



## A study of the relation of HbA1c levels in acute coronary syndrome and its complications

Authors

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### Abstract

**Introduction:** The risk of coronary artery disease (CAD) is higher in diabetic patients. In Indians, CAD occurs one decade earlier than the west. HbA1C is an easy marker of long term glucose regulation as it provides a good reflection of plasma glucose concentrations over 8 – 12 weeks. Abnormal glucose metabolism is associated with increased mortality and complications following ACS. This study was conducted in ICU of Govt. Medical College, Ernakulam among patients admitted following ACS using HbA1C in blood and observing the complications for first week.

**Materials and Methods:** 188 patients admitted with Acute Coronary Syndrome in Government Medical college, Ernakulam between January 2016 and December 2016, were evaluated clinically and with the investigatory facilities available at this institution. Their HbA1C levels were measured at the laboratory of Government Medical college Ernakulam. The clinical features and investigation results were noted. HbA1C levels in UNSTABLE ANGINA, NSTEMI, STEMI, and in complications like arrhythmias, cardiac failure, cardiogenic shock also were studied and the data analysed.

**Results and Discussion:** Out of 188 patients, 63.85% were males and 36.2% females. Mean age was 61.5±9.5. 42.6% had past H/O diabetes and 51.1% had past h/o CAD. 66% had HbA1C less than 6.5 and 11.2% had HbA1C greater than 8.5%; 22.9% had HbA1c level between 6.5% and 8.5%. Out of 188 patients, 63.3% had NSTEMI, 24.5% had STEMI and 12.2% had UNSTABLE ANGINA. Cardiac failure as a complication in 48 hrs, showed an increase as 17.7%, 53.5%, 66.7% within increase in HbA1C levels, <6.5, 6.5-8.5, >8.5 respectively. Cardiac failure as a complication after 3-7 days also showed an increase as 16.1%, 35.5%, 61.9% with increase in HbA1C levels, <6.5, 6.5-8.5, >8.5 respectively.

**Conclusions:** Acute coronary syndrome patients admitted in ICU of Government medical college Ernakulam had optimum long term glycemic control (HbA1C <6.5) in 66% of patients. NSTEMI is the most common acute cardiac state among ACS in this study which however not increased with increasing levels of HbA1c. Complications like cardiac failure in first 48 hrs and within 1 week was significantly higher in patients with higher HbA1C.

**Keywords:** Glycosylated haemoglobin, Acute coronary syndrome, STEMI, NSTEMI, Unstable angina, cardiac complications.

## Introduction

Diabetes mellitus has become the most common non communicable, life style associated disease world-wide. Diabetes mellitus is associated with an increased risk of micro and macro vascular complications and an approximate two-fold greater risk of mortality compared with the general population.<sup>(1)</sup> Complex interaction of genetics and environmental factors causes several types of diabetes. Broadly there are two types – type 1 and type 2. Type 1 is due to near total or complete absence of insulin. Type 2 DM is characterized by decreased insulin secretion, insulin resistance, and increased glucose production. Type 2 DM prevalence is increasing rapidly because of increasing obesity and inactivity. Diabetes is defined by the level of glycaemia above which diabetic specific complication occurs. Stress hyperglycaemia commonly occurs secondary to increased catecholamine levels.<sup>(2)</sup>

Cardiovascular disease is now the commonest cause of death in the world. Hyperglycemia accelerates atherogenesis by the formation of glycosylated proteins and advanced glycation end products (AGE) which increases endothelial dysfunction.<sup>(3)</sup> HbA1c level >6.5 definitely diagnoses Diabetes and could be considered as a good marker of glycosylated proteins. Higher HbA1c levels and increased cardiovascular morbidity occurs even before diagnosis of clinical diabetes.<sup>(4)</sup>

Thus, glycosylated haemoglobin (HbA1c) values may reveal diabetes in cases of AMI. So glycosylated hemoglobin A1c (HbA<sub>1c</sub>) is a better marker of sugar control as it provides a good reflection of plasma glucose concentrations over 8 – 12 weeks.

NICE guidelines recommend to offer all patients with hyperglycemia after ACS and without diabetes, to test for HbA1c level before discharge.<sup>(5)</sup> A significant proportion of ACS patients have diabetes, which may be undetected by current NICE criteria. Universal HbA1c testing offers utility as a simple and effective screening test for diabetes in the ACS population<sup>(6)</sup>.

