

Original Article

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Depressive symptoms and related factors in adults with heart failure: A multicenter cross-sectional study in northern Iran (2022–2023)

Abstract

Background: Depressive symptoms are frequent in patients with heart failure (HF), but estimates vary across settings. Clarifying their burden and related factors can inform integrated care. This study aimed to estimate the prevalence of depressive symptoms in adults with HF and identify associated factors.

Methods: We conducted a multicenter cross-sectional study (June 2022–February 2023) in cardiology wards and outpatient clinics of three hospitals affiliated with Babol University of Medical Sciences, northern Iran. Consecutive adults (≥ 18 years) with cardiologist-confirmed HF completed the 17-item Hamilton Depression Rating Scale (HAM-D-17); a score >7 was considered indicative of clinically relevant depressive symptoms. Baseline demographic and clinical characteristics were recorded. Independent correlates of depressive symptoms were examined using multivariable logistic regression.

Results: Of 250 participants (mean age 60.3 ± 15.1 years; 46.4% women), 51 (20.4%) had depressive symptoms (HAM-D-17 >7): mild 18.4%, moderate 1.6%, severe 0.4%. In unadjusted analyses, depressive symptoms were more common in women, in unemployed and unmarried participants, and in those with more advanced New York Heart Association (NYHA) functional class. In multivariable models, female sex (OR 6.57, 95% CI 2.91–14.85) and higher NYHA class were associated with depressive symptoms ($p < 0.01$), whereas left ventricular ejection fraction and HF etiology were not.

Conclusion: Approximately one fifth of adults with HF had clinically relevant depressive symptoms, particularly women and patients with worse functional status. Routine screening and integrated psychosocial care should be incorporated into HF management, with special attention to patients in advanced NYHA classes.

Keywords: Heart failure, Depressive symptoms, Prevalence, Cross-sectional study.

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Heart failure (HF) is a complex clinical syndrome characterized by impaired myocardial function and reduced cardiac output and remains a major global health challenge (1). Patients experience dyspnea, fatigue and edema; functional limitation is commonly graded by the New York Heart Association (NYHA) classification (I–IV), which informs prognosis and care (2). The prevalence of HF is rising with population aging and epidemiologic shifts. Globally, approximately 64 million people live with HF, with more than 300,000 deaths annually (3). The burden of HF is higher in low- and middle-income countries, particularly in Asia and Africa (3, 4). In Iran, its prevalence has been estimated to exceed 8%, which is higher than the regional average (5). HF is frequently accompanied by depression (6), one of the most common comorbidities in this population, affecting approximately 20–30% of patients (7), and more than 50% of those in advanced stages (4).



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These rates are substantially higher than in the general population and highlight the considerable comorbidity between HF and depression (8). The co-occurrence of depression with heart failure is linked to poorer self-care (9), lower treatment adherence (10), reduced quality of life (3), increased risk of short and long-term readmission (11), and mortality. Even with appropriate pharmacotherapy, it confers roughly 40–70% higher risks of hospitalization and death (12), resulting in an overall worse prognosis (3).

Despite extensive research, results on the prevalence and factors associated with depression in heart failure patients are inconsistent. Some studies have shown that depression increases the risk of mortality only in patients with low ejection fraction ($EF \leq 35\%$), while such an association was not observed in patients with higher EF (8). Also, the association of depression with decreased left ventricular function or ischemic etiology has been reported in some studies, but has not been replicated in other studies (13). This heterogeneity of findings, together with the lack of standardized screening protocols and the overlap between physical and psychological symptoms such as fatigue, reduced energy, and sleep disturbance have led to underdiagnosis of depression in many patients with HF and limited access to appropriate psychiatric care (14). Therefore, this multicenter study was conducted to investigate the prevalence of depressive symptoms, as assessed by the HAM-D-17, and to identify associated demographic and clinical factors in adults with heart failure in northern Iran.

Methods

Study design and reporting: This cross-sectional, descriptive–analytical study was conducted according to a predefined protocol and the STROBE guidelines. The study protocol was approved by the Ethics Committee of Babol University of Medical Sciences (IR.MUBABOL.HRI.REC.1401.014).

