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ORIGINAL ARTICLE

Occupational Variations in Vitamin D Status and its Correlation with Serum Lipids in Varying Glycemic Control Groups

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Abstract

Objective: The study focuses on the evaluation of the difference between the serum vitamin D3 levels, on the basis of sunlight exposure, in indoor and outdoor individuals and to find out the correlation between serum 1,25-OH-D and serum lipids of varying glycemic control subjects.

Methodology: We enrolled 221 participants. The serum 1,25-hydroxy-D3 was quantitated by immuno-fluorescence method. Blood HbA1c amount was analyzed by high performance liquid chromatography. Serum levels of cholesterol, triacylglycerols, high-density lipoprotein-cholesterol and low-density lipoprotein-cholesterol were estimated by spectrophotometric analysis. Very low-density lipoprotein cholesterol was computed using the Friedewald equation. The Statistical Package for Social Software 20.0 was chosen to statistically analyze the collected data.

Results: A significant dissimilarity in the levels of sun-born vitamin, the calcitriol, was calculated, among the sun-exposed and non-exposed group. The mean vitamin D value was measured higher in sun-exposure group than non-exposed to sun. There came to be known the interlink between glycemic control and vitamin D quantity. Serum vitamin D had an inverse relationship with serum cholesterol, triglycerides, LDL-C and VLDL-C, but a positive relation with HDL-C.

Conclusion: The present expanding insufficiency and deficiency of vitamin-D3 is bringing about the peril of prevalent dyslipidemia and poor glycemic control, hence jeopardizing the health of people. The current unforeseen falling off serum vitamin D levels in the principal part of the population, is needed to be overseen and treated accordingly.

Key words: Vitamin D, Sunlight, Diabetes mellitus, Lipid Profile

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Introduction

Metabolic syndrome (MetS), obesity and type-II diabetes mellitus are ubiquitous. Their prevalence is shooting up worldwide.[1] A total of 33 million persons in Pakistan, were suffering from diabetes in 2021.[2] T2DM hyperglycemic state is a sophisticated course of events and depends on multiple factors.[3] Nonetheless, it could be sublimated to escalating ruination of insulin sensitivity (increasing insulin resistance) and in agreement with this, the failure of pancreatic islets to perpetuate pertinent insulin output to recompense reduced insulin sensitivity.[4]

The World Health Organization (WHO), estimation states that every year, almost 2.6 million deaths happen by dyslipidemia.[5] The present-day world is facing the problem of obesity pandemic. Obesity is principally connected to the outcomes of insulin resistance and pro-inflammatory adipokines.[6] Free fatty acids (FFAs) released into blood circulation, are the usual ingredients for the synthesis of composite lipids or these FFAs are used for the β-oxidation in various body tissues. When each of these two metabolic pathways, is fed up of the extensive supply of FFAs, FFAs and their transitional metabolites set about rising up, within the cells. Thus, ectopic lipid deposition starts off. The consequential surge in insulin resistance starts off in liver and skeletal muscles.[7]

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"Metabolic related dyslipidemia" is a subtype of dyslipidemia, arisen as an outcome of obesity and

insulin resistance. It refers to raised serum level of VLDL-Cholesterol, triglycerides (TG), LDL-Cholesterol, along with comparatively diminished HDL-Cholesterol.[8]

Calciferol is one of the secosteroids, being fat-soluble.[9] Vitamin D (calciferol), is of two main configurations: Vitamin D2 and Vitamin D3. Our bare skin in sunlight, allows the UV B-photons to make way to epidermal cholesterol, forming cutaneous vitamin D. Cholesterol is the precursor to 7-dehyrocholesterol, which is a crude substance for vitamin D synthesis. This cholecalciferol is the principal root for vitamin D. [9, 10] If skin is laid bare in sunshine before 9 AM or after 3 PM, its end result is the only trifling synthesis of calcitriol within epidermis.[11-15] To tackle the vitamin D deficiency (VDD), the optimum time to go outside in the sun is around noon, since it has the lowest chance of causing cutaneous malignant melanoma (CMM).[13]

