Original Article

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Prevalence of Undiagnosed Diabetes Mellitus in Acute Coronary Syndrome Patients: A Hospital-based Study

Mohammad Ashraf[1], Sandeep Sharma[2], Aamir Rashid[3], Mohd Ismail[4], Masood Tanvir[5], Pooja Sharma[6], Aaqib Zaffar Banday[7]

[1]Lecturer, Department of Medicine, Government Medical College, Srinagar, Jammu and Kashmir, India, [2]Post-graduate Scholar, Department of Medicine, Government Medical College, Srinagar, Jammu and Kashmir, India, [3]Post Doctoral Fellow, Department of Paediatric Cardiology, Sree Chitra Tirunal Institute for Medical Sciences & Technology, Trivandrum, Kerala, India, [4]Associate Professor, Department of Medicine, Government Medical College, Srinagar, Jammu and Kashmir, India, [5]Professor, Department of Medicine, Government Medical College, Srinagar, Jammu and Kashmir, India, [6]Senior Resident, Department of Obstetrics and Gynaecology, Government Medical College, Srinagar, Jammu and Kashmir, India, [7]Post-graduate Scholar, Department of Paediatrics, Sher-I-Kashmir Institute of Medical Sciences, Srinagar, Jammu and Kashmir, India

Abstract

Introduction: Diabetes mellitus and cardiovascular disease are two widely connected entities. The prevalence of undiagnosed diabetes in and impact on survival of acute coronary syndrome (ACS) patients is largely unknown in our population.

Aims and Objectives: To study the prevalence of undiagnosed diabetes mellitus in ACS patients and study short-term all-cause mortality in different diabetic and non-diabetic subgroups - a hospital-based study.

Materials and Methods: The study was conducted in the Post-graduate Department of Medicine at Government Medical College, Srinagar, Jammu and Kashmir, India. It was prospective observational study. It included all patients, admitted as ACS in Medicine Department in between the period from April 2014 to August 2015 with a diagnosis of acute coronary syndromes which include ST-elevation myocardial infarction (STEMI), non-STEMI, and unstable angina. Patients were categorized into five groups known Type 2 diabetes mellitus, prediabetes, first time detected diabetes, non-diabetic ACS patients, and stress-induced hyperglycemia. All-cause 30 days mortality was seen in all patient taken under study.

Results: In our study, total of 693 ACS patients were enrolled. The mean age of patients was 61.20 ± 11.69 years. Males predominated in comparison to females with 4:1 ratio. 102 (14.7%) had undiagnosed (first time detected) diabetes. Diabetic and 1st time detected diabetic had double the mortality as compared to the normal and pre-diabetic group (10.8%, 8.8% vs. 5.8%).

Conclusion: Undiagnosed diabetes in patients with ACS is not uncommon in our population. Diabetic status profoundly affects the short-term mortality of ACS patients.

Key words: Acute coronary syndrome, Kashmiri population, Undiagnosed diabetes

INTRODUCTION

Diabetes mellitus (diabetes) and cardiovascular disease (CVD) are two widely interconnected entities.[1] The Euro Heart Survey on diabetes and the heart[1] indicates not only a high prevalence of diabetes but also the high rates of undiagnosed diabetes or pre-diabetic states such as impaired glucose tolerance or impaired fasting glucose in patients with stable or unstable coronary heart disease (CHD). With CHD ranking as the number one cause of death worldwide[2] with diabetes increasing by two to three times the risk of CHD[3] and with diabetes and the often preceding metabolic syndrome dramatically increasing their prevalence in Europe over the past 20 years, diabetologists and cardiologists have started to join their forces to improve the management of the millions of patients suffering

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Corresponding Author: Dr. Aamir Rashid, House No. 8, LD Colony, Rawalpora, Srinagar - 190 005, Jammu and Kashmir, India. Mobile: +91-8714809854. E-mail aamirrashid11@yahoo.co.in

from both diseases.[4] More than 18 million people in the United States have diabetes mellitus, and approximately 35% of the population is pre-diabetic.[5] More importantly, another 7 million Americans have undiagnosed diabetes and are at high risk of developing diabetic complications including CVD.[6]

Acute coronary syndrome (ACS) consists of three entities: (1) ST-segment elevated myocardial infarction (STEMI). (2) Non-ST-segment elevated myocardial infarction (NSTEMI). (3) Unstable angina (UA). In addition to being a risk factor for the development of coronary disease, diabetes influences outcomes following ACS. GUSTO Trial,[7] OASIS registry,[8] and GRACE registry observed an increased rate of post-MI complications and mortality among patients with diabetes compared with patients without diabetes.