Setting and participants: Participants were recruited from cardiology inpatient wards and outpatient clinics of three teaching hospitals (Shahid Beheshti, Rouhani, Shahid Yahyanejad) affiliated with Babol University of Medical Sciences) June 2022 - February 2023(. Recruitment took place at all three centers using identical eligibility criteria and consecutive screening procedures. Eligibility: adults (≥ 18 years) with HF confirmed by a cardiologist based on clinical assessment consistent with the American Heart Association/European Society of Cardiology diagnostic frameworks, supported by laboratory tests and echocardiography (AHA/ESC). Exclusion criteria were

inability to provide informed consent, major neurocognitive disorder or psychosis, severe sensory or language impairment, hemodynamic instability, or refusal to participate.

Demographic and clinical checklist: For each participant, baseline demographic (age, sex, marital and employment status) and clinical data were collected, including HF etiology (ischemic vs non-ischemic); HF duration; cardiovascular medications (categorized by drug class: ACE inhibitors (ACEIs), angiotensin-receptor blockers (ARBs), angiotensin receptor–neprilysin inhibitors (ARNIs), guideline-preferred β -blockers, mineralocorticoid-receptor antagonists (MRAs), loop diuretics, SGLT2 inhibitors, and hydralazine/nitrate), New York Heart Association (NYHA) functional class: I (no limitation), II (mild limitation with symptoms on ordinary activity), III (marked limitation with symptoms on less-than-ordinary activity), IV (symptoms at rest) (15), and left ventricular ejection fraction (LVEF). LVEF was obtained from echocardiography, recorded as a percentage, and categorized by guideline-based categories: heart failure with reduced ejection fraction (HFrEF, LVEF $<40\%$), mildly reduced ejection fraction (HFmrEF, LVEF 41–49%), preserved ejection fraction (HFpEF, LVEF $\geq 50\%$), and improved ejection fraction (HFimpEF, previous LVEF $\leq 40\%$ with current LVEF $>40\%$) (15–17).

Hamilton depression rating scale (HAM-D-17): Depressive-symptom severity was assessed using the 17-item HAM-D-17 (18). The total score ranges from 0 to 52; scores ≤ 7 indicate no or minimal depressive symptoms, 8–17 mild, 18–24 moderate, and ≥ 25 severe symptoms. For the main analyses, a score >7 was used to define clinically relevant depressive symptoms (binary outcome) (19). A validated Persian version was used; prior Persian-language studies have demonstrated strong convergent validity with the Montgomery–Åsberg Depression Rating Scale (MADRS), with correlations of $r = 0.92$ – 0.96 (20).

Outcomes: The primary outcome was the presence of clinically relevant depressive symptoms, defined as a HAM-D-17 score greater than 7. NYHA functional class (I–IV) and LVEF, analyzed as a continuous variable and categorized as HFrEF, HFmrEF, HFpEF, and HFimpEF, were identified a priori as key clinical covariates in the multivariable models.

Procedures: Following ethics approval from the Ethics Committee of Babol University of Medical Sciences, eligible patients were approached, the study procedures were explained, and written informed consent was obtained. The Demographic/Clinical Checklist was completed, and NYHA functional class was assigned according to standard

criteria. Heart failure pharmacotherapy was documented and coded by treatment intensity: (i) guideline-directed quadruple therapy (ACEI/ARB/ARNI, evidence-based β -blocker, MRA, SGLT2 inhibitor); (ii) extended therapy with the addition of a loop diuretic (e.g., furosemide) and, where applicable, digoxin; and (iii) high-intensity/polypharmacy regimens (>6 agents), which could include antiplatelets (e.g., aspirin), lipid-lowering agents, and anticoagulants. Cardiac function indices, including LVEF, were abstracted from 2D/Doppler echocardiography reports and recorded both as continuous values and as guideline-based categories.

Depressive-symptom severity was assessed using the 17-item HAM-D-17. All HAM-D-17 interviews were conducted face to face by a psychiatry resident who had received structured training in the administration and scoring of the scale. Assessments were performed after cardiologist-confirmed hemodynamic stabilization, either in a quiet area of the cardiology outpatient clinic or at the bedside in the cardiology ward, and were typically completed within 24–48 hours of eligibility confirmation. Privacy and confidentiality were ensured; interviews were conducted without family members present unless specifically requested by the patient.

