

# Prevalence and variables predictive of depressive symptoms in patients hospitalized for heart failure

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## Abstract

**Background:** *Our study set out to determine the prevalence of depressive symptoms and variables that influence its presence in patients hospitalized for heart failure. Depression is associated with a substantially increased risk of developing heart failure in individuals at risk, and has been related to adverse outcomes in patients with established heart failure. It is important to determine its prevalence in different populations and assess related causes.*

**Methods:** *We conducted a cross-sectional study of 103 patients with heart failure, admitted to public hospital, via a questionnaire that evaluates clinical variables, socio-demographics and we applied the Beck Depression Inventory to determine the prevalence of depressive symptoms and predictors of their presence. We used the  $\chi^2$ , Student test and considered significant when  $< 0.05$  and subjected to logistic regression analysis when between 0.05 and 0.1.*

**Results:** *The mean age of the patients in our study was  $65.4 \pm 13.6$ . Depressive symptoms were present in 69 (67%) patients: 35 (34%) had mild depressive symptoms, 22 (21.3%) had moderate symptoms and 12 (11.6%) patients presented severe symptoms. Marital status was significant when analyzed, and the predictors of depressive symptoms were marital status, sex, living arrangements and heart failure etiology.*

**Conclusions:** *Because depressive symptoms in patients hospitalized for heart failure are very common, it is important to detect these disorders. The prevalence of these varies according to socio-demographic and clinical data, and these factors should be taken into consideration when planning future studies, as well as screening and intervention programs for co-morbid depressive disorders in hospitalized patients with heart failure. (Cardiol J 2011; 18, 1: 18–25)*

**Key words:** depression, heart failure, hospitalized patients

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## Introduction

Heart failure (HF) is characterized by markedly compromised cardiac function, a high rate of complications, and decreased life expectancy [1]. Impaired cardiac function and neurohumoral activation are the defining characteristics of HF that contribute to clinical deterioration, and the focus of interventions has generally been on improving circulatory function and on blocking the rennin–angiotensin and sympathetic nervous systems [2].

The presence of depressive symptoms (DS) is widely considered a significant risk factor in patients with coronary heart disease [3]. DS is associated with a substantially increased risk of developing HF in individuals at risk [4] and has been associated with adverse outcomes in patients with established HF [5]. Most studies on DS in patients with HF have focused on hospitalized patients, with a prevalence ranging from 13–77.5% [5–8]. The factors associated with DS in patients with HF have been controversial. Freedland et al. [9] found that age, gender, employment status, past history of depression and functional severity of illness are associated with DS in hospitalized patients with HF. In later studies on outpatients, Gottlieb et al. [10] found significant association equally among depression and age, gender and functional status.

These studies have all been done in western cultures. Research of literature, both manual and electronic, reveals few studies on DS in Brazilian patients with HF. At the same time, studies have suggested that patients in developing countries (and those of lower socio-economic status) often report somatic symptoms and deny psychological symptoms more frequently than patients in western or developed countries [11, 12].

With the potential importance of DS in the quality of life of patients with HF, a DS prevalence and predictors study of Brazilian patients with HF is therefore warranted. This study aims to estimate the prevalence of DS and examine the socio-demographic and clinical factors associated with DS in Brazilian hospitalized patients with HF.

## Methods

This is a cross-sectional study of patients with HF consecutively admitted to the cardiology ward in three public hospitals. Patients were recruited over a period of three months. All patients admitted had a previous diagnosis of HF or were diagnosed when admitted through the Boston criteria. The ejection fraction of left ventricle was assessed

by transthoracic echocardiography with Simpson's method and those included in this were < 50%. Exclusion criteria included: concomitant diagnosis of serious cancer, use of antidepressants in the 30 days prior to admission, disorders that prevented understanding and communication with the researcher, history of alcohol abuse or dependence in the last six months, psychotic symptoms, history of psychosis, bipolar disorder, dementia (or mental state score < 23) or inability to sign the informed consent form.

## Procedures

Participants were first given a questionnaire regarding socio-demographic data such as age, sex, marital status, employment, educational level and monthly income. The disease assessment was made by evaluating the functional class of New York Heart Association (NYHA) and obtained information about the cardiovascular risk factors, etiology of HF and treatment administered. The patient's race was not considered, due to the mixed characteristic of the Brazilian population. We obtained informed consent from all patients. The study was approved by the ethics committee in research.

