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Correlation of Vitamin D with Severity of Coronary Artery Disease and Short-Term Outcome in Female Versus Male Patients with Coronary Artery Disease

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Abstract

Background: Coronary artery disease (CAD) is a worldwide health concern. Cardiovascular disease (CAD) continues to be the predominant cause of mortality and morbidity, despite the enhancement of the current preventive and therapeutic strategies. **This study aimed to** correlate between vitamin D (Vit D), CAD severity and short-term outcome in females versus males with CAD. **Methods:** This cross-sectional study was conducted on 200 cases who were categorized into 2 equal groups: group A (males) and group B (females). Vit D level was evaluated in all the cases studied, and they also underwent electrocardiography, coronary angiography, and calculation of Syntax. **Results**: There was a significant negative correlation between Syntax score and Vit D level, meanwhile there was a significant positive correlation between Syntax score and number of affected vessels. **Conclusion:** There is an association between Vit D and CAD as it can predict the CAD severity at cutoff value of ≤ 20 ng/ml, with 98.86% sensitivity, 84.82% specificity, 83.7% PPV and 99.0% NPV.

Keywords: Coronary Angiography; Coronary Artery Disease; Electrocardiography; Vitamin D.

Introduction

Coronary artery disease (CAD) is a global health issue. Despite the progress made in current preventive and therapeutic methods, cardiovascular disease (CVD) remains the primary cause of morbidity and mortality in both developed and developing countries (1). The prevention of CAD through primary and secondary measures necessitates the risk factors identification, including male sex, old age, DM, HTN, smoking, dyslipidemia, chronic renal disease, and a positive family history. However,

conventional risk factors do not occur in all patients with CAD, which suggests that there are alternative causes of their atherosclerosis. A substantial risk of CV events, myocardial infarction (MI), and mortality is associated with reduced vitamin D (Vit D), as demonstrated by extensive cross-sectional studies that have a long-term follow-up of over seven years (2).

Vit D deficiency has become more prevalent among the general population. It has been demonstrated that vit D has the capacity to directly or indirectly affect the renin–angiotensin system, inflammation, cytokine levels, and adaptive immune responses to inflammation. (3). Deficiency of Vit D may contribute to CVD through the mechanisms of impaired insulin sensitivity, inflammation, and increased renin–angiotensin levels. In patients who have coronary arteries and endure coronary angiography, subclinical atherosclerosis and endothelial dysfunctions have been associated with vit D deficiency. Insufficient vit D levels have been shown to exacerbate atherosclerosis, as well as cause vascular disease, smooth muscle cell proliferation, foam cell formation, and endothelial dysfunction (4).

The objective of this investigation was to establish a correlation between the CAD severity and vit D, short term outcome in female versus male CAD patients, relation between Vit D, ischemic and thrombotic burden and illustrate the extent of CAD and the gender-specific variations in vit D levels.

Patients and methods

The cross-sectional investigation was conducted on 200 patients with CAD, presented at Cardiology Department in Benha Insurance Hospital & Benha University Hospital. The patients provided written informed consent and received a confidential code number and an explanation of the study's purpose. The research was conducted with the approval of the Research Ethics Committee code MS 29-4-2024 at the Faculty of Medicine at Benha University from March 2024 to March 2025.

Inclusion criteria included adult patients aged 18 years or older, regardless of gender, who had CAD (acute ST-elevation MI, non-ST-elevation MI, old MI, and chronic stable or unstable angina pectoris).

Exclusion criteria included the administration of vit D and calcium supplements, parathyroid gland disorders, bone tumors or metabolic bone diseases, or a history of chronic kidney disease.

Grouping: Patients were assigned to two equal groups: **Group A (n=100):** including male patients. **Group B (N=100):** including female patients.

All studied cases were subjected to complete history including patient demographics, medical history and

previous medications for CAD management and symptoms review by

chest pain characteristics, symptoms of heart failure and other relevant symptoms. Risk factors including HTN which is diagnosed according to European society of cardiology (ESC) (5), symptoms suggestive of STEMI, time delay as patient related delay, diabetes mellitus ,chronic kidney disease, dyslipidemia which was diagnosed according to ESC (6), smoking status, previous history of CAD according to ESC (7) and family history of CAD (8). **Complete physical examinations** including general assessment, cardiovascular, respiratory, abdominal and extremities examinations. **Laboratory investigations** were conducted, including a complete blood count, kidney function assays (serum creatinine and blood urea), international normalized ratio, prothrombin time, partial thromboplastin time, hepatic function, fasting and random blood glucose levels, lipid profile, cardiac enzymes, electrolytes, and serum vit D deficiency (optimal value 40-80 ng/mL). The participants were divided into three categories: mild (20-30 ng/mL), moderate (10-20 ng/mL), and severe (<10 ng/mL). In addition, participants were classified as normal (>30 ng/mL) (9). Radiological investigations by electrocardiography (ECG), echocardiographic examination, and coronary angiography.

The LIAISON® Vit D assay (Diasorin Inc) was employed to evaluate Vit D levels using the chemiluminescence method. The laboratory established a normal range for 25(OH)D levels of 30 to 100 ng/ml. A value of less than 10 ng/ml was considered to indicate severe hypovitaminosis D.

A predetermined algorithm was employed to calculate syntax scores, which were subsequently supplemented with points. For this algorithm, six clinical variables were assessed: age, sex, left ventricular ejection fraction (LVEF), creatinine clearance (CrCl), chronic obstructive pulmonary disease, and peripheral artery disease. The lesions' complexity was indicated by higher scores, which ranged from 0 to over 60 (10).

12- lead surfaces ECG was conducted for each patient. STEMI was diagnosed based on presence of a new (or increasing) and persistent elevated ST-segment in at least two contiguous leads of ≥1 mm in all leads, with the potential exception of leads V2-V3. In the appropriate clinical context, the following cut-off values were applied; for males under 40 years are ≥2.5 mm, males over 40 years are ≥2 mm, and women of any age are ≥1.5 mm. Contiguous ECG leads were anatomically adjacent and symbolized a particular myocardial territory. Using modified Simpson methodologies, the EF% was evaluated during the echocardiographic examination. The endocardial borders were traced in both systole and diastole, and apical two-chamber and four-chamber views were

obtained. A computer algorithm partitioned the LV cavity into approximately 20 discs. LV volume was determined by the sum of the volumes of these discs. The LVEF was determined by dividing the disparity between the diastolic and systolic volumes by the diastolic volume (11).

At least one coronary stenosis that exceeded 50% was regarded as indicative of CAD. The presence of 3-vessel disease and/or left main disease was used to assess the CAD severity (12). Patients who had previously undergone percutaneous coronary interventions were believed to have a vessel that was diseased, and the treated lesion was believed to be as such. patients who had undergone prior bypass procedures were evaluated for the number of diseased vessels, as well as both native arteries and grafts, to ascertain the extent of CAD.

