Vitamin D deficiency increases risk of nephropathy and cardiovascular diseases in Type 2 diabetes mellitus patients

Hala Abdalazeem Aljack1,2, Mohammed Karrar Abdalla3, Omer Fadl Idris4, Amar Mohamed Ismail4

1Department of Clinical Chemistry, Faculty of Medical Laboratory Science, Omdurman Islamic University, 2Department of Clinical Chemistry, Faculty of Medical Laboratory Science, Al-Neelain University, 3Department of Clinical Chemistry, Faculty of Medical Laboratory Science, Sudan University of Science and Technology, 4Department of Biochemistry and Molecular Biology, Faculty of Science and Technology, Al-Neelain University, Khartoum, Sudan

Background: Vitamin D (VD) deficiency is associated with insulin function and secretion. It is linked with diabetes mellitus (DM) progression, and complications were also recorded. Therefore, the current study aimed to investigate serum VD level in Type 2 DM (T2DM) patients and its association with diabetic nephropathy and cardiovascular diseases (CVD). Materials and Methods: In this cross-sectional study, 205 patients with Type 2 diabetes age ranged from 39 to 75 years old were enrolled. Serum VD, high-sensitivity C-reactive protein (hs-CRP), and hemoglobin A1c (HbA1c) were measured. In addition, urinary albumin:creatinine ratio (ACR) was estimated. Results: Patients with Type 2 diabetes had a 78.5% VD level <30 ng/mL. ACR and hs-CRP levels were significantly increased in patients with diabetes with VD <30 ng/mL (P = 0.011 and P = 0.008, respectively). Female had significantly lower VD level than male (P < 0.001). Patients exposed to sunlight had significantly higher VD level and lower hs-CRP levels compared with less-exposed, P value (0.001 and < 0.001), respectively. Exercise significantly increased VD and decreased ACR levels in DM patients, P value (0.046 and 0.002), respectively. VD was positively associated with age (r = 0.355 P = 0.040) and negatively correlate with BMI (r = −0.502 P = 0.009), duration of disease (r = −0.498 P = 0.003), ACR (r = −0.384 P = 0.015), and HbA1c (r = −0.327 P = 0.032). Conclusion: The evidence from this study suggest that patients with Type 2 diabetes with VD deficiency are at higher risk for developing CVD and nephropathy.

Key words: Albumin:creatinine ratio, cardiovascular diseases, high-sensitive C-reactive protein, nephropathy, Sudan, type 2 diabetes mellitus, Vitamin D

INTRODUCTION

Vitamin D (VD) is being recognized recently as antiproliferative, stimulating cell differentiation, immunomodulatory, and anti-inflammation activity.[1] Therefore, it has a role in human health including cancer, infectious, respiratory, autoimmune, and cardiovascular diseases (CVDs).[3] Recently, VD has been linked with the development of Type 2 diabetes mellitus (T2DM), through its direct effect on pancreatic β-cell function, insulin secretion, and action.[3]

VD deficiency is highly prevalent worldwide,[4,8] about 1 billion in the world[8] and up to 50% of the adult population in developing countries lack VD.[10] In addition, the prevalence rate of hypovitaminosis D in the United States adults was 41.6%.[8] Many factors increase the deficiency of VD including less sunlight exposure, darkness skin, winter, elderly, use of clothes covering most of the body, female gender, and obesity.[11,12] Several previous studies proved that VD deficiency is highly prevalent in Type 1 and T2DM.[3,8] Few studies in Sudan reported an association between T2DM and VD deficiency. Furthermore, VD deficient is common in T2DM female than male.[13,14]

How to cite this article: Aljack HA, Abdalla MK, Idris OF, Ismail AM. Vitamin D deficiency increases risk of nephropathy and cardiovascular diseases in Type 2 diabetes mellitus patients. J Res Med Sci 2019;24:47.

