INTRODUCTION

Vitamin D deficiency (VDD) is a globally widespread pandemic [1] that affects the functions of various physiological systems. Over the past decade, the extraskletal effects of vitamin D are gaining importance. The discovery of vitamin D receptors (VDRs) in various organs coupled with the local synthesis of vitamin D strengthen this concept further [2]. VDD could well be a new risk factor for many diseases such as hypertension [3], cardiovascular disease [4,5], Type 1 and Type 2 diabetes [6], immune disorders, osteoporosis, and cancer [7].

Over 50% Type 2 diabetes mellitus (T2DM) patients have 20 ng/L of serum 25 hydroxyvitaminD (25(OH) D) level [8]. The American Diabetic Association and the American Heart Association strongly recommended the control of nonglycemic risk factors in diabetes patients to halt the onset as well as propensity of various complications [1]. Studies regarding the influence of serum vitamin D levels on diabetes and its associated dyslipidemia yielded conflicting results [9-11] and there are few comparative studies on the prevalence of VDD among individuals with and without diabetes [12]. In an attempt to address the same, this study is aimed to investigate the existence of VDD among diabetes patients as compared to nondiabetes individuals and its effect on both glycemic status and lipid profile.

METHODS

This is a hospital-based case-control study conducted on 200 subjects of both genders (100 Type 2 diabetes and 100 nondiabetes individuals) aged 40-60 years. The study protocol was approved by Institutional Ethics Committee (No. IEC KMC MLR 02-14/27) and the participants were enrolled after obtaining duly signed informed consent. Individuals who were on vitamin D supplementation and subjects with any acute or chronic illness as documented by history were excluded from the study. Fasting serum 25(OH) D levels (Diasource, USA) by enzyme-linked immunosorbent assay, fasting blood sugar (FBS), lipid profile including total cholesterol (TC), triglycerides (TG), high density lipoprotein (HDL), low density lipoprotein (LDL), TC/HDL, and very LDL were estimated. Atherogenic index of plasma (AIP) was calculated. Group comparisons were done by one-way analysis of variance followed by post-hoc Tukey's test and Student's independent t-test. Chi-square test was performed for categorical variables. Correlation was done by Pearson's analysis. p<0.05 was considered significant.

RESULTS

The average serum 25(OH) D levels were significantly (p<0.001) low in diabetes group. The prevalence of VDD and the percentage of insufficient and sufficient categories was significantly (p<0.001) high and low, respectively, in diabetes group. In the deficient category, diabetes group had severe VDD with significantly low-HDL and elevated TGs and there was an insignificant but negative association between serum vitamin D levels, FBS, HbA1c, TC, TG, LDL, TC/HDL, and AIP among diabetes patients.

Conclusion: The occurrence of severe VDD coupled with the independent association of the same with the glycemic and lipid profiles in Type 2 diabetes may further add to the aggravation of complications.

Keywords: Vitamin D deficiency, Type 2 diabetes, Glycemic and lipid indices.
the prevalence of VDD was significantly high in diabetes group (54% vs. 86%) and the percentage of insufficient and sufficient categories were also significantly low (5% and 9% vs. 25%, and 21%) respectively in diabetes group (Fig. 1). In the VDD category (n=140), the ratio of diabetes versus nondiabetic individuals was found to be 86:54 and the diabetes group had severe VDD with significantly low-HDL, elevated TGs, TC/HDL ratio, and AIP (Table 3). Although insignificant there was a negative association between serum vitamin D levels FBS, HbA1c, TC, TG, LDL, TC/HDL, and AIP among diabetes patients (Table 4).

