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Prevalence of vitamin D deficiency among acute coronary syndrome patients in Palestine

Iyad Ali[1,†,*]; *Ahmad Khalil* [1,†]; *Alaa Daibes*[1,†]; *Khaled Qushair* [1,†]; *Ahmed Al-Sabi*[2]; *Muhammad Yasser Alsedfy*[3.4]; *Hassan Kanj*[2]; *Mahmoud Abuissa*[1,†] & *Kamel Jebreen* [5.6,†,*].

[1]Department of Medical Sciences, Faculty of Medicine and Health Sciences, An-Najah National University, Nablus, Palestine. [2]College of Engineering and Technology, American University of the Middle East, Egaila 54200, Kuwait. [3]Alexandria University Cancer Research Cluster, Alexandria 21561, Egypt. [4]Electronics and Nano Devices lab, Faculty of Science - South Valley University, Qena 83523 Egypt. [4]Unité de Recherche Clinique Saint-Louis Fernand Widal Lariboisière, APHP, Paris, France. [5]Department of mathematics, An-Najah National University, Nablus, Palestine. [6]Department of mathematics, Palestine Technical University-Kadoorie, Hebron, Palestine.

†Contributed equally to this manuscript

*Corresponding authors: iyadali@najah.edu; k.jebreen@yahoo.com

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ABSTRACT

Introduction: Research has suggested that having low Vitamin D levels is associated with a higher likelihood of developing cardiovascular disease. Specifically, several observational studies have found that Vitamin D is linked to a decreased risk of coronary artery disease. Our study aimed to determine how prevalent Vitamin D deficiency is in Palestinian patients with acute coronary syndrome, a type of cardiovascular disease. **Methods:** This study used a cross-sectional design, which involved collecting 84 blood samples from patients diagnosed with acute coronary syndrome at two hospitals in Palestine. The blood samples were collected over approximately two months, from late January to late March 2021. They were analyzed to determine the patients' levels of vitamin 25(OH) D. The study also collected information on the patient's medical history, including any co-morbidities such as hypertension, diabetes mellitus, smoking, BMI, LDL, and TIA. The data was analyzed using point estimates, 95% confidence intervals, and frequency and proportion calculations for binary data. In addition, multivariate logistic regression analyses were performed to assess the factors associated with vitamin D status, including crude odd ratios and adjusted odd ratios for the relevant covariates. **Results:** In this study, it was found that 95% of the patients diagnosed with acute coronary syndrome had a deficiency in vitamin D. Of these patients, 50% had a severe deficiency, 32.14% had a moderate deficiency, and 8.33% had a mild deficiency. The study also found a significant relationship between male gender and vitamin D levels, with males having higher odds (OR: 7.07, 95% CI: 1.18–42.30, $P = 0.03$) of being deficient in vitamin D compared to females. Additionally, patients with a history of TIA (transient ischemic attack) were significantly associated with vitamin D deficiency (OR, 0.06, 95% CI, 0.-0.72). The study also showed that non-diabetic patients had higher levels of vitamin D compared to diabetic patients, and patients with hypertension (13.21±11.91 ng/ml) had slightly higher levels of vitamin D compared to those without hypertension (12.69±10.20 ng/ml). Non-smokers (14.36±13.97 ng/ml) and patients with low LDL (14.80±11 ng/ml) also had higher levels of vitamin D. Finally, patients who had suffered from TIA (24.40±25.03 ng/ml) had significantly higher levels of vitamin D compared to those who had not experienced a TIA (12.17±9.36 ng/ml). **Conclusion:** The findings of this study indicate that individuals diagnosed with ACS demonstrated a notable insufficiency of vitamin D. Although the number of studies on this topic is restricted, the outcomes of this research are largely consistent with prior investigations.

Keywords: Vitamin D, Acute Coronary Syndrome, Palestine, Deficiency.

INTRODUCTION

Vitamin D is considered a precursor of hormones. The active form of this vitamin is involved in regulating mineral ion hemostasis, particularly calcium, by boosting intestinal absorption of dietary calcium; hence, it is closely associated with growth, development, and bone health. Vitamin D plays a vital role in insufficient calcium intake by interacting with osteoblasts to signal osteoclast precursors to release calcium from bone stores. In addition to being present in the gut, vitamin D receptors are in numerous other human tissue types, including the bones, heart, vascular smooth muscles, brain, stomach, B and T lymphocytes, and pancreas (1).

