



## THE PREVALENCE AND SEVERITY OF DEPRESSION AND ANXIETY IN HEART FAILURE PATIENTS IN BULGARIA

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### ABSTRACT

**Background:** Depression and anxiety are common in patients with heart failure (HF). They are associated with adverse outcomes such as reduced adherence to treatment, poor ventricular function, increased hospitalizations, and higher mortality rate. However, despite the importance of these concomitant conditions, depression and anxiety often remain underdiagnosed and undertreated in patients with HF.

**Aim:** The aim of the study is to evaluate the prevalence and severity of depression and anxiety in patients with HF.

**Materials and methods:** 138 patients with chronic HF, a mean age of 70.29 ± 9.73 years and male/female ratio – 63 (45.7%)/75 (54.3%) were included in this cross-sectional study. Tests for depression (Hamilton Depression Rating Scale; HAM-D) and anxiety (Hamilton Anxiety Scale; HAM-A) were performed in all participants.

**Results:** 114 (82.6%) of the patients with HF have depression and 98 (71%) – anxiety disorder. Mild depression was found in 38 (33.3%) patients and moderate – in 49 (42.9%). Severe depression was found in 21 (18.4%) of the patients and very severe – in 6 (5.3%). In our cohort, women more often were diagnosed with depression than men (71.4% vs. 28.6%, (p<0.05)). Older age above 70 years was associated with an incidence of depression (AUC 0.75, 67% sensitivity and 64% specificity, p<0.05). Significant predictors of depression in HF patients were anemia (OR 2.74 (95% CI 1.23-4.56, p<0.05), CKD (OR 12.29 (95% CI 1.57-16.17, P<0.05), ejection fraction below 50% (OR 4.35 (95% CI 2.07-8.85, P<0.05) and alcohol consumption (OR 6.39 (95% CI 1.72 – 15.14, P<0.05)). Mild anxiety was diagnosed in 28 (28.6%) of the patients, 52 (53.1%) were with moderate and 18 (18.4%) – with severe anxiety. *Predictors of anxiety* in our HF cohort were poor controlled arterial hypertension (OR 2,18 (95% CI 1.26-5.57 P<0.05), alcohol consumption (OR 2,75, (95% CI 1.43-4.23, P<0.05), advanced HF (OR 4.57, (95% CI 2.02-7.66, P<0.05) and previous myocardial infarction (OR 3,25, (95% CI 1.89-5.53, P<0.05).

**Conclusions:** Our data shows that the key factors associated with the risk of developing depression in patients with HF are: CKD, anemia, alcohol use, ejection fraction < 50, while the most important factors associated with the development of anxiety are: uncontrolled hypertension, alcohol use, advanced HF and previous MI.

**Keywords:** Depression, anxiety, heart failure,

### BACKGROUND:

Heart failure (HF) is a chronic impairment of cardiac function and represents a serious burden to both patients and the healthcare system because of poor functioning and impaired health-related quality of life (QoL) [1], as well as frequent hospitalizations and high healthcare costs [2, 3]. Mortality remains high despite advances in treatment, with roughly 50% of HF patients dying within 5 years of diagnosis [4]. Psychiatric illnesses are prevalent in patients with HF and lead to negative health and cardiovascular outcomes in these patients.[5] The rate of depression in the general population with heart failure is 25%, but in patients with advanced HF, depression or depression-anxiety disorder rates are more than 50%. They are associated with adverse outcomes such as reduced adherence to treatment, poor function, increased hospitalizations, and higher mortality rate [6-8]. Depression and anxiety disorders -including generalized anxiety disorder (GAD), post-traumatic stress disorder (PTSD), and panic disorder - are the most common psychiatric conditions in HF patients [5]. The estimated prevalence of these diseases in HF patients is going to increase dramatically in the next several years, as will the economic burden [9, 10]. The association of depression/anxiety and HF multiply healthcare-related costs compared with either disease alone [11]. Several risk factors increase the risk for developing depression, including female gender, age, and previous depressive episodes [12-14]. Moreover, depression seems to increase the risk for HF, while HF increases the risk of depression. These mutual associations reveal a complex relationship between depression and HF. Although the detection of depression and anxiety in HF is challenging, it is important to recognize comorbid depression because it has been associated with significantly increased morbidity and mortality in HF [15]. However, despite the importance of these concomitant diseases, depression and anxiety often remain underdiagnosed and undertreated in patients with HF.

