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Methodological approach of weighing the prevalence of depression in heart failure patients: A case control study

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ABSTRACT

Background: People with heart failure may have associated comorbidities and illnesses, which are key risk factors for depression. In a tertiary care facility in Riyadh, Saudi Arabia, the relationship between heart failure, depression, and associated comorbidities will be methodologically evaluated. *Methods:* From January to July 2022, a case-control research was carried out. Patients who had heart failure were considered cases, whereas healthy individuals attending the primary care facility were considered as controls. The exposure was a prior history of heart failure as assessed by the PHQ-9 (Patient Health Questionnaire 9). Score was calculated, and depression severity was categorized (mild, moderate and severe). *Results:* A total of 800 participants were approached, out of whom 600 fulfilled the inclusion criteria and consented to participate, 420 (70%) participants were enrolled as cases and 180 (30%) as controls. For cases vs controls, mean (SD) age was 59.512± 15.417 and 31.06±5.992 years, 265 (63.1%) and 75 (41.7%) were males, respectively. Odds ratio (OR) (95% CI) of having heart failure and being depressed (PHQ-9) was 3.02 (2.44–3.83), p value <0.0001. The association remained significant even after adjusting for gender and age in Model 1 OR (95% CI): 2.82 (2.27–3.60), p value <0.0001, hypertension and stroke in Model 2 OR (95% CI): 2.87 (2.29–3.71), p value <0.0001 and malignancy and COPD in Model 3 OR (95% CI): 2.94 (2.31–3.85), p value <0.0001. *Conclusion:* Heart failure and depression had direct relation especially in individuals with certain associated comorbidities as hypertension, stroke, cancer, COPD, and older male patients.

Keywords: Depression, heart failure, associated comorbidities

1. INTRODUCTION

Associated comorbidities including diabetes and hypertension are significant risk factors for cardiovascular diseases and may be more common in people

with psychopathology (Sowers et al., 2001). Chronic types of comorbidities and heart failure are crucial in determining mental illness burden in the developing world (Savarese & Lund, 2017). In Saudi Arabia, the average prevalence of depressive disorders in the general population is 34 percent (Al-Qadhi et al., 2014). This exceeds the global lifetime prevalence of 8–12 percent (Alaqeel et al., 2022). Age related depression is reported to be 40.6 percent prevalent, with women being more likely than males to have it (50 percent vs. 32 percent) (Albert, 2015). Social circumstances and issues with the husband are the main causes of depression in women (Choi & Marks, 2008).

Studies on the connection between depression and heart failure have produced mixed results. According to some research people with depression disorders had an increased risk of developing heart failure, whereas other investigations found no such link (Rustad et al., 2013). There is ongoing debate over the relationship between heart failure and depression, and there are little data from Saudi Arabia. We propose that depression and/or not only cause heart failure but also affect other associated comorbidities and the stage at which they develop. In order to ascertain the relationship between heart failure and depressive illnesses, we thus devised this study.

2. MATERIALS AND METHODS

Study design and setting

From April 2022 to June 2022, a case control research was done on patients who visited outpatient medical clinics at a tertiary care facility in Riyadh, Saudi Arabia. Those patients were diagnosed with heart failure regardless the EF, while controls were selected as healthy cohort attending the primary care facility in the same hospital.

Study population

A total of 800 individuals were reached, and 600 (or 75% of them) met the requirements for inclusion and gave their agreement to take part. We enrolled 420 people (70 percent) as cases and 180 people (30 percent) as controls out of the people who were recruited for the research. Cases were individuals with an average age of 59.512 years in those who were receiving therapy. Controls were individuals with a mean age of 31.06 years who did not have heart failure, meaning that their EF was normal, which is between 55 and 70 percent. Additionally, the controls couldn't have had a heart failure diagnosis. The research excluded those with dementia or delirium who were confused because of electrolyte disturbance.

Patients with a clinical diagnosis of hepatic encephalopathy and those with persistent renal failure and end-stage renal disease (ESRD) were excluded from the study. Persistent acute renal failure is defined as the need for dialysis for more than four weeks, whereas ESRD is defined as the need for dialysis for longer than three months. The ethical review committee of KSUMC provided its permission (604-IMed-2022). After obtaining informed consent, all patients were enrolled.

