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3 **Angiographic profile and outcomes of Pakistani women with ST**  
4 **elevation myocardial infarction**

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12  
13 **Abstract**

14 **Objective:** To evaluate the angiographic profile and outcome of primary  
15 percutaneous coronary intervention in female patients with acute myocardial  
16 infarction.

17 **Method:** The cross-sectional study was conducted at the National Institute of  
18 Cardiovascular Diseases, Karachi, from July 1, 2017, to March 31, 2018, and  
19 comprised female patients presenting with acute myocardial infarction who  
20 underwent primary percutaneous coronary intervention and got enrolled in the  
21 National Cardiovascular Data Registry. Follow-up calls were made 1 year post-  
22 intervention and outcomes were noted. Data was analysed using SPSS 21.

23 **Results:** Of the 522 female patients with a mean age of  $57.41 \pm 11.14$  years,  
24 334(64%) were hypertensive, 202(38.7%) diabetic, 16(3.1%) had a family  
25 history of coronary artery disease, and 9(1.7%) were smokers. Single-vessel disease  
26 was observed in 183(35.1%) patients, and three-vessel disease in 144(27.6%).  
27 Post-procedure thrombolysis in myocardial infarction flow (0-II) was observed in 29(5.6%)  
28 patients, bleeding in 2(0.4%), and in-hospital mortality was in 22(4.2%).

29 Telephonic follow-up was successfully conducted in 436(87.5%) of the  
30 discharged patients, and, of them 15(3.4%) had expired and recurrence was  
31 reported by 10(2.3%) patients and 8(80%) of them underwent re-intervention.

32 **Conclusion:** More than half the female patients had multi-vessel disease and  
33 bifurcation lesion was observed in more than three-fourth of the sample.

34 **Key Words:** Coronary artery disease, Women, Percutaneous coronary  
35 intervention, Acute myocardial infarction, Angiography, Pakistan.

36

### 37 **Introduction**

38 The female gender was presumed to have a protective effect against coronary  
39 artery disease (CAD) in the reproductive age group, leading to the development  
40 of ischemic heart disease (IHD) 7-10 years later than men. Oestrogen is said to  
41 be protective against an increased level of low-density lipoprotein (LDL) and  
42 triglycerides (TG).<sup>(1,2)</sup>

43 Worldwide, cardiovascular diseases (CVDs) cause more deaths in women than  
44 all types of cancers combined, accounting for about 1 in every 5 female deaths  
45 in 2017 in the United States alone.<sup>(3)</sup> About 1 in 30 Asian women aged >20  
46 years has CAD.<sup>(4)</sup>

47 Constant efforts are made to reduce disease burden globally as well as at  
48 regional levels. Women are unique because they have atypical chest pain,  
49 delayed presentation, higher numbers of risk factors, different plaque  
50 composition and poor clinical outcome.<sup>(5)</sup> Primary percutaneous coronary  
51 intervention (PCI) has been established as the gold standard treatment for both  
52 men and women with ST elevation myocardial infarction (STEMI) when  
53 fulfilling the criteria.<sup>(6)</sup>

54 Although a lot of research in the developed world has been done to compare  
55 men and women in terms of their short-term and long-term outcomes with signs  
56 and symptoms, clinical presentation and angiographic profiles, women remain  
57 under-represented when studies are carried out.<sup>(7-11)</sup> Symptoms of ischemic

58 angina pain or CAD are usually distinct in women than their male counterparts.  
59 Women are also less likely to receive optimal treatment for certain heart  
60 conditions.

61 Evidence suggests women presenting with typical symptoms of acute coronary  
62 syndrome (ACS) with angina Canadian cardiovascular society classification IV (CCS IV)  
63 are more likely to have obstructive CAD found in angiography. Similarly,  
64 diabetes in females poses an added risk for CAD compared to males. Type II  
65 diabetes mellitus (T2DM) is found to be associated with poor prognosis and  
66 worse outcome in women.<sup>(12)</sup> Indian women presenting with myocardial  
67 infarction (MI) have diabetes, hypertension (HTN) and obesity as major risk  
68 factors, with the highest incidence among those aged 71-80 years.<sup>(13)</sup>

69 To the best of our knowledge, no prior women-specific dataset is available in  
70 Pakistan. The current was planned to fill the gap by evaluating the angiographic  
71 profile and outcome of primary PCI in female patients with acute MI.

