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ORIGINAL RESEARCH **INTENSIVE CARE**

Psychological assessment of the patients after intensive care unit discharge: a prospective cohort study

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ABSTRACT

Background & objective: Admission to an Intensive Care Unit (ICU) indicates a serious or even grave health-related condition of the patient. It is almost a stressful experience for a conscious patient, and might have adverse effects on the psychological status of the patients. This study aimed to determine the prevalence and associated factors of anxiety and depression in patients discharged from the ICU.

Methodology: It was a prospective cohort study of 93 ICU patients. All patients were required to answer a self–self-administered questionnaire which consisted of socio-demographic variables and the Hospital Anxiety Depression Scale (HADS) upon ICU discharge and subsequent 4 to 6 weeks. The study identified the prevalence of borderline and abnormal anxiety, as well as borderline and abnormal depression.

Results: The prevalence of borderline and abnormal anxiety was 21.5% and borderline and abnormal depression was 34.4% upon ICU discharge. Both parameters were improved after 4 to 6 weeks. The odds of abnormal anxiety at 4 to 6 weeks after discharge were 4.29-fold higher with medical diagnosis [adjusted OR 4.29 (95% CI 1.01, 17.76); P = 0.049] and 4.67-fold higher with patients on benzodiazepines (BDZ) [adjusted OR 4.67 (95% CI 1.21, 18.41); P = 0.026]. There were no significant factors in the multivariate analysis related to abnormal depression.

Conclusions: The prevalence of borderline and abnormal anxiety and depression was 21.5% and 34.4% respectively, upon ICU discharge and improved after 4 to 6 weeks. Medical diagnosis and benzodiazepine treatment were significant predictors of anxiety.

Abbreviations: BDZ: benzodiazepines, HADS: Hospital Anxiety Depression Scale, ICU: Intensive Care Unit,

Keywords: Anxiety; Depression; Intensive Care Unit; Benzodiazepines; Prevalence

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1. INTRODUCTION

Advancements in medical therapy have resulted in a higher survival rate among ICU patients. However, admission as well as the treatment in the ICU is very stressful to the patient and results in long-term psychological morbidity. Several studies have reported that post-ICU discharge, patients may experience psychological distress such as depression and anxiety, which may persist for some time.[1-3]

Depression is characterized by low mood or loss of interest for more than two weeks with a range of other symptoms .[4]). Anxiety is a normal emotion that may become persistent and inappropriate .[4]). The prevalence of anxiety ranges from 5% to 44% and for depression, it ranges from 7.5%-46%.[4,5]

It has been reported in many studies that several socio-demographic and clinical factors are associated with anxiety and depression in patients' post-ICU discharge. Rattray et al. (2005) reported that younger patients have higher anxiety scores.[6] Ramnarain et.al (2015) reported no strong association between age and depression and anxiety following ICU treatment.[7] A study showed that women have higher anxiety and depression scores.[6] Furthermore, unemployment is significantly associated with anxiety in ICU-discharged patients.[2]

There is a strong association between depression and patients who received benzodiazepines in ICU.[4]). Benzodiazepine is hypothesized to trigger depression by reducing central monoamine activity.[8] Myhren et al. (2010) reported there was no difference in anxiety and depression between medical, surgical, and trauma ICU patients.[2]

The requirement of mechanical ventilation during ICU admission has been associated with psychological morbidity after ICU discharge.[2] However, Rattray et al. (2005) reported there was no association between severity of illness (APACHE II score) and length of ICU stay with depression and anxiety post-ICU discharge.[6] Ramnarain et al. (2015) also reported there was no association between the length of ICU stay and depression and anxiety post-ICU discharge.[7]

These negative psychological morbidities can have a long-term impact on subsequent recovery and patient quality of life.[9,10] The quality of life in patients after ICU admission was found to be worse in prolonged mechanically ventilated patients, severe trauma, or sepsis patients.11 Several studies have suggested that early intra-ICU psychological intervention may help ICU patients recover from stressful experiences.[9,10] In addition, daily sedation withdrawal also offers benefits in the recovery of ICU patients.[9]

Scanning through the literature, this topic has been widely studied in developed countries for years. However, it gained very little concern among Asians and the Malaysian population in particular. One study in India reported a high level of depression and anxiety among ICU patients in comparison with patients in the general ward.[12] In Malaysia, several studies were conducted to assess psychological morbidity and quality of life among cancer patients.[13,14] However, no study has been conducted in Malaysia to assess the psychological morbidity in ICU-discharged patients.

