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Study of Serum Vitamin D Level In ST Segment Elevated Myocardial Infarction Patients Attending In A Tertiary Care Hospital, Kolkata.

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Abstract: ***Background:*** *Beyond the fundamental role in bone metabolism and calcium homeostasis, vitamin D influence several other medical conditions, including cardiovascular disease.Vitamin D deficiency has been independently associated with increased risk of developing acute myocardial infarction*

Aims And Objectives:*Vitamin D deficiency is emerging as a new risk factor forvarious cardiovascular diseases (CVDs), especiallyatherosclerotic vascular diseases. The aims of this study is to assess serum 25(OH)D level in cases of ST-segment elevated acute myocardial infarction patients admitted in the Department of Cardiology, R.G.KarMedical College ,Kolkata.*

Methods:*Randomly selected cases of STEMI irrespective of their age were recruited in the study. A questionnaire was administered to assess the risk factors of MI (Hypertension, Diabetes , smoking) .Acute MI was diagnosed if the patient had characteristic symptoms plus electrocardiogram changes indicative of a new MI (new pathologic Q waves, at least 1 mm ST elevation in any 2 or more contiguous limb leads or 2 mm ST elevation in precordial leads or a new left bundle branch block) with or without a elevated plasma level of creatine kinase-MB isoform (CK-MB) / Troponin T.*

Results*: Among the study population 65% were smoker, 57% were Diabetic and 72% were hypertensive. 37% patients were Vitamin D Deficient (< 20ng/ml), 41% were Vitamin D insufficient(20-30ng/ml) and only 22% had normal Vitamin D level. Only 36% study population had LVEF% more than 40% , rest (64%) had LVEF% less than 40%. Among the study population 38 patients had TVD among them 11 had LMCA involvement, DVD were found in 25 patients, SVD were in 26 patients. Only 11% patients had normal angiography. Majority of the Vitamin D deficient patients had TVD(73%) whereas majority of the Vitamin sufficient patients had either normal coronary angiography or SVD. Statistically significant correlation was found between Vitamin D deficiency or insufficiency and low LVEF% and the significance was still present when adjusted for other variables in multivariate logistic regression analysis.Inthis study 6 death occurred. All of them are either vitamin D deficient(5) or insufficient. No death occurred in vitamin D sufficient patient in my study population*

Conclusion:*This study reveals a very high prevalence of vitamin D deficiency among patients of acute MI. Despite the rampant hypovitaminosis, presence of severevitamin D deficiency was associated with risk of acute MI even after adjusting for conventional risk factors*

Keywords*: Vitamin D, Cardiovascular disease, Acute Myocardial Infarction,AMI*

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Abbreviations:STEMI : ST segment elevated myocardial infarction .DM : Diabetes mellitus. HTN : Hypertension FBS: Fasting blood sugar HDL: High density lipoprotein LDL : Low density lipoprotein TG : Triglyceride.. CVD : Cardiovascular diseases. CAD : Coronary artery diseases. CAG : Coronary angiography.SVD : Single vessel disease DVD : Double vessels disease .TVD : Triple vessel disease. LMCA : Left main coronary . EF : Ejection fraction.

I. Introduction

Beyond the fundamental role in bone metabolism and calcium homeostasis, vitamin D influence several other medical conditions, including cardiovascular disease. Indeed, vitamin D receptors have been found in the myocardium as well as in vascular cells, and hypovitaminosis D, a common finding in many industrialized countries, has been independently associated with increased risk of developing acute myocardial infarction[1].

Aims And Objectives: Vitamin D deficiency is emerging as a new risk factor forvarious cardiovascular diseases (CVDs), especiallyatherosclerotic vascular diseases.The aims of my thesis is to assess serum 25(OH)D level in cases of ST-segment elevated acute myocardial infarction patients admitted in the Department of Cardiology,R.G.KarMedical College ,Kolkata.

