

## ANALYSIS OF PSYCHO-SOCIAL RISK FACTORS IN PATIENTS WITH RECENT ACUTE CORONARY SYNDROME: A CASE-CONTROL STUDY

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### ABSTRACT

**Objective:** Although psycho-social factors are reported to be independently associated with myocardial ischemia in many studies, the majority of these were done in the western population. This was conducted in India to determine the impact of psycho-social factors in subjects with the recent acute coronary syndrome (ACS).

**Methods:** Patients with the first episode of ACS within 4 weeks of onset at LPS Institute of Cardiology, Kanpur, India between 2013 and 2015 were enrolled as cases. Control was community-based individuals without coronary artery disease. Both were compared for demographic variables, the psycho-social profile including annual income, education status, depression, stressful life events (using presumptive stressful life events scale, i.e. PSLES), and independent predictors were determined using multiple logistic regression analysis and were computed as odds ratio (OR).

**Results:** Between 200 cases and 200 controls, respectively, statistically significant difference was observed in mean annual income ( $2.74 \pm 1.95$  vs.  $2.23 \pm 1.22$  lac rupees;  $p < 0.05$ ), smoking exposure ( $13.93 \pm 16.17$  vs.  $4.88 \pm 3.10$  pack years;  $p < 0.05$ ), mean number of stressful life events ( $8.18 \pm 2.57$  vs.  $4.14 \pm 1.63$ ;  $p < 0.05$ ). Depression (48% vs. 27%;  $p < 0.05$ ) while education status was comparable. Further, odds of having myocardial infarction were higher for subjects with mild-to-moderate depression (OR: 2.45), family history of heart disease (OR: 2.25), hypertensive males (OR: 1.43), and diabetic females (OR: 1.22).

**Conclusion:** Psycho-social factors, particularly depression may have a significant role in the prognosis of ACS. Further systematic studies are warranted to provide more important insights regarding the magnitude of the association between psycho-social factors and the onset of ACS.

**Keywords:** Coronary artery disease, Depression, Psycho-social factors, Presumptive stressful life events scale, Stressful life events.

### INTRODUCTION

Coronary artery disease (CAD) is one of the leading causes of death all over the world [1,2], and acute coronary syndrome (ACS) is the most common presentation of CAD. A fundamental paradox has existed in the area of psycho-social risk factors and CAD for some time [3]. While several studies have indicated the underlying role of psycho-logical factors in the development and exacerbation of CAD, certain studies have also demonstrated psycho-social characteristics as a consequence of cardiac disease [3]. In addition, psycho-social factors tend to affect health-related behaviors such as smoking, physical activity, and diet; which in turn may influence the CAD risk. Furthermore, the level of education, monetary incomes, and social support may also have a role in access to and content of medical care [4,5]. Overall, these psycho-social factors can be divided into two general categories: Emotional factors (i.e. major depression and anxiety disorders as well as hostility and anger) and chronic stressors (i.e. low socio-economic status, illiteracy, work stress, marital stress, and caregiving strain) [6].

Although psycho-social factors are reported to be independently associated with CAD in many studies, the majority of the studies were performed in the western population [4]. It is also not clear whether the effect of psycho-social factors on the onset of CAD would be similar or different in individuals across countries, cultures, and ethnic groups as all these factors are of a subjective nature. In developing country like India, the relevance of these factors becomes, even more, important because of prevalent poverty, illiteracy, and rapid change toward western culture displayed by the formation of nuclear families, food fads, and daily-stress. With this background, there emerged a need to analyze the role of psycho-social factors in the onset of CAD. Hence, we conducted the present study to determine the psycho-social profiles in

subjects with recent ACS (within 4 weeks) presenting at a territory care center in India. Here, the psycho-social profile was based on depression, anxiety, stressful life events, annual income, and education.

