

PREVALENCE OF PERCEIVED DEPRESSIVE SYMPTOMS AND ITS ASSOCIATION WITH STAGES OF HEART FAILURE AMONG OUTPATIENTS IN A PUBLIC HOSPITAL IN MALAYSIA

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Published online: 16 Nov 2022

To cite this article: NG J. & ABDUL AZIZ F. (2022) Prevalence of perceived depressive symptoms and its association with stages of heart failure among outpatients in a public hospital in Malaysia, *Malaysian Journal of Pharmaceutical Sciences*, 20(2): 39–49, <https://doi.org/10.21315/mjps2022.20.2.4>

To link to this article: <https://doi.org/10.21315/mjps2022.20.2.4>

ABSTRACT

Heart failure (HF) patients with depression usually have poor prognosis. This study aimed to determine the prevalence of perceived depressive symptoms among outpatients with HF and its association with the New York Heart Association (NYHA) class. This was a cross-sectional survey conducted at the Heart Failure Clinic in Hospital Pulau Pinang (HPP) over 3 months period starting January 2020 using a convenience sampling method. All patients were included except patients under 18 years old, pregnant patients, diagnosed with psychiatric or depressive disorders and HF inpatients. A validated English and Malay version of Patient-Health Questionnaire-9 (PHQ-9) was used for screening of depressive symptoms. High scorers (≥ 10) were regarded as depressive. Results were reported in percentage (%) or median \pm interquartile range (IQR). Fisher's exact test with a 95% confidence interval was used. A total of 177 patients were recruited. The prevalence of perceived depressive symptoms among HF outpatients in HPP was 14.1%. The NYHA class was significantly associated with depressive status ($p = 0.003$). Depressive symptoms were common among these outpatients diagnosed with HF. A higher NYHA class suggested a higher depressive symptoms score. Screening for perceived depression especially patients with higher NYHA class was recommended.

Keywords: Heart failure, Prevalence, Depressive symptoms

INTRODUCTION

Globally, heart failure (HF) is found to affect 23 million people (Bui, Horwich and Fonarow 2011). Many population-based studies have reported the prevalence of HF about 1%–2% (Blair, Huffman and Shah 2013; Guo, Gregory and Amitava 2013; Ponikowski *et al.* 2014). HF is a complex clinical syndrome that often leads to hospitalisation, readmission and

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mortality. In Thailand, HF is accounted for 19% of total hospitalisations (Laothavorn *et al.* 2010; Reyes *et al.* 2016). More than 1 million HF hospitalisations were reported in the United States in 2010 (Mozaffarian *et al.* 2015). The rate of readmission within 30 days ranged from 3%–15% in Taiwan, whilst 8% was reported in Malaysia (Reyes *et al.* 2016). A high mortality rate of 5%–10% had been reported during hospitalisation and more than half of patients died within 5 years of the first HF hospitalisation (Tribouilloy *et al.* 2008). Findings from a study by Reyes *et al.* (2016) reported that the cost of hospitalisation due to HF varied across regions, from as low as USD813 per patient in Indonesia to nearly USD9,000 per patient in South Korea, suggesting higher expenditure in a more developed region. Nevertheless, the cost is expected to continue rising due to global population ageing.

In Malaysia, HF is accounted for 6%–10% of all acute admissions and is considered as an important cause of hospitalisation (Reyes *et al.* 2016; Ministry of Health Malaysia 2019). Ministry of Health (2019) reported that 1.8% of the nation's total health expenditure, equivalent to RM785 million, is attributed to the treatment of HF. Given the health and economic burden, proper management of HF and timely prevention should be undertaken to reduce hospital admissions.

Patients with HF present the symptoms differently based on the severity of the disease. They are often grouped based on exercise capacities specified under New York Heart Association (NYHA) functional classification. HF patients in NYHA Class I usually have no limitation in exercise. Ordinary physical activity does not cause undue fatigue, dyspnoea or palpitation. NYHA class II patients are comfortable at rest. However, ordinary physical activity will cause fatigue, palpitation, dyspnoea or angina. As heart function further deteriorates, patients in NYHA Class III are comfortable at rest but will experience symptoms with less than ordinary activity. Patients with symptoms at rest are classified under NYHA Class IV. They are unable to carry on any physical activity without discomfort (Reyes *et al.* 2016).

Evidence from Braunstein *et al.* (2003) showed that the risk of hospitalisation increased with the number of chronic diseases. In the same study, non-cardiac comorbidities such as depression, renal failure and diabetes mellitus are shown to be associated with a higher risk for hospitalisation and mortality in HF patients.

