Assessment of demographics, treatment strategies, and evidence-based medicine use among diabetic and non-diabetic patients with acute coronary syndrome: A cohort study

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ABSTRACT

Objectives: To evaluate and compare clinical and epidemiological characteristics, treatment strategies, and utilization of evidence-based medicine (EBM) among coronary artery disease (CAD) patients with or without diabetes. **Materials and Methods:** Prospective observational cohort study from a tertiary care hospital in India among patients with CAD (myocardial infarction, unstable angina, or chronic stable angina). Data included demographic information, vital signs, personal particulars, risk factors for CAD, treatment strategies, and discharge medications. We evaluated epidemiologic characteristics and treatment strategies for diabetic and non-diabetic patients. **Results:** Of 1,073 patients who underwent angiography, 960 patients (30% diabetic) had CAD. Proportion of hypertensive patients was higher among diabetic patients (58 vs 35% non-diabetic, $P < 0.001$). Similar proportion of patients received medical management in diabetic vs non-diabetic CAD patients (35 vs 34%, $P = 0.091$); in diabetics the use of surgical procedure was higher (22 vs 17%, $P = 0.0230$) than interventional strategy (percutaneous transluminal coronary angioplasty, 43 vs 49%, $P = 0.0445$). Key medications (antiplatelet agents, angiotensin-converting enzyme inhibitor (ACEI)/angiotensin receptor blocker (ARB), beta-blockers, and ahtihyperlipidemic agents) were prescribed in 95, 53/12, 67, and 91% diabetic ($n = $ 252) and 96, 51/8, 67, and 94% non-diabetic ($n = 673$) patients, respectively on discharge. **Conclusions:** Clustering of several risk factors at presentation, typically diabetes and hypertension, is common in CAD patients. Though diabetic patients are managed more conservatively, utilization of EBM for diabetic and non-diabetic patients is consistent with the recommendations.

Key words: Acute coronary syndrome, coronary artery disease, diabetes, evidence-based medicine

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INTRODUCTION

Cardiovascular disease (CVD), a leading cause of death in India,[1] leads to premature death, disability, and financial catastrophe due to high out-of-pocket expenditures for acute cardiovascular care.[2] Diabetes has been recognized as an independent risk factor associated with increased

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mortality during hospitalization, short- and long-term follow-up among patients with acute coronary syndrome (ACS).[3-6]

It has also been reported that patients with ACS require secondary prevention and pharmacological therapy could play crucial role following an acute event.[7] A set of medicines has been recognized and recommended by the treatment guidelines based on the findings of major clinical trials to prevent death and secondary complications after ACS: Angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) as appropriate, beta blockers, lipid-lowering medications (statins), and aspirin.[7,8] The studies have demonstrated that, in eligible patients with ACS, pertinent prescribing of these evidence-based medicine (EBM) reduces morbidity and mortality.[9] Diabetes also influences outcomes following ACS, and therefore, secondary prevention in diabetic individuals is more critical.

In light of this background, the present study was focused to (1) assess and compare the baseline clinical characteristics of ACS patients presented with or without diabetes; and (2) assess and compare interventional strategies for ACS and current trend of utilization of key EBM at discharge for ACS patients presented with or without diabetes.

MATERIALS AND METHODS

This was a prospective observational study conducted between January 2011 and January 2012 at a tertiary care hospital from Jaipur (India).

Inclusion criteria
Consecutive patients of both the genders, age ≥18 years, admitted at cardiac intensive care unit (ICU) of a tertiary care hospital were considered.

Patients who underwent coronary angiography (CAG), and diagnosed as myocardial infarction (MI), unstable angina, or chronic stable angina on final diagnosis using standard definitions, were considered to have coronary artery disease (CAD).[10] Patients were identified as known case of CAD on the basis of at least one of the following criteria:[7] History of documented angina/infarction, ECG findings suggestive of silent MI, a positive treadmill test or stress echocardiography-highly suggestive of silent MI, history of angina/MI with ECG confirmation, or angiographic evidence of CAD or history of PTCA/CABG. Patients were identified as diabetics if they met any of the following criteria: At least one prescription of anti-diabetic drug or monitoring supply; or elevated HbA1C level. Patients with history of hypertension and/or on treatment for hypertension or at least 2 elevated BP measurements were considered hypertensive.