II. Materials and Methods

1. STUDY AREA Admitted patients , Department of Cardiology , R.G.Kar Medical College, Kolkata.
2. STUDY POPULATION – Patients of STEMI admitted in Department of Cardiology, R.G.Kar Medical College, Kolkata
3. STUDY PERIOD – March 2016 – August 2017
4. SAMPLE SIZE – 100 patients of STEMI of both gender.
5. SAMPLE DESIGN – Simple Random Selection
6. STUDY DESIGN- A Hospital based Longitudinal/ Prospective study
7. STUDY TYPE- Descriptive Analytical study
8. STUDY TECHNIQUE-Randomly selected cases of STEMI irrespective of their age were recruited in the study. A questionnaire was administered to assess the risk factors of MI (Hypertension, Diabetes , smoking) and a fasting blood sample was collected within 24 h of admission to the hospital. Acute MI was diagnosed if the patient had characteristic symptoms plus electrocardiogram changes indicative of a new MI (new pathologic Q waves, at least 1 mm ST elevation in any 2 or more contiguous limb leads or 2 mm ST elevation in precordial leads or a new left bundle branch block) with or without a elevated plasma level of creatine kinase-MB isoform (CK-MB) / Troponin T. Glucose was measured by glucose oxidase method usingcommercially available kits (RANDOX, UK). Total Cholesterol was measured from serum samples by CHOD-PAP enzymaticmethod using commercially available kits(RANDOX,UK). HDL Cholesterol was measured from serum samples by phosphotungistic precipitating method. Triglyceride was measured from serum samples by enzymatic GPO-PAP method using commercially available kit (RANDOX, UK). 25 (OH) D was measured within 24 hours of admission by chemiluminescent immunoassay method using commercially available kit. When the facility for serum 25(OH)D estimation was hampered due to any reason then it was done in outside reliable laboratory and the expenditure was provided by me. All included patients underwent Echocardiography (2D, M mode and colourdoppler study) to assess the Left ventricular function and Conventional Coronary Angiography to detect the extent of coronary artery disease.The patients were followed up until discharge or death.

9.PARAMETERS WERE STUDIED :

Study Parameters :

i. Laboratorial Examination
ii. Electrocardiography
iii. Echocardiography
iv. Coronary Angiography

Study tools:

a) Blood Examination
- Complete Haemogram
- Serum 25(OH) Vitamin D
- Fasting Blood Sugar(FBS)
- Blood urea
- Serum creatinine
- Lipid Profile
- Cardiac Troponin

b) 12 Leads ECG with Long lead II

c) Echocardiography-2D , M-Mode& Colour
d) Coronary Angiography

11. ANALYSIS OF DATA: The following standard statistical method was used for data analysis.
Statistical analysis was done using SPSS version 20.0. Descriptive statistics were calculated as frequency, percentage, mean and standard deviation. Descriptive data were represented using various tables, diagrams etc. For inferential statistics, various tests of significance were used according to the type of variables dealt with. For all the statistical tests of significance, p value of <0.05 was considered to reject the null hypothesis. Chi-square test was used to determine the association between categorical variables . For dichotomous outcomes, logistic regression analysis was used. Firstly, a univariate analysis was done to ascertain the relationship with other variables. Then, all the variables found to be significant in univariate analysis were also entered into a multiple logistic regression.

INCLUSION CRITERIA :
- Patients with STEMI
- Biomarker evidence of myocardial injury (elevated troponins or CKMB)
- Supporting evidence of AMI (eg., prolonged ischemic signs or symptoms, electrocardiographic ST-segment changes)
- Ability and willingness to participate based on information given to patient and to health facility.