72

### 73 **Patients and Methods**

74 The cross-sectional study was conducted at the National Institute of  
75 Cardiovascular Diseases (NICVD), Karachi, from July 1, 2017, to March 31,  
76 2018. After approval from the institutional ethics review committee, data was  
77 extracted from a prospectively collected hospital-based registry with  
78 consecutive inclusion of patients. Those included were female patients aged 18-  
79 75 years presenting with acute MI who underwent primary PCI <12 hours of  
80 symptom onset, and who got themselves enrolled in the National Cardiovascular  
81 Data Registry (NCDR)<sup>14</sup>. Prior to inclusion in NCDR, informed consent was  
82 obtained and those who refused to give consent were automatically excluded  
83 from any subsequent analysis. Pharmacological management during hospital  
84 stay as well as medical management at discharge were according to the American  
85 Heart Association (AHA) and European Society of Cardiology (ESC) management of STEMI guidelines  
86 2017.<sup>(6)</sup>

87 All the primary PCI procedures were performed by consultant cardiologists.  
88 Culprit artery was attempted in the index hospitalisation and for patients with  
89 multi-vessels disease (MVD), subsequent staged PCI was planned. Bifurcating  
90 lesions were managed with the major strategy of one-stent technique with final  
91 kissing balloon (FKB) inflation with provisional backup of second stenting, if  
92 required.

93 The variables and details of the proforma used for data collection are already  
94 defined.<sup>(14)</sup> Data regarding demographic characteristics, angiographic profile,  
95 and in-hospital outcomes and complications were retrieved from the online  
96 NCDT portal<sup>14</sup>. All the patients were referred to in-house cardiac rehabilitation  
97 centre, and smokers were counselled regarding smoking cessation. Follow-up  
98 calls were made to all the discharged patients with their verbal consent to obtain  
99 the outcome of primary PCI after one year.

100 The sample size for the study was estimated using the World Health  
101 Organisation (WHO) calculator version 2.0<sup>(15)</sup>, with expected hospital mortality  
102 rate of 10%<sup>(16)</sup>, 95% confidence level and 3% margin of error. In view of the  
103 observational nature of the study, the required sample size was inflated by a  
104 judgmental proportion of 30% to account for the design effect. The study  
105 duration was dependent on fulfilling the sample size requirement.

106 Data was analysed using SPSS 21. Descriptive statistics, such as frequencies  
107 and percentages, mean  $\pm$  standard deviation (SD) or median and interquartile  
108 range (IQR) were calculated as required. Chi-square test, independent sample t-  
109 test and Mann–Whitney U test were applied, as appropriate, for comparisons.  
110  $P < 0.05$  was taken as statistically significant.

111

## 112 **Results**

113 Of the 522 female patients with a mean age of  $57.41 \pm 11.14$  years, 27(5.2%)  
114 were aged  $< 40$  years, 165(31.6%) were obese, 334(64%) were hypertensive,  
115 202(38.7%) were diabetic, 16(3.1%) had a family history of CAD, and 9(1.7%)

116 were smokers. Prior history of MI was found in 15(2.9%) patients and prior  
117 history PCI in 6(1.1%) (Table 1).

118 Single-vessel disease (SVD) was found in 183(35.1%) patients, two-vessel in  
119 186(35.6%), and three-vessel in 144(27.6%). Bifurcation lesion was observed in  
120 123(23.6%) patients, and thrombus was present in 411(78.7%) patients. Pre-  
121 procedure thrombolysis in myocardial infarction (TIMI) flow was 0 in 310(59.4%) patients.  
122 Mean pre-procedural left ventricular ejection fraction (LVEF) was  
123 42.73±10.05% and post-procedure LVEF within 24 hours post-procedure was  
124 45.42±11.49% (Table 2).

125 Post-procedure TIMI flow (0-II) was observed in 29(5.6%) patients, bleeding  
126 complication in 2(0.4%), and in-hospital mortality in 22(4.2%) cases (Table 3).  
127 In 4(18.2%) of the mortality cases, the age was >65 years (Table 4).

128 Telephonic follow-up was successful in 436(87.2%) patients out of 500  
129 discharged patients. Loss to follow-up cases were 64(12.8%), and in 55(85.9%)  
130 of those case, the contact number was either 'switched off' or 'not available',  
131 while the remaining 9(14.1%) contact numbers were wrong numbers.

132 Mean follow-up duration was 377±69 days. Among the successfully followed  
133 patients, 15(3.4%) had expired, 10(2.3%) had MI recurrence, 8(1.8%)  
134 underwent re-intervention, 6(1.1%) underwent coronary artery bypass grafting  
135 surgery (CABG), and bleeding and cerebrovascular accidents (CVAs) were  
136 reported by 1(0.2%) patient each. Among the 15 post-discharge mortality case,  
137 3(20%) were aged >65 years (Table 5).

