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Research Article

Vitamin D Deficiency and its Association with Nephropathy in Type 2 Diabetes Mellitus Patients: A Cross Sectional Study

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A B S T R A C T

Background: Vitamin D (VD) deficiency is linked to insulin activity and its release. It is associated with uncontrolled diabetes and more complications in diabetic patients. So, this study will prove importance of investigating serum VD level in Type 2 DM (T2DM) patients and its relation to complication of diabetic nephropathy.

Materials and Methods: Total 1025 patients with Type 2 diabetes were enrolled in this study. Age limit was from 40 to 76 year. Investigations for serum VD, haemoglobin A1c (HbA1c), high-sensitivity C-reactive protein (hs-CRP) and urinary Albumin: Creatinine Ratio (ACR) were done in each patient.

Result: It was found that most of the patient (77.89%) were having VD<29.88 ng/m along with significantly higher ACR and hs-CRP levels in these patients (P=0.012 and P=0.007, respectively). VD was observed significantly lesser in females than males P < 0.001. Those patients who were exposed to sunrays had significantly more VD values and lesser hs-CRP values in comparison to less-exposed ones, P-value (0.001 and <0.001), respectively. Physical activity significantly raises VD and decreases ACR levels in diabetic patients, P-value (0.045 and 0.001), respectively. Except age (r=0.356 P=0.041) all other factors like BMI (r=−0.503 P=0.008), duration of disease (r=−0.489 P=0.004), ACR (r=−0.295 P=0.016) and HbA1c (r=−0.330 P=0.031) were negatively correlated with VD.

Conclusion: This study concluded that Type 2 diabetes with VD deficiency are prone for the development of nephropathy.

Keywords: Type 2 Diabetes Mellitus, HbA1C, Vitamin D, Nephropathy, Albumin: Creatinine Ratio, High-Sensitivity C-Reactive Protein

Introduction

In recent years Vitamin D (VD) is known for its antiproliferative, immunomodulatory, anti-inflammation and stimulating cell differentiation functions.[1] So that, it plays major role in protection of body health with infections, malignancies, autoimmune disorders, respiratory and Cardiovascular Diseases (CVDs).[2] Recently, it was also reported that VD is associated with the progression of Type 2 Diabetes Mellitus (T2DM), as VD has direct role in pancreatic β-cell activity, insulin release and action.[3]

VD deficiency is found in most of the part of the world.[4,5] It is estimated that about 1 billion peoples have VD deficiency worldwide[6] and 50% of the adults in developing countries have absence of VD.[7] While in developed nations, the prevalence rate of VD deficiency is about 41.6%.[4] Factors associated with VD deficiency includes lesser sunlight exposure, dark skin, elderly, winter season, use of clothes covering most of the body, obesity and female gender.[8,9] Occurrence of VD deficiency in Type 1 and T2DM is already proven by some studies.[5] Studies done in Sudan also found correlation of VD deficiency and development of T2DM. VD deficiency is more common in female diabetics.[10]

VD inhibits the endothelial destruction in the kidney. Damage of endothelium causes Microalbuminuria (MAU), due to its role in negative regulation of renin-angiotensin-aldosterone system. So many reports are there correlating between MAU and VD deficiency in T2DM.[11] As VD deficiency increases, albuminuria aggravates.[12]

Early finding and correction of VD deficiency will prevent T2DM complications. So, the current study aimed to search whether VD has diagnostic and predictive role in defining nephropathy in T2DM subjects.

Material and Methods

This cross-sectional study was done on randomly selected subjects with confirmed diagnosis of Type 2 diabetes mellitus who were attending medicine outdoor patient department of King George's Medical University, Uttar Pradesh, India. Consent was taken from each subject and blood was investigated for 1025 clinically diagnosed subjects including of 470 males and 555 females. Excluded T2DM patients were those with pre-existing inflammation, renal diseases, cardiovascular diseases, liver diseases and those who were on VD supplementation. Diagnosis of T2DM was made on behalf of history, previous records, clinical examinations and investigations. Questions about the patient's age, sex, economic lifestyle, family history, education level and sunrays exposure were asked. Sugar status, BMI and VD values were compared for every subject. Those with Haemoglobin A1c (HbA1c) ≤8% were considered as sugar controlled and those with >8% as sugar uncontrolled. BMI was classified as normal weight 18.5-25 kg/m,^{2} overweight >25-30 kg/m^2 and obese >30 kg/m.^{2} Meanwhile, VD values ≤30 ng/ml put as deficient and >30 ng/ml as adequate.

