Original Article

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Vitamin-D Levels of Patients with ST-elevation Myocardial Infarction and Association with In-hospital Prognosis: An Exploratory Observational Study in Southern India

Internal Medicine Section

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ABSTRACT

Introduction: The role of vitamin-D in various diseases, including heart disease, has been a subject of interest in recent years. Many studies revealed low vitamin-D status in patients with Acute Coronary Syndrome (ACS). Studies have shown statistically significant low Vitamin-D levels in patients with Myocardial Infarction (MI) in recent years with some studies showing association of vitamin-D deficiency with worse outcome in patients with severe deficiency.

Aim: To determine serum vitamin-D levels in patients with acute ST-Elevation Myocardial Infarction (STEMI), and its association with in-hospital prognosis.

Materials and Methods: An exploratory observational study was conducted in 100 patients with STEMI consulting a General Medicine Department, JSS Hospital (Tertiary Healthcare Centre), Mysuru, Karnataka, India, from May 2015 to June 2016. The patients were followed-up for in-hospital prognosis. Serum vitamin-D was estimated by Enhanced Chemiluminiscence Immunoassay (ECLIA) method. Electrocardiogram (ECG), Echocardiogram (ECHO) and Coronary Angiogram (CAG) were done in all patients using standard procedures. In-hospital prognosis of the subjects with vitamin-D deficiency and those with normal vitamin-D levels were compared. Data was analysed using Statistical Package for the Social Sciences (SPSS) software version 21.0.

Results: Of total 100 patients, majority (n=59, 15.36%) were in the age group of 50-69 years and there were 81 males and 19 females. The results showed 72% of the subjects were deficient and 19% had insufficient vitamin-D levels, therefore, a total of 91% of the STEMI patients had abnormally low vitamin-D levels. Those with Diabetes Mellitus (DM) (n=52) and past Ischaemic Heart Disease (IHD) (n=9) had significantly low vitamin-D levels, suggesting that the association of vitamin-D deficiency with these risk factors may also contribute to the role of vitamin-D deficiency in STEMI. Among those with cardiac failure (44%), 86.3% had deficient and 11.6% had insufficient vitamin-D levels.

Conclusion: Vitamin-D deficiency was seen in majority of the STEMI patients. Significantly deficient level of vitamin-D was observed in STEMI patients who progressed to cardiac failure (44%) as a complication.

Keywords: Acute coronary syndrome, Cardiac failure, Liver function tests

INTRODUCTION

Vitamin-D is involved in the regulation of Renin Angiotensin Aldosterone System (RAAS) pathway display, immunomodulatory, anti-inflammatory and insulin resistance property. The extent of vitamin-D deficiency has been linked to a range of metabolic disorders, infections, acute and chronic conditions and mortality. There is an increasing trend in the low vitamin-D status worldwide. Data from study based on United States (US) population suggests a 45% of the population have serum 25-hydroxyvitamin D concentrations ≤20 ng/mL [1,2]. Studies from India also show a high prevalence of vitamin-D deficiency in our population [3,4].

Vitamin-D receptors are present in many organs including major cardiovascular cells and there is a prevailing interest in understanding the cardiovascular benefits of vitamin-D [5,6]. Clinical studies have demonstrated an independent association between vitamin-D deficiency and various manifestations of degenerative cardiovascular disease. Interest in the role of vitamin-D in Cardiovascular Diseases (CVD) arose from evidence of adverse cardiovascular effects of vitamin-D deficiency in animal models and epidemiological studies reporting the increase in cardiovascular events in winter and at increasing distance from the equator [5,6].

Vitamin-D deficiency increases the chance of coronary artery disease and the association between IHD and vitamin-D deficiency remains significant even after adjustment for cardiovascular risk factors such as diabetes, smoking, obesity, physical activity and high blood cholesterol [6]. The role of vitamin-D in various diseases including heart disease has been a subject of interest in recent years. Clinical studies have evidenced significant association of low vitamin-D levels in patients with ACS undergoing coronary angiography and severe deficiency correlating with adverse outcomes [7]. However, the precise understanding of the cause-and-effect relationship and the CV risk benefits of vitamin-D supplementation in prone individuals is lacking. With this background the study aimed to determine serum vitamin-D levels in patients with acute STEMI, and its correlation with in-hospital prognosis.