## METHODS

We performed this study to evaluate the prevalence and severity of depression and anxiety in patients with HF. The study was conducted between December 2020 and December 2022. The study population comprised 138 patients admitted with decompensation of chronic HF. We included in this cross-sectional study adults 18 years of age and older. The mean age of the patients was  $70.29 \pm 9.73$  years, and the male/female ratio – 63 (45.7%)/75 (54.3%). Echocardiography for evaluation of HF according to ESC protocol and tests for depression (Hamilton Depression Rating Scale; HAM-D) and anxiety (Hamilton Anxiety Scale; HAM-A) were performed in all participants. All participants signed informed consent.

### Statistical analysis

Categorical variables were expressed as numbers and percentages. All categorical variables were compared for the study outcome using the Chi-square test. Continuous variables with a normal distribution were expressed as mean and standard deviation (SD). We compared normally distributed continuous variables using the Student t-test, and the Mann–Whitney test was used to compare variables with a non-normal distribution. Both univariate and multivariate logistic regression analyses were done to identify predictors of depression and anxiety. Confidence intervals were calculated at 95% interval levels, and differences were considered statistically significant at a p-value less than 0.05. All statistics were generated with SPSS Version 22.0.

## RESULTS:

Hypertension was the most prevalent comorbidity, seen in 133 (96.4%) participants. Only 36 (26.1%) patients had a history of ischaemic heart disease. Ejection fraction was preserved in 86 (62.3%), mid-range in 27(19.6%) and reduced in 25 (18.1%). The *alcohol drinking* history have 69 (50.0%). Most of the patients (92.7%) were in the New York Heart Association (NYHA) functional class III. Diabetes mellitus was presented in 58 (42.0%) of the patients with HF. 114 (82.6%) of the patients with HF have depression. Mild depression was found in 38 (33.3%) patients and moderate – in 49 (42.9%). Severe depression was found in 21 (18.4%) of the patients and very severe – in 6 (5.3%) (Tabl. 1).

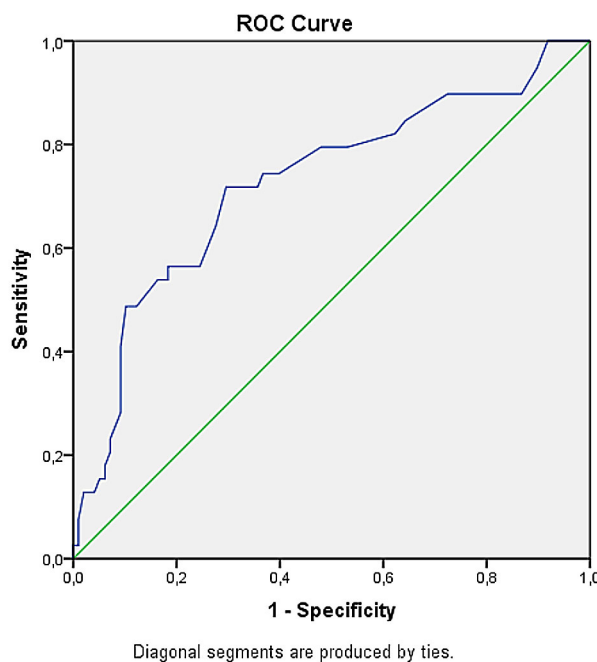
**Table 1.** Stages of depression in HF patients

Stage of depression	N	%
Mild	38	33.3
Moderate	49	42.9
Severe	21	18.4
Very severe	6	5.3

Note: N – number of patients

Older age above 70 years was associated with the incidence of depression (AUC 0.75, 67% sensitivity and 64% specificity,  $p < 0.05$ ) (Fig. 1).