This study was approved by the Local Ethical Committee of hospital. Written pre-informed consent was taken from each study participants.

Calculation of BMI, VD, hsCRP, HbA1C and ACR Values

- Body Mass Index (BMI) was measured by dividing body weight in kilograms by body height in meters square (kg/m^2).
- Serum VD values were estimated by competitive inhibition enzyme-linked immunosorbent assay or ELISA.
- Serum levels of high-sensitivity C-reactive protein (hs-CRP) was estimated by the particle-enhanced immunoturbidimetric assay method Cobas C-311®. Human CRP agglutinates with latex particles which are already lodged with monoclonal anti-CRP antibodies. The formed precipitate was estimated turbidimetrically.
- As per the manufacturer, urine albumin and creatinine were calculated by Cobas C-311® fully automated analyser. Within the blood sample anti-albumin antibodies cross react with antigen and results in formation of antigen-antibody complexes which were analysed turbidimetrically. Reaction of creatinine to picrate in alkaline medium results in yellow-red product whose rate of synthesis is directly proportional to the creatinine value in the blood sample, which is further analysed by photometrically.
- HbA1c measurement was done in fully automated closed system - Roche Cobas C-311®. Total haemoglobin and HbA1c values were calculated after haemolysis of the anticoagulated whole blood sample. Spectrophotometer analysed total haemoglobin while HbA1c was measured by immune turbidimetrically. The ratio of both above values resulted in the final percentage of HbA1c.

Statistical Analysis

Statistical analysis was performed using SPSS Statistics software. Base line characteristics were assessed with standard descriptive statistics. Data were presented in the form of frequencies, percentage, and means±standard deviation. The Student's *t*-test was used to compare mean levels of study parameters between groups. Categorical variables were compared using Chi-square and multiple regression tests. Pearson's correlation coefficient test used to calculate the correlation between continuous variables. $p<0.05$ was considered statistically significant.

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Result

Demographic and Baseline Features of Study Participants

Among total 1025 studied, 555 (54%) were female and 470 (54%) were male. 805 (78.5%) had VD deficient while 220 (21.5%) were having adequate VD. Maximum number of patients were with higher BMI values and were categorised in overweight 472 (46%), obese 317 (31%) and normal weight 236(23%) patients. Total 705(68.8%) subjects were with uncontrolled blood sugar level. Of all 1025 patients, 893 (87.1%) were having sun bath of less than 5 hours. 534 (52.1%) were having no any physical activity Table 1.

Table 1.Demographic and baseline features of study participants

S. No.	Characteristics	Frequency (%)
1.	Male	46% (470)
2.	Female	54% (555)
3.	<55 years age	47% (480)
4.	>55 years age	53% (545)
5.	Normal weight	23% (236)
6.	Overweight	46% (472)
7.	obese	31% (317)
8.	Controlled sugar	31% (320)
9.	Uncontrolled sugar	68.8% (705)
10.	Low qualification	18% (185)
11.	Moderate qualification	65% (666)
12.	High qualification	17% (174)
13.	Low life style	35% (359)
14.	Moderate life style	57.40% (588)
15.	Good life style	7.6% (78)
16.	Do physical exercise	47.9% (491)
17.	Not do physical exercise	52.1% (534)
18.	Sun exposure <5 hours	87.1% (893)
19.	Sun exposure <5 hours	12.9% (132)
20.	Family history of DM 1st degree	36.5% (374)
21.	Family history of DM 2nd degree	46.3% (474)
22.	No Family history of DM	17.2% (176)
23.	Family history of CVD-Yes	14.1% (145)
24.	Family history of CVD-No	85.9% (880)
25.	On cholesterol lowering drug	47.2% (484)
26.	Not on cholesterol lowering drug	52.8% (541)
27.	VD deficient	78.5% (805)
28.	VD sufficient	21.5% (220)

DM: Diabetes Mellitus, CVD: Cardiovascular Disease.

Association of Nonparametric Variables with Vitamin D Levels

It was observed that BMI, sex and sun exposure were significantly linked with VD deficiency (P=0.004, P<0.001 and P=0.006, respectively). Also these parameters increases the risk of VD deficiency (sex - Odd Ratio [OR]: 3.89 with Confidence Interval [CI]: [1.89-7.98]; BMI - OR: 5.97 with CI: [1.79-19.79]; and sun exposure - OR: 3.5 with CI: [1.45-8.39]) (Table2).