MATERIALS AND METHODS

An exploratory observational study was conducted in the Department of General Medicine, JSS Hospital (Tertiary Healthcare Centre), Mysuru, Karnataka, India, from May 2015 to June 2016 in patients with STEMI. The Institutional Ethics Committee had approved the study (IEC letter No: JSS/MC/PG/6109, meeting date 30.10.2014). Serum levels of 25-hydroxy vitamin-D (25-OHD) <20 ng/mL indicate vitamin-D deficiency and levels above 30 ng/ mL are considered optimal while vitamin-D levels of 21-29 ng/mL are considered insufficient [8,9]. Serum vitamin-D levels 10 ng/mL is considered severe deficiency according to Mayo Medical Laboratories reference ranges for total serum 25-hydroxy vitamin-D [9].

Sample size calculation: Assuming the overall prevalence of vitamin-D deficiency in patients with acute Myocardial Infarction (MI)

to be 75% [10] with an alpha error 5% and confidence level of 95% at least 75 or more subjects needs to be studied. The final sample size was taken as 100.

Inclusion criteria: Patients above 18 years of age, with clinical features of MI, confirmed to have STEMI based on Electrocardiogram (ECG) findings and elevated troponin levels with symptoms of ischaemia or echocardiographic Regional Wall Motion Abnormalities (RWMA) abnormality on Echocardiogram (ECHO) were included in the study.

Exclusion criteria: Pregnant women, patients with renal disease or hepatic dysfunction {history of chronic liver disease or deranged Liver Function Tests (LFT)}, patients on vitamin-D supplementation, bisphosphonates or hormone replacement therapy within past six months from the conduct of the study were excluded from the study.

Study Procedure

Data was collected in a pretested proforma. Detailed history, general physical examination, systemic examination, and investigations like Troponin-T, blood urea and serum creatinine, serum electrolytes and LFT were carried out from non heparinised venous blood sample. Serum vitamin-D was estimated by Electrochemiluminescence Immunoassay (ECLIA) method. ECG, ECHO and Coronary Artery Angiography (CAG) were done in all patients using standard procedures. In-hospital prognosis of the subjects with vitamin-D deficiency and those with normal vitamin-D levels were compared.

Assessment of in-hospital prognosis: The patients included in the study were followed-up till the time of discharge for complications namely cardiac failure, arrhythmias including conduction abnormalities, cardiogenic shock, mechanical complications, ischaemic complications such as stent thrombosis and postinfarction angina, Left Ventricular (LV) apical clot formation, embolic complications, pericarditis and major bleeding as well as mortality. A note was also made of other complications that the patients developed such as contrast induced nephropathy.

STATISTICAL ANALYSIS

Data was analysed using statistical SPSS software version 21.0 and were expressed as descriptive statistics such as mean, median and standard deviation for parametric variables and actual frequencies and percentages for non parametric data. Comparisons between groups were done using Chi-square test, one-way Analysis of Variance (ANOVA) test, Mann-Whitney U test and Kruskal-Wallis test (KW test). A p-value <0.05 was considered as statistically significant.

RESULTS

The study was conducted in 100 STEMI patients. [Table/Fig-1] presents the demographic characteristics of the included participants. The mean vitamin-D levels were 15.6 ng/mL with almost three-fourth of population having vitamin-D deficiency (normal-9%, insufficient-19%, deficient-72%). Vitamin-D levels of females were 8.4 ng/mL which was lower than males (17.2 ng/mL). Vitamin-D deficiency was maximum in housewives.

Significantly low vitamin-D levels were seen in those with DM and history of IHD [Table/Fig-2]. Duration of hospitalisation was significantly longer among the vitamin-D deficient group. Complications like cardiac failure, arrythmias, cardiogenic shock, heart block, contrast induced nephropathy, LV apical clot, stent thrombosis were noted, among those who developed complications (56% of the total population), 75% were vitamin-D deficient and 23.2% had insufficient levels. Vitamin-D deficiency therefore, had a statistically significant association with the risk of development of complications in patients with acute MI.