Coronary atherosclerotic vascular disease is the major cause of mortality and morbidity in patients with type 2 DM. Mechanic features unique to DM are vascular effects of hyperglycemia<sup>(7)</sup>. In population-based studies, including diabetic and nondiabetic cohorts, HbA1c has been reported as an independent predictor of all-cause and cardiovascular disease mortality<sup>(8)</sup>.

Quality of diabetes care is sub-optimal (HbA1c >8%) amongst 42-50 per cent of diabetes patients.<sup>(9)</sup> In patients with AMI, elevated glucose and HbA1c levels on admission are associated with higher ischemic scores and increased mortality rates compared with patients with normal levels on admission<sup>(10)</sup>. HbA1c >6.5 in patients of ACS is associated with more complication rate, high mortality and angiographically more severe disease.<sup>(11)</sup> HbA1c estimation at the time of admission to ICU clearly and quickly differentiates MI patients stress induced hyperglycemia from diabetics<sup>(12)</sup>. In population-based studies including diabetic and non-diabetic cohorts, HbA1c has been reported as an independent predictor of all-cause and cardiovascular disease mortality.<sup>(13)</sup>

Prevalence of coronary artery disease in Kerala is 7.5% in rural and 11% in urban areas in previous studies. Prevalence of CAD was 21.4% in diabetic south Indian subjects.<sup>(14)</sup>

There is no study regarding HbA<sub>1c</sub> levels and ACS in Kerala. Government Medical College, ERNAKULAM is an institution which gets drainage of patients from both rural and urban areas of Ernakulam. No data is available regarding the status of diabetic control and its impact on ACS complications.

This study intends to find the relation of HbA1c levels in acute coronary syndrome and to find the proportion of high HbA1c with ACS and its relation with complications of ACS.

## Aim of the Study

To study the relation of HbA1c levels in acute coronary syndrome and its complications

## Materials and Methods

This is a Cross sectional study conducted at the Intensive care unit, Department of medicine, Government Medical College, Ernakulam, Kerala from January 2016 to December 2016. All acute coronary syndrome patients admitted in ICU between age 30 to 70 years were included in the study.

### Exclusion criteria

- 1) Known cases of congenital heart diseases
- 2) Rheumatic Heart diseases
- 3) Haemoglobinopathies
- 4) Hemolytic anemia
- 5) Sepsis

**Sample Size** was calculated as 188 samples.

### Sampling technique :

All patients who get admitted in ICU with features of acute coronary syndrome satisfying the inclusion and exclusion criteria were included consecutively till the required sample size was achieved

### Procedure in Detail

Proposed study was conducted over a period of one year in Govt. Medical College, Ernakulam. All patients admitted with ACS *which refers to* STEMI, NSTEMI and unstable angina in ICU who fulfilled the inclusion criteria were recruited to the study with informed consent. Relevant history and clinical details were obtained from each patient, as per proforma.

### Patient Recruitment

Once the patient was admitted, history was taken and data collected in pre-structured proforma. Details of history, examinations and laboratory and technical investigations reports were noted from time to time. Patients were treated specifically and symptomatically.

HbA<sub>1c</sub> testing was done by immuno assay method.

Patients were stratified according to HbA<sub>1c</sub> levels

- 1) HbA<sub>1c</sub> levels less than 6.5
  - 2) HbA<sub>1c</sub> level 6.5 to 8.5
  - 3) HbA<sub>1c</sub> level more than 8.5
- 1) the relation between different HbA<sub>1c</sub> levels and spectrum of ACS (unstable angina, NSTEMI,

STEMI) studied and 2) the relation between HbA<sub>1c</sub> levels and complications in first week such as arrhythmias, cardiac failure and cardiogenic shock were also studied.

### Data Analysis

The data were numerically coded and entered in Microsoft Excel spread sheet. The analysis was done using the software SPSS (Statistical package for social sciences) to find out the relation between HbA<sub>1c</sub> levels and ACS. Chi-square test has been used to find the significance of study parameters on categorical scale between two or more groups.