Participants with HAM-D-17 scores >7 were informed of their screening result and, with their permission, were referred to the hospital psychiatry service for further clinical evaluation and management as part of routine care. These subsequent clinical assessments were not part of the study protocol, and their findings were not systematically collected or analyzed as research data.

Sample Size: Based on prior evidence (21), we set the expected prevalence (p) at 0.20 and estimated the sample size for a single proportion with 5% absolute precision at 95% confidence ($Z=1.96$, $d=0.05$). The calculation yielded $n=245.9$, rounded to 246; allowing 2% non-response, the final target sample was $N=250$.

$$n = \frac{Z^2 \cdot p \cdot (1 - p)}{d^2}$$

Sampling: A non-probability, consecutive sampling strategy was used. During the study period, all adults with cardiologist-confirmed HF who attended the cardiology inpatient wards or outpatient clinics of the three teaching hospitals and met the eligibility criteria were screened and approached in the order of admission or clinic visit. Eligible patients were invited to participate until the target sample size ($N=250$) was reached. To avoid duplicate enrolment across centers, patient identifiers were cross-checked and unique study codes were assigned. Refusals and reasons for

non-participation were documented, and participant flow was tracked throughout the study.

Bias mitigation: Selection bias was minimized through consecutive recruitment at all three hospitals and systematic documentation of non-participation. Information bias was reduced by using a standardized, interviewer-administered HAM-D-17. The assessor received structured training on standardized administration and scoring of the HAM-D-17 prior to study initiation and was not involved in cardiology care or aware of detailed LVEF categories and pharmacotherapy at the time of assessment. Potential confounding (age, sex, HF duration and etiology, NYHA class, LVEF) was addressed using multivariable modeling, and data quality was supported by standardized checklists and periodic monitoring.

Statistical analysis: Analyses were conducted using SPSS Version 22 (IBM Corp., Armonk, NY, USA). A two-sided α of 0.05 was considered statistically significant. The distribution of continuous variables was assessed using the Shapiro–Wilk test with inspection of Q–Q plots, and homogeneity of variances was evaluated using Levene’s test. Normally distributed variables are presented as mean $\pm$ standard deviation (SD) and were compared using independent-samples t tests or one-way ANOVA, as appropriate. Non-normally distributed variables are summarized as median [interquartile range, IQR] and were compared using the Mann–Whitney U test or Kruskal–Wallis test. Categorical variables are presented as n (%) and were compared using Pearson’s χ^2 test or Fisher’s exact test, with linear-by-linear χ^2 for ordered categories. Associations between candidate predictors and screen-positive depressive symptoms (HAM-D-17 >7) were examined using binary logistic regression to estimate odds ratios (ORs) with 95% confidence intervals (CIs). Candidate predictors were specified a priori on clinical grounds (sex, marital and employment status, HF etiology, NYHA class, LVEF, HF duration, medication count, anti-ischemic therapy, RAAS therapy, and SGLT2 inhibitor use) and entered using a forward likelihood-ratio procedure. Model assumptions (linearity of the logit and multicollinearity) were checked, and model calibration (Hosmer–Lemeshow) and discrimination (C-statistic/area under the curve) were evaluated.

Missing data: Missing data were handled according to a prespecified plan. Complete-case analysis (no imputation) was applied to variables with <5% missingness, consistent with methodological guidance (22). The extent and pattern of missingness were assessed before modeling, and multivariable analyses were restricted to observations with complete data on all included covariates.

Results

After exclusion of cases with we incomplete file data and Baseline characteristics for the 250 patients with heart failure are presented overall and stratified by depressive-symptom status, followed by prespecified bivariate analyses and multivariable logistic regression (two-sided $\alpha=0.05$), selected according to variable type and distribution.

Baseline characteristics by depressive-symptom status:

When comparing groups defined by HAM-D-17 >7 (table 1), participants with depressive symptoms were more often female, unmarried, and unemployed; had a higher

proportion of non-ischemic HF; showed worse functional status (more NYHA class III–IV); and had lower LVEF and longer HF duration. These differences were statistically significant (table 1).

Prevalence and severity of depressive symptoms: Using HAM-D-17 >7 , 51 of 250 (20.4%) participants had clinically relevant depressive symptoms. Most symptomatic patients were in the mild range, whereas moderate and severe symptom levels were uncommon. HAM-D-17 data were complete (0% missing) (table 2).