Statistical analysis:

SPSS v27 (IBM©, Armonk, NY, USA) was used to conduct statistical analysis. Shapiro-Wilks' test and histograms were used to verify the normality of the data distribution. The quantitative parametric data was analyzed using an unpaired student t-test, which was based on the mean and standard deviation (SD). The Mann Whitney test was used to assess quantitative non-parametric data, which was presented using the interquartile range (IQR) and median. To analyze the qualitative variables, which were reported as frequencies and percentages, we utilized Fisher's exact test or the Chi-square test as appropriate. A two-tailed P value below 0.05 was used to assess statistical significance. Pearson or spearman correlation to measure the degree of relationship between two numerical variables. Receiver operating characteristic (ROC) curve which extends from the lowest left corner to the highest left corner and subsequently to the highest right corner. Area under the curve, also known as area under the curve (AUC), is a measure the diagn0ostic performance; an AUC more than 50% indicates satisfactory performance, and an AUC close to 100% indicates excellent performance.

Results

The females' age was significantly greater than that of the males, while other demographic data were insignificantly different between both groups. The risk factors, smoking, history of MI, previous percutaneous coronary intervention (PCI), history of MI, HTN, and CABG in males were significantly increased than females. There was an insignificant difference between both groups regarding the other risk factors. The medications history, the presenting symptoms and the vital signs were comparable between two groups. High-density lipoprotein (HDL) in males was significantly lower compared to females however triglycerides, total cholesterol and LDL in females were significantly higher than males. There was an insignificant difference between both groups regarding the other

laboratory investigations. The Vit D level in males was significantly decreased compared to females. In comparison to females, the Vit D levels of the moderate and severe deficiency groups were significantly elevated in males. The ECG findings on admission were significantly different between both groups. The angiographic findings, 1-vessel CAD and lesion severity <50% in females were significantly greater than males, while SYNTAX score, LAD, LCX, RCA affected vessels, lesion length, severity (50-70%, >70%), and Males had significantly higher rates of chronic occlusion than females. There was an insignificant difference between both groups regarding the EF, the other angiographic findings, and the adverse events. **Table 1**

In comparison to the normal and mild deficiency, the occurrence of smokers was elevated in the severe and moderate deficiency in both males and females, and it was significantly higher in the severe deficiency than in the moderate deficiency ($P<0.001$) among males, while smoking in females was insignificantly different. Males with severe deficiency exhibited significantly higher clopidogrel levels than those with moderate deficiency. The ASA levels in the mild and moderate deficiency groups were significantly lower than those in the normal group. The severe group exhibited a significantly higher HbA1c value than the normal, mild, and moderate deficiency groups. Notably, the moderate deficiency group exhibited a significantly higher HbA1c value than the normal group however HbA1c was insignificantly different between the other groups and each other's. Triglycerides and LDL in severe deficiency were significantly higher than normal, mild, and moderate deficiency groups. Compared to the normal group, HDL levels were significantly lower in moderate and severe deficiency, with an insignificant difference between the other groups and each other's in female. The baseline characteristics, the other risk factors, the presenting symptoms, the other medications, and the other laboratory investigations were insignificantly different from the studied. **Table 2**

Among both males and females, the ECG on admission was insignificantly different among the studied groups. The EF of females was significantly lower in the moderate and severe deficiency groups than in the normal group, and it was significantly decreased in the severe deficiency groups over the mild deficiency groups. The EF of males in the severe deficiency group was lower than that of the normal, mild, and moderate deficiency groups. was significantly lower in mild and moderate deficiency groups than normal groups. In the severe deficiency group, the syntax score was significantly greater than that of the other groups. Similarly, the moderate deficiency group exhibited a significantly higher syntax score than the normal and mild groups. The severity of CAD (50-70%, >70%) was the highest in severe groups, while the remaining angiographic findings were

insignificantly different among the studied groups. The adverse events including reinfarction and mortality in severe deficiency group were significantly higher than the other groups. Bleeding was insignificantly different among the studied groups. **Table 3**

A significant relation was found between syntax score and severity, Since the syntax score was higher in patients with a severity level exceeding 70% than in those without a severity level, and those with <50%, and was insignificantly different than those with 50-70%. Syntax score was significantly higher in patients with severity 50-70% than patients with no severity and those with <50% and was significantly higher in patients with severity <50% than patients with no severity. There was an insignificant relation between syntax score and affected vessels. **Table 4**

A significant negative correlation was observed between the Syntax score and Vit D level (r=-0.751, P<0.001), whereas a significant positive correlation was observed between the number of affected vessels and the Syntax score (r=0.305, P<0.001). **Table 5, Figure 1**

Vit D level can significantly predict the severity of CAD with AUC of 0.936, at cutoff value of ≤ 20 ng/ml, with 98.86% sensitivity, 84.82% specificity, 83.7% PPV and 99.0% NPV. **Figure 2,3.**

The multivariate logistic regression analysis showed that sex (male), smoking, chronic occlusion, Syntax score and vit D level were significant predictors for CAD severity. **Table 6**

Table 1: Baseline characteristics, risk factors, medications history, vital signs, presenting symptoms, laboratory investigation, vitamin D level, ECG on admission, ejection fraction and angiographic and adverse events findings of the studied groups

	Male group (n=100)	Female group (n=100)	P-value
Baseline characteristics			
Age (years)	58.05±4.1	69.11 ± 4.71	**<0.001***
Weight (kg)	78.68±10.18	78.03 ±10.13	0.651
Height (m)	1.67 ± 0.04	1.66 ±0.04	0.146
BMI (kg/m^2)	28.36 ±3.97	28.44 ±4.14	0.878
Risk factors			
Smoking	52 (52%)	2 (2%)	**<0.001***
HTN	65(65%)	47(47%)	**0.044***
DM	46 (46%)	40 (40%)	0.319
Dyslipidaemias	62 (62%)	59 (59%)	0.664
Atrial fibrillation	11 (11%)	15 (15%)	0.400
Family history	38 (38%)	26 (26%)	0.068
History of MI	33 (33%)	16 (16%)	**0.005***
Previous PCI	31 (31%)	18 (18%)	**0.032***
Previous CABG	18 (18%)	7 (7%)	**0.018***
COPD	5 (5%)	9 (9%)	0.267
Medications history			
ACE inhibitors	32 (32%)	29 (29%)	0.645
ARBs	20 (20%)	23 (23%)	0.605