**Fig. 1.** ROC curve of age.

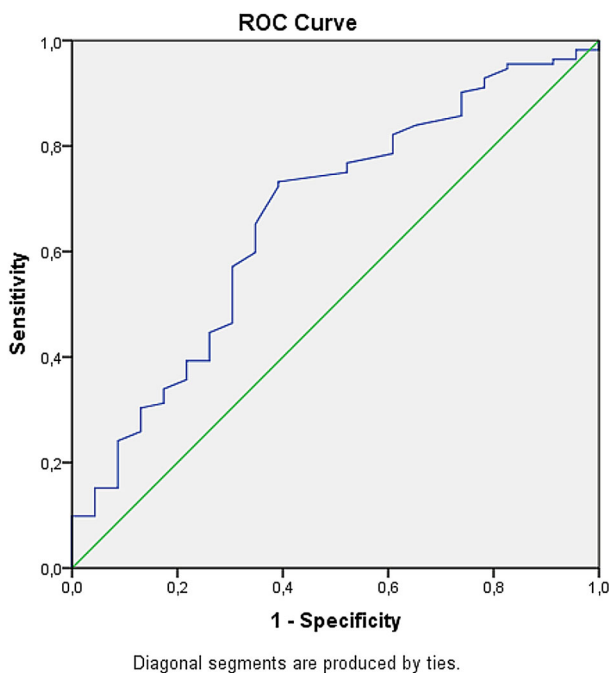


Note:ROC-Receiver operating characteristic curve

Mild depression was more often observed in patients with valvular heart diseases, especially aortic stenosis (13.5 vs 8.0%, ( $p < 0.05$ )), mitral insufficiency (26.7% vs. 15.2% ( $p < 0.05$ )) and moderate depression in those with aortic insufficiency (18.2% vs. 9.4%, ( $p < 0.05$ )). In patients with mild and moderate depression, conduction diseases were found more frequent: left anterior fascicular block (18.4% vs 5.0%, ( $p < 0.05$ )) and left bundle branch block (8.1% vs. 1.0%, ( $p < 0.05$ )). The findings of our study show that patients with heart surgery were more likely to experience mild depression (after aortic valve surgery 2.6% vs 1.0%, ( $p < 0.05$ ), after mitral valve surgery 7.9% vs 0%, ( $p < 0.001$ ), combined mitral and tricuspidal surgery 2.6 % vs 0.5%, ( $p < 0.05$ ) and aortocoronary bypass 5.3% vs 0.5%, ( $p < 0.001$ )). In our cohort, women more often were diagnosed with severe depression than men (71.4% vs. 28.6%, ( $p < 0.05$ )). Severe depression was diagnosed more frequently in patients with valvular heart diseases (11.7% vs 3.6% ( $p < 0.05$ )), especially mitral valve diseases (11.6% vs. 3.6% ( $p < 0.05$ )) and patients with atrial fibrillation – paroxysmal (33.3% vs 13.7%, ( $p < 0.05$ )) and permanent (33.3 vs. 28.7, ( $p < 0.05$ )). Patients with previous myocardial infarction (33.3% vs. 7.6% ( $p < 0.05$ )) and previous stroke (66.7% vs. 17.4% ( $p < 0.05$ )) suffer more often from very severe depression. Clinically significant depression was present in patients with heart failure with mid-range ejection fraction (HFmEF) (33.3% vs 17.1%, ( $p < 0.05$ )) and heart failure with reduced ejection fraction (HFrEF) (50.0% vs. 16.7%, ( $p < 0.05$ )). Diabetes mellitus (8.6% vs 1.3% ( $p < 0.05$ )) and chronic kidney disease (CKD) (50.0% vs. 18.9% ( $p < 0.05$ )) were also associated with very severe depression. Heavy alcohol consumption was common in those with very severe depression (16.7 vs 12.9%, ( $p < 0.05$ )). Our data showed that anemia with hemoglobin below 117 g/l (AUC 0.66, 72% sensitivity and 68% specificity,  $p < 0.05$ ) is associated with an increased risk of

developing depression (fig. 2) and patients with hemoglobin below 100g/l develop very severe depression (16.7% vs 5.4%, (p<0.05)).

**Fig. 2.** Roc curve of hemoglobin.



Note: ROC-Receiver operating characteristic curve

Significant predictors of depression in HF patients were anemia, CKD, ejection fraction below 50% and alcohol consumption (Tabl.2).

