

# Association of Serum Vit D level with in-Hospital Outcome in Patients with Acute Myocardial Infarction

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## ABSTRACT

**Background:** Low Vitamin D (Vit D) level is associated with disease severity amongst critical acute myocardial infarction (AMI) patients. This leads to the hypothesis that Vit D plays a role in the emergence of cardiac risk factors, contributing to worsening AMI patients' short- and long-term prognoses. Therefore, there is still unclear data showing the potential impact of Vit D insufficiency or deficiency on the morbidity and mortality of AMI patients. So far, there has been no research conducted in Pakistan examining whether or not Vit D status are association to the outcome of hospitalization for coronary artery disease.

**Objective:** The objective of the study is to examine the relationship between Vit D status on hospital admission and subsequent mortality and morbidity among patients with acute myocardial infarction.

**Study Design:** Cross sectional observational study

**Study Setting:** This study was conducted in the department of Interventional Cardiology, National Institute of Cardiovascular Diseases (NICVD), Karachi from 1st August 2022 to 31st January 2023.

**Methodology:** Total 250 subjects were enrolled in the study and divided in to two groups. Group A with normal Vit D (30ng/ml or above) and Group B included lower Vit D level than 30ng/ml, all patients were suffering from AMI. Baseline demographic characteristics, including age, and gender (male/female), was recorded. The patients were tested for Vit D status and distributed in their respective groups. The history, complications, and clinical data were included. The stay in the hospital and any adverse outcomes that appeared during the stay were also recorded. The clinical results include HDL, TG, and troponin I of every patient were noted for the clinical correlation of AMI patients with adequate and deficiency of Vit D level. All the data was collected in the form of a questionnaire. The statistical analysis was done by using SPSS version 20.

**Results:** Participants' mean ages were 53.8 and 5.9 years old. Group A (patients with low Vit D status) averaged 59.6 years of age, whereas Group B (58.9 years) had normal Vit D status. The analysis showed a statistically non- significant ( $p > 0.05$ ) difference in average age between the groups. There were 250 patients, with male 43.6% and female 56.4%. Men (63.2%) and women (36.8%) were in Group A. There were 71.4% males and 28.6% females in Group B. We found out the 137(60.6%) significant adverse hospital outcomes ( $p < 0.001$ ) in Group B and had a more significant proportion of patients with diabetes mellitus and who had smoked ( $p = 0.002$  and  $0.001$ , respectively). In a multivariate logistic regression smoking, diabetes, Troponin I and low vitamin showed the significant risk association ( $p < 0.001$ ).

**Practical Implication:** There is still a lack of conclusive evidence on the relationship between vitamin D insufficiency or deficiency and the morbidity and mortality of AMI patients. Until far, there has been no research in Pakistan linking serum vitamin D levels to in-hospital outcomes for patients suffering from acute myocardial infarction.

**Conclusion:** The research shows an association between low Vit D status, adverse outcomes, and clinical parameters after AMI. A low blood Vit D level is independently associated to an increased risk of developing severe clinical outcomes during hospitalization, including death after an AMI.

**Keyword:** Vit D, AMI, Vit D deficiency, low Vit D, Cardiovascular disease

## INTRODUCTION

The cardiovascular disease more specifically acute myocardial infarction (AMI) remains the leading cause of death and disability in the developing countries.<sup>1</sup> New risk factors for AMI development such as Vit D deficiency which may have significant role in the disease progression<sup>2</sup> The widespread prevalence of Vit D insufficiency, or inadequacy is well-documented. In Pakistan, there is 73% population is suffering from Vit D deficiency and 20% are suffering from AMI.<sup>3</sup> The consequences of low Vit D status have often been studied on osteoblast formation and calcium status of the body.<sup>4</sup> Preliminary investigations reveal a probable association between Vit D deficiency and AMI's short- and long-term outcomes.<sup>5, 6</sup> Vit D deficiency appears to predispose to in-hospital and recurrent unfavorable cardiac events. This is likely due to its relationship with the number of damaged coronary arteries, AMI complications, and cardiac remodelling in individuals with AMI.<sup>7, 8</sup>