Address for correspondence: Hala Abdalazeem Aljack, Department of Clinical Chemistry, Omdurman Islamic University, Faculty of Medical Laboratory Science, Alshigla Street, Khartoum 11111, Sudan. E-mail: hala.abdalazeem@yahoo.com; amarqqqu@yahoo.com

Received: 26-05-2018; Revised: 13-11-2018; Accepted: 17-02-2019

© 2019 Journal of Research in Medical Sciences | Published by Wolters Kluwer - Medknow
VD prevents the endothelial damage of the kidney which leads to microalbuminuria (MAU), by its role in negative regulation of renin–angiotensin–aldosterone system.[15] One study suggested that patients with Type 2 diabetes and chronic renal disease have an exceptionally high rate of severe VD deficiency.[16] A number of observations have reported a correlation between MAU and VD deficiency in T2DM,[16] and the prevalence of albuminuria was enhanced with decreased levels of VD.[17] Moreover, VD deficiency independently associated with prevalent of CVD in patients with Type 2 diabetes with mild kidney dysfunction.[18]

Early detection of nephropathy and CVD risks provides the way for early intervention to reduce T2DM complications. Therefore, the present study aimed to investigate whether VD has diagnostic and predictive risk factors for diabetic nephropathy and CVD in T2DM patients.

**MATERIALS AND METHODS**

This is a cross-sectional study conducted on randomly selected patients with Type 2 diabetes attending Military Hospital in Khartoum State (hospital for referring to it from all States of Sudan). After informed consent, blood samples were collected from 205 clinically diagnosed patients and consist of 94 males and 111 females. Patients with diabetes with known inflammatory, cardiovascular, liver, renal diseases, and/or with VD supplement were excluded from the study. The diagnoses were based on clinical history records. Before the demographic determination and classification instructed questionnaire was used, we asked the patients about age, sex, education level, lifestyle (based on the economic status), sun exposure, and family history. Moreover, glycemic control, BMI, and VD status were classified based on the reference range of each. Hemoglobin A1c (HbA1c) ≤8% considered as controlled and >8% as uncontrolled. Whereas, BMI 18.5–25 kg/m² defined as normal weight, >25–30 kg/m² overweight, and >30 kg/m² obese. Meanwhile, VD level ≤30 ng/ml considered as deficient and >30 ng/ml as sufficient.

**Ethical consideration**

The study was approval by the Local Ethical Committee of Al-Neelain University (issued on May 5, 2015) and Military Hospital Managers and carried out in accordance to International Ethical Guideline. Written informed consent was obtained from all participants.

**Measurement of body mass index**

Body mass index (BMI) was calculated by dividing weight in kilograms by height in meters squared (kg/m²).

**Measurement of Vitamin D**

Serum VD level was measured using the competitive inhibition enzyme-linked immunosorbent assay or ELISA (EUROIMMUN AG, Germany). Brief according to manufacturer’s protocol, 200 μl sample was added into biotin-coated monoclonal anti-VD antibodies, followed by competitive binding of 100 μl VD-labeled. Unbound VD were washed. Streptavidin-peroxidase (100 μl) was added to detect bound biotin labeled 25-OH VD, and then, peroxidase substrate tetramethylbenzidine (100 μl) was added to promote a color reaction. The color intensity was inversely proportional to the 25-OH VD concentration in the sample. Samples results were calculated using standard curve. The detection limit is 1.6 ng/mL (sensitivity) and specifically detects 25-VD and VD₃.

**Measurement of high-sensitivity C-reactive protein**

Serum levels of high-sensitivity C-reactive protein (hs-CRP) in patients were measured using the particle-enhanced immunoturbidimetric assay method Cobas C-311®. Human CRP agglutinates with latex particles coated with monoclonal anti-CRP antibodies, and then, the precipitate was determined turbidimetrically.

**Measurement of albumin:creatinine ratio**

According to the manufacturer, urine albumin and creatinine were analyzed by Cobas C-311® fully automated analyzer. Anti-albumin antibodies react with antigen in the sample to form antigen-antibody complexes, following agglutination, and then, complexes were measured turbidimetrically. Moreover, creatinine reacts with picrate in alkaline solution to form a yellow-red adduct. The rate of the dye formation is directly proportional to the creatinine concentration in the specimen and is measured photometrically.

