**ABSTRACT**

Introduction: The depression is common among patients who have an ACS with prevalence ranges from 16% to 23%. The rate is substantially higher than in the general population and primary care patients. Depression in cardiac patients is often both chronic and recurrent. Despite its frequency, this psychiatric problem often goes unrecognized and can persist for months to years, substantially impacting quality of life. In the setting of ACS, where great attention has been given to its frequent coexistence and prognostic import, rate of depression recognition is unknown.

Objective: To recognize incidence and prevalence of depression in ACS

Methods: All patients presenting with acute coronary syndrome were assessed for depression.

Conclusion: The study suggested that depressive symptoms should be included in the group of modifiable post-ACS risk factors that have a negative impact on patients' quality of life and should therefore be considered in efforts to improve the health of these patients. Assessment of depressive symptoms in coronary patients should be performed independently of other cardiovascular risk factors, particularly in the elderly, men, and those who have the modifiable risk factors for cardiovascular disease.

KEYWORDS

Dexamethasone, Supratentorial tumour, Haemodynamics, Emergence reactions

INTRODUCTION

The term acute coronary syndrome (ACS) refers to any group of clinical symptoms compatible with acute myocardial ischemia and includes unstable angina (UA), non-ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI). Each year in the United States, approximately 1.36 million people are hospitalized for ACS, of which 0.81 million are for myocardial infarction (MI) and the remainder are for UA. Roughly two-thirds of patients with MI have NSTEMI; the rest have STEMI. Of one third of STEMI patients die within 24 hours of onset of ischemia. The morbidity and mortality is lower in UA/NSTEMI patients. Almost 18% of men and 23% of women over age 40 may die within 1 year following MI.

The depression is common among patients who have an ACS. Its prevalence ranges from 16% to 23%. This rate is substantially higher than that seen in the general population (4% to 5%) or primary care patients (8% to 10%). Rather than being a transient reaction to having cardiac disease, depression in cardiac patients is often both chronic and recurrent. The Sertraline Antidepressant Heart Attack Randomized Trial (SADHART) found that, among ACS patients who entered the hospital with major depression, 94% had been depressed for over one month, 61% had been depressed for over six months and more than half had a prior major depressive episode.

Furthermore, depressive symptoms are not transient after myocardial infarction, but instead persist if untreated. Two studies have found that depressive symptoms are essentially stable over the year following MI, with little reduction of symptoms over this period in untreated patients. Two pathways (“direct” and “indirect”) are proposed which link the association of depression and ACS. "Direct" pathway refers to influences of depression on physiological factors that may lead to atherosclerosis or coronary events and consists of the autonomic imbalance and activation of the Hypothalamic Pituitary Axis. Depression leading to dysregulation of immunologic mechanisms (eg, proinflammatory cytokines such as interleukins [IL-1, IL-6] or tumor necrosis factor [TNF]), which are associated with an increased risk of CHD and coagulation abnormalities and vascular endothelial dysfunction leading to the development or the progression of atherosclerosis in depressed people.

Indirect pathways refer to psychosocial and behavioral mediators, which correlate with depression and CHD. Depression is associated with poor health behavior, maladaptive coping style, social isolation, and chronic life stress. Behavioral risk factors such as smoking, low physical activity, poor diet and the failure to adhere to medical recommendations mediate the relationship of depressive disorders with CHD.

Depression has been independently associated with negative cardiac outcomes in patients with acute cardiac events and indeed, across the spectrum of cardiac disease. Depression in healthy persons without cardiac disease have been associated with the development of coronary artery disease. Numerous studies of healthy men and women linking depression to the onset of cardiac illness; have found that depression was associated with a 60% increase in cardiac disease.

Among patients with existing cardiac disease, depression has been associated with progression of the illness. Patients found to have depression when diagnosed with coronary artery disease are more likely to have acute cardiovascular/ischemic events than non-depressed patients and hypertensive patients with depression are more likely to die of their cardiac disease.

