Serum Vitamin D Level in Patients Undergoing Coronary Artery Catheterization

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Submitted 4 May 2021 Accepted 16 June 2021 Published 30 June 2021

Abstract

Background: Vitamin D deficiency may be a risk factor for coronary artery disease (CAD). We aimed to measure the prevalence of vitamin D deficiency in CAD and its association with severity of angiographic proven CAD.

Methods: This prospective, cross-sectional study included 106 consecutive patients who were admitted for typical angina and had signs of myocardial injury (ECG findings and/or elevated troponin I or CK-MB) and who underwent coronary angiography at the university hospital of BPKIHS from August 2020 to April 2021. Patients were categorized into angiographic proven CAD group and angiographic normal coronary artery group. Serum vitamin D level was classified as normal (≥ 30 ng/ml) and deficiency (< 30 ng/ml).

Results: Out of 106 patients, 78 patients (73.6%) had vitamin D deficiency and 28 (26.4%) had normal vitamin D level (p = 0.39). Vitamin D level (mean ± SD) in patients with angiographic normal coronary artery and angiographic proven CAD were 25.94 ± 11.63 ng/ml and 26.07 ± 12.90 ng/ml respectively (p = 0.97). Prevalence of vitamin D deficiency was 75.0% and 64.3% in significant CAD group and normal coronary artery group respectively (p = 0.39). Similarly, frequency of vitamin D deficiency were 68.6%, 78.3% and 88.90% in single, double, and triple vessel disease respectively (p = 0.21). The vitamin D level (mean ± SD) in single, double and triple vessel disease were 27.31 ± 14.02 ng/ml, 25.69 ± 12.72 ng/ml, 23.08 ± 9.45 ng/ml respectively.

Conclusion: The prevalence of vitamin D deficiency in both angiographic normal coronary artery and angiographic proven CAD were high but comparable. There was no association of vitamin D deficiency with severity of angiographic proven CAD.

Keywords: Coronary angiography; Coronary artery disease; Vitamin D deficiency
Coronary artery disease (CAD) is a leading cause of death despite significant progress in primary prevention and treatment strategies [1]. Although it has been associated with hypertension, diabetes mellitus, dyslipidemia and smoking, the search for newer preventable, modifiable risk factors continues in order to decrease cardiovascular morbidity and mortality [2]. Vitamin D deficiency is reported to be associated with cardiovascular disease (CVD) and many of its risk factors [3, 4].

Vitamin D is important in calcium and phosphate metabolism which facilitates bone mineralization, muscle contraction, nerve conduction and general cellular function [5]. Growing evidence suggests more diversified role of vitamin D than previously believed. Vitamin D deficiency has been shown to result in cardiac hypertrophy and fibrosis by elevation of matrix metalloproteinase enzyme [6, 7]. It also predisposes to hypertension by up regulation of the renin-angiotensin system [8]. Similarly, it is also involved in promoting the formation of atheromatous plaque by increasing the uptake of lipids by macrophages and their conversion into foam cells [4]. Hence, it’s deficiency increases the risk of CVD and CAD.

Vitamin D deficiency is recognized as a major public health problem globally [5]. Its prevalence is up to 73% in Nepalese population and variably reported as 51.2% to 95% in CAD [9-11]. In South Asian population, CAD has an early onset and is aggressive [12]. However, only a few studies have explored the role of vitamin D deficiency in CAD patients and the results are conflicting. In this cross-sectional study, we aimed to measure prevalence of vitamin D deficiency in CAD and to assess association of vitamin D deficiency with angiographically proven CAD.

