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ANTIPLATELET ADHERENCE AT SIX MONTHS AFTER PRIMARY PERCUTANEOUS CORONARY INTERVENTION PERFORMED AT A RURAL SATELLITE CENTER

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Contribution
SFM conceived the idea and designed the study. Data collection and manuscript writing was done by SFM, JUR, JAS, RAP, and MK. All the authors contributed equally to the submitted manuscript.

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ABSTRACT

Objectives: To determine the frequency of dual antiplatelet adherence at six months after primary PCI performed at rural satellite center.

Methodology: This was a descriptive study conducted at Rural Satellite Center (Larkana) of the National Institute of Cardiovascular Disease, Pakistan from October 2017 to March 2018. Patients of either gender between the ages of 20-80 years who underwent primary Percutaneous Coronary Intervention (PCI) at least six months ago were included in this study. Compliance with antiplatelet therapy was assessed by interview at follow up. Patients were labeled as compliant if they took both aspirin and clopidogrel at the time of follow up at six months.

Results: Of the total of 241 patients, 208 (86.3%) were male. The mean age of the patients was 53.37 ± 11.07 years. Hypertension was present in 170 (70.5%), 101 (41.9%) were diabetic, 104 (43.2%) were smokers and 18 (7.5%) were obese. The most common culprit artery was left anterior descending (LAD) artery, 149 (61,8%), followed by the right coronary artery (RCA) in 83 (34.4%) patients. Nearly 12.1% (31) patients had the three-vessel disease, whereas, 53.9% (130) patients had single-vessel involved. Compliance with antiplatelet therapy at six months was found to be 89.6%, 219 (90.9%) were compliant to aspirin while 218 (90.5%) were compliant to clopidogrel.

Conclusion: In our population, a significant number of patients (10.4%) were not compliant with dual antiplatelet therapy after six months of primary PCI. The dual antiplatelet adherence, in our population, is lower than in developed countries. Therefore, efforts should be made to increase compliance.

Keywords: ACS, Aspirin, clopidogrel, Dual antiplatelet, Myocardial infarction

INTRODUCTION

Coronary artery disease (CAD) is on the rise in developing countries.[1] It is estimated that CAD-related mortality rates will double from 1990 to 2020, due to an increase in deaths mainly from the developing world.[2] A large number of Pakistani population is suffering from CAD.[3,4] Percutaneous coronary artery intervention (PCI) is nowadays widely used procedure for both acute coronary syndrome (ACS) and stable coronary artery disease.[5] Primary PCI in ST-segment elevation myocardial infarction (STEMI) is recommended and favorable therapy in the majority of the cases. Nowadays a large number of PCI procedures are performed in developing countries. Dual antiplatelet therapy is recommended after stenting; therefore strict compliance to dual antiplatelet is necessary.[6]

However non-adherence to dual antiplatelet is still a problem. Non-adherence can be due to many reasons, one study has divided non adherence into Cessation as discontinuation (physician recommendation), interruption (for surgery) or disruption (due to non-compliance or bleeding).[7] One study conducted in Saudi Arabia and reported that still a good number of patients are not adherent to dual antiplatelet.[8]

Owing to the easy availability of PCI in developing countries financial burden of dual antiplatelet is an issue, for example in cases of ACS where some centers, like ours, may provide free of cost primary or early invasive angioplasty but the patient has to bear the cost of subsequent dual antiplatelet therapy for a prolonged time. Therefore, adherence to dual antiplatelet may be different in a predominantly lower socioeconomic setup. Secondly, the literacy rate is low in our population; many studies have found an inverse relationship between lack of knowledge and drug adherence.[9] Non-affordability and illiteracy may cause different rates of drug adherence in our population.

Therefore, this study was undertaken to determine the frequency of antiplatelet adherence in patients after primary PCI for STEMI in low socioeconomic settings. Results may highlight the magnitude of the problem, hence, a justification for corrective measures to increase drug compliance in these patients.

METHODOLOGY

This was a descriptive study conducted at a Rural Satellite Center (Larkana) of the National Institute of Cardiovascular Disease, Pakistan from October 2017 to March 2018. Patients of either gender between the ages of 20-80 years who underwent primary Percutaneous Coronary Intervention (PCI) at least six months ago were included in this study after informed consent. Patients with prior cardiac-related surgery, chronic kidney diseases (CKD), and congenital heart disease were excluded. Patients with active GI bleeding were also excluded.

Coronary angiography was performed mostly through radial as a preferred route. The procedures were performed within 90 minutes of hospital arrival for the patients who arrived hospital within 24 hours of the onset of chest pain and diagnosed with STEMI. The aim of the primary PCI procedure was to open the culprit vessel(s) and restore the TIMI (thrombolysis in myocardial infarction) III flow. The decision regarding stenting and type of stent was left on the treating consultant. In the case of hemodynamic instability PCI of the non-culprit artery was undertaken at the discretion of the consultant.