Given that current therapeutic modalities can effectively reduce depressive symptoms, its recognition as a co-morbidity in patients with ACS has the potential to improve patients' depression-related morbidity. In fact, recent updates to the American College of Cardiology/American Heart Association guidelines recommend routine assessments of depressive symptoms so that appropriate interventions and follow-up can be instituted. However, in the setting of ACS, where great attention has been given to its frequent coexistence and prognostic import, rate of depression recognition is unknown.

There is lack of literature linking Depression and ACS in the Indian population, this study was undertaken to determine the prevalence of depression in ACS patients.

METHODS

A total of 100 patients presenting with acute coronary syndrome were enrolled in the study after informed consent.

The demographic and patient characteristics were collected and data on patient complaints, presenting illness and its duration were recorded. Risk factors like Hypertension, Dyslipidemia, Diabetes were assessed.
Mellitus, Family history, Smoking and Alcohol were noted. Treatment history of any drugs for past psychiatric illness was also recorded.

Case definition of acute coronary syndrome 27

1. Myocardial infarction

a. ST elevation MI (ECG)
b. Non ST elevation MI (Cardiac marker)

2. Unstable angina

a. Rest angina or angina with minimal exertion, usually lasting at least 20 minutes.
b. New onset severe angina, usually defined as occurring within the last month.
c. Crescendo angina, defined as previously diagnosed angina that has become distinctly more frequent, longer in duration or more severe in nature.

The severity of depression was measured by using Hamilton Psychiatric Rating Scale For Depression 28.

The scoring was done in the following manner:

- 0 – 50 : Total score
- 7 or less : Normal
- 8 – 13 : Mild
- 14 – 18 : Moderate
- 19 – 22 : Severe
- 23 and above : Very severe

STATISTICAL ANALYSIS:

All the information was collected using a structured proforma and entered in computer software. Crosschecking and data cleaning was done.

- Nominal data such as demographic data were presented as number and percentages.
- Continuous data (age, duration of disease, pulse BP) were expressed as mean, standard deviation and range.
- Chi-Square test was applied as appropriate for comparison of nominal data.
- P value of 0.05 was considered as statistically significant.

RESULTS

In our study, majority of patients were 40 to 70 years of age. Mean age of patients being 57.25 years, with a standard deviation of 10.38. We found that significantly high number of male patients were present(76% vs 24%) in our study group which was similar to Vural et al who had 82 patients with ACS (54 males and 28 females), mean age being 61.9±12.1 years 27.

The studies by Dias et al 35 and Yadav 31 also found significant male predominance with mean age of 59.4 and 56 years.

The major risk factors for ACS in the study group was alcoholism (43%) and Hypertension (43%), followed by DM (34%), smoking (34%) and hypercholesterolemia (33%). In a study by Yadav, tobacco consumption (65%) was a major risk factor followed by hypertension (33%), diabetes mellitus (16%), family history of coronary artery disease (14%) obesity (13%) and dyslipidemia (12%).

Frasure-Smith et al. demonstrated that depression is in itself an independent risk factor for cardiac events, particularly after infarction, patients with depression having a threefold increase in cardiac mortality, regardless of age and other risk factors.

Our study found that significantly high number of patients having ACS had depression (mild to severe) (37%), mean HAM-D score being 8.36 with a standard deviation of 5.54.

Bearing in mind that the prevalence of depression at some stage in life in the general population is estimated at 17%, these percentages may seem high, but the results are in agreement with data published from other studies that report major depression in 25% of patients following myocardial infarction and symptoms of minor or major depression in 27%-65%.

Amin et al 32 and Dias et al 29 found that the prevalence of moderate/severe depressive symptoms was 17.6% and 41.6% respectively.

Drago et al 35 showed that women had a higher prevalence of depression than men (35% vs 9%; p<0.01).

Amin et al 32 showed depressed patients were more likely to be younger, female, of a minority race, and to have a lower level of education as compared with nondepressed patients.

