# Study on Vitamin D deficiency in patients of diabetes mellitus presenting with Acute Coronary syndrome in a tertiary care hospital in South India



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# ABSTRACT

Background: Vitamin D, a fat-soluble vitamin has its receptor present in myriad of tissues and it modulates multiple cellular processes. Vitamin D deficiency is reported to be associated with coronary artery disease. Cardiovascular disease is the leading cause of mortality worldwide. Aims and Objective: The primary outcome was to investigate if there is a correlation of 25-OH levels with the percentage of luminal stenosis, as measured with coronary angiogram. The secondary outcome was to determine the differences in angiographically proven luminal stenosis across categories of 25-OH vitamin D levels. Materials and Methods: Thirty patients with acute coronary syndrome with diabetes mellitus were included in this cross-sectional descriptive study. All patients were tested for fasting vitamin D levels, fasting blood sugar, HbA<sub>1c</sub> and serum creatinine. Detailed history of the patients was recorded. Data was analyzed by the statistical software SPSS version 19 and p value < 0.05 was considered significant. Statistical tests like Chi- square, independent t test and log regression was used. Results: In this study 30 patients undergoing coronary angiography for acute coronary syndrome, Vitamin D levels showed severe deficiency in 6.7% (2) cases while mild deficiency was seen in 50% of the cases. Patients with single vessel disease on the coronary angiogram had lower mean HbA<sub>10</sub>(9.18)levels in our study. Patients with triple vessel disease had poorly controlled mean HbA<sub>1c</sub>levels (10.42). Conclusion: In this study we did not find any significant difference between the serum Vitamin D deficiency levels with patients with angiographic severity of the coronary artery disease. Patients with poorly controlled diabetes mellitus had more severe angiographic proven coronary artery disease.

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Key words: Coronary angiogram; Vitamin D; Diabetes Mellitus,  $HbA_{1C}$ 

### INTRODUCTION

Vitamin D, a fat soluble vitamin has its receptor present in myriad of tissues and it modulates multiple cellular processes. Vitamin D acts on the renin-angiotensin aldosterone system and effects changes in cardiomyocytes as a result of the presence of its receptor in this type of cell which may explain its effect on the cardiovascular system. Coronary artery disease (CAD) is one of the common causes of death and disability in developed countries. Experimental evidence points to the involvement of

multiple factors in coronary plaque formation, including vitamin D.<sup>3</sup>The study aimed to examine the association of coronary artery disease with vitamin D level in patients with diabetes mellitus.

### **MATERIALS AND METHODS**

The study was approved by the ethics committee of Father Muller Charitable College Institution. It was conducted according to the standards of the declaration

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of Helinski. It was a prospective study done in a tertiary hospital from February 2019 to February 2020. Thirty patients of diabetes mellitus presenting with acute coronary syndrome were included in this study. All patients presenting with acute coronary syndrome underwent coronary angiogram. The angiogram was evaluated by the cardiologist as single, double or triple vessel disease. In these entire patient's vitamin D levels assay, fasting blood sugar, HbA<sub>1C</sub>, serum creatine and fasting lipid profile tests was done. Only patients who signed informed consent were included in the study. The study was approved by the institutional review board. HbA<sub>1C</sub> levels less than 7was taken as well controlled diabetes mellitus. HbA<sub>1C</sub> levels between 7 to 8.9 was taken as out of control (uncontrolled) diabetes mellitus. Above 9 was taken as poorly controlled diabetes mellitus in this study. All patients presenting with acute coronary syndrome will undergo coronary angiogram .Presence of significant vessel disease CAD was defined as at least>70% stenosis at one or more major coronary arteries (left anterior descending, left circumflex and right coronary artery) Coronary angiogram will be evaluated by the cardiologist as single, double or triple vessel disease. Serum 25(OH) Vitamin D concentrations was analysed by Roche Hitachi COBAS 6000 automatic machine by electrochemiluminescence method and the values was expressed in ng/ml. The values less than 10ng/ml were considered as severe vitamin D deficiency while 10-20ng/ml was considered as vitamin D deficiency.