Beta blockers		33 (33%)	25 (25%)	0.212
Nitrates		28 (28%)	31 (31%)	0.471
Statins		36 (36%)	29 (29%)	0.344
Calcium antagonists		18 (18%)	11 (11%)	0.159
Diuretics		13 (13%)	10 (10%)	0.638
ASA		37 (37%)	30 (30%)	0.494
Clopidogrel		12(12%)	9 (9%)	0.471
Presenting symptoms				
Chest pain		77(77%)	69(69%)	0.202
Dyspnea		23(23%)	31(31%)	
Vital signs				
HR (beats/min)		82.3 ± 7.95	82.56 ± 7.14	0.808
SBP (mmHg)		138.1 ± 10.12	137.2 ± 10.06	0.529
DBP (mmHg)		79.2 ± 7.74	80.2 ± 7.38	0.351
HR (beats/min)		82.3 ± 7.95	82.56 ± 7.14	0.808
Laboratory investigation				
Hb (g/dL)		13.45 ± 0.63	13.35 ± 0.6	0.272
WBCs (*109/L)		7.23 ± 1.1	7.46 ± 1.13	0.156
Platelets (*109/L)		300.13 ± 27.07	300.27 ± 27.33	0.971
HbA1c (%)		6.0 ± 1.17	6.03 ± 1.15	0.870
Serum creatinine (mg/dL)		0.98 ± 0.12	0.98 ± 0.12	0.793
Urea (mg/dL)		34.1± 8.67	33.99 ± 9.1	0.930
CRP (mg/dL)		1.78 ± 0.32	1.81 ± 0.31	0.530
PT (sec)		11.71 ± 0.45	11.78 ± 0.48	0.246
PTT (sec)		28.98 ± 2.94	29.96± 3.1	0.397
INR		0.99 ± 0.14	0.99 ± 0.14	0.844
ALT (U/L)		32.56 ± 4.77	32.75± 4.72	0.777
AST (U/L)		28.52 ± 6.44	29.99± 6.16	0.101
Cholesterol (mg/dL)		180.56± 20.44	157.57± 9.81	**<0.001***
Triglycerides (mg/dL)		174.6± 51.25	120.72± 17.71	**<0.001***
HDL (mg/dL)		39.83± 3.04	47.11± 5.15	**<0.001***
LDL (mg/dL)		105.81± 17.94	86.32± 8.43	**<0.001***
Vitamin D level				
Vit D level (ng/mL)		19.49 ± 12.44	23.76 ± 11.87	**0.014***
Normal (>30 ng/mL)		24 (24%)	34 (34%)	**0.044***
Mild deficiency (20-30 ng/mL)		16 (16%)	25 (25%)	
Moderate deficiency (10-20 ng/mL)		31 (31%)	25 (25%)	
Severe deficiency (<10 ng/mL)		29 (29%)	16 (16%)	
ECG on admission				
STEMI		14 (14%)	9 (9%)	**0.005***
Non-STEMI		29 (29%)	18 (18%)	
Old myocardial infarction		13 (13%)	10 (10%)	
Chronic stable angina pectoris		12 (12%)	34 (34%)	
Unstable angina pectoris		32 (32%)	29 (29%)	
Ejection fraction and angiographic findings				
EF (%)		56.89 ± 4.79	57.1 ± 4.82	0.758
Syntax score		23.35± 11.89	19.78± 11.11	**0.029***
Affected vessels	**1-vessel CAD**	37 (37%)	55 (55%)	**0.011***
	2-vessel CAD	30 (30%)	20 (20%)	0.102
	3-vessel CAD	33 (33%)	25 (25%)	0.212
Type of vessel	**LAD**	57 (57%)	29 (29%)	**<0.001***
	LCX	46 (46%)	18 (18%)	**<0.001***
	RCA	34 (34%)	12 (12%)	**<0.001***
	OM	21 (21%)	13 (13%)	0.132
	Diagonal	19 (19%)	10 (10%)	0.555
	PDA	12 (12%)	9 (9%)	0.070

	Ramus intermedius	7 (7%)	4 (4%)	0.352
Lesion characteristics	**Lesion length (mm)**	26.13 ± 6.5	20 ± 5.85	**<0.001***
	Severity <50%	7 (7%)	24 (24%)	**<0.001***
	50-70	14 (14%)	7 (7%)	**0.040***
	>70%	30 (30)	6 (6%)	**<0.001***
	Chronic occlusion	14 (14%)	4 (4%)	**0.013***
	Thrombus	4 (4%)	2 (2%)	0.407
Adverse events	**Bleeding**	**3 (3%)**	1 (1%)	0.312
	Reinfarction	**8 (8%)**	4 (4%)	0.233
	Mortality	**5 (5%)**	2 (5%)	0.445

Data presents as mean ± SD or frequency (%). *Statistically significant difference as p value <0.05. BMI: Body mass index, HTN: hypertension, DM: diabetes mellitus, MI: myocardial infarction, PCI: percutaneous coronary intervention, CABG: coronary artery bypass graft surgery, COPD: chronic obstructive pulmonary disease, ACE: angiotensin-converting enzyme, ARBs: angiotensin receptor blockers, ASA: acetylsalicylic acid , HR: heart rate, SBP: systolic blood pressure, DBP: diastolic blood pressure, Hb: hemoglobin, WBCs: white blood cells, HbA1c: glycated hemoglobin, CRP: c-reactive protein, PT: percussion therapy, PTT: Partial thromboplastin time, INR: international normalized ratio, ALT: alanine aminotransferase, AST: aspartate aminotransferase, HDL: high-density lipoprotein, LDL: low-density lipoprotein, STEMI: ST-elevation myocardial infarction, EF: Ejection fraction, CAD: coronary artery disease, LAD: left anterior descending artery, LCX: left circumflex artery, RCA: right coronary artery, OM: obtuse marginal, PDA: posterior descending artery.

Table 2: Baseline characteristics, risk factors, medications, presenting symptoms according to vit D status, vital signs, and laboratory investigation.

