Epidemiology and Management Cost of Myocardial Infarction in North Punjab, Pakistan

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Background: Coronary heart disease (CHD) is an important cause of morbidity and mortality in Pakistan. The temporal trends in the risk factors for myocardial infarction (MI) and the impact of socioeconomic status on these risk factors remain ambiguous.

Objectives: The objectives of the present analysis were to investigate the potential association between various risk factors and MI in North Punjab, Pakistan, and to assess the status of the control of the risk factors associated with MI in this population.

Patients and Methods: The present study included 515 patients admitted to the coronary care units or equivalent cardiology wards of the participating hospitals between 2011 and 2012 in North Punjab, Pakistan. The analysis was focused on identifying the socioeconomic status, lifestyle, family history of MI, and risk factors (i.e. hypertension, diabetes, smoking, and hyperlipidemia). A structured questionnaire was designed to collect data. The lipid profile was recorded from the investigation chart of every patient. For statistical analysis, the Kruskal Wallis, Mann-Whitney U, Wilcoxon, and chi-square tests were used.

Results: MI was common in the males at the age of 41 - 60 years as compared to the females (P = 0.015). Patients with a positive parental history of CHD experienced MI at a younger age (P = 0.0001) at a body mass index (BMI) $\leq 25 \, kg/m^2$. Sedentary lifestyle (70%) and smoking (60%) had a male predominance. Hypertension accounted for nearly 37%, hyperlipidemia 26%, and diabetes 19.4% of the rural and urban subjects (P < 0.01). High-density lipoprotein cholesterol decreased (up to 34 mg/dl), while low-density lipoprotein cholesterol and hypertension increased with age. The mean monthly cost of medicines and physicians' fees per patient was 2381.132 Pakistani Rupees (24.24 USD).

Conclusions: Higher BMI, positive family history, smoking, hypertension, hyperlipidemia, and diabetes were the strong predictors of MI in North Punjab, Pakistan. Preventive efforts are needed to start early in life and continue throughout the life course.

Keywords: Myocardial Infarction; Smoking; Hypertension; Diabetes

1. Background

Coronary heart disease (CHD) is the cause of 17.1 million deaths per year throughout the world (1). Thus, CHD is today the largest single contributor to global mortality and will continue to dominate mortality trends in the future. It has been reported that the majority of deaths (39%) in low- and middle-income countries under the age of 70 years are due to CHD (2). Myocardial Infarction (MI) is one of the major complications of CHD. The Asian population is more susceptible to MI (3, 4). It has been estimated that MI is 50% higher in South Asians than in white people in the UK (5).

Pakistan is a developing South Asian country with a population of over 187 million (6). The majority of the population of Pakistan (67.5%) live in rural areas and bear the greatest burden of heart disease (7). The Framingham study (1961, cited in Kannel) reported that obesity, hypertension, smoking, diabetes mellitus, and hypercholesterolemia were the major risk factors for the onset of CHD (8). Another study showed that the high prevalence of MI risk factors in Pakistan with more than 30% of the population over 45 years of age is affected by this disease (2).

Punjab is the most developed and populated province accounting for more than 45% of the entire population of Pakistan (9). However, there is a paucity of data on the estimates of CHD risk factor burden or of its control status in Punjab, Pakistan. Moreover, only a little information on MI risk factors has been reported in Peshawar and Rahim yar khan, Pakistan (7).

2. Objectives

The objectives of the present study were to collect epidemiological data on MI in North Punjab and to evaluate the environmental risk factors responsible for MI with a view to lessening the disease burden through modifications in lifestyle.

3. Patients and Methods

3.1. Study Design

This population-based study was carried out in six re-

gions of North Punjab, Pakistan. The urban population from Lahore and Islamabad and the rural population from Faisalabad, Gujranwala, Gujrat, and Sialkot were included in this survey. A total of 515 MI patients were included in this study and divided into 250 urban and 265 rural MI patients.