**Measurement of hemoglobin A1c**

The analysis of HbA1c was done in fully automated closed system – Roche Cobas C-311®. Total hemoglobin and HbA1c concentrations are determined after hemolysis of the anticoagulated whole blood specimen. The total hemoglobin was measured using spectrophotometer. HbA1c was determined by immune turbidimetrically. The ratio of both concentrations was yield the final percentage of HbA1c results. The anticoagulated whole blood specimen was hemolysed with HbA1c hemolysis reagent. The released Hb was proteolytically degraded by pepsin, to make the β-N-terminal structures more accessible for the immunoassay. In addition, the heme portions are oxidized for the Hb assay. Total Hb was determined in the hemolysate using a cyanide-free colorimetric method based on the formation of a brownish-green chromophore (alkaline hematin D-575) in alkaline detergent solution. The color intensity was proportional to the Hb concentration. HbA1c is measured using monoclonal antibodies attached to latex particles. The antibodies bind the β-N-terminal fragments of HbA1c. Remaining free antibodies were agglutinated with a synthetic polymer carrying multiple copies of the
β-N-terminal structure of HbA1c. The change in turbidity was inversely related to the amount of bound glycopeptides and is measured turbidimetrically at 550 nm. The test sensitivity is 3%. Acetylated Hb, carbamylated Hb, and labile HbA1c do not affect the assay result. Glycated HbF is not detected.

**Statistical analysis**
The Statistical Package for the Social Sciences (SPSS) version 17.0 (SPSS Inc., Chicago, USA) was used for the data analysis. Data are presented as 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 was employed to evaluate the relationship between continuous variables. *P* ≤ 0.05 was used as the statistical significance.

**RESULTS**

**Demographic and baseline characteristics of study population**
Patients demographic analyses showed that, in total, 205 patients were recruited, 111 (54%) were female and 94 (46%) were male. Of 205 patients with Type 2 diabetes, 161 (78.5%) had VD deficient and 44 (21.5%) had VD sufficient. High frequency of BMI status was reported in overweight 94 (46%) followed by obese 64 (31%) and normal weight 47 (23%). Of all patients, 141 (68.8%) were sun exposed <5 hr. Likewise, patients had not physical exercise 101 (52.1%). Demographic and baseline characteristics are summarized in Table 1.

**Nonparametric association of study variables in groups classified according to Vitamin D status**
The results of the study revealed that gender, BMI, and sun exposure were significantly associated with VD deficient (*P*<0.001, *P*=0.004, and *P*=0.006, respectively). Furthermore, they increased the risk of VD deficient (gender – 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]). The results of the association were shown in Table 2.

**Comparison of study parameters in groups classified based on Vitamin D status, gender, sun exposure, physical exercise, and glycemic control**
The mean values of hs-CRP and albumin: creatinine ratio (ACR) levels were significantly higher in patients with diabetes with VD deficient than in those with VD sufficient (*P*=0.008 and *P*=0.011, respectively). However, the mean value of HbA1c level revealed insignificant difference.