Depression is a medical illness that negatively affects how we feel, think or act (Parekh 2017). It is common in HF patients (Yancy *et al.* 2013). The rate of depression among hospitalised patients with HF is ranging from 13%–77.5%, whereas other small studies have reported 13%–42% among outpatients with HF (Rumsfeld *et al.* 2003; Gottlieb *et al.* 2004). Yancy *et al.* (2013) stated that such emotional distress may worsen the patient's perception of abnormal physical, emotional or cognitive state, making them to feel even more ill. Hence, depression may cause low adherence to medications (Moser *et al.* 2010; Wu *et al.* 2013), leading to failure of treatment and increased hospitalisation rate (Jiang *et al.* 2001). Evidence from Yancy *et al.* (2013) showed that depression is associated with lower health-related quality of life and worse clinical outcomes. A systematic review from Rutledge *et al.* (2006) reported a higher rate of depression among HF Class IV than Class I (42% versus 11%). These findings suggested the importance of detecting depressive symptoms among HF patients and its association with the disease state. However, there were limited studies related to these aspects in local setting within Malaysia. Therefore, this study aimed to determine the prevalence of perceived depressive symptoms and their association with the New York Heart Association (NYHA) class among HF outpatients in Hospital Pulau Pinang (HPP).

METHODS

Study Design and Setting

This was a cross-sectional survey conducted at the Heart Failure Clinic in HPP from January 2020 to March 2020.

Ethical Approval

An ethical approval was obtained from the Medical Research Ethics Committee (MREC), Ministry of Health (MOH), Malaysia with registration number NMRR-19-3116-51217 (IIR).

Study Population

The target population for this study was HF outpatients who came for follow-up at the cardiac clinic in HPP from January 2020 to March 2020.

Eligibility Criteria and Sampling Method

Inclusion criteria were all HF outpatients in HPP regardless of ejection fraction value and those who were 18 years old and above. Patients who refused did not give consent, were below 18 years old, were diagnosed with psychiatric or depressive disorders or were under follow-up at a psychiatric clinic, pregnant patients, and HF inpatients were excluded. Eligible patients were recruited through convenience sampling.

Sample Size Determination

The number of samples required was determined based on the formula with finite population correction, as shown below (Daniel 1999):

$$n' = \frac{NZ^2 P(1 - P)}{(d^2(N - 1) + Z^2 P(1 - P))}$$

where,

- n' = Sample size
- N = Population size
= 406 (based on HPP Cardiology Clinic Census 2018)
- Z = Z statistic for 95% level of confidence
= 1.96
- P = Expected proportion
= 0.215 (Rutledge *et al.* 2006)
- d = Precision
= 0.05

Accounting for 10% dropout, the sample size recruited was 177.

Data Collection and Study Variables

Eligible HF outpatients were asked for their willingness to participate in the study. After obtaining signed informed consent, each participant was given a questionnaire. The

researchers read aloud to those who were illiterate or with vision problems and helped them to fill in the questionnaires. The completed questionnaires were collected and tabulated by the researchers.

The questionnaire consisted of two sections. Part 1 determined the demographic data of patients whereas Part 2 evaluated the depressive symptoms among participants. Validated English (Cronbach's $\alpha = 0.89$) and Malay (Cronbach's $\alpha = 0.70$) versions of Patient-Health Questionnaire-9 (PHQ-9) was used as a tool which served for screening of depressive symptoms (Kroenke, Spitzer and Williams 2001; Sherina, Arroll and Goodyear-Smith 2012). There were nine questions in PHQ-9 with 4-point scale, each indicating the frequency of encountering the problems for the past 2 weeks; 0 (not at all), 1 (several days), 2 (more than half of the days) and 3 (nearly every day). The total score range for nine questions was 0–27. Based on the total score, it was categorised into two groups using a cut-off point of 10, low score group (< 10) and high score group (≥ 10) (Sherina, Arroll and Goodyear-Smith 2012). Patients in the low score group were said to be non-depressive whereas those in the high score group were depressive. The nine questions were as follow:

1. Little interest or pleasure in doing things.
2. Feeling down, depressed or hopeless.
3. Trouble falling or staying asleep or sleeping too much.
4. Feeling tired or having little energy.
5. Poor appetite or overeating.
6. Feeling bad about yourself—or that you are a failure or have let yourself or your family down.
7. Trouble concentrating on things, such as reading the newspaper or watching television.
8. Moving or speaking so slowly that other people could have noticed? Or the opposite—being so fidgety or restless that you have been moving around a lot more than usual.
9. Thoughts that you would be better off dead or of hurting yourself in some way.