		Normal	**Mild deficiency**	**Moderate deficiency**	**Severe deficiency**	**P value**
			Baseline characteristics			
Age (years)	**Males**	58.21 ±4.23	56.25 ±3.86	58.71 ±4.06	58.21 ±4.07	0.267
	Females	70.15±4.45	68.04 ±4.58	69.04 ±4.95	68.69 ±5.08	0.386
Weight (kg)	**Males**	79.54 ±9.71	78.20 ±9.92	78.84 ±9.59	81.24±10.39	0.692
	Females	77.74±10.07	78.08 ±11.75	79.52 ±9.04	76.25 ±9.74	0.791
Height (m)	**Males**	1.67 ±0.05	1.67 ±0.04	1.66 ±0.04	1.67±0.04	0.651
	Females	1.67 ±0.05	1.64 ±0.04	1.67±0.05	1.65 ±0.04	0.066
BMI (kg/m^2)	**Males**	28.68 ±3.83	26.14 ±4.37	28.64 ±3.78	29 ±3.82	0.106
	Females	28.04±4.14	29.02±4.67	28.61±3.71	28.13±4.14	0.819
			Risk factors			
Smoking	**Males**	3 (12.5%)	3 (18.8%)	19(61.29%)	27 (93.10%)	**<0.001*** P1=0.588 **P2<0.001*** **P3<0.001*** **P4<0.001*** **P5<0.001*** **P6<0.001***
	Females	0 (0%)	0 (0.0%)	1 (4.0%)	1 (6.3%)	0.061
HTN	**Males**	14 (58.3%)	11 (68.8%)	16 (51.6%)	24 (82.8%)	0.071
	Females	20 (58.8%)	11 (44.0%)	10 (40.0%)	6 (37.5%)	0.381
DM	**Males**	7 (29.2%)	8 (50.0%)	19 (61.3%)	12 (41.4%)	0.111
	Females	17 (50.0%)	7 (28.0%)	9 (36.0%)	7 (43.8%)	0.365
dyslipidaemia	**Males**	14 (58.3%)	10 (62.5%)	22 (71.0%)	16 (55.2%)	0.621
	Females	21 (61.8%)	17 (68.0%)	16 (64.0%)	5 (31.3%)	0.098
Atrial fibrillation	**Males**	4 (16.7%)	1 (6.3%)	3 (9.7%)	3 (10.3%)	0.747
	Females	5 (14.7%)	3 (12.0%)	6 (24.0%)	1 (6.3%)	0.436
Family history	**Males**	10 (41.7%)	4 (25.0%)	15 (48.4%)	9 (31.0%)	0.347
	Females	6 (17.6%)	5 (20%)	9 (36%)	6 (37.5%)	----
History of MI	**Males**	11 (45.8%)	4 (25.0%)	11(35.5%)	7 (24.1%)	0.338
	Females	5 (14.7%)	5 (20.0%)	3 (12.0%)	3 (18.8%)	0.867
Previous PCI	**Males**	11 (45.8%)	5 (31.3%)	9 (29.0%)	6 (20.7%)	0.265
	Females	5 (14.7%)	6 (24.0%)	4 (16.0%)	3 (18.8%)	0.817
Previous CABG	**Males**	6 (25.0%)	3 (18.8%)	6 (19.4%)	3 (10.3%)	0.574
	Females	0 (0.0%)	4 (16.0%)	2 (8.0%)	1 (6.3%)	0.126
COPD	**Males**	0 (0.0%)	1 (6.3%)	1 (3.2%)	3 (10.3%)	0.352
	Females	2 (5.9%)	4 (16.0%)	2 (8.0%)	1 (6.3%)	0.556
			Medications			
ACE	**Males**	5 (20.83%)	6 (37.5%)	14 (45.2%)	7 (24.1%)	0.180

inhibitors	**Females**	10 (29.4%)	7 (28%)	8 (32%)	4 (25%)		0.969
ARBs	**Males**	3 (12.5%)	3 (18.8%)	7 (22.6%)	7 (24.1%)		0.729
	Females	7 (20.6%)	5 (20%)	9 (36%)	2 (12.5%)		0.305
Beta	**Males**	8 (33.3%)	7 (43.8%)	9 (29%)	9 (31%)		0.775
blockers	**Females**	8 (23.5%)	8 (32%)	6 (24%)	3 (18.8%)		0.792
Nitrates	**Males**	6 (25%)	4 (25%)	12 (38.7%)	6 (20.7%)		0.438
	Females	8 (23.5%)	6 (24%)	10 (40%)	7 (43.8%)		0.305
Statins	**Males**	10 (41.7%)	5 (31.3%)	9 (29%)	12 (41.4%)		0.680
	Females	8 (23.5%)	6 (24%)	8 (32%)	7 (43.8%)		0.458
Calcium	**Males**	5 (20.8%)	2 (12.5%)	9 (29.0%)	2 (6.9%)		0.142
antagonists	**Females**	4 (11.8%)	5 (20%)	1 (4%)	1 (6.3%)		0.295
Diuretics	**Males**	3 (12.5%)	1 (6.3%)	6 (19.4%)	3 (10.3%)		0.585
	Female	2 (5.9%)	4 (16%)	3 (12%)	1 (6.3%)		0.572
ASA	**Males**	12 (50%)	3 (18.8%)	13 (41.9%)	9 (31%)		0.188
	Females	17 (50%)	4 (16%)	5 (20%)	4 (25%)	**0.017***	**P1=0.007*** **P2=0.018*** P3=0.095 P4=0.713 P5=0.689 P6=0.706
Clopidogrel	**Males**	2 (8.3%)	1 (6.3%)	8 (25.8%)	1 (3.4%)	**0.038***	P1=1.00 P2=0.159 P3=0.584 P4=0.138 P5=1.00 P6=0.026*
	Females	3 (8.8%)	3 (12%)	2 (8%)	1 (6.3%)		0.929
			Presenting symptoms				
Symptoms	**Males**	17 (70.8%)	10 (62.5%)	26 (83.9%)	24 (82.8%)		0.286
		7 (29.2%)	6 (37.5%)	5 (16.1%)	5 (17.2%)		
	Females	17 (50.0%)	22 (88.0%)	18 (72.0%)	12 (75.0%)		**0.016***
		17 (50.0%)	3 (12.0%)	7 (28.0%)	4 (25.0%)		
			Vital signs				
HR (beats /min)	**Males**	82.25 ±7.62	79.69±7.73	84.52 ±8.27	81.41 ±7.76		0.213
	Females	83.03±7.022	82.24±7.73	82.04±7.65	82.88±6.11		0.950
SBP (mmHg)	**Males**	137.08±10.83	138.75±9.57	135.48±9.61	141.38±9.90		0.142
	Females	137.65±10.17	139.6±8.89	134±10.408	137.5±10.65		0.260
DBP (mmHg)	**Males**	78.33 ±8.68	78.75 ±7.19	78.39±7.35	81.03±7.72		0.514
	Females	80±7.38	80±7.638	80.8±7.59	80±7.30		0.975
			Laboratory investigation				
HbA1c (%)	**Males**	5.663 ±1.04	6.12 ±1.18	6.35 ±1.22	7.81 ±1.99	**0.040***	P1=0.209 P2=0.030* P3<0.001* P4=0.539 P5<0.001* P6=0.001*
	Females	5.25 ±1.14	5.716 ±1.22	6.02±1.087	6.97±1.38	**<0.001***	P1=0.146 P2=0.0114 **P3<0.001*** P4=0.370 **P5*=0.003*** **P6=0.018***
Serum creatinine (mg/dL)	**Males**	0.99± 0.11	0.92± 0.13	0.99± 0.12	0.99± 0.13		0.271
	Females	0.99 ±0.13	1.02 ±0.12	0.95 ±0.11	0.95 ±0.13		0.207
PT (sec)	**Males**	11.71± 0.42	11.54± 0.46	11.75± 0.41	11.75± 0.5		0.426
	Females	11.87 ±0.48	11.64 ±0.39	11.77±0.52	11.82 ±0.49		0.334
PTT (sec)	**Males**	29.5± 3.3	28.56± 2.83	28.81± 2.95	28.97± 2.76		0.762
	Females	30.29± 2.89	29.96± 3.42	29.64± 3.13	29.75± 3.19		0.869
INR	**Males**	1.02± 0.14	1.03± 0.15	0.95± 0.15	0.98± 0.13		0.218
	Females	0.98 ±0.13	1.01 ±0.14	0.95 ±0.16	1.04 ±0.15		0.229
Cholestero	**Males**	178.71± 19.8	176.5± 22.2	178.2± 21.4	186.6± 18.7		0.292