Therefore, this study aimed to determine the prevalence of depression and anxiety in patients upon ICU discharge, and 4 to 6 weeks after ICU discharge by assessing their symptoms via a psychometric instrument. Furthermore, this study aimed to find an association between the level of depression and anxiety 4 to 6 weeks after ICU discharge and sociodemographic and clinical factors.

The two group hypotheses were: i) there was no significant association between the level of depression and anxiety at 4 to 6 weeks after ICU discharge and sociodemographic factors: ii) there was no significant association between the level of depression and anxiety at 4 to 6 weeks after ICU discharge and clinical factors. Identifying these psychological morbidities and possible associated factors is important as measures can be implemented to reduce these incidents and hence provide a better psychological recovery and quality of life in ICU-discharged patients.

2. METHODOLOGY

The present study was a prospective cohort study, conducted from June 2018 to January 2019. The reference population was all patients admitted to the ICU of our hospital. The inclusion criteria were: subjects >18 years old, admitted to the ICU for more than 24 hours, able to read and understand a Malay version of the Hospital Anxiety Depression Scale (HADS) questionnaire, and lived within 20 km of the hospital. Those who refused to participate, sustained head injury, had underlying mental disorder, and substance abusers were excluded from the study. The recruitment of the subjects was based on convenience sampling, and a total of 93 subjects were voluntarily involved in this study.

The ethical approval and permission were granted from the Human Ethical Committee of Universiti Sains Malaysia [Reference: USM/JEPeM/17120682]. The objectives of the study were explained to the subjects, and the issues regarding confidentiality and anonymity were also addressed. The participation of subjects in this study was on a voluntary basis. The written, signed consent was obtained prior to their participation. The

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Table 1: Demographic data of study participants

Variables		N (%)
Age, year		48 ± 16
Gender	Male	40 (43.0)
	Female	53 (57.0)
Race	Malay	93 (100)
Education	Primary	15 (16.1)
	Secondary	66 (71.0)
	Tertiary	12 (12.9)
Employment		60 (64.5)
APACHE II Score		7 ± 3
Disease Category	Surgical	48 (51.6)
	Medical	45 (48.3)
ICU length of stay, day		4.0 ± 4.4
Use of Benzodiazepines		19 (20.9)
Mechanical Ventilation		74 (79.6)
Days of mechanical ventilation		2.8 ± 3.7

Data presented as n (%) or mean ± SD

total completion time of the questionnaire ranged between 15 to 20 min for each subject.

Sociodemographic information gathered included: gender, age, race, level of education, and employment status. The clinical information obtained included APACHE II score, disease category, length of ICU stays, and the use of benzodiazepines. The indication of mechanical ventilation and the duration of the mechanical ventilation were also noted.

In this study, the Malay validated Hospital Anxiety and Depression Scale (M-HADS) was used to assess the anxiety and depression levels among patients. In 2012, Lua and Wong translated and validated HADS in the Malay language for the purpose of local use.[15] The HADS consists of 14 items, seven for anxiety and seven for depression.[16] Three stages of anxiety and depression are classified based on a predetermined cut-off score. A total score of 0-7 indicates normal levels; 8-10 indicates the borderline abnormal level, and 11-21 indicates an abnormal level of anxiety and depression. The HADS instrument was found to perform well in assessing the severity and case level of anxiety disorder and depression in patients and gives meaningful results as a psychological screening tool.[17] Furthermore, several clinical and non-clinical studies have established the validity and reliability of M-HADS as a satisfactory psychometric instrument for anxiety and depression assessment among the Malaysian population.[18,19]

2.1. Statistical analysis

The responses from collected questionnaires were compiled into a set of systematic and computerized data via the IBM Statistical Package of Social Science (SPSS) version 22.0 software. The first component of analysis focuses on demographic data and stages of anxiety and depression among the subjects. Demographic data were presented descriptively in terms of mean ± standard deviation and frequency (percentage). The level of anxiety and depression at ICU discharge and 4-6 weeks post-ICU discharge were compared via Wilcoxon Signed-Rank Test.

