives: Osteoporosis is the most prevalent metabolic bone disease in postmenopausal women associated with reduced bone mass and increased bone fracture. OP is often associated with brittle fractures, with approximately 1/2 of women and 1/5 of men expected to experience an osteoporotic fracture during their lifetime. An awareness regarding the preventive, curative and rehabilitative care as well as a proper health policy is the need of hour. In the literature, scarce data investigate the link between 25-hydroxyvitamin D (25[OH]D), lipid profile and blood glucose level in the osteoporosis (OP) population. 25(OH)D, as a calcium-regulating hormone, can inhibit the rise of parathyroid hormone, increase bone mineralization to prevent bone loss, enhance muscle strength, improve balance, and prevent falls in the elderly. The aim of this study was to evaluate the independent relationship between serum 25-hydroxyvitamin D (25[OH]D), lipid profiles and fasting blood glucose levels (FBG) in a group of patients diagnosed with OP.

Materials & Methods: This is a cross sectional study recruiting 300 osteoporotic patients from orthopedic OPD. Mean, median, standard deviation, percentage and frequency will be used to describe demographic data. Chi square test was applied for analysis of categorical data and independent t test was applied for numerical data to compare the mean between two groups. Pearson's/ Spearman's correlation will be used to correlate Vitamin D, lipid profile and blood glucose level. For Non parametric data Kruskal Wallis test was applied.

Hypothesis: There is significant altered level of vitamin D and high density lipoprotein (HDL) level and significant relation among the parameters (vitamin D, lipid profile and blood glucose level) in osteoporosis.

Result: The mean age of the diagnosed osteoporotic patient was 59.81 years. In which 61% were female and 39% were male. There was significant high blood glucose level in osteoporotic female (192.47 ±61.76, *P* 0.00*) than osteoporotic male (163.77 ±39.09). Hypertriglyceridemia was seen in female (222.96 ± 100. 78, *P* 0.00*). The analysis also shows significant positive co-relation of fasting blood glucose level with age (*P*<0.05), TC(*P* <0.01),TG(*P* 0.05)

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and significant inverse correlation with vitamin D (P<0.01). This analysis also shows significant negative co-relation of vitamin D with HDL(p<0.01) in case of osteoporotic patient.

Conclusion: The status of Vitamin D is inversely proportional to hyperlipidemia and hyperglycemia with risks of cardiovascular disorders and hence chances of increase mortality rate. So, the importance of management of vitamin D deficiency or insufficiency with hyperglycemia to correct level of lipid profile and protection of CVS disorders in osteoporosis.

Keywords: *Osteoporosis(OP); Vitamin D; HDL- High density lipoprotein; LDL- Low density lipoprotein; TC- Total cholesterol; TG- Triaclyglyceride; Blood glucose level*

INTRODUCTION

Osteoporosis (OP) represents a skeletal sickness described by weakened bone mass and bone microarchitecture that quickly leads to bone fractures [1]. OP diagnosis is based on bone mineral density (BMD) [1]. Currently, one in three women and one in five men above the age of fifty will experience osteoporotic fractures, which makes osteoporosis a defining health problem of our aging society. These osteoporotic fractures predominantly occur at the level of the forearm, hip and lumbar spine bone and are associated with substantial morbidity and mortality. Hip fractures, for example, are responsible for a mortality rate up to 36% in the first year after the fracture occurred [2][3]. OP is often associated with brittle fractures, with approximately 1/2 of women and 1/5 of men expected to experience an osteoporotic fracture during their lifetime [4]. Osteoporosis and osteopenia are important health problems characterized by low bone mineral density (BMD), microarchitecture deterioration, and increased fracture risk [5].