Vitamin D exists in two forms, vitamin D2 and vitamin D3. Vitamin D2 is also recognized by the names ergocalciferol and calciferol. Cholecalciferol is also known as vitamin D3 (it derives from cholesterol). Vitamin D enters the body principally through the skin and through the diet. Either dietary vitamin D is absorbed and bound to chylomicron molecules in the gut. 7 dehydrocholesterol is produced in the skin in response to solar UV radiation (2).

Many risk factors are linked to vitamin D deficiency, such as aging, obesity, and low exposure to sunshine (3, 4). Severe vitamin D insufficiency results in rickets or osteomalacia increased PTH secretion due to low blood 1,25(OH)2D and low serum calcium, and an increased risk of fractures, particularly hip fractures (5). Recent research has shown a correlation between vitamin D insufficiency and coronary artery disease; however, vitamin D's protective effect mechanisms are not entirely understood. Recent mechanistic investigations reveal that vitamin D deficiency is connected to decreased endothelial function and vascular stiffness, inflammation, and many other factors that contribute negatively to the cardiovascular system. In addition to mechanistic studies, recent epidemiological research has focused more on the relationship between vitamin D insufficiency and coronary artery disease. Despite the debate surrounding some research, there is accumulating evidence linking low vitamin D levels with coronary artery disease (CAD) (6-9). This study examines the relationship between low vitamin D levels and Acute Coronary Syndrome (ACS) prevalence in Palestinian patients.

METHODS

A cross-sectional study was conducted at Arab Specialized Hospital (ASH) and An-Najah National University Hospital (NNUH) between January and March 2021. The study aimed to evaluate the incidence of vitamin D deficiency and explore a potential relationship between vitamin D insufficiency and acute coronary syndrome (ACS). The research included Palestinian patients diagnosed with ACS who consented to participate. Patients with chronic liver or kidney disease, parathyroid-related disorders, those taking vitamin D supplementation, or any medication that interferes with vitamin D were excluded from the study.

Our protocol (IRB2021D) has been approved by the institutional review board at An-Najah National University. To calculate our sample size, we utilized the Raosoft sample size calculator, with a 7% margin of error, a 90% confidence interval, and an 83.5% response distribution.

After being diagnosed by cardiologists based on clinical presentation, radiological, and laboratory investigations, including ECG and Troponin, 84 patients were included in the study. The study encompassed unstable angina, ST-elevated, and non-ST-elevated myocardial infarction. To obtain sociodemographic data, such as age and gender, as well as clinical history, including hypertension, diabetes mellitus, smoking, prior ischemic heart disease, and Body Mass Index, patients' medical records were utilized.

All patients included in the study had blood samples taken, which were then sent to the laboratory at NNUH to measure 25-OH-vitamin D in serum. Based on the vitamin D levels, which were classified as severe deficiency (<10 ng/ml), moderate deficiency (10-19 ng/ml), and mild insufficient deficiency (insufficient) (20-29 ng/ml), the patients were categorized (8).

Population Characteristics and Definition of Potential Risk Factors

The study recruited a total of 84 patients from a population with an age range of 35 to 87. Furthermore, we evaluated the patient's Body Mass Index (BMI), diabetes mellitus (DM) status, hypertension (HTN) status, gender, smoking status, low-density lipoprotein cholesterol (LDL), and transient ischemic attack (TIA). The BMI was classified according to the World Health Organization's criteria as Healthy Weight (18.5 - 24.9), Overweight (25-29.9), or Obese (> 29.9). Additionally, we divided the ages into two groups, those aged 65 and older or younger.

