#### **ORIGINAL ARTICLE**

# Depression as a Risk Factor for Coronary Artery Disease: Myth or Verity

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#### Author`s Contribution

All the authors contributed equally to this work; they designed the article, did data collection, did thorough search, analyzed the data, wrote, reviewed and approved the final

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#### ABSTRACT

**Objectives:** To determine the frequency of depression in patients with ischemic heart disease, subgroup analysis of prevalence of depression in patients with heart failure, acute STEMI and non STEMI-ACS and the effect of hospital stay and treatment of primary cardiac illness on depression scores.

**Methodology:** All patients with heart failure, acute STEMI and non STEMI-ACS, presenting to cardiology clinics over a period of March-August, 2016 with a precalculated sample size were enrolled into the study by consecutive sampling. HAM-D questionnaire was administered at the time of hospital admission and discharge. SPSS was used for data analysis.

**Results:** A total of 102 patients were included in the study out of which 47 (46%) were females and 55 (54%) were males. The mean age of the study population was 49.5±12 years. At the time of admission, 91/102 (89.2%) patients were found to be depressed, 32 (31.4%) had mild depression, 29 (28.4%) had moderate depression, 10 (9.8%) had severe depression and an alarming number (20 i.e. 19.6%) patients had very severe depression. At the time of discharge, 82/102 (80.3%) patients were found to be depressed, 35 (34.3%) had mild depression, 31 (30.4%) had moderate depression, 12 (11.8%) had severe depression and only 4 (3.9%) had very severe depression. The mean change in HAM-D score during hospital admission was -3.24±4 (Maximum +26, minimum -23). The difference in depression scores during hospital stay tended to inversely correlate with length of hospital stay. A greater proportion of patients with the diagnosis of STEMI had a severe or very severe depression.

**Conclusion:** Depression was found to be alarmingly prevalent in acute coronary syndrome affectees and hospital stay and treatment led to a mean fall in the depression scores.

**Keywords:** Depression, Coronary heart disease. risk factors.

## Introduction

Depression has long been known as an established risk factor for coronary artery disease but recent investigations on its prognostic significance in these patients have revealed a startling equivalence of its prognostic significance to that of left ventricular dysfunction and a history of previous myocardial infarction.<sup>1</sup> During the initial period following an acute myocardial infarction (6 months), the presence of coexistent depression increases the mortality risk 4 fold.<sup>1</sup> The

population specifically at risk for this is patients who have sustained ventricular arrhythmias and males less than 65 years of age which makes a sizeable proportion of such patients.<sup>2, 3</sup> In addition, it has also been established as a risk factor for recurrence of coronary events<sup>4</sup> and adverse outcomes after coronary artery bypass grafts.<sup>5</sup> An adverse prognosis for patients with heart failure as well as an increased risk of developing heart failure has also been demonstrated in various clinical studies.<sup>6, 7</sup> WHO, in 2007,

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highlighted the deleterious effects of depression by labeling it 1 of the 10 most important global health issues.8

Although smoking, drug non-compliance, lack of activity, decreased heart rate variability, and antidepressant drug adverse effects serve as the mediators for such effects in patients with depressive illness<sup>9, 10, 11</sup>, a direct link may be established by effects of depression on autonomic tone, increased hypothalamic-pituitary axis activity, increased serotonin levels and hence heightened platelet activation and inflammatory pathways.<sup>12, 13</sup> Around 15-20% patients with myocardial infarction are estimated to have co-morbid depression.<sup>14</sup> Women may increasingly be prone to develop depression after sustaining an acute myocardial infarction.<sup>15</sup> In comparison to a 4.8% prevalence of depression in patients with no medical illnesses, major depression has been found in as much as 9.3% in individuals with cardiac diseases.<sup>16</sup>

Primary care physicians and cardiologists face a markedly reduced chance of successful pharmacological and lifestyle interventions in patients with depressive illness associated with cardiac diseases. Targeting depression, therefore, seems a wise approach to reducing overall costs of treatment and health care utilization and improving the quality of life in cardiac patients. Despite an escalating need for recognizing and treating depression in cardiac patients, the authors, to their best of knowledge, failed to find any such studies on Pakistani population in literature.

