RELATIONSHIP BETWEEN SERUM VITAMIN D LEVEL AND ANGIOGRAPHIC SEVERITY IN CORONARY ARTERY DISEASE

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ABSTRACT

BACKGROUND

The aim of the study is to study the correlation of plasma 25-hydroxy vitamin D level with angiographic severity (Gensini score[1]) in Coronary Artery Disease (CAD). To determine the relation between vitamin D levels and angiographic severity of CAD[2,3,4] using Gensini score using patients with normal angiographic findings as controls. After appropriate consent, following measurement of vitamin D levels with ECLIA method in all subjects, coronary angiogram was done. Experimental data suggest that vitamin D levels influences thrombotic deficiency[5,6] and endothelial dysfunction,[7] which plays an important role in CAD. The results of angiographic study and vitamin D were then analysed in a double-blinded fashion by a third party.

MATERIALS AND METHODS

Place of Study- Department of General Medicine and Cardiology of Andhra Medical College, Visakhapatnam, India.
Type of Study- Prospective study.
Period of Study- November 2015 to December 2016.
This study was approved by the ethical committee of Andhra Medical College, Visakhapatnam, Andhra Pradesh State.

RESULTS

Our final results showed a trend towards increasing severity of CAD and LV dysfunction with progressive decrease in vitamin D levels, but unfortunately were not statistically significant. However, in a few subsets like elderly patients and diabetics, the values were significant. Further studies should be contemplated to determine exact role of vitamin D in atherosclerotic heart disease.

CONCLUSION

Our study showed that there is a trend towards increasing severity of CAD with decreasing levels of vitamin D in various subsets of patients with atherosclerosis. However, the results were not statistically significant, but the encouraging trend in our study should pave path for further studies to determine the optimal role of vitamin D in the pathogenesis and prognostication of patients with CAD.

KEYWORDS

Serum Vitamin D Level, Angiographic Severity, Gensini Score, 25-Hydroxy Vitamin D Coronary Artery Disease.

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BACKGROUND

The aim of the study is to study the correlation of plasma 25-hydroxy-vitamin D level with angiographic severity (Gensini score[1]) in coronary artery disease.[2,3,4]

Objectives of the Study

1. To study the levels of plasma 25-hydroxy-vitamin D in patients of coronary artery disease in various subsets including myocardial infarction (ST-Segment Myocardial Infarction (STEMI), Non-ST Segment Myocardial Infarction (NSTEMI)), coronary artery disease patients without myocardial infarction (Chronic Stable Angina (CSA), Unstable Angina (UA)) and patients with normal angiogram.
2. To correlate the levels of plasma 25-hydroxy-vitamin D with angiographic severity in coronary artery disease patients using Gensini score.
3. To compare the 25-hydroxy-vitamin D levels in various clinical subsets of coronary artery disease[8] with controls.

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MATERIALS AND METHODS

An observational, both retrospective and prospective, case-controlled study performed in a total of 100 hospitalised patients at the Departments of General Medicine and Cardiology of KGH of Andhra Medical College between November 2015 and December 2016.

Inclusion Criteria

The study population includes patients presenting as-

- Myocardial Infarction (MI) (STEMI and NSTEMI).
- CAD without MI (CSA and UA).
- Negative angiographic findings that comprise the control group.

Exclusion Criteria

Patients with-

1. Renal failure.
2. Hepatic failure.
3. Pregnancy.
4. Vitamin D supplementation.
5. Osteoporosis.
6. Patients not willing to participate will be excluded from this study.

Informed Consent

A written and oral informed consent will be taken from the patients after explaining the nature of the study. A detailed proforma for informed consent in English and Telugu are attached.

History, Physical Examination and Biochemical Tests- Weight, body surface area, body mass index and required biochemical tests like renal function tests, liver function tests will be done to include and exclude the patients.

Measurement of 25-OH-Vitamin D Levels- 2 mL of blood sample for 25-OH vitamin D were collected by venepuncture plasma 25-OH vitamin D levels were measured by using Electrochemiluminescence Immunoassay[9] (ECLIA) method. Serum concentration of 25-(OH) D correlates better with clinical outcomes than 1, 25-(OH) 2D concentration.[10]

Angiographic Data- Angiographic severity of coronary artery disease in patients undergoing Coronary Angiography (CAG) were evaluated using Gensini score as per the guidelines given by Merril Knudtson in his coronary scoring system[11] and Ian J Neeland et al.[12]

Statistical Analysis

Statistically significant in Chi-square test means the difference in the results did not occur by random chance. This is almost always represented by a lowercase p, which stands for probability. Cardiovascular risk factors like diabetes, hypertension, dyslipidaemias as well as vitamin D levels were studied. Bivariate correlation analysis was conducted in order to detect relationship between serum vitamin D levels with angiographic severity by Gensini score. p-value of less than 0.05 was considered significant.[13]

RESULTS

Demographic and Clinical Characteristics

A. Age Group- Majority of patients admitted for coronary angiogram were between 51-60 years as coronary artery disease is more prevalent in this age group.