### METHODS

#### Study design

#### Patient population

This case-control study was conducted between January 2013 and March 2015 at the LPS Institute of Cardiology, GSVM Medical College, Kanpur, India (26 months). In this study, the primary inclusion criterion for "cases" were patient, aged 25-75 years, presenting with the first episode of recent ACS within 4 weeks of onset. Here, the onset of ACS was diagnosed based on the symptoms of myocardial ischemia, characteristic of ischemia in the electrocardiogram, and elevation of cardiac markers such as cardiac troponin and creatinine phosphokinase-MB. Patients with prior history of angina, previous episode of ACS, signs of encephalopathy, unstable hemodynamic status, and those receiving inotropes were excluded. Another group, referred as "controls," comprised community-based age ( $\pm 5$  years) and sex-matched individuals with no past history suggestive of CAD. A ratio of 1:1 was established between cases and controls. In addition, established risk factors such as Type 2 diabetes mellitus and hypertension were matched as far as possible. Accordingly, a total of 200 cases and 200 controls were enrolled in the study.

#### Data collection

Enrolled participants were evaluated for demographic variables including age, gender body-mass index (BMI), annual income, education status, history and duration of hypertension and Type 2 diabetes mellitus, smoking habits and frequency of exposure, and

family history of CAD. Subsequently, all participants were assessed for psycho-social risk factors. Here, the International Classification of Disease-10 (ICD-10) criteria were used for diagnosis of depression and its classification into mild, moderate, and severe categories. Further, the presumptive stressful life events scale (PSLES), consisting of 51 items, was applied to measure the number of stressful life events in last 1 year.

### Statistical analysis

Continuous data are expressed as mean±standard deviation and are compared using the Mann-Whitney U test. Categorical data are presented as frequencies and percentages and are compared using the Chi-square test or Fisher exact test. The independent predictors of ACS were determined using multiple logistic regression analysis and were computed as odds ratio.  $p < 0.05$  was considered as statistically significant. The Statistical Package for Social Sciences (SPSS; Chicago, IL, USA) Program, Version 15 was used for statistical analysis.

## RESULTS

### Demographic variables

The baseline characteristics of cases and control group of patients are described in Table 1. In both groups, 172 (86%) patients were males and 28 (14%) were females, indicating a preponderance of male. The age range of included patients was 26-75 years. The mean age of subjects in the cases and control groups was comparable ( $54.38 \pm 11.33$  vs.  $55.00 \pm 10.66$  years). However, the difference between the mean age of male cases and male controls was statistically significant ( $53.61 \pm 11.20$  vs.  $59.46 \pm 11.16$  years;  $p < 0.05$ ). The majority of subjects were in the age group of 56-65 years (36.5%), followed by 46-55 years (30.5%). There were only 7% subjects below 35 years. Further, the difference in mean BMI was statistically significant between cases and controls ( $26.76 \pm 2.11$  vs.  $24.79 \pm 1.99$  kg/m<sup>2</sup>,  $p < 0.05$ ). However, comparison of mean BMI of female cases with female controls exhibited a non-significant difference ( $26.88 \pm 1.88$  vs.  $25.39 \pm 2.10$  kg/m<sup>2</sup>). The majority of subjects belonged to BMI category of 25-30 kg/m<sup>2</sup> (61.5%).

### Educational and economic status

About 50.5% of total subjects had an annual income between 1 and 3 lac rupees and about 21.5% of total subjects had annual income <1

lac rupees. The mean annual income was  $2.74 \pm 1.95$  lac rupees among cases  $2.23 \pm 1.22$  lac rupees among controls ( $p < 0.05$ ; Table 1). The difference was significant between cases and controls for both sexes. Analysis of educational qualification revealed that about 71.5% of subjects had completed matriculation, and 17% had completed post-graduation while 18.5% were illiterate. Overall, the difference between education status of cases and controls was not significant ( $p > 0.05$ ).

### Cardiovascular risk factors

Clinical comparison of cardiovascular risk factors between cases and control groups is given in Table 1. Positive family history of CAD was present in 40 (20%) cases and 20 (10%) controls ( $p < 0.05$ ). In both groups, 60 (30%) subjects were hypertensive. Type 2 diabetes mellitus was present in 66 (33%) of cases and 70 (35%) controls. Further, 30 (15%) cases and 34 (17%) controls were smokers. None of the female subjects had a history of smoking. The mean duration of hypertension and the mean duration of Type 2 diabetes mellitus were comparable between cases and controls groups. Smoking exposure was significantly more in cases than in controls ( $13.93 \pm 16.17$  vs.  $4.88 \pm 3.10$  pack years;  $p < 0.05$ ).