EXCLUSION CRITERIA:
- Chronic Kidney Disease
- Chronic Liver Disease
- Known endocrinal disorders (eg. Hypo/hyperparathyroidism etc.)
- Patients already on Calcium or Vitamin D supplementation
- Patients on medications like phenytoin, Isoniazid, Rifampicin etc.
- Who are not willing to give consent

III. Results and analysis

Table-1: Distribution of study population according to age and sex: (n=100)

			Sex		Total
			Male	Female	
Age in years	Less than 40	Count	23	3	26
		% within agegr2	88.5%	11.5%	100.0%
		% within Sex	28.0%	16.7%	26.0%
	More than 40	Count	59	15	74
		% within agegr2	79.7%	20.3%	100.0%
		% within Sex	72.0%	83.3%	74.0%
Total		Count	82	18	100
		% within agegr2	82.0%	18.0%	100.0%
		% within Sex	100.0%	100.0%	100.0%

Comments: Overall among the study population majority were male(82%). Mostly are more than 40 years.

Figure 1: Age and Sex distribution of study population(n=100)

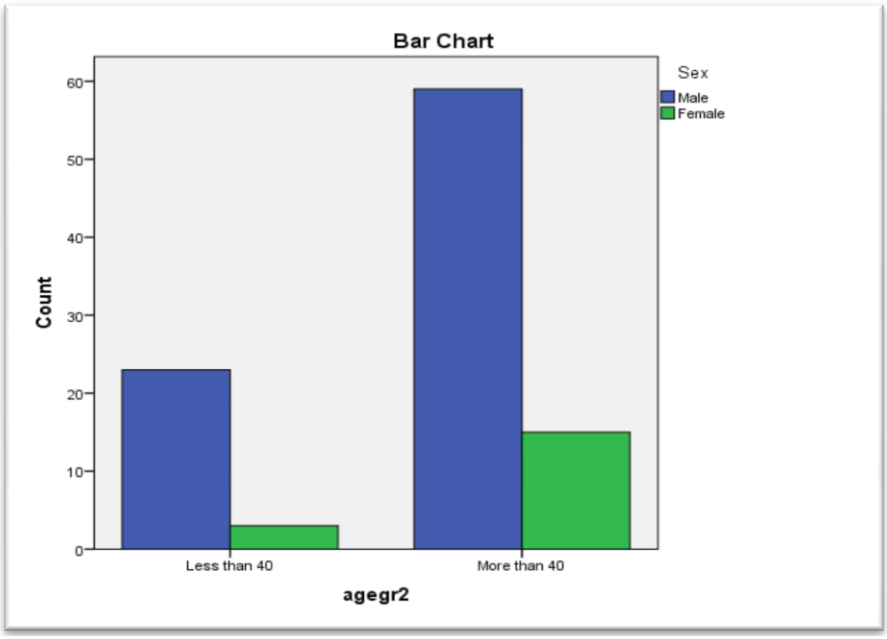


Table 2: Distribution of study population according to h/o Smoking, DM,HTN(n=100)

	Present	Absent	Total
	Frequency (%)	Frequency (%)	Frequency (%)
Smoking	65 (65%)	35	100
DM	57	43	100
HTN	72	28	100.0

Comments: Among the study population 65% had history of smoking, 57% suffered from Diabetes and majority had history of Hypertension(72%)

Table 3: Distribution of study population a/c to level of serum Vit D(n=100)

	Frequency	Percent	Valid Percent	Cumulative Percent
Deficient	37	37.0	37.0	37.0
Insufficient	41	41.0	41.0	78.0
Normal	22	22.0	22.0	100.0
Total	100	100.0	100.0	

Comments: Among the study population majority(41%) had Insufficient Vit D lelel followed by Deficient level in 37%. Only 22% study population had normal serum Vit D level.