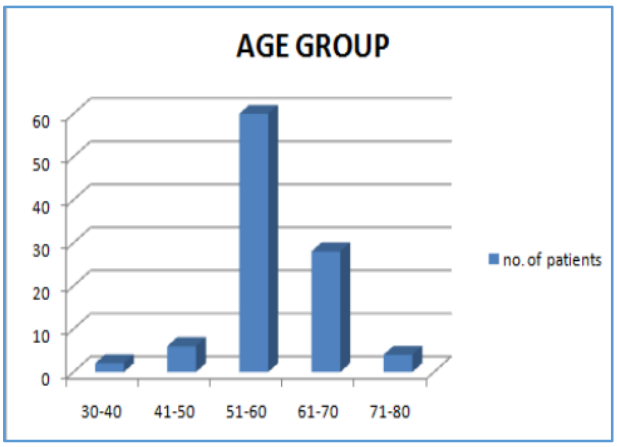


Figure 1. Age Group

B. Sex Prevalence- As coronary artery disease is more prevalent in males than female, our study showed similar trend and majority of patients admitted were males (85%).

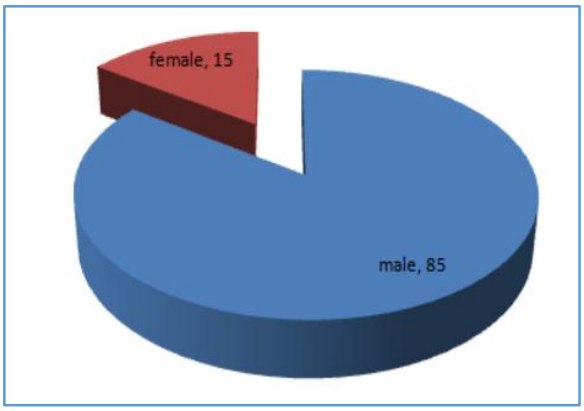


Figure 2. Sex Prevalence

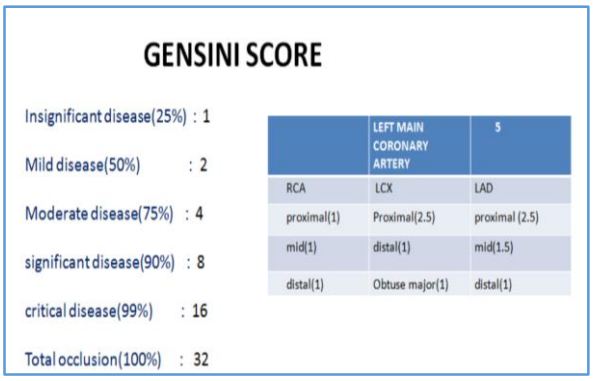


Figure 3. Gensini Score

C. Risk Factor Profile

In our study, prevalence of hypertension was more 84%, followed by diabetes mellitus 58%, followed by hyperlipidaemia 48%, followed by smoking 38%, followed by family history 34%.

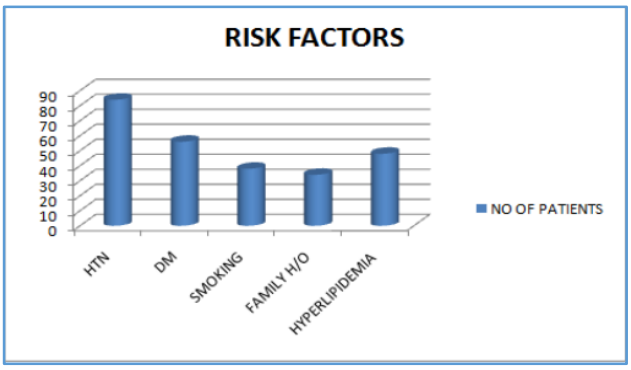


Figure 4. Risk Factors

D. Presenting Complaints

In our study, majority of patients presented with chest pain (87%), followed by Shortness of Breath (SOB) (76%), followed by palpitation (36%).