3.2. Data Collection

Data were collected by trained qualified staff from the patients admitted to coronary care units (CCU) or equivalent cardiology wards of the participating hospitals. The patients were screened to identify the MI cases. This study was conducted in accordance with the Good Clinical Practice (GCP) guidelines (declaration of Helsinki). The study protocol was approved by the Ethics Committee of Advanced Studies and Research (ref# AEG-A-AD-25-17/ZOOL/09). Written informed consent was obtained from all the participants. All the cases were enrolled between 2011 and 2012. The participation rate of the patients was 65%. Excluded subjects were 285 out of 800 because of incomplete data on variables. Thus, 515 subjects were included in this study. The inclusion criteria were comprised of MI as the principal diagnosis and admission via the CCU and emergency wards. The diagnosis of MI was based on severe chest pain of 30 minutes duration, characteristic electrocardiographic (ECG) patterns of MI, and significant elevation in cardiac enzymes such as creatine kinase-myocardial band (CK-MB). A structured questionnaire was designed to collect data. The analysis was focused on identifying the socioeconomic status (i.e. income and education), lifestyle (i.e. smoking, leisure time, and physical activity), dietary pattern, personal and family history of MI, and risk factors such as blood pressure, diabetes, high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C). At this point, arterial pressure was measured three times using a sphygmomanometer. According to the European Society of Hypertension/European Society of Cardiology (ESH/ESC) criteria, cases with systolic blood pressure > 140 mmHg and diastolic blood pressure > 90 mmHg as well as those with a previous history of hypertension and current consumption of antihypertensive medication for blood pressure control were considered hypertensive. Weight and height were also measured in order to calculate the body mass index (BMI) using the formula: weight (in kilograms) divided by the square of height (in meters). Cases with a BMI between 25 and 29 were considered overweight and subjects with a BMI $\geq$ were considered obese, while those with a total cholesterol level $\geq$ 200 mg/dl were considered hypercolesterolemics. Fasting blood samples (3 ml - 5 ml) of all the participants were collected by trained staff and were sent to the laboratories of the participating hospitals for lipid profile and blood sugar measurement. Subjects with a fasting glucose level $\geq$ 126 mg/dl were considered hyperglycemic, and those with a history of diabetes mellitus and using glucose-lowering medicines were considered diabetic. Disease treatment cost was expressed in Pakistani Rupees (Rs). Patients not willing to sign the consent form and those with previous illnesses associated with hepatic and renal failure, human immunodeficiency virus (HIV), or cancer were excluded from the study.

3.3. Data Analysis

Statistical analysis was performed using the R version 2.11. A descriptive analysis was conducted, and the study variables were checked for normal distribution. The Kruskal Wallis, Mann-Whitney U, and chi-square tests were utilized in order to check associations between the different variables. A two-sample two-tailed t-test (pooled variances) for a P value < 0.05 was considered statistically significant.

4. Results

The total number of the male patients was 356 (69.13%) as compared to 159 (30.88%) females in this study. The mean age of the participants from the rural areas was 56.8 ± 14.34 and from the urban areas was 55.7 ± 11.26 with a range of 20 - 80 years, while 53.79% of the patients were in the range of 41 - 60 years of age (P = 0.270) among the rural and urban populations in both genders. Tables 1 and 2 show that among the urban and rural populations, MI was much more common in the males than in the females (P = 0.015), which was highly statistically significant. However, the male MI patients were younger than their female counterparts. The relative difference regarding the MI prevalence between the sexes was greater among the younger subjects of up to 60 years old and smaller among the subjects of more than 60 years of age. The majority of the MI females were aged over 60 years. The demographic characteristics of the male and female subjects are summarized in Table 1.

4.1. Co-Morbid Conditions and Family History Related to Myocardial Infarction

Smoking was more common (Table 2) in the MI patients in the rural areas (33%) than those in the urban areas (28%) (P = 0.205). None of the female patients ever smoked as compared to the males. Twenty-six percent of the selected MI cases had hyperlipidemia (cholesterol level $\geq$ 200 mg/dl). The prevalence of hypertension was 36% as compared to diabetes (19.4%) in the MI patients (Table 2). As is evident in Tables 3 and 4, the HDL-C level reduced, while the LDL-C level and hypertension rose with age. As is shown in Figure 1, the patients with a first-degree relative positive family history experienced MI at a younger age at a BMI $\leq$ 25.

Table 1. Demographic Distribution of Myocardial Infarction [a,b,c]