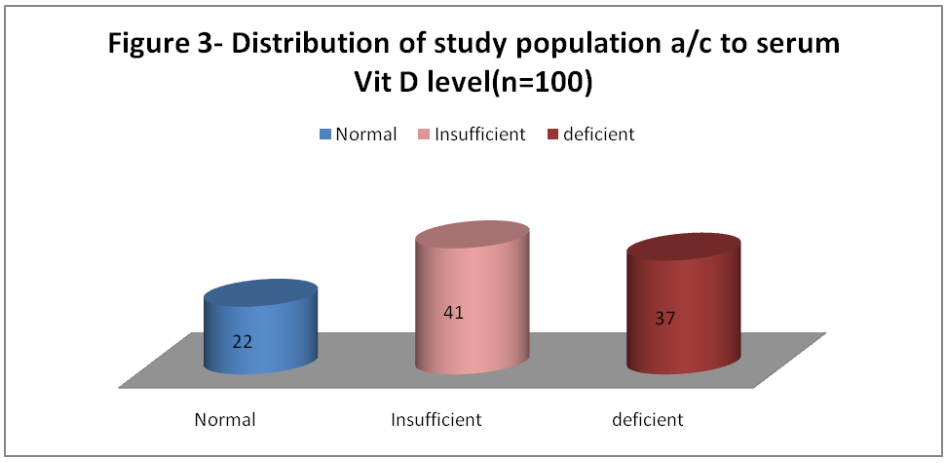


Table 4: Distribution of study population a/c to Type of STEMI from ECG(n=100)

	Frequency	Percent	Valid Percent	Cumulative Percent
L LWMI	4	4.0	4.0	4.0
IWMI	33	33.0	33.0	37.0
AWMI	63	63.0	63.0	100.0
Total	100	100.0	100.0	

Comments: Majority of the study population suffered from Anterior wall AMI(63%) followed by Inferior wall AMI (33%) & only 4% patients had Lateral wall AMI.

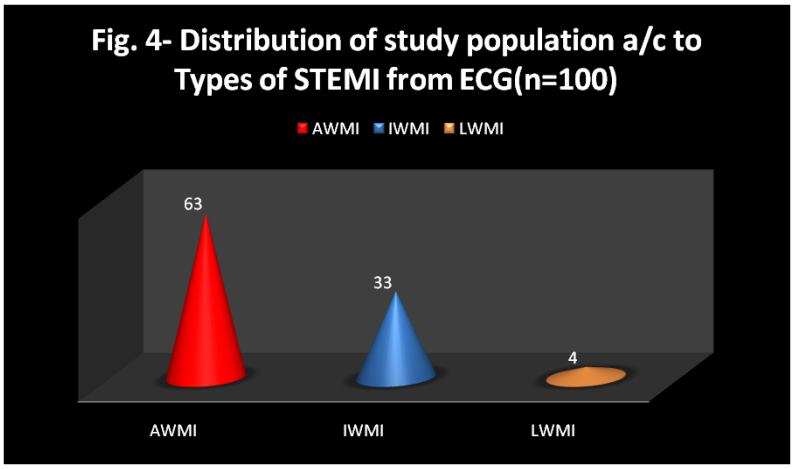


Table-5:Distribution of study population a/c to Outcome(n=100)

	Frequency	Percent
Alive	94	94.0
Death	6	6.0
Total	100	100.0

Comments: Among the study population 6% patients died during index hospital stay.

Table 6: Distribution of study population according to Angiographic findings(n=100)

	Frequency	Percent	Valid Percent
	Without LMCA	With LMCA	Total
Normal	11	0	11.0
SVD	25	1	26.0
DVD	24	1	25.0
TVD	27	11	38.0
Total	87	13	100.0

Comments: Among the study population Majority had Triple vessels disease (38%) diagnosed by Conventional Coronary Angiography Followed by single vessel Disease(26%) then Double Vessels Disease (25%). Only 11% study population had normal coronary angiography.

Fig-5: Distribution of STEMI patients according to Angiographic findings(n=100)