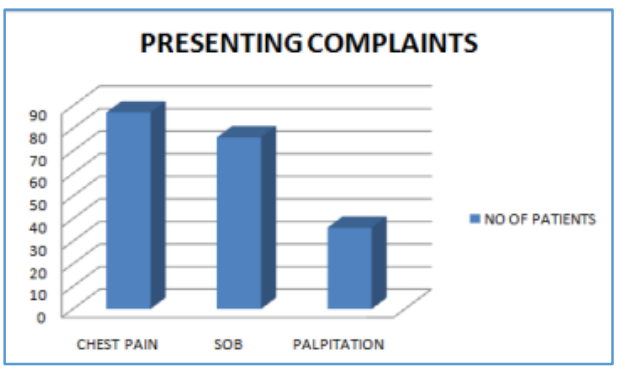


Figure 5. Presenting Complaints

Mode of Presentation

In our study, majority of patients were diagnosed as Chronic Stable Angina (CSA) 40%, followed by Unstable Angina (UA) 34%, followed by ST-Elevation MI (STEMI) 14%, NSTEMI 12%.

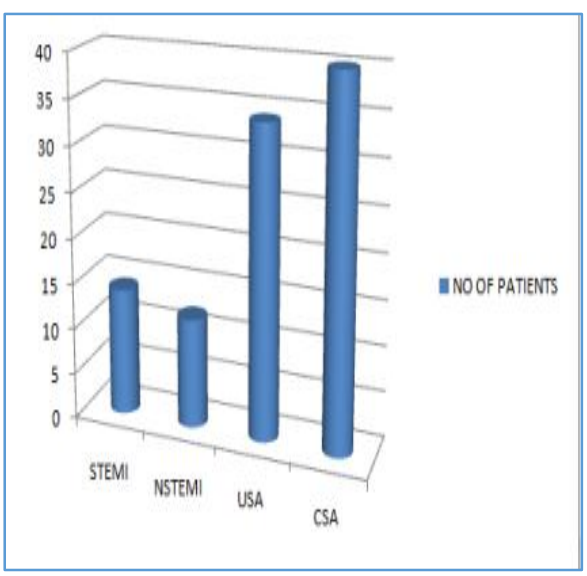


Figure 6. Mode of Presentation

Mode of Management

In our study, majority of patients with coronary artery disease were managed by Percutaneous Coronary Intervention (PCI) 59%. In patients with severe TVD and with co-morbid conditions were managed by Coronary Artery Bypass Grafting (CABG) 18%. In patients with mild CAD and normal coronaries were medically managed 23%.

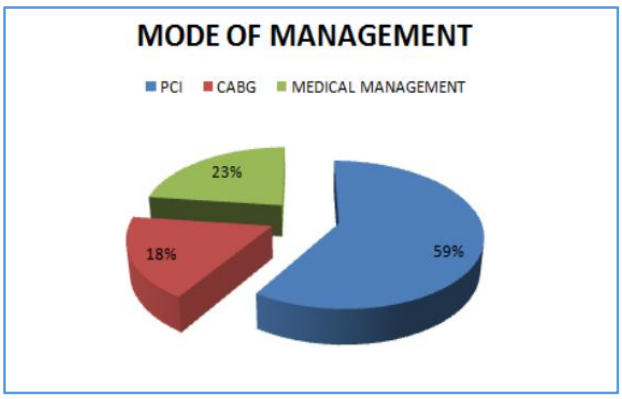
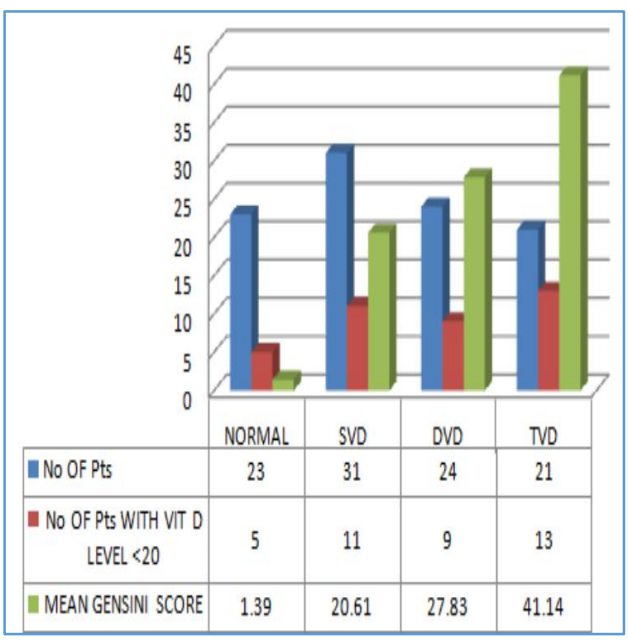