Study questionnaires and data collection

The Patient Health Questionnaire (PHQ)-9 is the major depressive disorder (MDD) module of the full PHQ-9 (Kroenke et al., 2001). Heart failure currently classified according to ejection fraction (EF). (PHQ-9) a commonly used instrument for evaluating psychological discomfort in patients and nonclinical populations was used to measure depression. The (PHQ-9) is a 9-item scale for depression that asks participants to verbally endorse answers that are then assessed as a measure of the degree of depression. A Likert scale with four points is used to rate each item. Each item receives a different score. The results were added together to create groups case control, one for each of the eight possible emotions: (PHQ-9). When a patient has an eight or above on the (PHQ-9), depression is diagnosed.

This has been applied in therapeutic contexts. The (PHQ-9)-ideal A's cutoff was 8, with sensitivity and specificity both at 0.89. Mother language, education and nationality were all recorded. To categorize cases and controls into patients with diabetes, stroke, ischemic heart disease, dyslipidemia, anemia, COPD, malignancy, thyroid disorders, renal impairment, hypertension, and smoking status, a personal, current, and previous medical history of physician diagnosed patients was documented. Residents who have received (PHQ-9) or questionnaire administration training entered the data. To detect a difference in percentage of 4.8 percent in depressive disorder, at an alpha of 0.05 and an 80 percent power, a minimum sample size of 420 cases and 180 controls was needed (Grimsrud et al., 2009).

Depression assessment

During their initial appointment, all patients were required to take the PHQ-9 questionnaire. One of the nine DSM-IV criteria for the diagnosis of major depression is matched to each of the survey questions on the PHQ-9. Respondents scored each question

according to their level of agreement (0 = not at all, 1 = a few days, 2 = more than half the days, and 3 = virtually every day). The survey was completed independently by the patients without help. We then divided respondents into four groups of depressed symptomatology based on the established cutoff PHQ-9 score of 10 to diagnose the presence of depression. Total PHQ-9 score: Low (0–4), medium ('5–9'), and moderate (10-14), and high (15–20), and grave (>20). Patients were additionally asked a yes/no question regarding obtaining counseling or antidepressant medication in addition to the PHQ-9 (Kroenke et al., 2001).

Statistical analysis

Analysis was performed using the (SPSS version 26®, International Business Machines Corporation (IBM), Armonk, NY). For quantitative data, mean and standard deviation were computed; for qualitative variables, frequency and percentage. On the (PHQ-9), a number code was issued in accordance with scale for each individual item question. The results of the 9-item (PHQ-9) questions were totaled. (PHQ-9) combined were then classed as 48 and 58, respectively.

The odds ratio (OR) was performed to investigate the relationship between heart failure and depression. Chi square analysis was used to compare qualitative and quantitative variables, respectively. The relationship between heart failure and (PHQ-9) was determined using multiple logistic regressions. Used as a dichotomous variable was (PHQ-9). Diabetes, stroke, ischemic heart disease, dyslipidemia, anemia, cancer, thyroid disorders, renal impairment, hypertension, and smoking status were the contributing factors, and the result was depression. These physiologically plausible explanatory variables that were significant (p value 0.05) on univariate analysis were used in the multiple regression models. For independent variables with more than two categories, dummy variables were generated.

3. RESULTS

Characteristics of participants

Mean age for cases was 59.512± 15.417 and 31.06±5.992 years for controls. In the study group 265 (63.1%) were males while in the control group they were 75 (41.7%), respectively (Table 1). The Mean ±SD of (PHQ-9) score was 4.66±3.13 for cases; 1.86±3.07 for controls, the cut-off value of PHQ-9 score that indicating depression was 4.9 average. The median (SD) score on the (PHQ-9) was 5.77 (3.5); 142 (40) had a score of 4.9, indicating depression. Comparing cases and controls (Table 2), 107 (33.8%) of the cases and 80 (31.3%) of the controls had (PHQ-9), with an OR (95 percent CI) of 2.12 (1.79-2.59), p value 0.051. In terms of (PHQ-9), 158 (49.5%) of the cases and 84 (30.8%) of the controls had (PHQ-9), with an OR (95 percent CI) of 3.02 (2.4-3.8) and a p value of 0.001.

Table 1 Basic Characteristics of case (n=420) and control (n=180).