The second component of analysis examined the interaction between demographics & clinical variables and the two clinical outcomes, i.e. borderline anxiety and borderline depression. Univariate analysis and multivariate logistic regression were used to study the interaction between them. A $P < 0.05$ is statistically significant for the analysis.

3. RESULTS

A total of 93 subjects were recruited in the present study and agreed to participate in the prospective follow-up study. Nonetheless, five subjects were lost to follow-up 4 to 6 weeks after being discharged from the ICU. Those who lost to follow-up were mostly aged 60 years old and above. The subjects were Malay, aged between 19 to 78 years old, with a mean age of 48 years (SD =16). The

Table 2: Anxiety and depression levels post-ICU stay

	Upon discharge	4 - 6 weeks post-discharge	P value
Anxiety			
Median (IQR)	1 (0)	1 (0)	0.02*
Frequency			
Normal	73 (78.5)	75 (85.2)	
Borderline abnormal	15 (16.1)	13 (14.8)	
Abnormal	5 (5.4)		
Depression			
Median (IQR)	1 (1)	1 (1)	0.01*
Frequency			
Normal	61 (65.6)	65 (69.9)	
Borderline abnormal	27 (29.0)	23 (24.7)	
Abnormal	5 (5.4)		

*Note: IQR=Interquartile range; *statistically significant via Wilcoxon signed-rank test*

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Table 3: Predictors of borderline anxiety 4 to 6 weeks post-ICU stay

Variables		Univariate analysis		Multivariate analysis	
		ORc (95% CI)	P value	ORa (95% CI)	P value
Age		0.988 (0.952, 1.025)	0.504		
Gender	Male	1			
	Female	0.372 (0.111, 1.250)	0.110		
Education		1.048 (0.347, 3.165)	0.934		
Employment	No	1			
	Yes	1.875 (0.475, 7.406)	0.370		
APACHE II Score		1.154 (0.999, 1.333)	0.052		
Disease category	Surgical	1			
	Medical	4.714 (1.174, 18.925)	0.029*	4.288 (1.007, 17.757)	0.049*
ICU length of stay, day		1.111 (0.997, 1.238)	0.056		
Use of Benzodiazepines	No	1			
	Yes	4.381 (1.364, 17.117)	0.015*	4.667 (1.207, 18.409)	0.026*
Mechanical Ventilation	No	1			
	Yes	3.789 (0.460, 31.185)	0.215		
Days of mechanical ventilation		1.089 (0.956, 1.240)	0.199		

Univariate and multivariate Logistic Regression (p < 0.05 is significant); ORc: Crude odds ratio; ORa: Adjusted odds ratio.

**The goodness of fit of the model was checked using the Hosmer-Lemeshow test, p = 0.520. This result gives no evidence of a lack of fit of the model.*

majority of them were females (57%), had a secondary education level (71%), and were employed (64%).

Subjects were mixed medical and surgical patients. Mean ICU stay was 4 days (± 4.4), and mean APACHE II score was 7 (± 3). The majority of the subjects did not receive benzodiazepines during ICU admission (72%). Most of them were on a mechanical ventilator (79 %) with a mean duration of mechanical ventilation of 2.8 (± 3.7) days. The demographic data of the subjects are shown in Table 1.

The prevalence of subjects with abnormal and borderline anxiety levels upon ICU discharge was 21.5%, while those with abnormal and borderline depression levels were 34.4%. There were changes in the anxiety (14.8%) and depression (24.7%) levels among subjects upon discharge from the ICU and 4 to 6 weeks after discharge from the ICU. The average anxiety and depression levels were reduced 4 to 6 weeks after ICU discharge (Table 2).

The interaction between demographic and clinical variables and borderline anxiety was analyzed via logistic regression analysis (Table 3). In the univariate logistic regression analysis, two variables showed significant associations with borderline anxiety level, i.e., disease category and the use of benzodiazepines. From the analysis, subjects with a medical diagnosis had 4.7-fold odds of getting borderline anxiety as compared to subjects with a surgical diagnosis. Subjects who received benzodiazepines during ICU stay will have 4.4-fold higher odds of getting anxiety, as compared to those who did not receive the drug. The two variables show a significant association with anxiety in multivariate analysis. The odds of getting anxiety for subjects with medical diagnoses and the use of benzodiazepines were 4.3- and 4.7-fold, respectively.