l (mg/dL)	**Females**	148.08± 10.7	153.4± 10.7	157.98± 9.3	167.6± 8.45	**<0.001***	P1=0.197 **P2=0.002*** **P3<0.001*** P4=0.370 **P5<0.001*** **P6=0.018***
Triglycerides (mg/dL)	**Males**	156.25± 50	155.6± 40.8	165.5± 49.9	195.9± 53.4	**0.013***	P1=1.00 P2=0.902 **P3=0.024*** P4=0.916 P5=0.004* P6=0.026*
	Females	110.62± 17.45	118± 15.8	119.6± 15.04	144.75± 15.14	**<0.001***	P1=0.309 P2=0.155 **P3<0.001*** P4=0.985 P5<0.001* P6<0.001*
HDL (mg/dL)	**Males** **Females**	39.88± 3.07 51.71± 6.55	39.56± 3.5 48.72± 4.87	39.55± 2.89 47.16± 4.48	38.93± 2.93 44.38± 3.61	 **<0.001***	0.715 P1=0.144 **P2=0.008*** **P3<0.001*** P4=0.722 P5=0.055 P6=0.355
LDL (mg/dL)	**Males**	98.17± 17.9	98.38± 13.6	103.5± 16.4	115.6± 17.9	**<0.001***	P1=1.00 P2=0.652 **P3=0.002*** P4=0.758 **P5=0.008*** **P6=0.032***
	Females	82.24± 8.33	85.96± 7.88	86.88± 8.06	94.5± 4.78	**<0.001***	P1=0.262 P2=0.107 **P3<0.001*** P4=0.974 **P5=0.004*** **P6=0.014***

Data presents as mean ± SD or frequency (%) *statically significant as p value <0.05. P1: P Value between Normal and Mild, P2: P Value between Normal and Moderate, P3: P Value between normal and Severe. P4: P Value between Mild and Moderate, P5: P Value between Mild and Severe, P6: P Value between Moderate and Severe. Normal (>30 ng/mL), mild deficiency (20-30 ng/mL), moderate deficiency (10-20 ng/mL), and severe deficiency (<10 ng/mL).). BMI: Body mass index. HTN: hypertension, DM: diabetes mellitus, MI: myocardial infarction, PCI: percutaneous coronary intervention, CABG: coronary artery bypass graft surgery, COPD: chronic obstructive pulmonary disease, MI: myocardial infarction, ACE: angiotensin-converting enzyme, ARBs: angiotensin receptor blockers, ASA: acetylsalicylic acid, HR: heart rate, SBP: systolic blood pressure, DBP: diastolic blood pressure,HbA1c: glycated haemoglobin, CRP: c-reactive protein, PT: percussion therapy, PTT: Partial thromboplastin time, INR: international normalized ratio, HDL: high-density lipoprotein, LDL: low-density lipoprotein.

Table 3: ECG on admission, ejection fraction, syntax score, angiographic findings and adverse events

			Normal	Mild deficiency	Moderate deficiency	Severe deficiency		P value
			ECG on admission					
Male	**STEMI**		2 (8.33%)	1 (6.25%)	5 (16.13%)	6 (20.69%)		0.715
	Non-STEMI		7 (29.17%)	6 (37.5%)	6 (19.35%)	10 (34.48%)		
	Old myocardial infarction		3 (12.5%)	1 (6.25%)	4 (12.9%)	5 (17.24%)		
	Chronic stable angina pectoris		4 (16.67%)	1 (6.25%)	5 (16.13%)	2 (6.9%)		
	Unstable angina pectoris		8 (16.67%)	7 (43.75%)	11 (35.48%)	6 (20.69%)		
Female	**STEMI**		1 (2.9%)	1 (4%)	3 (12%)	4 (25%)		0.272
	Non-STEMI		7 (20.6%)	3 (12%)	6 (24%)	2 (12.5%)		
	Old myocardial infarction		2 (5.9%)	3 (12%)	4 (16%)	1 (6.3%)		
	Chronic stable angina pectoris		15 (44.1%)	7 (28%)	7 (28%)	5 (31.3%)		
	Unstable angina pectoris		9 (26.5%)	11 (44%)	5 (20%)	4 (25%)		
Ejection fraction								
EF (%)	**Males**		60.75± 4.95	55.38± 4.16	53.42± 4.49	49.66± 3.59	**<0.001***	**P1=0.001*** **P2<0.001*** **P3<0.001*** P4=0.458 **P5<0.001*** **P6=0.006***
	Females		59.44± 5.22	57.08± 3.81	54.36± 4.32	53.06± 5.77	**<0.001***	P1=0.246 **P2<0.001*** **P3<0.001*** P4=0.191 **P5=0.049*** P6=0.832
Syntax score								
Males			10.79 ±5.39	10.19 ±4.83	27.65 ±3.23	36.41 ±4.62	**<0.001***	P1=0.097 **P2<0.001*** **P3<0.001*** **P4<0.001*** **P5<0.001*** **P6<0.001***
Females			12.50 ±6.82	12.40 ±6.22	27.92 ±6.04	34.06 ±7.27	**<0.001***	P1=1.00 **P2<0.001*** **P3<0.001*** **P4<0.001** **P5<0.001*** **P6=0.022***
Angiographic findings								
Affected vessels	**Males**	**1-vessel CAD**	12 (50%)	5 (31.25%)	12 (38.71%)	8 (27.59%)		0.736
		2-vessel CAD	6 (25%)	5 (31.25%)	10 (32.26%)	9 (31.03%)		
		3-vessel CAD	6 (25%)	6 (37.5%)	9 (29.03%)	12 (41.38%)		
	Females	**1-vessel CAD**	6 (25%)	6 (37.5%)	9 (29.03%)	12 (41.38%)		0.558
		2-vessel CAD	19 (55.9%)	15 (60.0%)	12 (48.0%)	9 (56.3%)		
		3-vessel CAD	7 (20.6%)	6 (24.0%)	3 (12.0%)	4 (25.0%)		
Type of vessel	**Male**	**LAD**	15 (62.5%)	8 (50%)	17 (54.8%)	17 (58.6%)		0.872
		LCX	7 (29.2%)	9 (56.3%)	18 (58.1%)	12 (41.4%)		0.140
		RCA	8 (33.3%)	8 (50%)	8 (25.8%)	10 (34.5%)		0.430
		OM	3 (12.5%)	3 (18.8%)	7 (22.6%)	8 (27.6%)		0.594
		Diagonal	6 (25%)	2 (12.5%)	5 (16.1%)	6 (20.7%)		0.748
		PDA	3 (12.5%)	2 (12.5%)	5 (16.1%)	2 (7.1%)		0.771
		Ramus intermedius	2 (8.3%)	1 (6.3%)	3 (9.7%)	1 (3.6%)		0.821
	Female	**LAD**	9 (26.47%)	5 (20%)	9 (36%)	6 (37.5%)		0.651
		LCX	6 (17.6%)	2 (8%)	6 (24%)	4 (25%)		0.417
		RCA	3 (8.8%)	3 (12%)	2 (8%)	4 (25%)		0.353