The most commonly encountered complication was cardiac failure (44%). Among those with cardiac failure, 86.3% had deficient and 11.6% had insufficient vitamin D levels which was statistically significant. The vitamin-D levels were significantly lower in patients who developed cardiac failure (mean vitamin-D level=12.55). All patients with cardiogenic shock, stent thrombosis, heart blocks and acute MR had abnormally low vitamin-D levels, though not statistically significant. Only one patient who expired had highest vitamin-D deficiency. There was no statistically significant correlation between the types of MI according to site of MI based on ECG findings and the vitamin-D levels in STEMI patients [Table/Fig-3]. There was no statistically significant correlation between the vitamin-D levels of patients and their CAG findings.

Among the patients whose duration of stay was longer than seven days, 87.5% (7 out of 8) were vitamin-D deficient and 12.5%

Variables	Total (N=100)	Normal (n=21) (reference range-30 ng/mL)	Insufficient (n=59) (reference range-21-29 ng/mL)	Deficient (n=20) (reference range-<20 ng/mL)
Age (years), n (%)				
30-49	21 (18.47)	1 (8)	8 (38.1)	12 (57.1)
50-69	59 (15.36)	6 (10.2)	10 (16.9)	43 (72.9)
>70	20 (13.31)	2 (10)	1 (5)	17 (85)
Gender distribution, n (%)				
Male	81	9 (11.1)	18 (22.2)	54 (66.7)
Female	19	0	1 (5.3)	18 (94.7)
Occupation, n (%)				
Farmer	32	4 (12.5)	11 (34.4)	17 (53.1)
Skilled workers	20	0	2 (10)	18 (90)
Homemakers	15	0	1 (6.7)	14 (93.3)
Professional	10	0	1 (10)	9 (90)
Businessmen	10	1 (10)	1 (10)	8 (80)
Manual labour	9	4 (44.4)	2 (22.2)	3 (33.3)
Shopkeeper	4	0	1 (25)	3 (75)

[Table/Fig-1]: Baseline characteristics of the study population.

Comorbidity/risk factors	Vitamin-D levels in deficient individuals				p-value
	With co-morbidities		Without co-morbidities		
	n	Mean±SD	n	Mean±SD	
DM	52	12.6±9.0	48	18.9±12.4	0.007
Hypertension	45	14.4±11.5	55	16.6±10.9	0.2
History of IHD	9	7.9±6.3	91	16.4±11.3	0.01
CVA	3	15.6±8.5	97	15.6±11.3	0.9
Smoking	43	20.1±13.5	57	12.2±7.5	0.005
Alcohol consumption	32	19.8±13.5	68	13.6±9.3	0.035
Lack of exercise	19	18.4±14.5	81	15±10.3	0.5
Family history of MI	14	16.9±8.7	86	15.4±11.6	0.3

[Table/Fig-2]: Vitamin-D levels (in ng/mL) in individuals with comorbidities or risk factors. *DM: Diabetes mellitus; IHD: Ischaemic heart disease; CVA: Cerebrovascular accident; MI: Myocardial Infarction

ECG/CAG	Total population	Normal	Insufficient	Deficient	p-value
ECG findings, n (%)					
Anterior wall MI	36	5 (13.9)	4 (11.1)	27 (75.0)	0.47
Anterior lateral MI	21	1 (4.8)	5 (23.8)	15 (71.4)	
Anteroseptal MI	12	0 (0)	4 (33.3)	8 (66.7)	
Inferior wall MI	18	0 (0)	5 (27.8)	13 (72.2)	
Inferoposterior MI	13	3 (23.1)	1 (7.7)	9 (69.2)	
CAG findings, n (%)					
Single vessel	63	9 (13.1)	10 (14.8)	44 (72.1)	0.16
Two vessels	17	0 (0)	6 (35.3)	11 (64.7)	
Three vessels	20	1 (5)	3 (15)	16 (80)	

[Table/Fig-3]: Association between ECG findings and vitamin-D levels in STEMI.

had insufficient vitamin-D levels. Among those with duration of stay between 5-7 days, 95.2% were vitamin-D deficient and remaining 4.8% had insufficient vitamin-D levels. Thus, vitamin-D deficiency was associated with significantly longer duration of stay (p-value=0.048). Moreover, mean duration of hospitalisation was also significantly longer among the patients with vitamin-D deficiency with p-value=0.008. Vitamin-D deficiency in STEMI patients was associated with a statistically significant increased risk of complications in general with p-value=0.01 [Table/Fig-4].