### Results

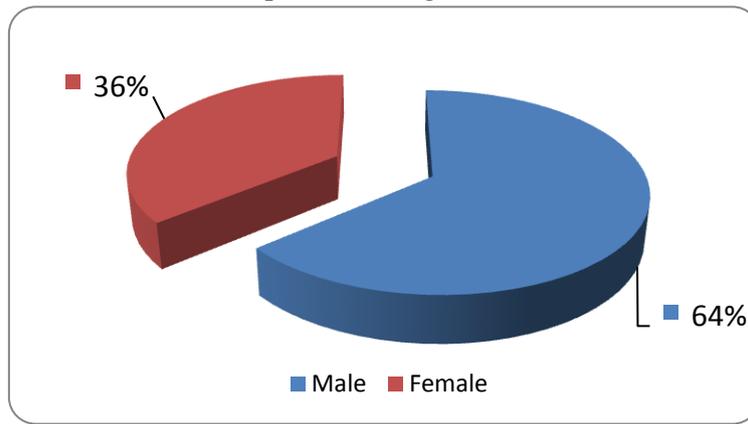
Total 188 patients were enrolled for the study. Majority of the patients (64.9%) belonged to the age group 61-70. The mean age of the study population was 61.5. (Table 1) Males comprised 64% of the study population and the rest were females. (Graph 1) History of CAD was observed in 51% of the patients and history of Diabetes Mellitus was seen in 42% of the patients.

Optimum glycemc levels were observed in the majority of patients. The mean HbA<sub>1c</sub> levels were 6.7. HbA<sub>1c</sub> levels <6.5 were noted in 66% of the patients. 23% had HbA<sub>1c</sub> between 6.5 and 8.5 and 11% patients had HbA<sub>1c</sub> >8.5. (Table 2) HbA<sub>1c</sub> levels were compared with various types of ACS. But there was no significant association. (Graph3, Table5)

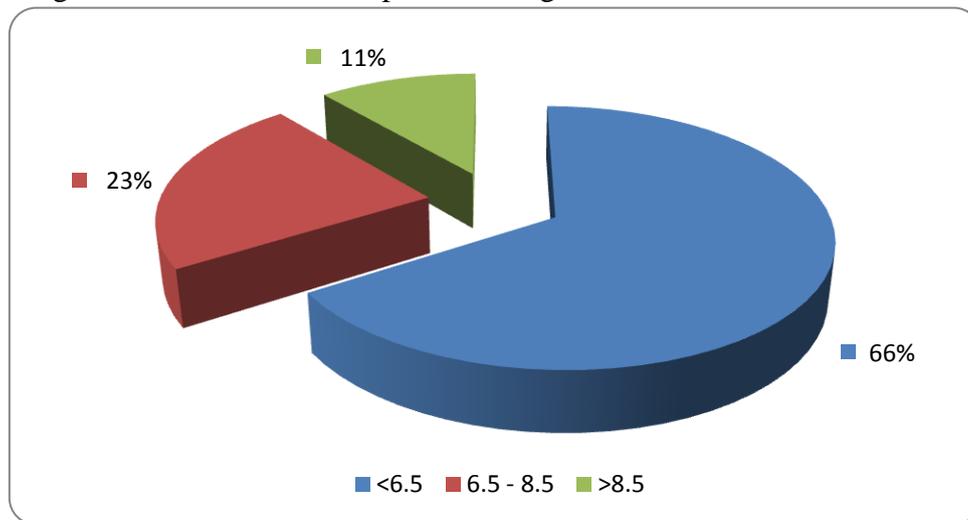
Out of the total study population 12%, 63% and 24.5% patients had Unstable angina, NSTEMI and STEMI respectively. Cardiac failure was the most common complication observed in 48 hours of presentation and during 3-7 days (Table 3,4). There was no significant association between types of ACS and HbA<sub>1c</sub> levels. (Table 5)

As the HbA<sub>1c</sub> levels increased there was a statistically significant increase in cardiac failure as a complication and was seen at 48 hours of admission and 3-7 days of hospital stay. (Table 6, 7, 8, 9)