Figure 7. Mode of Management

In our study, vitamin D levels were estimated in all patients undergoing CAG. Severe vitamin D deficiency <20 ng/mL was seen in total of 37 patients, out of which 32 patients were with severe Coronary Artery Disease (CAD) and 5 patients were with normal coronaries or mild CAD. Out of 32 patients with CAD, 13 patients were having Triple Vessel Disease (TVD), 9 patients were having Double Vessel Disease (DVD) and remaining 11 patients were having Single Vessel Disease (SVD). Gensini score was calculated in all patients undergoing CAG. Mean Gensini score was high in patients with TVD 41.14 followed by patients with DVD 27.83 followed by SVD 20.61 and in patients with near normal coronaries, score was very low 1.39.



	NORMAL	SVD	DVD	TVD
No OF Pts	23	31	24	21
No OF Pts WITH VIT D LEVEL <20	5	11	9	13
MEAN GENSINI SCORE	1.39	20.61	27.83	41.14

Figure 8

In our study, severe vitamin D deficiency <20 ng/mL was correlated to final management. Out of 18 patients undergoing CABG, low vitamin D levels were seen in 10 patients and out of 59 patients undergoing PCI, low vitamin D levels were seen in 22 patients. Out of 23 patients with medical management, low vitamin D levels were seen in 5 patients.

Patients, out of which 32 patients were with severe Coronary Artery Disease (CAD) and 5 patients were with normal coronaries or mild CAD. Out of 32 patients with CAD, 13 patients were having Triple-Vessel Disease (TVD), 9 patients were having Double-Vessel Disease (DVD) and remaining 11 patients were having Single-Vessel Disease (SVD). Gensini score was calculated in all patients undergoing CAG. Mean Gensini score is high in patients with TVD 41.14 followed by patients with DVD 27.83 followed by SVD 20.61 and in patients with near normal coronaries, score was very low 1.39.

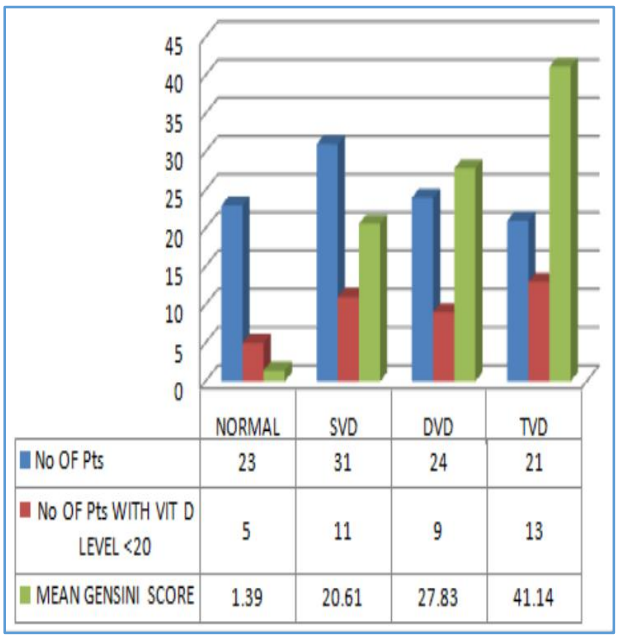


Figure 9

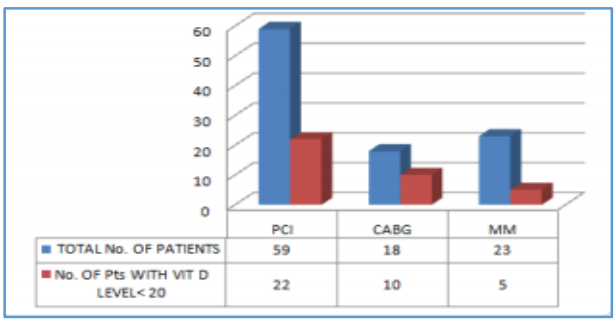


Figure 10

In our study, on subgroup analysis, severe vitamin D deficiency was found in 24 out of 56 diabetic patients (42.8%), 15 out of 38 smokers (39.4%) and 28 out of 48 hyperlipidaemic patients (58.3%).