The severity of HF was measured by functional class of NYHA [13]. This scale is used to quantify the degree of functional limitation imposed by HF. Four classes are assigned depending on the degree of effort required to cause symptoms. Patients may have symptoms of HF at rest (class IV) during daily activities (class III), when performing normal activities (class II) or only during those activities which limit normal individuals (class I) [14]. Demographic variables (age, sex, education level, marital status, housing conditions, presence or absence of fixed monthly income, living arrangements) were obtained by self-report at interview. No patients were in functional class I, because only hospitalized patients were included in the study. Co-morbidities and medications in use were studied.

To identify DS, the Beck Depression Inventory II was administered (BDI) [15, 16] to all patients in the study within five days of hospitalization. This scale, validated in Brazil and currently used in similar international studies, allows the identification of DS and their intensity via a score obtained by 21 indicator items. The score ranges from 0 to 63, according to Beck, distributed as follows: from 0 to 9 depression is considered absent, between 10 and 18 it is considered mild to moderate, between 19 and 29 it is considered moderate to severe, and above 30 it is considered severe. We considered as having DS those  $\geq 10$  points. The BDI [17] was used

to measure DS. This scale includes 21 symptoms and attitudes, covering emotions, behavioral changes, and somatic symptoms. In addition to the original scale, we computed the score excluding somatic symptoms (fatigue, sleep and appetite disturbances) that may result from HF rather than DS, and might therefore lead to an overestimation of the association between DS and heart failure stages. The application of the questionnaire was performed by physicians previously trained on the method [18].

The study was approved by the local bioethical committee and all patients gave their informed consent.

### Statistical analysis

Participants were classified as patients with DS, and without DS, based on the questionnaire adopted. The results were calculated as frequencies (%), mean and standard deviation. The  $\chi^2$  and Fisher's exact test were used to determine whether socio-demographic and clinical factors have any relation to DS. The level of significance was  $< 0.05$ . Variables with a value between 0.05 and 0.1 were included in logistic regression analysis to determine the predictive power of DS. The odds ratio (OR) and confidence interval (CI) 95% were calculated on predictor variables.

## Results

### Characteristics of the sample

Most patients were female (63.1%), married (50.5%), literate (73.8%) and less than half of them had a regular monthly income (43.7%). The vast majority belonged to functional classes II and III (75.2%). Hypertension was present in almost all samples (92.2%). Non-ischemic etiology was defined as the commonest cause of HF (57.3%). The baseline characteristics of the sample are presented in Table 1.

### Prevalence of depressive symptoms

The study sample was analyzed using the BDI: 69 (67%) patients with DS were identified. When evaluated, 35 (34%) had mild DS, 22 (21.3%) had moderate symptoms and 12 (11.6%) patients presented with severe symptoms.

### Correlates of depressive symptoms

Patients were divided into two groups with bases in the presence or absence of DS according to BDI. Univariate analyses were performed by  $\chi^2$  test or Fisher's exact test as presented in Tables 2 and 3. The only significant variable was marital sta-

**Table 1.** Baseline characteristics.

<b>Socio-demographic factors</b>		
Age (mean\SD)		65.4 (13.6%)
Sex	Male	38 (36.9%)
	Female	65 (63.1%)
Educational level	Illiterate	27 (26.2%)
	Literate	76 (73.8%)
Marital status	Married	51 (49.5%)
	Not married	52 (50.5%)
Monthly income	Have	45 (43.7%)
	Don't have	58 (56.3%)
Housing status	Homeowners	65 (63.1%)
	Not homeowners	38 (36.9%)
Living arrangements	Alone	29 (28.1%)
	Not alone	74 (71.9%)
<b>CV risk factors</b>		
Hypertension		95 (92.2%)
Diabetes mellitus		35 (34%)
Dyslipidemia		47 (45.6%)
Sedentary		85 (82.5%)
Smoking		36 (35%)
Alcohol consumption		22 (21.4%)
Family history of CV disorders		95 (92.2%)
<b>NYHA classification</b>		
II		35 (34%)
III		43 (41.2%)
IV		25 (24.3%)
<b>Drug treatment</b>		
ACEI		69 (67%)
Inhibitors of angiotensin II receptor		31 (30.1%)
Adrenergic beta-blockade		81 (78.6%)
Thiazide diuretics		21 (20.4%)
Aldosterone inhibitors		50 (48.5%)
Calcium channel blockers		20 (19.4%)
Oral nitrates		33 (32%)
Aspirin		66 (64.1%)
Oral anticoagulation		10 (9.7%)
Digitalis		45 (43.7%)
Thienopyridine		5 (4.8%)
Arterial vasodilators		2 (1.9%)
Statins		43 (41.7%)
Loop diuretics		59 (57.3%)
<b>Heart failure etiology</b>		
Ischemic		44 (42.7%)
Non-ischemic		59 (57.3%)

CV — cardiovascular; ACEI — angiotensin converting enzyme inhibitors

tus ( $p = 0.03$ ). When analyzing the variables for proper verification of the predictive variables for DS with  $p < 0.10$ , we considered gender, living arrange-

**Table 2.** Comparison between patients with depressive symptoms (DS) and without depressive symptoms related to clinical variables.