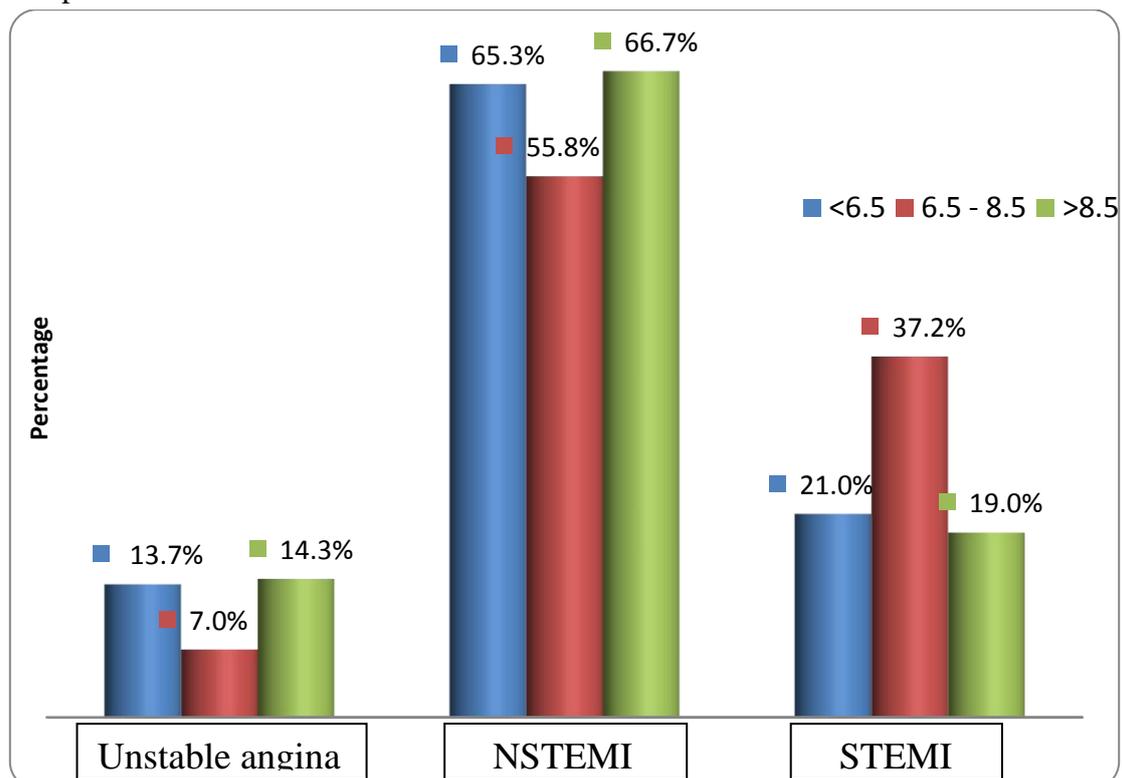
**Graph 1:** Percentage distribution of the sample according to sex



**Graph 2 :** Percentage distribution of the sample according to HbA1C



**Graph 3:** Comparison of ACS based on HbA1C



**Table 1:** Percentage distribution of the sample according to age

Age	Count	Percent
31 - 40	11	5.9
41 - 50	18	9.6
51 - 60	37	19.7
61 - 70	122	64.9
Mean ± SD	61.5 ± 9.5	

**Table 2:** Percentage distribution of the sample according to HbA1C

HbA1C	Count	Percent
<6.5	124	66.0
6.5 - 8.5	43	22.9
>8.5	21	11.2
Mean ± SD	6.7 ± 1.7	

**Table 3:** Percentage distribution of the sample according to complication in 48 hours

Complication_48 hrs	Count	Percent
Nil	115	61.2
Arrhythmia	7	3.7
Cardiac failure	59	31.4
Cardiogenic shock	3	1.6
Death	4	2.1

Cardiac failure was the most common complication observed in 48 hours of presentation and during 3-7 days.

**Table 4:** Percentage distribution of the sample according to Complication in 3-7 days

Complication_3-7 days	Count	Percent
Nil	118	62.8
Arrhythmia	3	1.6
Cardiac failure	56	29.8
Cardiogenic shock	6	3.2
Death	5	2.7

**Table 5:** Comparison of ACS based on HbA1C

ACS	<6.5		6.5 - 8.5		>8.5		$\chi^2$	p
	Count	Percent	Count	Percent	Count	Percent		
Unstable angina	17	13.7	3	7.0	3	14.3	5.49	0.241
NSTEMI	81	65.3	24	55.8	14	66.7		
STEMI	26	21.0	16	37.2	4	19.0		

Relation of HbA1c levels with the complications of acute coronary syndrome

**Table 6:** Distribution of complication in 48 hrs based on HbA1C

Complication in 48 hrs	<6.5		6.5 - 8.5		>8.5	
	Count	Percent	Count	Percent	Count	Percent
Nil	95	76.6	14	32.6	6	28.6
Arrhythmia	3	2.4	4	9.3	0	0.0
Cardiac failure	22	17.7	23	53.5	14	66.7
Cardiogenic shock	3	2.4	0	0.0	0	0.0
Death	1	0.8	2	4.7	1	4.8