The primary outcome was to investigate if there is a correlation of 25-OH levels with the percentage of luminal stenosis, as measured with coronary angiogram. The secondary outcome was to determine the differences in angiographically proven luminal stenosis across categories of 25-OH vitamin D levels. The gathered information was be analysed by the statistical software SPSS version 19 and p value<0.05 was considered to be significant. ANOVA, chi square test and fishers exact test were used to assess the relationship between the coronary angiogram reports and the Vitamin D levels.

### **RESULTS**

Out of the 30 patients in the study 46.7% (14) were above 60 years 36.7% (11) patients were in the age above 51 years 16.7% (5) patients were below 50 years as shown in Figure 1. 80% (24) patients were males and 20% (6) patients were females as shown in Figure 2. The HbA<sub>1C</sub>levels were out of control in 40% (12) patients and were poorly controlled in 60% (18) patients as shown in Table 1. None of the patients had HbA<sub>1C</sub> less than 7. Vitamin D reports analysed showed severe deficiency in 6.7% (2) cases while

Figure 1: Age stratification of the patients

46.7

46.7

46.7

46.7

46.7

46.7

46.7

46.7

46.7

51-60

Above 60

40-50

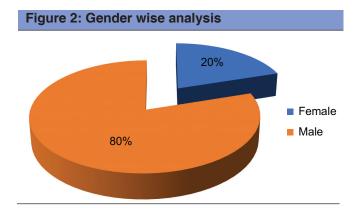


 Table 1: Analysis based on values of Glycated Hemoglobin (HbA<sub>1c</sub>)

 Frequency
 Percent

 Out of control
 12
 40.0

 Poorly control
 18
 60.0

 Total
 30
 100.0

mild deficiency was seen in 50% (15) cases. Vitamin D levels was normal in 43% (13) patients as shown in Figure 3.

Coronary angiogram report was analysed to single, double and triple vessel disease. Single vessel disease was seen in 43.3% (13) cases. Double vessel disease was seen in 26.7% (8) cases and triple vessel disease was seen in 30% (9) cases as shown in Table 2.

50% (15) patients in our study group had mild vitamin d deficiency and severe vitamin d deficiency was seen in 6.7% (2) cases and 43.3% (13) patients had normal vitamin D levels in this study.

In the subgroup elderly patients 14.3% (2) above age group 60 years had severe vitamin D deficiency. 57.1% (8) of the elderly patients had mild vitamin D deficiency. Mild vitamin D deficiency was seen in 36.4% (4) in the subgroup age group 51-

60 years. The vitamin D levels analysed with age group did not show any statistical significance in this study (p value=0.319). All the baseline characteristics are explained in Table 3.

8.3% (2) cases of the patients with severe vitamin D deficiency were males. In male patients mild vitamin D

Figure 3: Analysis based on values of Vitamin D

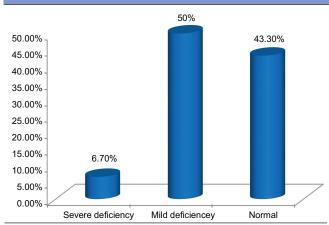


Table 2: Distribution of frequency of subjects based on Coronary Angiogram report

|        | Frequency | Percent |
|--------|-----------|---------|
| Single | 13        | 43.3    |
| Double | 8         | 26.7    |
| Triple | 9         | 30.0    |
| Total  | 30        | 100.0   |

deficiency was seen in 45.8% (11) cases and vitamin D levels were normal in 45.8% (11) cases. Vitamin D levels showed mild deficiency in 66.7%(4) of the female patients and 33.3% (2) had normal vitamin D levels.

There was no statistical significance between the gender of the patient and the vitamin D levels in this study.

