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A Cross-Sectional Study Exploring Perceived Depression, Anxiety and Stress among Chronic Pain Patients in a Malaysian General Hospital

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Abstract

Introduction: Chronic pain (CP) has caused substantial disabilities across populations worldwide. Depression, anxiety and stress have been known to afflict patients with CP. This study was aimed to determine the prevalence of perceived depression, anxiety and stress and its associated factors among CP patients in a Malaysian pain clinic. Methods: This cross-sectional study recruited 117 consecutive CP patients attending the pain clinic in a Malaysian general hospital during a one-year period. Clinical characteristics and assessments were evaluated by an experienced pain physician and derived from patient medical records. A self-administered questionnaire that consisted of items on socio-demographics, the validated 21-items Depression, Anxiety and Stress Scale (DASS-21) and the Visual Analogue Scale (VAS) was utilized. Multivariate linear regression analysis was employed to identify the factors associated with perceived depression, anxiety and stress. Results: The prevalence of perceived depression, anxiety and stress was relatively high, approximately 40% in our study sample. Younger age and higher pain score were significantly associated with depression, anxiety and stress, while having neck/cervical pain in the past 3 months was significantly associated

with depression and anxiety, and having hypertension was significantly associated with anxiety and stress. Conclusion: The relatively high prevalence of perceived depression, anxiety and stress in this sample was associated with socio-demographics, pain attributes and disease co-morbidities.

Keywords: Chronic Pain, Depression, Anxiety, Stress, Patients

Introduction

Chronic pain (CP) has been conceptualized as pain that persists beyond the normal healing time of tissue, lasting for more than 3 to 6 months "in the absence of other criteria [1, 2]." CP has led to higher psychiatric morbidities [3, 4], necessitating clinicians to recognize pain as a distinct disease entity of its' own [5]. The linkage between pain and psychiatric morbidities projected an alarming phenomenon, with almost 30%-60% of CP patients suffered depression [4, 6], 35% having anxiety related disorders [7] and nearly 63% suffered stress [8].

Socio-demographics and clinical characteristics were known to be associated with depression, anxiety and stress among CP patients. Higher rates of depression were correlated with advanced age, being female and lower education level [9-12]. Clinical characteristics like pain intensity, pain duration and pain locations were reported to be associated with depression [13-15], while pain intensity and education level were associated with anxiety [16-18]. Perceived stress was found to be correlated with pain intensity and socio-economic factors like employment, household income and education level [17, 19].

Despite their relevance, impact and clinical importance in practice, these psychiatric co-morbid conditions are often missed in busy pain clinics. This study was aimed to explore the prevalence of depression, anxiety and stress and their associated factors among a sample of CP patients in a Malaysian pain clinic.

Methods

Study design and setting

This cross-sectional study was conducted among 117 CP patients in an outpatient setting of pain clinic at the Tengku Ampuan Rahimah Hospital, Malaysia between January 2016 and December 2016. Consecutive adult patients aged 18 years or older who sustained chronic non-cancer pain as defined by the International Association for the Study of Pain (IASP) [1] with a definitive diagnosis as confirmed by a pain physician, who is also an investigator in this study (MP) were recruited. Patients with cognitive deficits, dementia, mental retardation, severe sensory or expressive impairment as documented in medical records were excluded.

Measures

A self-administered questionnaire was utilized in this study. Clinical health parameters (disease co-morbidities and co-existing medical conditions) were obtained from patients' medical records. Subject's pain characteristics were evaluated by an expert pain physician (MP, who is also an investigator in this study. Patients' socio-demographics such as gender, age,

marital status, monthly household income, education level, employment status and duration, and living arrangement were recorded.