Table 1. Baseline demographic and clinical characteristics by depressive-symptom status (depressive symptoms defined as HAM-D-17 >7).

Variable	Category/Metric	Total (N = 250)	Non-depressed (n = 199)	Depressed (n = 51)	P-value
Age (years)	Mean $\pm$ SD	60.3 $\pm$ 15.1	—	—	—
Sex	Female	116 (%46.4)	79 (%39.7)	37 (%72.5)	<0.001*
	Male	134 (%53.6)	120 (%60.3)	14 (%27.5)	
Marital status	Married	221 (%88.4)	181 (%91.0)	40 (%78.4)	0.044*
	Single	10 (%4.0)	6 (%3.0)	4 (%7.8)	
	Widowed	19 (%7.6)	12 (%6.0)	7 (%13.7)	
Employment	Not employed	183 (%73.2)	138 (%69.3)	45 (%88.2)	0.007*
	Employed	67 (%26.8)	61 (%30.7)	6 (%11.8)	
HF etiology	Ischemic	129 (%51.6)	111 (%55.8)	18 (%35.3)	0.009*
	Non-ischemic	121 (%48.4)	88 (%44.2)	33 (%64.7)	
NYHA class	I	96 (%38.4)	90 (%45.2)	6 (%11.8)	<0.001* ^a
	II	94 (%37.6)	76 (%38.2)	18 (%35.3)	
	III	44 (%17.6)	21 (%10.6)	23 (%45.1)	
	IV	16 (%6.4)	12 (%6.0)	4 (%7.8)	
LVEF (%)	Mean $\pm$ SD	26.5 $\pm$ 10.1	27.3 $\pm$ 9.7	23.4 $\pm$ 10.9	0.013*
HF duration (years)	Median [IQR]	4 [2–8]	4 [1–7]	6 [3–8]	0.002*

Values are n (%), mean $\pm$ SD, or median [IQR]. Categorical variables: Pearson's χ^2 or Fisher's exact; Age and LVEF: independent-samples t test (normal); HF duration: Mann–Whitney U (non-normal); ^a Trend across NYHA: linear-by-linear χ^2 ; two-sided: *p < 0.05. Abbreviations: HF: Heart failure; NYHA: New York Heart Association; LVEF: Left ventricular ejection fraction; SD: Standard deviation; IQR: Interquartile range.

Table 2. Prevalence of depressive-symptom categories based on the HAM-D-17 (N=250)

Outcome (HAM-D-17 categories)	N (%)
No depressive symptoms (≤ 7)	199 (%79.6)
Mild depressive symptoms (8–17)	46 (%18.4)
Moderate depressive symptoms (18–24)	4 (%1.6)
Severe depressive symptoms (≥ 25)	1 (%0.4)

Values are n (%). Depressive symptoms were defined and categorized using the 17-item Hamilton Depression Rating Scale (HAM-D-17). Abbreviations: HAM-D-17, 17-item Hamilton Depression Rating Scale.

Assumption checks & data quality: Missingness was <5% across analytic variables; we used complete-case analysis. Shapiro–Wilk (with Q–Q inspection) supported normality for age and LVEF ($p > 0.05$), while HF duration was non-normal ($p < 0.001$) and summarized as median [IQR] and analyzed non-parametrically. Levene’s tests supported variance homogeneity ($p \geq 0.05$). Diagnostics preceded comparative tests and regression.

Bivariate associations with depressive symptoms: In unadjusted (bivariate) comparisons by depressive-symptom status (HAM-D-17), depressive symptoms were more frequent in women and unemployed patients. Marital status differed significantly across depressive-symptom groups, with distinct distributions among married, single, and widowed participants (table 3). Depressive symptoms were also associated with non-ischemic HF etiology, higher NYHA class, lower LVEF, longer HF duration, and less use of anti-ischemic medication.