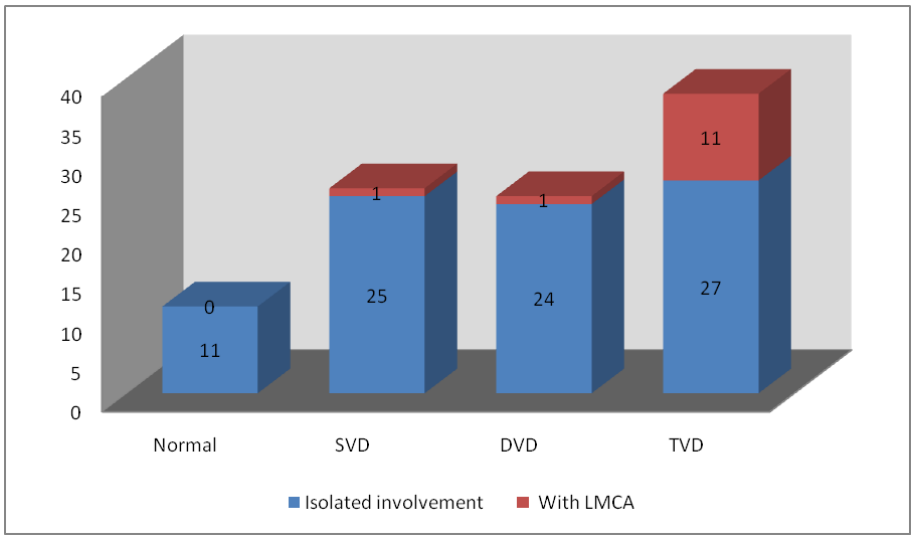


Table 7: Univariate Logistic Regression Analysis

Association of Left Ventricular EF% with Other Study Variables(n=100)

		EF		OR (95% CI)
		Preserved	Low	
Vit - D	**Deficient**	**6**	**31**	**17.56 (4.66 -66.15)**
	Insufficient	**13**	**28**	**7.32 (2.24 – 24.18)**
	Normal (Ref)	17	5	-
Age	**More than 40**	**17**	**57**	**9.101(3.275 -25.287)**
	Less than 4o (Ref)	19	7	-
Sex	**Male**	**33**	**49**	**0.297(0.080-1.107)**
	Female (ref)	**3**	**15**	--
Smoking	**Present**	**22**	**43**	**1.303(0.557-3.046)**
	Absent	14	21	--
Diabetes	**Present**	**10**	**47**	**7.188(2.875-17.971)**
	Absent	**26**	**17**	--
Hypertension	**Present**	**14**	**58**	**15.190(5.185-44.505)**
	Absent	**22**	**6**	--
HDL	**Present**	**11**	**44**	**5(2.065-12.108)**
	Absent	**25**	**20**	--

Comments:

I. Among the study population Statistically significant more risk of Low LVEF% was associated with Deficient & Insufficient level of Serum Vit D, Aged more than 40 yrs, History of Diabetes & Hypertension and Low Serum HDL Level

II. Vit –D Deficient patients are 17.56 times more prone to develop Low LVEF%(less than 40%) and Vit –D Insufficient patients are 7.32 times more prone to develop low LVEF% than the patients with Normal serum Vit-D level. This was statistically significant.

III. There is no correlation between sex and decreased LVEF%. Smoker are more prone to have Low LVEF% than the Nonsmoker patients although it is not statistically significant.

IV. Hypertensive patients are 15 times more chance of developing Low LVEF% than the nonhypertensive patient population .Diabetic patients are 7 times more prone to have low LVEF% than nondiabetic patients. Low HDL patients are 5 times more prone to develop decreased LVEF% than normal HDL patients. All these are statistically significant.

Table 8: Multivariate Logistic Regression Analysis

Association of Left Ventricular EF% with Other Study Variables(n=100)

		EF		Adjusted OR (95% CI)
		Preserved	Low	
Vit - D	**Deficient**	**6**	**31**	**1.6(1.7-6.91)**
	Insufficient	**13**	**28**	**2.1(2.6-9.34)**
	Normal (Ref)	17	5	-
Age	**More than 40**	**17**	**57**	2.871(0.555-14.847)

	Less than 4o (Ref)	19	7	-
Sex	**Male**	**33**	**49**	0.134(0.014-1.251)
	Female (ref)	**3**	**15**	--
Smoking	**Present**	**22**	**43**	3.656(0.866-15.435)
	Absent	14	21	--
Diabetes	**Present**	**10**	**47**	2.793(0.745-10.475)
	Absent	**26**	**17**	--
Hypertension	**Present**	**14**	**58**	**7.582(2.053-28.007)**
	Absent	**22**	**6**	--
HDL	**Present**	**11**	**44**	1.656(0.470-5.844)
	Absent	**25**	**20**	--

Comments:

I. Deficient and Insufficient Vit D and History of HTN were found to be major predictors of Low LVEF% in Multivariate Logistic Regression Model.

