JOURNAL OF PURE AND APPLIED MICROBIOLOGY, March 2016. Vol. **10**(1), p. 271-276

Comparing Vitamin D3 Serum Levels in Patients with Acute Cardiac Infarction and Elevated ST Segment with Healthy Patients

Farnaz Fariba*, Mehdi Moradi and Mohammad Mashhadi

Cardiovascular Research Centre of Ekbatan Hospital,
Hamadan University of Medical Sciences, Hamadan, Iran.

(Received: 13 June 2015; accepted: 19 September 2015)

Coronary artery diseases are considered to be the most common of cardiac illnesses as well as the most important factor contributing to acute myocardial infarction, which in turn is the most prevalent cause of death and disability in many countries. Although Epidemiologic studies have confirmed the role of many risk factors, such as hypercholesterolemia, diabetes, hypertension, smoking, obesity and increased blood glucose, there remains a variety of other parameters, such as vitamin D deficiency, which also increase the occurrence of coronary arterial diseases. This study aims to evaluate the level of vitamin D3 serum levels in patients suffering from acute myocardial infarction and comparing the finds to that of healthy individuals with no previous history of cardiac diseases. This case-control study was performed on patients suffering from acute myocardial infarction admitted to the Ekbatan hospital of Hamadan, Iran. Checklists were designed to gather data form 24 clauses of the subjects' medical files. Gathered data were processed and studied analytically. This research enrolled 40 patients with acute myocardial infarction as well as 40 healthy patients with no known history of cardiac diseases. Serum Vitamin D3 levels were lower in patients suffering from myocardial infarction than that of the control group (20.60 to 22.05), however this difference lacks statistical significance (P=0.284). Subjects with adequate serum levels of vitamin D3 had a 70% lesser chance of experiencing a myocardial infarction (chance ratio 0.30), however according to the Wald test, this relevance has no statistical significance (P=0.187). Higher levels of serum Vitamin D3 decreases the chance of acute myocardial infarction, although confirming this find as a clinical evidence requires repetition on larger groups.

Key words: Acute myocardial infarction, Vitamin D3 serum levels, Hamedan

Coronary artery diseases which are caused by the obstruction of coronary arteries are the most common of cardiac diseases as well as a main cause of acute myocardial infarction[1]. Myocardial infarctions are the leading cause of death and disability in most countries[2]. In medical terminology MI, heart stroke and myocardial infarction is defined as a permanent and irreversible death of cells in the myocardium of the heart, mainly due to blocked blood flow and severe ischemia[3]. This blockage may be spontaneous and have no indication of occurring, or may be accompanied by angina strokes[3]. Based on cardiography, there are two types of myocardial infarction: ST elevated strokes and non-ST elevated strokes.

Coronary artery diseases are amongst the most common illnesses throughout the world and it is anticipated that CAD will be the primary cause of death by 2020[4]. In Iran, reports also indicate an increase in CAD diseases, especially myocardial infarctions; CAD is currently the primary cause of death from the prospect of individuals killed per

* To whom all correspondence should be addressed.
E-mail: farnaz.fariba@gmail.com

year. Although Epidemiologic studies have confirmed the role of many risk factors, such as hypercholesterolemia, diabetes, hypertension, smoking, obesity, increased blood glucose and waist to hip ratio and reduced physical activity which are but a few of the many parameters contributing to atherosclerosis and coronary diseases, it is assumed that other factors such as vitamin D3 serum levels also play determining roles in the occurrence of Cardiac and arterial diseases[7-8]. Vitamin D are a family of lipid soluble hormone precursors which enter the body via sunlight, food and nutritional supplements. Vitamin D has two main forms: Vitamin D (ergosterol) and vitamin D3 (cholecalciferol). Exposure to sunlight leads to the synthesis of vitamin D from di-hydroxycholesterol in the kidneys. In addition cereal, eggs and fish are the most commonly available sources of vitamin D[9].

Vitamin D deficiency increases the chance of cancers of the breast and prostate, immune deficiency, worsening of arterial hypertension complications and also cardiac failure. Studies also suggest relevance between low vitamin D, especially 25 hydroxy vitamin D, levels and increased chance of cardiac and arterial diseases[10-12]. The United States cardiac and arterial diseases are mentioned as a complication resulting from vitamin D deficiency by the United States Institute of Medicine[13]. In 2012, Mahdavi et al studied the prevalence and prognostic role of vitamin D deficiency in patients with acute myocardial infarction residing in Ahwaz, Iran. The finds of this research show that serum vitamin D levels are significantly lower in AMI patients in comparison to healthy individuals[14]. In the same year, Bair et al studied 2910 AMI patients residing in the United States. The results indicate that regardless of symptoms and the severity of the condition, 25 hydroxy vitamin D deficiencies is common amongst the subjects[15]. In 2011, Rodriguez et al studied plasma Vitamin D levels in patients suffering from AMI and compared it to that of healthy subjects; no significant variation was seen between the two groups[16]. In 2009, Kendrick et al reached the conclusion that angina cardia, MI and cardiac failure has a higher prevalence in subjects with plasma vitamin D3 levels lesser than 20 nanograms per millilitres in comparison to subjects with higher and more adequate levels of vitamin D3[17]. In a study performed by Lee et all between 11th of April 2005 and 31st of December 2008 on 239 subjects with the aim of determining vitamin D deficiency prevalence in patients with acute myocardial infarction, it was revealed that 75% of the subjects had vitamin D levels lower than 20 nanograms per millilitre and another 21% were generally vitamin D deficient[18].