Multivariable logistic regression of depressive-symptom correlates: To assess independent associations with depressive symptoms (HAM-D-17 > 7), a multivariable logistic regression with forward stepwise (likelihood-ratio) selection was fitted (table 4). During multivariable

modeling, several clinically relevant covariates were tested but were not independently associated with depressive symptoms after adjustment and therefore were not retained in the final forward stepwise model. Female sex was associated with higher odds of depression (OR 6.57, 95% CI 2.91–14.85; $p < 0.001$). Compared with NYHA class IV, class I showed a protective (lower odds) effect (OR 0.12, 95% CI 0.03–0.56; $P = 0.007$), whereas classes II and III were not significant ($P = 0.271$ and $P = 0.098$, respectively). Multivariable binary logistic regression (forward LR). Outcome coded as 1 = HAM-D-17 > 7 . Values are odds ratios (OR) with 95% confidence intervals and two-sided p values (Wald test). Reference categories: male sex; NYHA class IV. * $p < 0.05$. Additional covariates (marital status, employment status, HF duration, LVEF, and HF etiology) were tested in the multivariable model but were not retained in the final model using forward likelihood-ratio selection. Abbreviations: OR: Odds ratio; CI: Confidence interval; NYHA: New York Heart Association. Additional covariates (marital status, employment status, HF duration, LVEF, and HF etiology) were examined in the multivariable model but were not retained in the final model using forward likelihood-ratio selection.

Table3. Bivariate associations with depressive symptoms (HAM-D-17 > 7)

Variable	Category/Metric	Total (N=250)	Non-depressed (n=199)	Depressed (n=51)	P-value
Sex	Female	116 (%46.4)	79 (%39.7)	37 (%72.5)	<0.001*
	Male	134 (%53.6)	120 (%60.3)	14 (%27.5)	
Marital status	Married	221 (%88.4)	181 (%91.0)	40 (%78.4)	0.044*
	Single	10 (%4.0)	6 (%3.0)	4 (%7.8)	
	Widowed	19 (%7.6)	12 (%6.0)	7 (%13.7)	
Employment	Not employed	183 (%73.2)	138 (%69.3)	45 (%88.2)	0.007*
	Employed	67 (%26.8)	61 (%30.7)	6 (%11.8)	
HF etiology	Ischemic	129 (%51.6)	111 (%55.8)	18 (%35.3)	0.009*
	Non-ischemic	121 (%48.4)	88 (%44.2)	33 (%64.7)	
No. of cardiac medications	≤ 4	110 (%44.0)	80 (%40.2)	30 (%58.8)	0.047*
	5–6	83 (%33.2)	72 (%36.2)	11 (%21.6)	
	> 6	57 (%22.8)	47 (%23.6)	10 (%19.6)	
β -blocker use	Yes	231 (%92.4)	183 (%92.0)	48 (%94.1)	0.604
Diuretic use	Yes	220 (%88.0)	176 (%88.4)	44 (%86.3)	0.671
Anti-ischemic medication	Yes	132 (%52.8)	113 (%57.1)	19 (%37.3)	0.011*
SGLT2 inhibitor (empagliflozin)	Yes	46 (%18.4)	34 (%17.1)	12 (%23.5)	0.289
NYHA class	I	96 (%38.4)	90 (%45.2)	6 (%11.8)	$p < 0.001^a$
	II	94 (%37.6)	76 (%38.2)	18 (%35.3)	
	III	44 (%17.6)	21 (%10.6)	23 (%45.1)	
	IV	16 (%6.4)	12 (%6.0)	4 (%7.8)	

Variable	Category/Metric	Total (N=250)	Non-depressed (n=199)	Depressed (n=51)	P-value
RAAS therapy ^b	None	18 (%7.2)	17 (%8.5)	1 (%2.0)	0.045*
	ACEi-ARB only	22 (%8.8)	17 (%8.5)	5 (%9.8)	
	MRA-only	33 (%13.2)	21 (%10.6)	12 (%23.5)	
	Both (ACEi/ARB + MRA)	177 (%70.8)	144 (%72.4)	33 (%64.7)	
LVEF, %	Mean±SD	26.5±10.1	27.3±9.7	23.4±10.9	0.013*
HF duration, y	Median [IQR]	4 [2–8]	4 [1–7]	6 [3–8]	0.002*