During hospitalization and after discharge, patients were prescribed with aspirin 300 mg for one month followed by 75 mg daily as a maintenance dose. Clopidogrel was advised 75 mg twice daily for one month followed by 75 mg daily as a maintenance dose. Antiplatelets were prescribed either separately or in combination according to the discretion of the consultant at the time of follow-up visit at one month. Beta-blockers, ACEI (angiotensin-converting-enzyme inhibitor), and statin were advised in different doses. At six months patients were called for a checkup. Patients who turned up for interview were asked about the compliance of different drugs and noted in proforma. Patients who were taking both antiplatelets were labeled as compliant. The primary outcome of interest was compliance with dual antiplatelet after six months of the primary percutaneous coronary intervention (PCI). And the secondary outcome was compliance with other anti-ischemic treatments like beta-blockers, Angiotensin-converting-enzyme inhibitors (ACEI), and statin.

Collected data were entered and analyzed using IBM SPSS Statistics for Windows, Version 21.0. (IBM Corp., Armonk, NY, US). Descriptive statistics such as mean ± standard deviation (SD) or median [interquartile range; IQR] or frequency and percentages were calculated appropriately. Chi-square test was applied to assess the association between outcome and baseline demographic and clinical characteristics. The calculated p-value of less than or equal to 0.05 was the significance criteria for the test.

RESULTS

Of the total of 241 patients, 208 (86.3%) were male. The mean age of the patients was 53.37 ± 11.07 years. Of the total sample, 101 (41.9%) were diabetic, hypertension was present in 170 (70.5%), 104 (43.2%) were smokers and 18 (7.5%) were obese. Baseline characters and details of occupation are given in Table 1.

The most common culprit artery was left anterior

Table 1: Demographic profile, baseline risk factors, and disease burden

Characteristics	Total (n = 271)
Age (years)	52.15 ± 10.56
Up to 40 years	39 (16.2%)
41 to 60 years	122 (50.6%)
More than 60 years	80 (33.2%)
Gender	
Male	208 (86.3%)
Female	33 (13.7%)
Risk factors	
Diabetes	101 (41.9%)
Hypertension	170 (70.5%)
Smoking	104 (43.2%)
Obesity	18 (7.5%)

descending (LAD) artery, 149 (61.8%), followed by the right coronary artery (RCA) in 83 (34.4%) patients. Nearly 12.1% (31) patients had the three-vessel disease, whereas, 53.9% (130) patients had single-vessel involved. Plain old balloon angioplasty (POBA) was done in nine (3.7%) patients and drug-eluting stent (DES) and bare-metal stent (BMS) were deployed in 51% (123) and 45.6% (110) patients respectively. Disease burden, localization of culprit lesion, and type of stent deployed during the procedure are presented in Table 2.

Table 2: Disease burden, localization of culprit lesion, and type of stent deployed during the procedure

Culprit Artery	
Left anterior descending (LAD)	149 (61.8%)
Right coronary artery (RCA)	83 (34.4%)
Circumflex artery (CX)	07 (2.9%)
Obtuse marginal (OM) branch	3 (1.2%)
Diagonal	1 (0.4%)
Number of Vessels Involved	
Single vessel disease (SVD)	130 (53.9%)
Two vessel disease (2VD)	80 (33.2%)
Three-vessel disease (3VD)	31 (12.1%)
Type of Stent Deployed	
Drug-eluting stent (DES)	123 (51%)
Bare-metal stent (BMS)	110 (45.6%)
Plain old balloon angioplasty (POBA)	09 (3.7%)

Compliance at six months was found to be 89.6%, 219 (90.9%) were compliant to aspirin while 218 (90.5%) were compliant to clopidogrel. Compliance with beta-blockers, ACEI, and statin was found to be 87.6%, 77.8% and 71.8 respectively. Compliance with dual antiplatelet and other anti-ischemic drugs are presented in Table 3.

Patients with left anterior descending artery stenting were more complaint while patients undergoing right coronary artery stenting were less complaint. Compliance rates after six months of the primary percutaneous coronary intervention (PCI) by baseline characteristics are presented in Table 4.