**Table 7 :** Comparison of complication in 48 hrs based on HbA1C

Complication in 48 hrs	<6.5		6.5 - 8.5		>8.5		$\chi^2$	p
	Count	Percent	Count	Percent	Count	Percent		
Nil	95	76.6	14	32.6	6	28.6	39.8**	0.000
Cardiac failure	22	17.7	23	53.5	14	66.7		
Others	7	5.6	6	14.0	1	4.8		

\*\*:- Significant at 0.01 level

**Table 8 :** Distribution of complication in 3-7 days based on HbA1C

Complication in 3-7 days	<6.5		6.5 - 8.5		>8.5	
	Count	Percent	Count	Percent	Count	Percent
Nil	96	77.4	16	37.2	6	28.6
Arrhythmia	1	0.8	2	4.7	0	0.0
Cardiac failure	20	16.1	23	53.5	13	61.9
Cardiogenic shock	5	4.0	0	0.0	1	4.8
Death	2	1.6	2	4.7	1	4.8

**Table 9 :** Comparison of complication in 3-7 days based on HbA1C

Complication in 3-7 days	<6.5		6.5 - 8.5		>8.5		$\chi^2$	p
	Count	Percent	Count	Percent	Count	Percent		
Nil	96	77.4	16	37.2	6	28.6	36.26*	0.000
Cardiac failure	20	16.1	23	53.5	13	61.9		
Others	8	6.5	4	9.3	2	9.5		

\*\*:- Significant at 0.01 level

## Discussion

The present study was based on analysis of acute coronary syndrome patients admitted in intensive coronary care unit of government medical college Ernakulam under department of general medicine during the study period of twelve months, the prime aim of the study was to study the relation of HbA1c levels in ACS and its cardiac complications.

A pilot study was conducted prior to the this study to find out the number of cases of acute coronary syndrome patients admitted per year and was found to be 300 per year with an average of 25 cases per year. According to previous study by Viswanathan Mohan et al- prevalence of CAD was 21.4% in south Indian subjects<sup>(15)</sup> Based on this sample size was calculated as 187.188 cases of cases between the ages 30 and 70 without the history of any congenital heart disease, Rheumatic heart disease, Haemolytic anemias, Haemoglobinopathies and sepsis were evaluated clinically.

All the subjects included in the study were evaluated with history, clinical examination ECG, HbA1 C levels in blood, CKMB, Trop I. 63.8% were males and 36.2% were females. Previous h/o

coronary artery disease was present in 51.1% and h/o diabetes in 42.6%. CKMB and TROP I elevation was 87.8% and 88.3% respectively. 124 patients out of 188 (66%) had HbA1c level below 6.5 indicating optimum glycemic control. 43% had HbA1c levels between 6.5-8.5(22.9%). 21 patients (11.2%) had HbA1c levels >8.5.

63.3%(119/189) had NSTEMI 46/189 and 23/189 had STEMI and Unstable angina respectively. Cardiac failure was the most common complication in 48 hours and within first week also 31.4% and 29.8% respectively.

In comparison of ACS based on HbA1C, NSTEMI showed an increase from 55.8% at levels 6.5-8.5 and 66.7% at >8.5 levels with p value 0.241.

Cardiac failure as a complication in 48 hours showed increase at HbA1c levels <6.5, 6.5-8.5, >8.5 from 17.7%, 53.5% to 66.7% respectively, significant at p value 0.01 level. Cardiac failure also increased in first week at HbA1c levels <6.5, 6.5-8.5, >8.5 from 16.1%, 53.5%, 61.9% respectively, significant at p value 0.01 level.

Dubey et al found Complications was present in 25% of patients the most common being left ventricular dysfunction.<sup>(16)</sup>

Vinitha et al also found Severity and complications of heart disease were significantly higher in diabetics and showed a significant correlation with HbA1c.<sup>(17)</sup>

Similar study by Sheetal et al mentioned that HbA1C > 6.5 in patients of acute coronary syndrome is associated with more complication rate, high mortality as well as angiographically more severe disease.<sup>(11)</sup> Recent study by Ramesh naidu et al also found that patient with HbA1c <6.5 percent 16 out of 56 developed complication like left ventricular failure, cardiogenic shock, arrhythmias as compared to 16 of 20 patients with HbA1c >8.5 % which was statistically significant.<sup>(18)</sup> Left ventricular failure was most common complication followed by cardiogenic shock and Arrhythmia in patient having ACS in this study.