### PSLES score

The mean number of stressful life events were  $8.18 \pm 2.57$  for cases and  $4.14 \pm 1.63$  for controls; the difference was statistically significant ( $p < 0.05$ ). In particular, 122 (61%) subjects in the cases group reported 5-8 stressful life events over the last 1 year, while 142 (71%) subjects in the control groups reported 3-6 stressful life events over the last 1 year.

### Prevalence and grading of depression

According to ICD-10 criteria, depression was noted in 96 (48%) subjects in the cases group, significantly higher than that noted in 54 (27%) subjects in the controls group ( $p < 0.05$ ). Cases had both lower percentage of mild and moderate depression compared to the control which was significant in itself (Fig. 1). Among depression in cases, 83% and 17% had mild and moderate depression, respectively (Fig. 2), which was 92% and 8% in control group (Fig. 3). Mild depression was displayed by 80 (40%) cases and 50 (25%) controls; moderate depression was present in 16 (8%) cases and 4 (2%) controls; and severe depression was present in no subjects from both groups.

### Predictors of myocardial infarction (MI)

The odds of having MI for subjects with family history of CAD were 2.25 times higher than those without a family history of CAD. The odds of having MI were also higher for hypertensive males (Odds ratio (OR)=1.43) and diabetic females (OR=1.22). Of significance, the odds of having MI were 2.45 times more if the subjects had mild or moderate depression (Fig. 4).

## DISCUSSION

Psycho-social risk factors are highly prevalent within cardiac patients, and they shaped the course of cardiac disease in both a positive and negative fashion. While physicians are accustomed to managing lifestyle behaviors such as overeating and physical inactivity, they are less likely to assess and treat psycho-social risk factors because of their limited familiarity with effective strategies and recommendations. Considering the widely-established role of psycho-social risk factors, it becomes necessary to evaluate the magnitude of the association between these factors and onset ACS in Indian population. Our study in this regard found that psycho-social factors, particularly depression may have a significant role in the prognosis of ACS.

Here, we examined 200 cases and 200 controls. There was a preponderance of male to female with a ratio of 6.14:1 in both the groups. The explanation for this may be the higher exposure of males to smoking and differences in health-care seeking behavior between males and females. Although we found no significant difference in overall age distribution between cases and controls, there was a significant difference in the mean age of male cases and male controls. Similar to our study, an analysis of 846 consecutive patients who

**Table 1: Comparison of baseline and clinical characteristics between cases and controls**

Characteristic	Cases (n=200)	Controls (n=200)	p value
<b>Demographic variables</b>			
Males	172 (86%)	172 (86%)	NS
Females	28 (14%)	28 (14%)	
Age (years)	$54.38 \pm 11.33$	$55.00 \pm 10.66$	NS
Age of males (years)	$53.61 \pm 11.20$	$59.46 \pm 11.16$	<0.05
BMI (kg/m <sup>2</sup> )	$26.76 \pm 2.11$	$24.79 \pm 1.99$	NS
<b>Coronary risk factors</b>			
Positive family history of CAD	40 (20%)	20 (10%)	<0.05
Hypertension	60 (30%)	60 (30%)	NS
Duration (years)	$8.55 \pm 5.14$	$7.68 \pm 4.43$	NS
Type 2 diabetes mellitus	66 (33%)	70 (35%)	NS
Duration (years)	$8.30 \pm 4.22$	$7.40 \pm 4.16$	NS
Smokers	30 (15%)	34 (17%)	NS
Smoking exposure (packs/year)	$13.93 \pm 16.17$	$4.88 \pm 3.10$	<0.05
<b>Educational-economic status</b>			
Illiterate	09	10	NS
Matriculates	23	21	NS
Post-graduates	68	69	NS
Mean annual income (Lac rupees)	$2.74 \pm 1.95$	$2.23 \pm 1.22$	<0.05
PSLES score	$8.18 \pm 2.57$	$4.14 \pm 1.63$	<0.05

CAD: Coronary artery disease, BMI: Body-mass index, PSLES: Presumptive stressful life events scale, NS: Non-significant