Variables	All patients	DS presence	No DS	P
<b>CV risk factors</b>				
Hypertension	95 (92.2%)	67 (70.5%)	28 (29.5%)	0.35
Diabetes mellitus	34 (33.0%)	23 (67.6%)	11 (32.4%)	0.56
Dislipidemia	47 (45.6%)	30 (63.8%)	17 (36.2%)	0.42
Sedentary	81 (78.6%)	56 (69.1%)	25 (30.9%)	0.44
Smoking	23 (22.3%)	13 (56.5%)	10 (43.5%)	0.23
Alcohol consumption	20 (19.4%)	17 (85.0%)	3 (15.0%)	0.08
<b>Other variables</b>				
Anemia	39 (37.9%)	29 (74.3%)	10 (25.7%)	0.26
COPD	12 (11.6%)	8 (66.7%)	4 (33.3%)	0.60
Hypothyroidism	6 (5.8%)	5 (83.3%)	1 (16.7%)	0.36
CRF	6 (5.8%)	6 (100%)	0 (0%)	0.09
Atrial fibrillation	21 (20.4%)	14 (66.7%)	7 (33.3%)	0.58
<b>Drug treatment</b>				
ACEI	69 (67.0%)	45 (65.2%)	24 (34.3%)	0.46
ARB II	31 (30.0%)	24 (77.4%)	7 (22.6%)	0.18
Adrenergic beta-blockers	83 (80.5%)	54 (65.0%)	29 (35.0%)	0.45
Thiazide diuretics	21 (20.3%)	15 (71.4%)	6 (28.6%)	0.45
Aldosterone inhibitors	50 (48.5%)	38 (76.0%)	12 (24.0%)	0.17
Calcium channel blockers	20 (19.4%)	15 (75.0%)	5 (25.0%)	0.33
Oral nitrates	33 (32.0%)	22 (66.7%)	11 (33.3%)	0.56
Aspirin	57 (55.3%)	45 (79.0%)	22 (21.0%)	0.55
Oral anticoagulation	10 (9.7%)	5 (50.0%)	5 (50.0%)	0.22
Digitalis	43 (41.7%)	30 (69.7%)	13 (30.3%)	0.45
Thienopyridine	5 (4.8%)	3 (60.0%)	2 (40.0%)	0.53
Hydralazine	2 (1.9%)	1 (50.0%)	1 (50.0%)	0.55
Loop diuretics	59 (57.2%)	46 (80.0%)	13 (22.0%)	0.12
<b>NYHA classification (FC)</b>				
II	36 (34.9%)	25 (69.4%)	11 (30.6%)	0.47
III	42 (40.8%)	27 (64.3%)	14 (35.7%)	
IV	25 (24.3%)	17 (68.0%)	8 (32.0%)	
<b>Heart failure etiology</b>				
Ischemic	43 (41.7%)	33 (76.7%)	10 (23.3%)	0.05
Non-ischemic	60 (58.3%)	36 (60.0%)	24 (40.0%)	

CV — cardiovascular; COPD — chronic obstructive pulmonary disease; CRF — chronic renal failure; ACEI — angiotensin-converting enzyme inhibitors; ARB — angiotensin receptor blockers; FC — functional class

ments, alcohol consumption, chronic renal failure and HF etiology. The variables that were not confirmed as a predictor of DS were alcohol consumption and chronic renal failure, presented in Table 4. The OR and CI 95% are presented in Table 5.

## Discussion

Many disturbances are common between HF and DS and they act during the continuum that leads up to overt HF. Particularly, neurohormonal acti-

vation is initially triggered as an adaptive response, but it eventually becomes maladaptive and perpetuates the process through a positive feedback mechanism. Moreover, precursors and risk factors for HF, namely coronary heart disease (as cause, consequence, and prognostic factor), hypertension [19], diabetes mellitus [20], obesity [21, 22], smoking [23], and excessive alcohol consumption [24], are, themselves, related to a higher prevalence of DS. If the higher prevalence of DS in HF patients is mainly a consequence of the association with

**Table 3.** Comparison between patients with depressive symptoms (DS) and without depressive symptoms related to socio-demographic variables.