Increased risk for subsequent adverse cardiac events in diabetic ACS patients may be explained by the observation that diabetic patients often have multiple comorbidities and tend to be hospitalized later after the onset of ACS symptoms.[9] Mechanistically, diabetic patients have reduced endothelium-dependent vasodilation and increased platelet reactivity with blunted response to antithrombotic therapy that may contribute to the development of ACS as well as post-ACS complications.[10] Furthermore, pathophysiological mechanisms involved with previously undiagnosed diabetes or prediabetes (such as impaired endothelial function and increased oxidative stress at the vessel wall leading to activation of platelets, inflammation, and thrombosis) might be affected more severely by the combination of hyperglycemia and ACS than has been observed in patients with known diabetes.[11,12]

Diabetes mellitus is associated with an increased risk of cardiovascular morbidity and mortality.[13,14] Findings of a meta-regression analysis suggest that even blood glucose levels below the threshold for diabetes are related to raised cardiovascular risk.[15] Patients with a longer duration of diabetes more frequently show signs of diabetic neuropathy that can result in atypical symptoms during MI. Thus, diagnosis of an ACS is more difficult in these patients and initiation of adequate therapy is often delayed.[15] Among patients with acute MI (AMI), diabetes mellitus is associated with higher mortality rates, both in-hospital[16] and during long-term follow-up.[16,17] This is the case across the whole spectrum of ACS.[18] In that study, ACS patients with diabetes had a higher risk of both death and re-infarction at 30 days than those without diabetes, and the rates of death or reinfarction at 6 months remained higher in the diabetic group, whether they presented with STEMI or NSTEMI. High blood glucose levels in patients admitted for ACS/AMI are common and are associated with an increased risk of death in both patients with diabetes[1,19-23] and patients without diabetes. Admission hyperglycemia is an even stronger predictor for mortality in patients without a medical history of diabetes.[19] The studies conducted earlier determine the correlation of diabetes with ACS, but the aim of our study is to determine the prevalence of undiagnosed diabetes in patient with ACS and to measure 30 days mortality among the patient with undiagnosed diabetes as compared to normal glycemic and known diabetic patients.

Aims and Objectives

To study the prevalence of undiagnosed diabetes mellitus in ACS patients and study short-term all-cause mortality in different diabetic and non-diabetic subgroups - a hospital-based study.

MATERIALS AND METHODS

The study was conducted in the Post-graduate Department of Medicine at Government Medical College, Srinagar, Jammu and Kashmir, India. It was prospective observational study. It included all patients, admitted as ACS (STEMI, NSETMI, UA) in medicine department in between the period from April 2014 to August 2015 with a diagnosis of acute coronary syndromes which include STEMI, NSTEMI, and UA. Patients were categorized into five groups: (1) ACS with known Type 2 diabetes mellitus (T2DM) (hemoglobin A1c [HbA1c] level ≥6.5 and fasting blood glucose values ≥126 mg/dl for all patients) or use of glucose-lowering drugs at admission). (2) ACS with prediabetes (fasting blood sugar: 100-125, HbA1c: 5.7-6.4). (3) ACS with first time detected diabetes/undiagnosed T2DM (fasting glucose ≥126 mg/dL or HbA1c ≥6.5% with no previous diabetes history). (4) Non-diabetic ACS patients (fasting glucose <100 mg/dl, HbA1c <5.7). (5) Stress-induced hyperglycemia (fasting glucose >126 mg/dl, HbA1c level <5.7). All-cause 30 days mortality was seen in all patient taken under study.

Inclusion Criteria

All adults ACS patients of either sex.

Exclusion Criteria

ACS due to substance abuse.

