

FREQUENCY OF CLINICAL DEPRESSION AND EFFECT OF ANTIDEPRESSANT TREATMENT ON OUTCOMES IN HEART FAILURE WITH REDUCED EJECTION FRACTION (HFREF) AT PIMS

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ABSTRACT

Background: Heart Failure with Reduced Ejection Fraction (HFrEF) is frequently associated with clinical depression, which adversely affects treatment adherence, self-care, healthcare utilization, and clinical outcomes. Evidence regarding the effect of antidepressant therapy on both psychological and cardiovascular outcomes among patients with HFrEF remains limited, particularly in Pakistan.

Objective: To determine the frequency of clinical depression and evaluate the effect of antidepressant therapy on depressive symptoms, medication adherence, heart failure-related hospital admissions, emergency department visits, and short-term mortality among patients with HFrEF presenting to the Pakistan Institute of Medical Sciences (PIMS), Islamabad.

Methods: A Cross Sectional study was conducted in the Department of Cardiology, PIMS, Islamabad, over three months. A total of 323 adult patients with HFrEF and clinical depression identified using the Patient Health Questionnaire-9 (PHQ-9) were enrolled through non-probability consecutive sampling. All participants received sertraline (50–100 mg/day) according to psychiatric assessment and were followed for three months. Depression severity, medication adherence, heart failure-related hospital admissions, emergency department visits, and all-cause mortality were evaluated before and after treatment. Statistical analysis was performed using SPSS version 23.0, with $p < 0.05$ considered statistically significant.

Results: The mean baseline PHQ-9 score significantly decreased from 13.9 ± 4.8 to 8.2 ± 4.1 after three months ($p < 0.001$). Good medication adherence improved from 57.3% to 86.1% ($p < 0.001$). Heart failure-related hospital admissions decreased from 29.1% to 14.6% ($p = 0.002$), while emergency department visits declined from 37.5% to 18.3% ($p < 0.001$). During follow-up, the all-cause mortality rate was 1.9%.

Conclusion: Sertraline therapy was associated with significant improvement in depressive symptoms and medication adherence, accompanied by reductions in heart failure-related hospital admissions and emergency department visits among patients with HFrEF. Routine depression screening and integrated psychiatric care may improve short-term clinical outcomes in this population. Larger multicenter studies with longer follow-up are warranted to confirm these findings.

KEYWORDS: Heart failure with reduced ejection fraction; HFrEF; Depression; Patient Health Questionnaire-9; PHQ-9; Sertraline; Antidepressant therapy; Heart failure; Mental health; Pakistan.

INTRODUCTION

Heart failure with reduced ejection fraction (HFrEF) is a major public health problem all over the world. Has been linked with high morbidity, mortality and health system costs globally. Worldwide, more than 64 million people suffer from heart failure, of which the majority have HFrEF. Although the many risk modification approaches, advanced and evidence-based therapies have been developed, patients with HFrEF remain poorly functional with high morbidity and mortality burden, and high burden on the healthcare system. {1} Heart failure with reduced ejection fraction (HFrEF) is one of the most common diseases in low and middle-income countries (LMICs) and is believed to be associated with high depression rates. Depression in patients with HFrEF is accompanied by a high level of comorbidities, medication adherence and physical activity, low level of self-care, suboptimal health care-seeking, utilization of emergency services, repeated emergency and inpatient care, and mortality. {2,3} Depression may be associated with poor health outcomes in patients with HFrEF due to an excess burden on the health care system, and antidepressant therapy is recommended to help alleviate the symptoms of depression. {1,4,5} The use of

antidepressants also improves compliance and mitigation of physical activities. The link between antidepressants and cardiovascular disease (CVD) is not known. However, some systematic reviews suggest antidepressants positively affect the psychological wellbeing of patients and the management of patients in routine care in cases of heart failure. {6} Although there are international recommendations that depression in heart failure patients should be routinely diagnosed and treated, many Low and Middle-Income Countries, including Pakistan, have limited mental health services integrated into cardiology. Heart failure with reduced ejection fraction (HFrEF) patients with depression exhibit worse adherence to treatment, self-care, quality of life, use of the emergency department, hospital re-admission and mortality. Studies have reported improvement in depressive symptomology with antidepressant treatment, but no evidence of the effect of antidepressant treatment on cardiovascular-related treatment adherence and adverse health outcomes in the near-term population.