Variables	All patients	DS presence	No DS	P
Age	65.43 (13.66%)	66.56 (13.18%)	63.14 (14.50%)	0.26
<b>Socio-demographic variables</b>				
Sex				
Male	38 (36.9%)	26 (68.4%)	12 (31.6%)	0.06
Female	65 (63.1%)	43 (66.1%)	22 (33.9%)	
Marital status				
Married	52 (50.5%)	31 (59.6%)	21 (40.4%)	0.03
Not married	51 (49.5%)	39 (76.4%)	12 (23.6%)	
Monthly income				
Have	45 (43.6%)	29 (64.4%)	16 (35.6%)	0.32
Don't have	58 (56.4%)	41 (70.7%)	17 (29.3%)	
Educational level				
Literate	75 (72.8%)	52 (69.3%)	23 (30.7%)	0.39
Illiterate	28 (27.2%)	8 (64.3%)	10 (35.7%)	
Living arrangements				
Live with others	74 (71.8%)	47 (63.5%)	27 (36.5%)	0.09
Live alone	29 (28.2%)	23 (79.3%)	6 (20.7%)	
Housing status				
Homeowners	63 (61.1%)	41 (65.0%)	22 (35.0%)	0.57
Not homeowners	37 (38.9%)	26 (70.3%)	14 (29.7%)	

**Table 4.** Logistic regression analysis to determine predictors of depressive symptoms in patients hospitalized for heart failure

Variables	$\beta$	t	p
Sex	0.55	4.4	< 0.0001
Living arrangements	0.45	3.19	0.002
Alcohol consumption	-0.46	-1.08	0.28
Chronic renal failure	-0.31	0.13	0.71
Heart failure etiology	0.74	5.98	< 0.0001

those risk factors, we would expect this effect to be already present in asymptomatic precursors of HF. If, however, DS acts mainly through changing perceptions and symptoms (that is, if depressed

patients are simply more sensitive to symptoms and express more severe fatigue, dyspnea and functional impairment with the same objective cardiac physiological abnormalities) then it should be associated only or mainly with symptomatic HF.

#### Depression prevalence and characteristics in patients with heart failure

In this study, 11.6% of the patients were considered as having severe DS and 21.3% as moderate. The prevalence of DS among patients with HF has varied widely, reflecting differences in populations and methods of diagnosing DS [8, 24–27]. Four studies that used the self-administered Center for Epidemiologic Studies Depression Scale reported depression prevalence from 24.4% to 58% [8, 28–30]. The one that used the self-administered Zung tool

**Table 5.** Variables predictive for depressive symptoms in patients with heart failure found in logistic regression.

Variable	Odds ratio (95% CI)
Sex: male vs female	1.10 (0.47–2.60)
Marital status: married vs not married	0.45 (0.19–1.06)
Living arrangements: live with another vs live alone	0.45 (0.16–1.25)
Heart failure etiology: ischemic vs non-ischemic	2.20 (0.91–5.28)

reported a 13% prevalence [31] and the one that used the self-reported Geriatric Depression Scale Short-Form reported a 77.5% prevalence [32]. Sullivan et al. [25] used the Primary Care Evaluation of Mental Disorder psychiatric diagnostic interview sections on depression, anxiety and alcohol disorders, finding a rate of 29% for 142 outpatients with advanced HF having major DS (16%), dysthymia (11%), and/or minor DS (8%). In our sample, the overall prevalence of DS was 69 (67%) patients.

Furthermore, although patients with non-ischemic etiology of HF were reported to have a lower prevalence of DS in a study of 396 patients [33], the prevalence of DS did not differ significantly by HF etiology in our study. The prevalence of DS likewise did not differ significantly by sex, although the recent National Comorbidity Survey reported a lifetime odds ratio for DS for women compared to men of 1.7 [34]. In another study, female gender was associated with DS when criteria for severe DS were used, but DS prevalence did not vary by sex when DS was defined as a BDI [9]. Three other studies have also found no significant link between sex and DS [8, 32, 33]. The pathophysiologic link between DS and HF therefore may not be related to sex. In our study, sex was considered a predictor variable for the DS presence, although it is still considered controversial.