It was observed that the mean values of hs-CRP and Albumin: Creatinine Ratio (ACR) were on higher side in T2DM patients with VD deficiency in comparison to patients with adequate VD. It was found significant (P=0.007 and P=0.001, respectively). However, the mean value of HbA1c was found non-significant in both groups. On comparing mean values of VD levels in males (30.2± 12.2 ng/ml) and females (20.0±8.90 ng/ml) there was significant reduction in females with P <0.001, while hs-CRP (5.91±2.61 mg/l) was considerably raised (3.54±2.55 mg/l) with P=0.004.

Sun exposed patients with <5 hours were having significantly lower mean VD level (23.6±11.2 ng/ml) in comparison to other group with sun exposer >5 hours (32.8±12.3 ng/ml), P=0.001. hs-CRP was significantly raised in patients with <5 hours sun exposer (5.15±6.48 mg/l) than with >5 hours (2.81±1.91 mg/l) with P <0.001.

Raised VD and lesser ACR levels with P=0.045 and P=0.002, respectively, were observed in physically exercising subjects. Also results were found that T2DM patients with uncontrolled blood sugar levels were having significantly more ACR with P=0.018; the results were presented in Table 3.

Two tails Student's t-test has been employed to compare between variables. The results expressed as mean±SD, and P<0.05 was statistically considered significant. VD=Vitamin D; HbA1c=Glycated haemoglobin; hs-CRP=High-sensitivity C-reactive protein; SD=Standard deviation; DM=Diabetes mellitus.

Correlation between Vitamin D Level and Age, BMI, Disease Duration, HbA1C and ACR

It was observed that VD and age (r=0.356; P=0.043) were significantly correlated in positive manner while VD was negatively correlated with BMI (r=−0.522; P=0.008), duration of disease (r=−0.499; P=0.004), ACR (r=−0.376; P=0.016) and HbA1c (r=−0.326; P=0.031).

Discussion

The observation of characteristics is that T2DM is more common in females, overweight, and most subjects were with physically inactive, uncontrolled blood sugar levels and less sun exposure. In this study it was found that there is high occurrence of VD insufficiency (78.5%) in

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our participants. Similar findings were also there in some previous studies on diabetics and non-diabetics.[13] Few other researches, supports that female sex is an independent indicator of VD deficiency.[14] So, speculated to a number of causes could lead to VD insufficiency, like physical activity, nutrition and spending more indoor times. Females had more hs-CRP in comparison to males in current research which supports previous studies.[15, 16]

Table 2.Nonparametric association of study variables in groups classified according to Vitamin D status

S. No.	Parameters	% Frequency VD Deficient	% Frequency VD Sufficient	OR/CI	P-values
1.	Male	38.7% (309)	71.10% (161)	3.89 (1.89-7.98)	<0.001
2.	Female	61.3% (490)	28.9% (65)		
3.	<55 years age	49% (392)	34.09% (88)	1.86 (0.92-3.73)	0.055
4.	>55 years age	51% (408)	65.91% (137)		
5.	Normal weight	19% (152)	40.4% (80)		
6.	Overweight	45.5% (364)	42.6% (78)	5.97 (1.79-19.79)	0.004
7.	obese	40.50% (324)	17% (27)	2.24 (0.76-6.59)	0.144
8.	Controlled sugar	31% (248)	36.36% (82)	0.78 (0.39-1.58)	0.312
9.	Uncontrolled sugar	69% (552)	63.64% (143)		
10.	Do exercise	44.65% (357)	56.52% (124)	0.62 (0.32-120)	0.106
11.	No exercise	55.35% (442)	43.48% (102)		
12.	<5 hours exercise	91.30% (730)	75% (163)	3.5 (1.45-8.39)	0.006
13.	>5 hours exercise	8.7% (69)	25% (63)		

Categorical variables reported as frequencies and percentage. Chi-square and multiple regression tests have been done to compare between variables. BMI: Body Mass Index; OR: Odd Ratio; CI: Confidence Interval, VD: Vitamin D.