Despite of its screening purpose, clinical diagnosis by clinicians was still required for establishing major depressive disorder.

The clinical characteristics of the patients were retrieved from each participant's outpatient medical record files and the information was recorded in a data collection form.

Statistical Analysis

The data collected was analysed using Statistical Package for Social Sciences (SPSS) version 24.0. Demographic data and clinical data were reported in percentage or median \pm interquartile range (IQR). Fisher's exact test with a 95% confidence interval was used to determine the association between NYHA classes and depressive status. A value of $p < 0.05$ was considered statistically significant.

RESULTS

Table 1 shows a total of 177 participants recruited with median age \pm IQR of 62 ± 17 years old. A major proportion of the population ($n = 152$, 85.9%) were in low score (< 10) category. The prevalence of the perceived depressive symptoms was 14.1% ($n = 25$).

More than half of the population ($n = 99$, 55.9%) was 60 years old and above. Nevertheless, the younger group was found to be more depressive as its proportion of high scorers ($n = 15$, 19.2%) almost doubled the older group ($n = 10$, 10.1%). HF seemed to affect more males ($n = 152$, 85.9%) than females ($n = 25$, 14.1%). Nonetheless, greater proportion of female patients were found to be depressive ($n = 5$, 20%) than male patients ($n = 20$, 13.2%). HF was common among Malay ($n = 76$, 42.9%), Chinese ($n = 68$, 38.4%) and Indians ($n = 33$, 18.6%). The proportion of high scorers among Malay patients ($n = 11$, 14.5%) was similar to that of Chinese ($n = 9$, 13.2%) and Indian ($n = 5$, 15.2%). Majority of the patients were married ($n = 140$, 79.1%). None of the widowed patients was depressive. Post-hoc Bonferroni test showed that marital status was not associated with depression status. Majority of patients were having children ($n = 146$, 82.5%). Majority of the patients were staying with family ($n = 159$, 89.8%) and at town area ($n = 137$, 77.4%). The proportion of patients staying alone who were depressive ($n = 4$, 22.2%) was greater compared to those staying with family ($n = 21$, 13.2%). Majority of patients received at least primary education ($n = 169$, 95.5%). Most of the patients were unemployed or retired ($n = 125$, 70.6%).

All patients had been diagnosed with HF with median \pm IQR of 2.00 ± 4.00 years. More than half of the patients ($n = 93$, 52.5%) were in NYHA Class I. The proportion of high scorers within NYHA Class I group was the lowest ($n = 6$, 6.5%), but it tripled in NYHA Class II ($n = 13$, 19.4%), increased up to 6-fold in Class III ($n = 6$, 37.5%). NYHA classes were significantly associated with depressive status ($p = 0.003$). Almost all the patients ($n = 171$, 96.6%) were having left ventricular ejection fraction (LVEF) $\leq 40\%$. LVEF was not associated with depressive status following post-hoc Bonferroni test. Comorbidities including hypertension, type 2 diabetes mellitus and ischaemic heart disease were common as more than half of the patients was reported to have at least one of these comorbidities (Table 1).

Table 1: Comparisons of demographic and clinical characteristics of patients based on depressive symptoms scores ($N = 177$).

Variables	Median \pm IQR or frequency (%)	Depressive symptoms scores, n (%)		p -value	
		Low score ($n = 152$)	High score ($n = 25$)		
Age (years old)	62.00 ± 17.00	–	–	–	
Age groups (years old)	Below 60	78 (44.1)	63 (41.4)	15 (60.0)	0.083
	60 and older	99 (55.9)	89 (58.6)	10 (40.0)	
Gender	Male	152 (85.9)	132 (86.8)	20 (80.0)	0.359 ^a
	Female	25 (14.1)	20 (13.2)	5 (20.0)	

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Table 1: (continued)

