Study of vitamin D deficiency prevalence in acute myocardial infarction

Satish Karur *, Virupakshappa Veerappa, Manjunath C. Nanjappa

Department of Cardiology, Sri Jayadeva Institute of Cardiovascular Sciences and Research, Bannerghatta Road, Jayanagar 9th Block, Bangalore, Karnataka 560069, India

A B S T R A C T

Background: Deficiency of 25-hydroxy vitamin D [25(OH)D] is a treatable condition that has been associated with coronary artery disease and many of its risk factors. A practical time to assess for 25(OH)D deficiency, and to initiate treatment, is at the time of an acute myocardial infarction (AMI). The prevalence of 25(OH)D deficiency and the characteristics associated with it in patients with acute myocardial infarction are unknown.

Methods: In this study 25(OH)D was assessed in 314 subjects enrolled in a Sri Jayadeva Institute of Cardiovascular Science and Research (SJICS&R). Patients enrolled from December 1, 2011 to February 28, 2012 had serum samples sent to a centralized laboratory for analysis using the ELECYS assay. Normal 25(OH)D levels are ≥ 30 ng/ml, and patients with levels < 30 and ≥ 20 ng/ml were classified as insufficient and those with levels ≤ 20 ng/ml as deficient. Vitamin D and other baseline characteristics were analyzed with T-test and chi-squared test.

Results: Of the 314 enrolled patients, 212 (67.5%) were 25(OH)D deficient and 50 (16%) were insufficient, for a total of 83.5% of patients with abnormally low 25(OH)D levels. No significant heterogeneity was observed among age or gender sub groups but 25(OH)D deficiency was more commonly seen in those with lower socioeconomic status, lower activity levels, diabetes, hypercholesterolemia (LDL), hypertriglyceridemia and in smokers.

Conclusion: Vitamin D deficiency is present in most of the patients with acute myocardial infarction and it is associated with many of its risk factors in our study.

© 2014 Published by Elsevier Ireland Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/3.0/).

1. Introduction

Vitamin D deficiency is highly prevalent worldwide [1], and is also noted to be high in India [2,3]. Low levels of 25(OH)D the principle circulating storage form of vitamin D, is present in as many as one third to one half of otherwise healthy middle aged to elderly population [1,4–6]. Limited cutaneous synthesis due to inadequate sun exposure or pigmented skin and inadequate dietary intake are the principle causes of low 25(OH)D levels.

Although the best characterised sequelae of vitamin D deficiency involve musculoskeletal system, growing evidence suggests that vitamin D axis affects vascular smooth muscle cell proliferation [6], endothelium [7] cardiomyocytes [18] inflammation, vascular calcification, renin-angiotensin system (RAS) [9,10], blood pressure and LVH [10–12] all of which affect the risk of cardiovascular diseases and myocardial infarction. However, the prevalence of vitamin D deficiency as well as the characteristics associated with it in patients presenting with acute myocardial infarction is unknown.

This is a prospective study undertaken at SJICS&R, Bangalore, India to describe the prevalence of vitamin D deficiency at the time of admission for acute myocardial infarction.

2. Methods

We evaluated the subjects enrolled in our study. We collected information of the patients admitted for AMI through chart abstraction, detailed patient interviews, and serum samples at SJICS&R from December 1, 2011 to February 28, 2012.

Inclusion criteria for the study are, age ≥ 20 years, biomarker evidence of myocardial injury (elevated troponins or CKMB), supporting evidence of AMI (eg., prolonged ischemic signs or symptoms, electrocardiographic ST-segment changes), and patients presenting within 24 h of symptoms onset. The study sample included 314 patients. Those patients with prevalent cardiovascular diseases and kidney diseases (serum creatinine > 1.6) were not included in the cohort. All the participants provided written informed consent. Detailed medical history examination and laboratory assessment of vascular risk factors were
performed. Patient data included demographics, age, gender, marital status, and education. Collected clinical variables included smoking, alcohol consumption, hypertension, diabetes mellitus, hypercholesterolemia, peripheral arterial disease, previous stroke, family history of coronary artery disease (CAD), chronic lung disease, chronic renal failure, chronic heart failure, previous angina, previous PTCA, and CABG. Hypertension was defined as systemic BP ≥ 140 mm Hg, diastolic BP ≥ 90 mm Hg, or use of anti-hypertensive therapy [13]. Criteria for diabetes mellitus were fasting glucose ≥ 126 mg/dL or use of insulin or hypoglycemic medications [14]. Current smoking denoted regular use of cigarettes in the preceding year. Hypercholesterolemia is defined as total cholesterol > 200 mg % and LDL cholesterol > 100 mg% [15]. Hypertriglyceridemia is defined as TGL > 150 mg.

The serum samples were obtained as soon as the patient got admitted to the hospital and before initiating medication (treatment). Data collected included, complete hemogram, random blood sugar, glycosylated hemoglobin, renal function tests, lipid pro- teins, CKMB, calcium, phosphorous and 25(OH)D levels. The serum 25(OH)D was determined by ECLIA from Elecsys Analyser. We classified the patients as per Table 1 [16–18].