Values are n (%), mean±SD, or median [IQR]; two-sided $\alpha=0.05$. Categorical: Pearson's χ^2 /Fisher's exact. Continuous: t (normal) or Mann-Whitney (HF duration). Superscripts: ^a = p for trend across NYHA classes (linear-by-linear χ^2); ^b = RAAS therapy labels (None; ACEi/ARB only; MRA-only; Both (ACEi/ARB + MRA)). Significance: a single asterisk marks p <0.05. Exact p-values are shown in the table. Abbreviations: HF: Heart failure; NYHA: New York Heart Association; RAAS: Renin-angiotensin-aldosterone system; SD: Standard deviation; IQR: Interquartile range; ACEi: Angiotensin-converting enzyme inhibitor; ARB: Angiotensin receptor blocker; MRA: Mineralocorticoid receptor antagonist; SGLT2: Sodium-glucose cotransporter-2.

Table 4. Multivariable logistic regression for depressive symptoms (HAM-D-17 >7)

Predictor	OR (CI %95)	P-value
Female sex (vs male)	6.57 (2.91–14.85)	<0.001*
NYHA class I (vs IV)	0.12 (0.03–0.56)	0.007*
NYHA class II (vs IV)	0.46 (0.12–1.82)	0.271
NYHA class III (vs IV)	3.26 (0.81–13.22)	0.098

New York Heart Association (NYHA).

Discussion

In this cross-sectional study of 250 adults with HF, about one in five participants screened positive for depressive symptoms on the HAM-D-17, predominantly in the mild range. After multivariable adjustment, female sex and poorer functional status were independently associated with higher depressive symptom burden, whereas HF etiology, LVEF, HF duration, marital status, employment status, and medication count were not. These results highlight sex and functional status as key determinants of depressive symptoms in this population.

Our observed prevalence of depressive symptoms (20%) is consistent with that reported in large cardiovascular cohorts (20–25%) (23), and falls within broader estimates for cardiac populations (approximately 31%) (24), and for inpatient or low- and middle-income country samples, in which rates up to 59% have been reported (25). Between-study variability likely reflects differences in assessment tools, cut-points, and case mix (outpatients' vs inpatients). Depressive symptoms also tend to increase with advancing NYHA class, with reported prevalence estimates of approximately 28% in class II, 46% in class III, and >50% in class IV (26). Taken together, these patterns underscore

the high burden of depressive symptoms in HF and support routine screening and the integration of mental health care into HF management. Female sex emerged as an independent correlate of depressive symptoms in our cohort. This is consistent with reports of higher depression rates and worse cardiac outcomes in women, including increased mortality and poorer treatment response (27, 28), as well as higher depressive-symptom scores among hospitalized systolic HF patients, although depression predicts adverse events in both sexes (29). Potential contributors include caregiving burden, chronic psychosocial stress, sociocultural factors, and biological influences (3). However, findings are not uniform, and some community-based studies report no sex difference (30) or even stronger associations in men (31), likely reflecting differences in setting (hospitalized vs community), HF phenotype, and depression measurement. Overall, screening should be universal yet sex-sensitive, with tailored follow-up for groups at higher risk.

A clear association was observed between HF functional status and depressive symptoms. Patients in NYHA classes III–IV were more likely to have depressive symptoms than those in class I; in our sample, class I patients were about

88% less likely to screen positive. This association remained robust after adjustment for sex and clinical factors. Other studies similarly link greater illness severity, poorer functional capacity, and higher rates of depression (25, 32). Depressive-symptom scores such as the PHQ-9 also worsen with functional decline (33). Beyond symptom scores, poorer functional status has been associated with lower quality of life, with depression and cognitive impairment potentially mediating this relationship (34). Notably, anxiety and depressive symptoms are reported across all HF ejection-fraction categories, but the severity of depression appears to be more closely related to NYHA class than to LVEF (35). The progression of HF, with chronic activation of neurohormonal and inflammatory pathways and distressing symptoms such as dyspnea and fatigue, can lead to anhedonia, reduced activity, and social isolation, all of which contribute to the development and maintenance of depression (27).

These findings reinforce the importance of systematically addressing mental health in HF care, particularly among patients in NYHA classes III–IV, and support routine depression screening as part of standard management (25). In contrast, LVEF itself showed no independent association with depressive symptoms in our study, consistent with evidence that mood symptoms track functional limitation and symptom burden more closely than systolic function. Depressive symptoms occur across both HFpEF and HFrEF, and their adverse prognostic impact appears similar across EF phenotypes (35). Prior studies also suggest that depressive symptoms correlate more strongly with personal and psychosocial factors than with LVEF or other echocardiographic indices (36), and may predict incident HF independent of baseline cardiac structure and function (37). These data support routine screening for depressive symptoms across EF phenotypes, with particular attention to patients with poor exercise tolerance or heavy symptom burden.