METHODOLOGY

The cross-sectional study was approved by the Research Evaluation Unit (REU), College of Physicians and Surgeons Pakistan (CPSP) and Institutional Ethical Review Board (IERB) Department of Cardiology, Pakistan Institute of Medical Sciences (PIMS) Islamabad. The study was carried out in a period of three months. The non-probability consecutive sampling technique was used to select patients with Heart Failure with Reduced Ejection Fraction (HFrEF) from the Outpatient Department (OPD) and Emergency Department (ED) of PIMS. The sample size consisted of 323 patients and was determined by applying the standard sample size calculation formula for the 95% confidence level, the 30% prevalence rate and the 5% margin of error. The patients included in this study were adult patients (18 to 60 years old) who were clinically depressed (Positive on the Patient Health Questionnaire-9: PHQ-9) with an ejection fraction (EF) < 40% with informed consent. Major depression patients with other psychiatric disorders, patients receiving psychotherapy who do not take antidepressants, patients who do not have cognitive impairments which impede the assessment, and who do not have terminal illnesses were included in the study. Data were collected after obtaining written and informed consent for participating in this research. This included demographic information, socioeconomic information, medical history, cardiovascular risk factor information (and depression information), and heart failure clinical information. The initial assessment for heart failure included age, gender, health history (hypertension and diabetes), smoking and sleep habits, physical activity, heart failure medications, and adherence to medications. It considered heart failure-related hospital visits and emergency visits. The condition of depression was evaluated with the use of PHQ-9 and classified as mild, moderate and moderate to severe or severe depression. Patients that were diagnosed with moderate to severe or severe depression were assessed by a consultant psychiatrist and the patients were prescribed sertraline (50-100 mg per day) after the clinical practice. Data was gathered after three months, including other clinical data, PHQ-9, and data on hospital visits, emergency visits and other deaths related to heart failure. Medical record review and clinical follow-up was the technique used to gather data. Data was gathered in a secure system and the confidentiality of data was ensured. Data collected were analysed using SPSS version 23. The findings of continuous data were presented as mean and standard deviation (SD) and the findings of categorical data were presented as frequency and percentage. A paired-samples t-test was used to analyze the PHQ-9 scores before and after the treatment. The Chi-square test was used to assess medication adherence. The other categorical data were analyzed by McNemar test. Pearson correlation was used to assess the correlation. A p-value of < 0.05 was used to consider the data statistically significant. The researchers adhered to the principles of confidentiality throughout the research process.

RESULTS

The study included 323 patients with Heart Failure with Reduced Ejection Fraction (HFrEF) and clinical depression. No one was excluded from the final analysis, and all the participants attended the initial and 3-month follow-up appointments. The average age of participants was 52.8 years (age range 29 years to 60 years) with 198 (61.3%) participants being male and 125 (38.7%) participants being female. Most of the participants had hypertension as a common condition (66.3%) followed by diabetes mellitus (43.0%). The number of participants who reported for cigarette smoking was 104 (32.2%) and for sleep disturbances, 89 (27.6%). Table 1 provides all necessary information about the participants. The average PHQ-9 score at baseline was 13.9. The participants were divided based on the PHQ-9 score as follows: 39 (12.1%) were classified as having mild depression, 112 (34.7%) participants had moderate depression, 118 (36.5%) participants had moderately severe depression and 54 (16.7%) participants had severe depression. The classification of participants by depression score is in Table 2. The mean score on the PHQ-9 after 3 months of sertraline was 8.2 (97.7% of the patients were in the non-remitting group). The paired-sample t test showed that the mean scores of depressions before and after treatment were statistically significantly different ($t = 31.48$, $p < 0.001$). Table 3 shows the comparison of the PHQ-9 scores taken at baseline and after 3 months. Initiation of antidepressants was associated with better heart failure therapy guideline adherence. Good adherence improved from a baseline of 185 (57.3%) to 278 (86.1%) at three-month follow-up ($p < 0.001$). Poor adherence declined from 138 (42.7%) to 45 (13.9%) after three months. Details are given in Table 6. Similarly, there was a reduction in

cardiovascular hospitalizations following an improvement in depressive symptoms. This decreased from 94 (29.1%) patients who had heart failure related hospitalization in the 3 months before the study entry to 47 (14.6%) within the three months follow up period ($P = 0.002$). Likewise, the number of patients who had heart failure-related EDP visits dropped from 121 (37.5%) before the intervention to 59 (18.3%) after 3 months ($p < 0.001$). More details are in Table 6. A total of 6 patients (1.9%) died, and 317 patients (98.1%) lived for the 3-month follow up. Please refer to Table 7 for more detail. Disturbed sleep patterns were associated with a disturbed sleep pattern score (PHQ-9) ($r = 0.29$, $p < 0.001$) and smoking status was associated with a score on the disturbed sleep pattern score (PHQ-9) ($r = 0.18$, $p = 0.002$), with the relationships both positive and weak. A negative and significant relationship with PHQ-9 score was seen with the level of regular physical activity ($r = -0.22$, $p < 0.001$). There was no significant relationship between age and depression scores ($r = 0.08$, $p = 0.146$). More details are in Table 4. At baseline, patients with diabetes mellitus and patients with disturbed sleep had significantly higher PHQ-9 scores (15.1 ± 4.5 ; 16.2 ± 4.3) than those without baseline (13.0 ± 4.6 ; 13.0 ± 4.5 , respectively; $p < 0.001$). The baseline PHQ-9 scores of females (14.4 ± 4.6) were higher than those of males (13.6 ± 4.9), however, the difference was not significant ($p = 0.118$). There was no significant correlation between severity of depression with participants having hypertension ($p = 0.274$). Subgroup analysis is reported in table 5.