OBSERVATION AND RESULTS

In our study, total of 693 ACS patients were enrolled. The distribution of various patients as per blood sugar status is shown in Table 1 and Figure 1. The mean age of patients was 61.20 ± 11.69 years. The mean age was comparable in various subgroups as shown in Table 2. Males predominated

in comparison to females with 4:1 ratio. The sex distribution is shown in Table 3. 102 (14.7%) had undiagnosed (first time detected) diabetes. Of various categories of ACS, STEMI was the most common. The distribution of types of ACS among various subgroups is shown in Table 4. First time detected diabetics had higher mean blood sugar (fasting) and HbA1c as compared to the diabetics as shown in Tables 5 and 6. Multi-vessel disease was more prevalent in diabetic and first time detected diabetic patients as shown in Table 7. Diabetic and first time detected diabetic come in more advanced Killip class (2-4) as a shown in Table 8. Diabetic and 1st time detected diabetic had double the mortality as compared to the normal and pre-diabetic group as shown in Table 9 and Figure 2.

Table 1: Distribution of ACS patients according to diabetic status

ACS	Number of patients (%)
Normal	313 (45.3)
Pre-diabetic	54 (7.7)
Diabetic	195 (28.2)
1st time detected diabetes	102 (14.7)
Stress-induced hyperglycemia	29 (4.1)

ACS: Acute coronary syndrome

Table 2: Age (mean) distribution of ACS patients

Age	*N*	Mean±SD	Minimum-maximum	*P* value
Normal	313	60.30±12.39	32-90	0.124
Pre-diabetic	54	60.33±12.20	35-85	
Diabetic	195	62.72±11.93	35-85	
1st time detected diabetes	102	61.70±13.69	40-85	
Stress-induced hyperglycemia	29	57.72±10.13	40-85	

ACS: Acute coronary syndrome, SD: Standard deviation

Table 3: Comparison of sex distribution in ACS patients

ACS category	*N* (%)			*P* value
	Male	Female	Total	
Normal	247 (78.9)	66 (21.1)	313 (100)	0.274
Pre-diabetic	36 (66.7)	18 (33.3)	54 (100)	
Diabetic	144 (73.8)	51 (26.2)	195 (100)	
1st time detected diabetes	74 (72.5)	28 (27.5)	102 (100)	
Stress-induced hyperglycemia	21 (72.4)	8 (27.6)	29 (100)	

ACS: Acute coronary syndrome

Table 4: ACS category

ACS category	*N* (%)				*P* value
	STEMI	NSTEMI	Unstable angina	Total	
Normal	220 (70.3)	81 (25.9)	12 (3.8)	313 (100)	0.002
Pre-diabetic	33 (61.1)	18 (33.3)	3 (5.6)	54 (100)	
Diabetic	114 (58.5)	72 (36.9)	9 (4.6)	195 (100)	
1st time detected diabetes	54 (52.9)	74 (72.5)	12 (11.8)	102 (100)	
Stress-induced hyperglycemia	24 (82.8)	21 (72.4)	0 (0.0)	29 (100)	

ACS: Acute coronary syndrome, STEMI: ST-elevation myocardial infarction, NSTEMI: Non-ST-elevation myocardial infarction

DISCUSSION

The increased risk of cardiovascular morbidity and mortality in diabetes mellitus has been validated in my studies.[13,24] Proposed mechanisms include platelets reactivity through variety of mechanisms[25,26] and endothelial dysfunction leading to decreased coronary reserve and increased platelet agreeability.[27] Diabetes mellitus can become the first time manifested in patients who develop ACS.

In our study, total of 693 ACS patients were enrolled. 102 (14.7%) had undiagnosed (first time detected) diabetes