Variables	Women		Men		Total
	Rural	**Urban**	**Rural**	**Urban**	
No.	95 (18.45)	64 (12.43)	170 (33.01)	186 (36.12)	515 (100)
Age, y					
20 - 40	11 (2.14)	4 (0.78)	27 (5.24)	21 (4.08)	63 (12.23)
41 - 60	54 (10.48)	26 (5.05)	82 (15.92)	115 (22.33)	277 (53.79)
≥ 61	30 (5.82)	34 (6.60)	61 (11.84)	50 (9.71)	175 (33.98)
BMI, Kg/m² [c]					
≤ 25	65 (12.62)	17 (3.30)	140 (27.18)	69 (13.40)	291 (56.50)
> 25	30 (5.82)	47 (9.13)	30 (5.82)	117 (22.72)	224 (43.50)
Mean ± Standard Deviation	23.75 ± 3.88	29.04 ± 5.46	22.60 ± 3.27	29.22 ± 22.89	26.00 ± 14.42
Family history					
-ve Family history	8 (1.55)	22 (4.27)	22 (4.27)	92 (17.86)	144 (27.96)
+ve Family History	87 (16.89)	42 (8.15)	148 (28.74)	94 (18.25)	371 (72.04)
Education					
Illiterate	50 (9.71)	36 (6.99)	49 (9.51)	66 (12.82)	201 (39.03)
Primary	27 (5.24)	11 (2.14)	50 (9.71)	48 (9.32)	136 (26.41)
College and above	18 (3.50)	17 (3.30)	71 (13.79)	72 (13.98)	178 (34.56)
Marital status					
Married	93 (18.06)	62 (12.04)	158 (30.68)	178 (34.56)	491 (95.34)
Single	2 (0.39)	2 (0.39)	12 (2.33)	8 (1.55)	24 (4.66)
Employment status					
Jobless	73 (14.17)	22 (4.27)	71 (13.79)	47 (9.13)	213 (41.36)
Laborer	5 (0.97)	20 (3.88)	3 (0.58)	56 (10.87)	84 (16.31)
Housewife	9 (1.75)	15 (2.91)	3 (0.58)	12 (2.33)	39 (7.57)
Office job/business	8 (1.55)	7 (1.36)	93 (18.06)	71 (13.79)	179 (34.76)

[a] Data are presented as No. (%) or mean ± SD.
[b] Rural, Rural Population (Faisalabad, Gujranwala, Gujrat, and Sialkot); Urban, Urban Population (Lahore and Islamabad).
[c] The body mass index was considered normal at ≤ 25 and overweight at > 25 for both men and women according to the World Health Organization. Bold letters denote greater values.

Table 2. Co-Morbid Conditions and Types of Myocardial Infarction [a,b,c]

Variables	Rural	Urban	Total	P Values
Number of patients	265 (51.4)	250 (48.5)	515 (100)	
STEMI	152 (30)	138 (27)	290 (56)	0.657
NSTEMI	113 (22)	112 (22)	225 (44)	0.657
Smoking				0.205
Smokers	169 (33)	145 (28)	314 (60)	
Non-smokers	96 (19)	105 (21)	201 (39)	
Life style				0.0001
Sedentary	151 (29)	213 (41)	364 (70)	
Physical activity	114 (22)	37 (7)	151 (29)	
Other Complications				1e-8 [c]
Diabetes	35 (7)	65 (13)	100 (19.4)	
Hypertension	90 (17)	100 (19.4)	190 (37)	
Hyperlipidemia	100 (19.4)	35 (7)	135 (26)	
Risk Factors ≥ 2	40 (8)	50 (8)	90 (17)	
Age, y				0.270
≤ 40	38	25	63	
41 - 60	136	141	277	
≥ 61	91	84	175	
Mean	56.83	55.79		0.523
Gender				
Male	170	186	356	0.0154
Female	95	64	159	

[a] Abbreviations; NSTEMI, Non-ST-Segment Elevation Myocardial Infarction; and STEMI, ST-Segment Elevation Myocardial Infarction.
[b] Data are presented as No. (%).
[c] P < 0.05.

Table 3. Risk Factors by Age Group and Gender in the Urban Population [a]

Age, y	≤ 40 (n = 25)		40 - 60 (n = 141)		> 60 (n = 84)	
Gender	**Male**	**Female**	**Male**	**Female**	**Male**	**Female**
BMI, mean ± SD	28.38 ± 5.42	29.28 ± 4.58	26.79 ± 5.41	28.26 ± 5.71	26.39 ± 4.27	29.61 ± 5.42
STEMI, n	11	3	69	12	28	15
NSTEMI, n	10	1	46	14	22	19
Non-smokers, n	4	4	30	24	12	31
Smokers, n	17	0	85	2	38	3
Family history, n	16	4	56	18	22	20
Sedentary life, n	14	2	100	25	41	31
Physical activity, n	7	2	15	1	9	3
Diabetes, n	4	1	37	8	1	5
Hypertension, n	10	1	24	28	27	10
Hyperlipidemia, n	6	0	12	2	11	3
HDL Cholesterol, mg/dl	37	45	34	38	32	34
LDL Cholesterol, mg/dl	135	124	140	130	145	148

[a] Abbreviations: BMI, Body Mass Index; HDL, High-Density Lipoprotein; LDL, Low-Density Lipoprotein; NSTEMI, Non-ST-Segment Elevation Myocardial Infarction; and STEMI, ST-Segment Elevation Myocardial Infarction.