Even though the importance and effect of vitamin D deficiency in cardiac diseases has been confirmed and documented, no previous studies have been performed in Iran which evaluate serum vitamin D levels in MI patients and compare it to that of healthy individuals. Thus, this study was designed and performed to evaluate serum 25 hydroxy vitamin D levels in elevated AMI patients with elevated ST segments and compare it to that of healthy patients with no previous history of cardiac diseases. In addition, this research has also studied the effect of age, gender, general body mass, history of smoking and diabetes.

MATERIALS AND METHODS

In this case control study, 40 patients with ST elevated acute myocardial infarction which were admitted to Ekbatan hospital, Hamedan, during summer 2013 were enrolled with 40 control patients with no previous history of cardiac diseases. Blood samples were gathered when subjects first entered the intensive care ward and sent to the laboratory for evaluation of serum vitamin D levels using an IDS kit. Enter criteria consisted of a minimum age of 30 years, no history of chronic renal complications, a maximum blood creatinine level of 1.8 milligrams per decilitres in both men and women, normal calcium levels, no intake of calcium supplements within the last 4 months, no currently present inflammatory disease such as infection or a condition of active autoimmunity, not being treated by cortones and also a signed consent agreeing to entering the study.

After obtaining a written consent, a previously designed 24 clause checklist was used to gather data from the medical file of these patients who were admitted to the angiography ward of Ekbatan hospital of Hamedan.

Data analysis was performed using STATA software V.13, parametric independent t-Test and the non-parametric chi-square test.

RESULTS

According to the results of the study, those with a history of AMI had lower serum Vitamin D3 levels compared to the control subjects(20.60 to 22.05), which is statistically insignificant (P=0.284).

The average level of serum vitamin D3 varied with age, the highest observed in those aged 71-86, however, this variation is also statistically insignificant (P=0.809).

The average serum level of vitamin D3 was higher in women in comparison to men, in those with a normal body mass when compared to the obese or anorexic, in those with no history of hypertension, diabetes type II, cigarette and opium smokers; however, the difference between vitamin D3 levels of these groups was not statistically significant (table 1).

Since this current research is a case control study and a double outcome (negative or present history of acute myocardial infarction) was predicted, in order to determine the effect of each of the parameters on the either of the outcomes, logistic regression and odds ratio estimation were employed. The crude (the individual impact of every parameter) and adapted (general impact of all parameters) results have been listed in tables 2 and 3, respectively. In short, adapted logistic regression analysis show that every unit of excess vitamin D3 reduces the chance of an AMI occurring by 0.11, which according to the Wald test, is insignificant.Amongst the other factors, those with a positive history of hypertension also face a 3.11 higher risk of AMI than others, a meaningful relevance according to the Wald test (P=0.021). Every additional WBC present in an ml of blood increases the chance of an AMI occurring by 1.001 (P<0.001). Every milligram of excess creatinine present in a dl of blood also elevates the chance of AMI occurring by 32.77 times the original rate (P=0.002). Every additional milligram of calcium, reduces this chance by 78% (P=0.027). All aforementioned relationships have been determined statistically meaningful by the Wald test. On the other hand, adapted regression

Table 1: Comparing the average serum levels of vitamin D3 in accordance with effective factors on AMI occurrence using one way Anova test

Single way anova test significance level	Standard deviation	Mean vitamin D3 serum level	Percent	Number of cases	Levels	Study parameter
0.284	12.79	20.65	50.00	40	Case	Study group
	8.65	22.05	50.00	40	Control	
0.806	10.26	20.00	32.50	26	40-55 y/o	Age
	22.80	17.31	47.50	38	56-70 y/o	
	10.62	23.71	20.00	16	71-86 y/o	
0.376	9.71	21.06	63.75	51	Male	Gender
	12.82	21.86	36.25	29	Female	
0.661	7.57	16.33	3.75	3	Anorexic (below 18.5)	BMI
	15.01	19.00	46.25	37	Normal (18.5-24.9)	
	10.01	17.50	37.50	30	Overweight (25-29.9)	
	11.26	17.9	12.50	10	Obese (above 30)	
0.259	9.04	20.77	35.00	28	Affirmative	Previous history of Hypertension
	13.75	22.43	65.00	52	Negative	
0.364	14.44	21.54	17.50	14	Affirmative	History of diabetes
	10.08	21.54	52.50	66	Negative	
0.115	12.03	19.29	33.75	27	Affirmative	History of smoking
	10.18	22.40	66.25	53	Negative	
0.528	14.26	21.53	18.75	15	Affirmative	History of opium addiction
	10.06	21.31	81.25	65	Negative	

