Original Article

Associated Factors of Anxiety among Acute Coronary Syndrome Patients in Kelantan and Terengganu

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(Received: 29 Aug. 2016; Revised: 7 Jul. 2017; Accepted: 24 Sept. 2017)

Abstract

Background and purpose: Anxiety is a common condition among acute coronary syndrome (ACS) patients. This syndrome often goes unrecognised and can persist for months to years, while impacting substantially the quality of life. Therefore, this study aimed to identify the associated factor of anxiety among ACS patients in Hospital Universiti Sains Malaysia (USM) and Hospital Sultanah Nur Zahirah (HSNZ).

Materials and Methods: This cross-sectional study involved ACS patients admitted to Hospital USM, Kelantan and HSNZ, Terengganu between August 2014 and May 2015. A standardised questionnaire was developed to interview the respondents. The questionnaire was separated into two sections. The first section comprised the socio-demographic details of the patients. The second section was the validated Depression Anxiety Stress Scale 21 (DASS-21) questionnaire. Simple and multiple logistic regressions were used for analysing the collected data.

Results: The mean (standard deviation (SD)) age of ACS patients was 60.4 (11.3) years and 61.2 (10.4) years in Hospital USM and HSNZ respectively. The majority of ACS patients who experienced anxiety were male (86.3%) with 84.9% of them Malay ethnicity and 85.9% of them married. The factor associated with anxiety among ACS patients was having a history of ischemic heart disease (adjusted odd ratio (OR): 2.20, as well as confidence interval (CI): 1.19, 4.10, p=0.013).

Conclusion: It was concluded that anxiety had myriad effects on cardiovascular physiology, which plays an important role in the increased incidence of ischemic events in patients. A screening tool should be created to refine and identify the psychological status of ACS patients, so that early treatment could be given.

Keywords: ACS; Anxiety; Kelantan; Terengganu

Citation: Wan-Nor-Asyikeen W, **Siti-Azrin AH**, Sulong ZR, Fauzi MH. Associated Factors of Anxiety among Acute Coronary Syndrome Patients in Kelantan and Terengganu 2017; 5 (4):1-9

1. Introduction

Acute coronary syndrome (ACS) is one of the leading causes of mortality globally including Malaysia (1, 2). In 2012, ACS cases accounted for 24.7% of all the recorded deaths in the country (3). These rates are poised to increase as disease patterns in this middle-income developing country become more similar to those of developed countries (4). ACS was commonly known as "heart attack", where it happens when there is an obstruction of the coronary arteries which results in restricted blood flow to the heart (5). It can be classified into three categories: unstable angina (UA); non-ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI) (5-7). In NSTEMI, the coronary arteries are partially or intermittently occluded, while in STEMI, there is full arterial occlusion (6). The risk factors for cardiac disease, and primarily an ACS, include male gender, age (over 45 years for male and 55 years for female), family history of cardiovascular disease, and modifiable risk factors, such as hypertension, hyperlipidaemia, diabetes, sedentary lifestyle and smoking (8). Besides, it has become increasingly clear that psychological factors, particularly anxiety, may play an important and independent role in the development of cardiac disease. About 20% to 50% of acute myocardial infarction (AMI) patients showed higher levels of self-reported anxiety following the events (9-11), while up to one-quarter of AMI patients experienced anxiety (12). Anxiety often persists after such cardiac events and among patients with anxiety shortly after ACS, many have clinically significant anxiety up to 2 years later (13-14). The patients with stable coronary heart disease have higher levels of anxiety than the general population, with prevalence rates ranging from 16% to 42 % (15). This finding is further an evidence of the pervasive nature of anxiety in coronary heart disease patients (16-18). Research on anxiety among ACS patients has been conducted quite extensively in other countries. However, the information about anxiety in ACS patients in Malaysia is scarce. The purpose of the current study was to identify the associated factors of anxiety among ACS patients. To this end, this study was conducted in hospital settings to examine the self-reported levels of anxiety.

2. *Materials and Methods*

This cross-sectional study involved all ACS patients admitted to all medical wards including Coronary Rehabilitation Ward (CRW) and Cardiac Care Unit (CCU) in Hospital USM and HSNZ from August 2014 until May 2015 that fulfilled the inclusion and exclusion criteria. Hence, convenience sampling method was applied in this study with the inclusion criteria of the age range of over 18 years old, in addition to literacy in Bahasa Melayu. However, the patients were excluded if they were intubated, had any altered mental status, were mentally retarded, or had psychological problem prior to ACS. After applying the inclusion and exclusion criteria, a total of 400 patients were determined to be eligible to participate in this study. There were 200 questionnaires distributed to ACS patients for each hospital.

A consent was taken from the ACS patients. The respondents were thoroughly justified on the research objectives. A Malay version of self-administered questionnaire of

Depression Anxiety Stress Scale 21 (DASS-21) was given to the respondents to answer in about 10 to 15 minutes. All information was kept confidential, and the individual data had no identification of the respondents.

