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25-hydroxycholecalciferol and dyslipidemia in type 2 Diabetic subjects

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ABSTRACT

Evaluating the 25-hydroxycholecalciferol and blood lipids and their relationship in type 2 Diabetic subjects. Observational study. Department of Medicine, Isra University Hospital and Consultant Clinics Hyderabad from January2014 to July 2014. A sample of 200 diagnosed type 2 DM were selected through non-probability purposive sampling. Blood lipids, blood urea nitrogen, serum creatinine, fasting blood glucose, alkaline phosphatase, serum calcium and phosphate were detected. 25-hydroxycholecalciferol was detected by ARCHITECT I 1000 system. Data was analyzed on SPSS version 21.0. Data was analyzed on SPSS version 22.0 at 95% confidence interval. Low 25-hydroxycholecalciferol was noted in 94% and dyslipidemia in 66.5% of 25-hydroxycholecalciferol deficient type 2 diabetic subjects. Pearson's correlation showed negative correlation of 25-hydroxycholecalciferol with LDLc, VLDLc, serum triglycerides, and cholesterol and positive correlation with HDLc. The present study reports 25- hydroxycholecalciferol deficiency and dyslipidemia in type 2 diabetic subjects. 25-hydroxycholecalciferol showed positive association with high density lipoprotein (HDLc) and inverse association with LDLc, serum cholesterol and triglycerides.

Introduction

Estimated world prevalence of 25-hydroxycholecalciferol deficiency in adults is approximately 50% with lowest reported prevalence of 2-30% in the Europe.[1] While 30- 50% is the estimate of insufficient 25-hydroxycholecalciferol reported in the general population.[2] The 25-hydroxycholecalciferol is major metabolite of vitamin D circulating in the blood. It approximates 95% of total Vitamin D3 and remaining is the vitamin D2. Estimated serum 25-hydroxycholecalciferol is a considered a sensitive measure of vitamin D.[3] Thus 25-hydroxycholecalciferol estimation is clinically used for the diagnosis, supplementation and treatment. It is a good indicator of dietary supply and sunlight production. Recently, 25-hydroxycholecalciferol has drawn major attention in normal and disease conditions. In the United States, deficient 25-hydroxycholecalciferol is reported in 36% and insufficiency in 57% of general medical patients.[4] Vitamin 25-hydroxycholecalciferol deficiency has now taken shapes of an epidemic in the USA.[5] Similar are the reports from the European continent with pockets of severe 25-hydroxycholecalciferol deficiency. One of three persons is 25-hydroxycholecalciferol deficient, has been reported from Australia.[6]

Similarly, Pakistani population is seriously suffering from 25-hydroxycholecalciferol deficiency.[7-9] Exact estimate of 25-hydroxycholecalciferol deficiency for Pakistan is seriously lacking and has not gained attention by the health authorities and the government. The condition is compounded by the fact that the people are not aware of 25-hydroxycholecalciferol deficiency, and its consequences and solution. In short, there is a total lack of public awareness[7-9]

25-hydroxycholecalciferol has been linked to the disease states such as; atherosclerosis, [10] stroke, 11, 12 systemic hypertension, [13] Diabetes mellitus,[14] obesity,[15] and the myocardial infarction. [16] Recently, dyslipidemia has been linked to be associated with 25-hydroxycholecalciferol deficiency. Dyslipidemia is an independent risk factor for the atherosclerotic disease such as myocardial infarction and stroke.[17-18] Recent studies had shown association of 25-hydroxycholecalciferol deficiency and dyslipidemia.[19-20]

Keeping in view the whole scenario, there is urgent need to highlight the issue as the 25-hydroxycholecalciferol deficiency is prevalent in Pakistan and similarly the Diabetes mellitus, dyslipidemia and associated complications. The Present study is a small scale study which was conducted to have a bird`s eye view of evaluating 25-hydroxycholecalciferol and association with the blood lipids in our indigenous type 2 diabetic population.

Subjects and Methods

The present observational study was conducted at the Department of Medicine, Isra University, and Hyderabad from January-July 2014. Diagnosed type 2 diabetic subjects were informed about the purpose of study, its advantages and disadvantages. Only volunteer subjects were informed in detail about the study protocol. Eventually, a sample of 200 diagnosed subjects was selected. Non probability purposive sampling was used for subject selection. Inclusion and exclusion criteria were exercised. Diagnosed type 2 diabetics, of 30-60 years of age and volunteers were inclusion criteria.