# Methodology

All patients with heart failure, acute STEMI and non STEMI-ACS, presenting to cardiology clinics (including inpatients) over a period of March-August, 2016 were enrolled into the study by consecutive sampling. The sample size was predetermined using WHO STEPS sample size calculator with the following statistics, anticipated population proportion 7.1%<sup>14</sup>, confidence interval 95%, power of test 80% which came out to be 102 patients. Patients less than 16 years of age, those already on treatment for depression or other psychiatric illnesses, patients with malignancies and those failing to provide consent were excluded from the study. A written informed consent was taken from each participant. The study was approved by the Ethical Review Board of the hospital. Baseline demographic features were noted for all patients. Pertinent history of primary cardiac illness and lab data including ECG, Echocardiography, Coronary angiography (where available), liver and kidney functions,

blood complete picture and thyroid function tests (if applicable) were obtained. The patients were then administered the Hamilton Rating Scale for Depression (HAM-D) questionnaire by one of the three trained investigators at the time of admission after clinical stabilization. The areas examined include mood, feelings of guilt, suicidal ideation, sleep, work and interests, psychomotor retardation, agitation, anxiety, somatic symptoms, weight loss and insight. A cumulative score of 0-7 is considered normal. Scores of 8-13 indicate mild depression, 14-18 moderate depression, 19-22 severe depression and >22 very severe depression. A repeat scoring was done at the time of discharge from the hospital.

Data were recorded and analyzed using SPSS v 22.0. Qualitative variables were reported using percentages and quantitative variables by using mean±standard deviation. HAM-D scores of patients on admission and discharge were compared by a paired sample T-test whereas Student T-test was applied to compare differences in depression scores for patients with heart failure, STEMI, and non STEMI-ACS. A p-value of <0.05 was considered to be statistically significant.

## Results

A total of 102 patients were included in the study out of which 47 (46%) were females and 55 (54%) were males. The mean age of the study population was  $49.5\pm12$  years. The presence of co-morbid illness in the cohort is described in Table I.

The patients had mean hemoglobin of  $13.7 \pm 2.05$  g/dL and a mean serum creatinine level of  $1.8 \pm 0.8$  mg/dL.

Patients included had one of the three admitting diagnosis; STEMI, non STE-ACS, Heart failure and this distribution is depicted in the table below (Table II).

At the time of admission, 91/102 (89.2%) patients were found to be depressed, 32 (31.4%) had mild depression, 29 (28.4%) had moderate depression, 10 (9.8%) had severe depression and an alarming number (20 i.e. 19.6%) patients had very severe depression.

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Table 1: Frequency of different co-morbid illness in the group of patients included in the study				
Factor	Patient Status	Frequency	Percentage	
Hypertension	No	38	37.3%	
	Yes	64	62.7%	
Diabetes	Non Diabetics	55	53.9%	
	Diabetics	47	46.1%	
Smoking	Yes	36	35.3%	
	No	66	64.7%	
Dyslipidemia	Yes	28	27.5%	
	No	74	72.5%	
Obesity	Yes	36	35.3%	
	No	66	64.7%	
Lifestyle	Sedentary	44	43.1%	
	Active	58	56.9%	
Socioeconomic	Lower	63	61.8%	
status	Middle	31	30.4%	
	Upper	8	7.8%	

Table 2: Distribution of patients according to diagnosis on admission			
Diagnosis	Frequency	Percentage	
STEMI	47	46.1%	
Non STE-ACS	33	32.4%	
Heart Failure	22	26.1%	

At the time of discharge, 82/102 (80.3%) patients were found to be depressed, 35 (34.3%) had mild depression, 31 (30.4%) had moderate depression, 12 (11.8%) had severe depression and only 4 (3.9%) had very severe depression.

The mean HAM-D score at the time of admission was  $16.30\pm8$  (Range 3-37) and that at the time of discharge was  $13.03\pm6$  (Range 1-31). The mean change in HAM-D score during hospital admission was  $-3.24\pm4$  (Maximum +26, minimum -23). A total of 66 patients had a fall in in their HAM-D scores will 36 had a net rise. The patients stayed in the hospital for a mean of  $4\pm1$  days. The difference in depression scores during hospital stay tended to inversely correlate with length of hospital stay (r=-0.082) but this finding was statistically insignificant.

A greater proportion of patients with the diagnosis of STEMI had a severe or very severe depression as illustrated in the chart below (Figure 1)

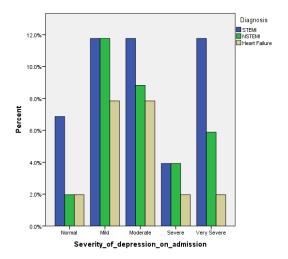


Figure 1: Clustered Bar Chart illustrating severity of baseline depression in relation to admitting diagnosis

The baseline depression score was found to correlate significantly with age (r=0.281, p value 0.049), gender (r=0.651, p value 0.038), presence of diabetes (r=0.183, p-value 0.05), lifestyle (r=0.211, p-value 0.034) and presence of obesity (r=0.142, p-value 0.03). No significant correlation to the presence of hypertension, smoking, socioeconomic status, anemia, creatinine levels and admitting diagnosis were found. The change in depression scores during hospital stay were found to correlate with gender and admitting diagnosis.