II. Association of Low LVEF% with Age, Diabetes and Low HDL level lost their significance when adjusted for other variables by Multivariate Logistic Regression Model.

Table 9: Distribution of Coronary artery Disease by Angiography with Degree of Serum Vit-D Level(n=100)

25(OH) Vit-D		Angiography				Total
		Normal	SVD	DVD	TVD	
Deficient	Count	0	5	5	27	37
	% within Vitdgr	0.0%	13.5%	13.5%	73.0%	100.0%
Insufficient	Count	0	11	19	11	41
	% within Vitdgr	0.0%	26.8%	46.3%	26.8%	100.0%
Normal	Count	11	10	1	0	22
	% within Vitdgr	50.0%	45.5%	4.5%	0.0%	100.0%
Total	Count	11	26	25	38	100
	% within Vitdgr	11.0%	26.0%	25.0%	38.0%	100.0%

Chi square value: 79.15, df: 6, P value: **<0.05**

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	79.152[a]	6	.000
Likelihood Ratio	80.098	6	.000
N of Valid Cases	100		

Comments:

I. Among the Vit-D Deficient patients majority have Triple Vessels Disease(73%)and no one has normal coronary angiography. Whereas among the Vit-D Insufficient patients majority have Double vessels Disease(46.3%). Both of them have statistically significant P-value.

II. Among the patients with normal vit-D level, majority have normal coronary angiography(50%) followed by Single Vessel Disease(45.5%) with P- value of less than 0.5

Fig.7: Distribution of Coronary artery Disease by Angiography with Degree of Serum Vit-D Level(n=100)

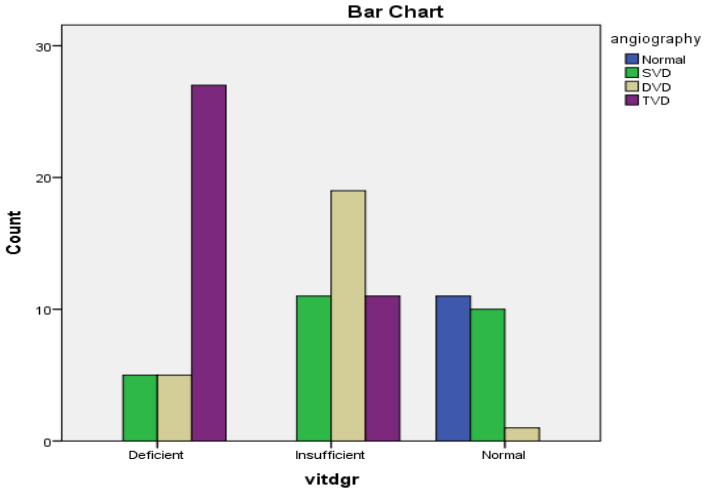


Table 10: Association of serum Vit D level with outcome of study population(n=100)

			Outcome		Total
			Alive	Death	
Vit-D	Deficient	Count	32	5	37
		% within vit D gr	86.5%	13.5%	100.0%
	Insufficient	Count	40	1	41
		% within vit D gr	97.6%	2.4%	100.0%
	Normal	Count	22	0	22
		% within vit D gr	100.0%	0.0%	100.0%
Total		Count	94	6	100
		% within vit D gr	94.0%	6.0%	100.0%