Parameters	Total population	Normal	Insufficient	Deficient
Mean duration of stay (days)	12.8 (N=100)	3.8 (9)	3.9 (19)	5.1 (72)
Duration of stay ≥8 days, n	8	0	1	7
5-7 days, n	21	0	1	20
Mortality, n	1	0	0	1
Complications, n (%)	56	1 (1.78)	13 (23.2)	42 (75)
Cardiac failure, n (%)	44	1 (2.3)	5 (11.4)	38 (86.3)
Arrythmias, n (%)	16	0	3 (18.7)	13 (81.3)
Cardiogenic shock, n (%)	4	0	0	4 (100)
Heart block, n (%)	4	0	2 (50)	2 (50)
MR	8	0	1 (12.5)	7 (87.5)
Contrast induced nephropathy, n (%)	3	0	0	3 (100)
LV apical clot, n (%)	2	0	2 (100)	0
Stent thrombosis, n (%)	2	0	0	2 (100)

[Table/Fig-4]: Outcomes.
*MR: Mitral regurgitation

There was statistically significant difference in vitamin-D status of patients who developed cardiac failure as compared to those without cardiac failure with p-value of 0.01. The patients who developed stent thrombosis (100%) were also vitamin-D deficient. All patients with cardiac arrhythmias, heart block and mitral regurgitation had abnormally low vitamin-D levels. All the patients (100%) who developed cardiogenic shock and contrast induced nephropathy following CAG were vitamin-D deficient. Although clinically significant, none of these findings were statistically significant which could be due to a small sample size. There was one mortality among the study population. The patient was an elderly male aged 72 years with anterolateral MI, had severe vitamin-D deficiency (vitamin-D level was 3.02 ng/mL). He also had hypertension, lifestyle habits of smoking and alcohol consumption, and had developed complications of cardiac failure and cardiac arrhythmia (ventricular fibrillation).

DISCUSSION

Multiple lines of evidence suggest a link between vitamin-D and cardiovascular disease. The risk of complications of coronary artery disease and MI is observed to be higher in patients with vitamin-D deficiency [2,11,12]. The present study observed a high prevalence of vitamin-D deficiency (72%) among STEMI patients. Vitamin-D deficiency and insufficiency reported by various studies fall in the range of 67-75% and 16-22%, respectively [13-16]. Similar to other observations, the mean vitamin-D levels in our study population of STEMI patients was 15.6 ng/mL. Vitamin-D deficiency is significantly associated with female sex and indoor occupations with less sun exposure.

In the present study, majority belonged to the age group 50 to 69 years, concordant with the general observation of incidence of coronary artery disease [14,15,17]. Although not statistically significant, vitamin-D levels seem to progressively decrease with age [10,13,15]. About 85% of individuals above 70 years and 73% of individuals in the age group of 50-69 years were deficient for vitamin-D with median levels of 8.9 and 12.5 IU, respectively.

Among STEMI patients with DM and history of IHD, it was observed that a significantly lower vitamin-D levels. Many of the earlier studies have evidenced vitamin-D deficiency in greater proportion of individuals with diabetes [10,11,15]. Although the underlying biological mechanisms are poorly understood, the association of low serum 25-hydroxy vitamin-D concentrations with type 2 diabetes may be mediated through effects on glucose homeostasis and a direct effect of vitamin-D on the β-cell function and thus insulin secretion. Several studies have suggested that low vitamin-D status also contributes to insulin resistance [18]. Contrary to the present study findings, Metrio MD et al., showed no significant association between vitamin-D levels and past IHD [14]. A positive correlation between lower vitamin-D levels and past IHD is suggestive of higher risk for recurrent MI in patients with vitamin-D deficiency and IHD long-term prospective studies are warranted to investigate this possibility. In the pool of conflicting evidence regarding the association of vitamin-D levels and hypertension in this study observations do not find a significant correlation [2,13,15,19,20]. Outcomes such as duration of hospital stay were significantly longer in patients and relatively in-hospital complications were higher among individuals with vitamin-D deficiency [13,14,20]. Cardiac failure is the most common complication and there was statistically significant association between cardiac failure and low vitamin-D levels in STEMI patients.

Lifestyle habits including smoking, alcohol consumption and regular exercise patterns are considered to be common factors [13,15]. A finding in the present study that contradicts previous studies is that vitamin-D deficiency was more in non smokers and non alcoholic patients as compared to smokers and alcoholics, with significantly higher vitamin-D levels in smokers and alcoholics. This needs to be further evaluated for possible effect of confounding factors such as occupation and sun exposure. In the present study, most (81%) of the patients did not exercise, though there was no statistically significant association between vitamin-D deficiency and lack of exercise.