Data analysis

The study's collected data was analyzed using R version 4.1.1. Descriptive statistical analysis was performed to compare the Vitamin D status of participants (normal, moderate, mild, severe). The distribution of participant information (n=84) was presented in Table (1), while Table (2) presented the vitamin D levels and deficiency status of the study population based on baseline characteristics. The Chi-squared test (denoted by *), ANOVA-test (denoted by **), or Mann-Whitney non-parametric test (denoted by ***) was used to compare quantitative and qualitative variables depending on their statistical distribution. Table (3) presents the results of the multivariate logistic regression analysis with Crude odd ratio (OR, 95% CI) and Adjusted Odd Ratio to the covariates (AOR, 95% CI) for factors associated with vitamin D status. Statistical significance was considered a two-sided P-value < 0.05. Chi-square was used to compare categorical variables between the two groups

RESULTS

Demographic characteristics of study participants

Among those assessed, 76 patients were diagnosed with ACS, accounting for 90.5%. Within this group, 50% were found to have a severe deficiency, 32.14% had a moderate deficiency, and 8.33% had a mild deficiency. The average age of the participants was 62.51±11.22, with a majority of them (54.76%) under the age of 65. The male population comprised over half of the participants (69.05%). The BMI calculation resulted in an average of 28.35±5.35, with 36.90% of participants classified as overweight, 35.71% as obese, and 27.37% within the healthy weight range. Most participants were diagnosed with type 2 diabetes mellitus (61.90%) and had hypertension (67.86%). Additionally, 60.71% of participants were smokers (Table (1)).

Table (1): Distribution of information of participants ($n = 84$).

Characteristics	Frequency (n)	Percent (%)
Vitamin D		
Mean ± SD	13.045 ± 11.36	
min, max	3, 64.29	
Vitamin D deficiency		
Normal	8	9.5
Moderate	27	32.14
Characteristics	**Frequency (n)**	**Percent (%)**
Vitamin D		
Mean ± SD	13.045 ± 11.36	
min, max	3, 64.29	
Mild	7	8.33
Severe Deficiency	42	50
Gender		
Male	58	69.05
Female	26	30.95
Age		
Mean ± SD	62.51 ± 11.22	
min, max	35,87	4
Age≥ 65		
No	46	54.76
Yes	38	45.24
BMI		
Mean ±s d	28.35 ± 5.35	
min, max	20,49	4
BMI		
Healthy Weight	23	27.38
Obese	31	36.9
Overweight	30	35.71
DM		
No	32	38.1
Yes	52	61.9
HTN		
No	27	32.14
Yes	57	67.86
Smoking		
No	33	39.29
Yes	51	60.71
LDL ≥ 100		
No	35	41.67
Yes	49	58.33
TIN		
No	78	92.86
Yes	6	7.14

The average vitamin D level was 13.05±11.36 ng/ml, ranging from 3 ng/ml to 64.29 ng/ml. Based on laboratory reference values, 50% of patients were severely deficient, 32.14% were moderately deficient, and 8.33% had a mild deficiency. The mean vitamin D levels were higher in females (15.75±15.82 ng/ml) than in males (11.83±8.56ng/ml), in patients aged 65 years or older (13.23±13.46 ng/ml) compared to patients under 60 years old (12.89±9.43 ng/ml), in non-diabetic patients (14.98±11.47 ng/ml) compared to diabetic patients (11.86±11.24 ng/ml), in patients with hypertension (13.21±11.91 ng/ml) compared to those without hypertension (12.69±10.20 ng/ml), in non-smokers (14.36±13.97 ng/ml), in patients with low LDL (14.80±11 ng/ml) compared to those with high LDL (11.79±11.56 ng/ml), and in patients who suffered from TIA (24.40±25.03 ng/ml) compared to those who did not (12.17±9.36 ng/ml) (Table (2)).

Table (2): Mean vitamin D levels and vitamin D deficiency status according to the baseline characteristics in the patients of ACS.