Seasons with less time spent outside in the sun (winter) have also been association to increased cardiovascular mortality rates assuming due to the deficiency of Vit D.<sup>9</sup> The cardiovascular reasons account for more significant deaths in individuals with chronic renal disease and primary hyperparathyroidism which are the two diseases associated to Vit D deficiency.<sup>10</sup> Importantly, Vit D deficiency with heart failure fatalities and abrupt cardiac deaths are also the evidence of mortality.<sup>11</sup> Evidence suggests that Vit D may play a role in several vital aspects of AMI, including acute ventricular dysfunction, heart failure progression, post-AMI ventricular remodeling, inflammation, thrombotic/bleeding balance,

and arrhythmias. Low Vit D level has been documented to have comparable prognostic importance in critically admitted patients, with an association between illness severity and mortality of AMI.<sup>12</sup>

<sup>13</sup> Together, these results confirm the theory that Vit D plays a role in the emergence of cardiac risk factors, contributing to worsening AMI patients' short- and long-term prognosis.<sup>14</sup> However, the correlation between Vit D status and clinical outcomes in AMI patients has only been the focused of a few studies. Therefore, there is still unclear data showing the potential impact of Vit D insufficiency or deficiency on the morbidity and mortality of AMI patients. So far, there has been no research conducted in Pakistan examining whether or not Vit D status are associated to the outcome of hospitalization for coronary artery disease.<sup>3</sup> The objective of the study is to examine the relationship between Vit D status on hospital admission and subsequent mortality and morbidity among patients with acute myocardial infarction. Furthermore, this study was to assess the serum Vit D status of patients admitted to the hospital with AMI and to determine whether or not these levels were associated with the development of complications during hospitalization.

## METHODS

**Study Design and Setting:** This was a cross sectional observational study conducted in the department of Interventional Cardiology, National Institute of Cardiovascular Diseases (NICVD), Karachi from 1st August 2022 to 31st January 2023 though the use of convenient purposive sampling technique.

**Sample Size:** Sample size calculation was done to compare proportions where the confidence interval was equal to 95 % with a 5% significance level, taking 80% power of the study. The 250 total sample size was calculated.

**Inclusion and Exclusion Criteria:** Participants willing to enroll in the study were included, aged 20 years, males, and females. Study participants who have received Vit D supplementation within the past few months, family history of cardiomyopathy and any severe co-morbid conditions such as liver disease, thyroid disorder, renal disease, malabsorption were excluded from the study.

**Study Participants:** Two hundred and fifty patients fulfilled the inclusion criteria and enrolled in the study after informed consent from parents. Patients with a blood Vit D level of 30 ng/ml or above were classified as "Group A," while those with a serum Vit D level of 30 ng/ml or below or a low Vit D level group were classified as "Group B." The relation between blood Vit D status and in-hospital complications of AMI were examined under the supervision of two cardiologists. All patients were monitored until discharge or death to study the associations/complications such as heart failure, cardiogenic shock, clinically significant tachy/bradyarrhythmia, and acute kidney injury.

**Data Collection:** Baseline demographic characteristics were recorded with the patient's Vit D status and distributed in their respective groups. The history, complications, and clinical data were included. The stay in the hospital and any adverse outcomes that appeared during the stay were also recorded. The clinical results include HDL, TG, and troponin I of every patient were noted for the clinical correlation of AMI patients with adequate and deficiency of Vit D level. All the data was collected in the form of a questionnaire.

**Statistical Analysis:** The data was collected and analysis through SPSS version 23. The qualitative data were calculated as frequency and percentages. Effectiveness between the groups compared through chi-square test and p-value  $\leq 0.05$  was taken as significant.

**RESULTS**

The 250 patients were divided into two groups, Group A consisting of those with blood Vit D status ( $>30$  ng/ml) and Group B consisting of those with low serum Vit D status (30 ng/ml). The ages of the respondents ranged from 20 to 70. Nearly half of the patients were between 40 and 60, with only 2% younger than 40. Participants' mean ages were 53.8 and 5.9 years old. Group A (patients with low Vit D status) averaged 59.6 years of age, whereas Group B (58.9 years) had normal Vit D status. The analysis showed a statistically non-significant ( $p>0.001$ ) difference in mean age between the groups. There were 250 patients, with male 43.6% and female 56.4%. Men (63.2%) and women (36.8%) were in Group A. There were 71.4% males and 28.6% females in Group B. The other demographic details are presented in Table I.