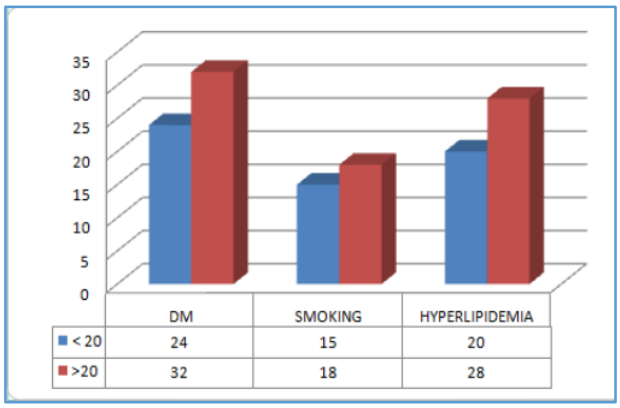


Figure 11

In our study, 2 patients had severe LV dysfunction, out of which one patient had severe vitamin D deficiency; 5 patients had moderate LV dysfunction, out of which 3 patients had severe vitamin D deficiency; 15 patients had mild LV dysfunction, out of which 8 patients had severe vitamin D deficiency; 78 patients had normal LV systolic function, out of which 25 patients had severe deficiency.

LV SYSTOLIC FUNCTION	No OF PT'S	No OF PT'S WITH VIT D < 20
NORMAL LV FUNCTIO N	78	25
MILD LV DYSFUNCTION	15	8
MODERATE LV DYSFUNCTION	5	3
SEVERE LV DYSFUNCTION	2	1

Figure 12

In our study, mean vitamin D levels are correlated with severity of coronary disease using Gensini score. There is a trend towards increasing severity of coronary artery disease with decreasing levels of vitamin D levels with odd's ratio of 2.5 with CI (0.86-7.6) with Z value of 1.69, but 'p' value obtained statistically not significant 0.09.

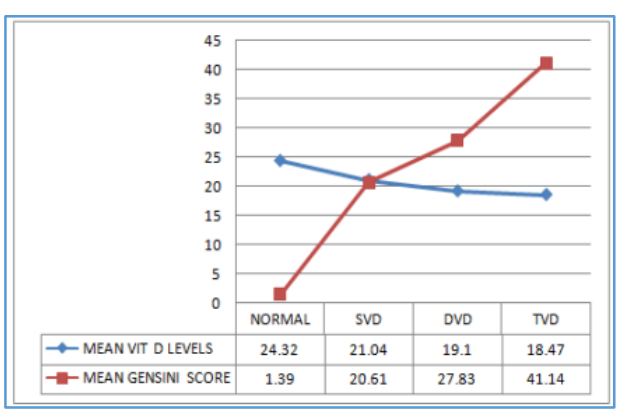


Figure 13

DISCUSSION

In our study, a single centre, double-blinded, both retrospective and prospective, case-controlled, observational study, the primary objective was to study the levels of plasma 25-hydroxy-vitamin D in patients of coronary artery disease in various subsets including myocardial infarction (ST-Segment Myocardial Infarction (STEMI), Non-ST Segment Myocardial Infarction (NSTEMI)), coronary artery disease patients without myocardial infarction (Chronic Stable Angina (CSA), Unstable Angina (UA)) with angiographic severity in coronary artery disease patients using Gensini score.

Low vitamin D levels (<20 ng/mL) seen in 5 patients (21.3%) with normal coronaries, 11 patients (35.4%) with SVD, 9 patients (37.5%) with DVD and 13 patients (61.9%) with TVD. Overall, low vitamin D levels are seen, 32 patients out of 77 patients (41.55%) with coronary artery disease.

In NHANES III, there was an U-shaped relationship between vitamin D and mortality risk with an apparent increase in mortality particularly in women with 25(OH)D levels >50 ng/L.[14]

Mean Gensini score in patients with normal coronaries is 1.39, with SVD is 20.61, with DVD is 27.83 and with TVD is 41.14. There is a trend towards increasing severity of coronary artery disease with decreasing levels of vitamin D levels with odds ratio of 2.5 with confidence interval (0.86-7.6) with Z value of 1.69, but 'p' value obtained is 0.09, which is statistically not significant.