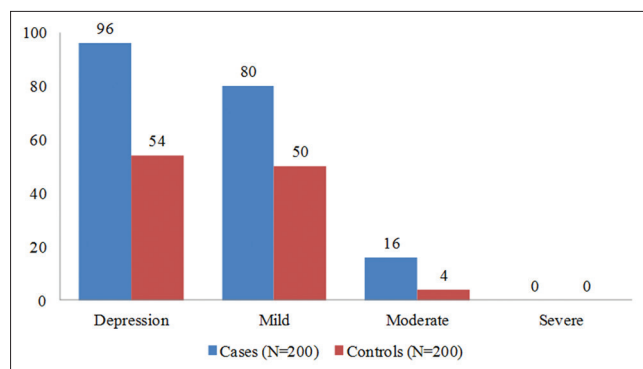


Fig. 1: Comparison of prevalence of depression between cases and controls

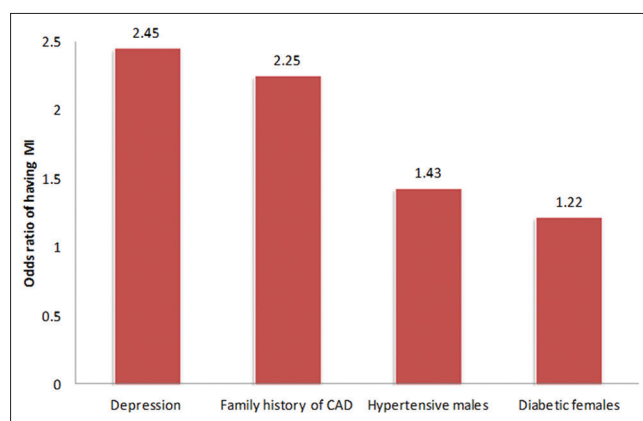


Fig. 2: Predictors of myocardial infarction, assessed as odds ratio for cases versus controls

underwent coronary angiography within 4 weeks of MI revealed that 83.3% of them were males, and the mean age of presentation was  $56.16 \pm 10.51$  years [7]. In another study involving 600 subjects in south India, the mean age of cases and controls was 47.2 years and 46.8 years, respectively, and there were 93% males in each group. These correlate well with the age and sex distribution in our study [8].

Obesity is a significant risk factor for CAD. The Framingham Heart Study showed that obesity is a CAD risk factor at the 14, 20, or 26 years follow-up, but not at the 6 or 8 years follow-up periods [9]. Thus, only long lasting obesity may increase the risk of acute MI (AMI). The Framingham study also demonstrated that weight reduction decreases other CAD risk factors such as hypertension, dyslipidemia, diabetes, and hyperuricemia. However, a case-control study from India showed no association between BMI and AMI among subjects aged 30-60 years [10]. In our study, obesity emerged as a significant CAD risk factor in men, but not in women, which may be partly explained by the fact that the number of female study subjects was small.

Recently, Rabi *et al.* has demonstrated that low-income groups were more likely to report a history of MI or congestive heart failure and low-income was associated with a greater degree of atherosclerosis and greater myocardial jeopardy in patients with diabetes [11]. Another epidemiology study concluded that CAD is more commonly associated with middle and higher socio-economic status which may be due to greater consumption of dietary fat and more sedentary lifestyle compared to lower socio-economic groups [12]. In contrast with these studies, our study shows that the mean annual income of cases was significantly more than that of controls. This can be attributed to selection bias inherent in our study, as it was a tertiary care hospital based study. The INTERHEART study also showed that family income, numbers of possessions, and non-professional occupation were only weakly or not at all independently