BMI and Depression:

Obesity and depression are interrelated health issues with numerous comorbidities worldwide 29. Our study found that the significantly high number of patients having ACS had high BMI (Overweight or obese). Mean BMI study group was 25.59 with standard deviation of 4.36. Our results are in the line with previous published literature.

However, none of the studies have assessed the association of BMI and depression in patients having ACS. We found that BMI and HAM-D score in our study group are correlated. The association is highly significant (p=0.032), indicating that in patients with ACS, HAM-D increases as BMI score increases. Our study is the first one to report the association of BMI and depression in patients having ACS.

We also found significant correlation between age and HAM-D score (p=0.000) which signifies as the age increases severity of depression increases, similar to the study by Dias et al 29 in which depressed patients were older than non-depressed patients (61.1 vs. 58.2 years, p = 0.06).

Risk factors and Depression:

Traditional risk factors have been identified in patients having ACS in multiple studies.

In our study with respect to association between ACS and depression, we found that the DM and hypercholesterolemia significantly affects the HAM – D score (p =0.000) however HT, alcohol and smoking does not affect the HAM – D score (p = 0.05).

These finding are similar to those reported in literature by Vural et al which showed correlation between DM and hypercholesteremia with depression.

Diabetes mellitus may place patients at risk for a depressive disorder through a biological mechanism linking the metabolic changes of this disease to changes in brain structure and function 36. Use of serotoninergic antidepressants (e.g., fluoxetine) to treat depression in diabetes has been found to reduce hyperglycemia, normalize glucose homeostasis, and increase insulin sensitivity 37. Therefore, the relationship between depression and diabetes mellitus is a bidirectional phenomenon. We believe that diabetes mellitus may also be regarded as a risk factor for depression and anxiety disorder following ACS.

As our findings indicated that a relationship exists between hypercholesterolemia and depression scores, however, we do not know the exact mechanism of this phenomenon. Many studies have investigated this association. Ledochowski et al. 38 showed that hypercholesterolemia may not necessarily increase the risk of depressive mood; conversely, increased intake of fat and carbohydrates by individuals with depressive mood may increase cholesterol levels. There are also controversies surrounding the possible relationship between hypercholesterolemia and depression 29.

One study has indicated that long-term cholesterol lowering therapy has different effects on serotonin transmission. This finding suggests that within this period some patients could be vulnerable to depression, violence, or suicide 39.

DISCUSSION

ACUTE CORONARY SYNDROME

The term acute coronary syndrome (ACS) refers to any group of clinical symptoms compatible with acute myocardial ischemia and covers the spectrum of clinical conditions ranging from unstable angina (UA) to non–ST-segment elevation myocardial infarction (NSTEMI) to ST-segment elevation myocardial infarction (STEMI). 41

Incidence and prevalence:

Men are slightly more likely to have cardiac illness than female. Age over 45 years for men and 55 years for women, family history of cardiovascular disease and modifiable risk factors like hypertension,
hypertension, diabetes, sedentary lifestyle, and smoking are alarming for developing ACS.

In addition to these risk factors, it has become increasingly clear that psychological factors, particularly depression, may play an important role in the development and propagation of cardiac disease. Depression is common in patients with acute coronary syndrome and is independently prognostic of a higher mortality and worse health status. Depression has been implicated in both the onset and outcome of acute coronary syndromes.

The prevalence of major depression ranges from 15% to 23%, which is approximately threefold higher than age-matched, community-based prevalence studies. Recovery from depression associated with ACS is extremely poor, with many patients remaining depressed months later. Moreover, women generally experience greater depressive symptomatology following ACS than men do,45-47 and this symptomatology may more detrimentally affect their prognosis and quality of life. Also untreated depression results in a poorer prognosis for patients with cardiovascular problems. 80