**Table 2.** Predictors of depression in HF patients

Predictors of depression	OR	95% CI	P
Anemia	2.74	1.23-4.56	<0.05
CKD	12.29	1.57-16.17	<0.05
Ejection fraction <50%	4.35	2.07-8.85	<0.05
Alcohol consumption	6.39	1.72 – 15.14	<0.05

Note: CKD - chronic kidney disease

Anxiety was diagnosed in 71 (71.0%). With mild anxiety were 28 (28.6%) of the patients, 52 (53.1%) were with moderate and 18 (18.4%) – with severe anxiety (Tabl. 3).

**Table 3.** Stages of anxiety in HF patients

Stage of anxiety	N	%
Mild	28	28.6
moderate	52	53.1
severe	18	18.4

Note: N – number of patients

Anxiety was found more frequently after aortocoronary bypass operation (5.0% vs 1.2%, (p<0.05)). Patients with hypertension with poor control of blood pressure manifested symptoms of anxiety (70.3% vs. 26.1%, (p<0.05)) and moderate depression (60.9% vs. 35.5%, (p<0.05)). Patients with hypertension treated with calcium channel blockers (CCB) more often are diagnosed with anxiety disorders (46.9% vs. 22.5%, p<0.05) and moderate depression (51.0% vs. 33.7%, (p<0.05)). Smoking was associated with an increased risk of new onset of mood and anxiety disorders in HF patients (45.0% vs. 29.6%, p<0.05). In patients with valvular heart diseases was observed mild anxiety (16.7% vs 12.1% (p< 0.05)). Patients with mitral stenosis experienced more frequent anxiety than those with VHD (10.7% vs. 2.7%, (p<0.05)). Severe anxiety was found in patients with previous myocardial infarction (22.2% vs. 6.7%, (p<0.05)). Our data showed that statin therapy increases the risk of developing anxiety - severe anxiety was observed in those treated with atorvastatin (27.8 vs 5.8%, (p<0.05)), while rosuvastatin therapy was associated with moderate anxiety (25.0% vs 11.6%, (p<0.05)). People with anxiety disorder have a substantially higher prevalence of alcohol consumption, which is more heavily than the overall population (38.3% vs. 5.6%, (p<0.05)). Advanced heart failure, especially functional class NYHA 4, have markedly higher prevalence rates of severe anxiety (16.7% vs. 3.3%, p<0.05) and very severe depression (50.0% vs. 3.0%, (p<0.001)) than other HF patients.

The multivariable analysis in our study showed that predictors of anxiety in the HF cohort were poor controlled arterial hypertension, alcohol consumption, advanced HF and previous myocardial infarction (Tabl. 4).

**Table 4.** Predictors of anxiety in HF patients

Predictors of anxiety	OR	95% CI	P
Poor controlled arterial hypertension	2.18	1.26-5.57	<0.05
Alcohol consumption	2.75	1.43-4.23	<0.05
Advanced HF	4.75	2.02-7.66	<0.05
Previous myocardial infarction	3.25	1.89-5.53	<0.05

## DISCUSSION

Our study demonstrates that the onset of depression and anxiety disorder are a common occurrence in HF patients. They have been linked to the development and progression of HF and other cardiovascular diseases. Also, depression is known as a poor prognostic marker in patients with a diagnosis of HF [16]. In the present study, we found depression was developed in 82.6% and anxiety in 71% of HF patients in our institution. This is significantly higher compared to most studies in high-income countries. In a community-based study conducted in the United States of America, the prevalence of depression in CHF patients was 17% [17]. Furthermore, Haworth et al.

studied 100 outpatients with heart failure in the United Kingdom and found the prevalence rate for anxiety and depression to be 18% and 29%, respectively [18]. The higher prevalence of symptoms of depression and anxiety in our patients is likely influenced by socioeconomic factors in the population in Bulgaria. Depression and anxiety are common yet underreported in CHF and should not be overlooked when managing these patients. This is particularly important since both conditions have been associated with poor outcomes with more robust evidence for depression [15].