The most commonly encountered complication was cardiac failure in individuals with vitamin-D deficiency, as reported by UK in-hospital prognosis study in 1259 MI which observed 80% of the patients who developed cardiac failure were vitamin-D deficient [2]. Although the mean vitamin-D levels were lower (12 ng/mL) in patients with cardiac arrhythmia during hospital stay there was no statistically significant correlation between development arrhythmias and vitamin-D deficiency [13]. This is contrary to the findings of some earlier studies which had reported statistically significant association of cardiac arrhythmias and vitamin-D deficiency in ACS patients [2,14,18]. All of the present study patients who developed cardiogenic shock and contrast induced nephropathy were vitamin-D deficient.

Out of the 100 patients in the present study only one patient died. In the study by Metrio MD et al., the in-hospital mortality was 2.6% but this study included both STEMI and Non ST-Elevation Myocardial Infarction (NSTEMI) patients and mortality was noted to be more in STEMI patients, and this is comparable to the present study. No significant association between vitamin-D levels and in-hospital mortality has been observed in most previous studies [13,15,19,20].

To the best of the present search, this study is the first one from South India that delved into the prevalence of vitamin-D deficiency and associated risk factors in STEMI patients and specifically on the in-hospital outcomes. Clinical interest derives from the fact that vitamin-D deficiency can be readily determined by blood testing and treated by supplementation. A single oral ultra-high dose of vitamin-D has been shown to restore normal 25 (OH)D levels within two days in critically ill patients, without causing adverse effects, thus providing the basis of an easy-to-administer dosing regimen for prospective intervention trials in acute cardiovascular settings [21]. The present study demonstrates high prevalence

vitamin D deficiency in patients presenting with STEMI as well as strengthens the evidence of a close association between low vitamin-D levels and increased risk of complications in patients with STEMI. Hence, it paves the way for studies based on pharmacologic supplementation of vitamin-D in selected high-risk ACS patients with severe vitamin-D deficiency, in order to improve their prognosis.

Limitation(s)

The major limitation in the present study was that there is no clearly defined control group in the study as majority of the patients in the study (91%) had abnormally low vitamin-D levels and only 9% of the patients had normal vitamin D levels. Even though the sample size was adequate to study the vitamin-D levels in patients with acute STEMI and outcome in general, a larger sample would have helped in a better understanding of the association of vitamin-D levels with the complications and in-hospital prognosis. Although clinically significant association could be noted, the association between vitamin-D levels and some of the complications individually such as cardiogenic shock, Artrioventricular (AV) conduction blocks, stent thrombosis could not be statistically demonstrated due to the low incidence of these complications in the present limited sample. The present study findings were based on single-centre population and would need to be verified in large cohorts. Moreover, this study is limited to complications and mortality during the hospital stay which varied from a period of 3-12 days. This is a relatively short period and further long-term follow-up after discharge as done in similar previous studies is lacking. The present study was only an observational study, further appropriately designed Randomised Controlled Trials (RCTs) are required to confirm if vitamin-D supplementation can help in improving outcome in STEMI patients and if it can be of help in prevention of MI in patients with risk factors for MI.

CONCLUSION(S)

Vitamin-D deficiency is associated with higher risk of STEMI and with worse outcome following STEMI. The correction of vitamin-D deficiency and maintenance of optimal vitamin-D levels may be a promising approach for prevention of MI in patients with risk factors and for improving the outcome in patients with acute MI. Further larger scale prospective studies and interventional trials studies are warranted to assess the potential role of vitamin-D supplementations in patients with STEMI and its risk factors.