Data from the Heart and Soul Study, a cross-sectional survey of 1024 people with CAD (coronary artery disease) revealed that those with depressive symptoms not only had increased risk of all-cause mortality, but also were more likely to report worse symptom burden, disease-specific quality of life, physical limitations, and overall health.51-52 Therefore it is not surprising that patients with CAD and depression have higher overall medical costs compared with similar patients without depression. 79

Studies in patients without known CAD have demonstrated that depression is linked to an increased risk of developing CAD. For example, a cohort of 81,875 patients from the Nurses’ Health Study showed that specifically in women with no previous history of CAD, there was a statistically significant age-adjusted trend for the association of increasingly more severe depression scores with fatal CAD, myocardial infarction, and sudden cardiac death. 79

Finally, patients with both CAD and depression have demonstrated lower adherence with treatment, diet and exercise, and smoking cessation, all of which can contribute to the negative consequences of depression in this population. 80-89 Recently, the impact of such negative behaviors in this population was further elucidated by the Heart and Soul Study investigators, who found a significant relationship between physical inactivity and cardiovascular events when adjusting for a number of variables including comorbid conditions, depression severity, smoking, and drug therapy compliance. 85

Though some cardiac illnesses may have associated impairments of appetite, concentration, sleep, and energy, true depression (with persistent depressed mood or anhedonia) is not a normal consequence of cardiac disease. Rather than being a transient reaction to having cardiac disease, depression in cardiac patients is often both chronic and recurrent. 90

The large Sertraline Antidepressant Heart Attack Randomized Trial (SADHART) trial 60 found that, among ACS patients who entered the hospital with major depression, 94% of such patients had been depressed for over one month, 61% had been depressed for over six months and more than half had a prior major depressive episode. Furthermore, depressive symptoms are not transient after myocardial infarction, but instead persist if untreated.

The Johns Hopkins Precursor study followed male medical students for 40 years and found depression to independently predict the subsequent development of cardiac disease and MI. Since that time, there have been numerous studies of healthy men and women linking depression to the onset of cardiac illness; a meta-analysis of this population found that depression was associated with a 60% increase in cardiac disease. 46

Among patients with existing cardiac disease, depression has been associated with progression of the illness. Patients found to have depression when diagnosed with coronary artery disease at cardiac catheterization are more likely to have acute cardiovascular/ischemic events than nondepressed patients and hypertensive patients with depression more likely to die of their cardiac disease. Also, patients with depression in the setting of acute myocardial ischemia (ACS) have substantially impaired medical/cardiac outcomes compared to those without depression.

One of the largest international case control studies ever performed with the aim of identifying the risk factors associated with coronary disease - the INTERHEART study - demonstrated that more than 90% of the overall risk for MI can be predicted on the basis of 9 risk factors. Psychosocial variables including stress and depression were important predictors of risk for MI (odds ratio [OR] 2.67; 99% confidence interval 2.21-3.22) in all age-groups, countries and ethnic groups, their effect being comparable to that of hypertension or abdominal fat. If this relationship is truly causal, it is much more important than previously thought, and a substantial proportion of MI's can be attributed to such factors.

A recent longitudinal study of post-ACS depression found that depression severity at 6 weeks after ACS was a strong and independent risk factor for cardiac mortality approximately 7 years after the index event. Findings from this study and others indicate that ACS patients whose depression is resistant to standard treatments appear to be at highest risk of suffering adverse cardiac outcomes. 62 It is unclear whether this is because the depression persists or whether this is a separate subtype of depression.

In addition to the long-term effects of post-ACS depression, it appears that depression may also have immediate detrimental effects among those admitted to the hospital with acute myocardial ischemia. In this regard, at least two studies have found that MI patients who enter the hospital with an ongoing major depressive episode are more likely to have an in-hospital cardiac complication. 63Though most studies of ACS patients have primarily evaluated depression after MI, depression in the setting of UA has also been specifically associated with cardiac morbidity and mortality.