The paramount concern of Vitamin D3, is to harmonize metabolites; calcium and phosphate by hormonal control.[16] Sun-born Vitamin, as was confined to be related to bone fitness, is now under meticulous look over because of Vitamin D receptors (VDRs) expression. These VDRs, customarily deal with gene transcription regulation. These genes are involved in modulation of several inflammatory elements and expression of immune cells that put up the prognosis of chronic disease, recovery from disease, or lead to mortality. Body tissues that accommodate hundreds of genes (making up to 5% of the human genome),have VDRs in their nuclei.[17] In addition to this, several in vivo and in vitro researches advocate the aptitude of vitamin D in maintaining glucose metabolism. For example, VDRs on β pancreatic cells invigorate insulin secretion, mediate immune retaliation and turn down the systematic inflammation. VDRs present in hepatocytes and bodily muscles quit the peripheral insulin resistance.[18,19] Vitamin D3, being an excellent antioxidant, is able to prevent T2DM.[20] Vitamin D has a fundamental role in maintaining fat deposition and balancing energy. It curbs transcription factors that promote adipogenesis. There existed more VDD in obese subjects.[21] The body mass index (BMI) and the serum 1,25-hydroxyvitamin-D, are associated inversely.[22]

VDD is going to be a worldwide health challenge.[23] Regardless of race or age, vitamin D deficiency affects about 1 billion individuals. [24] Anew consensus affirmation states that, VDD is designated to as serum 1,25(OH)D value below than 30 nmol/L (12 ng/mL). The vitamin D3 insufficiency is referred to as 1,25(OH)D value lying in between 30 nmol/L-50 nmol/L (12 – 20 ng/mL), while the values appraised to be all right and ample in accordance to general public skeletal fitness, should range between 50 nmol/L to 125 nmol/L (20 – 50 ng/mL).[25] Apart from obesity, VDD has a sturdy association with determinant of metabolic syndrome, like insulin resistance, dyslipidemia and arterial hypertension. [26]

There have been various reports, that diabetic individuals with VDD have lower LDL-C, higher TG and higher diastolic blood pressure as compared to the diabetic individuals with sufficient circulating vitamin D.[27] Vitamin D, via calcium production, proffers insulin and makes its secretion from pancreas, which affects glucose-levels in blood circulation. Vitamin D also activates lipoprotein lipase, which inhibits lipids production or increases lipid breakdown in adipose tissue. It also increases lipid usage in muscles. It also enhances the oxidation of lipids, bile juice production, and excretion of liver-resident cholesterol. [28]

The half-life of serum 1,25-(OH)-D3 roughly equals to 2-5 weeks, so the serum 1,25-(OH)-D3 is availed to estimate vitamin D3 status in human being.[29] The clinical outcomes and diabetic complication usually revolve around measuring HbA1c.[30] The standpoint of our study, is to shape the effect of sunlight exposure on the vitamin D level in diabetic and non-diabetic individuals and also to find out the correlation, between serum 1,25-(OH)-D and serum parameters of lipid, both in the diabetic and non-diabetic population of Pakistan.

Material and Methods

The cross-sectional, case-control study-design was adopted. The study was attempted to be carried out in the Pathology department of Aziz Bhatti Shaheed Teaching Hospital, Gujrat, Pakistan. The diabetic and non-diabetic citizens of Gujrat, Pakistan, with different occupations were included in the study. Occupations included, ranging from office setting, having rare exposure to sunshine, to laborers working in full sunshine. The demographic data of these participants were obtained. The sun-expose time was monitored and relative to it, two groups, one as the sun-exposed group and other as non-exposure, were devised. A total of 221 samples were

calculated for study. The technique adopted to collect samples and relative data was purposive sampling technique

Inclusion Criteria: Adults, having age above 18, with or without type-II diabetes mellitus.

Exclusion Criteria: Patients with Type 1 diabetes (having no response to oral hypoglycemic agents and showing response to only insulin with age; < 30 years)

- Gestational diabetes (having no history of diabetes before pregnancy)
- Recently diagnosed diabetes (HbA1c ranging 5.7-7.0)
- Chronic disorders like CKD, CLD and bone disorders etc.
- Those on Vitamin D supplementation or having injectable vitamin D.
- Patients taking lipid lowering agents from long duration

A proforma, containing the demographic data, clinical findings and study variable was used to collect information from the participating subjects.