An Elecsys vitamin D total assay is intended for quantitative determination of the total 25-hydroxy vitamin D in human serum and plasma. The electrochemiluminescence immunoassay “ECLIA” is intended for use in Elecsys and cobas e immunoassay analysers. Levels of 25(OH)D and other baseline characteristics were analyzed using T-test and chi-squared test.

### 3. Results

During the enrolment period of December 1, 2011 to February 28, 2012, 314 patients admitted to SJICS&R Hospital consented to baseline blood work and had 25(OH)D levels assessed via ECLIA method. The mean age for the total population in deficient group was 54.09 ± 12.26 years and for insufficient and sufficient groups was 52.23 ± 12.13 years (Table 2). 82.48% of the enrolled subjects were men and 17.5% were women (Table 2).

No significant heterogeneity was observed among age or gender subgroups, but vitamin D deficiency was more commonly seen in patients with low social support and lower activity level and diabetes (Table 2).

### 4. Discussion

This study evaluated vitamin D status in patients admitted for AMI at SJICS&R—a tertiary care centre. Our data suggested that there is high prevalence of vitamin D deficiency or insufficient (83.5%) in AMI patients. This data is consistent with data associating CAD and many of its risk factors with 25(OH)D deficiency [16,19]. Studies have shown that individuals with vitamin D deficiency were at higher risk of ischemic heart disease [20–22]. There is a significant association between osteoporosis and vascular calcification and vitamin D levels are inversely related to vascular calcification which in turn may affect AMI risk [23].

Our data also noted that there is more vitamin D deficiency in patients who are having diabetes mellitus, confirming previously described associations [24]. Vitamin D deficiency with dietary calcium deficiency has been associated with impaired fasting glucose and possibly type 2 diabetes mellitus which is a risk factor for cardiovascular disease [25,26] which possibly explains the increased prevalence of vitamin D deficiency in our diabetic subgroup.

Animal studies have shown that vitamin D regulates RAS by suppressing renin gene expression, deficiency leading to increased renin production and hypertension [27,12], though in our study hypertension was equally distributed between the two groups.

Skin pigmentation has a vital role in vitamin D production. Darker skin individuals produce less vitamin D with same ultraviolet B radiation as compared to fairer skin [28]. This explains the higher prevalence of vitamin D deficiency in our cohort as all the study subjects were Indians with dark skin.

Patients with high cholesterol high triglyceride levels and who smoke are high risk factors for cardiovascular disease and these are associated with vitamin D deficiency and myocardial infarction.

Other observations made from the study were lower socioeconomic status patients and sedentary life style were other risk factors for vitamin D deficiency. Low vitamin D levels in lower socioeconomic status patients may be because of poor dietary intake of nutritional supplements and sedentary patients may have less sun exposure for adequate 25(OH)D production.

Vitamin D can adversely affect many aspects of health, especially musculoskeletal and immunological function. Although there are no randomised trials to explain that normalising vitamin D levels will improve cardiovascular health and prognosis, it is reasonable to screen AMI patients for vitamin D deficiency and to correct deficient levels.
according to nationally established consensus guidelines to optimize overall health.

Limitations of the study include small number of study group done especially during the early part of the year. The study was not conducted throughout the year, so that we are unable to comment on the seasonal variation and its influence on the vitamin D levels.

Another limitation of the study is lack of an adequate control group with normal vitamin D levels. Because of large proportion of patients who were vitamin D deficient or insufficient, we did not have an adequate group for comparison.

5. Conclusions

Vitamin D deficiency is present in most of the patients with acute myocardial infarction and it is associated with many of its risk factors in our study. Prospective studies are needed to investigate benefits of screening and treatment of this very common vitamin deficiency for prevention of cardiovascular diseases.