There was a statistically significant correlation between the sexes in the research groups ( $p=0.021$ ). Amongst Group B patients the Vit D status were significantly lower in female patients (19.9 ng/ml) as compared to 28.1 ng/ml in male patients ( $p=0.036$ ). Vit D insufficiency, a blood level between 11 and 20 ng/ml, was present in almost half of the patients (45.5%). Serum Vit D status ranged from 11 to 46 ng/ml, with an average of 24.62 ng/ml in all patients enrolled in the study. We found out the 137(60.6%) significant adverse hospital outcomes ( $p<0.001$ ) in Group B and had a more significant proportion of patients who had previously been diagnosed with diabetes mellitus and who had smoked ( $p = 0.002$  and  $0.001$ , respectively). We also noticed that the patients with Vit D status between 9 and 22 ng/ml (38.1%) were more likely to have heart failure, followed by those with levels between 23 and 30 ng/ml (23.6%). The mean difference between the two groups was statistically significant ( $p=0.001$ ), with Group B having a more extended mean hospital stay (7.3) as compared to Group A with 5.6 days. Patients in the research spent an average of 6.35 days in the hospital.

Table 1: Demographic details of the patients

Variables	Frequency	Percentage
Vit D		
Normal Vit D	24	9.6
Low Vit D	226	90.4
Gender		
Male	109	43.6
Female	141	56.4
History of Patients		
Hypertension	28	11.2
Smoking	188	75.2
Diabetes Mellitus	22	8.8
Dyslipidemia	9	3.6
Family history of coronary artery disease	3	1.2
Adverse outcomes		
Heart failure	61	24.4
Cardiogenic shock	108	43.2
Arrhythmia	51	20.4
AF	3	1.2
VT	7	2.8
1st degree AV block	5	2.0
Complete AV block	5	2.0
Trifascicular block	3	1.2
AKI	5	2.0
Death	2	.8
Clinical Variables		
Age>50 years	14	5.6
Female gender	14	5.6
Smoking	41	16.4
Diabetes	55	22.0
Low HDL-C	45	18.0
Elevated TG	32	12.8
Elevated Troponin I	31	12.4
Presence of low Vit D level	18	7.2

Table 2: Chi Square Test was to Calculate Data

Adverse in Hospital outcome	Group A (n=24) Number (%)	Group B (n=226) Number (%)	Total (n=250) Number (%)	P value
Present	14 (58.3)	137 (60.6)	151 (60.4)	<0.001
Absent	10 (41.7)	89 (39.4)	99 (39.6)	

means significant ( $p<0.05$ )

The clinical variables in-hospital outcome was used as dependent variable in a multivariate logistic regression analysis with age  $>50$  years, female gender, smoking, diabetes mellitus, low HDL-C, increased TG, high Troponin I, and the presence of low Vit D level as independent factors. Where age, smoking, diabetes, Troponin I and low vitamin are showing the risk association.

Table 3: Multivariate Logistic Regression was Used to Calculate Data.

Variables	Standardized Coefficient (a)	OR	95% CI	P value
Age>50 years	0.776	1.01	4.86 – 6.89	0.001**
Females	0.456	0.23	0.59 – 1.02	0.459
Smoking	1.043	2.86	1.23 – 3.56	0.043*
Diabetes	2.044	3.37	5.55 – 31.3	0.001**
Decreased HDL	0.443	0.450	0.44 – 1.96	0.714
Increased TG	0.560	0.730	0.89 – 2.046	0.998
Increased Troponin I	3.600	1.692	1.263– 1.63	0.002*
Low Vit D level	8.204	6.700	9.72 – 35.776	0.001*

means significant ( $p<0.05$ ) and \*means not significant ( $p>0.05$ )

**DISCUSSIONS**

This cross-sectional observational research was conducted to determine whether or not a correlation exists between a low blood Vit D level and an increased risk of complications during hospitalization for patients with acute myocardial infarction. Our findings show that low Vit D status are associated with an increased risk of adverse hospital outcomes following AMI risk factors. Vit D insufficiency, a blood level between 11 and 20 ng/ml, was present in almost half of the patients (45.5%). Serum Vit D status ranged from 11 to 46 ng/ml, with an average of 24.62 ng/ml in all patients enrolled in the study. We found that the Vit D status of female patients were significantly lower than male patients. Women often have lower 25(OH)D levels than men showed in a study conducted by Yu Chao et al.<sup>15</sup> Differences in body fat composition, insufficient nutritional intake, pregnancy, and menopause are all possible causes.<sup>16</sup> In addition, minimizing sun exposure might lead to lower levels of Vit D produced naturally in