Characteristics	Case group(N=420)	Control Group(N=180)			t-statistic	P value
	Mean ±SD	Mean ±SD				
Age(Years)	59.512± 15.417	31.06±5.992			23.526	<0.000
	N	%	N	%	Chi square	P value
Gender						
Male	265	63.1	75	41.7	23.5617	<0.000
Female	155	36.9	105	58.3		
Nationality						
Saudi	356	84.8	141	78	3.6619	<=0.050
Non-Saudi	64	15.2	39	22		
Depression						
Low (Non-minimal)	107	25.5	92	51.1	4.13	0.025*
Medium (Mild)	45	10.7	47	26.1		
Moderate	19	4.5	28	15.6		
High (Moderately severe)	9	2.1	7	3.9		
Grave (Severe)	3	0.7	6	3.3		
Hypertension (HTN)						
Yes	176	97.8	9	95	306.142	<0.000

No	2	1.1	171	5		
Diabetes mellitus (DM)						
Yes	259	61.7	176	97.8	86.9323	<0.000
No	152	36.2	2	1.1		
Pre-diabetic	0	0	2	1.1		
Smoking						
Yes	299	71.2	154	85.6	32.1851	<0.000
No	112	26.7	19	10.6		
Pre-smoker	0	0	6	3.3		

P values were base on t test and chi square, P value<0.05 is significant; *p-value represent insignificant

Table 2 Testing for the linearity of the model.

Model	Case Group		Control Group	
	Standardized	P-value	standardized	P-value
(Constant)	3.093	0.098	1.736	0.000
Gender	0.091	0.577	0.199	0.244
DM	0.125	0.501	0.317	0.354
HTN	-0.148	0.433	0.065	0.418
Smoking	0.284	0.12	-0.074	0.687
Renal impairment	-0.06	0.762	N/A	N/A
Thyroid	-0.197	0.374	N/A	N/A
Stroke	-0.896	0.13	N/A	N/A
COPD	-0.087	0.832	N/A	N/A
Malignancy	0.166	0.684	N/A	N/A
Dyslipidemia	N/A	N/A	0.009	0.984
Anemia	0.161	0.335	N/A	N/A
Age	-0.004	0.507	-0.008	0.56
R^2	0.316		0.123	

Depression Severely; Non minimal=1, Mild=2, Moderate=3, Moderately severe=4, severe=5, Predictor; No=0, yes=1, pre=1.

Modified models for the relationship between (PHQ-9) and heart failure on a univariate logistic regression with depression as the outcome, the OR (95 percent confidence interval) for (PHQ-9) was 3.02 (2.4-3.8), p value 0.001; age 2 (1.9-2.02); male gender 2.22 (1.8-2.7); history of smoking 2.51 (1.9-3.3); history of diabetes mellitus 2.26 (1.90-2.7); elevated cholesterol 1.66 (1.4-1.9); history of hypertension 1.49 (1.2-1.8); and history of renal impairment Table 3 provides detailed information on nationality and educational levels. Among 420 cases, 215 had low grade depression in comparison to 46/180 controls (51.1% vs 25.5% respectively). 110 cases had medium depression in comparison to 19 controls (26.1% vs 10.7% respectively). 65 cases had moderate depression in comparison to 8 controls (15.6% vs 4.5% respectively). 16 cases had high depression in comparison to 4 controls (3.9% vs 2.1% respectively). 14 cases had grave depression in comparison to 1 control (3.3% vs 0.7% respectively) Figure 1.

Table 3 Ordinal logistic Regression of Depression.

Variable		CASE GOUP		Control Group	
		OR(CI)	P value	OR(CI)	P value
Age		-.007(-.031, .017),	0.553	-.011(-.061, .038)	0.553
Gender	Male	-.251(-.898, .396)	0.447	-.421(-1.042,0.200)	0.447
	Female	0[a]	.	0[a]	.
DM	Yes	-.016(-.766, .733)	0.966	-1.841(-4.370, .687)	0.966
	No	0[a]	.	-21.654(-21.654,-21.654)	.

	Pre-Diabetes			0[a]	
HTN	Yes	.193(-.572, .957)	0.621	-.739(-2.038, .560)	0.621
	No	0[a]	.	0[a]	.
Smoking	Yes	-.675(-1.468, .118)	0.095	1.388(-.851, 3.627)	0.095
	No	0[a]	.	1.917(-.429, 4.264)	.
	Pre-smoking	N/A		0[a]	
Renal impairment	Yes	.057(-.742,0.857)	0.888	N/A	N/A
	No	0[a]	.	N/A	N/A
Thyroid	Yes	.348(-.507, 1.202)	0.425	N/A	N/A
	No	0[a]	.	N/A	N/A
stroke	Yes	1.537(-.657, 3.732)	0.17	N/A	N/A
	No	0[a]	.	N/A	N/A
COPD	Yes	-.024(-1.708, 1.660)	0.977	N/A	N/A
	No	0[a]	.	N/A	N/A
malignancy	Yes	-.435(-2.180, 1.310)	0.625	N/A	N/A
	No	0[a]	.	N/A	N/A
anemia	Yes	-.371(-1.051, .310)	0.286	N/A	N/A
	No	0[a]	.	N/A	N/A
Dyslipidemia	Yes	N/A	N/A	-.045(-1.700, 1.609)	
	No	N/A	N/A	0[a]	