Exclusion criteria
Patients who did not undergo CAG, diagnosed with normal coronary artery after CAG and/or diagnosed with atypical chest pain on diagnosis were excluded.

Discharge summaries of patients were reviewed to collect demographic information, vital signs, and details of other risk factors for CAD such as presence of diabetes, hypertension, and prior history of CAD. Information pertaining treatment strategies (percutaneous transluminal coronary angioplasty (PTCA), coronary artery bypass grafting (CABG), or medical management) were collected. For assessment of treatment strategy: If intervention procedure or surgery was performed in-house or recommended on discharge, then patients were assigned in PTCA (performed or recommended) or CABG (performed or recommended) respectively; all other patients were considered for medical management.

For all the patients medications prescribed on discharge were collected from hospital discharge summary. Beta-blockers were defined as all beta-blockers available as single or combination products; aspirin, prescribed either as single-ingredient aspirin formulations or combination drugs containing aspirin (excluding those medications indicated for acute analgesia).

We compared demographics, medical history, and clinical presentation for all CAD patients presented with or without diabetes. Also, we present a subgroup analysis to compare treatment strategies and utilization of for utilization of key EBM (ACEIs/ARBs, beta-blockers, statins, and aspirin) as per current guidelines among diabetic or non-diabetic ACS patients.[7]

Statistical analysis
The statistical tests were performed using Statistical Package for Social Sciences (SPSS; version 17.0). Differences in demographic information, medical history, and clinical characteristics among the comparison groups were examined using Chi-square (χ^2) test and Student's t-test for discrete and categorical variables, respectively. $P < 0.05$ in either case was considered as statistically significant; whereas, $P < 0.001$ was considered as highly significant.

RESULTS

A total of 1,166 consecutive patients admitted in cardiac ICU between January 2011 and January 2012 were considered. Of these 1,073 patients underwent CAG, of which 113 (10.5%) patients had atypical chest pain or normal coronaries as final diagnosis, leaving 960 eligible patients with CAD for the further analysis [Figure 1].

Demographics, medical history, and clinical presentation

Approximately one-third patients (27.1%) were diabetic with majority (around 80%) male patients [Table 1]. Proportion of hypertensive patients among diabetic subgroup was found to be significantly higher as compared to non-diabetics (57.7 vs 34.9%, $P < 0.001$). The difference between mean systolic BP for diabetics and non-diabetics was found to be statistically significant ($P = 0.037$). Around 40% of all patients with CAD had single vessel disease (SVD) on CAG. More than one-third diabetic patients (35%) had triple vessel disease (TVD) on CAG, whereas the proportion was only 24% among non-diabetic patients. Overall 3 to 4% patients were diagnosed with chronic stable angina on final diagnosis. For both, diabetic and non-diabetic patients more than 60% patients were diagnosed to have unstable angina as final diagnosis. The proportion of patients diagnosed with ST-elevation MI was higher in diabetic patients (9.5% (seven out of 74 MI patients) vs 8.3% (24 out of 289 MI patients) for non-diabetic patients).

Treatment strategy and EBM use for ACS patients

Of 925 ACS patients, 252 (27%) patients had diabetes. Thirty-five percent of diabetic and non-diabetic patients were put on medical management [Figure 2]. For revascularization, PTCA was preferred for almost half of the non-diabetic patients (49 vs 43% diabetic patients, $P = 0.045$); while CABG was preferred for 17% non-diabetic patients vs 22% diabetic patients ($P = 0.023$).