During subgroup analysis in patients with depression and diabetes, non-diabetics tended to have milder depression severities as compared to diabetics and this relation has been depicted in the figure below (Figure 2)

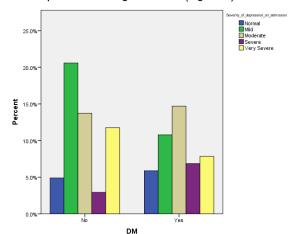


Figure 2: Stratification of diabetics and non-diabetics according to severity of depression

Similar sub-group analysis for smokers and obese yielded the same relationship and has been shown in figure 3 & 4.

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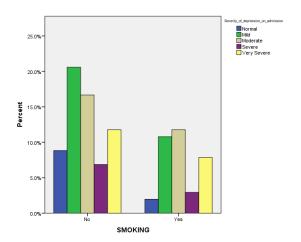


Figure 3: Relationship between smoking status and severity of depression

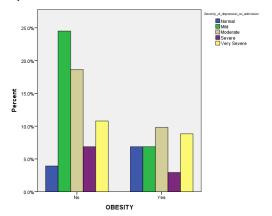


Figure 4: Relationship between obesity and severity of depression

A higher proportion of patients with low socioeconomic status fell into more severe strata on the severity of depression as shown in figure 5.

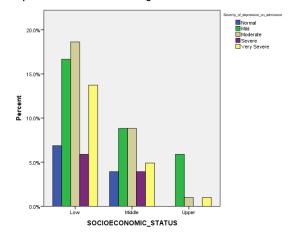


Figure 5: Socioeconomic status and severity of diabetes

# Discussion

The concomitant occurrence of heart disease and depression is not a hitherto unstudied area. Not only is the presence of co-morbid depression known to affect the prognosis of patients with heart disease 18, a significant impediment to treatment is also posed by suboptimal compliance to drug therapy and a lack of willful participation in requisite lifestyle interventions and adherence to follow up visits by the patients with heart disease who have co-morbid major depression. 19, 20 The importance of a prompt diagnosis and proper treatment can thus not be over-emphasized. Moreover, the possibility of existence of a causal association between the two highly prevalent illnesses can open the avenues for screening of depression to become a routine practice in patients with heart disease and its treatment may potentially cause a decline in the incidence of coronary artery disease.

This study was carried out in a cardiology equipped tertiary care center, Shaheed Zulfiqar Ali Bhutto Medical University (PIMS), Islamabad that caters to an enormous patients turn over from all social strata alike from Rawalpindi, Islamabad and a wide catchment area surrounding the twin cities.

Depression was alarmingly prevalent in patients with heart disease at the time of admission (89.2%). This is consistent with the results published by Thomas et al. 21 where depression was found to be 3 times as prevalent in patients with STEMI as in the general population. It is also known that 15% of all patients admitted with STEMI fulfill the criteria for major depression 22 which is mirrored by our findings as well (12.1%), A striking difference in this prevalence between the two genders as demonstrated by our study has also been well documented in literature for general population [23] and those with coronary artery disease [24]. Higher prevalence for depression in heart failure patients than that in acute coronary syndromes previously reported in literature [25] is in contrast to our findings of a higher frequency in patients with STEMI. This difference may have arisen owing to higher in-hospital cost of treatment for patients with acute coronary syndrome and a higher proportion of patients with lower social status catered to by our hospital. But also noteworthy is the fact that the bias that arises due to bi-

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directional association between depression and coronary artery disease may lead to over estimation of the prevalence of either in the patients of these illnesses.

Lack of a significant correlation between depression scores and gender, smoking status and physical activity is consistent with previously published data <sup>[26]</sup>. Findings relatively novel to our study included a higher prevalence of major depression as compared to that of milder degrees in patients with both higher and lower social class, diabetics and smokers.

The aetiopathogenesis of depression in heart disease patients is postulated to be due to an upregulated sympatho-adrenal activity <sup>27</sup>, enhanced platelet reactivity <sup>[28]</sup> and alterations of serotonergic neurotransmission.<sup>29</sup>

# Conclusion

A startling prevalence of depression has been noted in patients with acute coronary syndromes; both at the time of admission and discharge from hospital for the index event. Also noted is the fact that treatment for this ailment leads to, more often than not, a fall in the severity of depression as objectified by depression scores. Hence, depression should be taken into account while treating for cardiovascular diseases as such practices are expected to improve prognosis, decrease event rate, ensure adherence to treatment and enhance the quality of life for these patients. Furthermore, a lower instead of a higher threshold for institution of pharmacotherapy for depression should be kept by the cardiologists to facilitate early and effective risk factor modification and restoration of customary activities after a cardiac event.

Recommendations: Depression should be taken into account while treating for cardiovascular diseases as such practices are expected to improve prognosis, decrease event rate, ensure adherence to treatment and enhance the quality of life for these patients.

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