Table 3: compliance to dual antiplatelet and other anti-ischemic drugs

Drug Compliance	
Dual antiplatelet compliance	216 (89.6%)
Asprin	219 (90.9%)
Clopidogrel	218 (90.5%)
Other anti-ischemic drugs	
Beta Blocker	211 (87.6%)
ACE inhibitor	187 (77.6%)
Statin	173 (71.8%)

ACE = angiotensin-converting-enzyme

Table 4: compliance after six months of the primary percutaneous coronary intervention (PCI) by baseline characteristics

Characteristics	Base N	Outcome		P-value
		compliant	noncompliant	
Age				
Up to 40 years	39	35 (89.74%)	04 (10.26%)	
41 to 60 years	122	110 (90.16%)	12 (9.84%)	0.950
More than 60 years	80	71 (88.75%)	09 (11.25%)	
Gender				
Male	208	185 (88.9%)	23 (11.1%)	0.544
Female	33	31 (93.9%)	02 (6.1%)	
The culprit left anterior descending (LAD)				
Yes	149	140 (93.95%)	09 (6.04%)	0.008*
No	92	76 (82.6%)	16 (17.4%)	
Culprit right coronary artery (RCA)				
Yes	83	69 (83.13%)	14 (16.86%)	0.025*
No	158	147(93.03%)	11 (6.97%)	
Number of Vessels Involved				
Single vessel disease (SVD)	130	117 (96.58%)	13 (3.42%)	
Two vessel disease (2VD)	80	73 (91.25%)	07 (8.75%)	0.543
Three-vessel disease (3VD)	31	26 (83.87%)	05 (16.13%)	
Type of Stent Deployed				
Drug-eluting stent (DES)	123	113 (91.86%)	10 (8.14%)	
Bare-metal stent (BMS)	110	97 (88.18%)	13 (11.82%)	0.237
Plain old balloon angioplasty (POBA)	09	07 (77.77%)	02 (22.2%)	

*significant at 5% level of significance

p-values are based on Chi-Square test

DISCUSSION

Dual antiplatelet therapy is very important during the initial days of PCI.[10,11] Latest Guidelines recommend that dual

antiplatelet therapy should be continued for at least one-year in ACS patients.[12] At our center, we use drug-eluting stents (DES) for the primary PCI of most of the patients. Continuation of dual antiplatelet at least for 12 months is very necessary in case of DES implantation[13,14] otherwise the risk of stent thrombosis and in-stent restenosis (ISR) increases.[15,16]

Dual antiplatelet compliance was 90% at six months. One study from the developed world has shown almost 95% of drug compliance to dual antiplatelet after acute myocardial infarction (AMI),[17] which is much higher than our population.

Many studies from developed nations also report a higher adherence rate for long term dual antiplatelet therapy.[18-20] The reasons for higher adherence to dual antiplatelet in developed countries can be multifold. One of the possible reasons for their success may be the strict fellowship of guidelines. Their healthcare system from general practitioners to tertiary care is well organized and coordinated. General practitioners (GP's) are the backbone of the healthcare system. If GP's are aware of updated guidelines regarding dual antiplatelet therapy they can impact adherence a lot. For example, they may not stop dual antiplatelet for complications like minor dyspepsia or minor surgical procedure which can be done with minimum risk of bleeding while the patient continues to have dual antiplatelet.

Secondly, developed countries have a well-developed medical insurance system in place. On the contrary, our patients solely rely on public sector hospitals for free provision of medicines. The free provision of medicine, after a patient is discharged, is not without its own perils. Misuse of the facility is often reported in the shape of the medicine being sold to commercial pharmacy stores. Because of the lack of monitoring pharmacy stores do purchase these medicines from patients at lower rates and sale these medicines to customers. Hence free provision of medicine may not be the only solution to increase adherence. Rather a well-coordinated structure for monitoring and avoidance of misuse of the facility may give better results.

On the contrary, less compliance with dual antiplatelet in our population can be due to two main reasons, the first reason is the non-affordability of patients. Most of our patients belong to poor socioeconomic status. Our center is a public sector hospital and the initial treatment cost included PCI and medicine was provided free of cost. But after discharge, the patient had to buy medicine from his pocket and the cost of prolonged dual antiplatelet therapy is not affordable for most of our low-income classes. Therefore, the financial burden of long term dual antiplatelet is significant considering the overall economic condition of our population. The second reason may be lack of knowledge. The majority of our patients were not educated. They were expected to be less aware of complications if dual antiplatelet is stopped prematurely. Many studies have shown that poor social background and lack of education[21,22] are two important causes of drug noncompliance. In our population both of these factors are common.

Apart from non-affordability other important reasons can be disease-related. The majority of the patients presenting with STEMI had never been on chronic medications before. In most of these patients, this was the first sudden incident of health issues. PCI often provide prompt relief in symptom in these patients. After discharge as the memories of the initial shock period slowly become dimmer, patients start negligence in drug adherence. Many of these patients don't have subsequent symptoms. Lack of symptom is a major factor for drug non-adherence, as a strong urging factor for drug compliance is lost. Therefore prompt and subsequent relief of symptoms caused by primary PCI makes it difficult for them to take regular medications, which have no apparent effect on symptoms. Rather side effects of drugs can easily make them noncompliant.

CONCLUSIONS

In our study, a significant number of patients were not compliant with dual antiplatelet therapy after six months of primary PCI. The dual antiplatelet adherence, in our population, is lower than in developed countries. Therefore, efforts should be made either by free of cost provision of medicine or increasing patient education to increase compliance.

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