### Table 1: Demographic and baseline characteristics of Type 2 diabetes mellitus patients

| Characteristic                  | Frequency (%) |
|--------------------------------|---------------|
| **Gender**                     |               |
| Male                           | 94 (46)       |
| Female                         | 111 (54)      |
| **Age (years)**                |               |
| <55                            | 96 (47)       |
| >55                            | 109 (53)      |
| **BMI**                        |               |
| Normal weight                  | 47 (23)       |
| Overweight                     | 94 (46)       |
| Obese                          | 64 (31)       |
| **Diabetic control**           |               |
| Controlled                     | 64 (31.2)     |
| Uncontrolled                   | 141 (68.8)    |
| **Education status**           |               |
| Low                            | 36 (18)       |
| Moderate                       | 132 (65)      |
| High                           | 35 (17)       |
| **Lifestyle**                  |               |
| Low                            | 69 (35.0)     |
| Moderate                       | 113 (57.40)   |
| Good                           | 15 (7.6)      |
| **Physical exercise**          |               |
| Yes                            | 93 (47.9)     |
| No                             | 101 (52.1)    |
| **Sun exposure**               |               |
| <5 h                           | 176 (87.1)    |
| >5 h                           | 26 (12.9)     |
| **Family history of DM**       |               |
| First degree                   | 108 (36.5)    |
| Second degree                  | 137 (46.3)    |
| No                             | 51 (17.2)     |
| **Family history of CVD**      |               |
| Yes                            | 26 (14.1)     |
| No                             | 159 (85.9)    |
| **Cholesterol-lowering agent** |               |
| Yes                            | 84 (47.2)     |
| No                             | 94 (52.8)     |
| **VD status**                  |               |
| VD deficient                   | 161 (78.5)    |
| VD sufficient                  | 44 (21.5)     |

The mean level of VD (20.0 ± 8.90 ng/ml) was significantly reduced in females compared to that in males (30.2 ± 12.2 ng/ml) with *P* = 0.000, whereas hs-CRP (5.91 ± 2.61 mg/l) was considerably elevated (3.54 ± 2.55 mg/l) with *P* = 0.005.

The mean VD level (23.6 ± 11.2 ng/ml) was significantly lower in group exposed to sun <5 h compared to sun exposed >5 h (32.8 ± 12.3 ng/ml) with *P* = 0.001; in contrast, hs-CRP was significantly elevated (5.15 ± 6.48 mg/l) than (2.81 ± 1.91 mg/l) with *P* = 0.000.
Patients on physical exercise significantly had higher VD and lower ACR levels, with $P = 0.046$ and $P = 0.002$, respectively. On the other hand, uncontrolled patients with diabetes had significantly higher ACR with $P = 0.019$; the results were presented in Table 3.

### DISCUSSION

Latest studies in Sudan revealed a higher prevalence of VD deficiency among T2DM patients, which attributed to nutritional, skin color, sun exposure times, and uses of sun blockers. This finding signifies the need to determine a possible relationship between VD, ACR, hs-CRP levels, and study variables. Therefore, monitoring of VD was valuable for the diagnosis, supplementation regimen if necessary and thus prevention of T2DM complication.

The results of characteristics demonstrated that T2DM is more common in females, overweight, and most patients

![Image of correlation graphs](image-url)

**Figure 1:** Pearson’s correlation coefficient test has been used to correlate between Vitamin D and variables indicative cardiovascular diseases, nephropathy, and glycemic control. ($r^+$)=Pearson correlation; ($r^-$)=Negative correlation; BMI = Body Mass Index; hs-CRP = high-sensitivity C-reactive protein; HbA1c = Glycated hemoglobin.

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

| Parameter         | Frequency (%) | OR (CI) | $P$  |
|-------------------|--------------|---------|------|
| Gender            |              |         |      |
| Male              | 62 (38.70)   | 32 (71.10) | 3.89 (1.89-7.98) | <0.001 |
| Female            | 98 (61.30)   | 13 (28.90) |         |       |
| Age (years)       |              |         |      |
| <55               | 79 (49.01)   | 15 (34.09) | 1.86 (0.92-3.73) | 0.054 |
| >55               | 82 (50.99)   | 29 (65.91) |         |       |
| BMI               |              |         |      |
| Normal weight     | 30 (19.00)   | 19 (40.40) |         |       |
| Overweight        | 72 (45.50)   | 20 (42.60) | 5.97 (1.79-19.79) | 0.004 |
| Obese             | 56 (40.50)   | 8 (17.00)  | 2.24 (0.76-6.59) | 0.143 |
| Diabetic control  |              |         |      |
| Controlled        | 50 (31.00)   | 16 (36.36) | 0.78 (0.39-1.58) | 0.310 |
| Uncontrolled      | 111 (69.00)  | 28 (63.64) |         |       |
| Physical exercise |              |         |      |
| Yes               | 71 (44.65%)  | 26 (56.52%) | 0.62 (0.32-1.20) | 0.105 |
| No                | 88 (55.35%)  | 20 (43.48%) |         |       |
| Sun exposure (h/day) |      |         |      |
| <5                | 147 (91.30)  | 33 (75.00)  | 3.5 (1.45-8.39) | 0.006 |
| >5                | 14 (8.70)    | 11 (25.00)  |         |       |