CLINICAL RISK FACTORS OF OSTEOPOROSIS

Patients who have suffered one or more fragility fractures at any site are at increased risk of having subsequent fracture for any given value of bone mineral. The earlier the age at fracture and the greater the number of previous fractures, the greater the subsequent risk. The risk of vertebral fractures is particularly high in those with prevalent vertebral fractures and is at least 2-fold increased. A wrist fracture doubles the risk of hip fracture and triples the risk of vertebral fracture [6]. A very large number of other risk factors for low bone mass or fracture have been identified (Table 1)

Table 1: Factors contributing to osteoporosis [7]

Genetic or constitutional White or asiatic ethnicity
Family (maternal) history of fractures
Small body frame Long hip axis length
Premature menopause (B45 years)
Late menarche
Lifestyle and nutritional
Nulliparity
Prolonged secondary amenorrhea
Smoking
Excessive alcohol intake
Inactivity
Prolonged immobilization
Prolonged parenteral nutrition
Low body weight
Medical disorders
Anorexia nervosa
Malabsorption due to gastrointestinal and hepatobiliary diseases
Primary hyperparathyroidism
Thyrotoxicosis
Primary hypogonadism
Prolactinoma
Hypercortisolism

Osteogenesis imperfecta
Rheumatoid arthritis
Chronic obstructive lung disease
Chronic neurological disorders
Chronic renal failure
Mastocytosis Type I diabetes
Post transplantation
Drugs Chronic corticosteroid therapy
Excessive thyroid therapy
Anticoagulants Chemotherapy
Gonadotropin-releasing hormone agonist or antagonist
Anticonvulsant
Chronic phosphate binding antacid use

Several hormonal and biochemical factors known to affect bone metabolism have been shown to change with age in men in parallel with their age-related decline in bone mineral density (BMD). These parameters have therefore been implicated in the pathogenesis of aging bone loss, although whether they are causal or simply epiphenomena is still not known.

Vitamin D and calcium are essential for maintaining bone health, and their deficiency is an important risk factor for the development of osteoporosis. Vitamin D is naturally produced in human skin upon exposure to sunlight. Due to a modern lifestyle, there is insufficient exposure to sunlight for the synthesis of vitamin D [8], resulting in particularly low seasonal concentrations of 25-Hydroxy-Vitamin D3 (25(OH)D3), usually during winter and spring [9]. Prevalence of vitamin D deficiency in elderly patients with hip fractures varies from 50 to 62% in different population in various geographical areas.

Osteoporosis and cardiovascular (CVDs) may be linked. Osteoporosis and CVDs share many risk factors, such as advancing age, premature menopause, genetics, a sedentary lifestyle and smoking, etc. [10]. There is also vitro evidence suggesting lipids are involved in the development of osteoporosis [11]. However, the association between lipid profile and osteoporosis in human studies is still controversial [11]. Majority of human studies suggested that there were negative associations between lipid biomarkers and bone mineral density (BMD) [12,13].

Type 2 diabetes mellitus (T2DM) and OP are both highly prevalent chronic diseases, and the association between the two is an area of active research. Diabetes is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. T2DM, which accounts for 90–95% of those with diabetes previously referred to as non–insulin-dependent diabetes, T2DM, or adult-onset diabetes, encompasses individuals who have insulin resistance and usually have relative (rather than absolute) insulin deficiency[14]. Furthermore, the fracture risk in patients with T2DM is increased[15].

Vitamin D deficiency is associated with various diseases harmful to bone health, including diabetes, chronic obstructive pulmonary disease, a variety of autoimmune diseases and dyslipidemia [15]. There is paucity of literature on association of vitamin D status, lipid profile and blood glucose level prevalence of VDD and bone mass status in Indian patients with fragility hip fracture. If the association is confirmed, the clinical management of blood glucose in OP patients with serum 25(OH)D deficiency, dyslipidemia has instructive implications.