Samples were drawn in EDTA and serum vials. The sample types for HbA1c were contained in EDTA vial and were well mixed on the roller mixer before testing. The samples, for serum vitamin D3 estimation and lipid profile assessment, were used from serum vials. The serum was obtained by centrifuging the clotted blood in serum vials, at 3400 R.P.M for 7 minutes.

HbA1c was performed on "ac6601 hba1c" of jiangso audicam medical technology co., ltd. The testing method was ion exchange high pressure liquid chromatography (HPLC). Serum vitamin D was performed on I Chroma-III, Boditech. The testing principle is based on quantitative determination of total 1,25(OH)D3 level, in human serum / plasma, through immunofluorescence assay. Serum lipid profile, including total-cholesterol, total-triglycerides, HDL-C and LDL-C, were performed on "Selectra Pro M Lite" of ELITech group. The testing was based on spectrophotometric measurement of analytes. The value for VLDL-C, was calculated by Friedewald equation, stated below

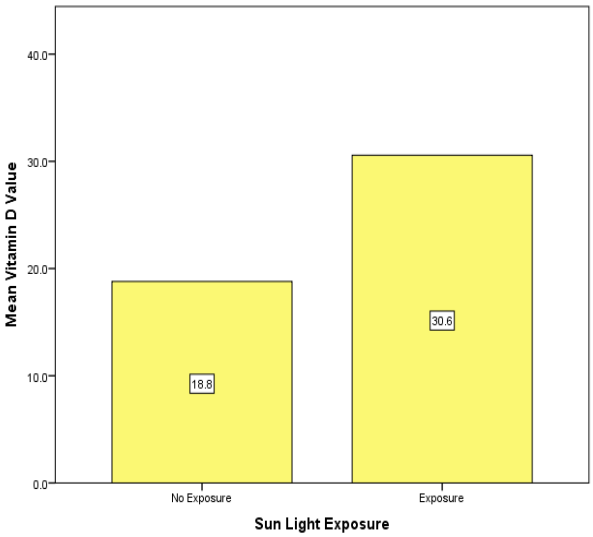
- VLDL-C= Triglycerides/5 (mg/dl|)

Results

I221 respondents were enrolled in the study, of them 89 (40.3%) were male individuals and 132 (59.7%) were female individuals. Of 221 participants 146 (66.1%) had no diabetes, 30 (12.6%) had diabetes but with desirable control (HbA1c value, falling between 7.0 to 9.0) and 45 (20.4%) patients were diabetic with poor control (HbA1c value: > 9.0). Out of 221 respondents, 26 (11.6%) had hypovitaminosis D (<10 ng/ml serum 1,25-OH-D), 123 (56.7%) presented with vitamin D insufficiency (Vitamin D3 level ranging 10ng/ml to 30 ng/ml). However, the sufficient vitamin-D3 level was observed in 72 (32.6%) participants

The sunlight exposure association with vitamin D status

59 (26.7%) of 221 participants had a little or no exposure to sunlight, rest 162 (73.3%) had adequate sunlight exposure in their daily routine life.



Graph1. The association between sunlight exposure and vitamin D status

The mean value of vitamin D for the group with no sunlight exposure was 18.8 ng/ml and that for the exposure group, it was 30.6 ng/ml (Graph 1). This shows that, with adequate sunlight, the serum vitamin D level is higher than the serum vitamin D level, with inadequate exposure to sunshine (Graph 1).

"The two independent sample T-Test" was performed to check the mean difference between vitamin D values of sunlight exposure and non-exposure group. The means difference calculated was -11.7818 (P value: .000). This shows that there is a significant difference in serum concentration of 1,25(OH) D3 of respondents exposed to sunlight in their routine life than the respondents, who don't expose to sunlight in their day routine.

The vitamin D3 status was grouped as; deficiency, insufficiency and sufficiency. These three groups, were compared with that of sunlight exposed and non-exposed groups, by crosstabulation (Table I)

In no exposure group 13 (22.0%) of 59 had deficient serum vitamin D3 level. 40 (67.8%) were found to suffer vitamin D insufficiency. Only 6 (10.1%) had adequate vitamin D amount.