We observed increased risk of ischaemic heart disease, myocardial infarction and angiographic severity of CAD with decreasing plasma 25-hydroxy vitamin D levels. However, on analysis of the results, 'p' value obtained is 0.09, which is not statistically significant.

On subgroup comparative analysis, we found that the mean vitamin D levels are much lower in particular subsets of CAD patients like men >70 yrs., patients with diabetes mellitus, smokers, patients with significant dyslipidaemia when compared with matched subsets.

Elderly men >70 yrs. with multivessel disease and higher Gensini score, the mean value of vitamin D was significantly lower than younger patients with CAD (p value 0.04).

In smokers with CAD irrespective of age presenting with acute coronary syndrome, the mean vitamin D levels were significantly lower (p value 0.05), even lower values were seen in patients admitted with STEMI.

Diabetics with severe vitamin D deficiency had higher Gensini scores and multivessel involvement when compared with diabetics with lesser degree of vitamin D deficiency (p 0.04).

In our study, demographic and clinical characteristics of patients showed similar profiles as that of recent trails.[15,14] Predominant age group being 50-60 years with male preponderance and the risk profile of patients were similar to trend of coronary artery disease with hypertension (84%), diabetes mellitus (58%), hyperlipidaemia (48%), smoking (38%) and family h/o CAD (34%). Our study also showed a nonlinear relationship between vitamin D level and ejection fraction across various subsets of CAD patients with decreasing vitamin D levels, there was a higher incidence of LV dysfunction, however, p value was not significant (0.08).

Diastolic dysfunction parameters showed no relation with vitamin D levels as majority of CAD patients had diastolic dysfunction.

Overall, severe vitamin D deficiency was seen among 32% and 54% of patients with normal and decreased LV function, respectively.

Sanjay Kumar Syal et al[7] in their study found out that there was vitamin D deficiency, 53% of CAD of double-vessel disease, 38% in CAD of triple vessel.

Irafan Sahin et al[16] in their study using Gensini score in CAD revealed the overall prevalence of 25-OH-D was less than 15 ng/mL was 34.8% (n=47) with 11% having vitamin D levels less than 10 ng/mL.

Akin F, Aya B et al in their study revealed the 83% of the study population had the vitamin D levels less than 30 ng/mL, which remained as a significant predictor for the severity of the CAD.

Dabaprasad Dhibar et al[17] study revealed that the frequency of vitamin D deficiency was higher in patients with normal coronary artery (89.30%) as compared to the patients with CAD (81.70%), but statistically insignificant (p=0.29).

Some limitations of our study should be noted. First, sample size was small; second, our study was observational; and patients were not randomised. MACE events were not studied. It is possible that confounding factors played a role, which were not accounted. Also, there were some demographic differences, which appeared, however, to be very minor.

SUMMARY

In our observational case-control study, we studied 100 patients between November 2015 to December 2016 admitted in Departments of General Medicine and Cardiology, King George Hospital of Andhra Medical College, Visakhapatnam, with a diagnosis of CAD (ACS and CSA) to determine the relation between vitamin D levels and angiographic severity of CAD using Gensini score using patients with normal angiographic findings as controls. After appropriate consent, following measurement of vitamin D levels with ECLIA method in all subjects, coronary angiogram was done. The results of angiographic study and vitamin D were then analysed in a double-blinded fashion by a third party. Our final results showed a trend towards increasing severity of CAD and LV dysfunction with progressive decrease in vitamin D levels, but unfortunately were not statistically significant. However, in a few subsets like elderly patients and diabetics, the values were significant. Further studies should be contemplated to determine exact role of vitamin D in atherosclerotic heart disease. Several studies show that vitamin D supplementation for those with vitamin D deficiency might beneficially reduce inflammation.[18,19]

Significant associations between low vitamin D status and both prevalent and incident degenerative CVD have

been reported in large-scale studies using composite end points.[20,21]

CONCLUSION

Despite wide ranges experimental and epidemiological evidence implicating 1, 25(OH)2D in many aspects of cardiovascular health, a metaanalysis of 51 trials of vitamin D in the prevention of various cardiovascular outcomes showed no overall result.[22] At present, it is unclear whether vitamin D supplementation can reduce the risk of consequences of CVD and it is not recommended for this indication.[23] Our study showed that there is a trend towards increasing severity of CAD with decreasing levels of vitamin D in various subsets of patients with atherosclerosis. However, the results were not statistically significant, but the encouraging trend in our study should pave path for further studies to determine the optimal role of vitamin D in the pathogenesis and prognostication of patients with CAD.

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