We also did not find independent associations between HF etiology (ischemic vs non-ischemic), HF duration, or medication count and depressive symptoms once functional status and sex were taken into account. Prior work suggests that depressive and anxiety symptoms occur across HF etiologies and EF phenotypes, whereas functional status is a more reliable indicator of psychological risk (35). Etiologic signals reported in some studies likely reflect confounding by disease severity, comorbidities, polypharmacy, and social context (3, 25). Similarly, HF duration may function as a proxy for accumulated disease burden such as repeated hospitalizations and lifestyle restrictions rather than as a direct causal determinant of

depressive symptoms (38). Medication count chiefly reflects illness severity and regimen complexity, and prior studies have shown that polypharmacy can be associated with depression in some settings (3), although lower adherence among depressed patients may paradoxically reduce the number of medications actually taken (10). Interpreting raw medication counts therefore requires caution and clinical contextualization (3).

After adjustment, marital and employment status were not independently associated with depressive symptoms in our sample. Nonetheless, prior studies link single status in hospitalized HF patients with poorer survival (39), and unemployment with higher cardiac mortality, especially when depressive symptoms are present (40). Evidence on readmissions and the role of social support suggests that these variables act as markers of social vulnerability rather than direct causal determinants, underscoring the value of comprehensive screening combined with psychosocial support for at-risk patients (36, 41, 42). Taken together, our findings and prior literature emphasize that depressive symptoms in HF should be understood within a broader biopsychosocial framework, in which functional impairment, sex, and social context intersect to shape risk.

Clinical implications: Regular, structured screening for depressive symptoms should be integrated into heart failure care across all ejection-fraction phenotypes, with prioritized follow-up for women and for patients in NYHA classes III–IV. Brief psychiatric assessment and clear referral pathways within cardiac services may help reduce missed cases and improve treatment adherence. Multidisciplinary collaboration and linkage to community resources are particularly important in low-resource settings.

Future directions: Trials of collaborative-care models, stratified by sex and NYHA class, are needed to evaluate effects on depression remission, adherence, re-hospitalization, quality of life, and mortality. Incorporating psychosocial measures (e.g. social support, health literacy) and objective activity indices could refine risk stratification and guide implementation strategies.

Limitations: This cross-sectional study cannot establish causal relationships, and single-region recruitment from three teaching hospitals may limit generalizability. Symptom overlap between HF and somatic items of the HAM-D-17 may have led to some misclassification. The screen-positive subgroup was relatively small ($n=51$), which may have limited statistical power for detecting weaker associations. Important psychosocial factors (e.g. social support, health literacy, and medication adherence) were not assessed; therefore, residual confounding remains possible. Larger, multicenter longitudinal studies with more

comprehensive diagnostic and psychosocial assessments are needed to confirm and extend these findings.

Conclusions: In this study, approximately one fifth of adults with HF had clinically relevant depressive symptoms on the HAM-D-17, with higher prevalence in women and in those with worse functional status. Depressive symptoms were associated with female sex and disease severity, independent of LVEF or ischemic etiology, supporting routine screening and the integration of psychosocial services, particularly for women and patients in advanced NYHA classes.

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Ethics approval: The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Babol University of Medical Sciences (IR.MUBABOL.HRI.REC.1401.014). All participants received written information about the study aims, procedures, and potential risks/benefits, and provided written informed consent. Confidentiality and the right to withdraw at any time were assured.

Conflict of interests: The authors declare no conflicts of interest.

Authors' contribution: RH and NG conceived and designed the study, supervised the project, and critically revised the manuscript. HS developed the statistical analysis plan, performed the analyses, and contributed to interpretation of the findings and drafting of the Methods and Results. MGA coordinated data collection, conducted the investigation, and drafted sections of the manuscript. All authors approved the final version and take responsibility for the integrity of the work.

Data availability: Data are available from the corresponding author on reasonable request.

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