Table 3.Study parameters in patients group classified according to Vitamin D status, gender, sun exposure, physical exercise, and glycemic control

	Study parameters in case group classified according to VD status			
S. No.	**Parameters**	**VD deficient (mean±SD)**	**VD sufficient (mean±SD)**	**p**
1.	HbA1c (%)	9.46± 2.43	8.82 ±2.63	0.159
2.	hsCRP mg/l	4.24± 4.11	2.72± 2.61	0.007
3.	ACR mg/g	47.8 ±117	19.9 ±22.7	0.001
	Patients classified according to sex			
	Parameters	Male (mean±SD)	Female (mean±SD)	**p**
1.	Vitamin D (ng/ml)	30.2±12.2	20.0±8.90	<0.001
2.	hsCRP mg/l	3.54±2.55	5.91±2.61	0.004
3.	ACR mg/g	30.6±8.60	42.9±7.21	0.269
	Patients classified according to sun exposure			
	Parameters	Sun exposure <5 h/day (mean±SD)	Sun exposure >5 h/day (mean±SD)	**p**
1.	Vitamin D (ng/ml)	23.6±11.2	32.8±12.3	0.001
2.	hsCRP mg/l	5.15±6.48	2.81±1.91	<0.001
3.	ACR mg/g	38.6±6.33	24.0±5.79	0.09
	Patients classified according to physical exercise			
	Parameters	Patients with physical exercise (mean±SD)	Patients without physical exercise (mean±SD)	**p**
1.	Vitamin D (ng/ml)	27.0±12.4	23.3±11.0	0.045

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2.	hsCRP mg/l	4.29±5.35	5.20±6.91	0.31
3.	ACR mg/g	21.1±41.5	48.6±77.4	0.002
	Patients classified according to glycemic control			
	Parameters	**Controlled DM (mean±SD)**	**Uncontrolled DM (mean±SD)**	**p**
1.	Vitamin D (ng/ml)	25.7±11.4	24.3±11.9	0.463
2.	hsCRP mg/l	4.06±2.63	5.12±2.65	0.266
3.	ACR mg/g	20.6±6.59	43.8±7.21	0.018

In addition, physical exercise and exposure to sunrays significantly raises VD and lowers hs-CRP values. Current research findings confirmed by previous results, indicating that lower values of duration of sun exposure and physical inactivity significantly affects VD levels in the body. Physical exercise may raise serum values of VD by increasing skin exposure to sunrays,[17] more lipolysis and increasing mobilization of stored VD from the fat compartments.[18]

Concurrent with prior studies, the current research resulted that subjects with type 2 diabetes mellitus having VD deficiency had raised values of hs-CRP in comparison to those with VD sufficieny. The previous researches has reported that VD deficiency may lead to systemic inflammation,[19] because VD prevents the formation of inflammatory markers like interleukin 2 (IL-2), interferon-gamma and IL-5 through Th-1 lymphocytes, and it also prevents the formation of IL-6 by monocytes, as it is the first stimulant of hs-CRP generation.[7] VD deficiency causes macrovascular and microvascular complications by causing inflammation of the vessels.[1]

Here we find that the mean ACR was significantly raised in diabetic with VD deficiency than those with VD sufficient. Moreover, the reciprocal relation of ACR and VD was established. These results were incompatible with prior results that subjects with type 2 diabetes mellitus had higher values of ACR; on the other side, VD supplementation decreases ACR.[6] ACR is an early marker for nephropathy, and VD function as proteinuria homeostasis[20] hence VD deficiency is linked with nephropathy in T2DM subjects. Physical activity significantly reduces ACR values. Prior reports signify same results of physical activity link with decreased albumin excretion in the T2DM patients despite unknown mechanism of exercise on ACR; possibly it is because of its action on the vascular endothelium that is due to nitric oxide acting as vaso-relaxant.[21]

This research aims to compare mean VD values of uncontrolled diabetes with that of controlled. Although there was an insignificant difference was observed, yet, it favours with prior studies showing insignificant differences in mean HbA1c between groups of VD status.[19] Likewise, Pearson's regression analyses resulted that VD and HbA1c are negatively correlated. As VD enhances pancreatic β-cell secretion of insulin and activation from proinsulin to insulin, it might help in insulin function by simulating the insulin receptors expression and control of the calcium level.[22] So, VD must be known for blood sugar homeostasis and hence complications of diabetes.

Actually, VD values are negatively associated with BMI, disease duration, and sugar control.[2] In other researches, there was significant relation of VD deficiency and albuminuria, and we could calculate low VD level on nephropathy development.[23] Also, study on drug trial proved reduction of proteinuria after the administration of VD in patients with Type 2 diabetes.[24]

The drawbacks of this study were investigating some haematological parameters related to VD control like phosphorus, parathyroid hormone and calcium values. The major drawback of current research was that subjects were selected on the basis of their previous clinical data, and no pre investigations were done to diminish confounding factors of drawback.

