

High Prevalence of Vitamin D Deficiency in Patients with Acute Myocardial Infarction: An Iraqi Single-Center Study

Shwan Othman Amen¹, Soza Tharwat Baban², Salah Hassan Yousif³, Zana Tharwat Baban⁴, Ahmed Himdad Hawez¹, Dlovan Mustafa Fateh Jalal⁵

¹Cardiac Catheterization Laboratory, Surgical Specialty Hospital - Cardiac Center; ²College of Health Sciences, Hawler Medical University; ³Cardiac Catheterization Laboratory, Surgical Specialty Hospital - Cardiac Center; Department of Surgery, College of Medicine, Hawler Medical University; ⁴Cardiac Surgery Department, Surgical Specialty Hospital - Cardiac Center; ⁵Erbil Directorates of Health, Erbil, Iraq

Abstract

Background: Coronary artery disease (CAD) is the leading cause of morbidity and mortality worldwide despite current advances in primary preventive and state-of-the art interventional strategies for effective CAD treatment. The major manifestation of CAD is the acute myocardial infarction (AMI). Vitamin D deficiency is associated with an increased risk of coronary atherosclerosis and AMI. **Objectives:** The major aim of this study was to determine the association of Vitamin D deficiency with AMI in Iraqi patients living in this region. **Materials and Methods:** Vitamin D level status was determined in 148 patients presented with AMI and 148 of healthy controls. Measurement of serum 25-hydroxyvitamin D (25(OH) D) levels was performed using enzymatic immunoassay method. Normal serum 25(OH) D level is ≥ 30 ng/ml, while patients with level of 20–30 ng/ml was classified as insufficient, and those with level 10–20 ng/ml as deficient. The severe Vitamin D deficiency in patients was defined when serum 25(OH) D level was ≤ 10 ng/ml. **Results:** The mean of 25(OH) D level was significantly lower in patients with AMI (8.73 ng/ml) as compared to healthy controls (13.60 ng/ml). Notably, the prevalence of severe deficiency of 25(OH) D level (<10 ng/ml) was higher in patients with AMI (67.6%) as compared to that in healthy controls (51.4%). This difference was statistically significant. Similar trend was observed for the prevalence of deficient Vitamin D level (≥ 10 – <20 ng/ml) in cases (28.4%) as compared to control group (24.3%). Moreover, 4.1% of AMI patients showed insufficient 25(OH) D level in comparison to 13.5% in healthy individuals of control group. Interestingly there were no AMI patients with sufficient 25(OH) D level (30–100 ng/ml) while 10.8% of healthy individuals in the control group showed sufficient 25(OH) D level. **Conclusions:** This study concludes that Vitamin D deficiency is a highly prevalent condition in patients with AMI among Iraqi population and it is an emerging new risk factor associated with AMI.

Keywords: Acute myocardial infarction, prevalence, Vitamin D deficiency

INTRODUCTION

Coronary artery disease (CAD) represents the greatest leading cause of morbidity and mortality throughout the world despite current advances in primary preventive and state-of-the art interventional strategies for effective CAD treatment.^[1] The major cause of CAD is the atherosclerosis of coronary arteries.^[2] Atherosclerosis is characterized by endothelial dysfunction, vascular inflammation and the formation of atherosclerotic plaque.^[3] This build-up of atherosclerotic plaque causes an inadequate supply of oxygen to myocardial tissue leading to myocardial hypoxia. Consequently, the plaque rupture and atherothrombosis cause further narrowing of coronary arteries and almost occluding the blood flow leading to fatal acute coronary syndromes.^[4] The most evident manifestation of CAD is the Acute myocardial infarction (AMI). Extensive research studies, the foremost among them is the Farmingham

heart study findings had clarified the cause of cardiovascular diseases and emphasized on the critical role of classical risk factors in the development of CAD such as hyperlipidemia, hypertension, diabetes mellitus, smoking, diet, physical inactivity, and obesity.^[5,6]

It should be pointed out; however, these risk factors can explain only a proportion of morbidity or mortality from CAD

Address for correspondence: Dr. Shwan Othman Amen, Surgical Specialty Hospital - Cardiac Center, Erbil, Iraq. E-mail: amenshwan@yahoo.com

Submitted: 02-Nov-2019 **Accepted:** 06-Oct-2020
Published: 14-Dec-2020

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Amen SO, Baban ST, Yousif SH, Baban ZT, Hawez AH, Jalal DM. High prevalence of vitamin D deficiency in patients with acute myocardial infarction: An Iraqi single-center study. Med J Babylon 2020;17:358-62.