60% (18) of patients in our study had poorly controlled diabetes mellitus. In this group 50 % (9) had normal vitamin d levels 38.9% (7) had mild vitamin D deficiency and 11.1% (2) had severe vitamin D deficiency. 40%(12) of patients in this study had out of control diabetes mellitus. In this group 66.7% (8) patients had mild vitamin Deficiency and 33.3% (4) had normal vitamin D levels. There was no statistical significance between vitamin D levels and the HbA<sub>10</sub> levels as shown in Table 4.

Coronary angiogram report was analysed with the vitamin D reports. 6.7% (2) patients with triple vessel disease had severe vitamin D deficiency,50% patients showed mild vitamin D deficiency and 43.3% (13) had normal vitamin D levels. In this group of patients with mild vitamin D deficiency 46.7% (7) patients had single vessel disease on the coronary angiogram report, double vessel disease was seen in 26.7% (4) patients and 26.7% (4) patients had triple vessel disease.

43.3% (13) patients had normal vitamin D levels. In this group 46.2%(6) patients had single vessel disease on the coronary angiogram 30.8% (4) patients had double vessel

|                             |                | VIT D  |         |            |                 |         |            |        |         |            |
|-----------------------------|----------------|--------|---------|------------|-----------------|---------|------------|--------|---------|------------|
|                             |                | Severe |         |            | Mild deficiency |         |            | Normal |         |            |
|                             |                | Count  | Row N % | Column N % | Count           | Row N % | Column N % | Count  | Row N % | Column N % |
| Age                         | 40 – 50        | 0      | .0      | .0         | 3               | 60.0    | 20.0       | 2      | 40.0    | 15.4       |
|                             | 51 – 60        | 0      | .0      | .0         | 4               | 36.4    | 26.7       | 7      | 63.6    | 53.8       |
|                             | Above 60       | 2      | 14.3    | 100.0      | 8               | 57.1    | 53.3       | 4      | 28.6    | 30.8       |
|                             | Total          | 2      | 6.7     | 100.0      | 15              | 50.0    | 100.0      | 13     | 43.3    | 100.0      |
| Gender                      | F              | 0      | .0%     | .0         | 4               | 66.7    | 26.7       | 2      | 33.3    | 15.4       |
|                             | M              | 2      | 8.3     | 100.0      | 11              | 45.8    | 73.3       | 11     | 45.8    | 84.6       |
|                             | Total          | 2      | 6.7     | 100.0      | 15              | 50.0    | 100.0      | 13     | 43.3    | 100.0      |
| HbA <sub>1C</sub>           | Out of control | 0      | .0      | .0         | 8               | 66.7    | 53.3       | 4      | 33.3    | 30.8       |
|                             | Poorly control | 2      | 11.1    | 100.0      | 7               | 38.9    | 46.7       | 9      | 50.0    | 69.2       |
|                             | Total          | 2      | 6.7     | 100.0      | 15              | 50.0    | 100.0      | 13     | 43.3    | 100.0      |
| Single<br>Double_<br>Triple | Double         | 0      | .0      | .0         | 4               | 50.0    | 26.7       | 4      | 50.0    | 30.8       |
| , .                         | Single         | 0      | .0      | .0         | 7               | 53.8    | 46.7       | 6      | 46.2    | 46.2       |
|                             | Triple         | 2      | 22.2    | 100.0      | 4               | 44.4    | 26.7       | 3      | 33.3    | 23.1       |
|                             | Total          | 2      | 6.7     | 100.0      | 15              | 50.0    | 100.0      | 13     | 43.3    | 100.0      |

| Table 4: Vitamin D analysis with other variables |                                    |    |  |  |  |  |
|--------------------------------------------------|------------------------------------|----|--|--|--|--|
| Vitamin D with following parameters              | Chi square/Fishers<br>exact test p |    |  |  |  |  |
| Age                                              | 0.319                              | NS |  |  |  |  |
| Gender                                           | 0.580                              | NS |  |  |  |  |
| HbA <sub>1C</sub>                                | 0.234                              | NS |  |  |  |  |
| Single_Double_Triple                             | 0.280                              | NS |  |  |  |  |