**Table 4.** Risk Factors by Age Group and Gender in the Rural Population [a]

Age, y	≤ 40 (n = 25)		40 - 60 (n = 141)		> 60 (n = 84)	
Gender	**Male**	**Female**	**Male**	**Female**	**Male**	**Female**
BMI, mean ± SD	22.36 ± 2.53	23.06 ± 6.00	23.28 ± 3.36	24.39 ± 3.43	21.80 ± 3.27	22.85 ± 3.63
STEMI, n	18	5	48	29	38	14
NSTEMI, n	9	6	34	25	23	16
Non-smokers, n	9	11	37	54	35	23
Smokers, n	18	0	45	0	26	7
Family history, n	22	9	74	49	52	29
Sedentary life, n	16	5	44	34	37	15
Physical activity, n	11	6	38	20	24	15
Diabetes, n	3	2	5	5	10	10
Hypertension, n	7	5	20	20	26	12
Hyperlipidemia, n	8	1	23	18	36	14
HDL Cholesterol, mg/dl	30	38	40	43	40	42
LDL Cholesterol, mg/dl	121	125	130	128	140	141

[a] Abbreviations; BMI, Body Mass Index; HDL, High-Density Lipoprotein; LDL, Low-Density Lipoprotein; NSTEMI, Non-ST-Segment Elevation Myocardial Infarction; and STEMI, ST-Segment Elevation Myocardial Infarction.

4.2. Economic Burden

Figure 2 depicts the relationship between the monthly income and the overall cost (i.e. ECG, computerized tomography (CT scan), angiography, surgery, and medication) of the MI patients (P = 0.917). According to the Kruskal test, however, this relationship did not constitute statistical significance. The mean monthly cost of medicines and physicians' fees was 2381.132 Rs (24.24 USD).
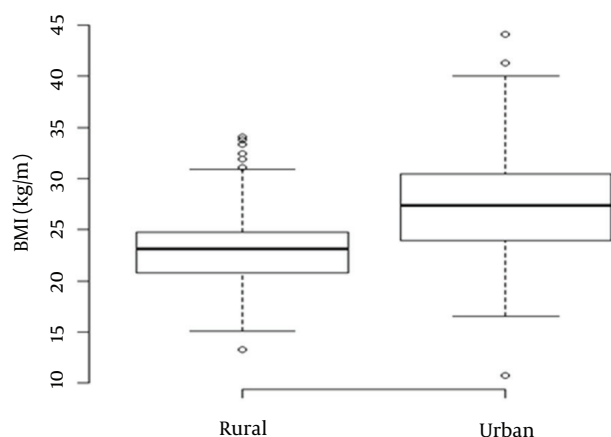
Figure 1. Relationship between the Body Mass Index (kg/m²) and Family History

Figure 2. Relationship Between the Surgery Cost and Monthly Income of the Myocardial Infarction Patients
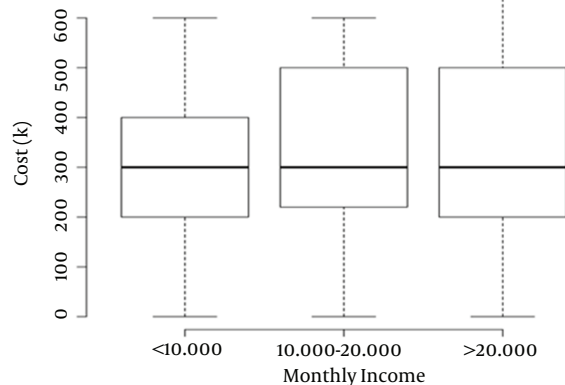
K: means over one hundred.

5. Discussion

Risk factors associated with CHD in the Pakistani population have been relatively insufficiently studied (10). Nevertheless, a thorough knowledge of these factors in the different regions of Punjab, Pakistan, is of a great importance in order to develop national health strategies for their control. The current study found that CHD and its risk factors such as hypertension, diabetes, and obesity are on the increase in our country. Our data revealed that the male MI patients from the rural and urban areas of Punjab, Pakistan, were relatively young (41 - 60 years). Gender difference was also common among our study population (P = 0.015), which chimes in with previous studies reporting that middle-aged men have 2 to 5 times higher risk of MI than women (11, 12). Women of young age are protected from the risk of CHD (13), and hormone replacement therapy reduces the risk of heart disease in postmenopausal women (14). Estrogen is thought to be a major contributor to premenopausal women's tendency to have normal blood pressure, higher levels of HDL-C, and lower triglyceride levels compared to men (15, 16).