OR - represent odd ratio, CI - Confident Interval of the Odd Ratio.

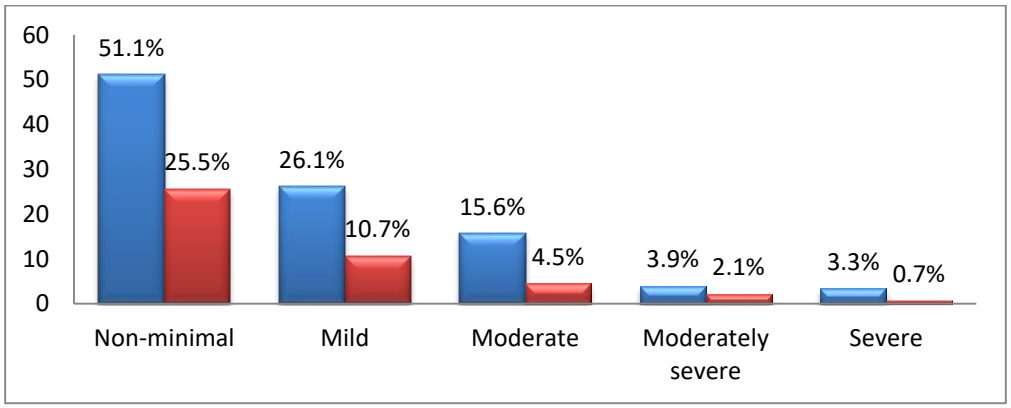

Figure 1 Comparison of Depression severity between Case (blue bars) and Control Groups (red bars)

After correcting for age and gender, the OR (95 percent confidence interval) for (PHQ-9) on multiple logistic regression for outcome of heart failure and (PHQ-9) as the primary exposure variable in Model I was 2.82 (2.2-3.6), with a p value of 0.0001. In Model II, after further correcting for thyroid conditions and stroke, the OR (95 percent CI) for (PHQ-9) was 2.87 (2.2-3.7), with a p value is of 0.0001. After adjusting for diabetes, stroke, ischemic heart disease, dyslipidemia, anemia, COPD, malignancy, thyroid diseases, renal impairment, hypertension, and smoking status in Model III, the final model, (PHQ-9) remained significantly associated with COPD with OR (95 percent CI): 2.94 (2.3-3.8), p value 0.001.

