



2020

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Recommended Citation

Alsumih, Norah; Alqahtani, Rahaf; Almutairi, Faisal; Faraj, Rakan; Alsubeai, Turki; Alghanim, Ahmed; Alharbi, Shmylan; and Almodaimegh, Hind (2020) "The Use of Antidepressants in Patients with Heart Failure," *Journal of the Saudi Heart Association*: Vol. 32 : Iss. 1 , Article 9.

Available at: <https://doi.org/10.37616/2212-5043.1008>

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The Use of Antidepressants in Patients with Heart Failure

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Abstract

Background: Heart failure (HF) is a chronic disease affecting patients' quality of life (QoL) and may cause depression. Recent studies reported that the prevalence of depression in patients with HF is 21.5%. Antidepressants, mainly selective serotonin reuptake inhibitors, are usually prescribed for HF patients diagnosed with depression. Some evidence supports antidepressant's role in improving symptoms by enhancing the psychological aspect of their QoL. Depression screening and treatment are important in the multidisciplinary management; however, their survival benefits are inconsistent. In our study, we aim to investigate the prevalence of depression and the use of antidepressants in patients with HF as well as to determine the acceptance of using antidepressants in such patients.

Methods: This is a cross-sectional study conducted by interviewing HF outpatients at National Guard Hospital in Riyadh. Patients were assessed using Hamilton depression rating scale.

Results: A total of 306 patients were included, with the majority (69%) being male and aged >61 years (60%). Patients' medical history was classified into different groups, with the largest proportion (39.9%) in the diabetic-hypertensive group, followed by a diabetic group (21.2%) and a hypertensive group (10.8%). Patients were classified according to the New York Heart Association Functional Classification, and most patients were in Class I (61.8%). Some of the patients (8.5%) had been diagnosed with depression. There was no statistically significant association between HF and depression ($p > 0.05$). However, 5.6% of patients had been prescribed antidepressants and 17.1% of patients believed that they required antidepressants. Moreover, there was a statically significant association between medical history and development of depression ($p = 0.014$).

Conclusions: The prevalence of depression in HF patients in our population was lower than reported. There was no association between HF stage, depression, and antidepressant use.

Keywords: Antidepressants, Heart failure, Depression, Quality of life, Selective serotonin uptake inhibitors

1. Introduction

Heart failure (HF) is a disease that results in the gradual deterioration of the heart's muscle contractility and overall function,

eventually leading to advanced HF [1]. Due to the debilitating effect of HF on patients and their quality of life (QoL), an association between HF and depression has been reported in the literature. A meta-analysis reported that the

Received 31 August 2019; revised 23 September 2019; accepted 29 September 2019.
Available online 17 April 2020

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prevalence of depression in patients with HF is 21.5%, with a higher prevalence in women [2]. The study also reported higher rates of mortality and rehospitalization in patients suffering from severe depression [3]. A second study recruited 391 patients with HF (age, >50 years) and found that patients with severe depression have an 82% higher risk of death or functional decline [3] (Table 1).

A study performed by O'Connor et al [4] concluded that depression, without using antidepressants, may be related to increased mortality in HF patients. Efficacy and safety must be considered while prescribing an antidepressant. In terms of efficacy, there is no significant difference between the different classes of antidepressants or agents in the same class, but there is a difference in terms of safety and adverse effects [5]. Hypotension is one of the most prominent side effects of antidepressant use, especially with tricyclic antidepressants (TACs) due to their α -adrenergic blocking activity [6]. Glassman et al [7] report that using imipramine, a member of TACs, in 15 depressed HF patients caused orthostatic hypotension in 7 of the 15 patients. Hypotension may increase the risk of falls in elderly patients with HF, potentially increasing the