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.
were poorly glycemic control, physically inactive, and less sun exposure. Meanwhile, the current study reported a high prevalence of VD deficiency (78.5%) in our population. These findings have been documented in many previous studies that obese and females are more vulnerable to VD deficiency; these findings were reported in nondiabetic and patients with diabetes.\(^{[19,20]}\) Moreover, supported with another study that female gender is an independent predictor of VD deficiency.\(^{[21]}\) Therefore, speculated to many factors could lead to VD deficiency, such as nutritional, physical activity, and spend more indoor times despite dark skin color. Furthermore, supporting with previous observations,\(^{[22,23]}\) the results of the current study demonstrated that, females had increased hs-CRP than males.

In addition, exposure to sunlight significantly increased VD and decreased hs-CRP levels. Likewise, physical exercise increases the VD level. Our study confirmed by previous observations, suggesting that low level of sun exposure and physical inactivity affected VD status.\(^{[24]}\) Furthermore, physical exercise may increase serum level of VD by increasing skin exposure to sunlight,\(^{[24]}\) increasing lipolysis, and enhancing mobilization of deposited VD from the fat compartments.\(^{[25]}\)

Concurrent with previous findings, the present study demonstrated that patients with diabetes with VD deficient had higher levels of hs-CRP than those with VD sufficient. The previous study has shown that VD deficiency may contribute to systemic inflammation,\(^{[24]}\) due to its role to inhibit production of inflammatory markers such as interferon-gamma, interleukin 2 (IL-2), and IL-5 by Th-1 lymphocytes, and it also inhibits synthesis of IL-6 by monocytes, which is the primary stimulant of hs-CRP production.\(^{[19]}\) Moreover, VD deficiency associated with inflammation-linked vascular endothelial dysfunction that leads to macrovascular and microvascular complications.\(^{[1]}\)

The study provides evidence that mean ACR was significantly higher in diabetic with VD deficient than those with VD sufficient. Moreover, the negative association between ACR and VD was demonstrated. These findings incompatible with previous report that patients with diabetes had increased level of ACR; on the other hand, VD supplementation diminished ACR.\(^{[9]}\) Since ACR considered as an early predictor marker for nephropathy, and VD has a role in proteinuria homeostasis.\(^{[27]}\) Therefore, suggesting that, VD deficiency associated with nephropathy in T2DM patients. Furthermore, these findings have been reinforced by the negative association between VD level and duration of DM. In addition to that, physical exercise significantly decreased ACR level. Previous reports revealed similar finding that physical activity is associated with lower

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

| Parameter                              | Study parameters in case group classified according to VD status                                                                 |
|----------------------------------------|-----------------------------------------------------------------------------------------------------------------------------|
|                                        | VD deficient (mean±SD)                                                                                                         |
|                                        | VD sufficient (mean±SD)                                                                                                         |
|                                        | P                                                                                                                            |
| HbA1c (%)                              | 9.46±2.43                                                                                                                  |
|                                        | 8.82±2.63                                                                                                                  |
|                                        | 0.159                                                                                                                       |
| hs-CRP (mg/L)                          | 4.24±4.11                                                                                                                  |
|                                        | 2.72±2.61                                                                                                                  |
|                                        | 0.008                                                                                                                       |
| Albumin:creatinine ratio (mg/g)        | 47.8±117                                                                                                                   |
|                                        | 19.9±22.7                                                                                                                  |
|                                        | 0.011                                                                                                                       |