REFERENCES

[1] Forrest KYZ, Stuhldreher WL. Prevalence and correlates of vitamin D deficiency in US adults. Nutrition research (New York, N.Y.). 2011;31(1):48-54.
[2] Giovannucci E, Liu Y, Hollis BW, Rimm EB. 25-hydroxyvitamin D and risk of myocardial infarction in men: A prospective study. Archives of Internal Medicine. 2008;168(11):1174-80.
[3] Harinarayan CV, Sachan A, Reddy PA, Satish KM, Prasad UV, Srivani P. Vitamin D status and bone mineral density in women of reproductive and postmenopausal age groups: A cross-sectional study from south India. The Journal of the Association of Physicians of India. 2011;59:698-704.
[4] Sachan A, Gupta R, Das V, Agarwal A, Awasthi PK, Bhatia V. High prevalence of vitamin D deficiency among pregnant women and their newborns in northern India. The American Journal of Clinical Nutrition. 2005;81:1060-64.
[5] Kamili M, Dar I, Ali G, Wazir H, Hussain S. Prevalence of coronary heart disease in Kashmiris. Indian Heart Journal. 2007;59(1):44-49.
[6] Judd SE, Tangpricha V. Vitamin D deficiency and risk for cardiovascular disease. The American Journal of the Medical Sciences. 2009;338:40-44.
[7] Ismail HM, Algrafi AS, Amoudi O, Ahmed S, Al-Thagfan SS, Shora H, et al. Vitamin D and its metabolites deficiency in acute coronary syndrome patients undergoing coronary angiography: A case-control study. Vascular Health and Risk Management. 2021;17:471.
[8] Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP. Evaluation, treatment, and prevention of vitamin D deficiency: An endocrine society clinical practice guideline. The Journal of Clinical Endocrinology & Metabolism. 2011;96(7):1911-30.
[9] Kennel KA, Drake MT, Hurley DL. Vitamin D deficiency in adults: When to test and how to treat. Mayo Clinic Proceedings. 2010;85(8):752-57.
[10] Lee JH, Gadi R, Spertus JA, Tang F, O'Keefe JH. Prevalence of vitamin D deficiency in patients with acute myocardial infarction. The American Journal of Cardiology. 2011;107(11):1636-38.
[11] de Boer IH, Kestenbaum B, Shoben AB, Michos ED, Sarnak MJ, Siscovick DS. 25-hydroxyvitamin D levels inversely associate with risk for developing coronary artery calcification. Journal of the American Society of Nephrology. 2009;20(8):1805-12.
[12] Hosseinpanah F, Yarjanli M, Sheikholeslami F, Heibatollahi M, Eskandary PS, Azizi F. Associations between vitamin D and cardiovascular outcomes; Tehran lipid and glucose Study. Atherosclerosis. 2011;218(1):238-42.
[13] Metrio MD, 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. Medicine. 2015;94:e857.
[14] Ng LL, Sandhu JK, Squire IB, Davies JE, Jones DJL. Vitamin D and prognosis in acute myocardial infarction. International Journal of Cardiology. 2013;168:2341-46.
[15] Karur S, Veerappa V, Nanjappa MC. Study of vitamin D deficiency prevalence in acute myocardial infarction. IJC Heart & Vessels. 2014;3:57-59.
[16] Kim DH, Sabour S, Sagar UN, Adams S, Whellan DJ. Prevalence of hypovitaminosis D in cardiovascular diseases (from the National Health and Nutrition Examination Survey 2001 to 2004). The American Journal of Cardiology. 2008;102(11):1540-44.
[17] Lee JH, O'Keefe JH, Bell D, Hensrud DD, Holick MF. Vitamin D deficiency an important, common, and easily treatable cardiovascular risk factor? Journal of the American College of Cardiology. 2008;52(24):1949-56.
[18] Dalgård C, Petersen MS, Weihe P, Grandjean P. Vitamin D status in relation to glucose metabolism and type 2 diabetes in septuagenarians. Diabetes Care. 2011;34(6):1284-88.
[19] Mahdavi K, Amirajam Z, Yazdankhah S, Majidi S, Adel MH, Omidvar B, et al. The prevalence and prognostic role of vitamin d deficiency in patients with acute coronary syndrome: A single centre study in south-west of Iran. Heart, Lung and Circulation. 2013;22:346-51.
[20] Mohammed H, El-Ashmawy H, Mohamed ES, Mostafa A. The prognostic value of serum 25-hydroxyvitamin D level in patients with ST-segment elevation myocardial infarction. Egyptian Journal of Obesity, Diabetes and Endocrinology. 2015;1:49.
[21] Amrein K, Sourij H, Wagner G, Holl A, Pieber TR, Smolle KH, et al. Short-term effects of high-dose oral vitamin D3 in critically ill vitamin D deficient patients: A randomized, double-blind, placebo-controlled pilot study. Critical care (London, England). 2011;15(2):R104.

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