Abbreviations

HF	Heart Failure
QOL	Quality of Life
HAMD	Hamilton Depression Rating Scale
NYHA	New York Heart Association
TACs	Tricyclic Antidepressants
SSRIs	Selective Serotonin Reuptake Inhibitors
KAMC	King Abdulaziz Medical City
KACC	King Abdulaziz Cardiac Center
ACICU	Adult Cardiac Intensive Care Unit
QN	Question Numbers
IQR	interquartile range
DM	Diabetes Mellitus
HTN	Hypertension

risk of hip fractures. In Glassman's study, six of the seven hypotensive HF patients suffered from falls [7]. However, hypotension is not an adverse event for another class of antidepressant, selective serotonin reuptake inhibitors (SSRIs). For all agents in this class, hypotension does not occur because there is almost no effect on blood pressure and cardiac conduction even in a case of overdose. SSRIs are considered the safest choice for HF patients with depression. There are some evidences demonstrating that SSRIs are related to decreased mortality and improved heart function [8]. The most frequently prescribed SSRIs are fluoxetine, paroxetine, sertraline, and citalopram (Table 2).

Several studies have been conducted to evaluate the use of antidepressants in patients with HF to improve their QoL, but the results are contradictory. According to a study evaluating the relationship between the long-term use of antidepressants and mortality in HF patients, 30.0% of the participants were depressed and 24.2% were taking antidepressants. The outcome of the study was that depressed HF patients who were not taking antidepressants had an increased mortality rate compared with those who were using antidepressants [4]. A study conducted between 1997 and 2010 that included 121,252 patients found that more HF patients use antidepressants after being discharged from hospital, with or without a diagnosis of clinical depression. They found that the use of antidepressants

Table 1. Baseline patient characteristics.

Variables		Number	Percentage (%)
Sex	Male	210	69.3
	Female	93	30.7
Age (y)	21–30	5	1.6
	31–40	17	5.6
	41–50	29	9.5
	51–60	71	23.2
	61–70	91	29.7
	71–100	91	29.7
Diagnosed with Depression	Yes	26	8.5
	No	279	91.5
NYHA Class	I	168	54.9
	II	92	30.1
	III	10	3.3
	IV	2	0.7
	Missing	34	11.1
Medical History	Dyslipidemia		2.6
	DM		21.2
	DM-Dyslipidemia		1.0
	DM-HTN		39.9
	DM-HTN-Dyslipidemia		8.2
	HTN		10.8
	HTN-Dyslipidemia		2.0
	Missing		6.9
Other		2.6	

DM = diabetes mellitus; HTN = hypertension; NYHA = New York Heart Association.

Table 2. Participants' scores for Hamilton depression rating scale.

Categories	Frequency	Percentage (%)
No-to-Mild Depressive Symptomatology	80	26.1
Moderate Depressive Symptomatology	133	43.5
Severe Depressive Symptomatology	93	30.4
Total	306	100.0

increased for a long period after the diagnosis of HF, and the use of antidepressants was associated with an increased mortality rate after being discharged [9]. Another study suggests that the use of antidepressants worsened the outcome of patients who still had symptoms of depression [10]. Moreover, another study found that the use of antidepressants and benzodiazepines is safe in terms of survival with HF, whereas the use of antidepressant was not found to be independently associated with mortality [11]. In 2007, a study conducted to evaluate the relationship between antidepressants and death or hospitalization in HF patients found that the use of antidepressants is associated with increased mortality or cardiovascular-related hospitalization [12]. Angermann et al [13] compared patients taking escitalopram ($n = 185$) and patients taking placebo ($n = 187$) and concluded that escitalopram did not significantly reduce all-cause mortality or hospitalization, and there was no significant improvement in depression (Table 3).

A randomized controlled trial compared the use of sertraline with that of a placebo in HF patients diagnosed with depression and reported that it did not improve short- or long-term morbidity and mortality [14]. However, another randomized study showed that paroxetine reduces depression in HF patients by improving the psychological aspect in their QoL [15]. Evidence shows that the treatment and screening of depression are important in the multidisciplinary management of patients with HF [16]; however, the pharmacological treatment outcomes are not resolved yet [17] (Table 4).

In our study, we aim to determine the prevalence of depression and the use of antidepressants in patients with HF as well as to explore the acceptance of using antidepressants in this patient group.

Table 3. Correlation between heart failure stage and depression.