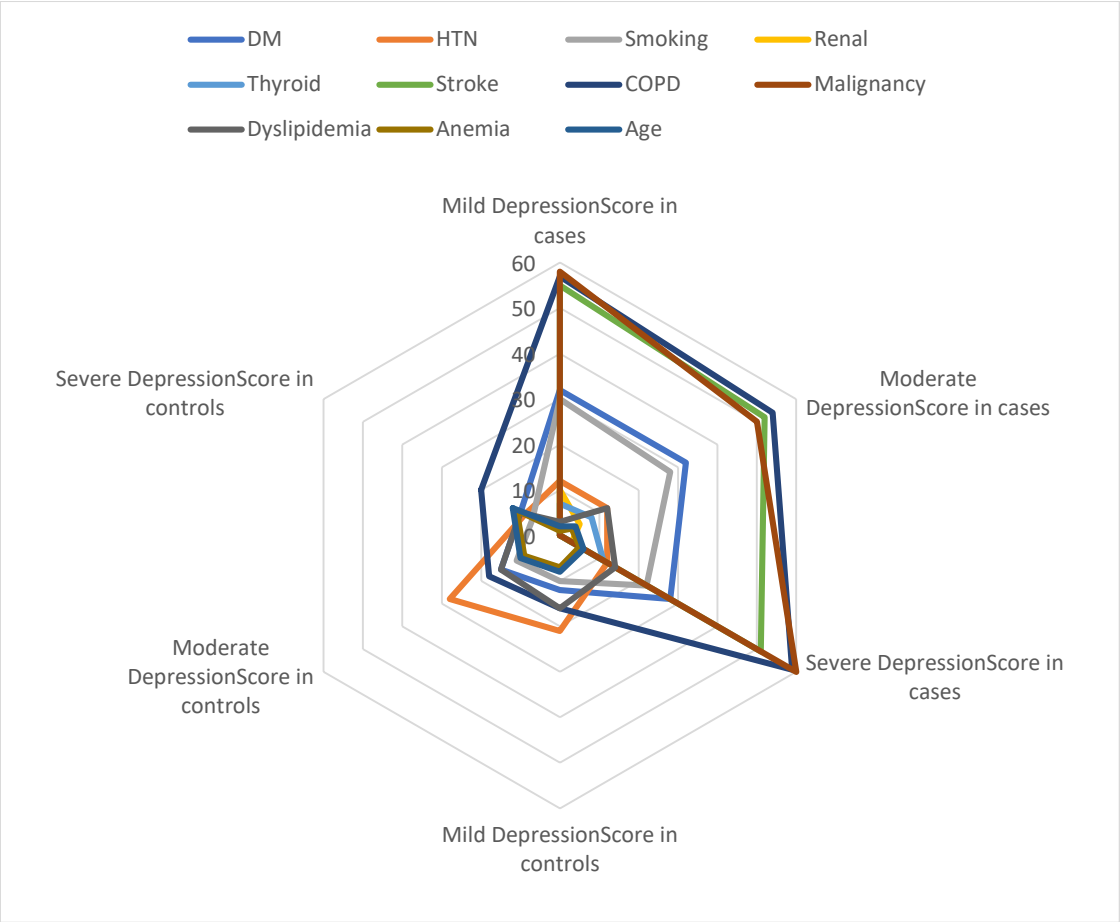

Figure 2 radar chart showed the scoring system of mild moderate severe depression among patients with heart failure and other associated comorbidities (cases vs controls)

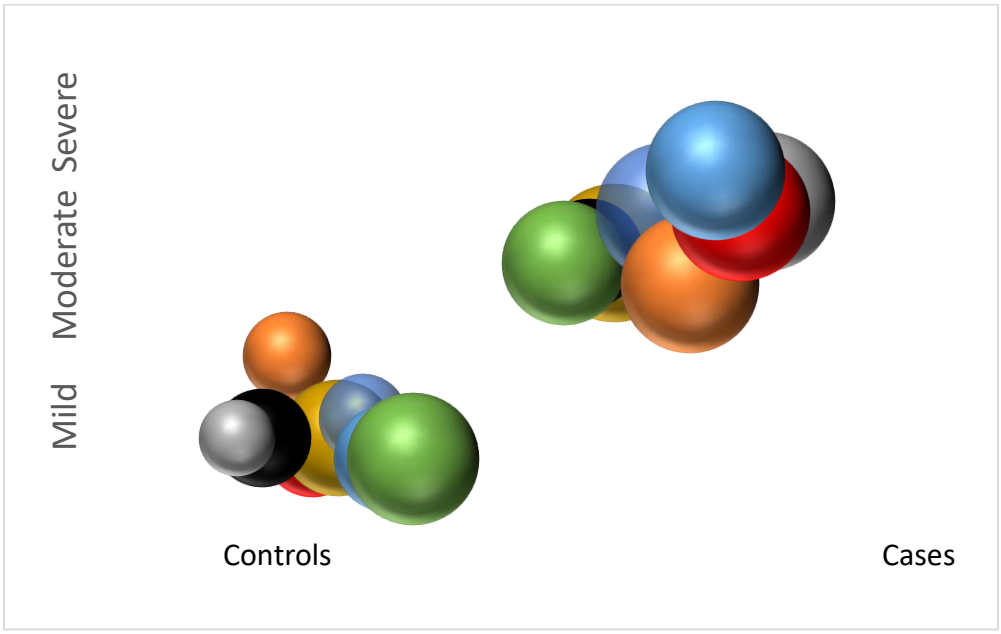

Figure 3 showed the statistical weight and classification of degree of depression in relation to associated comorbidities among cases vs controls (Age, Malignancy, COPD, Stroke, DM, HTN, Smoking, Renal impairment).