Conclusion

In this study we concluded that the number of VD deficiency in our population is more. ACR and hs-CRP are raised in type 2 diabetics with VD <30 ng/ml. Moreover, VD values were negatively related with BMI, duration of disease, ACR, and HbA1c values. As a result, VD deficiency may cause nephropathy in patients of Type 2 diabetes mellitus. Therefore, investigating and VD administration should be done.

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Conflicts of Interest: None

References

1. Mao L, Ji F, Liu Y et al. Calcitriol plays a protective role in diabetic nephropathy through anti-inflammatory effects. *Int J Clin Exp Med* 2014; 7: 5437-44. Available From: https://www.researchgate.net/publication/272097445_Calcitriol_plays_a_protective_role_in_diabetic_nephropathy_through_anti-inflammatory_effects. [Google Scholar, PubMed].

2. Ahmadieh H, Azar ST, Lakkis N, et al. Hypovitaminosis d in patients with type 2 diabetes mellitus: A relation to disease control and complications. *ISRN Endocrinol* 2013; 2013: 641098. [PubMed/ Google Scholar].
3. Kulie T, Groff A, Redmer J et al. Vitamin D: An evidence-based review. *J Am Board Fam Med* 2009; 22: 698-706. Available From: https://www.jabfm.org/content/22/6/698. [Google Scholar, PubMed].
4. Long M, Wang C, Liu D. Glycated hemoglobin A1C and Vitamin D and their association with diabetic retinopathy severity. *Nutr Diabetes* 2017; 7: e281. Available From: https://www.semanticscholar.org/paper/Glycated-hemoglobin-A1C-and-vitamin-D-and-their-Long-Wang/6fa3eb25c4ed126716a655679ffb4f26df866120. [Google Scholar/ PubMed].
5. Alcubierre N, Valls J, Rubinat E et al. Vitamin D deficiency is associated with the presence and severity of diabetic retinopathy in type 2 diabetes mellitus. *J Diabetes Res* 2015; 2015: 374178. Available From: https://www.hindawi.com/journals/jdr/2015/374178/. [Google Scholar/ PubMed].
6. Nakashima A, Yokoyama K, Yokoo T et al. Role of Vitamin D in diabetes mellitus and chronic kidney disease. *World J Diabetes.* 2016; 7: 89-100. Available From: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4781904/ [Google Scholar/ PubMed].
7. Liefaard MC, Ligthart S, Vitezova A et al. Vitamin D and C-reactive protein: A mendelian randomization study. *PLoS One.* 2015; 10: e0131740. Available From: https://journals.plos.org/plosone/article/figure?id=10.1371/journal.pone.0131740.g002. [Google Scholar/ PubMed].
8. Mandarino NR, Júnior FD, Salgado JV et al. Is Vitamin D deficiency a new risk factor for cardiovascular disease? *Open Cardiovasc Med J* 2015; 9: 40-9. Available From: https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.107.706127. [Google Scholar/ PubMed].
9. Lee JH, O'Keefe JH, Bell D et al. Vitamin D deficiency an important, common, and easily treatable cardiovascular risk factor? *J Am Coll Cardiol* 2008; 52: 1949-56. Available From: https://www.sciencedirect.com/science/article/pii/S0735109708031756 [Google Scholar/ PubMed].
10. Yousif NM, Ismail AM. Alanine aminotransferase and gamma-glutamyl transferase activity as predictor markers for hepatocellular damage in Vitamin D deficient type 2 diabetes mellitus patients-cross-sectional study. *Am J Med Med Sci* 2014; 4: 186-91.Available From: https://www.researchgate.net/publication/274632736_Alanine_Aminotransferase_and_Gamma-glutamyltransferase_Activity_as_Predictor_Markers_for_Hepatocellular_Damage_in_Vitamin_D_Deficient_Type_2_Diabetes_Mellitus_Patients_-_Cross-sectional_Study. [Google Scholar].
11. Shaafie IA, Hesham RA, Basha AA. Vitamin D status in type 2 diabetic patients and its association with glycemic control, lipids & microalbuminuria: A pilot study. *GMJ, ASM* 2013; 2(S1): S6-13. Available From: https://pdfs.semanticscholar.org/8faf/b3a972b5292b6d393313b92c9c760bc179b5.pdf. [Google Scholar].
12. Tiryaki Ö, Usalan C, Sayiner ZA. Vitamin D receptor activation with calcitriol for reducing urinary angiotensinogen in patients with type 2 diabetic chronic kidney disease. *Ren Fail* 2016; 38: 222-227. Available From: https://www.tandfonline.com/doi/full/10.3109/0886022X.2015.1128250. [Google Scholar/ PubMed].
13. Rafiq S, Jeppesen PB. Body mass index, Vitamin D, and type 2 diabetes: A Systematic review and meta-analysis. *Nutrients*. 2018; 10: pii-E1182. Available From: https://www.researchgate.net/publication/327277096_Body_Mass_Index_Vitamin_D_and_Type_2_Diabetes_A_Systematic_Review_and_Meta-Analysis [Google Scholar/ PubMed].
14. Rolim MC, Santos BM, Conceição G et al. Relationship between Vitamin D status, glycemic control and cardiovascular risk factors in Brazilians with type 2 diabetes mellitus. *Diabetol Metab Syndr* 2016; 8: 77. Available From: https://www.researchgate.net/publication/310471063_Relationship_between_Vitamin_D_status_glycemic_control_and_cardiovascular_risk_factors_in_Brazilians_with_type_2_diabetes_mellitus. [Google Scholar/ PubMed].
15. Qasim AN, Budharaju V, Mehta NN et al. Gender differences in the association of C-reactive protein with coronary artery calcium in type-2 diabetes. *Clin Endocrinol (Oxf)* 2011; 74: 44-50. Available From: https://www.researchgate.net/publication/46577152_Gender_Differences_in_the_Association_of_C-Reactive_Protein_with_Coronary_Artery_Calcium_in_Type-2_Diabetes. [Google Scholar PubMed].
16. Mahajan A, Tabassum R, Chavali S et al. High-sensitivity C-reactive protein levels and type 2 diabetes in urban North Indians. *J Clin Endocrinol Metab* 2009; 94: 2123-2127. Available From: https://academic.oup.com/jcem/article/94/6/2123/2597228. [Google Scholar/ PubMed].
17. Almehmadi B, Fallata E, Alqahtani S, et al. The effects of physical activity and sun exposure on Vitamin D status among children from Jeddah, Saudi Arabia. *J Pediatr Care* 2016; 2: 1-4. Available From: http://pediatrics.imedpub.com/the-effects-of-physical-activity-and-sun-exposure-on-vitamin-d-status-among-children-from-jeddah-saudi-arabia.php?aid=8822/. [Google Scholar].
18. Kavadar G, Demircioğlu DT, Özgönenel L et al. The relationship between Vitamin D status, physical