Hypertension (HTN) is the main risk factor for cardiovascular mortality, morbidity, and disability that adversely impacts both human capital and medical costs [16]. Globally, the prevalence of hypertension is increased with economic development and acceleration of population ageing, as well as modifications in lifestyle. According to reported data, HTN is a major cause of ischemic heart disease, stroke, and premature deaths [17]. A possible association between osteoporosis and the lipid profile could be explained at a molecular level as well: Franceschi described the ‘global reduction in the capacity to cope with a variety of stressors and a concomitant progressive increase in proinflammatory status’ (the “inflammaging” theory) which can lead to age related diseases such as osteoporosis (18). Another theory, based on the epidemiological link between hyperlipidemia, visceral obesity and

osteoporosis, supports these findings through the 'osteo-lipo-vascular interactions' which exist due to the common origin of osteoblasts, vascular smooth muscle cells and adipocytes (19).

In this study, we sought to gain additional information beyond what has been reported so far. While clinical studies, especially on a population such as ours, are lacking regarding the independent relation of vitamin D, lipid profile and blood glucose level in osteoporotic patient.

MATERIALS AND METHODS

Patients of age 40 to 70 years diagnosed with osteoporosis attending tertiary care hospital of MIHS, Janakpur, Nepal. The demographics (i.e age and sex), clinical laboratory parameters (lipid profiles, fasting blood glucose level, vitamin D) were taken in fasting state from 6 am to 10 am, prescribed and dispensation drugs were recorded from 20th April 2024 to 20th October 2024. We studied 300 osteoporotic patient in which 61% were female and 39% were male. This cross-sectional study has general obejective i) To find the level of 25(OH)vit-D level, lipid profile and blood glucose in diagnosed case of osteoporotic patient ii) To investigate the relationship among the 25(OH)vit-D level, lipid profile and blood glucose level and specific objective i) To find the association of osteoporosis with demographic profile (age, sex).

Subjects with established diagnosis of osteoporosis were included in this research and patient under medication of vitamin D, Anti hyperlipidemic drug were excluded from the analysis. Taking the reference from the study done in China, Vitamin D deficiency is prevalent in the middle-aged and elderly northwestern Chinese population and is largely attributed to CHD, obesity, dyslipidemia, older age, female sex, and smoking. The prevalence of vitamin D deficiency in osteoporosis was 75.2% [8]. A self-generated proforma will be filled by interviewing the patients only after taking their informed written consent.

The informed consent were taken from the patients fulfilling inclusion criteria. After collecting the blood sample in plain vial. It will be centrifuged at 3000 RPM for 10 minutes to separate the serum. The serum were stored at -20 ºC till the analysis of Biochemical parameter. Estimation of VIT-D was done by Chemiluminiscence immunoassay technology. And Lipid profiles and urea, creatinine, calcium, phosphate, sodium blood glucose will be done by $fully\ automatic\ COBAS\ C311$. All the data will be entered in Microsoft Excel 2010 and statistical analyses will be done using SPSS 11.0. Normality test will be performed using Kolmogorov Smirnov test. Gender is expressed in frequency and percentage. Descriptive statics i.e. mean ± SD or median, inter-quartile range are used to represent the biochemical parameters (Vitamin D,Total cholesterol,Triacylglycerol,HDL,LDL). Chi square test is applied for categorical data and independent t test will be applied for numerical data to compare the mean between two groups. Spearman's correlation is used to correlate Vitamin D, lipid profile and blood glucose. For Nonparametric Mann Whitney U test is applied. p value ≤ 0.05 will be considered as statistically significant.

RESULT

This is a hospital based descriptive cross-sectional study among osteoporotic patient at Madhesh institute of health sciences, Janakpur, Nepal. The study was conducted in the department of biochemistry in collaboration with the department of orthopedic. A total no. of 300 subjects were selected as the study group for the present study. Level of vitamin D, total cholesterol, triacylglycerol, HDL, LDL and blood glucose level were estimated for all the samples of the study group.

Table 2: General characteristics of participants.