**DISCUSSION**

VDD is considered as a global pandemic and has been reported in healthy population. More than 90% of relatively healthy Indians have low 25(OH) D levels. The common causes for VDD in apparently healthy individuals are low dietary intake and indoor life style with minimal exposure to sunlight [13]. It has been proposed that low serum vitamin D levels predispose individuals to T2DM [14]. Studies also demonstrated higher prevalence of VDD among diabetes patients compared to nondiabetic individuals [14]. In this study, more than half (54%) of the nondiabetic individuals were found to have VDD whereas the extent of VDD was much higher (86%) in diabetic group (Fig. 1). These findings reiterate the previous reports of widespread VDD even among apparently healthy subjects and those affected by diabetes are more severely affected. Diabetes patients are more prone to VDD has been supported by previous studies where Boucher B et al., Isaia G et al., Mattila C et al., reported correlation of low serum 25(OH) D concentrations with impaired glucose tolerance and an increased risk of Type 2 diabetes [14-16]. Evidence from cross-sectional studies showed that low serum 25-(OH)D levels are linked to impaired glucose tolerance and diabetes [18]. A meta-analysis of 21 prospective studies concluded that lower serum vitamin D levels are associated with hyperglycemia and insulin resistance [19]. The presence of VDR and vitamin D binding proteins (VDBP) in pancreatic tissues strengthen the concept of vitamin D being essential for insulin synthesis and secretion [14]. The probable mechanisms for VDD among diabetes patients could be obesity, vitamin D being fat soluble gets sequestered in adipose tissue leading to low serum levels) decreased VDBP secondary to reduced function or availability of megalin or low density lipoprotein-related protein 2 (hasten the metabolism and elimination of active form of vitamin D) [20].

Vitamin D was proposed to exert favorable actions in Type 2 DM patients through the following pathways, (i) Improved β-cell function
Data from previous studies pointed the role of serum 25(OH) D levels in dyslipidemia. Nevertheless, the exact mechanism(s) relating VDD with dyslipidemia are not well known and there exist disparity [27]. In the current study, there was no significant difference in serum lipid profile across the vitamin D categories of both the groups (Tables 1 and 2) but in the diabetes group the deficient category had elevated TGs, AIP, and low-HDL compared to other two categories. Similar to the glycemic profile the lipid profile was also better in insufficient category which may be related to the specific pharmatherapy of these patients. Jorde R, Grimnes G [28] reported a positive correlation between vitamin D status and HDL whereas, Xinyan B et al [11] found no such association but they reported a significant inverse relation between TC/HDL, LDL/HDL ratios and serum 25(OH) D levels. In this study, insignificant but negative and positive associations were reported between serum 25(OH) D levels, TC, TGs, TC/HDL ratio, AIP and HDL respectively, among the diabetes patients (Table 4). An AIP above 0.5 has been a suggestive of atherogenic risk [29]. Although diabetes patients of deficient category had higher AIP compared to nondiabetes group irrespective of the vitamin D status it is within the specified cut off. Saedisomeila et al [30] established a statistically insignificant positive relation between serum 25(OH) D levels, LDL, and TC. They also showed an inverse relationship between serum 25(OH) D and TG levels in diabetes individuals. Venkatesh G et al showed that exposure to sun light had no significant changes on lipid profile of prediabetes subjects. The authors highlighted the need for appropriate vitamin D supplementation with intensive life style changes for the prevention or delay of T2DM progression [31].

The modulatory effects of vitamin D on lipid profile has been through direct and indirect effects and its role in attenuation of serum TGs may be due to the regulatory action that increases the lipoprotein lipase activity in adiposity [31]. The role of calcium-mediated regulation of cholesterol and other components of lipid profile is not well known. In a study conducted by Querfeld et al [32] they reported that vitamin D supplementation had a significant effect over specific components of lipid profile and revealed 8% (0.28 mmol/L) increase in serum LDL-C and a 16% (0.22 mmol/L) decrease in serum TG compared to the placebo group.

The strengths of the study are comparison of serum vitamin D levels between diabetes and nondiabetes individuals with reference to the severity of VDD among diabetes patients with an emphasis on deficient category between the groups. The limitation is the influence of diabetes, drug therapy and other comorbidities on the study variables was not considered.

CONCLUSION

The occurrence of severe VDD coupled with the negative association of the same although insignificant with the glycemic and lipid profiles excluding HDL in diabetes population may further add to the aggravation of complications in already compromised situation. Hence, maintenance of adequate serum vitamin D levels should be a priority especially in diabetes individuals.

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