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RESEARCH ARTICLE

A STUDY OF VITAMIN D LEVELS IN PATIENTS PRESENTING WITH ACUTE CORONARY SYNDROMES

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ABSTRACT

Introduction: Vitamin D deficiency is highly prevalent worldwide, and is also noted to be high in India. 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. Vitamin D, known primarily as a factor of bone metabolism, can affect the transcription of a number of genes, which play a vital role in the development of ACS and pathogenesis of CAD. The vitamin D axis affects vascular smooth muscle cell proliferation, inflammation, vascular calcification, the renin-angiotensin system (RAS), and blood pressure, all of which affect risk of CVD and myocardial infarction (MI). Endothelial dysfunction plays an important role in pathogenesis of CAD and vitamin D deficiency is postulated to promote endothelial dysfunction Because hypovitaminosis D is prevalent and easily correctable, establishing the relationship between vitamin D and risk of MI is important.

Objectives: 1. To assess the levels of Vitamin D in patients with acute coronary syndromes. 2. To elucidate a possible correlation between the levels of Vitamin D in patients with acute coronary syndromes.

Methods: A prospective study of 50 patients admitted in Basaveshwar Hospital, Kalaburagi with acute coronary syndromes were studied between December 2013 and May 2015. The Vitamin D levels were analyzed in all the patients and correlated with different parameters for statistical significance.

Results: The mean age of the study group was 57.96±9.6 years. Of the 50 patients, 28 were males with a male: female ratio of 1.2:1. Our study group had 17 patients who had a smoking history and 15 who consumed alcohol. AWMI was the most common presentation that was observed in 20/50 patients and NSTEMI was seen least in 9/50 patients. Vitamin D deficiency was seen in 78% of patients with acute coronary syndrome. 26 patients had Vitamin D deficiency levels (<20 ng/ml) while 13 patients had insufficiency (vitamin D levels 21-30 ng/ml). 57.7% of females had Vitamin D deficiency. This was significant when compared to the male population. Vitamin D deficient patients had a higher incidence of diabetes (57.69%) and hypertension (69.23%). Contrary to many studies, we could not elicit any significant association between total cholesterol levels or triglyceride levels. One patient in our study expired within 24 hours. He had an AWMI who presented in cardiogenic shock. His Vitamin D level was 20.2 ng/ml.

Conclusions: There is a high prevalence of Vitamin D deficiency (78%) among ACS patients. Vitamin D deficiency, along with increasing the prevalence of traditional risk factors for ACS, might also be an independent risk factor for ACS.

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INTRODUCTION

Vitamin D deficiency is highly prevalent worldwide (Holick, 2006), and is also noted to be high in India (Harinarayan *et al*., 2004; Goswami *et al*., 2000). 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 (Holick, 2006; Malabanan *et al*., 1998; Chapuy *et al*., 1997; Merke *et al*., 1987). 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. Vitamin D deficiency has a bearing not only on skeletal but also on extra skeletal diseases. Cultural and social taboos often dictate lifestyle patterns such as clothing – that may limit sun exposure and vegetarianism – which certainly limits vitamin D rich dietary options. Most Indians are vegetarians. Although a consensus regarding the optimal level of serum 25(OH)D has not been established, most experts define 25(OH)D deficiency as a level <20 ng/ml and vitamin D insufficiency as 21- 29ng/ml (Zittermann *et al*., 2006; Weishaar and Simpson, 1987). For studied end points such as incident MI or all-cause mortality a level of ≥30ng/ml is considered optimal. It is now increasingly recognized that adequate vitamin D status is not only important for bone health and the prevention of osteoporosis but also for optimal function of many other organs and tissues throughout the body, including the cardiovascular (CV) system (Zittermann *et al*., 2006).

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Cardiac myocytes have cytosolic vitamin D receptors (VDR) (Zittermann *et al*., 2003) that bind active vitamin D (1,25 dihydroxy vitamin D), but unlike vascular smooth muscle cells, cardiacmyocytes lack 1a-hydroxylase activity (Hewison *et al*., 2004), an enzyme that converts inactive vitamin D(25 hydroxy vitamin D) to active vitamin D. Hence cardiac muscle is strongly dependent upon circulating active vitamin D or calcitriol levels. In the past, several *in vitro* studies have shown that calcitriol regulates intracellular calcium metabolism and thus myocardial contractility (Weishaar and Simpson, 1987; Weishaar and Simpson, 1989; Wu *et al*., 1995). Consequently, 25(OH) D deficiency has been associated with aberrant cardiac contractility, cardiomegaly and increased ventricular mass due to myocardial collagen deposition, effects on blood pressure (Weishaar and Simpson, 1989). Apart from its effects on the myocardium, 25 (OH)D deficiency also leads to enhanced atherosclerosis secondary to vascular smooth muscle cell (VSMC) proliferation (Mitsuhashi *et al*., 1991; Mohtai and Yamamoto, 1987) and increased production of pro inflammatory cytokines (IL-6 and TNF-alfa) (Muller *et al*., 1992). There is growing body of evidence from clinical studies that 25(OH)D deficiency also plays an important role in the genesis of coronary risk factors, including hypertension (HTN), type-2 diabetes (DM-2) and the metabolic syndrome.