138 There was no statistically significant association of clinical and angiographic  
139 characteristics with in-hospital and post-discharge mortality except bifurcating  
140 lesions, which was found to be associated with increased in-hospital mortality  
141 and decreased post-discharge mortality ( $p<0.05$ ).

## 142 Discussion

143 The majority of patients in the current study were in the middle age group  
144 (71%) which is in contrast with literature that shows women get MI 10 years

145 later than the average age of men having MI.<sup>(2)</sup> This is alarming and needs  
146 further research to identify the changing trend in women and its cause especially  
147 in our part of the world. Hypertension, diabetes and raised body mass index  
148 (BMI) are part of standard modifiable cardiovascular risks factors, (SMuRFs)  
149 extensively studied earlier<sup>(17)</sup>, and were found to be higher in the current study.

150 Other less known risk factors, like dyslipidemia, family history of CAD and  
151 smoking, were also negative in the sample, like previous similar studies.<sup>(18)</sup> The  
152 female gender is more likely to present in emergency departments either with  
153 atypical symptoms or because of unawareness regarding symptoms despite  
154 having underlying MI.<sup>(19)</sup> Majority of the current sample (43%), also presented  
155 with absence of typical MI symptoms despite having ST elevation on  
156 electrocardiogram (ECG). This may explain one reason of delay in seeking medical  
157 care in this patient group.<sup>(20)</sup>

158 MVD was found more frequent in the current study (>50%), which is similar to  
159 another Pakistani study.<sup>(21)</sup> We found negligible cases having left main as the  
160 culprit artery, which was also seen in an earlier study<sup>(22)</sup> which reported  
161 frequency of left main as 1.01%. In-hospital mortality was 4.2% in the current  
162 data, while it was significantly variable owing to percentage representation of  
163 females in different studies.<sup>(23,24)</sup> One-year follow-up mortality was 3.4% which  
164 is similar as reported earlier.<sup>(25)</sup>

165 Angiographic findings, like multi-vessel involvement, presence of thrombus and  
166 bifurcating lesions signifying increased lesion complexity, were associated with  
167 in-hospital and 1-year mortality which are comparable to prior evidence.<sup>(26,27)</sup>

168 An improved hospital record and strict follow-up strategy are needed for  
169 monitoring the changing trends and for bring about improvement in cardiac  
170 health of Pakistani women population.

171 The current study has limitations that need consideration. Unlike majority of  
172 studies done on similar samples, the current study had no male comparison  
173 group. Also, time variables were not taken into consideration. Besides, similar

174 to other observational registries, the current study carries a risk of selection bias,  
175 non-randomised data, and missing or incomplete information. ACS patients who  
176 died before or shortly after admission were not included, and the same was the  
177 case with patients who did not have coronary angioplasty but were given  
178 medical treatment or referred for CABG. Though the study cite is a high-  
179 volume tertiary care cardiac centre, results may not be generalisable.

180

### 181 **Conclusion**

182 More than half of the female patients presenting with acute MI had MVD, and  
183 bifurcation lesion was observed in more than three-fourth of them. Early and  
184 short-term outcomes of primary PCI in the study population were comparable  
185 with low mortality, re-infarction and re-intervention rates.

186

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190

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289 **Table 1: Baseline Characteristics**

<b>Characteristics</b>	<b>Total (n = 522)</b>
<b>Age (years)</b>	
Mean ± SD	57.41 ± 11.14 years
18 to 40 years	27(5.2%)
41 to 65 years	371(71.1%)
More than 65 years	124(23.8%)
<b>Body Mass Index (BMI)</b>	
Mean ± SD	25.86 ± 4.74 kg/m <sup>2</sup>
Underweight (<18.5 kg/m <sup>2</sup> )	26(5%)
Healthy (18.5 to 22.9 kg/m <sup>2</sup> )	117(22.4%)
Overweight (23 to 27.49 kg/m <sup>2</sup> )	214(41%)
Obese (≥ 27.5 kg/m <sup>2</sup> )	165(31.6%)
<b>Risk Profile</b>	
Diabetes	202(38.7%)
Hypertension	334(64%)
Family History of CAD	16(3.1%)
Smoker	9(1.7%)
Dyslipidemia	5(1%)
Current Dialysis	1(0.2%)
Prior myocardial infarction	15(2.9%)
Prior heart failure	1(0.2%)
Prior PCI	6(1.1%)
Prior CVD	7(1.3%)
Prior PAD	1(0.2%)
Chronic Lung Disease	5(1%)
<b>Angina Classification in past 2 weeks</b>	
CCS I	25(4.8%)
CCS II	70(13.4%)
CCS III	103(19.7%)
CCS IV	100(19.2%)
No symptoms, no angina	224(42.9%)

290 SD: Standard deviation, CAD: Coronary artery disease, PCI: Percutaneous coronary  
 291 intervention, CVD: Cardiovascular disease, PAD: Peripheral artery disease, CCS: Canadian  
 292 cardiovascular society classification.