HF stage		Have been diagnosed with depression?		
		No	Yes	Total
Missing	Count	42	4	46
	Percentage (%)	91.3	8.7	100.0
B	Count	31	2	33
	Percentage (%)	93.9	6.1	100.0
C	Count	204	20	224
	Percentage (%)	91.1	8.9	100.0
D	Count	2	0	2
	Percentage (%)	100.0	0.0	100.0
Total	Count	279	26	305
	Percentage (%)	91.5	8.5	100.0

HF = heart failure.

Table 4. Patients' insight regarding antidepressant need.

Do You Think You Need Antidepressant Drugs?	Frequency	Percentage (%)
No	No	No
Yes	Yes	Yes
Missing	Missing	Missing
Total	Total	Total

2. Methods

2.1. Study sample and general procedures

We studied 306 patients admitted to King Abdulaziz Medical City (KAMC), Riyadh, Saudi Arabia. KAMC has a bed capacity of 1501 and has been operational since May 1983. While continuing to expand, it has been providing services for a rapidly growing patient population in all its catchments areas. Ambulatory Care Services and Primary Health Care Services provide preventive health services including health education and behavioral modifications to adopt healthy lifestyles. King Abdulaziz Cardiac Center (KACC) consists of 32 beds as well as an adult cardiac intensive care unit. KACC is one of the largest cardiac centers in the region with an average of 500 adult cardiac surgeries per year. Inclusion criteria for the study were patients aged >18 years and diagnosed with HF for at least a year. Patients diagnosed with HF for <1 year were excluded. King Abdullah International Medical Research Center approved the study.

2.2. Study measure

Depressive symptoms in patients were assessed using Hamilton depression rating scale. A questionnaire containing 20 questions about the feelings or behavior of the participant during the previous week was distributed to patients with HF. The symptoms were classified into nine groups; each group of symptoms was associated with a specific question number in the scale (QN = question numbers):

- Dysphoria: QN 2, 4, 6
- Anhedonia: QN 8, 10
- Appetite: QN 1, 18
- Sleep: QN 5, 11, 19
- Worthlessness: QN 9, 17
- Fatigue: QN 7, 16
- Agitation: QN 12, 13
- Suicidal ideation: QN 14, 15
- Thinking/concentration: QN 3, 20

2.3. Data management and analyses

Data management and analysis were performed using SPSS 21.0 (Release 21.0.0.0, IBM, USA). Descriptive statistical analyses were also performed. Continuous variables were summarized as mean (standard deviation) and median (interquartile range). Proportions and percentages were used for categorical variables. Interferential statistics were performed using a Chi-square test to compare frequencies with a 95% confidence interval. Statistical significance was considered at $p < 0.05$.

3. Results

The aim of the study is to explore the prevalence of depression in HF patients and the use of antidepressant in eligible patients. A total of 306 patients were included, with the majority (69%) of the participants being male. Furthermore, the highest proportion of patients was aged 61–70 years (29.9%) and 71–100 years (29.9%), followed by 23.2% in the 51–60 years age group.

The participants' medical history was classified into different groups (Fig. 1), with the highest proportion (39.9%) of the participants in the diabetic-hypertensive group, followed by the diabetes only (21.2%) and hypertensive only (10.8%) groups. From the medical history, the majority of the participants with HF have a history of both diabetes and hypertension.

Regarding the classification of HF, most of the participants were classified in the New York Heart Association Functional Classification Class I. When asked if they have been diagnosed with depression,

only 26 patients (8.5%) responded positively. To assess the prevalence of depression in the participants with HF, a cross tabulation table was created to indicate the percentage of participants diagnosed with depression in each HF stage. Relatively small proportions, 6.1% for stage B and 8.9% for stage C HF patients, were diagnosed with depression. However, no participant in stage D was diagnosed with depression. No relationship between the HF stages and depression was observed ($p > 0.05$).

Regarding the use of antidepressants, only 5.6% of the participants were prescribed antidepressants. All participants were asked whether they believed that they needed antidepressants, and 17.1% of patients responded positively. The study found no statistical relationship between HF stages and antidepressant use ($p = 0.530$).