Parameters	All subjects(n=300)	Normal range
Age(years)	59.81	
Female(%)	61	
Male(%)	39	
Vitamin D(ng/ml)	19.78± 7.74	30-100
TC(mg/dl)	251.65±57.45	150-250
TG(mg/dl	211.29±102.29	50-130
LDL(mg/dl)	170.28±49.75	50-130

HDL(mg/dl)	30.1±14.5	40-75
Glucose (mg/dl)	181.28±55.78	70-100

Table 2 depicts the baseline characteristics of the study population. Median age of the participants with osteoporosis was 59.81. There were 61% female and 39 % male in our study. The mean value of vitamin D in the study is 19.78± 7.74, indicative of vitamin D deficiency and the value of lipid profiles (TC,TG,LDL) is high and low HDl level indicative of hyperlipidemia in the cases. Whereas blood glucose level is 123.64±49.17, indicative of hyperglycemia among the patient of osteoporosis.

Table 3: Differences between men and women in Vitamin D level, lipid profile, glucose level and age in osteoporotic patients (n=300).

Parameters	**Gender**		**p-value***
	Female (n=183)	**Male (n=117)**	
FBS(mg/dl)	192.47± 61.76	163.77± 39.09	0.00*
TC(mg/dl)	257.14± 61.46	243.06± 49.59	0.81
TG(mg/dl)	222.96± 100.78	193.03± 102.39	0.00*
HDL(mg/dl)	30.13± 14.92	30.05± 13.88	0.53
LDL(mg/dl)	182.41± 54.72	174.4± 40.52	0.403
VIT D(ng/ml)	19.9± 7.31	19.6± 8.4	0.62
Age	62.35±7.81	55.83±12.22	0.00*

*Mann-Whitney U test; p-value<0.05 is statistically significant

Table 3 shows the differences between men and women in different biochemical parameters where the age of female is 62.35±7.81 which is more than the age of male and has significant differences. It also resulted that FBS was significantly high in female (p=00.00*) than in male. Similarly, the value of triglyacylglyceride was also significantly high in female(p=0.00*) than in male.

Table 4: correlation of different parameters(n=300)

Characteristics	**Spearman's correlation**	**Age**	**FBS**	**TC**	**TG**	**HDL**	**LDL**	**VIT D**
Age	r	1.000						
	p-value	-						
FBS	r	**0.12***	1.000					
	p-value	**<0.05**	-					
TC	r	-0.04	**0.16****	1.000				
	p-value	0.44	**<0.01**	-				
TG	r	-0.10	**0.11***	**0.458*****	1.000			
	p-value	0.06	**<0.05**	**<0.01**	-			
HDL	r	0.1	0.01	**0.17****	**-0.15****	1.000		
	p-value	0.08	0.74	**<0.01**	**<0.01**	-		
LDL	r	-0.03	0.142	**0.91****	**0.16****	-0.03	1.000	
	p-value	0.53	0.01	**<0.01**	**<0.01**	0.6	-	
VIT D	r	-0.59	**-0.25****	-0.04	-0.005	**0.15****	-0.09	1.000

	p-value	0.3	**<0.01**	0.42	0.92	**<0.01**	0.08	-
r=Spearman's Correlation								
**. Spearman's Correlation is significant at the 0.01 level (2-tailed).								
*. Spearman's Correlation is significant at the 0.05 level (2-tailed).								

Table 4 elucidated the correlation of different parameters in osteoporotic cases and shows that there is significant positive correlation of fasting blood glucose level with age (<0.05), TC (<0.01), TG (<0.05) and significant inverse correlation with vitamin D($p<0.01$) . This analysis also revealed significant negative correlation of vitamin D with HDL($p<0.01$) in case of osteoporotic patient.

DISCUSSION

In this retrospective cross-section study, we found that in the osteoporotic population, the common age group in Madhesh institute of health sciences was 55.39 which were more common in female age group.