The interaction between demographic and clinical variables and borderline depression was analyzed via logistic regression analysis (Table 4). In the univariate logistic regression analysis, three variables showed significant associations with borderline depression level, i.e., ICU length of stay, use of benzodiazepines, and days of mechanical ventilation. From the analysis, an increase in ICU stay and mechanical ventilation by one day will incur about 21% probability of getting borderline depression. Subjects who used benzodiazepines during ICU admission had 6-fold higher odds of getting depression, as compared to those who did not take the drug. Nonetheless, the three variables did not show a significant association with depression in multivariate analysis. The three variables could be independent risk

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Table 4: Predictors of borderline depression 4 to 6 weeks post-ICU stay

Variables		Univariate analysis		Multivariate analysis	
		OR (95% CI)	P value	OR (95% CI)	P value
Age		0.987 (0.958, 1.017)	0.384		
Gender	Male	1			
	Female	0.421 (0.160, 1.110)	0.080		
Education		1.608 (0.647, 3.998)	0.306		
Employment	No	1			
	Yes	0.742 (0.277, 1.989)	0.554		
APACHE II Score		1.111 (0.978, 1.263)	0.106		
Disease category	Surgical	1			
	Medical	2.287 (0.848, 6.165)	0.102		
ICU length of stay, day		1.207 (1.037, 1.404)	0.015*	1.350 (0.913, 1.996)	0.133
Use of Benzodiazepines	No	1			
	Yes	6.154 (1.970, 19.220)	0.002*	3.509 (0.849, 14.507)	0.083
Mechanical Ventilation	No	1			
	Yes	2.177 (0.571, 8.299)	0.255		
Days of mechanical ventilation		1.206 (1.014, 4.434)	0.034*	0.776 (0.491, 1.226)	0.276

Univariate and multivariate Logistic Regression ($p < 0.05$ is significant); ORc: Crude odds ratio; ORa: Adjusted odds ratio.

**The goodness of fit of the model was checked using the Hosmer-Lemeshow test, $p = 0.520$. This result gives no evidence of a lack of fit of the model.*

factors for borderline depression 4 to 6 weeks post-ICU discharge.

4. DISCUSSION

In the present study, the prevalence of subjects with a significant level of depression and anxiety upon ICU discharge was 34.4% and 21.5% respectively. At 4 to 6 weeks following ICU discharge the prevalence of subjects with significant level of depression (24.7%) and anxiety (14.8%) were reduced and consistent with study by Mc Kinley et al.[20] The prevalence of anxiety and depression at 4 to 6 weeks post ICU discharge in present study however were lower compared to previous study conducted among mechanically ventilated ICU patient at 2 months pot ICU discharge.[5] Most of the similar studies were conducted at 6 and 12 months intervals post ICU discharge and reported there were still significant levels of depression and anxiety up to 1 year post ICU discharge.[1,3] A significant number of subjects experienced borderline depression (24.7%) and borderline anxiety (14.8%) levels and the symptoms may persist for sometimes impose a long term impact on subsequent recovery and patient quality of life.[1] Therefore they warrant an assessment and management by expert as reported by previous studies, as an early intra ICU psychological intervention may help ICU patients recover from stressful experience.[9,10]

From the present study, there was no significant association between socio-demographic factors and borderline anxiety and borderline depression levels at 4 to 6 weeks post-intensive care discharge. These present findings are similar to previous findings.[7,21,22] However Mc Kinley et.al reported that female gender was associated with worse psychological recovery for ICU survivors.[20]

In the univariate logistic regression analysis, two clinical variables showed significant associations with borderline anxiety level, i.e. disease category and usage of benzodiazepines during intensive care admission. These two clinical variables show a significant association with anxiety in multivariate analysis. Whereas, for borderline depression level at 4 to 6 weeks post ICU discharge, in the univariate logistic regression analysis, 3 clinical variables showed significant association i.e., ICU length of stay, use of benzodiazepines, and days of mechanical ventilation. Nonetheless, these three clinical variables did not show a significant association with depression in multivariate

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analysis and could be independent risk factors for borderline depression 4 to 6 weeks post-ICU discharge.