| Table 5: Angiogram report with Glycated haemoglobin (HbA <sub>1c</sub> ) levels |    |        |                |      |    |  |
|---------------------------------------------------------------------------------|----|--------|----------------|------|----|--|
|                                                                                 | N  | Mean   | Std. Deviation | Р    |    |  |
|                                                                                 |    | HBA1C  |                |      |    |  |
| Single                                                                          | 13 | 9.185  | 2.0663         | .244 | NS |  |
| Double                                                                          | 8  | 10.338 | 1.7952         |      |    |  |
| Triple                                                                          | 9  | 10.422 | 1.6784         |      |    |  |
| Total                                                                           | 30 | 9.863  | 1.9202         |      |    |  |

| Table 6: Angiogram report with Vitamin D levels |        |           |                |      |    |  |  |
|-------------------------------------------------|--------|-----------|----------------|------|----|--|--|
|                                                 | N Mean |           | Std. Deviation | Р    |    |  |  |
|                                                 |        | Vitamin D |                |      |    |  |  |
| Single                                          | 13     | 18.8908   | 7.87096        | .660 | NS |  |  |
| Double                                          | 8      | 18.4375   | 6.41829        |      |    |  |  |
| Triple                                          | 9      | 16.1111   | 6.81107        |      |    |  |  |
| Total                                           | 30     | 17.9360   | 7.06313        |      |    |  |  |

disease on the coronary angiogram had normal vitamin D levels while 23.1%(3) with triple vessel disease on the coronary angiogram had normal vitamin D levels. There was no statistical significance between the abnormal coronary angiogram report in patients and the vitamin D levels as shown in Table 5 and Table 6.

Patients with single vessel disease on the coronary angiogram had lower mean HbA<sub>1C</sub>(9.18) levels in our study. Patients with triple vessel disease had poorly controlled mean HbA<sub>1C</sub>levels (10.42)

Patients with single vessel disease on coronary angiogram had higher mean Vitamin D (18.89) levels as shown in the above table. Patients with triple vessel disease had lower mean vitamin D levels (16.11).

# **DISCUSSION**

In this study we did not find any significant difference between the serum vitamin D deficiency levels with patients with angiographic severity of the coronary artery disease. In a study done by Dhibar<sup>4</sup> et al it was concluded that vitamin D deficiency was prevalent in subjects with angiography – proven normal coronary artery, and vitamin D deficiency and severity of deficiency does not correlate with angiographic severity of the disease. Similar study

done by T. Akhtaret al<sup>5</sup> showed vitamin d deficiency does not correlate with the severity of coronary artery disease. Syal etal. reported a higher prevalence of vitamin D deficiency in angiographically proven CAD patients and noted a positive association with severity of CAD and endothelial dysfunction with vitamin D deficiency, but their study lacks a control group.

The study done by Darraj H<sup>7</sup> et al showed significant correlation between HbA1Clevels with Vitamin D deficiency in diabetic patients. In a study done by Dossariet al<sup>8</sup> Vitamin D deficiency was seen in patients with poor glycemic control with type 2 diabetes. Patients with high HbA<sub>1C</sub>levels had very low vitamin d deficiency levels in study done by Saif – Elnasaret al.<sup>9</sup>In this study patient with triple vessel disease on angiography had higher HbA<sub>1C</sub>levels (10.42) as compared with patients with double vessel and single vessel disease and also had lower vitamin d levels though was not statistically significant.

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## **CONCLUSION**

In this study we did not find any significant difference between the serum Vitamin D deficiency levels with patients with angiographic severity of the coronary artery disease. Patients with poorly controlled diabetes mellitus had more severe angiographic proven coronary artery disease.

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AB- Concept and design of the study; interpreted the results, prepared the manuscript and critical revision of the manuscript; AR- statistically analyzed, interpreted, reviewed the literature; PP- concept, coordination, analyzed the angiogram; ARA- Design of the study, statistically analyzed and interpreted, and revision of the manuscript.

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