We explored that in the study done by Sozen et al [20], It was estimated that 50% women and 20% of men over the age of 50 years will have an osteoporosis-related fracture in their remaining life.

In the study done by Guo Tang et al[21] done in 2023, stated that the status of vitamin D levels (OR: 0.787, 95% CI: 0.674-0.918, P=0.002), and outdoor activity time (OR: 0.556, 95% CI: 0.338-0.915, P=0.021) were negatively correlated with postmenopausal osteoporosis. Which is also related to our study depicted the vitamin D status as 17.80±8.15.

This research has revealed that in the studied osteoporotic patients, the blood serum levels of Vitamin D were inversely linked with the attention of TG. In contrast,25(OH)D levels were positively linked with the HDL concentrations. Jungert et al. [22] established that 25(OH)D concentrations were negatively related to TC and LDL-C in old German females. J-m Wang et al. also found that vitamin D serum levels were adversely linked with TC and LDL-C in diabetic individuals [23].

Our results showed a negative link between 25(OH)D and blood glucose concentration in osteoporotic individuals. Similarly in the study done by Yao-Wei Ye et al[24], In his retrospective cross-sectional study done at tertiary referral center , 2084 osteoporotic patients analyzed in their study. There was a linear significantly negative association between serum 25(OH)D and FBG (β, - 0.02; 95% CI - 0.03 to - 0.01; P = 0.0011) in the fully adjusted models. Specifically, when serum 25(OH)D level was less than 23.39 ng/mL, FBG decreased by 0.04 mmol/L for every 1 ng/mL increase of serum 25(OH)D level.

In the retrospective cross-sectional study done by Si-ming Xu et al[24] done at Kunshan Hospital of Jiangsu University, including 2063 OP patients, reported that in the OP patients, the serum 25(OH)D levels were inversely connected with blood TGs concentration, whereas they were positively associated with the HDL, apolipoprotein-A, and lipoprotein A levels. Meanwhile, the researcher also found a nonlinear relationship and threshold effect between serum 25(OH)D and TC, LDL-C. Furthermore, there were positive correlations between the blood serum 25(OH)D levels and the levels of TC and LDL-C when 25(OH)D concentrations ranged from 0 to 10.04 ng/mL. which is proved by our research that there was negative correlation of vitamin D level and triacylglyeceride. And the nonlinear relation of vitamin D with TC and LDL.

In the retrospective analysis done by Hao-han et al[25] conducted on 710 patients shows $1,25(OH)_2D_3$ negatively correlates with TC, LDL-C, and Castelli index. This suggests that individuals with osteoporosis, their bone formation capacity may be weakened, which is not beneficial for bone health. Therefore, individuals with low Vitamin D should take early preventive measures against osteoporosis.

In general, more extensive data, rigorous experimental and multi-center designs are needed in future to verify that serum HDL-C is negatively correlated with osteoporosis, as well as more fundamental studies on the molecular level of HDL-C and bone metabolism to obtain a relatively more objective and reliable evidence-based basis.

CONCLUSION

The present study demonstrated that status of Vitamin D is inversely proportional to hyperlipidemia and hyperglycemia with risks of cardiovascular disorders and hence chances of increase mortality rate. So, the importance of management of vitamin D deficiency or insufficiency with hyperglycemia to correct level of lipid profile and protection of CVS disorders in osteoporosis. However, future prospective intervention studies are necessary with large sample size to confirm this hypothesis.

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LIMITATIONS

Our study had several limitations. First, the dietary quality and lifestyle factors that might be associated with the level of Vitamin D and the prevalence of osteoporosis were not documented in the study questionnaire. Second, smoking, drinking, diet, coffee and tea consumption, method and frequency of exercise, and statin use as well as stress level, among others, were not documented in this study but might be associated with the prevalence of osteoporosis. Third, because this is a cross-sectional study, associations might be determined but causation could not be. Therefore, explanations for the results of this study should be taken with caution.

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