Variables	Frequency n (%)	Mean ± SD	Vitamin D deficiency status		*P value*
			No	Yes	
Gender					
Female	26 (30.95)	15.75 ± 15.82	5 (62.5%)	21 (27.6%)	0.04 *
Male	58 (69.05)	11.83 ± 8.56	3 (37.5%)	55 (72.4%)	
Total			8 (100.0%)	76 (100.0%)	
Age					
n (miss)			8 (0)	76 (0)	0.51**
Mean ± Std-Dev			65 ± 12.5	62.2 ± 11.1	
Median (Q1-Q3)			61.5 (56-74.25)	62.5 (54-70)	
Min, Max			51, 87	35, 85	
Age ≥ 65					
No	46 (54.76)	12.89 ± 9.43	5 (62.5%)	41 (53.9%)	
Yes	38 (45.24)	13.23 ± 13.46	3 (37.5%)	35 (46.1%)	0.65 *
Total	84 (100%)		8 (100.0%)	76 (100.0%)	
BMI					
n (miss)			8 (0)	76 (0)	0.44***
Mean±Std. Dev			26.9 ± 3.7	28.5 ± 5.5	
Median (Q1-Q3)			26.75(25.42-28.42)	28 (24.48-31.21)	
Min, Max			21, 33	20, 49	
BMI [c]					
Healthy Weight	23 (27.38)	13.37 ± 10.27	2 (25.0%)	21 (28.4%)	
Obese	31 (36.9)	10.82 ± 7.68	2 (25.0%)	29 (39.2%)	0.76 *
Over Weight	30 (35.71)	15.78 ± 15.08	4 (50.0%)	24 (32.4%)	0.54 *
Total	84 (100%)		8 (100.0%)	74 (100.0%)	
DM					
no	32 (38.1)	14.98 ± 11.47	4 (50.0%)	28 (36.8%)	
yes	52 (61.9)	11.86 ± 11.24	4 (50.0%)	48 (63.2%)	0.47 *
Total	84 (100%)		8 (100.0%)	76 (100.0%)	
HTN					
no	27 (32.14)	12.69 ± 10.30	3 (37.5%)	24 (31.6%)	
yes	57 (67.86)	13.21 ± 11.91	5 (62.5%)	52 (68.4%)	0.73 *
Total	84 (100%)		8 (100.0%)	76 (100.0%)	
Smoking					
no	33 (39.29)	14.36 ± 13.97	4 (50.0%)	29 (38.2%)	
Yes	51 (60.71)	12.19 ± 9.35	4 (50.0%)	47 (61.8%)	0.52 *
Total			8 (100.0%)	76 (100.0%)	
LDL ≥ 100					
No	35 (41.67)	14.80 ± 11	4 (50.0%)	31 (40.8%)	
Yes	49 (58.33)	11.79 ± 11.56	4 (50.0%)	45 (59.2%)	0.62 *

Variables	Frequency n (%)	Mean ± SD	Vitamin D deficiency status		*P value*
			No	Yes	
Total	84 (100%)		8 (100.0%)	76 (100.0%)	
TIA					
No	78 (92.86)	12.17 ± 9.36	6 (75.0%)	72 (94.7%)	
Yes	6 (7.14)	24.395 ± 25.03	2 (25.0%)	4 (5.3%)	0.04 *
Total	84 (100%)		8 (100.0%)	76 (100.0%)	

c: variables were categorized

Risk Factors for Vitamin D Deficiency

To determine the possible association between risk factors and vitamin D status, both univariable and multivariable logistic regression models were utilized to estimate the crude and adjusted Odds Ratios (ORs), as shown in Table (3). Diabetes mellitus, hypertension, BMI, smoking, gender, age, LDL, and TIA were identified as clinical risk factors for vitamin D deficiency and were all adjusted in the multivariable regression models regardless of statistical significance. The results of the binary logistic regression model revealed a significant association between gender and vitamin D status, with males being seven times more likely to have a vitamin D deficiency compared to females (OR: 7.07, 95% CI: 1.18–42.30). Furthermore, a significant association was observed between TIA and vitamin D status, with an OR of 0.06 (95% CI: 0. - 0.72).

Table (3): Crude OR (95%CI) and AOR (95%CI) for the association between vitamin D status and other covariates from Logistic Regression Analysis.

Variable	OR (95% CI)	P Value	AOR (95% CI)	P Value
Gender				
Male	4.37 (0.96,19.90)	0.06	7.07 (1.18,42.3)	0.03
Female	Ref		Ref	
Age				
Yes	1.42 (0.32, 6.38)	0.65	3.77 (0.49,28.82)	0.2
No	Ref		Ref	
BMI				
Overweight	0.57 (0.09, 3.44)	0.54	0.59 (0.06,5.43)	0.64
Obese	1.38 (0.18,10.61)	0.76	1.65 (0.15,18.65)	0.68
Healthy Weight	Ref		Ref	
DM				
Yes	1.71 (0.40, 7.40)	0.47	2.39 (0.28,20.1)	0.42
No	Ref		Ref	
HTN				
Yes	1.30 (0.29, 5.89)	0.73	1.74 (0.25,12)	0.57
No	Ref		Ref	
Smoking				
Yes	1.62 (0.38, 6.99)	0.52	0 (0, Inf)	0.99
No	Ref		Ref	
LDL				
Yes	1.45 (0.34, 6.25)	0.62	0.82 (0.11,6.29)	0.85
No	Ref		Ref	
TIA				
Yes	0.17 (0.03, 1.10)	0.06	0.06 (0,0.72)	0.03
No	Ref		Ref	