Overall, antiplatelet agent, ACEI/ARB, beta-blocker, and antihyperlipidemic agents were prescribed in 95.7, 51.9/9.0, 66.9, and 93.2%, respectively for all patients with CAD at discharge. Significantly higher proportion of ACS patients with diabetes were prescribed ARBs compared to non-diabetic patients (12 vs 8%, $P = 0.030$) [Table 2].
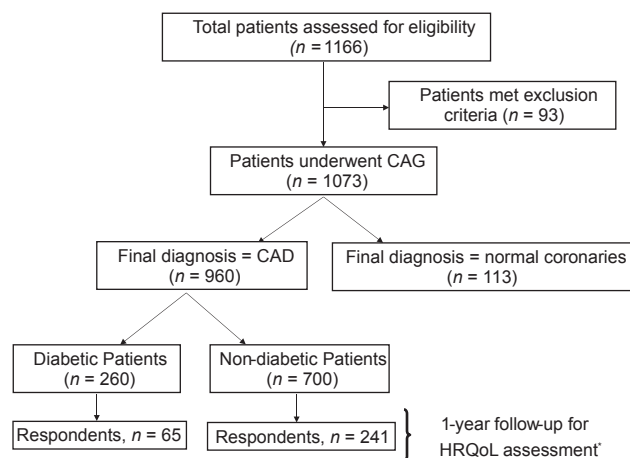
Figure 1: Study cohorts and patient flow.
*EQ-5D questionnaire, a standardized generic instrument, was administered at 1-year follow-up via telephonic interview to assess HRQoL (results are being reported separately). CAD = Coronary artery disease, CAG = coronary angiography, HRQoL = Health-related quality of life

DISCUSSION

Multiple risk factors and CAD

CVD remains an important non-communicable disease (NCD) globally. India is predicted to bear the greatest burden of

Table 1: Demographics, medical history, clinical presentation, and angiography results

	All patients	Patients with diabetes	Patients without diabetes	P value
N	960	260	700	
Gender, male	757 (78.9)	202 (77.7)	555 (79.3)	0.591
Age, years	58.4±10.1	59.6±9.2	57.9±11.3	0.037
Blood pressure (mmHg)				
Systolic	129.3±19.9	131.4±18.7	128.5±20.3	0.034
Diastolic	77.8±10.8	78.3±9.3	77.6±10.4	0.321
Medical history				
Diabetes	260 (27.1)	-	-	
Hypertension	394 (41.0)	150 (57.7)	244 (34.9)	<0.001
Known case of CAD	264 (27.5)	71 (27.3)	193 (27.6)	0.935
Smoking	148 (15.4)	37 (14.2)	111 (15.9)	<0.001
Prior CHF	157 (26.7)	38 (26.0)	119 (27.0)	0.821
Coronary angiography results (disease)				
Single vessel	238 (42.0)	52 (37.1)	186 (43.7)	0.029
Double vessel	129 (22.8)	32 (22.9)	97 (22.8)	
Triple vessel	150 (26.5)	49 (35.0%)	101 (23.7)	
Minimal/ noncritical	49 (8.7)	7 (5.0)	42 (9.9)	
Final diagnosis				
ACS*	925 (96.4)	252 (96.9)	673 (96.1)	
Chronic stable angina	35 (3.6)	8 (3.1)	27 (3.9)	

Data are number (%) or mean±standard deviation. *P* value for comparison between patients with and without diabetes. ACS=Acute coronary syndrome, CABG=Coronary artery bypass grafting, CAD=Coronary artery disease, CHF=Congestive heart failure, DM=Diabetes, PTCA=Percutaneous transluminal coronary angioplasty, *Myocardial infarction or unstable angina
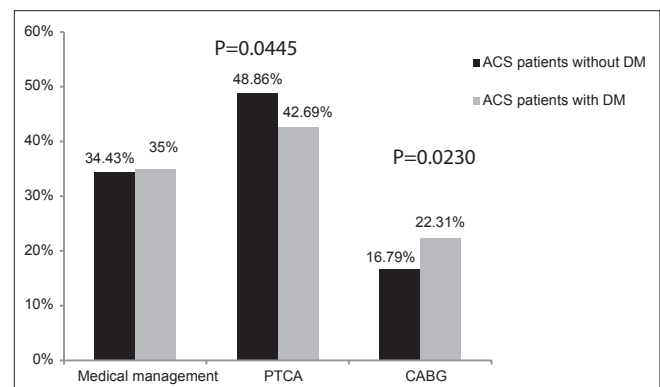
Figure 2: Comparison of treatment strategies among diabetic and non-diabetic ACS patients. ACS = Acute coronary syndrome, CABG = Coronary artery bypass grafting, DM = Diabetes mellitus, PTCA = Percutaneous transluminal coronary angioplasty