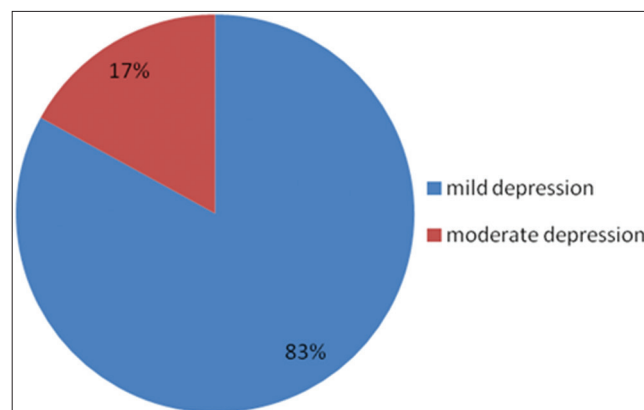


Fig. 3: Category of depression in cases

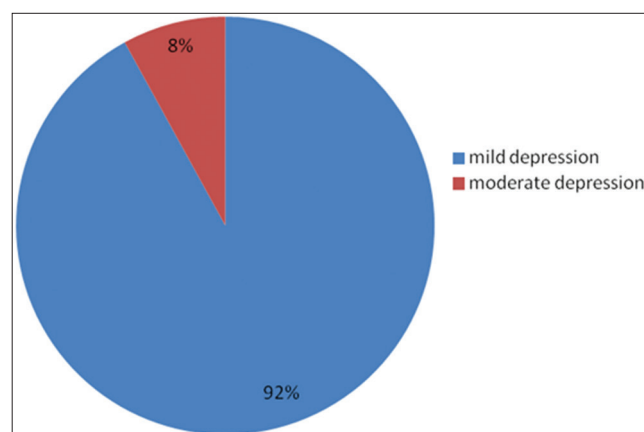


Fig. 4: Category of depression in control

related to AMI [1,4]. However, the study indicated that low education was most consistently associated with increased risk for AMI globally. The determinants of MI onset study investigators [13] also showed that the relative risk (RR) was twice as high among those with less than high school education (RR: 3.3; 95% confidence interval (CI): 2.0-5.4) compared with patients with at least some college education (RR: 1.6; 95% CI: 0.9-2.9). In our study, the difference between education status of cases and controls was not significant. We strongly believe that people with low socio-economic status in a country like India might not avail the health services due to financial constraints.

In our study, we made an effort to match cases and controls with respect to history or established risk factors for CAD like Type 2 diabetes mellitus and hypertension. Despite this, males with hypertension had a slightly higher risk for having AMI as compared to normo-tensive males (OR=1.43) and diabetic females had a slightly higher risk for having AMI as compared to non-diabetic females (OR=1.22). We also observed that positive family history of CAD was significantly more in cases than controls, and the odds were 2.25. This correlates well with previous studies done in India and abroad [4,7,14]. In addition, a study of 9,328 adult males and 10,062 adult females have shown that the hazard ratio of having CAD was 1.75 (95% CI: 1.59-1.92) for men and 1.83 (95% CI: 1.60-2.11) for women with one or more first-degree relatives with MI as compared with subjects without a family history. In addition, we observed no difference in proportions of smokers between cases and controls. However, the exposure to smoking was significantly more in cases. The above findings co-related well with findings of INTERHEART study, which showed that smoking 1-5 cigarettes daily increases the risk of AMI by 40% [1,4].

Stressful life events represent a very important category of psychosocial stress. Sudden changes in an individual's lifestyle can be traumatic

and may collectively represent a tremendous source of stress [15]. Few studies have showed that a psycho-social stress is a significant risk factor for AMI, but measure of stress may not be suitable for different countries, cultures, and ethnic groups [15-17]. In our study, 61% of cases had 5-8 stressful life events over the last 1 year. The mean number of stressful life events for cases were nearly twice than for controls. Another case-control study from Kolkata, India has also reported a significant link between stressful life events and subsequent MI. They showed that an MI patient was likely to experience 4.16 stressful life events, which were twice as much as 2.24 events reported in the control group. The MI subjects were more likely to have experienced stressful life events than the controls [17].

Similarly, depression is strongly associated with cardiac morbidity and mortality in patients with a recent history of ACS. In our study, depression was identified as the strongest predictor of AMI (OR:2.45). Mild-to-moderate depression was noted in diagnosed in 48% of cases and 27% of controls. It becomes vital to identify the characteristics or subtypes of depression that are associated with the highest risk of cardiac events [18-20]. We are of the strong opinion that treatment of depression in patients with recent ACS can improve patient care.

There are certain limitations of our study. Since there is no a consensus on either the definition or measurement of psycho-social stress, issues related to validity, and accuracy of measurement persists, which may lead to potential bias. Further, the selection bias inherent in our study could be another major limitation of our study.

## CONCLUSIONS

We conclude that psycho-social factors, particularly depression may have a significant role in the prognosis of ACS. Further systematic studies are warranted to provide more important insights regarding the magnitude of the association between psycho-social factors and the onset of ACS.

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