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Diabetic nephropathy, renal failure, vitamin D supplements, diuretic and β-blockers drugs were exclusion criteria. Smokers were also excluded. Normal, insufficient and deficient 25-hydroxycholecalciferol were categorized as >30ng/dl, 20-30 ng/dl and <20ng/dl respectively. Systolic and diastolic blood pressure >140mmHg and >90mmHg was defined as systemic hypertension. Fasting blood glucose >110mg/dL were considered as diabetic.[21] Dyslipidemia was defined as cholesterol >200mg/dL, LDL-C >130mg/dL, HDL-C <40mg/dL, VLDL-C >30mg/dL, and triglycerides >150mg/dL respectively. Venous blood samples were drawn from ante cubital vein by 24 Gauge disposable syringes (Becktin Dickinson, USA) after alcohol swab was applied. Saniplast was applied after procedure. The blood was centrifuged at 4000rpm for 10 minutes and serum was frozen at -20°C. Blood and sera were used for detection of blood lipids, BUN, SERUM creatinine, blood glucose, alkaline phosphatase, and serum calcium and serum phosphate by standard biochemical testing. Serum cholesterol by colorimetric method, blood glucose by glucose oxidase method, serum triglycerides by enzymatic method, HDLc by precipitant method, and LDLc by the Fried Ewald's formula.[22] 25-hydroxycholecalciferol was detected by ARCHITECT I 1000 system. Ethical approval and informed consent protocol was obeyed. Proforma was designed for data collection, which was entered in SPSS version 21.0. Data was analyzed by student's t test and chi square test for the numerical and categorical variables. Pearson's correlation was used for the correlation of variables. P value significance was defined as < 0.05.

Results

The present study was conducted at the Department of Medicine, Isra University Hyderabad, and Sindh. 200 diagnosed cases of type 2 Diabetes mellitus (DM) were selected according to criteria and were studied for the 25-hydroxy cholecalciferol, dyslipidemia and their possible association. Age, gender, BMI, body weight, Blood urea nitrogen (BUN), serum creatinine, systemic hypertension and dyslipidemia are shown in table 1. Age of study subjects noted was 48±11.7 years. Mean± S.D of 25-hydroxycholecalciferol was found low noted as 28.20±5.30 ng/dl (95% CI 17.90-33.1). Graph 1 shows the frequency of normal, insufficient and deficient 25-hydroxycholecalciferol as 6%, 4.5% and 84.4% respectively (p=0.0001). Mean± S.D of 25-hydroxycholecalciferol in 3 categories was noted as 37.6± 1.7, 26.2±2.7 and 11.13± 4.17 ng/dl respectively (p=0.0001). 25-hydroxycholecalciferol values as low as 4.32 ng/dl were noted in the diabetic population of the present study. Low 25-hydroxycholecalciferol was noted in 94% of diabetic subjects. Table 2 shows the blood lipids and other biochemical parameters in subjects with normal and low 25-hydroxycholecalciferol. LDL-c, serum cholesterol, and triglycerides were raised in subjects with low 25-hydroxycholecalciferol. HDL was reduced in 25-hydroxycholecalciferol deficient subjects. VLDL showed no differences as shown in table 2. Dyslipidemia was noted in 66.5% of total study subjects (table 1). Pearson's correlation showed negative correlation of 25- hydroxycholecalciferol with LDLc, VLDLc, serum triglycerides, and cholesterol. A positive correlation was noted for HDLc and 25-hydroxycholecalciferol.

Table. 1. Characteristics in study subjects (n=200).

Age	48±11.7 years
Male	130 (65%)
Female	70 (35%)
BMI (kg/m^2)	29±4.5
Weight (kg)	69±23.8
Systemic hypertension	77 (38%)
Dyslipidemia	133 (66.5%)
Blood urea nitrogen (mg/dl)	10.5±2.4
Serum creatinine (mg/dl)	1.1±0.3

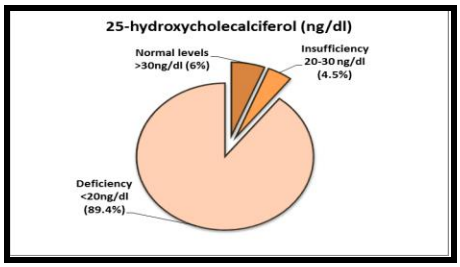
Table. 2. Blood lipids and biochemical parameters in study subjects (n=200).