In a systematic review evaluating the prevalence, variance, and measurement tools for anxiety in patients with heart failure, the pooled prevalence from 38 studies ranged from 6.3 to 72.3% [7]. In our study, anxiety and depression coexisted in 54.6% of patients. Such a finding emphasizes the need to screen for both conditions since the treatment plan differs between the two conditions. This study indicated that those heart failure patients with NYHA class III and IV are more likely at risk of depressive/anxiety disorders compared to those who had NYHA class I and II. The possible explanation could be individual heart failure patients with advanced stage might be worried about their worsening symptom, illness-related complication, dietary restriction and inability to do any activity, and they are always dependent on others. This might directly or indirectly lead to depression and anxiety. This finding is supported by a study done in Ethiopia [19] and a study done in Greece 2020 [20]. Notably, the univariate logistic regression model indicated that NYHA class IV increased the odds of in-hospital anxiety by 4.57-fold; while a recent systematic review by Moradi M et al. [21] showed that odds of depression with any severity in HF patients was significantly 2.5 times higher with NYHA class III, IV compared to with NYHA class I, II.

Older age was documented as one of the contributing factors for depression in various patient populations [22, 23], and especially this problem was prevalent in older adults [24]. This point was reasonable when older adults were common in our sample size of HF patients. In our study population with HF, we saw that older age was significantly associated with a greater prevalence of depression. It is consistent with previous studies [25,26].

Our data revealed that those heart failure patients who experienced high alcohol intake showed a strongly positive association with depressive (OR 6.39 (95% CI 1.72 – 15.14,  $P < 0.05$ ) and anxiety disorder (OR 2.75, (95% CI 1.43-4.23,  $P < 0.05$ ), than those who have not experienced alcohol use. This might be due to the fact that alcohol use exposes to depression and anxiety. Most alco-

hol users might be affected by physiological, psychological, social and economic behaviour that can alters the metabolic condition of individual life and as a result of conflict to family and society at large. This finding is supported by research done in England [27], which contradicts research done in the United Kingdom, which showed no significant association between alcohol intake and depression.

In our study, depression rates in women are particularly high [28]. Comparably, a study of the year 2020 has found a significant gender-based association of HF with depression, where a high incidence is noted among females accompanied by a high fatality rate. Chronic comorbidities may potentially be a major factor in the progression of depression and anxiety in the HF population.

The current study revealed high depression and anxiety rates in HF patients who were afflicted with VHD and hypertension, also DM and CKD increased the risk of developing depression. In coherence, Bahall M. (2019) also signified hypertension and DM as the most common risk factors linked to depression in the HF cohort [29]. Coronary heart disease is strongly associated with depression [30] and is the principal risk factor for the development of HF. In our study, the most affected were those who experienced previous myocardial infarction. We also found that patients who underwent surgical procedures had a higher rate of depression and anxiety. Based on the current evidence, a positive correlation between depression/anxiety and HF can be established. The severity of HF may promote these psychiatric disorders. Management of mild to moderate depression/anxiety can be performed by implying early screening, cognitive behavioral therapy, and exercise. The severity of the disease can be additionally supported by antipsychotic drugs. High-risk depression/anxiety may require immediate psychiatric care and brain simulations.

## CONCLUSIONS:

Depression and anxiety are common, unrecognized, and associated with adverse outcomes in Bulgarian patients with HF. Our data shows that the key factors associated with the risk of developing depression in patients with HF are: CKD, anemia, alcohol use, ejection fraction  $< 50$ , while the most important factors associated with the development of anxiety are: uncontrolled hypertension, alcohol use, advanced HF and previous MI. The early diagnosis and treatment of these disorders, as well as an interdisciplinary approach, can contribute to an improvement of the health condition and quality of life in this group of patients.

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*Please cite this article as:* Kolev V, Manov E, Runev N, Stoimenov B, Onchev G, Pancheva R. The Prevalence and Severity of Depression and Anxiety in Heart Failure Patients in Bulgaria. *J of IMAB*. 2023 Oct-Dec;29(4):5208-5213. [Crossref - <https://doi.org/10.5272/jimab.2023294.5208>]

Received: 07/07/2023; Published online: 13/11/2023



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