Furthermore, large epidemiological studies, including the Health Professionals Study and the Framingham Offspring Study, have shown that low 25(OH)D levels (<15ng/ml) as compared with levels ≥30ng/ml, were independently associated with twice the risk of incident myocardial infarction (MI) and a higher risk of incident cardiovascular events including fatal and nonfatal stroke. Moreover, the risk of allcause mortality was higher among subjects with vitamin D levels <17.8ng/ml in NHANES III as compared with subjects having levels >32 (Forman *et al*., 2005; Scragg *et al*., 2004).

MATERIALS AND METHODS

A total of 50 patients admitted with an event of acute coronary syndrome in Basaveshwar Teaching & General Hospital, Kalaburagi were included in the study. This study was conducted from Dec 2013-May 2015. All patients admitted in our hospital diagnosed clinically, ECG wise, ECHO wise and with the help of cardiac enzymes as Acute Coronary Syndrome who gave consent o be a part of the study were included in the study. Patients who were known case of Vitamin D deficiency, on Vitamin D supplements, Known case of renal disease, Pregnantwomen, Patients with underlying malignancies, Patients who are not willing to be a part of the study were excluded. Following investigations were done on patients Complete hemogram, Renal function tests, Cardiactroponins, Liver function tests, Vitamin D levels, Serum calcium and phosphate, FBS, PPBS, HbA1C, Fasting lipid profile, 2D ECHO. Statistical analysis was done using SPSS 16 software. Results were interpreted using paired and unpaired t tests and chi square tests.

RESULTS

During our study period 50 patients were assessed as mentioned above. The mean age of our study group was 57.9±9.69 years. Of the study population there were 22 female patients and 28 were males accounting to 44% and 56% respectively. Our youngest patient was a 40 year old male who presented with NSTEMI and the oldest patient was a 75 year old male who also had NSTEMI. The youngest patient to have a STEMI (AWMI) was 53 years in our study and the oldest patient in our study to have a study was 73 years who presented to us with an AWMI. In our study, 11 patients had NSTEMI, 30 patients had STEMI and 9 patients had UA accounting to 22%, 60% and 18% respectively.

Table 1. Sex wise distribution of cases

Valid Gender	Frequency	Percent	Valid Percent	Cumulative Percent
Female	22	44.0	44.0	44.0
Male	28	56.0	56.0	100.0
Total	50	100.0	100.0	

In our study 60% patients were hypertensive and only 44% patients were diabetics. Among the hypertensive patients, nearly 70% patients had Vitamin D deficiency and among our diabetic patients 57.6% had Vitamin D deficiency.

Table 2. Hypertension

Valid	Frequency	Percent	Valid %	Cumulative %
NO	20	40.0	40.0	40.0
YES	30	60.0	60.0	100.0
Total	50	100.0	100.0	

We analyzed the ECG finding of our patients and found that 40% of our patients had AWMI, 20% of our patients, 18% had NSTEMI and ECG was normal in 22% of our patients

Table 3. Frequency of ACS

	Frequency	Percent	Valid Percent	Cumulative Percent
NSTEMI	11	22.0	22.0	22.0
STEMI	30	60.0	60.0	82.0
UA	9	18.0	18.0	100.0
Total	50	100.0	100.0	

Table 4. ECG findings

	Frequency	Percent	Valid Percent	Cumulative Percent
AWMI	20	40.0	40.0	40.0
IWMI	10	20.0	20.0	60.0
NORMAL	11	22.0	22.0	82.0
NSTEMI	9	18.0	18.0	100.0
Total	50	100.0	100.0	

We evaluated the triglyceride as an individual risk factor for our patients and concluded that 76% of our patients have a triglyceride value >150 mg%.

Table 5. Hyper Triglyceridemia

	Frequency	Percent	Valid Percent	Cumulative Percent
No	12	24.0	24.0	24.0
Yes	38	76.0	76.0	100.0
Total	50	100.0	100.0	

Only 34% patients were smokers and only 30% of our patients had a history of alcohol consumption. 13 out of the 50 patients had both smoking and alcohol as risk factors. There was evidence of anterior wall hypokinesia in 5 patients while septum and apical hypokinesia was seen in 20 patients. IWMI was seen in 5 patients as evidenced by inferior wall hypokinesia. Posterior wall hypokinesia was observed in 2 patients whereas the ECHO was normal in 18 patients We assessed the Vitamin D levels in our patients and 26 patients of

our study were deficient in Vitamin D and 13 patients were insufficient in Vitamin D levels. 11 patients had a value more than 30 ng/ml. thus there was a high prevalence of Vitamin D deficiency in acute coronary syndrome patients which came up to 78%. Thus in our study, we have 26 patients in our study with a Vitamin-D deficiency and 24 patients with non-deficiency. We compared the different parameters with respect to Vitamin D deficient individuals and in those where the values were ≥20 ng/ml The mean age of patients with Vitamin D ≤20 was 58.65±9.4 years whereas the mean age of patients with Vitamin D levels >20 was 57.02±10.1 years. This mean age among the 2 groups was not significant with a p value of 0.782. 57.7% of Vitamin D deficient patients were females. Thus Vitamin D deficiency was seen more among females when compared to males with a significant p value of 0.042.