References

[1] Holick MF. Prevalence of vitamin D inadequacy and implication for health. Mayo Clin Proc 2006;81:355–73.
[2] Harinarayan CV, Ramalakshmi T, Venkataprasad u. High prevalence of low dietary calcium and low vitamin D status in healthy Indians. Asia Pac J Clin Nutr 2004;13(4):359–64.
[3] Goswami R, Gupta N, Goswami D, Marwaha RK, Tandon N, Kochupillai N, et al. Prevalence and significance of low 25(OH)D concentration in healthy subjects in Delhi. Am J Clin Nutr 2000;72:472–5.
[4] Malabanan A, veronikis IE, Holick MF. Redefining vit D insufficiency. Lancet 1998;351:805–6.
[5] Chapuy MC, Preziosi P, Maamer M, Arnaud S, Ganal P, Herebergs S, Mernier PJ. Prevalence of vit D insufficiency in an adult normal population. Osteoporos Int 1997;7:439–43.
[6] Merk J, Hoffman W, Goldsmitd D, Ritz E. Demonstration of 1,25(OH)2 vit D3 receptors and actions in vascular smooth muscle cells in vitro. Calcif Tissue Int 1987;41:112–4.
[7] Merk J, Milde P, Lewicka S, Hugel U, Klaus G, Mangeldorf DJ, Haussler MR, Ranterberg EW, Ritz E. Identification and regulation of 1,25(OH)2D3 receptors activity and biosynthesis of 1,25(OH)(2)D3; studies in cultured bovine aortic endothelial cells and human dermal capillaries. J Clin Invest 1989;83:1903–15.
[8] O'Connor TU, Berry JF, Jarvis AK, Simpson RU. 1,25(OH)2D3 regulation of cardiac myocyte proliferation and hypertrophy. Am J Physiol 1997;272:H1751-8.
[9] Sigmund CD, Okuyama K, Ingelfinger J, Jones CA, Mullins JJ, Kane C, et al. Isolation and characterization of renin-expressing cell lines from transgenic mice containing a renin-promoter viral oncogene fusion construct. J Biol Chem 1990 Nov 15;265(32):19916–22.
[10] Li YC, Kong J, Wei M, Chen ZF, Liu SQ, Cao LP. 1,25-Dihydroxy vitamin D(3) is a negative endocrine regulator of the renin-angiotensin system. J Clin Invest 2002;110:229–38.
[11] Wu J, Garami M, Cao L, Li Q, Gardner DG. 1,25(OH)2D3 suppresses expression and secretion of ANP from cardiac myocytes. Am J Physiol 1995;268(pt1):E1108–13.
[12] Xiang W, Kong J, Chen S, Cao LP, Qiao G, Zheng W, et al. Cardiac hypertrophy in vit D receptor knockout mice: role of the systemic and cardiac renin-angiotensin systems. Am J Physiol Endocrinol Metab 2005;288:E125–32.
[13] Chobanian AV, Ballin GI, Black HR, GreenLA, Jl Jizzo, Jone DW, Matron Wright JT, Roccella EJ. The seventh report of the Joint Nation Committee on prevention, detection, evaluation and treatment of high blood pressure. Hypertension 2003;42:1206–52.
[14] Report of the expert committee on the diagnosis and classification of diabetes mellitus. Diabetes Care 1997;20:1183–97.
[15] Third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation and treatment of high blood cholesterol in adults (Adult treatment panel III). NIH publication No. 01-3670; may 2001.
[16] Lee JH, O‘Keefe JH, Bell D, Hensrudd DD, Holick MF. Vitamin D deficiency: an important, common and easily treatable cardiovascular risk factor. J Am Coll Cardiol 2008;52:1945–56.
[17] Bischoff-Ferrari HA, Giovannucci E, Willet WC, Dawson hughes B. Estimation of optimal serum concentrations of 25-hydroxy vitamin D for multiple health outcomes. Am J Clin Nutr 2006;84:18–28.
[18] Chapuy MC, Preziosi P, Maamer M, Arnaud S, Ganal P, Hereberg S, et al. Prevalence of vitamin D deficiency in an adult normal population. Osteoporos Int 1997;7:439–43.
[19] Carl J, Lavic MD, John H, Lee MD, Richard V, Milani MD. Vitamin D and cardiovascular disease. JACC 2011;58(15):1547–56.
[20] Lund B, Badskjaer J, Lund B, Soerenson OH. Vitamin D and ischemic heart disease. Horm Metab Res 1978;10(6):553–6.
[21] Scragg R, Jackson R, Holdaway IM, Lim T, Beaglehole R. Myocardial infarction is inversely associated with plasma 25-hydroxy vitamin D3 levels: a community based study. Int J Epidemiol 1990;19(3):559–63.
[22] Vik B, Try K, Thelle DS. Forde OH Tromso Heart study; vitamin D metabolism and myocardial infarction. Br Med J 1979;2(6183):176.
[23] Warison KE, Abrolat ML, Malone LL, Hoeg JM, Doherty T, Detrano R, et al. Active serum vitamin D levels are inversely correlated with coronary calcification. Circulation 1997;96(6):1755–60.
[24] Ciogolini M, Iagulli MP, Microni V, Gallorto M, Lombardi S, Targher G. Serum 25-hydroxy vitamin D3 concentrations and prevalence of cardiovascular diseases among type 2 diabetic patients. Diabetes Care 2006;29:722–4.
[25] Pittas AG, Harris HS, Stark PC, Dawson-Hughes B. The effect of calcium and vitamin D supplementation on blood glucose and markers of inflammation in non diabetic adults. Diabetes Care 2007;30(4):980–6.
[26] Maghbooli Z, Hossein-Nezhad A, Karimi F, Shafaei AR, Larijani B. Correlation between vitamin D3 deficiency and insulin resistance in pregnancy. Diabetes Metab Res Rev 2008;24(1):27–32.
[27] Li YC, Qiao G, Işıkovic M, Xiang W, Zheng W, Kong J, Vitamin D: a negative endocrine regulator of the renin angiotensin system and blood pressure. J Steroid Biochem Mol Biol 2004;89–90(1–5):387–92.
[28] Matsuoka LY, Wortsman J, Hadda JG, Kolpin PM, Hollis BW. Racial pigmentation and the cutaneous synthesis of vitamin D. Arch Dermatol 1991;127:536–8.