	Normal 25-hydroxy-D_3	Low 25-hydroxy-D_3	p-value
HDLc (mg/dl)	40.3±7.5	32.4±7.37	0.005
LDLc (mg/dl)	91.2±17.3	112.9±27.5	0.001
VLDL (mg/dl)	39.78 ± 13.9	38 ± 17.23	0.31
Triglycerides (mg/dl)	129.7±41.9	213.2±90.3	0.0001
Total cholesterol (mg/dl)	149.2±21.6	211.3±34.4	0.0001
Fasting blood glucose (mg/dl)	117.7±15.3	123.7±29.3	0.001
Serum calcium (mg/dl)	9.8±1.6	7.1±1.5	0.001
Serum phosphorus (mg/dl)	2.45±0.7	2.3±0.21	0.002
Alkaline phosphatase (IU)	100.5±10.78	121.7±5.6	0.0001

Table 3. Pearson's correlation of 25-hydroxcholecalciferol (n=200).

	r-value	p-value
HDLc (mg/dl)	0.481	0.0001
LDLc (mg/dl)	-0.367	0.001
VLDL (mg/dl)	-0.281	0.01
Triglycerides (mg/dl)	-0.372	0.001
Total cholesterol (mg/dl)	-0.412	0.0002

r-value= correlation coefficient



Graph 1. Pie chart showing the frequency of 25-hydroxycholecalciferol.

Discussion

First conclusive finding of present study is low 25-hydroxycholecalciferol which was noted in approximately 94% of study subjects. And second important finding of clinical significance is the dyslipidemia which was noted in 66.5% of the study subjects. Low 25-hydroxycholecalciferol is consistent to previous studies reported from Pakistan.[23-25] A previous study[26] showed normal, insufficiency and deficiency of 25-hydroxycholecalciferol in 3%, 10% and 87% subjects respectively, this is parallel to present findings of 6%, 4.5% and 89.4% respectively. 25-hydroxycholecalciferol of 90.1% has been reported in a previous study from Karachi.[27] The epidemic of 25-hydroxycholecalciferol deficiency is very pertinent to Pakistan, but reports from developed countries also show its deficiency.[1,5] A report from Australia concluded

1 out of 3 persons is suffering from 25-hydroxycholecalciferol deficiency.[6] In general, various factors have been implicated in the 25-hydroxycholecalciferol deficiency such as traditional dressing, prevents form exposure to sunlight, increasing age, dietary deficiency, hot foods, skin screens, beauty creams, etc. are a few noticeable causes of modern era. 25-hydroxycholecalciferol deficiency has now taken the shape of global epidemic which is particular to the developing countries like Pakistan.[28,29] Many systemic disorders have been associated with 25-hydroxycholecalciferol deficiency such as atherosclerosis,[10] brain stroke[11,12], systemic hypertension,[13] Diabetes mellitus,[14] obesity,[15] myocardial infarction[16] and malignancy, particularly of the intestine and prostate.[30,31]

LDL-c, serum cholesterol, and triglycerides were raised in subjects with low 25- hydroxycholecalciferol. HDL was reduced in 25-hydroxycholecalciferol deficient subjects. VLDL showed no differences as shown in table 2. Dyslipidemia was noted in 66.5% of total study subjects. Mean fasting blood glucose levels were higher in 25-hydroxycholecalciferol deficient diabetics; this is in agreement with previous report.[13,32,33] Findings of low 25-hydroxycholecalciferol are consistent to previous studies reported from Pakistan[34,35] and India.[23] Mean alkaline phosphatase was raised (121.7±5.6 IU) in 25-hydroxycholecalciferol deficient diabetics, this is consistent to previous reports.[1,23,36]

LDL-c, serum cholesterol, and triglycerides were raised in subjects with low 25- hydroxycholecalciferol. HDLc was reduced in 25-hydroxycholecalciferol deficient subjects, the findings are supported by previous studies.[23,37,38] Positive correlation of HDLc observed in present study is also a consistent finding to previous studies.[37-42] Negative association of LDLc, Serum cholesterol, and triglycerides is also supported by previous studies.[42,43]

In the light of above discussion, the present study reports 25-hydroxycholecalciferol deficiency and dyslipidemia is prevalent in type 2 diabetic subjects. Dyslipidemia was noted in diabetics with 25- hydroxycholecalciferol deficiency; however, the cause effect relationship cannot be ascertained due to study design. Further studies are recommended.

Conclusion

The present study reports 25- hydroxycholecalciferol deficiency and dyslipidemia in type 2 diabetic subjects. 25-hydroxycholecalciferol showed positive association with high density lipoprotein (HDLc) and inverse association with LDLc, serum cholesterol and triglycerides. For the cause effect relationship of 25- hydroxycholecalciferol deficiency and dyslipidemia, further studies are recommended. If such association really exists, then types 2 diabetics are prone to more cardiovascular events than diabetics without 25-hydroxycholecalciferol deficiency.

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