It was obvious in our findings that certain diseases when accompanied with heart failure together causing high score of depression. Cases with malignancy, stroke, COPD, HTN and old aged males showed high score of severe to moderate depression in comparison with other diseases like thyroid, diabetes, renal impairment and anemia. Figure 2 when we tried to discover the weight

of correlations and statistical methodological approach toward weighing of relations between degree of depression in relation to associated comorbidities among cases vs controls, we found positive results between degree of depression and certain diseases accompanied with heart failure, such as malignancy, stroke, COPD, HTN and old aged males Figure 3.

4. DISCUSSION

We write that (PHQ-9) results showing heart failure have a correlation with depression. Even after correcting for socioeconomic position, education level, concomitant illnesses such diabetes, is chemic heart disease, dyslipidemia, anemia, COPD, cancer, thyroid disorders, renal impairment, hypertension, and smoking history, the link remained significant. A cute cardio vascular complications such myocardial infarction, congestive heart failure, and isolated systolic hypertension are more common in those with major depression (Okam et al., 2020). Numerous researches have been conducted to determine the connection between depression and heart failure. These also include of sizable cohort studies where individuals with depression who were monitored for more than five years discovered to have incident heart failure (Freedland et al., 2011).

In this case control research, we describe the relationship between heart failure and depression. All patients who were known to have heart failure were included in this. A paper focused on the connection between heart failure and depression. This study found that the heart failure group had greater ratings for impulsivity, sadness, expressing anger, and stress (Ishak et al., 2020). In a research, involving 31495 individuals, participants with heart failure and a common mental condition had the highest chance of dying from CVD (Hamer et al., 2010). However, this study also included a control group and concentrated on prevalent mental diseases in general. The probabilities of getting heart failure were 1.9 times greater in those with depression after controlling for all other covariates, as shown by the modeling pattern in multiple logistic regressions, in contrast to this. Furthermore, patients with heart failure had higher (PHQ-9) scores. Additionally, several investigations have demonstrated that heart failure and depression are unrelated (York et al., 2009).

According to a significant longitudinal study that tracked 36530 people for 11 years, for absence of depression, signs of depression were predictive of poor cardiac function (Aziz & Steffens, 2013). In this study, we evaluated depression using the (PHQ-9). Our finding showed a strong correlation between “depression” and “heart failure”. The explanation for this would be that we included heart failure patients and a control group, whereas the aforementioned study recruited not only heart failure patients therefore this case control study was explicitly created to explore the relationship between “depression” and “heart failure”. On the one hand, depressed patients' incapacity to adhere to treatment plans and a healthy lifestyle might be the cause of this (De Hert et al., 2018). On the other hand, these heart failure patients experience psychological discomfort and a sense of helplessness related to heart failure management (Dekker et al., 2009). This depressed behavior that causes heart failure may be caused by increased sympathetic stimulation.

A continuous upsurge in dominant concerned efferent instincts to the ganglia caused by stress may provide the recurrent high frequency pre synaptic activity necessary to induce sympathetic ganglia, according to animal experiments on rats (Zhang & Anderson, 2014). It would thus be necessary to do more study in people because we did not examine such underlying causes and processes. It's also questionable if depression and heart failure are related. Heart failure patients scored higher on impulsivity, sadness, expressing anger, and stress (Rohyans & Pressler, 2009). It has also been claimed that there is a connection between heart failure and panic attacks, indicating that heart failure is a risk factor for panic attacks (Celano et al., 2016). While more study is needed, one possibility is that individuals with depression may or may not be better able to take heart failure medications than those without depression.

The case control approach of this study, which primarily included heart failure patients and sought to understand the association amid unhappiness and heart failure, is its strength. The study has a number of restrictions. Due to the fact that there is only one study center, the study cannot be applied to the full Saudi Arabian population. Second, we did not account for socioeconomic level when analyzing the elements that may have contributed to this group of patients' depressions. Third, we failed to track therapeutic compliance for anti heart failure.

5. CONCLUSION

Depression and heart failure have been linked. The connection is affected by comorbidities as well as demographic factors. In cases of heart failure, treating depression early on may be helpful. Large scale research is required to both confirm this link and investigate the underlying processes.

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Author Contributions

All authors contributed equally in methods, writing and statistical analysis.

Ethical approval

The study was approved by the Medical Ethics Committee of KSUMC (Ethical approval code: (604-IMed-2022).

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Conflict of interest

The authors declare that there is no conflict of interests

Data and materials availability

All data associated with this study are present in the paper.

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