In our study we also found cardiac failure as the most common complication followed by cardiogenic shock in HbA1c levels above >8.5% and positive correlation between HbA1c levels and complications like cardiac failure.

### Conclusions

Acute coronary syndrome patients admitted in ICU of Government medical college Ernakulam had optimum long term glycemic control (HbA1C<6.5) in 66% of patients. NSTEMI is the most common acute cardiac state among ACS in this study which however not increased in increasing levels of HbA1c .Complications like cardiac failure in first 48 hrs and within 1 week was significantly higher in patients with higher HbA1C.

### Limitations of the Study

- The study period was one year only.
- Being a Tertiary care centre in metro city, study may not always represent actual situation in the community.

**Conflicts of interest:** Nil

### Bibliography

1. Mulnier HE, Seaman HE, Raleigh VS, Soedamah , Muthu SS. Mortality in people with type 2 diabetes in the UK. *Diabet Med* 2006;23:516–521.
2. Husband DJ, Alberti KG, Stress hyperglycaemia during acute Myocardial infarction: An indicator of pre-existing diabetes? *Lancet*, 1983; 2: 179-81
3. Brownlee M. Advanced glycosylation in diabetes and aging. *Ann Rev Med* 1988; 46: 223-4.
4. Haffner SM, Lehto S, Ronnema T, Pyorala K. Mortality from coronary heart disease in subjects with type 2 diabetes and in non diabetic subjects with and without prior myocardial infarction. *N Engl J Med* 1998;339:229-34.
5. HYPERGLYCEMIA IN ACS Management; NICE Guidelines.; nice.org.uk/guidance/cq130
6. McCune C, Maynard S, McClements B Lindsay HbA1c for Diabetes Screening in Acute Coronary Syndrome:time for a reappraisal of the guidelines? *Ulster Med J* 2015;84(3):154-156
7. MEDICINE UPDATE 2010;Vol 20
8. Kishore P, Kim SH, Crandall JP. Glycemic control and cardiovascular disease: what's a doctor to do? *Curr Diab Rep* 2012; 12: 255-264 [PMID: 22467273 DOI: 10.1007/s11892-012-0268-5]
9. Mohammed K. Ali, K.M. Venkat Narayan& Nikhil Tandon Diabetes & coronary heart disease: Current perspectives *Indian J MedRes* 132, November 2010, pp 584-597 .
10. Mahmut Cakmak MD, Nazmiye Cakmak MD, Sebnem Cetemen MD The value of admission glycosylated hemoglobin level in patients with acute myocardial infarction *Can J Cardiol* 2008;24(5):375-378.
11. Sheetal D Vora,et al A Study of Glycosylated Hemoglobin in acute

- coronary syndrome. National journal of community medicine vol 7 issue 2 feb 2016
12. Nayak Rashmi and Chauhan Vinay Singh. Glycosylated Haemoglobin as a diagnostic marker of diabetes mellitus in acute myocardial infarction and correlation with dietary pattern, international research journal of medical sciences vol 3(6) 1-4 june 2015
  13. Chiara Lazzeri, Serafina Valente, Marco Chiostri. Clinical significance of glycated hemoglobin in the acute phase of ST elevation myocardial infarction. World J Cardiol 2014 April 26; 6(4): 140-147
  14. Viswanathan Mohan et al. "epidemiology of cardiovascular disease in type 2 diabetes: the Indian Scenario" journal of Diabetes Science and Technology' vol 4 issue 1 jan 2010 }
  15. Amitani M Sultanqaboos University Med J. Aug 2013 vol 13 ISS 3, PP 368-370 E Pub 25 Jun 13 Sub 21 May 13,
  16. T. N. Dubey, Kaustubh Mundada, A Arya. Correlation of HbA1c with mortality and severity in acute coronary syndrome. International Journal of Contemporary Medical Research 2016; 3(8): 2244-2247.
  17. Vinita Elizabeth Mani\*, Mary John\*\*, Rajneesh Calton. Impact of HbA1c on Acute Cardiac States. JAPI • JUNE 2011 • VOL. 59
  18. Y. Ramesh Naidu, Y. Sharmila, Y. Nischal, V. Srinivas, V. Satyaprasad. "Study of HbA1c levels in Acute Coronary Syndrome". Journal of Evolution of Medical and Dental Sciences 2015; Vol. 4, Issue 77, September 24; Page: 13274-13278, DOI: 10.14260/jemds/2015/1909