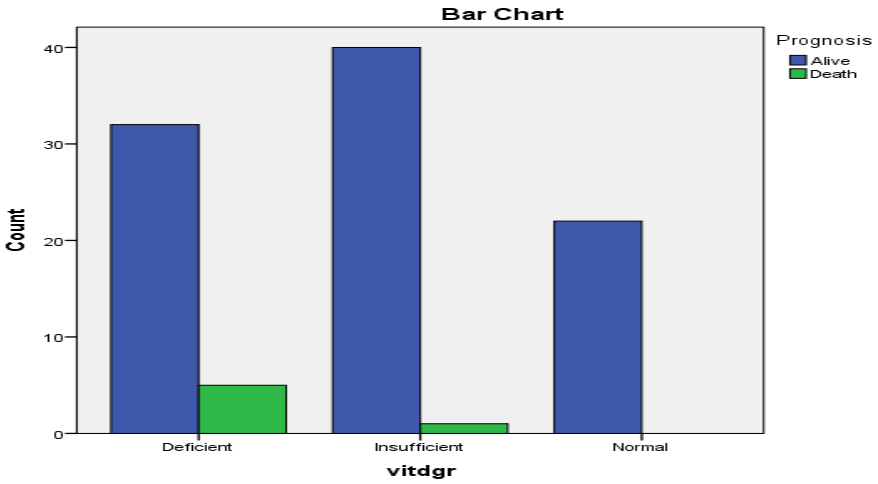
Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	6.030[a]	2	.049
Likelihood Ratio	6.685	2	.035
N of Valid Cases	100		

Comments:

Among the study population total 6 death occurred ofwhich 5 occurred in Vit-D deficient patients and 1 death in Vit-D Insufficient patient. No death occurred in Vit-D adequate patient. All of them are marginally statistically significant with P value of 0.049.

Fig-6: Association of Serum Vit –D level with Outcome of study population(n=100)



IV. Discussion

This study evaluated vitamin D status in patients admitted with STEMI at R.G.Kar Medical college & Hospital- a tertiary care centre.Our data suggested that thereis high prevalence of vitamin D deficiency or insufficiency (78%) in

STEMI patients.The high prevalence of vitamin D deficiency found in this

study is consistent with other studies from India. A ruralprevalence study in North Indians showed that thoughvitamin D levels in rural subjects were significantly higherthan in urban Indians, the prevalence of vitamin D deficiency[serum 25(OH) vitamin D < 20 ng/ml] in them was as high as 70%.[2] Another study from Delhi, in healthy individuals above50 years of age, revealed deficiency [serum 25(OH) vitaminD< 20 ng/ml] in 91.2% including severe deficiency [serum25(OH) vitamin D < 10 ng/ml] in 62% and vitamin D insufficiency[serum 25(OH) vitamin D levels 20-30 ng/ml] inadditional 6.8% of the population.[3]A study from AndhraPradesh similarly reported a very high prevalence of vitamin D deficiency.[4]The causes for high prevalence of VitaminD deficiency in Indians is attributed to dark-skin, lack ofadequate direct skin exposure to sunlight and lack of vitaminD in predominant Indian diet.

Our data also noted that there is more vitamin D deficiency inpatients who are having diabetes mellitus, confirming previouslydescribed associations [5]. Vitamin D deficiency with dietary calciumdeficiency has been associated with impaired fasting glucose and possiblytype 2 diabetesmellitus which is a risk factor for cardiovascular disease[6,7] which possibly explains the increased prevalence ofvitamin D deficiency in our diabetic subgroup.

Conventionally patients with high cholesterol, high triglyceride levels and whosmoke are high risk factors for cardiovascular disease and our study shows these areassociated with vitamin D deficiency and myocardial infarction.In my study statistically significant decreased left ventricular systolic function was associated with insufficient or deficient serum vitamin D level, increased age of the patient(more than 40 years), Diabetes, Hypertension and low HDL level in Univariate logistic regression analysis. But when adjusted for other risk factors with low LVEF% , most of them lost their statistical significance except insufficient/ deficient serum vitamin D level and hypertension which are still present with the decreased left ventricular systolic function.No statistical significance was found among male and female patients.