METHODS

This prospective, cross-sectional study was conducted at a university hospital of B. P. Koirala Institute of Health Sciences (BPKIHS), Dharan, Nepal from August 2020 to April 2021. All consecutive patients aged ≥ 20 years visiting emergency department or cardiology out patient unit for typical angina and ECG showing signs of ischemia and/or biomarker evidence of myocardial injury (elevated troponin I or creatine kinase-MB (CK-MB)) who underwent coronary angiography (CAG) were enrolled. Patients having severe valve disease, liver or kidney failure, diseases related to bone metabolism, primary or secondary hyperparathyroidism, malignancy or osteoporosis, or taking vitamin D supplements or drugs like rifampicin, phenytoin, barbiturate, and thiazide diuretics which may interfere with vitamin D metabolism were excluded. Patients were recruited as per medical ethics and informed written consent was taken from each patient. Institutional Review Committee had approved the study protocol before recruitment of patients.

Sample size was estimated based on the prevalence of vitamin D deficiency in CAD as 51.2% as shown by a previous study [10]. Using Z value of 1.96 for confidence interval of 95% with 80% power and precision of 10%, the estimated sample size was 106 patients, including 10% dropout.

A detailed socio-demographic data and relevant clinical information were recorded in a structured data collection tool. All patients underwent thorough detailed medical history, clinical evaluation, blood sampling, electrocardiography (ECG) and echocardiography. All patients had undergone CAG as per American College of Cardiology American Heart Association (ACC/AHA) guidelines [13]. Random blood sugar (RBS), fasting blood sugar (FBS), post-prandial blood sugar (PPBS), glycosylated hemoglobin (HbA1c), renal function tests, lipid profile, troponin I and CK-MB of all patients were performed by standard methods. Blood samples for relevant baseline investigations were collected at the time of admission and before initiating medication. Samples for lipid profile and vitamin D were drawn after eight hours of fasting on the next day of admission.

The vitamin D level was determined by fully automated chemiluminescence immunoassay (CLIA) analyzer from Snibe Diagnostic MAGLUMI 2000 in the standard biochemistry laboratory. The principle of operation of vitamin D assay is a two-incubation chemiluminescence immunoassay. Two milliliters of blood was centrifuged at room temperature. Collected serum was incubated twice, after which the washed sample underwent chemiluminescent reaction to measure relative light units that gave the measure of 25-OH-vitamin D in serum. Vitamin D level ≥ 30 ng/ml was considered as normal whereas the level < 30 ng/ml as deficiency. Vitamin D levels between 20-30 ng/ml were considered as mild deficiency, 10-20 ng/ml as moderate deficiency and < 10 ng/ml as severe deficiency.

All 106 patients were grouped as angiographic proven CAD group and normal coronary artery group based on the CAG finding. Angiographic proven CAD was defined as coronary artery stenosis ≥ 50% in one or more major coronary arteries. It was further grad-
ed as single vessel disease (SVD), double vessel disease (DVD) and triple vessel disease (TVD) depending upon the number of vessels involved. Angiographic normal coronary artery was defined as coronary artery luminal diameter narrowing < 50% or normal coronary artery.

**OPERATIONAL DEFINITIONS**

Case definition of CAD was based on the WHO European Acute Myocardial Infarction Registry criteria [14]. Hypertension was defined as per 2017 ACC/AHA task force guideline [15]. Diabetes was defined as per 2017 American Diabetes Association guidelines [16]. Dyslipidemia was defined as per 2017 American Association of Clinical Endocrinologists guidelines [17]. Smokers were defined as anyone who has smoked 100 cigarettes in his or her lifetime and who currently smokes cigarettes [18].

The collected data was entered in Microsoft excel 2007 and uploaded into Statistical Package for Social Sciences version 17 (SPSS Inc; Chicago, IL, USA). Values were expressed as number, percentage, mean ± standard deviation or median (IQR). The chi-square test was used to compare categorical variables and the Student’s t-test was used to compare normally distributed data. A two-sided p-value of < 0.05 was considered as statistically significant with 95% confidence interval.