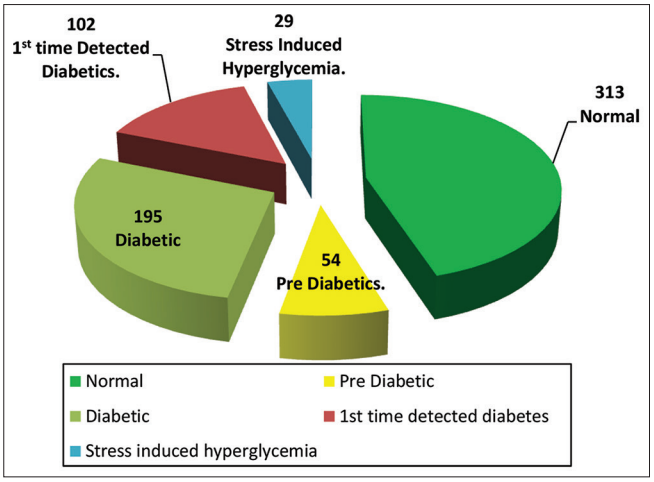

Figure 1: Patient population according to glycemic status

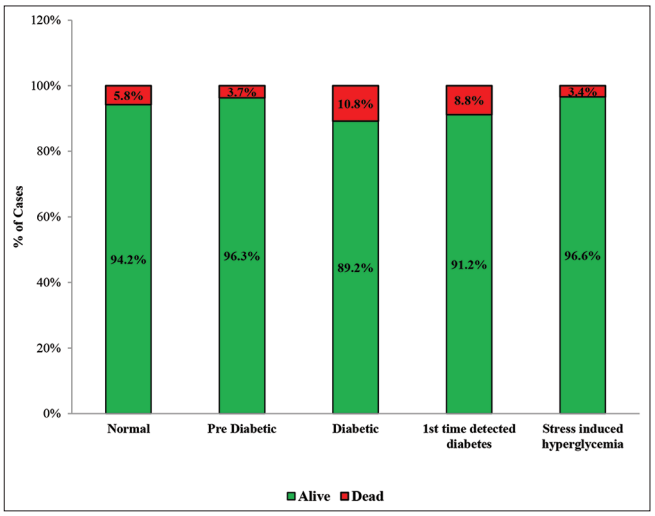

Figure 2: Comparison of 30 days mortality

Table 5: Comparison of mean blood sugar fasting among groups

Normal	Pre-diabetic	Diabetic	1st time detected diabetes	Stress-induced hyperglycemia	*P* value
87.52±6.73	115.55±5.01	196.04±39.06	227.21±48.16	162±30	p<0.001

Table 6: Comparison of Mean Hba1c among groups

Normal	Pre-diabetic	Diabetic	1st time detected hyperglycemia	Stress-induced hyperglycemia	*P* value
5.2±0.00	5.97±0.125	8.74±1.05	9.43±0.94	5.19±0.22	<0.001

Table 7: Coronary involvement in different glycemic groups

CAG	Normal (%)	Pre-diabetic (%)	Diabetic (%)	1st time detected diabetes (%)	Stress-induced hyperglycemia (%)
Single vessel disease	68.4	59.3	29.2	49.0	55.2
Double vessel disease	24.0	37.0	58.4	45.1	20.7
Triple vessel disease	7.7	3.7	15.4	5.9	24.1

CAG: Coronary Angiogram

Table 8: Killip class comparison

Killip class	Normal (%)	Pre-diabetic (%)	Diabetic (%)	1st time detected diabetes (%)	Stress-induced hyperglycemia (%)
1	61.0	53.7	34.5	52.0	41.4
2	26.5	25.9	29.2	24.5	44.8
3	8.6	16.7	32.3	20.6	10.3
4	3.8	3.7	3.1	2.9	3.4

Table 9: Comparison of 30 days mortality

30 days mortality	Normal (%)	Pre-diabetic (%)	Diabetic (%)	1st time detected diabetes (%)	Stress-induced hyperglycemia (%)
Alive	94.2	96.3	89.2	91.2	96.6
Dead	5.8	3.7	10.8	8.8	3.4

which was consistent with studies of Roberto *et al.* (2013), Abdullatef *et al.* (2013), and Conaway *et al.* (2005).