Access this article online

Quick Response Code:



Website:
www.medjbabylon.org

DOI:
10.4103/MJBL.MJBL_67_19

disease. A better understanding of CAD pathophysiology might have a considerable impact on clinical management. Recent attention has been focused on new emerging risk factors with therapeutic implications, including an inflammatory biomarker, Vitamin D.^[7] Beyond involvement of Vitamin D level in skeletal health such as bone metabolism and calcium homeostasis, growing evidence has linked Vitamin D deficiency to increased risk of CAD development.^[8] An important factor for worldwide high prevalence of Vitamin D deficiency is because of insufficient sun exposure and limited induced Vitamin D production in the skin and low Vitamin D intake by nutrition.^[9] Recent studies have demonstrated that Vitamin D deficiency is observed in patients suffering from CAD, and its major manifestations such as AMI.^[10] A case-control study conducted on Danish population, which examined 53 patients hospitalized with AMI and compared them to 409 control subjects, and it was observed that Vitamin D levels were lower in patients with AMI as compared to healthy subjects.^[11] In a similar study examined 30 patients with AMI matched with control subjects with age and gender, and showed a linearly decreasing risk of AMI associated with higher Vitamin D levels.^[12] Another cross-sectional study had also elucidated that low levels of Vitamin D are correlated with increased severity of cardiovascular pathology, prevalent myocardial dysfunction and heart failure. Thus, suggesting that Vitamin D supplementation is useful for treatment and prevention of CAD.^[13]

The association between Vitamin D deficiency and CAD is most likely attributed to the following recent findings.^[14] First, Vitamin D receptors (VDRs) are present in most cardiac tissues such as cardiomyocytes and vascular smooth muscle and maybe involved in the regulation of blood pressure and proliferation of vascular smooth muscle cells, myocytes, and regulation of cardiac cell growth. Moreover, VDR antagonists inhibit the development of atherosclerosis, calcification of the arteries, heart muscle hypertrophy and thrombosis.^[15,16] Second, the proportional increase in prevalence of CAD, diabetes, hypertension and Vitamin D deficiency or insufficiency to the distance from the equator. Moreover, reduced sunlight exposure leads to Vitamin D deficiency because ultraviolet-B induced Vitamin synthesis in the skin is the main factor of circulating 25-hydroxyvitamin D (25(OH) D) concentration that are measured to assess Vitamin D status.^[17,18] Third, Vitamin D deficiency has a role in the development and increase of traditional cardiovascular risk factors such as hypertension and diabetes mellitus. It has been shown that patients with other underlying disease conditions that are associated with Vitamin D deficiency are at higher risk of death, CAD events, and hospitalization compared to those related to their underlying diseases alone.^[19] According to the significant association of Vitamin D deficiency with cardiovascular disease, it is imperative to determine the role of Vitamin D deficiency which can be potential therapeutic target for the treatment and prevention of CAD, and its major manifestation such as AMI. It is well-known that Vitamin D insufficiency

or deficiency is a prevalent disease worldwide, and it is noted to be a highly prevalent health problem in most parts of Iraq.^[20] However, the associations of Vitamin D deficiency with increased prevalence of AMI in Iraqi population have not yet been studied. The aims of this case-control study are to determine the prevalence of Vitamin D deficiency in Iraqi AMI patients and to investigate the association between Vitamin D deficiency and AMI in Iraqi patients.

MATERIALS AND METHODS

Study population

The study sample included 148 patients presented with acute AMI admitted to the causality department of the Surgical Specialty Hospital-Cardiac Center within 12 h of clinical signs and symptoms onset from March to May 2018. Diagnostic criteria of AMI were followed according to the guidelines of the European Society of Cardiology. The inclusion criteria consisted of patients of 20 years old and above, with evident myocardial injury biomarkers such as elevated troponins or creatine kinase myocardial band, prolonged heart ischemic signs or symptoms, electrocardiographic ST-segment changes and patients presenting within 24 h of symptoms onset of AMI. The control group consisted of 148 age-and gender-matched individuals without ischemic heart disease.