DISCUSSION

The study found that the average vitamin D levels were lower in men than in women (15.75±15.82). A previous study in Palestine reported a high prevalence of vitamin D deficiency in females of reproductive age, associated with several risk factors, such as obesity, type 2 diabetes, dyslipidemia, smoking, and systemic hypertension (10, 11). Regarding our knowledge, we found one cross-sectional study that focused on 2026 Norwegians who required weight loss treatment. The study reported that men had considerably greater chances of having vitamin D deficiency than women (12). Our findings are consistent with the previous study, as we also found that men have higher odds of having vitamin D deficiency than women. Specifically, our study reported an odds ratio of 4.37 (0.96, 19.90) for men and 7.07 (1.18, 42.3) for women after adjusting for various risk factors.

Previous global studies have established a connection between low vitamin D levels and diabetes mellitus. Bayani et al. reported that patients with diabetes had a higher incidence of vitamin D insufficiency than those without diabetes (13). In another study by Lee et al., it was found that vitamin D insufficiency was common among 305 type 2 diabetic patients (14). Moreover, a population-based prospective study in Australia found that non-diabetics had higher serum vitamin D concentrations than people with diabetes (15). The presence of vitamin D receptors in β cells and vitamin D-dependent calcium-binding proteins in pancreatic tissue suggests a role for vitamin D in insulin secretion (14, 15). In both in vitro and in vivo models, it has been demonstrated that vitamin D is essential for normal insulin release in response to glucose levels in the blood and for maintaining glucose tolerance.

Conversely, it has been widely observed that low vitamin D levels are associated with hypertension. Our data corroborate previous reports indicating a high prevalence of vitamin D insufficiency in patients with hypertension (16, 17). Our findings also confirm that smoking is a risk factor for vitamin D deficiency, as previously reported (18, 19).

As we had limited resources, such as incomplete lipid profiles of patients, our study had a relatively small sample size. Nonetheless, we established a negative association between serum LDL levels and vitamin D levels by using LDL levels as a dyslipidemic indicator. This finding is consistent with recent research (20-22).

Low serum vitamin D levels are associated with an increased stroke risk (23). However, our results show a significant correlation between Vitamin D deficiency and TIA. The ORs showed that TIA is less likely to happen in Vitamin D deficiency patients. The correlation between Vitamin D status and TIA is controversial to many previous similar studies (20, 24, 25). These findings should pave the way for further investigations in the future.

The regression analysis showed that the predictors and ACS were closely linked. Low serum concentrations of 1,25(OH)2D and 25(OH)D strongly predicted the development of ACS. High systolic blood pressure and high total cholesterol (TC), and HDL-C substantially predicted ACS. On the other hand, neither the D2 nor the D3 substantially predicted the occurrence of ACS. Acute coronary syndromes are separately linked to vitamin D insufficiency, which may also be a separate risk factor for ACS.

CONCLUSION

Despite the few works on vitamin D deficiency and ACS that have been done in this regard, the results are largely consistent with the previous works in this field where the prevalence of vitamin D deficiency among patients of ACS in our study was sufficiently high. Admitting patients with acute coronary syndrome should be checked for vitamin D inadequacy, and treatment should be prescribed accordingly.

Ethics approval and consent to participate

The study followed proper procedures and protocols, including obtaining approval from the Institutional Review Board at An-Najah National University to ensure compliance with ethical guidelines such as the Declaration of Helsinki and the US Federal Policy for the Protection of Human Subjects. Written informed consent was obtained from participants before collecting any samples or data. The participants' identities were kept confidential, and all samples and data were processed anonymously.