Table 2: Key medications prescribed on discharge

Medication	All ACS patients	ACS patients with diabetes	ACS patients without diabetes	P value
N	925	252	673	
Antiplatelet agent	885 (95.7)	239 (94.8)	646 (96.0)	0.445
ACEI	480 (51.9)	134 (53.2)	346 (51.4)	0.633
ARB	83 (9.0)	31 (12.3)	52 (7.7)	0.030
Beta-blocker	619 (66.9)	168 (66.7)	451 (67.0)	0.921
Antihyperlipidemic agent	862 (93.2)	230 (91.3)	632 (93.9)	0.156

Data are number (%). ACS=Acute coronary syndrome, ACEI=Angiotensin-converting enzyme inhibitor, ARB=Angiotensin receptor blocker

NCDs and its clearly evident from the fact that burden of CAD have reached epidemic proportions in Indian population.[11,12] The epidemiological studies from various parts of India have reported rising trends and a high burden in the levels of conventional risk factors for CAD including diabetes and hypertension.[13-15] The prevalence of diabetes among CAD patients has been greatly varying across the studies for Indian population over a period of time. Earlier studies reported prevalence of diabetes from 5 to 20% in patients with CAD.[16,17] We observed that one-third of total patients admitted with CAD had diabetes. This finding is quite comparable with similar studies.[18-20] Diabetic patients without any history of heart disease bear the same risk for future cardiovascular death as non-diabetic patients with a history of MI.[21] These observations, plus the fact that the prevalence of diabetes increases the risk of cardiovascular outcomes and mortality in patients with established CAD[3-5] render diabetes as a considerably important cardiovascular risk factor following acute event.

Another important finding of our study was higher prevalence of conventional comorbidities in patients with CAD who had diabetes. Typically CAD patients with diabetes had significantly higher prevalence of hypertension. Overall the higher prevalence of diabetes and hypertension as reported in the recent studies may be attributed the comparatively higher development[22] and increasing prevalence of conventional risk factors for epidemic of CAD in India. Coexistence of diabetes and hypertension, which is generally observed in CAD patients and also seen in the present study, is important multiplicative risk factor for macro- and microvascular disease, resulting in increased morbidity and mortality.[23] The worse prognosis in CAD patients with ACS from India, as reported in CREATE registry, at least in part, could be attributed to clustering of multiple conventional risk factors.[18]

Treatment strategies−diabetics vs non-diabetics

We observed that surgery was more frequently preferred in diabetic patients diagnosed with ACS. This trend is not surprising considering the fact that in present study population proportion of patients with advanced CAD (e.g., TVD) was significantly higher in diabetic subgroup.

Selection of appropriate therapeutic management for diabetic patients following acute coronary event is critical. It has been established that use of surgery is advantageous over the interventional procedure for diabetic patients.[24,25] For non-diabetic patients, angioplasty remained standard of care if the revascularization was needed for an acute event. This strategy is also aligned with the current guidelines, which recommend coronary artery revascularization with coronary stents for the patients presented with a minimum stenosis diameter of <20% (as visually assessed by angiography).[26,27] Further, patients with noncritical lesion were managed conservatively and were put on medical management from both diabetic and non-diabetic patients in present study cohort.