the body.<sup>17</sup> The prevalence of smoking was more significant among CAD risk factors (64.1%), whereas the prevalence of hypertension (34.8%) and diabetes mellitus (33.8%) were closer together.<sup>18</sup> Low Vit D status were associated with an increased risk of patients with a history of smoking and diabetes mellitus ( $p < 0.043$  and  $p < 0.001$ , respectively). Cigarette smoking was revealed to be the leading cause of AMI risk (OR=1.043). Similar to our study, Malakar, Arup Kr et al.,<sup>19</sup> found that smoking was the most common risk factor among CAD patients. Patients with diabetes were more likely to have Vit D deficiency than patients without diabetes or individuals with insufficient Vit D. Vit D insufficiency has been associated to type 2 diabetes in the working elderly, according to research done by Bener Abdulbari et al.<sup>20</sup>

Our research population had a high prevalence of Vit D deficiency. Patients with AMI were more likely to have a Vit D level below 30 ng/ml than above. In previous study, Vit D insufficiency was found in 39.5% of patients compared to 26% in the control group, and inadequate Vit D status were found in 18% of patients compared to 11% of the control population, as reported by Kumar et al. (2016).<sup>21</sup> Javadzadegan, Hassan et al., found that 67.5% of individuals with low Vit D status were deficient, while 16.5% had inadequate levels.<sup>22</sup> According to research by Ferrari Davide et al., Vit D status in 83% of individuals were below 30 ng/ml.<sup>23</sup> There is 7% of participants had adequate Vit D status, while 93% had Vit D deficiency or insufficiency. The widespread lack of Vit D, or hypovitaminosis D, contributes to its high incidence in previous studies.<sup>23, 24</sup> Complications of Acute Coronary Syndrome that occurred during hospitalization after the index event were considered adverse in this study.<sup>25</sup> These included heart failure, tachy/bradyarrhythmia, acute kidney injury, cardiogenic shock, and death.<sup>26</sup> Patients with low Vit D status were more likely to have adverse hospital outcome (60.6%) than those with normal Vit D status and this was a statistically significant ( $p = 0.001$ ). The results of this research provide credence to the hypothesis that AMI patients with low Vit D status upon hospital presentation had a worse prognosis. Patients with 25 (OH) D deficiency had a 5-fold increased risk of diabetes which remained true even after considering other significant independent factors associated with AMI. We found a statistically significant ( $p = 0.001$ ) correlation between low Vit D status and an increased risk of heart failure. Patients with AMI with a deficiency in Vit D were more likely to have arrhythmias. Reportedly, chronic ventricular tachycardia and cardiomyopathy were controlled after treating Vit D deficiency and hypocalcemia. Vit D-resistant rickets has been associated to a highly unusual occurrence of fetal atrial flutter.<sup>27</sup> The adverse hospital outcome for AMI patients above the age of 50 years was significantly associated with Vit D status ( $p < 0.001$ ) with normal Vit D status developing heart failure with Vit D deficiency. Vit D deficiency was more common in HF patients than in the control group, according to research by Bahrami Leila Sadat et al.<sup>28</sup> Vit D can also influence cardiac function through its effects on parathyroid hormone and serum calcium levels. Dialysis patients were the first to provide proof in people.<sup>29-31</sup> Treatment with 1 gram of 1-alpha-hydroxycholecalciferol once a day for six weeks decreased parathyroid plasma levels and increased fractional fiber shortening on M-mode echocardiography in individuals with uremic cardiomyopathy.<sup>32</sup>

There was a very significant correlation between low Vit D status and the occurrence of AMI with all patients who had adverse outcome having low Vit D status. More research is needed to determine whether or not a lack of Vit D contributes to cardiogenic shock after an AMI. Patients with Vit D status in the deficient range of AMI patients who died as a result of adverse outcomes, whereas patients with normal Vit D status did not.<sup>33</sup>

This study's finding is consistent with the hypothesis, although other considerations might have influenced the outcome. The study was not conducted on a large sample size. The more clinical parameter would be included as a secondary outcome mediated the association between Vit D status and cardiovascular risk.

## CONCLUSION

The research shows an association between low Vit D status, adverse outcomes, and clinical parameters after AMI. A low blood Vit D level is independently associated to an increased risk of developing severe clinical outcomes during hospitalization, including death after an AMI. The role of Vit D deficiency as a risk marker or risk factor has yet to be established. These results showed the pathophysiology of cardiovascular risk and determined whether restoration of Vit D deficiency might help prevent cardiovascular disease.

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