The association between medical history and depression was evaluated. Traditionally, it has been reported that medical history may influence an individual's depression level. In this study, the Chi-square test revealed a significant association between patients' disease history and depression ($p = 0.014$); however, the analysis of variance (ANOVA) results indicated no significant association between the patients' history and depression level. Despite the insignificant ANOVA results, the third null hypothesis is accepted. Therefore, we can state that there is a significant association between the medical history and a diagnosis of depression. Previous research has assessed the relationship between medical history and HF; however, no significant association between the two variables was found in the current study.

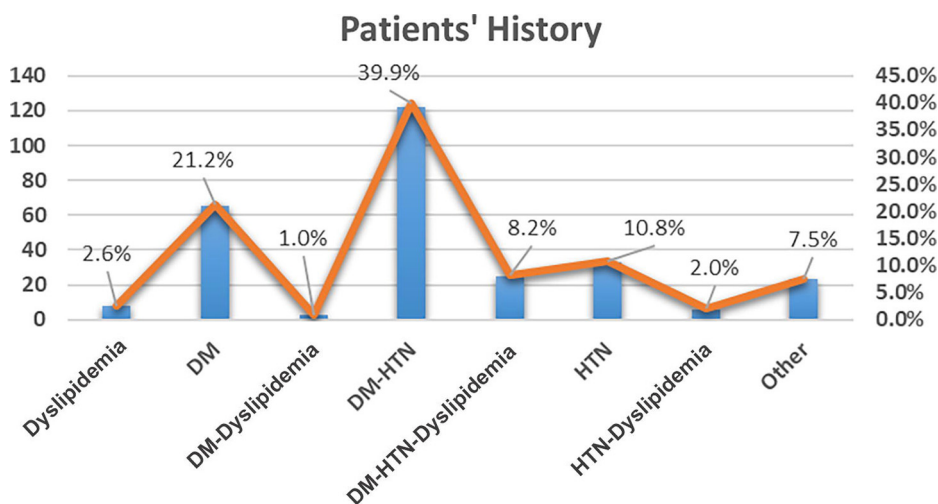


Fig. 1. Participants' Medical History. DM = diabetes mellitus; HTN = hypertension.

4. Discussion

The prevalence of depression in our patients with HF was 8.5%, which was lower than that reported previously in a meta-analysis by Rutledge et al (21.5%) [2]. Our study did not find a statistically significant relationship between HF and depression. In addition, there was no statistically significant association between the various stages of HF. However, depression was more prevalent in stage C than in earlier, more asymptomatic stages.

The majority of the HF participants were also diagnosed with diabetes or hypertension or both. Both diabetes and hypertension can cause left ventricular hypertrophy, a risk factor for developing HF [18]. A significant association was found between medical history and depression in this sample.

Only a small percentage of the HF participants (5.6%) were using antidepressants. It is unclear why all the depressed patients with HF were not treated pharmacologically. Notably, 17% of the participants believed that they required antidepressants, which was higher than the proportion with diagnosed depression in this sample. This raises the question whether depression may be underdiagnosed in patients with HF as well as undertreated.

In addition to the lack of an association between the HF stage and depression, we found no association between the HF stage and antidepressant use.

Our study had some limitations; it was a single-center study with a limited sample size. In addition, participants were evaluated using depression scales, not an extensive professional interview. All the participants were consulting on an outpatient basis, with no inclusion of an inpatient population.

5. Conclusion

The prevalence of depression in HF patients in our study was lower than that reported in the meta-analysis. There was no association between the HF stage, depression, and antidepressant use. There was, however, a significant association between the medical history and the development of depression in this population. This study highlights the possibility that depression might be underdiagnosed in this population.

Acknowledgements

None.

Financial support

This research received no specific grant from any funding agency, commercial or not-for-profit sectors.

Conflict of interest

The authors declare no conflict of interest.

Ethical standards

The data collected were kept with the principal investigator. Access to the data was restricted to the principal investigator, biostatistician, and the data collectors.

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