This data is consistent with data associating CAD andmany of its risk factors with 25(OH)D deficiency [8,9]. Studies have shown that individuals with vitamin D deficiency were at higher riskof ischemic heart disease [10-12].The association of vitamin D with cardiovascular health has been reported extensively recently. A large populationbased study reported by Brøndum-Jacobsen et al, comparingindividuals with plasma 25(OH) vitamin D levels at the 1st to4th percentile to individuals with levels at the 50th to 100thpercentile, revealed that the multivariable adjusted risk wasincreased by 40% for ischemic heart disease, by 64% formyocardial infarction, by 57% for early death and by 81% forfatal ischemic heart disease/myocardial infarction in individualswith low vitamin D.[13] In the meta-analyses of 18studies in the same paper, the authors found that the risk ofischemic heart disease and early death were increased by 39%and 46% for lowest versus highest quartile of 25(OH) vitamin Dlevel.Our study shows out of 78 Vit D Insufficient or deficient study population majority have low left ventricular ejection fraction(<40%), only 19 patients have LVEF>40% which is statistically significant. Another observation of my study is that among the Vit D deficient patients , majority(73%) have Triple vessels disease & no one has normal coronary angiography. Similarly a study by Syal et al from North India in100 patients undergoing coronary angiography revealed moresevere coronary artery disease and greater endothelialdysfunction among individuals with low vitamin D.[14]Among the Vitamin- D insufficient patients majority(46.3%) have Double Vessels Disease whereas Vitamin D sufficient patients have either normal coronary angiography or Single vessel disease(95.5%). Regarding Arrhythmias out of 17 patients with rhythm disorder patients 16 have either Vitamin-D deficiency or insufficiency. So from my study it can be said that among the STEMI patients who are Vitamin- D deficient or insufficient they are more prone to develope decreased left ventricular systolic function, increased incidence of extensive coronary artery disease by conventional coronary angiography and also more likely to have arrhythmic disorderthan the patients with sufficient serum Vitamin D level.

Although vitamin D deficiency has been strongly associated with CV risk factors, inflammation, and adverse CV outcomes, randomized trials have not yet been done todemonstrate that normalizing vitamin D levels will improve CV health and prognosis. Large scale randomised trials like VITAL study are ongoing for evaluation of cardiovascular benefits of vitamin D supplementation. However, vitamin D deficiency adversely affects many aspects of general health, especially with regard to musculoskeletal and immunologic function.[15] Thus, it is reasonable to screen patients with AMI with a vitamin D level and correct deficient levels according to nationally established consensus guidelines to optimize overall health.

V. Summary

Vitamin D deficiency is emerging as a new risk factor forvarious cardiovascular diseases especiallyatherosclerotic vascular diseases. With growing urbanisation and adoption of a westernised lifestyle, the prevalence of both CVD and Vitamin D deficiency are increasing. There is also emerging body of evidence linking vitamin D deficiency to early mortality , with vitamin D being considered as one of the possible treatable cardiovascular risk factors.

VI. Study Limitations

1. This study was done in relatively small number of study population
2.Another limitation of the study is lack of an adequate control group with normal vitamin D levels. Because of large proportions of patients who were vitamin D deficient or insufficient, we did not have adequate control group for comparison.
3.Although this study is a longitudinal study but it was done only during index hospitalisation (from admission to discharge/death) average duration of hospital stay 7 days. For determining prognosis of the patients with STEMI (both vitamin D deficient and sufficient) long term longitudinal follow up study needed.

VII. Conclusion

This study reveals a very high prevalence ofvitamin D deficiency among patients of acute MI.Despite the rampant hypovitaminosis, presence of severevitamin D deficiency was associated with risk of acute MIeven after adjusting for conventional risk factors. This associationneeds to be tested in larger cross-sectional and

cohortstudies from India. Prospective studies are needed to investigate benefits of screening and treatment of this very common vitamin deficiency for prevention of cardiovascular diseases.

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