Disease co-morbidities (diabetes, hypertension or dyslipidemia) were derived from patient medical records. Baseline clinical parameters adopted were as follows: (1) Patients with fasting plasma glucose level of 7mmol/L (126mg/dL) or above and prescribed with oral hypoglycaemic agents or insulin regimen as documented in medical records were classified as having diabetes [20]; (2) Patients were hypertensive if they were previously diagnosed with hypertension and administered with anti-hypertensives as documented in medical records [20]; (3) Dyslipidemia was defined as total cholesterol more than 5.2 mmol/L with high plasma triglyceride concentration (>1.7mmol/L), low high-density lipoprotein cholesterol concentration (<1.0 mmol/L for men; <1.3 mmol/L for women) and increased concentration of low-density lipoprotein cholesterol (>2.6 mmol/L with cardiac risk factors) with patients currently on statins as documented in medical records [21].

Other co-existing medical conditions reported in the current sample include pre-existing asthma/COPD, heart problems (cardiac ischemia, heart failure or arrhythmias), and renal problems. Diagnostic symptoms consistent with asthma or COPD, include airflow limitations in spirometry with a significant response to bronchodilators as documented in patient medical records [22]. Patients with identified cardiac conditions (myocardial ischemia, heart failure or arrhythmias) were characterized based on ischemia or failure symptoms, chest radiography, echocardiography, irregular heart beat or abnormal electrocardiogram findings as documented in medical records [23]. Renal problems were identified according to abnormal renal profile (increased creatinine or urea level) as documented in medical records.

Assessment of pain parameters (pain duration and intensity) were based on subjective reports of patients. The visual analogue scale (VAS) was utilized to measure current pain intensity. Pain regions were evaluated and confirmed by the pain physician in this study and as documented in patients' medical records: head, face, neck/cervical, shoulder, upper limbs, thoracic anterior, thoracic posterior, abdominal, lumbar, pelvic/anal/perineal and lower limbs. If the pain regions are overlapped, we marked this as pain present in both or multiple sites. Pain type (neuropathic, muscle, inflammatory, mechanical or compressive) were evaluated based on symptoms presented by the patients as classified by IASP [1], and a confirmed diagnosis by the pain physician in this study.

Perceived depression, anxiety and stress were evaluated using the validated 21-items Depression, Anxiety and Stress Scales (DASS-21) [24]. DASS-21 consist a set of three self-report sub-scales designed to measure perceived emotional states of depression, anxiety and stress symptoms. Each of the three DASS-21 sub-scales contains 7 items, scored on a 4-point Likert scoring (ranged from 0-did not apply to me at all to 3- applied to me very much or most of the time). Scores for depression, anxiety and stress were calculated by summing the scores for the relevant sub-scale items and multiplied by 2 to achieve a final score [24]. Perceived depression was defined as anhedonia (reduced positive affect) [20]. The American Psychological Association characterizes perceived anxiety and stress by

feelings of tension, worried thoughts, and physical changes [25]. Anxiety is related to autonomic arousal, skeletal muscle tension and situational aspects, whereas stress is more related to irritability, impatience and difficulty in relaxing [26].

Data analysis

Data were analyzed using SPSS software version 23.0. Normality tests were conducted using statistical and graphical methods, and all quantitative data were found to be normally distributed. Descriptive statistics were conducted for all variables. To determine the prevalence of perceived depression, anxiety and stress, we categorized total scores into two groups. The "normal' score for each category of the DASS-21 was considered as a single group, while the "mild," "moderate" and "severe" scores for each category were grouped together.

Considering the principles of parsimony and biological plausibility for variable selection, multivariate linear regression analysis using backward elimination technique was performed to obtain the factors associated with perceived depression, anxiety and stress in CP patients. Assumptions of linear regression, including multi-collinearity between independent variables were tested. A p-value of less than 0.05 ($p<0.05$) was considered as statistically significant.

Results

Socio-demographic characteristics of participants

Majority of the respondents were females (59%, 69/117), married (82.1%, 96/117), and lived with their family (i.e spouse, siblings, parents, children or other close relatives) (93.2%, 109/117). Majority were unemployed (63.2%, 74/117), with a monthly income of >1000 RM (69.2%, 81/117) (RM 1000 being the minimum wage in Malaysia at the time of the study), and had attained secondary education or lower (86.3%, 101/117). The mean age of participants was 50.41 ± 11.5 years, with a mean employment duration of 14.88 ± 12.9 years (Table 1).