As compared to the non-sunlight exposure group, the sunlight exposure group had only 13 (8.0%) of 162 individuals, presented with vitamin D deficiency. 83 (51.2%) of 162 had insufficient serum 25(OH) D level. 0f 162 exposure group

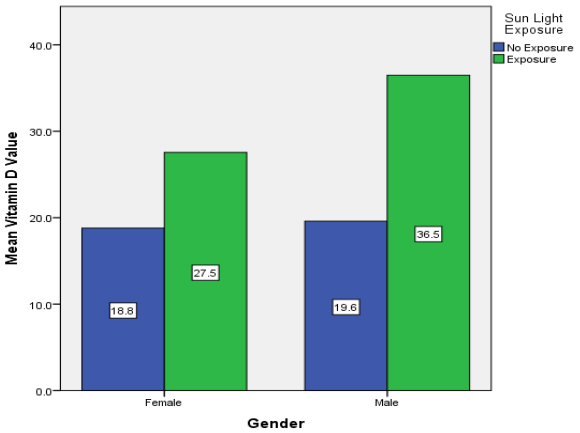
respondents, 66 (40.7%) appeared to be sufficient in 25 Hydroxy Vitamin D3 (Table I).

Table I: Vitamin D Status * Sun Light Exposure Cross tabulation				
		Sun Light Exposure		Total
		No Exposure	Exposure	
Vitamin D Status	Deficiency	13	13	26
	Insufficiency	40	83	123
	Sufficiency	6	66	72
Total		59	162	221

The relationship between the sunlight exposure and vitamin D status, was established by applying Pearson Chi-Square test (Table II). The test came about with significant relation (P value .000).

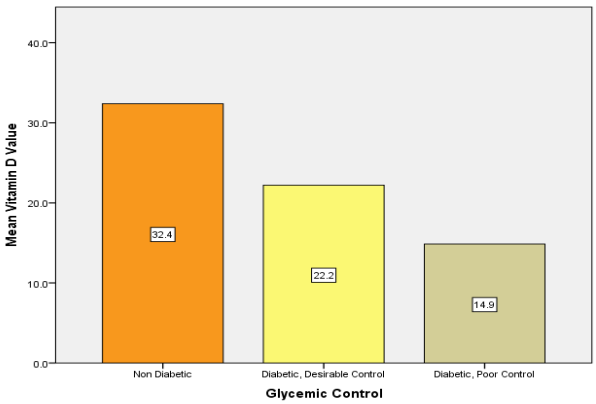
Table II. Pearson Chi-Square Test to observe relationship of sunlight exposure with Vitamin D status *Chi-Square Tests			
	Value	**df**	**Asymp. Sig. (2-sided)**
PearsonChi-Square	21.753a	2	.000
N of Valid Cases	221		
0 cells (.0%) have expected count less than 5. The minimum expected count is 6.94.			

Graph 2 shows the percentage of deficiency, insufficiency and sufficiency of vitamin D3 status according to sunlight exposure. Vitamin D3 deficiency was observed equally (5,88%) in both sun-exposed and non-exposed groups. Insufficient vitamin D was spotted 18.10% in inadequate sun-exposed group and 37.50% in sun-exposed group. Vitamin D sufficiency was reported 2.71% and 29.86% in no-exposure and exposure group, respectively.



Graph 3. Gender wise mean vitamin D value in both sun-exposed and non-exposed groups

The mean levels of serum 1,25-OH-D varied among glycemic control groups. Those categorized as non-diabetic had the mean value of vitamin D as 32.4 ng/ml. The category of individual group, having desirable control but being diabetic resulted in the mean outcome of 22.2 ng/ml of serum level of vitamin D. The last one group, is the diabetics with no or poor control, for which the mean level of vitamin D3 calculated, was 14.9 (Graph 4).



Graph 4. The mean Vitamin D level in different glycemic control groups.

Vitamin D Correlation with The Lipids:Pearson correlation table showed satisfactory results. Vitamin D level can affect the lipid status, primarily, in the patients with diabetes, having poor glycemic control.