Variables		Median ± IQR or frequency (%)	Depressive symptoms scores, <i>n</i> (%)		<i>p</i> -value
			Low score (<i>n</i> = 152)	High score (<i>n</i> = 25)	
Race	Malay	76 (42.9)	65 (42.8)	11 (44.0)	0.96
	Chinese	68 (38.4)	59 (38.8)	9 (36.0)	
	Indian	33 (18.6)	28 (18.4)	5 (20.0)	
Marital status	Single	23 (13.0)	18 (11.8)	5 (20.0)	0.036 ^{a†}
	Married	140 (79.1)	123 (80.9)	17 (68.0)	
	Widowed	8 (4.5)	8 (5.3)	0 (0.0)	
	Divorced	6 (3.4)	3 (2.0)	3 (12.0)	
Having children	Yes	146 (82.5)	128 (84.2)	18 (72.0)	0.157 ^a
	No	31 (17.5)	24 (15.8)	7 (28.0)	
Living status	Alone	18 (10.2)	14 (9.2)	4 (16.0)	0.291 ^a
	With family	159 (89.8)	138 (90.8)	21 (84.0)	
Living location	Town	137 (77.4)	120 (78.9)	17 (68.0)	0.225
	Rural	40 (22.6)	32 (21.1)	8 (32.0)	
Education level	No formal education	8 (4.5)	6 (3.9)	2 (8.0)	0.759 ^a
	Primary education	33 (18.6)	29 (19.1)	4 (16.0)	
	Secondary education	109 (61.6)	93 (61.2)	16 (64.0)	
	Tertiary education	27 (15.3)	24 (15.8)	3 (12.0)	
Employment status	Employed	52 (29.4)	46 (30.3)	6 (24.0)	0.524
	Unemployed/ Retired	125 (70.6)	106 (69.7)	19 (76.0)	
Duration of HF (years)	Median ± IQR	2.00 ± 4.00	–	–	–
NYHA classes	I	93 (52.5)	87 (57.2)	6 (24.0)	0.003 ^{a†}
	II	67 (37.9)	54 (35.5)	13 (52.0)	
	III	16 (9.0)	10 (6.6)	6 (24.0)	
	IV	1 (0.6)	1 (0.7)	0 (0.0)	
LVEF categories	≤ 40%	171 (96.6)	149 (98.0)	22 (88.0)	0.038 ^{a†}
	> 40%	6 (3.4)	3 (2.0)	3 (12.0)	

(continued on next page)

Table 1: (continued)

Variables		Median \pm IQR or frequency (%)	Depressive symptoms scores, <i>n</i> (%)		<i>p</i> -value
			Low score (<i>n</i> = 152)	High score (<i>n</i> = 25)	
Types of HF (<i>N</i> = 151)	Ischaemic	127 (71.8)	110 (83.3)	17 (89.5)	0.739
	Non-ischaemic	24 (13.6)	22 (16.7)	2 (10.5)	
Comorbidities	Hypertension	121 (68.4)	103 (67.8)	18 (72.0)	0.673
	Type 2 diabetes mellitus	99 (55.9)	84 (55.3)	15 (60.0)	0.658
	Ischaemic heart disease	131 (74.0)	113 (74.3)	18 (72.0)	0.805
	Kidney diseases	32 (18.1)	27 (17.8)	5 (20.0)	0.782 ^a

Notes: ^aFisher's exact test; **p* < 0.05

DISCUSSION

In this study, the prevalence of perceived depressive symptoms among HF outpatients was found to be 14.1%. This was considerably higher than the prevalence reported (1.8%; 95% CI: 1.5–2.1) among general adult population (aged 16 years old and above) who was not institutionalised (in hospitals, hostels, etc) in Malaysia (Malaysian Healthcare Performance Unit 2017). This suggested that presence of depressive symptoms was more common among individuals with existing health problems. In fact, the prevalence rates for HF patients in studies conducted abroad varied across a wide range, from 9% to 60% (Vaccarino *et al.* 2001; Pihl *et al.* 2005; Rutledge *et al.* 2006). The heterogeneity of the prevalence rates between current study and other studies could be explained by the differences in depression assessment methods (questionnaires or diagnostic interview) and diagnostic thresholds (cut-off points) being applied (Rutledge *et al.* 2006).

Prevalence of 14.1% reported from our current study was lower than that being reported by Gottlieb *et al.* (2004) with depression rate of 48%. The later was conducted at a HF outpatient clinic in the United States with sample size of 155. The mean age of patient group was 64 \pm 12 years old and 79% were men. These patients' characteristics in Gottlieb *et al.* (2004) were similar to our current study. However, NYHA Class I patients were excluded. The study population included patients with more severe NYHA class, therefore leading to greater depression rate. Beck Deck Inventory (BDI) questionnaire (cut-off point \geq 10) was used instead of PHQ-9. In fact, the cut-off point being used could affect the results. The liberal cut-off point of 10 in BDI questionnaire might not explicitly screen for patients with only moderate to severe depression, but also those with mild depression. In PHQ-9, the cut-off point of 10 reflects to moderate to severe depression (Kroenke, Spitzer and Williams 2001).