Consent for publication

Not Applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Authors' contributions

Iyad Ali: conceptualization, writing-original draft, data curation, funding acquisition, investigation, methodology, project administration, resources, supervision, validation, visualization, and writing review & editing. **Ahmad Khalil**: conceptualization, writing-original draft, data curation, formal analysis, investigation, methodology, resources, software, validation, visualization, and writing review & editing. **Alaa Daibes**: conceptualization, writing-original draft, data curation, formal analysis, investigation, methodology, resources, software, validation, visualization, and writing review & editing. **Khaled Qushair**: conceptualization, writing-original draft, data curation, formal analysis, investigation, methodology, resources, software, validation, visualization, and writing review & editing. **Mahmoud Abuissa**: conceptualization, writing-original draft, data curation, funding acquisition, investigation, methodology, project administration, resources, supervision, validation, visualization, and writing review & editing. **Ahmed Al-Sabi**: Writing-original draft, data curation, formal analysis, investigation, methodology, resources, software, validation, visualization, and writing review & editing. **M. Yasser Alsedfy**: Writing-original draft, data curation, formal analysis, investigation, methodology, resources, software, validation, visualization, and writing review & editing. **Hassan Kanj**: Writing-original draft, data curation, formal analysis, investigation, methodology, resources, software, validation, visualization, and writing review & editing. **Kamel Jebreen**: Writing-original draft, data curation, formal analysis, investigation, methodology, resources, software, validation, visualization, and writing review & editing.

Conflict of interest

The authors declare no conflict of interest.

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REFERENCES

1] Holick, M. F. (2003) Vitamin D: A millenium perspective. *Journal of cellular biochemistry* **88**, 296-307.

2] Atef, S. H. (2018) Vitamin D assays in clinical laboratory: Past, present and future challenges. *The Journal of Steroid Biochemistry and Molecular Biology* **175**, 136-137.

3] Kanj, H. (2016) Contribution to risk analysis related to the transport of hazardous materials by agent-based simulation. Université Grenoble Alpes.

4] Kanj, H., Aly, W. H., and Kanj, S. (2022) A Novel Dynamic Approach for Risk Analysis and Simulation Using Multi-Agents Model. In *Applied Sciences* Vol. 12.

5] Lips, P. (2006) Vitamin D physiology. *Progress in biophysics and molecular biology* **92**, 4-8.

6] Chen, W. R., Qian, Y. A., Chen, Y. D., Shi, Y., Yin, D. W., Wang, H., Zhu, P., Liu, H. W., and Sha, Y. (2014) The effects of low vitamin D on coronary artery disease. *Heart, lung & circulation* **23**, 314-319.

7] Judd, S. E., Nanes, M. S., Ziegler, T. R., Wilson, P. W., and Tangpricha, V. (2008) Optimal vitamin D status attenuates the age-associated increase in systolic blood pressure in white Americans: results from the third National Health and Nutrition Examination Survey. *The American journal of clinical nutrition* **87**, 136-141.

8] Shor, R., Tirosh, A., Shemesh, L., Krakover, R., Bar Chaim, A., Mor, A., Boaz, M., and Golik, A. (2012) 25 hydroxyvitamin D levels in patients undergoing coronary artery catheterization. *European journal of internal medicine* **23**, 470-473.

9] Vacek, J. L., Vanga, S. R., Good, M., Lai, S. M., Lakkireddy, D., and Howard, P. A. (2012) Vitamin D deficiency and supplementation and relation to cardiovascular health. *The American journal of cardiology* **109**, 359-363.

10] Aasheim, E. T., Hofso, D., Hjelmesaeth, J., Birkeland, K. I., and Bohmer, T. (2008) Vitamin status in morbidly obese patients: a cross-sectional study. *The*

American journal of clinical nutrition **87**, 362-369.

11] Carlin, A. M., Rao, D. S., Meslemani, A. M., Genaw, J. A., Parikh, N. J., Levy, S., Bhan, A., and Talpos, G. B. (2006) Prevalence of vitamin D depletion among morbidly obese patients seeking gastric bypass surgery. *Surgery for obesity and related diseases : official journal of the American Society for Bariatric Surgery* **2**, 98-103; discussion 104.