Table 1. Socio-demographic characteristics of participants (n=117)

Characteristics	Frequency (n)	Percentage (%)
Gender		
Male	48	41.0
Female	69	59.0
Age (years)	50.41 ± 11.5*	
≤50	58	49.6
>50	59	50.4
Marital status		
Single	21	17.9
Married	96	82.1
Monthly income (RM)	2258.85 ± 1846.1*	
≤1000	36	30.8
>1000	81	69.2
Education level		
Secondary or lower	101	86.3

Tertiary	16	13.7
Employment status		
Employed	43	36.8
Unemployed	74	63.2
Employment duration (years)	14.88 ± 12.9*	
≤10	60	51.3
>10	57	48.7
Living arrangement		
With family	109	93.2
Alone	8	6.8

**Mean ± SD*

Distribution of clinical characteristics, depression, anxiety and stress scores of participants

Table 2 provides a summary of the distribution of clinical characteristics (pain site, type, intensity, duration, co-morbidities), depression, anxiety and stress scores of the respondents. About half of respondents had lumbar (47.9%, 56/117) and lower limb pain (47.0%, 55/117) over the 3 months preceding assessment, while about one in five complained of upper limb (20.5%, 25/117) and pelvic/anal/perineal pain (19.7%, 23/117), respectively. Slightly over half of respondents had either peripheral neuropathic pain (53.8%, 63/117) or muscle pain (51.3%, 60/117). The average pain duration was 70.94 ± 49.9 months, with slightly over half of the respondents (52.1%, 61/117) having had the pain for 60 months or less. About 4 out of every 5 respondents (80.3%, 94/117) had pain of greater than moderate to severe intensity. The most common co-morbidities reported by the participants were hypertension (44.4%, 52/117), dyslipidemia (43.6%, 51/117) and diabetes (37.6%, 44/117). The mean depression score of the respondents was 9.85 ± 9.8 (Min = 0, Max = 36), while the mean anxiety score was 9.42 ± 8.2 (Min = 0, Max = 38), and mean stress score was 13.54 ± 12.0 (Min = 0, Max = 90) (Table 2). Overall, about half (50.4%, 59/117) of the respondents in the sample had symptoms of anxiety (score of ≥8), while the prevalence of depression symptoms (score of ≥10) and stress (score of ≥15) symptoms were about 44.4% (52/117) and 39.3% (46/117), respectively. Of respondents who were either depressed, anxious or stressed, slightly more than one-third had severe forms of these emotional states/symptoms (severe depression = 34.7%; severe anxiety = 40.7%; severe stress = 39.2%).

Table 2. Distribution of clinical characteristics, depression, anxiety and stress scores of participants (n=117)

Characteristics	Frequency (n)	Percentage (%)
Pain type		
Peripheral neuropathic pain (Yes)	63	53.8
Central neuropathic pain (Yes)	11	9.4
Muscle pain (Yes)	60	51.3
Inflammatory pain (Yes)	11	9.4
Mechanical/compressive pain (Yes)	52	44.4

Pain site (past 3 months)		
Head (Yes)	5	4.3
Face (Yes)	13	11.1
Neck/cervical (Yes)	19	16.2
Shoulder (Yes)	20	17.1
Upper limb (Yes)	25	20.5
Thoracic anterior (Yes)	3	2.6
Thoracic posterior (Yes)	9	7.7
Abdominal (Yes)	9	7.7
Lumbar (Yes)	56	47.9
Pelvic/anal/perineal (Yes)	23	19.7
Lower limb (Yes)	55	47.0
Pain duration (months)	70.94 ± 49.9*	
≤60	61	52.1
>60	56	47.9
Pain intensity score	7.43 ± 1.9*	
0-5 (None to moderate)	23	19.7
6-10 (More than moderate to severe)	94	80.3
Have Diabetes (Yes)	44	37.6
Have Asthma/COPD (Yes)	13	11.1
Have Hypertension (Yes)	52	44.4
Have Heart problems (Yes)	18	15.4
Have Renal problems (Yes)	3	2.6
Have Dyslipidemia (Yes)	51	43.6
Depression score	9.85 ± 9.8*	
Normal	65	55.6
Depressed	52	44.4
Anxiety score	9.42 ± 8.2*	
Normal	58	49.6
Anxiety	59	50.4
Stress score	13.54 ± 12.0*	
Normal	71	60.7
Stress	46	39.3