Those patients and control subjects with existing inflammatory or autoimmune diseases, pregnancy, anaemia, and acute or chronic liver and kidney diseases were not included in the study. All the AMI patients and control subjects provided written informed consent. Detailed medical history examination and laboratory assessment of vascular risk factors were performed. Case and control data were collected in the questionnaire including their personal histories, major risk factors, history of ischemic heart disease, and provided blood samples for laboratory analysis.

Laboratory analysis

Blood sampling for serum levels of 25(OH) D was obtained in ethylenediaminetetraacetic acid tubes as soon as the patient got admitted to the hospital and before initiating treatment. The level of total 25(OH) D (the major storage form of Vitamin D in the body) in patient's serum was quantitatively measured by 25(OH) D enzymatic cycling immunoassay method using Cobas Integra system (Roche Diagnostics). Following collection, the samples were centrifuged immediately at 4000 g for 10 min. The serum was separated and immediately stored at -20°C until further analysis. Other laboratory biochemical parameters such as Lipid profile test including total cholesterol (mg/dL), high-density lipoprotein cholesterol (mg/dL), low-density lipoprotein cholesterol (mg/dL), triglyceride (mg/dL) and hemoglobin A1C test for diabetes, were measured by enzymatic colorimetric method using Roche Cobas system. We classified the patients as per Table 1.

Statistical analysis of data

Data were analysed using the SPSS statistical software version 21 (SPSS, IBM Company, Chicago, IL, USA).

Differences in variables were tested using Student's *t*-test (continuous data) or the Chi-square test (categorical data). A $P \leq 0.05$ was considered as statistically significantly different.

Ethical consideration

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. It was carried out with patients verbal and analytical approval before sample was taken. The study protocol and the subject information and consent form were reviewed and approved by a local ethics committee. This study was approved by the Ethics Committee of Hawler Medical University.

RESULTS

This study consisted of 148 consecutive patients with AMI (case group) (102 males and 46 females), mean age: 55.9 ± 12.8 years and 148 healthy individuals (control group) (34 males and 114 females), mean age: 60.5 ± 10.5 years. Patients in both case and control groups were separated into four subgroups according to their serum 25(OH) D levels, as described in [Table 1]. The mean of 25(OH) Vitamin D level was significantly lower in patients with AMI in case group (8.73 ng/ml) as compared to healthy individuals in the control group (13.60 ng/ml).

There was a significant difference in the prevalence rate of Vitamin D deficiency among the case and control groups, as shown in [Figure 1]. The prevalence of severe deficiency of 25(OH) D level (<10 ng/ml) was significantly higher in patients with AMI (67.6%) as compared to that in healthy individuals (51.4%) in the control group. Similar trend was observed for the prevalence of deficient Vitamin D level (≥ 10 to <20 ng/ml) in cases (28.4%) as compared to control group (24.3%). Moreover, 4.1% of AMI patients showed insufficient 25(OH) D level in comparison to 13.5% in healthy individuals of control group. Interestingly there were no AMI patients with sufficient 25(OH) D level (30–100 ng/ml) while 10.8% of healthy individuals in the control group showed sufficient 25(OH) D level.

The prevalence of severe Vitamin D deficiency was higher in female patients with AMI (75.0%) than male patients (62.7%). This difference was statistically significant ($P < 0.001$), as described in Figure 2.

Furthermore, the prevalence of Vitamin D levels according to the age of AMI patients is shown in Figure 3. Results showed that among patients with AMI in case group, the highest rate

of severe Vitamin D deficiency level was in age group of 60–69 years (36.0%). The highest rate of deficient Vitamin D level was observed in age group of 50–59 years (40.9%). Whereas, the highest rate of insufficient Vitamin D level was observed in age group of 70–79 years (66.7%). There was significant difference between the age groups ($P < 0.05$).

It was observed that 44.4% of female AMI patients in age group of 60–69 years showed high prevalence of severe Vitamin D deficiency level. Similarly, 50% of female AMI patients in age group of 50–59 years were observed with deficient Vitamin D level, as shown in [Table 2].