Table 1. Baseline demographic and clinical characteristics (n=323)

Variable	Value
Age (years), Mean $\pm$ SD	52.8 $\pm$ 7.4
Male	198 (61.3%)
Female	125 (38.7%)
Hypertension	214 (66.3%)
Diabetes mellitus	139 (43.0%)
Family history of CAD	87 (26.9%)
Smoking	104 (32.2%)
Regular exercise	96 (29.7%)
Healthy diet	118 (36.5%)
Disturbed sleep	89 (27.6%)

Table 2. Baseline depression severity according to PHQ-9

PHQ-9 Category	n (%)
Mild (5–9)	39 (12.1%)
Moderate (10–14)	112 (34.7%)
Moderately severe (15–19)	118 (36.5%)
Severe (20–27)	54 (16.7%)
Mean PHQ-9 score	13.9 $\pm$ 4.8

Table 3. Comparison of PHQ-9 scores before and after treatment

Variable	Baseline	3 Months	Mean Difference	t	p-value
PHQ-9 score	13.9 $\pm$ 4.8	8.2 $\pm$ 4.1	5.7 $\pm$ 3.2	31.48	<0.001

Table 4. Correlation between selected variables and baseline PHQ-9

Variable	r	p-value
Age	0.08	0.146
Smoking	0.18	0.002
Disturbed sleep	0.29	<0.001
Regular exercise	-0.22	<0.001

Table 5. Subgroup analysis of baseline PHQ-9 score

Variable	Mean PHQ-9 $\pm$ SD	p-value
Male	13.6 $\pm$ 4.9	0.118
Female	14.4 $\pm$ 4.6	
Diabetes present	15.1 $\pm$ 4.5	0.001
Diabetes absent	13.0 $\pm$ 4.6	
Hypertension present	14.1 $\pm$ 4.7	0.274

Hypertension absent	13.5 ± 4.8	
Disturbed sleep	16.2 ± 4.3	<0.001
Normal sleep	13.0 ± 4.5	

Table 6. Cardiovascular outcomes before and after antidepressant therapy

Outcome	Baseline	3 Months	p-value
Good medication adherence	185 (57.3%)	278 (86.1%)	<0.001
HF-related hospital admissions	94 (29.1%)	47 (14.6%)	0.002
Emergency department visits	121 (37.5%)	59 (18.3%)	<0.001

Table 7. All-cause mortality during follow-up

Outcome	n (%)
Alive	317 (98.1%)
Deaths	6 (1.9%)

DISCUSSION

The aim of this study was to assess the prevalence of clinical depression and the effects of antidepressant therapy on psychological function and short-term cardiovascular outcomes in HFrEF. The data indicated that depressed patients who took sertraline had a significant reduction in depression symptoms by the end of three months, and the patients also had a better response to medication, fewer hospitalizations for heart failure, fewer visits to the emergency department and a low mortality risk, within a few months. The results show that the integration of mental health treatment within the existing cardiovascular treatment is beneficial. {5,6} Patients with HFrEF are depressed, and some negative effects on important cardiovascular outcomes and increased health care utilization, and depression has been linked to poorer quality of life and self-care and treatment adherence. The present review confirms that depression is reduced in patients with heart failure, and it has been established that sertraline and other SSRI's are effective in treating depression in heart failure patients. {6,10,11} Many of the previous systematic reviews have been focused on early depression management to improve the efficiency of heart failure management. This study found that antidepressants resulted in higher adherence with medications. Depression negatively impacts motivation and adherence to self-care behaviors and important treatments. This leads to low treatment compliance. It is, therefore, expected that the decongestion of heart failure and decrease of the need for emergency medical treatment would be the result of improved compliance to treatment of depression. Many previous studies that have assessed the management of depression in heart failure have documented the same. {6,10,13} In this regard, it could be concluded that the effective management of depression has a positive effect on the health of the cardiovascular system because of the reduction of emergency department visits and hospitalizations. Better psychological well-being can help ensure adherence to treatment, improve the chances of desired proactive health actions and, ultimately, reduce the disease burden and health service costs. Although, there were low death rates in the follow-up, short duration studies, limit the long-term survival prognosis. {6,8,10} In agreement with existing studies with the addition of disturbed sleep and smoking, poor psychological health correlates with more severe degrees of depression, while physical exercise is protective. {14-19} The main limitation is a single-center study with a short follow-up. To validate these results and to examine the effect of depression reduction on cardiovascular morbidity and mortality, larger studies with multiple centers and prolonged follow-up will be necessary. {20,21}

CONCLUSION

Patients with Heart Failure with Reduced Ejection Fraction (HFrEF) are very likely to have Clinical Depression. This makes it extremely crucial to find out how it affects the management of this disease. After three months treatment with sertraline, improvement in depressive symptoms was noted in this study. Improved depression symptoms are associated with improvements in adherence to antidepressants, reduced hospitalizations for HF, reduced ED attendance and reduced low short-term mortality. These results back up the need for regular depression screenings during heart failure management with the goal of starting psychiatric treatment as soon as possible. Further research is required with a larger number of sites and patients and longer follow up period, to examine the sustained impact of antidepressants on heart health and cardiac effects of antidepressants.

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