The questionnaire was divided into two sections. The first section was meant to provide the socio-demographic details including age, gender, race, occupation, marital status, and co-morbid. The second section was the DASS-21. The Depression Scale measures hopelessness, low self-esteem, and low positive affect. The Anxiety Scale assesses autonomic arousal, physiological hyperarousal, and the subjective feeling of fear. The Stress Scale items measure tension, agitation, and negative affect. The scales are considered to approximate facets of diagnostic categories, as follows: Depression Scale for mood disorders, Anxiety Scale for panic disorder, and Stress Scale for generalized anxiety disorder (19). The content validity of the questionnaire was assessed by Musa R et al. (2007) (20). They translated, validated, and measured psychometric properties of DASS-21 in the adapted Bahasa Malaysia (BM) version. The reliability coefficients (Cronbach's alpha) of the BM version had very good values of 0.74 for anxiety (20). The data were entered, cleaned, and analyzed using SPSS 22.0 for Windows. Mean (SD) and median (interquartile range) were used for the continuous variables to describe the characteristic of ACS patients, depending upon the normality of distribution, whereas frequency and percentage was used for categorical variables. Simple and multiple logistic regression were also used to identify the associated factors of anxiety with the outcome of total score.

The logistic regression which was used to analyze the data in the current study involved binary outcome (in which there are only two possible outcomes: normal and abnormal anxiety). The independent variables were screened one by one by using simple logistic regression. Only the variables which were statistically important with p-value less than 0.25, or the ones which were clinically important were included to proceed with multiple logistic regression. For anxiety, gender, education status, occupation status, household income, diabetes mellitus, hypertension, dyslipidemia, stroke, and ischemic heart disease (IHD) variables were included to proceed with multiple logistic regression. The results are presented as the crude and with adjusted odd ratios (OR), 95% confidence interval (CI) and *p*-value. The *p*-value < 0.05 was considered to indicate statistical significance.

3. *Results*

The socio-demographic characteristics of the ACS patients are shown in Table 1. The mean (SD) age of patients was 60.4 (11.3) years in Hospital USM and 61.2 (10.4) years in HSNZ. The preponderance of anxious-ACS patients were of Malay ethnicity (84.9%) with 86.3% males, and 85.9% of them were married. The unemployed patients also contributed to the larger amount of anxiety (85.8%).

About 91.4% of ACS patients who experienced anxiety had a stroke, 90.6% had IHD, 87.6% had diabetes mellitus, 86.7% had hypertension, and 82.9% had hyperlipidaemia. The patients with other co-morbid, such as chronic kidney disease, peptic ulcer disease, gastritis, and chronic lung disease were 93.0%. The associated factor of anxiety among ACS patients also had a history of IHD (OR: 2.20, p=0.013).

Table 1. Socio-demographic of ACS patient in Hospital USM and HSNZ (n=400)

Variables	Anxiety category	
	Normal n (%)	**Abnormal** n (%)
Gender		
Female	23 (15.1)	129 (84.9)
Male	34 (13.7)	214 (86.3)
Race		
Non-Malay	8 (10.7)	67 (89.3)
Malay	49 (15.1)	276 (84.9)
Marital Status		
Single	2 (15.4)	11 (84.6)
Married	39 (14.1)	237 (85.9)
Divorced/Widow	16 (14.4)	95 (85.6)
Occupation		
Unemployed	20 (14.2)	121 (85.8)
Government	4 (8.3)	44 (91.7)
Private	7 (12.7)	48 (87.3)
Others	26 (20.6)	130 (79.4)
Comorbid		
Diabetes Mellitus	30 (12.4)	212 (87.6)
Hypertension	40 (13.3)	260 (86.7)
Hyperlipidaemia	32 (17.1)	155 (82.9)
Stroke	6 (8.6)	64 (91.4)
Ischemic Heart Disease	16 (9.4)	155 (90.6)
Others	6 (7.0)	80 (93.0)

Table 1. The associated factor of anxiety among ACS patients (n=400)

Variables	Simple Logistic Regression			Multiple Logistic Regression		
	b	**Crude Odd Ratio (95% CI)**	**p-value**	**b**	**Adjusted Odd Ratio (95% CI)**	**p-value**
Comorbid						
Ischemic Heart Disease	0.75	2.11 (1.14, 3.91)	0.017	0.79	2.20 (1.19, 4.10)	0.013

4. *Discussion*

Anxiety is a common condition experienced by ACS patients. Anxiety is a state of uneasiness, accompanied by dysphoria, somatic signs and symptoms of tension which focus on the apprehension of possible failure, misfortune or danger (22). Anxiety in ACS patients can have a negative impact on health outcomes.

The analysis of data in the present study revealed that intense subjective distress and fear of dying, immediately after ACS, increased the risk of anxiety (23). Some patients had a family history of the death of their parents as a result of same illness. The history was often associated with the conscious fantasy that the patient's death at the age of which their parents died was inevitable, leading to considerable vigilance, avoidance, and other anxiety behaviours (24). Emotional upsets often trigger off the pathophysiological changes underlying plaque rupture, the formation of a pro-thrombotic vascular environment,

thrombus formation, and other neuroendocrine and autonomic processes, which results in cardiac rhythm disturbances which subsequently lead to anxiety symptoms (25).