### Predictors of depressive symptoms

Marital status was the risk factor for DS in our study. Although advancing age was associated with increasing DS, it was not related to a higher prevalence. This has been noticed in some previous studies [8, 9] but not in others [32, 33]. Koenig [8] found that a composite measure of medical illness severity independently predicted DS in patients with HF, whereas others reported that patients with greater HF symptoms were more likely to be depressed [9, 32–35]. A link between DS and NYHA classification (but not ejection fraction) may explain why some patients with HF with lower ejection fractions remain asymptomatic, while others with higher ejection fractions are physically limited because of significant fatigue or dyspnea. Such findings suggest each of them has independent predictability for survival. Depressive symptoms are a risk factor for ischemic heart disease development as well as for poor prognosis, once it is manifested [36]. In our study, we submitted the following variables to logistic regression analysis: sex, living arrangements, alcohol consumption, chronic renal failure and HF etiology. Variables that were confirmed as predic-

tors of DS in our sample were sex, living arrangements and HF etiology.

Havranek et al. [23] identified four independent predictors associated with the development of depressive symptoms among 245 outpatients with HF, as measured by the Medical Outcomes Study-Depression tool: (1) living alone, (2) alcohol abuse, (3) perceived financial burden from medical care, and (4) worse baseline HF-specific health status as measured by the Kansas City Cardiomyopathy Questionnaire. Patients who developed depressive symptoms at one-year follow-up were more likely to live alone (40% vs 23%,  $p = 0.015$ ), have a history of alcohol abuse (23% vs 11%,  $p = 0.013$ ), and perceive medical care as an economic burden (60% vs 34%,  $p = 0.003$ ). The Kansas City Cardiomyopathy Questionnaire summary scores of 60 vs 71 were worse in patients who developed significant depressive symptoms at one year ( $p < 0.001$ ). For patients with one, two, and three risk factors, the incidence of significant depressive symptoms at one year was 16%, 36%, and 69%, respectively. There were no significant differences between the patients who developed depressive symptoms and the patients who did not regarding age, race or marital status [23].

These include high activation of the hypothalamic-pituitary-adrenal axis and intra-abdominal fat content [37, 38], elevated plasma norepinephrine, increased heart rate, reduced heart rate variability [39, 40], increased platelet aggregation [41], and elevated plasma levels of proinflammatory cytokines such as tumor necrosis factor, interleukin-1, the interleukin-6 family [42, 43] and C-reactive protein [44]. Mental stress-induced myocardial ischemia, a risk factor for the poor prognosis of cardiac patients, is found to be associated with DS [45]. Moreover, DS adversely affects patient adherence to recommended interventions.

In contrast to its strong association with functional class, severe DS is associated with medical co-morbidity. However, the variables in our sample were not related to severe DS in the univariate analysis and were not retained as independent correlates. There was no difference in terms of education, income, housing conditions or beta-blockade. Beta-blockers improve prognosis in HF, but doctors may be reluctant to prescribe them for depressed patients. If this increases the risk of morbidity and mortality it should be investigated. Independent predictors included sex, living arrangements and etiology of HF. Most of the correlations of major depression also correlate with minor depression, but not so strongly [43, 44].

## Limitations of the study

Unlike the previous studies of depressive disorders in hospitalized patients with HF, both of which were restricted to elderly patients, this one also includes young patients. Because of its more inclusive sample, the present findings provide better estimates of the prevalence of DS in the population of patients hospitalized with HF when compared to earlier studies. The small sample may imply limitations on the representativeness of the results. Furthermore, this report identifies a number of patient characteristics that help to explain why the observed prevalence of severe DS has varied so widely across the studies.

Despite the cross-sectional design, the classification of subjects according to evolving stages of HF allowed us to come closer to a longitudinal perspective and to demonstrate higher scores on a depression scale in women at early, asymptomatic stages of HF. These results show that the association between DS and HF is not merely explained by the emotional effect of medical illness. If future studies confirm that depression contributes to a more likely or faster progression of symptomatic HF, we can make a clearer prediction of future HF.

## Conclusions

Depressive symptoms are very common in hospitalized patients with HF. Its prevalence varies according to how DS is defined and according to the patient's demographic, medical and social characteristics. Predictive factors such as gender, marital status, lifestyle and etiology of HF were important to the presence of DS in the sample. These factors should be taken into consideration when planning future studies as well as screening and intervention programs for co-morbid depressive disorders in hospitalized patients with HF.

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