EBM for post-ACS period

As a consequence of high prevalence and being a major cause of mortality and morbidity for patients with CVD, the effective management of ACS has been challenging. To provide standards for diagnosis, treatment, and to optimize patient outcomes after ACS, the clinical practice guidelines have been developed.[21] Since availability of data on efficacy of various therapies and clinical outcomes constitute the primary basis for the recommendations of guidelines, the treatment of ACS is repeatedly evolving. Despite clear and consistent evidence, secondary prevention medical therapies are underutilized in patients receiving conventional care following ACS and may contribute to substantial adverse outcomes following an acute event.[9,28] Dissemination of new information and its implementation into practice may differ and the variation in the utilization of the EBM recommended by the guidelines is quite possible.

Published data from the registries for ACS patients from India, CREATE and Kerala ACS registry, have reported relatively lower utilization of these key medications.[18,19] However, head-to-head comparison with these findings suggests reasonably higher utilization of EBM in our study population compared to the local registries. For instance, antiplatelet agent was prescribed in 52% ACS patients in national CREATE registry[18] versus 96% of patients in our study. Similarly, while comparing our findings with Kerala ACS registry, we found that adherence to guideline was fairly high in terms of ACE/ARB use at discharge in our study (60 vs 25% patients from Kerala ACS registry).[19] Although, use of beta-blockers was similar for the present study (67%), CREATE registry (59%)[18] and Kerala ACS registry (63%),[19] use of statin was highest in patients from CREATE registry (98%). In global context, it is worth comparing our findings with the international registry. The comparison of our study with the European Action

on Secondary Prevention through Intervention to Reduce Events (EuroASPIRE)-III survey indicate comparable findings for the use of antiplatelet agent (96% patients in our study vs 93% patients in EuroASPIRE III) and antihyperlipidemic agent (93 vs 89%); but indicates scope for improvement for the use of ACEI/ARB (60 vs 74%) and beta-blocker (67 vs 89%) for secondary prevention in patients with CAD.[28] Overall, the findings demonstrate the awareness on utilization of EBM and confirm adherence in regional practice with little variation. It also suggests that care offered by a specialized physician definitely provides a superior adherence to consensus guidelines to serve patients better. It has been claimed that along with the awareness about the treatment guidelines, the wide availability and the relatively low cost of generic drugs is also equally important for the adherence to the guidelines in India.[18]

Moreover, the comparison for utilization of key medications on discharge among ACS patients with and without diabetes was done. Our findings suggest that prescription of different key EBM at discharge for secondary prevention was not different for the diabetic and non-diabetic ACS patients in our study cohort; except for use of ARB therapy. More frequent use of ARBs in diabetic patients can be explained by taking into account the fact that significantly higher proportion of diabetic patients were hypertensive and ARBs have shown beneficial effect in such population.[29]

Limitations

Though perhaps this is the first hospital-based study comparing baseline characteristics and utilization of EBM among diabetic and non-diabetic patients with ACS from India; while interpreting the results of this study, certain limitations have to be taken into consideration: First, because of the observational study design, no information regarding missing data can be provided. We neither examine the effects of other potential confounders nor assessed outcomes, which could, otherwise have stated the results in terms of outcomes. The diagnosis of diabetes was based on the review of medical records alone; no information was available about diabetes duration or adequacy of control, and patients with undiagnosed diabetes may have been misclassified.

CONCLUSIONS

Diabetes is highly prevalent among patients with CAD and the worse prognosis in such patients from India may be attributed to clustering of several cardiovascular risk factors at presentation (typically diabetes and hypertension). It is observed that the diabetic patients presented with ACS are being managed more frequently with surgical therapy (CABG) compared to non-diabetic counterpart. Utilization of EBM for both diabetic and non-diabetic ACS patients is consistent with the guidelines and recommendations and is not differing among the diabetic and non-diabetic population; except for the higher use of ARB therapy in diabetic patients. This observational study might serve as a maneuver to the current practice and highlights the awareness on the adherence to the recommendations from the guidelines. Nevertheless, outcome studies should be planned to collect more evidence-based treatment records in large population to assess and direct the management of ACS patients with diabetes.

ACKNOWLEDGMENT

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