**Mechanisms linking depression and myocardial ischemia:** Overall, there are two mechanistic categories that likely contribute to link depression and myocardial ischemia: physiologic effects and behavioral effects. (Figure 2)

Physiologic effects of depression have shown its correlation with platelet hyperreactivity and aggregation mediated by serotonin, elevations of other inflammatory markers (eg, IL-1, IL-6, and TNF-α) diminished HRV, sympathetic nervous system dysregulation 67, Endothelial dysfunction 68.

Following studies assessed the impact of depression after a cardiac event. It is seen that the depression as having a negative influence on outcome criteria such as cardiac morbidity, cardiac mortality, or total mortality. (Figure 1)

**Hamilton Rating Scale for Depression:** The Hamilton Rating Scale for Depression (HRSD), also known as the Hamilton Depression Rating Scale (HDRS) or abbreviated to HAM-D, is a multiple choice questionnaire that clinicians may use to rate the severity of a patient's major depression. Max Hamilton originally published the scale in 1960 and reviewed and evaluated it in 1960, 1967, 1969, and 1980. The questionnaire rates the severity of symptoms observed in depression such as low mood, insomnia, agitation, anxiety and weight loss. The questionnaire is presently one of the most commonly used scales for rating depression in medical research.

Unlike other depression measures, the Hamilton Rating Scale for Depression was developed in a medical setting and, for more than 30 years, used concurrently with antidepressant medication to evaluate treatment response.

**Description of the Rating Scale:** The variables are measured either on five-point or three-point scales, the latter being used where quantification of the variable is either difficult or impossible. No distinction is made between intensity and frequency of symptom, the rater having to give due weight to both of them in making his judgment. Various problems are to be found with specific symptoms. Thus considerable difficulty is found with the depressive triad: depressive mood, guilt, and suicidal tendencies. These are so closely linked in description and judgment as to be very difficult to separate. It is very important to avoid the halo effect by
The study also suggested that depressive symptoms should be included in the group of modifiable post-ACS risk factors that have a negative impact on patients’ quality of life and should therefore be considered in efforts to improve the health of these patients. Assessment of depressive symptoms in coronary patients should be performed independently of other cardiovascular risk factors, particularly in the elderly, men, and those who have the risk factors (DM, hypercholesterolemia etc.) The large prospective studies are required to substantiate the fact of our study.

ACKNOWLEDGEMENT:
None

CONFLICT OF INTEREST
No conflict of interest

ETHICAL APPROVAL
Ethical clearance was obtained by the respective institution.

Table 1: Body Mass Index (BMI) was calculated as weight (kg) divided by height in meters squared (m^2).

<table>
<thead>
<tr>
<th>Stage</th>
<th>BMI (kg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>&lt;18.5</td>
</tr>
<tr>
<td>Healthy weight</td>
<td>18.5-24.9</td>
</tr>
<tr>
<td>Overweight</td>
<td>25.0-29.9</td>
</tr>
<tr>
<td>Obesity</td>
<td>30.0-34.9</td>
</tr>
<tr>
<td>Extreme Obesity</td>
<td>≥35.0</td>
</tr>
</tbody>
</table>

Table 2: Hypertension based on JNC 7 classification

<table>
<thead>
<tr>
<th>Classification</th>
<th>Diastolic mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;80</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>80-89</td>
</tr>
<tr>
<td>Stage 1</td>
<td>90-99</td>
</tr>
<tr>
<td>Stage 2</td>
<td>≥100</td>
</tr>
</tbody>
</table>

Figure 1: Pathophysiology of acute coronary syndrome
The figure shows the pathophysiology of acute coronary syndrome leading to acute myocardial infarction or unstable angina. (CPK-MB: Creatine kinase –MB)

Figure 2: Putative mechanisms linking depression/anxiety and cardiac outcomes in acute coronary syndrome (ACS) patients.
The figure represents the various mechanisms linking the correlation between depression and acute coronary syndrome.
The figure explains the odds ratio of depression as a univariate variable for a risk factor for mortality in coronary heart disease patients. (CHD: coronary heart disease), (HR: Hazards ratio)

REFERENCES