The use of benzodiazepines was reported to be strongly associated with depression and anxiety among ICU survivors.[4] Kam et al. reported a higher mean daily benzodiazepine dose associated with depressive symptoms. Benzodiazepine is hypothesized to trigger depression by reducing central monoamine activity.[8] Therefore, pharmacological modification i.e. avoidance of benzodiazepine usage during ICU stay, would offer benefit for psychological recovery among ICU-discharged patients.

Several studies reported disease category had no significant association with anxiety.[2,22] However, the present study showed medical subjects had 4.7 odds of getting borderline anxiety as compared to non-medical subjects. A possible explanation is that most of the medical subjects had underlying chronic medical illness. However, we have no data to support this.

From the present study, an abnormal level of depression at 4–6 weeks after ICU discharge was associated with length of ICU stay and days of mechanical ventilation. This is consistent with a study by Ramona et.al, which reported depression among ARDS survivors at 1 year associated with duration of mechanical ventilation.[23] However, several studies showed that the length of ICU stay had no significant association with depression.[7,22] From the present study, most of the subjects who required prolonged mechanical ventilation stayed longer in the ICU and received benzodiazepines for sedation. Most subjects who were mechanically ventilated for a short period of time (1-3 days) received sedation other than benzodiazepines. However, these three clinical variables did not show a significant association with depression in multivariate analysis.

The severity of illness at the time of admission did not show any significant association with level of depression and anxiety at 4 -6 weeks after ICU discharge, and it is consistent with other previous studies.[7,21,22]

Box 1: Hospital Anxiety and Depression Scale	
Anxiety	
1.	I get a sort of frightened feeling as if something awful is about to happen:
2.	Worrying thoughts go through my mind:
3.	I can sit at ease and feel relaxed:
4.	I get a sort of frightened feeling like 'butterflies' in the stomach:
5.	I feel restless as I have to be on the move:
6.	I get sudden feelings of panic
Depression	
1)	I enjoy the things I used to enjoy:
2)	I can laugh and see the funny side of things:
3)	I feel cheerful:
4)	I feel as if I am slowed down:
5)	I have lost interest in my appearance
6)	I look forward with enjoyment to things:
7)	I can enjoy a good book or radio

5. LIMITATIONS

The presence study has several limitations. Since all the subjects in the present study were Malay, the findings were not relevant to other ethnicities in Malaysia. Therefore, the present findings are only applicable to Malay population in Malaysia, and further similar studies involving other ethnicities in Malaysia are recommended.

Secondly, the self-reported questionnaire was another limitation. Self-reported questionnaires have excellent sensitivity but poor specificity compared with a structured psychiatric interview. However, due to the limitation of time, self-reported questionnaires were used as a tool for the subjects who cannot spend much time in this present study.

Furthermore, this present study did not measure prior psychological symptoms, as this is a predictor of psychological distress in several studies. In addition, no assessment of delirium and cognitive failure was performed in subjects involved, as these two factors may contribute to the outcome.

In addition, the present study should follow up with the patient for some period of time, i.e. 3 to 12 months post-ICU discharge for further information about changes in anxiety and depression levels over time.

6. CONCLUSION

In conclusion, early assessment and treatment of psychological distress in discharged ICU patients is needed as the prevalence of depression and anxiety is high. This finding also warrants a multi-disciplinary collaboration involving the ICU team, the primary team, and the psychiatric team to ensure a better recovery and quality of life for ICU-discharged patients. In addition, pharmacological measures such as avoidance of benzodiazepines should be encouraged to reduce this psychological burden to ICU patients

7. Data availability

The numerical data generated during this research are available from the authors on request.

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8. Conflict of interest

All authors declare that there was no conflict of interest.

9. Funding

The study utilized the hospital resources only, and no external or industry funding was involved.

10. Authors' contribution

MAI: manuscript writing and editing

RHNZ: Designing the study, correction of manuscript

FA: conducting the study and analyzing the data

MMZ: Analyzing the data

All authors have read the final proof and approved it.

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