**Patients classified according to gender**

| Parameter                              | Male (mean±SD)                                                                 | Female (mean±SD)                                                                 |
|----------------------------------------|------------------------------------------------------------------------------|------------------------------------------------------------------------------|
|                                        | P                                                                            | P                                                                            |
| Vitamin D (ng/ml)                      | 30.2±12.2                                                                    | 20.0±8.90                                                                    |
|                                        | <0.001                                                                        | <0.001                                                                        |
| hs-CRP (mg/L)                          | 3.54±2.55                                                                    | 5.91±2.61                                                                    |
|                                        | 0.005                                                                        |                                                                               |
| Albumin:creatinine ratio (mg/g)        | 30.6±8.60                                                                    | 42.9±7.21                                                                    |
|                                        | 0.271                                                                        |                                                                               |

**Patients classified according to sun exposure**

| Parameter                              | Sun exposure <5 h/day (mean±SD)                                                                                     |
|----------------------------------------|------------------------------------------------------------------------------------------------------------------|
|                                        | Sun exposure > 5 h/day (mean±SD)                                                                                   |
|                                        | P                                                                                                                |
| Vitamin D (ng/ml)                      | 23.6±11.2                                                                                                         |
|                                        | 32.8±12.3                                                                                                         |
|                                        | 0.001                                                                                                             |
| hs-CRP (mg/L)                          | 5.15±6.48                                                                                                         |
|                                        | 2.81±1.91                                                                                                         |
|                                        | <0.001                                                                                                             |
| Albumin:creatinine ratio (mg/g)        | 38.6±6.33                                                                                                         |
|                                        | 24.0±5.79                                                                                                         |
|                                        | 0.092                                                                                                             |

**Patients classified according to physical exercise**

| Parameter                              | Patients with physical exercise (mean±SD)                                                                 |
|----------------------------------------|----------------------------------------------------------------------------------------------------------|
|                                        | Patients without physical exercise (mean±SD)                                                            |
|                                        | P                                                                                                         |
| Vitamin D (ng/ml)                      | 27.0±12.4                                                                                                 |
|                                        | 23.3±11.0                                                                                                 |
|                                        | 0.046                                                                                                     |
| hs-CRP (mg/L)                          | 4.29±5.35                                                                                                 |
|                                        | 5.20±6.91                                                                                                 |
|                                        | 0.309                                                                                                     |
| Albumin:creatinine ratio (mg/g)        | 21.1±4.15                                                                                                 |
|                                        | 48.6±77.4                                                                                                 |
|                                        | 0.002                                                                                                     |

**Patients classified according to glycemic control**

| Parameter                              | Controlled DM (mean±SD)                                                                                       |
|----------------------------------------|--------------------------------------------------------------------------------------------------------------|
|                                        | Uncontrolled DM (mean±SD)                                                                                     |
|                                        | P                                                                                                            |
| Vitamin D (ng/ml)                      | 25.7±11.4                                                                                                  |
|                                        | 24.3±11.9                                                                                                 |
|                                        | 0.462                                                                                                      |
| hs-CRP (mg/L)                          | 4.06±2.63                                                                                                  |
|                                        | 5.12±2.65                                                                                                 |
|                                        | 0.267                                                                                                      |
| Albumin:creatinine ratio (mg/g)        | 20.6±6.59                                                                                                  |
|                                        | 43.8±77.4                                                                                                 |
|                                        | 0.019                                                                                                      |

Two-tailed 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 hemoglobin; hs-CRP=High-sensitivity C-reactive protein; SD=Standard deviation; DM=Diabetes mellitus.
albumin excretion in the diabetic population despite unknown mechanism of physical exercise on ACR; it may be due to its effects on the vascular endothelium that mediated by nitric oxide which acts as a vasorelaxant.[28]

The present study focused to compare mean VD level of uncontrolled diabetic patients with controlled. In spite of an insignificant difference was found, yet, it agreed with previous a study that demonstrated insignificant differences in mean HbA1c between groups of VD status.[26] Likewise, Pearson’s regression analyses revealed that VD level negatively correlated with HbA1c. Since the role of VD in pancreatic β-cell functions, which acts to enhance insulin secretion and conversion from proinsulin to insulin, VD might facilitate insulin action by simulating the insulin receptors expression and regulation of the calcium pool.[29] Therefore, VD must be considered in blood glucose homeostasis and thus diabetic complications.[30]