**RESULTS**

Out of the 106 enrolled patients, 14 (13.2%) had angiographic normal coronary artery. Among the 92 (86.8%) patients with angiographic proven CAD, 51 (48.1%) patients had SVD, 23 (21.7%) had DVD and 18 (17.0%) had TVD. Thirty-two patients (30.2%) were diagnosed as chronic stable angina (CSA); 74 patients (69.8%) as acute coronary syndrome (ACS). The age, gender distribution and presence of hypertension, diabetes mellitus, smoking and dyslipidemia was comparable between angiographic proven CAD and angiographic normal coronary artery groups. FBS, PPBS and HbA1c were significantly higher in patients with angiographic proven CAD compared to angiographic normal coronary artery group (Table 1).

The vitamin D level [median (IQR)] among the 106 patients was 22.75 (18.41, 31.01) ng/ml with minimum of 6.4 ng/ml and maximum of 78.85 ng/ml. Both groups of patients with angiographic normal coronary artery and angiographic proven CAD had low vitamin D levels (Fig. 1).

Prevalence of vitamin D deficiency in 106 patients was 73.6%. The prevalence of vitamin D deficiency in

| Table 1: Baseline characteristics of patients according to coronary angiography profile. Values are expressed as mean ± SD or n (%) |
|-----------------|-----------------|-----------------|-----------------|-----------------|
| Parameters      | Angiographic normal coronary artery (n = 14) | Angiographic proven CAD (n = 92) | p-value |
| Age (y)         | 62.14 ± 10.51   | 64.15 ± 11.49   | 0.51*          |
| Male/ Female (57/ 49) | 9 (15.8%)/ 5 (10.2%) | 48 (84.2%)/ 44 (89.8%) | 0.39*          |
| ACS/ CSA (74/ 32) | 5 (6.8%)/ 9 (28.1%) | 69 (93.2%)/ 23 (71.9%) | 0.003          |
| Diabetics (n = 36) | 2 (5.6%) | 34 (94.4%) | 0.09*          |
| Hypertensive (n = 27) | 13 (16.5%) | 66 (83.5%) | 0.09*          |
| Smoker (n = 38) | 4 (10.5%) | 34 (89.5%) | 0.54*          |
| Alcoholic (n = 14) | 4 (28.6%) | 10 (71.4%) | 0.06*          |
| Dyslipidemic (n = 15) | 1 (6.7%) | 14 (93.3%) | 0.41*          |
| FBS (mg/dl)     | 106 ± 13.29     | 120.26 ± 38.10  | 0.01*          |
| PPBS (mg/dl)    | 141.64 ± 19.87  | 180.19 ± 59.28  | < 0.001*       |
| HbA1c (%)       | 5.421 ± 0.706   | 6.40 ± 1.63     | < 0.001*       |
| Creatinine (mg/dl) | 1.121 ± 0.30  | 1.10 ± 0.39     | 0.90*          |
| LDL (mg/dl)     | 121.78 ± 34.42  | 121.77 ± 42.05  | 0.99*          |
| HDL (mg/dl)     | 42.357 ± 6.640  | 40.02 ± 11.19   | 0.29*          |
| Vitamin D (ng/ml) | 25.942 ± 11.638 | 26.078 ± 12.905 | 0.96*          |

patients with angiographic proven CAD (75%) was comparable (p = 0.39) to that of patients with angiographic normal coronary artery (64.3%). The frequency of vitamin D deficiency in SVD, DVD and TVD patients were 68.6%, 78.3% and 88.9% respectively (p = 0.21) (Table 2).

Out of 74 patients of ACS, 56 (75.7%) patients had vitamin D deficiency and 18 (24.3%) had normal vitamin D level. Similarly, out of 32 patients of CSA, 22 (68.8%) patients had vitamin D deficiency and 10 (31.3%) had normal vitamin D level (Fig. 2).

DISCUSSION

We found that out of 106 patients, 86.8% had angiographic proven CAD and 13.2% had angiographic normal coronary artery. The prevalence of vitamin D deficiency in angiographic proven CAD group (75%) and angiographic normal coronary artery (64.3%) were comparable. In addition, vitamin D deficiency was not associated with severity of angiographic proven CAD.