In the current study, a high prevalence of overweight was found among the patients from the urban areas (P = 0.0041) as compared to those from the rural areas. This may be due to less physical inactivity and unhealthy dietary practice, encompassing the high consumption of saturated fats and refined carbohydrates as well as the low consumption of fruits and vegetables among the residents of urban areas. Gupta et al. (17) reported that a higher BMI had a positive relationship with MI. Our data on the BMI demonstrated that the patients with a positive family history of MI suffered heart disease even at a lower BMI ≤ 25, which may be due to consanguineous marriages in Pakistan (18).

Our results showed that a 56% ST-elevation myocardial infarction (STEMI) continues to be a major public health concern in Pakistan. Badran et al. (19) also underlined STEMI, by comparison with non-ST-elevation myocardial infarction (NSTEMI), as a major issue in Pakistan.

In our study, sedentary lifestyle (70%) and smoking (60%) were reported predominantly among the male MI patients. Smoking deteriorates HDL-C (14), raises the blood pressure, and releases free radicals which are injurious to heart's health. Wu et al. (20) reported that the cessation of smoking can reduce the risk of heart disease by 65%. Non-smokers exposed to passive smoking are also at great risk of MI. Faisal et al. (21) reported a 26% prevalence rate of sedentary lifestyle among patients with CHD in Peshawar, Pakistan. Furthermore, smokers of all age groups have 2 - 3 times higher death rates than non-smokers (22). It has also been proven by an animal study that physical exercise improves the left ventricular function (23).

In the present study, hypertension (36%) emerged as the most important risk factor for the onset of MI, and its incidence was much higher among the patients from the urban areas than among those from the rural regions. This finding is concordant with the results of a previous study reporting that hypertension is much higher in Pakistan than in the other South Asian countries (24). Hypertension is one of the most important risk factors responsible for atherosclerotic events (25). Similar to serum cholesterol, the blood pressure also tends to increase with age, and more prominently in women than in men (26). In our study, hyperlipidemia and diabetes were detected in 26% and 19.4% of our MI patients, respectively. According to the INTERHEART study, hyperlipidemia is a significant risk factor for CHD in South Asia (27). Type II diabetes is a major public health issue in Pakistan (28) and is an important cause of cardiovascular disease (29, 30). The data available in the literature show a more frequent occurrence of other CHD risk factors among diabetic patients (31). Our data showed that LDL-C increased with age. An earlier study

reported that plasma LDL-C increases by about 40% between 20 and 60 years of age (32).

Low- and middle-income individuals are faced with a great socioeconomic burden in the pursuit of their treatments. The diagnosis of heart disease via ECG, CT scan, echocardiography, and angiography is costly, while the main burden of disease faced by the patient is at the time of surgery. Our data showed that the mean calculated cost per patient for surgery was 600000 Rs (6108.19 USD), which sometimes drastically affects the financial capacity of the patient. The treatment of CHD is a constant, life-long process. Indeed, patients have to consult their physicians every month, and medicines as well as physicians' fees are expensive. In our study, the mean calculated monthly cost of medicines and physicians' fees per patient was 2381.132 Rs (24.24 USD). Even low-income patients are compelled to pay these high expenses, which may contribute to hypertension. One-third of Pakistani people live in poverty and as such cannot afford the increasing burden of such a costly disease.

Our data demonstrated that the MI patients living in the urban areas, in comparison with those living in the rural regions, had a high level of MI risk factors (i.e. physical inactivity, hypertension, and diabetes) and should, therefore, be treated as a high-risk group for prevention and treatment. Moreover, this study demonstrated that effective risk factor control is still poor in Punjab, Pakistan. Accordingly, public health programs, comprising lifestyle interventions and different pharmacological therapies, should be implemented in order to reduce the risk of CHD in Pakistan. Preventive efforts are needed to start early in life and should continue throughout the life course.

The most significant limitation of the present study is its small sample size of MI patients from Punjab Province, Pakistan. Be that as it may, our findings could assist in future well-targeted intervention and awareness campaigns, aimed at residents of urban areas in particular, with a view to lessening the burden of CHD. Our findings, however, require confirmation by further research.

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