DISCUSSION

Vitamin D deficiency is a highly prevalent condition worldwide. A growing number of data indicate that Vitamin D deficiency

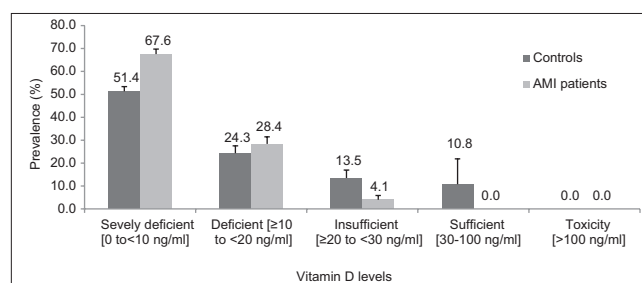


Figure 1: Distribution of Vitamin D levels in patients with acute myocardial infarction and control subjects

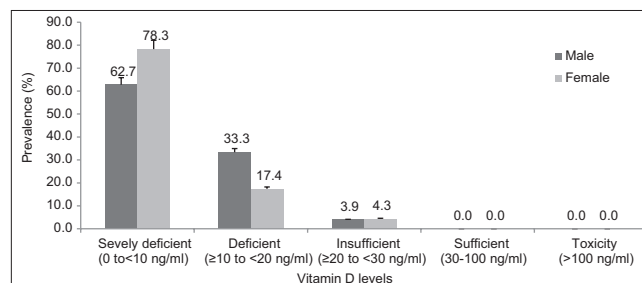


Figure 2: Distribution of Vitamin D levels in patients with acute myocardial infarction in relation to gender

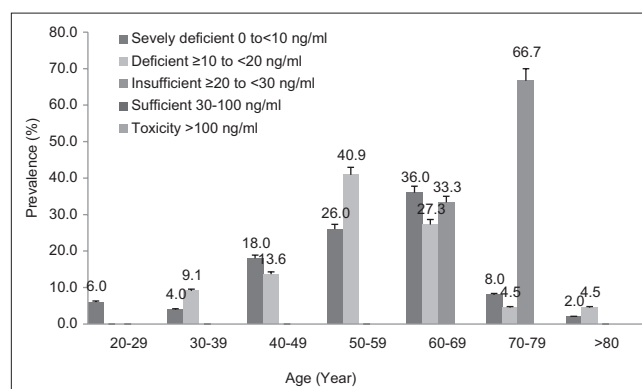


Figure 3: Distribution of Vitamin D levels in relation to age of patients with acute myocardial infarction

Table 1: Classification of 25-hydroxyvitamin D levels

Vitamin D status	Serum 25(OH)D (ng/ml)
0–<10 ng/ml	Severely deficient
≥10–<20 ng/ml	Deficient
≥20–<30 ng/ml	Insufficient
30–100 ng/ml	Sufficient
>100 ng/ml	Toxicity
25(OH)D: 25-hydroxyvitamin D	

Table 2: Distribution of Vitamin D levels in patients with acute myocardial infarction in relation to gender and age

Age	Severely deficient, <i>n</i> (%)		Deficient, <i>n</i> (%)		Insufficient, <i>n</i> (%)		Sufficient, <i>n</i> (%)		Toxicity, <i>n</i> (%)		Total, <i>n</i> (%)
	0–<10 ng/ml		≥10–<20 ng/ml		≥20–<30 ng/ml		30–100 ng/ml		>100 ng/ml		
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	
20–29	6 (9.4)	0	0	0	0	0	0	0	0	0	6 (4.1)
30–39	4 (6.3)	0	4 (11.8)	0	0	0	0	0	0	0	8 (5.4)
40–49	12 (18.8)	6 (16.7)	4 (11.8)	2 (25.0)	0	0	0	0	0	0	24 (16.2)
50–59	14 (21.9)	12 (33.3)	10 (29.4)	4 (50.0)	0	0	0	0	0	0	40 (27.0)
60–69	20 (31.3)	16 (44.4)	12 (35.3)	0	2 (50.0)	2 (100.0)	0	0	0	0	52 (35.1)
70–79	6 (9.4)	2 (5.6)	2 (5.9)	2 (25.0)	2 (50.0)	0	0	0	0	0	14 (9.5)
>80	2 (3.1)	0	2 (5.9)	0	0	0	0	0	0	0	4 (2.7)
Total	64 (62.7)	36 (78.3)	34 (33.3)	8 (17.4)	4 (3.9)	2 (4.3)	0	0	0	0	148 (100)

is present in up to 50% of healthy children^[1] and remains common in young adults.^[21] Epidemiological studies suggest Vitamin D deficiency or insufficiency may adversely affect cardiovascular health. Vitamin D has significant roles beyond bone and calcium metabolism. Because VDRs are involved in the expression of nearly 3000 human genes, a deficiency could potentially affect numerous disease processes.^[22]