12] Johnson, L. K., Hofso, D., Aasheim, E. T., Tanbo, T., Holven, K. B., Andersen, L. F., Roislien, J., and Hjelmesaeth, J. (2012) Impact of gender on vitamin D deficiency in morbidly obese patients: a cross-sectional study. *European journal of clinical nutrition* **66**, 83-90.

13] Bayani, M. A., Akbari, R., Banasaz, B., and Saeedi, F. (2014) Status of Vitamin-D in diabetic patients. *Caspian journal of internal medicine* **5**, 40-42.

14] Lee, J. I., Oh, S. J., Ha, W. C., Kwon, H. S., Sohn, T. S., Son, H. S., and Cha, B. Y. (2012) Serum 25-hydroxyvitamin D concentration and arterial stiffness among type 2 diabetes. *Diabetes research and clinical practice* **95**, 42-47.

15] Gagnon, C., Lu, Z. X., Magliano, D. J., Dunstan, D. W., Shaw, J. E., Zimmet, P. Z., Sikaris, K., Grantham, N., Ebeling, P. R., and Daly, R. M. (2011) Serum 25-hydroxyvitamin D, calcium intake, and risk of type 2 diabetes after 5 years: results from a national, population-based prospective study (the Australian Diabetes, Obesity and Lifestyle study). *Diabetes care* **34**, 1133-1138.

16] Alkhatatbeh, M. J., Abdul-Razzak, K. K., Khasawneh, L. Q., and Saadeh, N. A. (2017) High Prevalence of Vitamin D Deficiency and Correlation of Serum Vitamin D with Cardiovascular Risk in Patients with Metabolic Syndrome. *Metabolic syndrome and related disorders* **15**, 213-219.

17] El-Menyar, A., Rahil, A., Dousa, K., Ibrahim, W., Ibrahim, T., Khalifa, R., and Abdel Rahman, M. O. (2012) Low vitamin d and cardiovascular risk factors in males and females from a sunny, rich country. *The open cardiovascular medicine journal* **6**, 76-80.

18] Gorter, E. A., Krijnen, P., and Schipper, I. B. (2016) Vitamin D deficiency in adult fracture patients: prevalence and risk factors. *European journal of trauma and emergency surgery : official publication of the European Trauma Society* **42**, 369-378.

19] Parva, N. R., Tadepalli, S., Singh, P., Qian, A., Joshi, R., Kandala, H., Nookala, V. K., and Cheriyath, P. (2018) Prevalence of Vitamin D Deficiency and Associated Risk Factors in the US Population (2011-2012). *Cureus* **10**, e2741.

20] Gannage-Yared, M. H., Chedid, R., Khalife, S., Azzi, E., Zoghbi, F., and Halaby, G. (2009) Vitamin D in relation to metabolic risk factors, insulin sensitivity and adiponectin in a young Middle-Eastern population. *European journal of endocrinology* **160**, 965-971.

21] Han, Y. Y., Hsu, S. H., and Su, T. C. (2021) Association between Vitamin D Deficiency and High Serum Levels of Small Dense LDL in Middle-Aged Adults. *Biomedicines* **9.**

22] Ponda, M. P., Dowd, K., Finkielstein, D., Holt, P. R., and Breslow, J. L. (2012) The short-term effects of vitamin D repletion on cholesterol: a randomized, placebo-controlled trial. *Arteriosclerosis, thrombosis, and vascular biology* **32**, 2510-2515.

23] Zhou, R., Wang, M., Huang, H., Li, W., Hu, Y., and Wu, T. (2018) Lower vitamin D status is associated with an increased risk of ischemic stroke: a systematic review and meta-analysis. *Nutrients* **10**, 277.

24] Gupta, A., Prabhakar, S., Modi, M., Bhadada, S. K., Lal, V., and Khurana, D. (2014) Vitamin D status and risk of ischemic stroke in North Indian patients. *Indian journal of endocrinology and metabolism* **18**, 721-725.

25] Kuhn, T., Kaaks, R., Teucher, B., Hirche, F., Dierkes, J., Weikert, C., Katzke, V., Boeing, H., Stangl, G. I., and Buijsse, B. (2013) Plasma 25-hydroxyvitamin D and its genetic determinants in relation to incident myocardial infarction and stroke in the European prospective investigation into cancer and nutrition (EPIC)-Germany study. *PloS one* **8**, e69080.