activity and insulin resistance in overweight and obese subjects. *Bosn J Basic Med Sci* 2015; 15: 62-66. Available From: https://www.researchgate.net/publication/277780100_The_relationship_between_vitamin_D_status_physical_activity_and_insulin_resistance_in_overweight_and_obese_subjects. [Google Scholar/ PubMed].

19. Haidari F, Zakerkish M, Karandish M et al. Association between serum Vitamin D level and glycemic and inflammatory markers in non-obese patients with type 2 diabetes. *Iran J Med Sci* 2016; 41: 367-373. Available From: https://www.researchgate.net/publication/307576913_Association_between_Serum_Vitamin_D_Level_and_Glycemic_and_Inflammatory_Markers_in_Non-obese_Patients_with_Type_2_Diabetes. [Google Scholar/ PubMed].
20. Prabhu RA, Saraf K. Vitamin D in diabetic nephropathy. *J Postgrad Med* 2018; 64: 5-6. Available From: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5820815/.
21. Robinson ES, Fisher ND, Forman JP et al. Physical activity and albuminuria. *Am J Epidemiol* 2010; 171: 515-521. Available From: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2842220/ [Google Scholar].
22. Swamy M, Ganiger A, Prasad SD et al. Serum 25-hydroxy Vitamin D levels in type 2 diabetes mellitus - A comparative study. *Int J Clin Biochem Res* 2016; 3: 255-258. [Google Scholar].
23. Zoppini G, Galletti A, Targher G et al. Lower levels of 25-hydroxyvitamin D3 are associated with a higher prevalence of microvascular complications in patients with type 2 diabetes. *BMJ Open Diabetes Res Care* 2015;3:e000058. Available From: https://www.researchgate.net/publication/275663635_Lower_levels_of_25-hydroxyvitamin_D3_are_associated_with_a_higher_prevalence_of_microvascular_complications_in_patients_with_type_2_diabetes [Google Scholar/ PubMed].
24. Momeni A, Mirhosseini M, Kabiri M et al. Effect of Vitamin D on proteinuria in type 2 diabetic patients. *J Nephropathol.* 2017; 6: 10-14. Available From: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5106877/ [Google Scholar].

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