		OM	4 (11.76%)	3 (12%)	3 (12%)	3 (18.8%)	0.798
		Diagonal	3 (8.8%)	1 (4%)	3 (12%)	3 (18.8%)	0.734
		PDA	3 (8.8%)	1 (4%)	3 (12%)	2 (12.5%)	0.363
		Ramus intermedius	0 (0%)	1 (4%)	2 (8%)	1 (6.3%)	0.445
Lesion characteristics	**Male**	**Lesion length (mm)**	24.83 ± 7.27	25.25 ± 6.6	25.65 ± 6.13	28.21 ± 5.96	0.225
		Severity	**<50%** 1 (4.17%)	1 (12.5%)	4 (12.9%)	1 (3.45%)	0.470
			50-70 0 (0%)	0 (12.5%)	6 (19.35%)	8 (27.59%)	**0.008***
			>70% 0 (0%)	2 (12.5%)	11(35.48%)	17 (58.62%)	**<0.001***
		Chronic occlusion	3 (12.5%)	4 (25.0%)	4 (12.9%)	3 (10.3%)	0.571
		Thrombus	1 (4.2%)	2 (12.5%)	0 (0.0%)	1 (3.4%)	0.228
	Female	**Lesion length (mm)**	20.65 ± 5.29	20.36 ± 6.1	18.40 ± 5.94	20.56 ± 6.45	0.475
		Severity	**<50%** 4 (11.8%)	5 (20%)	10 (40%)	5 (31.3%)	0.072
			50-70 1 (2.9%)	1 (4%)	1 (4%)	4 (25%)	**0.023***
			>70% 0 (0%)	0 (0%)	1 (4%)	5 (31.3%)	**<0.001***
		Chronic occlusion	2 (5.9%)	1 (4.0%)	0 (0.0%)	1 (6.3%)	0.667
		Thrombus	0 (0.0%)	1 (4.0%)	0 (0.0%)	1 (6.3%)	0.363
Adverse events							
Bleeding	**Males**		0 (0%)	0 (0%)	1 (3.2%)	2 (6.9%)	0.431
	Females		0 (0%)	0 (0%)	0 (0%)	1 (6.3%)	0.151
Reinfarction	**Males**		0 (0%)	0 (0%)	2 (6.5%)	6 (20.7%)	**0.019***
	Females		0 (0%)	0 (0%)	1 (4%)	3 (18.8%)	**0.009***
Mortality	**Males**		0 (0%)	0 (0%)	0 (0%)	5 (17.2%)	0
	Females		0 (0%)	0 (0%)	0 (0%)	2 (12.5%)	**0.013***

STEMI: ST-elevation myocardial infarction, EF: ejection fraction, LAD: left anterior descending artery, LCX: left circumflex artery, RCA: right coronary artery, OM: obtuse marginal and PDA: posterior descending artery.

Table 4: Relation between syntax score and severity and the affected vessels

		Syntax score	P-value	
Severity	**No**	16.61± 10.06	**<0.001***	**P1=0.023***
	<50%	22.35± 10.74		**P2<0.001***
	50-70	29.83± 9.42		**P3<0.001***
	>70%	31.59± 8.64		**P4=0.033*,**
				P5=0.001*,
				P6=0.911
Affected vessels	**1-vessel CAD**	22.00 ± 11.7	0.886	
	2-vessel CAD	21.28 ± 12.2		
	3-vessel CAD	21.12 ± 11.1		

Data was presented as statistically significant different as p value <0.05, P1: P Value between 0 and <50%, P2: P Value between 0 and 50-70%, P3: P Value between 0 and >70%. P4: P Value between <50 and 50-70%, P5: P Value between <50% and >70%, P6: P Value between 50-70% and >70%.CAD: coronary artery disease

Table 5: Correlation between Syntax score and other parameters

	Syntax score	
	r	**P**
Number of affected vessels	0.305	**<0.001***
Vit D level (ng/ml)	-0.751	**<0.001***

Data was presented as statistically significant different as p value <0.05.r: correlation coefficient

Table 6: Multivariate logistic regression analysis for prediction of CAD severity

	OR	**95% CI**	**P value**
Age (years)	0.9583	0.8759 to 1.0485	0.354
Sex	0.1513	0.0324 to 0.7073	**0.016***
Smoking	0.1789	0.0505 to 0.6339	**0.008***
HTN	0.6941	0.3196 to 1.5073	0.356
Cholesterol (mg/dL)	1.0149	0.9950 to 1.0351	0.144
Triglycerides (mg/dL)	1.0144	0.9946 to 1.0346	0.155
HDL (mg/dL)	1.0277	0.9825 to 1.0750	0.234
LDL (mg/dL)	0.9780	0.9419 to 1.0155	0.247
Chronic occlusion	6.535	1.7393 to 24.5544	**0.005***
Lesion length	0.969	0.9116 to 1.0300	0.312
Syntax	1.0170	1.0013 to 1.0329	**0.033***
Vessel affected	1.1171	0.7035 to 1.7737	0.639
Vit D (ng/ml)	1.0176	1.0018 to 1.0337	**0.028***

HTN: hypertension, HDL: high density lipoprotein, LDL: low density lipoprotein, OR: odds ratio, CI: confidence interval, *: statistically significant as p value <0.05.