The prevalence of 14.1% found in current study was comparatively lower than that reported in a meta-analysis (21.5%) by Rutledge *et al.* (2006). This meta-analysis included inpatients, outpatients and combined groups. However, in current study, HF inpatients were excluded due to consideration of different measurement method that may lead to measurement bias. According to Rutledge *et al.* (2006), questionnaires are more likely to be used to assess depression among HF outpatients. On the other hand, interview session is more often performed among hospitalised HF patients to detect depressive disorders. One example is the use of diagnostic interview schedule in previous study of major depression among HF inpatients by Koenig (1998). Additionally, Freedland *et al.* (2003) suggested that further clinical reviews after DIS are necessary to reduce the risk of overdiagnosis of depression in medically ill HF inpatients. Generally, inpatients would be expected to have more comorbidities and clinically unstable. They might have more severe NYHA class and more depressive compared to outpatients. This could be explained by the exacerbation of HF that caused obvious functional disability and hospitalisation, contributing to mental stress, and affecting the NYHA class of the patient during hospital admission. Notably, this study showed that younger patients were more depressive than older group. We expected that demised of friends or family members, reduced strength, loneliness, loss of active income, diminishing health, targetless living might lead to higher prevalence of depressive symptoms among elderly, however it was the other way round, as proven by previous studies and current study. Gottlieb *et al.* (2004) conducted a study among HF outpatients and found that depressive patients (62 ± 14) years old were younger than non-depressive patients (65 ± 11) years old ($p = 0.086$). Another study by Freedland *et al.* (2003) on HF inpatients reported that age was significantly associated with major depression and the prevalence was higher among those below 60 years old (60%) compared to those above 60 years old (47%) ($p = 0.003$).

Current study showed that depressive status was associated with NYHA classes ($p = 0.003$). Jiang *et al.* (2001) reported consistent result that the prevalence of depression was higher among patients with higher NYHA classes. A similar trend was observed in study by Gottlieb *et al.* (2004) in outpatients setting, whereby more depressive patients were found in NYHA Classes III and IV than Class II ($X^2 = 6.51$ (2); $p = 0.038$). A meta-analysis consisting of five studies by Rutledge *et al.* (2006) also showed that the depression rate in NYHA class III was nearly double of Class II. Higher NYHA class indicates a greater reduction of cardiopulmonary function, therefore greater degree of functional impairment. Such disability reduces quality of life and increases mental stress. Therefore, patients in higher NYHA class (Class III or IV) were more likely to be depressive.

Limitations

During the data collection process, we found that the degree of understanding on the PHQ-9 questionnaires varied among participants. Some requested clarification from researcher and a verbal form of explanation was given upon enquiry. This might lead to response bias in answering the questions among participants. Even though the questionnaires had been validated in Malaysian population, there was possibility that different patient groups might have different understanding levels due to variances in education level.

There was only one patient in NYHA Class IV in current study. Such unequal patient distribution could affect the result of the analysis. Two proportions sample size formula could be used to ensure adequate samples in both groups but there was no data to be utilised for this formula. In fact, the findings from current study could help to fill this gap.

CONCLUSION

Depressive symptoms were common among HF outpatients and were significantly associated with NYHA class. In view of increasing number of patients and limited time and resources available, screening patients for perceived depression especially those with higher NYHA class was recommended as it could possibly detect early depressive symptoms and trigger prompt action. Ultimately, outcomes such as hospitalisation, healthcare cost and death would be reduced.

ACKNOWLEDGEMENTS

We would like to express a sincere gratitude to Dr. Sabariah Noor Harun from the School of Pharmaceutical Sciences, USM; Assoc. Prof. Dr. Balamurugan Tangiisuran from the National Poison Centre, USM; Dr. Muhamad Ali SK. Abdul Kader from the Department of Cardiology, Hospital Pulau Pinang; Ms Choong Shiau Fenn and Ms Chia Pooi Yin, pharmacists from the Heart Failure Clinic in Hospital Pulau Pinang, for the kind assistance in the study process. The participation of patients in the study is very much appreciated.

The study findings had been presented in the form of e-poster in International Conference of Pharmacy and Health Sciences 2020, 3rd Joint Conference UNAIR-USM.

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