In fact, that VD level was negatively related with BMI,[31] duration of disease,[32] and glycemic control.[33] In other studies, the significant association between hypovitaminosis D and albuminuria was reported, and the possible effect of low VD level on nephropathy progression can be determined.[33] In addition, drug trial study proved that the administration of VD in patients with Type 2 diabetes with hypovitaminosis D leads to normalization of serum VD level and decrease proteinuria.[34]

The limitations of this study the number of sample size. Other limitations of this study were measuring some laboratory parameters related to VD regulation such as parathyroid hormone, phosphorus, and calcium levels. The major limitation of this study was that patients selected depending on their previous clinical data, no preinvestigations have done to overcome drawback confounding factors.

CONCLUSION
The data of the present study suggest that the frequency of VD deficiency is higher in our population. Type 2 diabetic with VD<30 ng/ml had higher levels of ACR and hs-CRP. Moreover, VD level was inversely associated with BMI, duration of disease, ACR, and HbA1c. Therefore, VD deficiency might be a risk factor for developing CVD and nephropathy in patients with Type 2 diabetes. Therefore, monitoring and VD supplementation regimens are recommended.

Acknowledgment
The authors gratefully acknowledge Dr. Nazik Mahmoud (Specialist of Diabetes and Endocrinology) at diabetic center of military hospital for her valuable assistance in this study.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES
1. Mao L, Ji F, Liu Y, Zhang W, Ma X. Calcitriol plays a protective role in diabetic nephropathy through anti-inflammatory effects. Int J Clin Exp Med 2014;7:5437-44.
2. Ahmadieh H, Azar ST, Lakkis N, Arabi A. Hypovitaminosis d in patients with type 2 diabetes mellitus: A relation to disease control and complications. ISRN Endocrinol 2013;2013:641098.
3. Kulie T, Groff A, Redmer J, Houmshell J, Schrager S. Vitamin D: An evidence-based review. J Am Board Fam Med 2009;22:698-706.
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.
5. Alcubierre N, Vals J, Rubiniat E, Cao G, Esquerda A, Traveset A, 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.
6. Fanari Z, Hammami S, Hammami MB, Hammami S, Abdellatif A. Vitamin D deficiency plays an important role in cardiac disease and affects patient outcome: Still a myth or a fact that needs exploration? J Saudi Heart Assoc 2015;27:264-71.
7. Joergensen C, Gall MA, Schmedes A, Tarnow L, Parving HH, Rossing P, et al. Vitamin D levels and mortality in type 2 diabetes. Diabetes Care 2010;33:2238-43.
8. Lavie CJ, Lee JH, Milani RV. Vitamin D and cardiovascular disease will it live up to its hype? J Am Coll Cardiol 2011;58:1547-56.
9. Nakashima A, Yokoyama K, Yokoo T, Urashima M. Role of Vitamin D in diabetes mellitus and chronic kidney disease. World J Diabetes 2016;7:89-100.
10. Liefaard MC, Ligthart S, Vitezova A, Hofman A, Uitterlinden AG, Kieffe-de Jong JC, et al. Vitamin D and C-reactive protein: A mendelian randomization study. PLoS One 2015;10:e0131740.
11. Mandarino NR, Júnior FD, Salgado JV, Lages JS, Filho NS. Is Vitamin D deficiency a new risk factor for cardiovascular disease? Open Cardiovasc Med J 2015;9:40-9.
12. Lee JH, O’Keefe JH, Bell D, Hensrud DD, Holick MF. Vitamin D deficiency an important, common, and easily treatable cardiovascular risk factor? J Am Coll Cardiol 2008;52:1949-56.
13. Yousif NM, Ismail AM. Alanine aminotransferase and gamma-glutamyltransferase activity as predictor markers for hepatocellular damage in Vitamin D deficient type 2 diabetes mellitus patients-cross-sectional study. Am J Med Sci 2014;4:186-91.
14. Mohammed MS, Ismail AM. Evaluation of lipid profile in Vitamin D deficiency diabetes mellitus type 2. Eur Acad Res 2014;2:12074-84.
15. 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-S13.
16. Ushuogullari CA, Balkan F, Caner S, Ucler R, Kaya C, Ersoy R, et al. The relationship between microvascular complications and Vitamin D deficiency in type 2 diabetes mellitus. BMC Endocr Disord 2015;15:33.
17. Tiryaki O, 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;38:222-7.
18. Chonchol M, Cigolini M, Targher G. Association between 25-hydroxyvitamin D deficiency and cardiovascular disease in type 2 diabetic patients with mild kidney dysfunction. Nephrol Dial Transplant 2009;23:269-74.