In the normal glycemic control group, vitamin D has a weak negative correlation with serum cholesterol level (Pearson correlation value -0.145), but there was an insignificant correlation (P value 0.079). Similar to this, diabetics with desirable glycemic control (HbA1c: 7.0-9.0) have the same results (Pearson correlation value -0.112 and P value 0.556). However, diabetic patients, with poor glycemic control (HbA1c: >9.0) had moderate negative correlation (Pearson correlation value -0.480)and it was significant correlation (P value 0.001) (Table III).

Table III: Correlation of vitamin D3 with Cholesterol Vitamin D Level*Cholesterol Value.				
Glycemic Control Group	Pearson Correlation Value	Result	P Value	Conclusion
Non-Diabetics	-0.145	Weak-Negative Correlation	0.079	Insignificant Correlation
Diabetics, With Desire Control	-.112	Weak-Negative Correlation	.556	Insignificant Correlation
Diabetics, With Poor Control	-.486	Moderate-Negative Correlation	.001	Significant Correlation

There existed a moderate positive correlation, between 1,25 hydroxy vitamin-D3 and high-density lipoprotein=cholesterol (HDL-Cholesterol) in all groups viz, non-diabetic, desirable glycemic control individuals and the poor glycemic control population (Pearson correlation values 0.363, 0.435 and 0.486 respectively). Also, the data showed significant correlation among two of all three glycemic control groups. The desirable control group had an insignificant correlation,

between the vitamin-D3 level and HDL-Cholesterol; (P value; non-diabetic: 0.000, desirable: glycemic control individuals: 0.016 and poor glycemic control population:0.001) (Table IV).

Table IV: Correlation of vitamin D3 with HDL-cholesterol Vitamin D Level*HDL-C Value.

Glycemic Control Group	Pearson Correlation Value	Result	P Value	Conclusion
Non-Diabetics	.363	Moderate-Positive Correlation	.000	Significant Correlation
Diabetics, With Desire Control	.435	Moderate-Positive Correlation	.016	Insignificant Correlation
Diabetics, With Poor Control	.486	Moderate-Positive Correlation	.001	Significant Correlation

In triglycerides case, the results were consistent in each of three groups. The evaluation shows that there existed a weak-inverse correlation in between the vitamin D3 status and triglycerides, but insignificant correlation was estimated. The Pearson correlation value -0.126 for non-diabetics (P value: 0.130), -0.101 for desirable control diabetics (P value: 0.596) and -0.048 for poor control diabetics (P value:.752) (Table 5).

Table VI: Correlation Analysis between Vitamin D3 Status and Triglycerides in Different Glycemic Control Groups"

Vitamin D Level*Triglycerides Value				
Glycemic Control Group	Pearson Correlation Value	Result	P Value	Conclusion
Non-Diabetics	-.126	Weak Negative Correlation	.130	Insignificant Correlation
Diabetics, With Desirable Control	-.101	Weak Negative Correlation	.596	Insignificant Correlation
Diabetics, With Poor Control	-.048	Weak Negative Correlation	.752	Significant Correlation

In all three groups; non-diabetic, diabetics with desirable control and diabetics with poor control, there was a weak correlation between vitamin D3 level and low-density lipoprotein-cholesterol (LDL-C), having Pearson correlation value -0.203, -0.278 and -0.175, respectively. Nonetheless the correlation was insignificant in all three cases. (P value 0.014, 0.131 and 0.214 for non-diabetic, diabetics with desirable control, and diabetics with poor control, respectively) (Table VI).

Table VI: Correlation of vitamin D3 with LDL-cholesterol.

Vitamin D Level*LDL-C Value				
Glycemic Control Group	Pearson Correlation Value	Result	P Value	Conclusion
Non-Diabetics	-.203	Weak Negative Correlation	.014	Insignificant Correlation
Diabetics, With Desire Control	-.278	Weak Negative Correlation	.137	Insignificant Correlation
Diabetics,With Poor Control	-.175	Weak Negative Correlation	.251	Insignificant Correlation

For VLDL-C, the results were same as for LDL-C i.e., weak negative correlation, with insignificant (P value 0.581 for non-diabetic, 0.801 for diabetics with desirable control and 0.743 for poor glycemic control diabetics), came about between the serum 1,25(OH)D and serum VLDL-C. The Pearson correlation value for all three categories, namely; the non-diabetic, diabetics with desirable control and diabetics were, -0.056, -0.048, and -.050, respectively (Table 7).