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296 **Table 2: Angiographic Characteristics**

<b>Characteristics</b>	<b>Total (n = 522)</b>
<b>Number of Diseased Vessels</b>	

<b>Normal angiogram</b>	9(1.7%)
Single vessel disease	183(35.1%)
Two-vessel disease	186(35.6%)
Three-vessel disease	144(27.6%)
<b>Infarct Related Artery</b>	
Left anterior descending artery (LAD)	266(51%)
Right coronary artery (RCA)	198(37.9%)
Circumflex artery (CIRC)	52(10%)
Posterior descending artery (PDA)	1(0.2%)
Ramus intermedius	3(0.6%)
Left main artery (LM)	2(0.4%)
<b>Bifurcation Lesion</b>	
No	399(76.4%)
Yes	123(23.6%)
<b>Dominance</b>	
Co-dominant	24(4.6%)
Left	42(8%)
Right	451(86.4%)
Information not available	5(1%)
<b>Thrombus Present</b>	
No	111(21.3%)
Yes	411(78.7%)
<b>Pre procedure TIMI flow</b>	
TIMI - 0	310(59.4%)
TIMI - 1	49(9.4%)
TIMI - 2	87(16.7%)
TIMI - 3	76(14.6%)
<b>Pre-procedural left ventricular ejection fraction (LVEF)</b>	
Mean $\pm$ SD	42.73 $\pm$ 10.05%
Information not available	281(53.8%)
<b>Stenosis (pre procedural)</b>	95.73 $\pm$ 7.09%

297 SD: Standard deviation, TIMI: Thrombolysis in myocardial infarction

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302 **Table 3: In-hospital outcome of primary percutaneous coronary intervention (PCI).**

<b>Characteristics</b>	<b>Total (n = 522)</b>
<b>Access Site</b>	
Femoral	378(72.4%)
Radial	144(27.6%)

<b>Contrast Volume</b>	138.4 ± 46.43 ml
<b>Fluoroscopic Time</b>	13.83 ± 7.21 minutes
<b>Post procedure TIMI flow</b>	
TIMI - 0	2(0.4%)
TIMI - 1	7(1.3%)
TIMI - 2	20(3.8%)
TIMI - 3	493(94.4%)
<b>In-hospital Outcome</b>	
Bleeding Complication	2(0.4%)
Emergency CABG	0(0%)
Mortality	22(4.2%)

TIMI: Thrombolysis in myocardial infarction, CABG: Coronary artery bypass grafting.

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**Table 4: In-hospital mortality**

Characteristics	Alive (n = 500)	Deceased (n = 22)	P-value
Age ≥ 65 years	133(26.6%)	4(18.2%)	0.38
Obese (≥ 27.5 kg/m <sup>2</sup> )	154(30.8%)	11(50%)	0.058
Hypertension	323(64.6%)	11(50%)	0.163
Diabetes	193(38.6%)	9(40.9%)	0.828
CCS III or IV (P2W)	193(38.6%)	10(45.5%)	0.519
Multi Vessels Diseased	314(62.8%)	16(72.7%)	0.345
Bifurcating Lesions	113(22.6%)	10(45.5%)	0.013*
No Flow	293(58.6%)	17(77.3%)	0.081

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CCS: Canadian cardiovascular society classification

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**Table 5: Post-discharge mortality.**

Characteristics	Alive (n = 421)	Deceased (n = 15)	P-value
Age ≥ 65 years	112(26.6%)	3(20%)	0.568
Obese (≥ 27.5 kg/m <sup>2</sup> )	132(31.4%)	2(13.3%)	0.137
Hypertension	270(64.1%)	9(60%)	0.743
Diabetes	159(37.8%)	6(40%)	0.861
CCS III or IV (P2W)	162(38.5%)	3(20%)	0.147
Multi Vessels Diseased	270(64.1%)	8(53.3%)	0.393
Bifurcating Lesions	103(24.5%)	0(0%)	0.028*
No Flow	247(58.7%)	10(66.7%)	0.536

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CCS: Canadian cardiovascular society classification

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