analysis reveals that if every other parameter remains constant, every additional WBC present in a ml of blood increases the chance of an AMI occurring by 1.02 times, which according to the Wald test is exceptionally meaningful (P<0.040). In addition and under the condition that other parameters remain unchanged, every milligram of excess creatinine within a decilitre of blood increases this chance by 99 times (P=0.017). Also, every excess milligram of non-fasting blood glucose is able to increase this chance by 1.03 times, if other parameters remain constant (P=0.05). These relationships are statistically meaningful according to the Wald test.

Table 2: estimating the crude odds ration of the parameters effective in the occurrence of AMIs

The average serum level of vitamin D3in the case group (subjects with a present history of AMI) is about 2 nanograms per decilitres lower than that of the control group (those with no known history of AMI). Although not statistically

Table 2. Estimating the crude odds ration of the parameters effective in the occurrence of AMIs according to logistic regression

Wald test P-value	Un-adapted logistic regression		Comparison criterion Odds ratio 95% of confidence interval	Variable
0.644	0.30	0.05-1.75	Adequate to severe deficiency	Vitamin D3 serum level
0.597	0.69	0.13-3.39	Mild to severe deficiency	
0.187	0.64	0.12-3.25	Moderate to severe deficiency	
0.465	1.01	0.97-1.05	Increase by one year	Age
0.816	0.90	0.36-2.23	More women compared to men	Gender
0.22	1.07	0.96-1.18	Increase by one unit	BMI
0.021	3.11	1.18-8.19	Affirmative against negative	History of hypertension
0.011	1.03	1.06-1.07	Every mm-Hg increase	Systolic blood pressure
0.012	1.07	1.01-1.03	Every mm-Hg increase	Diastolic blood pressure
0.087	3.00	0.83-10.54	Affirmative against negative	History of past or present diabetes
0.10	2.21	0.85-5.47	Affirmative against negative	History of smoking
0.159	2.33	0.71-7.58	Affirmative against negative	Addiction to opium
<0.0001	1.001	1.0001-1.0003	Increase of number in every ml of blood	WBC count
0.012	1.02	1.005-1.04	Every mg of Increase in every ml of blood	Fasting BG
0.002	32.77	3.50-306.00	Increase in every deciliter of blood	Creatinine
0.027	0.22	0.05-0.84	Increase in every deciliter of blood	Calcium
0.05	1.001	0.97-1.01	Every milligram of increase in every dl	Cholesterol

Table 3. Estimating the adapted odd ratio of the parameters involved in the occurrence of an AMI using logistic regression

Wald test pvalue	adapted logistic regression criterion		Comparison	Variable
	Odds ratio	95% of confidence interval	Increase by one unit	BMI
0.316	1.16	1.86-1.56	Every mm-Hg increase	Systolic blood pressure
0.573	1.06	0.86-1.30	Every mm-Hg increase	Diastolic blood pressure
0.581	2.19	0.13-35.00	Affirmative against negative	History of smoking
0.040	10.2	1.0001-1.0021	Increase of number in every ml of blood	WBC count
0.05	10.3	0.99-1.06	Every mg of Increase in every ml of blood	Fasting BG
0.017	99	12.04- 827	Increase in every deciliter of blood	Creatinine

significant (P=0.284), the difference between the average serum levels of vitamin D3 in the two groups is of profound clinical importance. The limited sample population used in this research may reduce the statistical potential of the study and also affect its P values so that the correct level of significance cannot be determined via analysis. In general, 15 subjects (18%) had adequate levels of vitamin D3 in their blood while 10 percent suffered from severe vitamin D3 deficiency.

DISCUSSION

When comparing the serum level of Vitamin D3 in the study and control group in accordance with age, gender and a history of some underlying conditions, no statistically significant variation was observed. However, this may be due to the limited study population which in turn, reduces the statistical potential of the research. Mahdavi et al performed a study in 2012 in south-western regions of Iran (Ahwaz); the results indicate that the 72% of the study group have vitamin D deficiency while 27.4% of the control group face this deficit (14). In the current study, 52.5% of the main subjects and 42.5% of the control group faced moderate to severe vitamin D3 deficiency (lower than 20 nanograms per decilitres of blood), the prevalence in the control group being significantly higher than that of Mahdavi's control group.