Table 6. Vitamin D levels in different types of ACS

Vitamin D	≤20	>20	Total
AWMI	9	11	20
IWMI	7	3	10
Normal	4	7	11
NSTEMI	4	5	9
Total	24	26	50

We plotted the relationship between HDL values and Vitamin D levels and analyzed using chi square test and concluded that the levels were not significant statistically among Vitamin D deficient and non-deficient patients with a p value of 0.2. We decided to see if the Vitamin D levels would lead to any particular type of involvement in the type of ACS as in AWMI or NSTEMI. The Fisher exact chi square value was 2.7 with a chi square value of 0.459 thus having no statistical significance. There was no significant association between total cholesterol levels in both the group of patients with a p value of 0.29. There was no positive co relation between the levels of LDL cholesterol between the 2 groups. However hypertension was prevalent more in patients with Vitamin D deficiency with a statistically significant p value of 0.017. Diabetes was also significantly higher in patients with Vitamin D deficiency. 57.6 % of diabetics belonged to the deficient group as compared to the 29.2% in the non-deficient group. This had a significant p value of 0.042. Habits such as smoking and alcohol did not have any statistical significant correlation with Vitamin D levels in the present study with a p value of 0.272 and 0.266 respectively.

DISCUSSION

With acute coronary syndromes being one of the leading causes of mortality and morbidity all over the world, science has spread its arms in every possible direction to unsheathe the hidden reversible risk factors for ACS. Vitamin D levels have been the point of interest for many authors for a very long time. In our study the mean age was 57.9 years with the mean age in Vitamin D deficient patients being slightly higher (58.65 years). The male female ratio was almost equally distributed in our study with the male: female ratio being 1.2:1. We found a significant Vitamin D deficiency in female patients compared to male patients. In our study 57.7% of Vitamin D deficient patients were females. Our data suggested that there is high prevalence of vitamin D deficiency or insufficiency (78%) in acute coronary syndrome patients. This data is consistent with a study by Satyamurthy *et al*. (2012) who reported a 72% Vitamin D deficiency in AMI patients. We found that there was a significant association between diabetes and hypertension and Vitamin D levels (p value= 0.042, 0.017 respectively). Vitamin D has been implicated in the pathogenesis of diabetes via mechanisms like reduced insulin production, increased insulin resistance and reduced insulin sensitivity due to reduced calcitonin (Tea Skaaby, 2015).

In various other studies like

Siadat *et al*. and Giovannucci *et al*. hypertension was significantly associated with reduced Vitamin D levels. Krause *et al* studied 18 subjects with stage I hypertension exposed to UVA and UVB (which stimulate vitamin D formation with skin) for 6 weeks and demonstrated a significant fall in systolic and diastolic blood pressure in subjects receiving UVB therapy (Kannel *et al*., 1979). Similar results were demonstrated in a tanning study, exposure to UVB radiation three times a week for 3 months led to a nearly 200% increase in 25(OH)D levels and a 6 mm Hg decrease in blood pressure (Kannel *et al*., 1979). A study of patients with T2DM and low baseline 25(OH) vitamin D levels demonstrated that on supplementation by a single dose of 100,000 IU vitamin D2 results in reduction of systolic blood pressure by 14 mm Hg and improvement of endothelial function (Suzanne *et al*.,). In the Framingham study on 3,890 nondiabetic individuals, the prevalence of vitamin D deficiency (25[OH]D<20 ng/mL) was threefold higher in those with higher level of subcutaneous adipose tissue and visceral adipose tissue than in those with lower level (Pittas *et al*., 2010). Similarly, a cross-sectional study on 8,018 nonsmoking subjects showed significant positive associations between serum 25(OH) vitamin D and serum total cholesterol, high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) and significant negative associations between serum 25(OH) vitamin D and both LDL-C/HDL-C ratio and TG (Pittas *et al*., 2007). We, in our study tried to establish a correlation between Vitamin D levels and the type of MI vis a vis AWMI, NSTEMI, IWMI in our patients and could not find any significance of the same (p value= 0.439).

Conclusion

1. Vitamin D deficiency, along with increasing the prevalence of traditional risk factors for ACS, is an independent risk factor for ACS.
2. There is a high prevalence of Vitamin D deficiency (78%) among acute coronary syndrome patients.

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