Here, we assessed the prevalence of Vitamin D deficiency in patients with AMI among Iraqi population. Findings of this study present significant high prevalence of severe Vitamin D deficiency (67.6%) in AMI patients as compared to control group (51.4%). This indicates that there is a strong association between Vitamin D deficiency and developing risk of AMI. This study provides the first evidence that Vitamin D deficiency represents a novel risk factor for CAD and AMI.

The high prevalence of Vitamin D deficiency found in this study in AMI is consistent with other epidemiological observational studies. A study by Ng *et al.*^[23] showed that 74% of patients with AMI had low Vitamin D levels, and of note, 36% of them had a severe deficiency. In line with this, a multicenter study reported that 96% of patients with acute coronary disease had low Vitamin D levels. Studies by Aleksova *et al.*^[24] and De Metrio *et al.*^[25] were similarly demonstrated a high prevalence of Vitamin D deficiency in patients with AMI of 68% and 89%, respectively. Moreover, a recent study conducted in Karbala province of Iraq reported high significant prevalence of Vitamin D deficiency in patients with AMI compared to healthy controls.^[26] Contrary to our study findings, a recent study by Mohammad *et al.*^[27] and Rodriguez *et al.*^[28] observed no significant difference in mean plasma Vitamin D levels between patients with CAD and healthy control group.

Correlation between Vitamin D deficiency and patient's gender has been investigated in this study. The female gender was associated with more severe cases of Vitamin D deficiency in comparison to male patients with AMI and this was consistent with findings of a study by Lips *et al.*^[29] Moreover, a lower serum 25(OH) D concentration among older patients with AMI (age group of 60–69 years) were observed and this could partly be due the insufficient capacity of the skin to form Vitamin D after sunlight exposure. In conclusion, this

study confirms the association of Vitamin D deficiency with increasing risk of CAD and AMI. New studies are necessary to determine the association of Vitamin D deficiency with conventional risk factors in patients with AMI.

CONCLUSIONS

Taken together, the present study supports the association between Vitamin D deficiency with increased risk of AMI development as severe Vitamin D deficiency is present in almost all patients with AMI in comparison to healthy controls. This study shed the light on primary prevention and control of CAD and AMI through screening for Vitamin D level in these patients and treatment of this very common vitamin deficiency.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Holick MF. Vitamin D deficiency. *N Engl J Med* 2007;357:266-81.
- Scheen AJ. From atherosclerosis to atherothrombosis: From a silent chronic pathology to an acute critical event. *Rev Med Liege* 2018;73:224-8.
- Libby P, Buring JE, Badimon L, Hansson GK, Deanfield J, Bittencourt MS, *et al.* Atherosclerosis. *Nat Rev Dis Prim* 2019;5:56.
- Crea F, Liuzzo G. Pathogenesis of acute coronary syndromes. *J Am Coll Cardiol* 2013;61:1-11.
- Dawber TR, Meadors GF, Moore FE Jr. Epidemiological approaches to heart disease: The Framingham Study. *Am J Public Health Nations Health* 1951;41:279-86.
- Larsson B. CHD and its risk factors: The pooling project. *Lakartidningen* 1979;76:2286-8.
- Mandarino NR, Monteiro F Jr., Salgado JV, Santos LJ, Salgado FN. Is Vitamin D deficiency a new risk factor for cardiovascular disease? *Open Cardiovasc Med J* 2015;9:40-9.
- Merk J, Milde P, Lweicka S, Hugel U, Klaus G, Mangelsdorf DJ, *et al.* Identification and regulation of 1,25(OH) 2D3 receptors activity and biosynthesis of 1,25(OH) 2D3; studies in cultured bovine aortic endothelial cells and human dermal capillaries. *J Clin Invest* 1989;83:1903-15.
- Garcia VC, Martini LA. Vitamin D and cardiovascular disease. *Nutrients* 2014;2:426-37.
- Zittermann A, Schleithoff SS, Koerfer R. Vitamin D insufficiency in congestive heart failure: Why and what to do about it? *Heart Fail Rev*