High prevalence of vitamin D deficiency in our population is reflective of the generalized high prevalence rates of hypovitaminosis D in Nepal [9]. The high prevalence rates in our country despite its sunny climate and darker skin complexion of the population may be due to generalized malnutrition, vegetarian food habits, inadequate sun exposure, and lack of vitamin D food fortification program.

Multiple studies showed that vitamin D deficiency is directly or indirectly associated with CAD [19, 20]. Recent meta-analyses have been conflicting, with both positive and neutral associations reported [21, 22]. Moreover, data on severity of vitamin D deficiency and extent of angiographically determined CAD are limited.

In our study, the prevalence of vitamin D deficiency was high in both angiographic proven CAD group and angiographically normal coronary artery (75% vs 64.3%). In addition, there was no statistically significant difference in the prevalence of vitamin D deficiency among SVD, DVD and TVD patients. However, there was a trend towards lower mean vitamin D level with increasing severity of CAD. Further study with a larger

**Table 2:** Prevalence of vitamin D deficiency among patients with various coronary angiography profiles (n=106). Values are expressed as n (%)

<table>
<thead>
<tr>
<th>Coronary angiography profile</th>
<th>Vitamin D &lt; 30 ng/ml (n=78)</th>
<th>Vitamin D ≥ 30 ng/ml (n=28)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Coronary (n = 14)</td>
<td>9 (64.3%)</td>
<td>5 (35.7%)</td>
<td>0.39</td>
</tr>
<tr>
<td>CAD (n = 92)</td>
<td>69 (75%)</td>
<td>23 (25%)</td>
<td></td>
</tr>
<tr>
<td>SVD (n = 51)</td>
<td>35 (68.6%)</td>
<td>16 (31.4%)</td>
<td>0.21</td>
</tr>
<tr>
<td>DVD (n = 23)</td>
<td>18 (78.3%)</td>
<td>5 (21.7%)</td>
<td></td>
</tr>
<tr>
<td>TVD (n =18)</td>
<td>16 (88.9%)</td>
<td>2 (11.1%)</td>
<td></td>
</tr>
</tbody>
</table>

* chi-square test. CAD: Coronary artery disease, SVD: Single vessel disease, DVD: Double vessel disease, TVD: Triple vessel disease.
Among the patients undergoing CAG in Ludwigshafen Risk and Cardiovascular Health study cohort, low levels of vitamin D were independently associated with heart failure, all-cause and cardiovascular mortality. However, the relationship between vitamin D and angiographic severity of CAD was not reported [23, 24]. A higher prevalence of vitamin D deficiency in angiographically proven CAD patients and positive association with severity of CAD with vitamin D deficiency have been reported, but the study lacked a control group [25]. Similarly, a study reported lower vitamin D levels in patients with CAD than in controls and also revealed protective association of vitamin D with CAD after adjusting for conventional risk factors [26]. Similar to our study, an Indian study revealed a high prevalence of vitamin D deficiency in patients with CAD (81.70%) and no association of vitamin D deficiency with angiographic severity of CAD [27]. Comparable to our study, prevalence of vitamin D deficiency was 64.7% in patients with ACS and mean vitamin D level was 27.99 ± 11.77 ng/ml in another study [28].

Our study had several limitations. Firstly, our sample size was small and the study was restricted to a single center. Secondly, we did not have outcome-related data. Thirdly, we took patient with angiographic normal coronary group as control which was disproportionately small in size. Perhaps, an age matched cohort who attended cardiac outpatient department with no symptoms suggestive of ischemia could have been a better control group for comparison. Fourthly, it is very difficult to prove association of vitamin D deficiency with CAD in a population, where prevalence of vitamin D deficiency is itself very high.

CONCLUSION

The prevalence of vitamin D deficiency in both angiographic normal coronary artery and angiographic proven CAD were high but comparable. There was no association of vitamin D deficiency with severity of angiographic proven CAD.

References

Vitamin D in patients undergoing angiography