In our study, all-cause 30 days mortality in known diabetic ACS patients was 10.8% and those of first time detected diabetic ACS patients was 8.8%, which is almost double of the normal glycemic ACS patients (5.8%). In patients with prediabetes, the mortality was 3.7% and that of stress-induced hyperglycemia was 3.4%, which was comparable with normal glycemic patients. Although many studies have shown hyperglycemia as an independent risk factor for mortality in ACS, Aleksandar *et al.* (2012) in his study concluded that stress-induced hyperglycemia has higher mortality, similar results could not be reproduced in our study because of small number of patients having stress-induced hyperglycemia. Our study concluded that diabetic status has a significant impact on short-term (30 days) mortality among ACS patients. Our study results were consistent with a study from Donahoe *et al.* (2007) showing mortality at 30 days was significantly higher among patients with diabetes than without diabetes presenting with STEMI 8.5% versus 5.4%. Giraldez *et al.* (2013) showed that all-cause mortality at 30 days in NSTEMI patients with known diabetes was 3.7% and for undiagnosed diabetes was 3.6% as compared to group with normal glycemic status, which was 1.8% thus mortality was almost double in diabetic and undiagnosed group and pre-diabetic group equaled that of normal population.

As CREATE-ECLA study clearly demonstrated that elevated glucose at hospital admission was a predictor of worse outcomes among non-diabetic patients but not among diabetic patients but early strict control of sugars can reduce early mortality as our study showed that in the undiagnosed group, early glycemic control did not let mortality exceed to that belonging to the diabetic group.

The prevalence of stress-induced hyperglycemia increased to 82.8% in patients with STEMI, which is consistent with Timmer *et al.* showing hyperglycemia in 70% of patients with STEMI patients. Another study by Abdullatef *et al.* (2013) showed stress-induced hyperglycemia in acute STEMI was 66.7%. In patients with UA, hyperglycemia was not documented as our sample size for this group was small to comment. Similarly, the frequency of first time

detected diabetes was more in STEMI 52.9% compared to NSTEMI 35.9% and UA 11.8%. There is no literature, which shows the frequency of different ACS groups, but overall prevalence of STEMI-ACS is more in our study which is consistent with Nuti *et al.* (2014) showing higher prevalence of STEMI (86%) in Chinese population, and the prevalence of NSTEMI is more in diabetic group as compared with patients having normal sugars.

Diabetic status had a significant impact on morbidity status of the patients with ACS in our study. Patients with diabetes and first time detected diabetes had more number of patients in advanced Killip class (Killip class 3-32.3% and 20.6%, respectively) compared to patients with normal blood sugar (8.6%). A number of patients in Killip class 4 were comparable in all groups; no logical inference can be made from this data as number of patients presenting in Killip class 4 were very less. Shehab *et al.* (2012) in his study showed higher Killip class (2-4) belonged to the diabetic group (27.3%). Another study Sean *et al.* showed higher Killip class (2-4) in diabetes group 13.6% as compared to the non-diabetic group about 9.6%.

In our study, we concluded that male sex is a risk factor for ACS irrespective of glycemic status. Male to female ratio in our study was 4:1 in all groups approximately. Our results are consistent with Sharma *et al.* (2014), in which male population in ACS was 79.5%.

In our study, the prevalence of multi-vessel disease (double vessel disease and triple vessel disease) is almost double in diabetic, newly detected diabetes (63.8%, 51%) as compared to normal glycemic status group, in which double vessel disease plus triple vessel disease is 31.7% which is consistent with study conducted by Donahoe *et al.* (2007) which showed that in diabetic group multi-vessel disease is 62% as compared to non-diabetic group in which multi-vessel disease is approximately 48%. Another study by Dubey *et al.* (2013) showed that diabetic patients had more multi-vessel disease 64.2%. Another study by Hegde *et al.* (2014) showed that multi-vessel disease is more common among diabetes as compared to the normal glycemic group (44% vs. 16%).

Mean HbA1c level among first time detected diabetes was more as compared to known diabetic groups in our study. Mean HbA1c level among first time detected diabetes was 9.43 ± 0.94 consistent with Abdullatef *et al.* (2013) which shows mean HbA1c among first time detected diabetes was 8.7 ± 1.9. The higher HbA1c level at presentation was associated with high risk of ACS as shown by Narayana *et al.* (2015), so undiagnosed population are more prone to develop acute coronary events and worse outcomes.

CONCLUSION

Undiagnosed diabetes in patients with ACS is not uncommon in our population. Diabetic status profoundly affects the short-term mortality of ACS patients.

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