**Mean ± SD*

Multivariate linear regression analysis of socio-demographic and clinical characteristics on depression score

In a multivariate regression analysis, we examined the association of socio-demographic and clinical characteristics of respondents with their depression score. All the assumptions of multivariate linear regression analysis were tested and met. The final multivariate regression model (Backward Elimination Technique) was statistically significant ($F = 4.224$, $p=0.001$), and explained 14.3% of the variance in depression scores. Overall, Table 3 shows that there were three statistically significant factors associated with depression scores in the model. We

observed that for every unit increase in age, depression score was significantly decreased by 0.186 units (β = -0.186, 95% CI = -0.358 - -0.014, p=0.035). In contrast, respondents who reported neck/cervical pain in the past 3 months had a significant increase in depression score of about 8.708 units (β = 8.708, 95% CI = 4.013 – 13.404, p<0.001), while depression score significantly increased by 1.091 units for every unit increase in pain score (β = 1.091, 95% CI = 0.158 – 2.024, p=0.022). Given that the regression coefficients may be compromised by collinearity, we checked the variance inflation factor (VIF) as an indicator for collinearity. Traditionally, a VIF higher than 10 is indicative of high collinearity and our results suggest that a VIF was not present in model (Table 3).

Table 3. Multivariate linear regression analysis; factors associated with depression score (n=117)

Variable	B	SE	95% CI for β	T statistic	P value	Tolerance	VIF
Age (years)	-0.186	0.087	-0.358 – -0.014	-2.140	0.035*	0.722	1.386
Muscle pain	-3.240	1.782	-6.771 – 0.291	-1.818	0.072	0.894	1.119
Neck/cervical pain past 3 months	8.708	2.369	4.013 – 13.404	3.675	0.0001*	0.928	1.077
Abdominal region pain past 3 months	5.990	3.404	-0.757– 12.736	1.795	0.081	0.861	1.161
Pain score	1.091	0.471	0.158 – 2.024	2.318	0.022*	0.911	1.098
Have hypertension	3.746	2.010	-0.237 – 7.730	1.864	0.065	0.711	1.407

Adjusted R squared = 14.3%
**Significant at p<0.05*
Model: F=4.224, p=0.001

Multivariate linear regression analysis of socio-demographic and clinical characteristics on anxiety score

Using a multivariate regression analysis, we also explored the association between anxiety score and clinical and socio-demographic characteristics of the respondents. All the assumptions of multivariate linear regression analysis were tested and met. The final multivariate regression model (Backward Elimination Technique) was statistically significant (F = 4.587, p=0.001), and explained 13.4% of the variance in anxiety scores. Overall, Table 4 shows that there were four statistically significant factors associated with anxiety scores in the model. We observed that for every unit increase in age, anxiety score was significantly decreased by 0.232 units (β = -0.232, 95% CI = -0.373 - -0.090, p=0.002). In contrast, anxiety score significantly increased by 0.895 units for very unit increase in pain score (β = 0.895, 95% CI = 0.120 – 1.671, p=0.024). Respondents who experienced neck/cervical pain in the past 3 months had a significant increase in anxiety score of about 4.623 units (β = 4.623, 95% CI = 0.709 – 8.536, p=0.021). Similarly, respondents who had hypertension had a significant increase in anxiety score of about 3.666 units (β = 3.666, 95% CI = 0.323 – 7.009, p=0.032). There was no evidence suggestive of collinearity, as the VIF was far below 10 (Table 4).