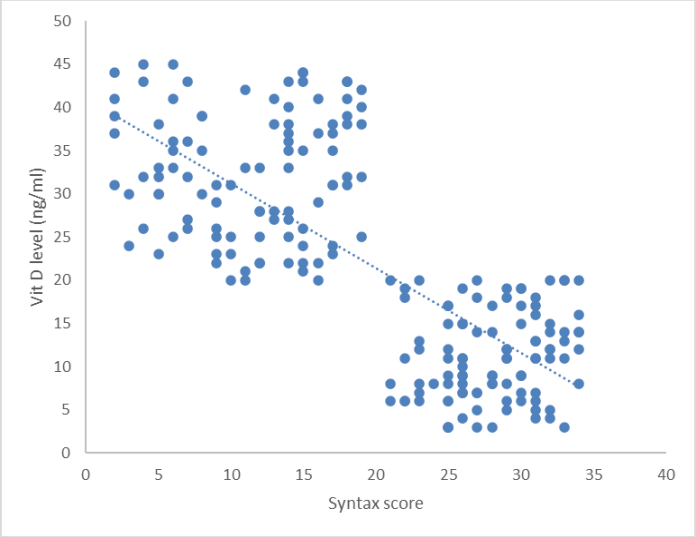

Figure 1: Correlation between Syntax score and Vit D level.

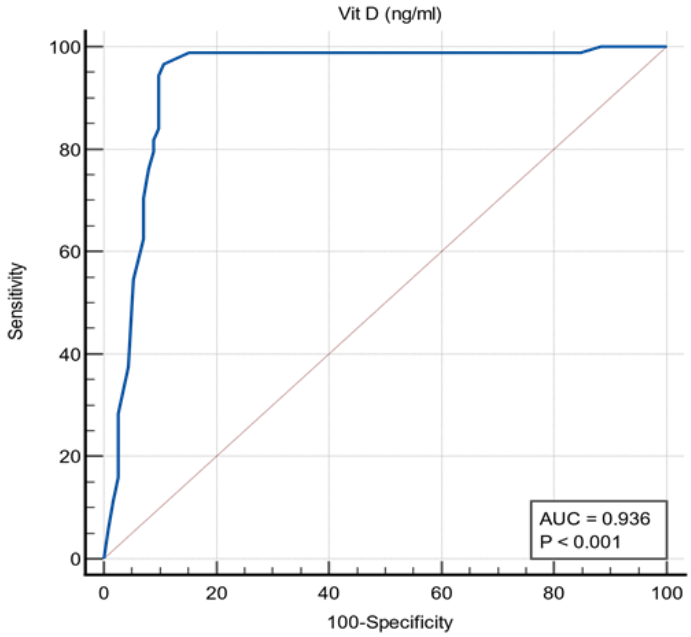

Figure 2: ROC curve analysis of Vit D level for prediction of Severity of CAD

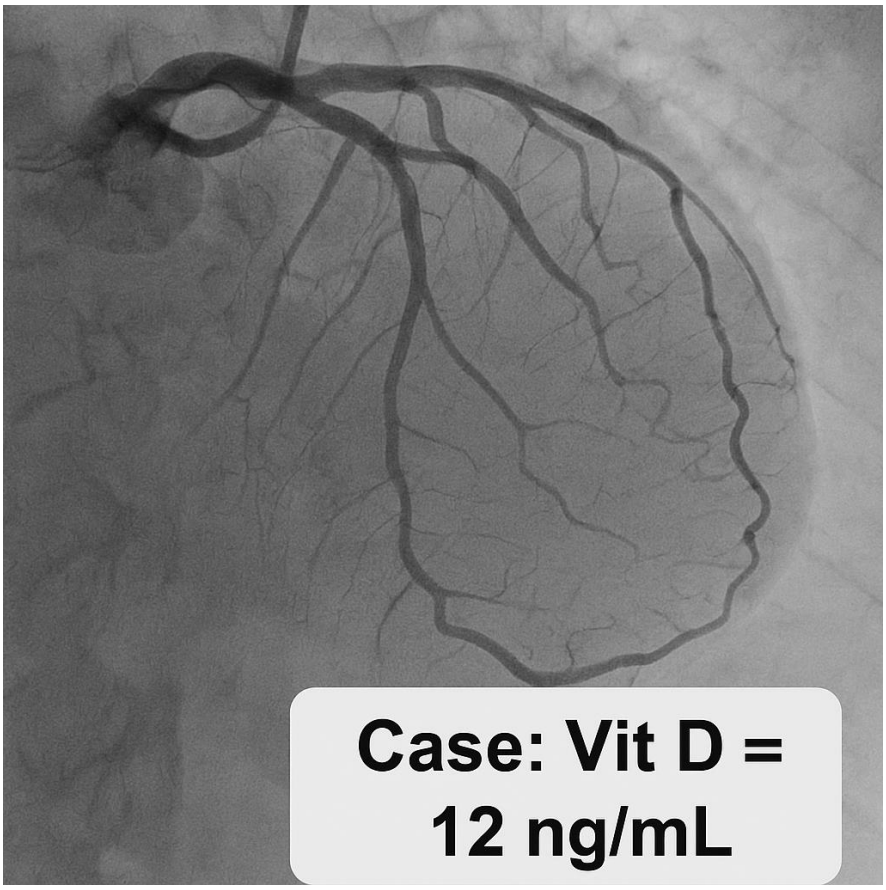

Figure 3. Representative grayscale coronary angiography image illustrating the left and right coronary arteries opacified with radiopaque contrast. The case presented shows a serum 25-hydroxyvitamin D level of 12 ng/mL, which falls within the severe deficiency range (<10–20 ng/mL), and is associated with a higher SYNTAX score and increased coronary artery disease complexity according to the study findings**.**

Discussion

Our research revealed that the average age of females was significantly higher than that of males (P<0.001). These results are parallel to Gilabert-Garcia et al., (13) who noted that men are generally at a higher risk of CAD than women, especially in younger years, the risk increases in both sexes as they age, and by age 65 and older, the prevalence and impact of CAD are similar in both men and women.

Regarding the risk factors, smoking, history of MI, HTN, history of MI, previous PCI and CABG in males were significantly higher than females (P<0.05). According to our findings, Yasmin et al., (14) proved that males are more susceptible to having a history of MI in the context of CAD than females. This is reflected in both higher incidence rates of MI in men and a greater likelihood of presenting with a history of MI compared to women.

Contrary, Jeong et al., (15) demonstrated that in comparison to non-smokers, female smokers have a 25% higher incidence of CAD than male smokers.

Regarding the results, total cholesterol, triglycerides, and LDL were significantly increased in females than males (P<0.05). HDL was significantly lower in males than females (P<0.001). Additionally, Holven & van Lennep al., (16) revealed that women have higher HDL-C levels and lower LDL-C levels, while LDL-C levels increase and HDLC levels decrease in men from early adulthood to middle age.