The current study found that there was a significant association between IHD and anxiety. Patients with elevated anxiety had higher rates of subsequent development of coronary heart disease than non-anxious persons (15). In particular, the worry was a component of anxiety that appears to be especially associated with cardiac disease (26, 27). Platelet activity and aggregation were found to be the key components of AMI. The link between anxiety and platelet hyper-reactivity (and subsequent aggregation) may be mediated by serotonin (15). Serotonin is found in the whole blood and platelets, and plays a vital role in platelet activation. When serotonin binds to 5-hydroxytryptamine-2 (5HT-2) receptors on platelets, it causes the release of pro-coagulant factors stored in the platelets and enhances platelet aggregation, leading to clot formation (15).

In normal coronary arteries, thrombus formation and ischemia are prevented by serotonin's stimulation of the endothelium to release nitric oxide, which results in vasodilation in the area surrounding the clot. In atherosclerotic arteries, however, damage to the endothelium prevents the release of nitric oxide with the result that serotonin leads to vasoconstriction (28). So, it is not surprising that elevated blood serotonin levels have been associated with IHD and cardiac events (29). The patients with phobic anxiety have then been found to have abnormalities in the coagulation and fibrinolytic system leading to a hypercoagulable state (30). Furthermore, abnormalities in blood serotonin levels, platelet serotonin transporters, and platelet intracellular calcium levels in response to stimulation (increasing sensitivity to pro-coagulant factors) have been reported in patients with specific anxiety disorders (15).

Inflammation also plays an essential role in the pathogenesis of acute ischemic events (15). Inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α), and interleukin-1 (IL-1) are actively involved in the pathogenesis of atherosclerosis, and elevations of inflammatory markers, especially C-reactive protein (CRP), and they are independently associated with mortality following ACS (31). In ACS patients who have experienced anxiety, the levels of circulating inflammatory markers are abnormal. A large study of healthy adults revealed that the elevated levels of anxiety were associated with abnormalities of multiple inflammatory markers (32). Besides, women with diabetes who had phobic anxiety had also experienced higher levels of inflammatory cytokines (33), and generalized anxiety disorder, which was associated with elevated levels of CRP among patients with cardiac disease (34).

Based on the results of the current study, it was also observed that hyperactivity of the sympathetic nervous system led to an increase in the release of catecholamine in the periphery. This activity, in turn, resulted in vasoconstriction, blood pressure elevation, platelet activation, and arrhythmia, all of which can have harmful effects on cardiovascular stability. It was then concluded that acute anxiety and chronic worry could lead to sympathetic nervous system hyperactivity and autonomic dysregulation, providing another potential causative relation between these disorders and adverse cardiac events (35, 36).

It was also found that endothelial dysfunction had a significant impact on cardiovascular health. Indeed, endothelial dysfunction in patients with cardiovascular illness has been independently associated with higher rates of cardiac mortality (37-39). Endothelial dysfunction also has been reported in patients with elevated levels of anxiety, particularly in the elderly (40, 41). Abnormal vascular function in the setting of anxiety could certainly lead to adverse cardiovascular physiology and outcomes. A study in Turkey found that panic-agoraphobia following ACS treatment were associated with female gender and some pre-hospital factors, such as the presence of diabetes or hypercholesterolemia, and a history of cardiovascular disease (42). The theory behind this phenomenon was that premenstrual hormonal fluctuations might partially explain the higher incidence of panic disorder in women. Progesterone metabolites have anxiolytic effects due to their agonistic effect on g-aminobutyric acid (GABA)/benzodiazepine receptors. There was also a greater panic response in females suffering from the premenstrual dysphoric disorder. This finding indicated that a possible concurrent dysregulation of the GABA/benzodiazepine receptor complex may underlie aspects of both the panic response and the disorders related to the female reproductive cycle. Premenstrual hormonal fluctuations may also explain the increased frequency of respiratory-related symptoms in women with panic disorder (42).

The present study had several limitations, since it was only limited to two hospitals and involved small study samples. The results of the study could then not be generalizable to the entire national population, as the data were collected from only two centers which were Hospital USM and HSNZ. This study was conducted over a ten-month period. To obtain comprehensive results, a more extensive study should then be carried out to recruit more patients into the study over a larger geographical area including many districts in Kelantan and Terengganu.

In conclusion, it should be said that anxiety has myriad effects on cardiovascular physiology via sorts of mechanisms, and these effects play an essential role in the increased incidence of ischemic events. Furthermore, the effects of anxiety on health-promoting behaviour clearly play a role in these patients' poor cardiac outcomes. Therefore, it is suggested that a screening tool to be created to refine and identify the psychological status of ACS patients, so that early treatment could be given.

Acknowledgement

We would like to thank the following individuals who have contributed to this study: staff in Hospital USM and HSNZ, Director of both hospitals and Ethical Committee.

Conflict of Interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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