Table 4. Multivariate linear regression analysis; factors associated with anxiety score (n=117)

Variable	B	SE	95% CI for β	T statistic	P value	Tolerance	VIF
Age (years)	-0.232	0.071	-0.373 – -0.090	-3.239	0.002*	0.749	1.335
Neck/cervical pain past 3 months	4.623	1.975	0.709 – 8.536	2.341	0.021*	0.941	1.062
Lumbar pain past 3 months	-2.429	1.437	-5.276 – 0.418	-1.690	0.094	0.969	1.032
Pain score	0.895	0.391	0.120 – 1.671	2.287	0.024*	0.929	1.077
Have hypertension	3.666	1.687	0.323 – 7.009	2.173	0.032*	0.711	1.407

Adjusted R squared = 13.4%
**Significant at p<0.05*
Model: F=4.587, p=0.001

Multivariate linear regression analysis of socio-demographic and clinical characteristics on stress score

We also explored the association of stress score with participants' socio-demographic and clinical characteristics using multivariate linear regression analysis. All the assumptions of multivariate linear regression were tested and met. The final multivariate model (Backward Elimination Technique) was statistically significant (F = 8.299, p<0.001), and explained 20.1% of the variance in stress scores. Overall, Table 5 shows that there were three statistically significant factors associated with stress score in the model. We observed that for every unit increase in age, stress score was significantly decreased by 0.492 units (β = -0.492, 95% CI = -0.690 - -0.294, p=0.0001). In contrast, stress score significantly increased by 1.128 units for very unit increase in pain score (β = 1.128, 95% CI = 0.039 – 2.216, p=0.042). Similarly, respondents who had hypertension had a significant increase in stress score of about 7.367 units (β = 7.367, 95% CI = 2.648 – 12.051, p=0.002). There was no evidence suggestive of collinearity, as the VIF was far below 10 (Table 5).

Table 5. Multivariate linear regression analysis; factors associated with stress score (n=117)

Variable	B	SE	95% CI for β	T statistic	P value	Tolerance	VIF
Age (years)	-0.492	0.100	-0.690 – -0.294	-4.922	0.0001*	0.755	1.324
Neck/cervical pain past 3 months	5.428	2.765	-0.050 – 10.905	1.963	0.052	0.947	1.057
Pain score	1.128	0.549	0.039 – 2.216	2.053	0.042*	0.929	1.077
Have hypertension	7.367	2.364	2.684 – 12.051	3.117	0.002*	0.713	1.402

Adjusted R squared = 20.1%
**Significant at p<0.05*
Model: F=8.299, p<0.001

Discussion

Core summary findings

Perceived depression, anxiety and stress were relatively high in our study population, with as much as 40% of the respondents suffering from each of these psychological states. Factors associated with depression, anxiety and stress scores were younger aged and higher pain scores. Having neck/cervical pain in the past 3 months was significantly associated with depression and anxiety scores, while being hypertensive was significantly associated with anxiety and stress scores.

Comparison with existing literature

Prevalence of perceived depression, anxiety and stress

CP patients suffer higher rates of depression and anxiety as compared to the general population [27, 28]. Not only does pain affect normal functioning, treatment response and quality of life, it is also believed to be predictive of subsequent depression, anxiety and stress related states [29]. The prevalence of depression among CP patients has been reported to range from 31.5% in China [4] to 60.8% in the UK [30]. The depression rate found in this study fell within this established range, and consistent with a study conducted in Tunisia [31]. Even more prevalent than depression is anxiety [32-34], which is believed to be caused by responsiveness to pain intensity and duration. Anxiety rate in the current study was 50.4%, consistent with a previous Malaysian study conducted among patients attending multidisciplinary pain and rheumatology clinics [18]. As suggested by the stress process model [35], the presence of anxiety and depression may trigger a stress response to overcome the collapse of coping mechanisms. Perceived stress in this study was reported to be 39.3%.

Covariates of depression, anxiety and stress scores

This study found that younger age was significantly associated with depression, anxiety and stress scores among CP patients. While this finding is supported by reports from other studies conducted in the UK [30] and China [4], some inconsistencies regarding this association was established [34, 36]. Although a previous study conducted among a community sample in the United States reported that participants with chronic pain and depression were likely to be older [37], the investigators also found that younger participants with chronic and co-morbid pains were more likely to have depression than participants with chronic pain only.