In the study performed by Lee et al in 2008, 96% of the cases faced Vitamin D deficiency (serum levels lower than 30 nanograms per decilitres)[18]. Similar to Lee's study, 82% of the subject enrolled in this study was also deficit considering serum levels of vitamin D.

In 2011, Rodriguez et al evaluated the serum levels of vitamin D in patients suffering from acute myocardial infarction. There endeavours revealed no significant variation between the average values of serum Vitamin D in the two groups (22.06 against 22.24 with a p value of 0.618) (16). Although the study population of the at hand study was smaller than that of Rodriguez's, the gap between the average value of serum vitamin D of the study and control group was considerably greater (20.65 against 22.05), although like theirs, these results are also statistically insignificant.

One of the prominent downsides of this research is the limited study population and as a result a reduced statistical potential in terms of determining the difference between the averages values of the two groups. Financial complications, such as the high price of IDS kits which were used to evaluate serum levels of vitamin D3 in the subjects, were among the factors which prohibited researchers from enrolling more subjects.

Therefore, the clinically significant variations between the two groups emphasises the importance of performing such studies in larger groups, which need to be financially supported by the respective authorities, so that more solid evidence may be obtained considering the role of vitamin D deficiency in the occurrence of cardiac diseases and also to increase the general health state of this country, which a great population of whose are vitamin D deficit.

ACKNOWLEDGMENTS

Authors take sincere thanks to clinical research Centre of Ekbatan Hospital for their help and financial support.

REFERENCES

1. Icahn School of Medicine at Mount Sinai. Fighting Coronary Artery Disease. 2014 [cited 2014 0611]; Available from: http://www.mountsinai.org/patient-care/service-areas/heart/areas-of-care/heart-attack-coronary-artery-disease.
2. WHO. Cardiovascular disease. 2014; Available from: http://www.who.int/cardiovascular_diseases/en/.
3. Topol EJ, Califf RM. Textbook of cardiovascular medicine: Lippincott Williams & Wilkins; 2007.
4. Azizi F, Janghorbani M, Hatami H. Epidemiology and control of common disease in Iran. Tehran: Eshtiagh. 2010;1380:10-22.
5. Statistics of Heart Attack [cited 2015 2801]. Available from: https://www.floridahospital.com/heart-attack-myocardial-infarction/statistics
6. Sowers JR, Epstein M, Frohlich ED. Diabetes, hypertension, and cardiovascular disease an update. *Hypertension*. 2001;**37**(4):1053-9.
7. Pittas AG, Chung M, Trikalinos T, Mitri J, Brendel M, Patel K, et al. Systematic review: vitamin D and cardiometabolic outcomes. *Annals of internal medicine*. 2010;**152**(5):307-14.

8. Naesgaard PA, De La Fuente RAL, Nilsen ST, Woie L, Aarsland T, Brede C, et al. Serum 25 (OH) D is a 2-year predictor of all-cause mortality, cardiac death and sudden cardiac death in chest pain patients from Northern Argentina. *PloS one*. 2012;**7**(9):e43228.
9. Lilly LS. Braunwald's heart disease: a textbook of cardiovascular medicine: Elsevier Health Sciences; 2012.
10. Wang TJ, Pencina MJ, Booth SL, Jacques PF, Ingelsson E, Lanier K, et al. Vitamin D deficiency and risk of cardiovascular disease. *Circulation*. 2008;**117**(4):503-11.
11. Rich MW. Treatment of acute myocardial infarction. The American journal of geriatric cardiology. 2001;**10**(6):328-36.
12. Norman AW, Wong RG. Biological activity of the vitamin D metabolite 1, 25-dihydroxycholecalciferol in chickens and rats. *The Journal of nutrition*. 1972;**102**(12):1709-18.
13. Sowers JR. Obesity as a cardiovascular risk factor. *The American journal of medicine*. 2003; **115**(8): 37-41.
14. 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**(5):346-51.
15. Bair TL, Horne B, Anderson J, May H, Lappe D, Muhlestein J. Do Levels OF Vitamin D Differ Among Patients With Coronary Artery Disease Based on Initial Clinical Presentation? Journal of the American College of Cardiology. 2012; **59**(13s1):E1386-E.
16. Rodriguez G, Starr AZ, Czernuszewicz GZ, Manhas A, Alhariri A, Willerson JT, et al. Determinants of plasma vitamin D levels in patients with acute coronary syndromes. *European journal of clinical investigation*. 2011; **41**(12):1299-309.
17. Kendrick J, Targher G, Smits G, Chonchol M. 25-Hydroxyvitamin D deficiency is independently associated with cardiovascular disease in the Third National Health and Nutrition Examination Survey. *Atherosclerosis*. 2009; **205**(1): 255-60.
18. 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): 1636-8.