- 2006;11:25-33.
11. Lund B, Badskjaer J, Lund B, Soerensen OH. Vitamin D and ischaemic heart disease. *Horm Metab Res* 1978;10:553-6.
12. Scragg R, Jackson R, Holdaway IM, Lim T, Beaglehole R. Myocardial infarction is inversely associated with plasma 25-hydroxyvitamin D3 levels: A community-based study. *Int J Epidemiol* 1990;19:559-63.
13. Pilz S, März W, Wellnitz B, Seelhorst U, Fahrleitner-Pammer A, Dimai HP, *et al.* Association of Vitamin D deficiency with heart failure and sudden cardiac death in a large cross-sectional study of patients referred for coronary angiography. *J Clin Endocrinol Metab* 2008;93:3927-35.
14. Huang J, Wang Z, Hu Z, Jiang W, Li B. Association between blood Vitamin D and myocardial infarction: A meta-analysis including observational studies. *Clin Chim Acta* 2017;471:270-5.
15. Kienreich K, Tomaschitz A, Verheyen N, Pieber T, Gaksch M, Grubler MR, *et al.* Vitamin D and cardiovascular disease. *Nutrients* 2013;5:3005-21.
16. Wu-Wong JR, Nakane M, Ma J, Ruan X, Kroeger PE. Effects of Vitamin D analogs on gene expression profiling in human coronary artery smooth muscle cells. *Atherosclerosis* 2006;186:20-8.
17. Holick MF. Prevalence of Vitamin D inadequacy and implication for health. *Mayo Clin Proc* 2006;81:355-73.
18. Nair R, Maseeh M. Vitamin D: The "sunshine" vitamin. *J Pharmacol Pharmacother* 2012;3:118-26.
19. Mozos L, Marginean O. Links between Vitamin D deficiency and cardiovascular diseases. *Biomed Res Int* 2015;2015:109275.
20. Mohammed SJ. Association between Vitamin D and body weight in Iraqi population: Case-control study. *J Obes Weight Loss Ther* 2018;8:377.
21. Tangpricha V, Pearce EN, Chen TC, Holick MF. Vitamin D insufficiency among free-living healthy young adults. *Am J Med* 2002;112:659-62.
22. BouillonR, Carmeliet G, Verlinden L, Etten EV, Verstuyf A, Luderer HF. Vitamin D and human health: Lessons from Vitamin D receptor Null Mice. *Endocr Rev* 2008;29:726-76.
23. Ng LL, Sandhu JK, Squire IB, Davies JE, Jones DJ. Vitamin D and prognosis in acute myocardial infarction. *Int J Cardiol* 2013;168:2341-6.
24. Aleksova A, Belfiore R, Carriere C, Kassem S, La Carrubba S, Barbat G, *et al.* Vitamin D Deficiency in patients with acute myocardial infarction: An Italian single-center study. *Int J Vitam Nutr Res* 2015;85:23-30.
25. De Metrio M, Milazzo V, Rubino M, Cabiati A, Moltrasio M, Marana I, *et al.* Vitamin D plasma levels and in-hospital and 1-year outcomes in acute coronary syndromes: A prospective study. *Medicine (Baltimore)* 2015;94:e857.
26. Al-Tu'ma FJ, Mohammed ZM, Al-Sarraf HH. Evaluation of Vitamin D3 level and Apo B/Apo A1 ratio in acute myocardial infarction patients in kerbala province. *Int J Chem Tech Res* 2017;10: 472-79.
27. Mohammad AM, Shammo NA, Jasem JA. Vitamin D status in acute myocardial infarction: A case-control study. *Cardiovasc Endocrinol Metab* 2018;7:93-6.
28. Rodriguez G, Starr AZ, Czernusiewicz GZ, Manhas A, Alhariri A, Willerson JT, *et al.* Determinants of plasma Vitamin D levels in patients with acute coronary syndromes. *Eur J Clin Invest* 2011;41:1299-309.
29. Lips P, Hosking D, Lippuner K, Norquist JM, Wehren L, Maalouf G, *et al.* The prevalence of vitamin D inadequacy amongst women with osteoporosis: An international epidemiological investigation. *J Intern Med* 2006;260:245-54.