19. Rafiq S, Jeppesen PB. Body mass index, Vitamin D, and type 2 diabetes: A Systematic review and meta-analysis. Nutrients 2018;10. pii: E1182.

20. Dix CF, Bauer JD, Martin I, Rochester S, Duarte Romero B, Prins JR, et al. Association of sun exposure, skin colour and body mass index with Vitamin D status in individuals who are morbidly obese. Nutrients 2017;9. pii: E1094.

21. Rolim MC, Santos BM, Conceição G, Rocha PN. Relationship between Vitamin D status, glycemic control and cardiovascular risk factors in Brazilians with type 2 diabetes mellitus. Diabetol Metab Syndr 2016;8:77.

22. Qasim AN, Budharaju V, Mehta NN, St Clair C, Farouk S, Braunstein S, 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.

23. Mahajan A, Tabassum R, Chavali S, Dwivedi OP, Bharadwaj M, Tandon N, et al. High-sensitivity C-reactive protein levels and type 2 diabetes in urban North Indians. J Clin Endocrinol Metab 2009;94:2123-7.

24. Almehmadi B, Fallata E, Alqahtani S, Al-Agha A. 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.

25. Kavadar G, Demircioğlu DT, Özgünene L, Emre TY. The relationship between Vitamin D status, physical activity and insulin resistance in overweight and obese subjects. Bosn J Basic Med Sci 2015;15:62-6.

26. Haidari F, Zakerkash M, Karandish M, Saki A, Pooraziz S. Association between serum Vitamin D level and glycemic and inflammatory markers in non-obese patients with type 2 diabetes. Iran J Med Sci 2016;41:367-73.

27. Prabhu RA, Saraf K. Vitamin D in diabetic nephropathy. J Postgrad Med 2018;64:5-6.

28. Robinson ES, Fisher ND, Forman JP, Curhan GC. Physical activity and albuminuria. Am J Epidemiol 2010;171:515-21.

29. Swamy M, Ganiger A, Prasad SD, Ratna S. Serum 25-hydroxy Vitamin D levels in type 2 diabetes mellitus - A comparative study. Int J Clin Biochem Res 2016;3:255-8.

30. Ucak S, Sevim E, Ersoy D, Sivritepe R, Basat O, Atay S, et al. Evaluation of the relationship between microalbuminuria and 25-(OH) Vitamin D levels in patients with type 2 diabetes mellitus. Aging Male 2018; 22:1-5.

31. Cimbek A, Gürsoy G, Kirnap NG, Acar Y, Kiliç Z, Gümüş F, et al. Relation of obesity with serum 25 hydroxy Vitamin D3 levels in type 2 diabetic patients. J Res Med Sci 2012;17:1119-23.

32. Kishore PK, Choudhary I, Satyanarayana P, Singh UN. Association of Vitamin D with insulin resistance in type 2 diabetic mellitus patients International Journal of Biomedical Research 2017;8:200-3.

33. Zoppini G, Galletti A, Targher G, Brangani C, Pichiri I, Trombetta M, 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.

34. Momeni A, Mirhosseini M, Kabiri M, Kheiri S. Effect of Vitamin D on proteinuria in type 2 diabetic patients. J Nephropathol 2017;6:10-4.