Table VII. Correlation of vitamin D3 with VLDL-cholesterol

Glycemic Control Groups	Pearson Correlation Value	Result	P Value	Conclusion
Non-Diabetics	-.046	Weak-Negative Correlation	.581	Insignificant Correlation
Diabetics, With Desire Control	-.048	Weak-Negative Correlation	.801	Insignificant Correlation
Diabetics,With Poor Control	-.050	Weak-Negative Correlation	.743	Insignificant Correlation

Discussion

The World Health Organization describes ameloblastoma as a benign lesion with a fibrous stroma and a follicular or plexiform appearance. It is typically described as a benign ectomesenchymal-free odontogenic epithelial tumour. Additionally, it exhibits invasive local behaviour and recurs frequently. Ameloblastoma does not differentiate between sexes, but it is more common in patients between the ages of 30 and 40.[11,12]

Studies showed an average age of conventional ameloblastoma presentation to be 33.2 years for Brazilian, 30.4 years for African and 42.3 years for European populations.[13] Also, there was an equal sex distribution seen in our study. These findings are all consistent with current literature.[14] The results of this present study are in agreement with these findings. The mean age of group A was similar to group B (26.097 ± 5.742 vs. 25.121 ± 5.112), without statistically significant difference. This mean age shows that in our population this disease is more prevenient at lower age as compared to other studies. But the findings of no significance relationship of disease with gender is also parallel to our results.

This tumour can be a major challenge for clinicians due to its biological invasive behavior, available treatment approaches, reconstructive complexities, requirement for long term follow-up, and patient compliance.[15] It is generally accepted that the first operation affords the best chance of cure. Both primary and recurrent ameloblastomas are treated by either conservative or radical surgery. Conservative procedures

include enucleation, curettage, cryotherapy or marsupialization, which are used for intraluminal unicystic ameloblastomas and in children or medically compromised patients, as it preserves patient's normal tissues, minimises facial disfiguration and supports adequate quality of life after surgery. However, the disadvantage of conservative procedures is a higher recurrence rate, especially in conventional ameloblastomas and the mural unicystic type.[16]

In this study, the posterior part of the mandible is by far the most damaged area, and although there is occasionally a little female preponderance, men and women do not vary significantly in the majority of the series.[6,10] Similar findings were obtained in earlier research.[17] Patients affected by ameloblastomas often exhibit a wide age range with a peak incidence in the third and fourth decades of life. The surgical treatment of ameloblastomas is complicated since it must be vigorous and invasive to prevent recurrence. Enucleation or curettage may be used in the conservative method, which is occasionally followed by marsupialization. Unsolved is the issue of the rate of recurrence following conservative therapy.[18]

The results of this present study support that enucleation with chemical fixation has significantly better outcomes as compared to enucleation alone. The success rate in terms of no recurrence of combination group of enucleations with chemical fixation had a significantly less rate of recurrence (16.42% vs. 31.34%, P-value = 0.043) in comparison to enucleation alone group. These findings are quite consistent with other researches, such as study conducted by Blanas et al, showed that enucleation along with the application of Carnoy's solution is a least invasive procedure having lowest recurrence rate. It is recommended that application of Carnoy's solution for five minutes in the cavity of cyst can significantly reduce the recurrence rate.[19] Gosau et al[20] claim that the administration of Carnoy's solution in addition to enucleation decreased the recurrence rate compared to simple enucleation also corroborated this. The goal of utilizing Carnoy's solution is to completely remove any epithelial residues that could lead to recurrences.[21]

Conclusion

It may be concluded that all subtypes of unicystic ameloblastoma like mural subtypes can be treated conservatively with significantly increased success rate with bone curettage along with Carnoy's solution application. This surgical procedure has shown improved or similar results as compared to other more aggressive techniques. Conservative therapy in combination with Carnoy's solution and timely intervention can significantly improve outcome and other potential complication of the surgery. Longer follow-up times and larger investigations are necessary to corroborate this finding. Additionally, additional research may be done to demonstrate how this conservative strategy affects the traditional kind of ameloblastoma.

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