According to our investigation, males showed significantly lower Vit D levels than females (P=0.014). The Vit D status of both groups was significantly different (P=0.044) as males exhibited a significantly higher prevalence of moderate and severe deficiency than females.

As well, Haitchi et al., (17) conducted a retrospective study and found that Vit D levels in males were significantly lower than those of the females.

Our study found that the ECG findings on admission were significantly different between both groups (P=0.005). Carbone et al., (18) confirmed our results as they showed that ECG findings in (CAD) can differ between males and females, impacting diagnostic accuracy and interpretation. While some findings are similar, others are more prevalent in one sex than the other.

Regarding the angiographic findings, SYNTAX score, LAD, LCX, RCA affected vessels, lesion length, severity (50-70%, >70%), and chronic occlusion in males were significantly higher than females (P<0.05) while 1-vessel CAD and lesion severity <50% were significantly higher in females than males (P=0.011, <0.001). These results are agreed with Chiha et al., (19) who demonstrated that women may have a higher prevalence of mild, single-vessel CAD than men. Also, severe CAD, particularly high-risk CAD like left main artery stenosis, three-vessel disease, or two-vessel disease with proximal LAD involvement, is more frequent in men.

Based on the vit D status, smoking was significantly higher in the moderate and severe deficiency than normal among males (P<0.001, <0.001), was significantly higher in the moderate and severe deficiency than mild deficiency (P<0.001, <0.001), and smoker number was significantly higher in the severe deficiency than moderate deficiency (P<0.001). In alignment with our study, Yang et al., (20) illustrated that smoking negatively affects circulating Vit D levels in adults.

Based on the vit D status, among females, ASA was significantly lower in mild and moderate deficiency groups than normal group (P=0.007, 0.018) and among males, clopidogrel was significantly higher in severe deficiency than moderate deficiency group (P=0.026).

Based on the vit D status, among males, Triglycerides and LDL in the severe group were significantly higher than the normal, mild, and the moderate deficiency groups (P<0.05), HbA1c was significantly higher in moderate deficiency than normal group (P=0.030). HbA1c and total cholesterol in females, were significantly higher in severe deficiency than normal, mild, and moderate deficiency groups (P<0.05), was significantly higher in moderate deficiency than normal group (P<0.05). HDL was significantly lower in moderate and severe deficiency compared to normal group (P=0.008, <0.001).

These findings are in accordance with Hwang et al., (21) who determined that severe Vit D deficiency is associated with a significant increase in HbA1c levels, particularly in individuals with abnormal HbA1c values. This suggests that Vit D deficiency may contribute to poorer glycemic control in diabetic men, potentially leading to higher blood glucose levels over time.

On the other hand, Autier P et al. (22) conducted a meta-analysis that revealed that, Vit D supplementation did not produce a statistically significant difference in total cholesterol, triglycerides, LDL-C, and HDL-C.

On the basis of Vit D status, the EF of males was significantly lower in the severe deficiency group than in the normal, mild, and moderate deficiency groups (P<0.001, <0.001, 0.006), and in the mild and moderate deficiency groups than in the normal group (P=0.001, <0.001). In the moderate and severe deficiency groups, EF was significantly lower than that of the normal group among females (P<0.001, 0.001), and it was significantly lower in the severe deficiency group than in the mild deficiency group (P=0.049).

These results are consistence by Wu et al., (23) who asserted that chronic vit D deficiency may lead to a reduced ejection fraction (EF) in specific heart failure patients, particularly those with a reduced ejection fraction (HFrEF). The syntax scores of the severe deficiency group were significantly higher than those of the other groups (P<0.05), and the moderate deficiency group was significantly higher than the normal and mild groups (P<0.05) based on the vit D status of males and females.

In terms of the angiographic findings, the severity of CAD was significantly different among the studied groups (P<0.05) for males and females (50-70%, >70%), with the severe group exhibiting the highest severity. In agreement with the current findings, Candemir et al., (24) SYNTAX scores were independently predicted by 25(OH)D levels, as determined by a multivariable regression analysis. 25(OH)D levels were significantlly reduced in the group with the highest SYNTAX scores. Both the 25(OH)D levels and the SYNTAX scores demonstrated significant negative correlations.

Regarding the adverse events, severe deficiency group had higher incidence of reinfarction and mortality than the other groups (P<0.005).

Similarly, Correia et al., (25) found that severe Vit D deficiency is associated with increased incidence of reinfarction and mortality in CAD patients. Specifically, individuals with severe Vit D deficiency have a significantly higher risk of in-hospital cardiovascular mortality compared to those with sufficient levels. This increased risk is independent of other cardiovascular risk factors and persists even after accounting for factors like the GRACE score and Gensini angiographic score.

Our study showed that the relation between syntax score and severity was significant (P<0.001), Patients with a severity of >70% exhibited a statistically higher syntax score than those with no severity or a severity of <50% (P<0.001, 0.001), while the difference between patients with 50-70% severity was not statistically significant. The syntax score was significantly increased in patients with a severity of 50-70% compared to those with no severity and a severity of <50% (P<0.001, 0.033), and it was also significantly elevated in patients with a severity of <50% compared to those with no severity (P=0.023).

These findings are assured by Rasheed et al., (26) who declared that there is a significant relationship between SYNTAX score and the CAD severity. Higher SYNTAX scores indicate more complex and severe CAD and are associated with poorer prognosis and increased need for revascularization.

In our investigation, the Syntax score and Vit D level were found to have a significant negative correlation. The Syntax score and the number of afflicted vessels exhibited a significant positive correlation. Furthermore, Sahani and Gupta al., (27) in patients with CAD, a significant negative correlation was observed between the Syntax score and Vit D levels. This means that patients with reduced Vit D levels had elevated SYNTAX scores, resulting in more severe and complex CAD.

In our results, Vit D level can significantly predict the severity of CAD with AUC of 0.936 (P<0.001), at cutoff value of ≤ 20 ng/ml, with 98.86% sensitivity, 84.82% specificity, 83.7% PPV and 99.0% NPV.

In accordance with the results, Candemir rt al., (24) showed that specific Vit D levels, like 13.87 ng/mL, have been shown a high sensitivity (81%) and 80.6% specificity in predicting high SYNTAX scores, in the assessment of CAD.

The limitations of the current study were single-center nature, the relatively small sample size, and the absence of a study on the therapeutic effect of Vit D deficiency on CAD outcome.

Therefore, this study recommended further investigations with larger and stratified sample size, multi-center study

and future studies assessing therapeutic effect of Vit D deficiency on CAD outcome.

Conclusions

There is an association between Vit D and as it can predict the severity of CAD at cutoff value of ≤ 20 ng/ml, with 98.86% sensitivity, 84.82% specificity, 83.7% PPV and 99.0% NPV.

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