Higher pain scores/intensity was significantly associated with depression, anxiety and stress scores in this study. Multiple studies that explored the associations between pain intensity with depression, anxiety and stress among CP patients found similar findings [4, 18, 28, 31, 36, 38]. Pain duration has been reported to have a direct relationship with depression and anxiety [31, 36, 39], but in our study – like the study from UK [30] – failed to confirm this association. It is possible that the relationship between duration of pain and these psychological states as reported by the earlier studies might be mediated by age at onset of pain, type, site and severity of pain, all of which are independent predictors of depression, anxiety and stress among CP patients.

This study found that pain site, particularly having neck/cervical pain in the past 3 months was significantly associated with depression and anxiety ($p<0.05$), but only

marginally predictive of stress (p=0.05). We observed that respondents who experienced neck/cervical pain in the past 3 months were likely to have higher depression, anxiety and stress scores of up to 8.7, 4.6 and 5.4 units, respectively. This finding is supported by the results of a longitudinal study conducted among 614 participants in the Netherlands, in which the authors reported that the onset of depression and anxiety was significantly associated with 6 pain locations (neck, back, head, orofacial area, abdomen, and joints; hazard ratio [HR] = 1.96 to 4.02; P<0.05) [38]. Beyond this, literature suggests some inconsistencies with regards to the associations between specific pain sites and onset of depression, anxiety and stress. For example, some studies conducted in the UK [30] and the United States [37] found no significant association between pain sites and depression. Differences in methodological approaches (such as studies focusing on specific patient groups like those with chronic low back pain, rheumatoid arthritis, etc.) might have been responsible for the heterogeneity in findings regarding the association between specific pain sites and onset of depression, anxiety and stress. A more consistent association of onset of depression, anxiety and stress with multiple pain sites or increasing number of pain locations has been reported [30, 38, 40-43]. Our findings highlight the importance for clinicians to understand that while chronic low back pain or generalized pain may be more prevalent in practice, as was the case in this study and several previous studies, focused symptomatic screening for early detection and treatment of neck/cervical pain would not only impact onset of depression, anxiety and stress among CP patients, but also improve integrated management and outcomes in these patients.

This study also found significant associations between anxiety and stress with the presence of medical co-morbidity such as hypertension among CP patients. Previous studies have established a significant dose-dependent relationship between levels of comorbidity and severity of pain, impact of pain, severity of depression, anxiety and physical functioning, especially in older CP patients with comorbid hypertension or cardiovascular diseases [44, 45]. This relationship is further exaggerated by the presence of several comorbidities in the same patient [46]. This has significant implications for patient management to enhance better outcomes and improve quality of life.

Strengths & Limitations

The major strength of this study was the structured approach to our inquiry, which included the use of internationally validated DASS-21 instrument for the assessment of the study outcomes and in combination with objective clinical assessment of pain characteristics by a specialist physician. Our study also extends current knowledge on association of pain site and co-morbidities with depression, anxiety and stress, which could potentially impact clinical management of CP sufferers, especially in Malaysia. This study is not without limitations. Beyond the small sample size of our study, we did not evaluate the potential impact that different pain management modalities may have on the onset of depression, anxiety and stress. The small sample from a single center study limits the generalizability of the study findings.

Conclusions

Our study revealed a higher prevalence of anxiety symptoms than depression and stress

symptoms among CP sufferers attending a Malaysian outpatient pain clinic. Patients were more likely to present with severe forms of these emotional states, and associated with younger age, higher pain intensity, neck/cervical pain and co-morbid hypertension. Our findings underscore the need for routine symptomatic screening for depression, anxiety and stress (and where practically feasible neck/cervical pain) among CP sufferers to enhance early detection and treatment, improved quality of life and better treatment outcomes. Attention to other co-morbid conditions such as hypertension, diabetes, asthma/COPD etc, may also impact long-term management of pain, depression, anxiety and stress among CP sufferers, and is therefore encouraged.

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Conflict of Interests

None declared.

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