

A PROSPECTIVE STUDY ON THE PSYCHOLOGICAL ASSESSMENT IN COVID-19 PATIENTS DURING AND POST-INTENSIVE CARE UNIT AND NON-INTENSIVE CARE UNIT DISCHARGE

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LIST OF SYMBOLS AND ABBREVIATIONS

ICU	Intensive Care Unit
HRPZ	Hospital Raja Perempuan Zainab
SpO ₂	Oxygen saturation
Tx modalities	Treatment modalities
RT-PCR	Reverse Transcriptase-Polymerase Chain Reaction
M-HADS	Malay validated Hospital Anxiety Depression Score
IES-R	Impact of Event Scale-Revised (Malay validated)
HFNC	High Flow Nasal Cannula
HFMO	High Flow Mask Oxygen
ARDS	Acute Respiratory Distress Syndrome
=	equal to
±	standard deviation
<i>p</i>	<i>p</i> -value
%	percent
<	less than

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ABSTRACT

Background: COVID-19 pandemic outbreak has been creating havoc and has imposed a sense of severe insecurity and panic situation. Patients with COVID-19 have different degrees of psychological distress, such as anxiety and depression, which may have been related to their prognosis. This study aimed to assess psychological distress among COVID-19 patients during and post-intensive care unit (ICU) and non-ICU discharge.

Method: This was a prospective cohort single-centre observational study of 118 adult patients infected with COVID-19 who were admitted to Hospital Raja Perempuan Zainab II, Kota Bharu, Kelantan between September 2021, and March 2022. 59 patients were admitted to the ICU (Group 1) and another 59 to the isolation COVID-19 ward (non-ICU – Group 2). All the patients received the Malay validated Hospital Anxiety Depression Scale (M-HADS) questionnaire twice, during discharge from ICU or isolation COVID-19 ward and 1 month after discharge from the hospital. Both anxiety scores and depression scores for the Group 1 and Group 2 were compared using repeated measure ANOVA and linear regression was used to control confounding factors.

Results: In Group 1; 13 (22.03%) was admitted as category 4b, 41 (69.50%) as category 5a and 5 (8.47%) as category 5b, while in Group 2; 7 (11.86%) as category 2, 7 (11.86%) as category 3, 17 (28.81%) as category 4a and, 28 (47.46%) as category 4b. Mean depression score based on COVID-19 categories during discharge; in Group 1, category 4b (7.62 ± 2.220), category 5a (8.49 ± 2.040), and category 5b (7.40 ± 1.340), while in Group 2, category 4b (7.21 ± 1.770). Post-discharge; in Group 1, category 4b (5.69 ± 1.440), category 5a (6.05 ± 1.280), and category 5b (6.40 ± 0.550), while in Group 2, category 4b (5.71 ± 1.330). Mean anxiety score based on COVID-19 categories during discharge; in Group 1, category 4b (9.92 ± 2.060), category 5a (11.73 ± 2.950), and category 5b (11.80 ± 1.300), while in Group 2, category 4b (10.29 ± 1.560). Post-discharge; in Group 1, category 4b (8.08 ± 1.800), category 5a (9.32 ± 2.330), and category 5b (9.20 ± 1.640), while in Group 2, category 4b (7.68 ± 1.280). Prevalence of depression during discharge in Group 1; was mild (52.54%) and moderate (10.17%) with a mean depression score was (8.20 ± 2.049), otherwise, in Group 2; mild (40.68%), and moderate (1.69%) with mean depression score (6.98 ± 1.624). Prevalence of depression post-discharge in Group 1; was mild (1.69%) and another 98.31% no depression with a mean depression score was (6.00 ± 1.273), otherwise, in Group 2; no depression (100%), with a mean depression score (5.54 ± 1.250).

Prevalence of anxiety during discharge, in Group 1; was mild (25.42%), moderate (61.02%), and severe (6.78%) with a mean anxiety score was (11.34 ± 2.752), otherwise, in Group 2; mild (45.76%), and moderate (38.98%) with mean anxiety score (9.53 ± 2.104). Prevalence of anxiety post-discharge in Group 1; was mild (40.68%), and moderate (27.12%) with a mean anxiety score was (8.97 ± 2.197), otherwise, in Group 2; mild (33.90%), and moderate (1.69%) with mean depression score (7.20 ± 1.540). Gender (p-value = 0.033), an education level (p-value = 0.018), and oxygen level (p-value = 0.008) were associated with depression during discharge, and age (p-value < 0.001) were associated with depression post-discharge. Social support (p-value = 0.010), oxygen level (p-value = 0.010), and treatment modalities (p-value = 0.027) were associated with anxiety during discharge, and oxygen saturation (p-value = 0.005), and treatment modalities (p-value = 0.090) were associated with anxiety post-discharge. Prevalence of PTSD; 10.17% had mild symptoms in the psychological domain, otherwise, no patients had symptoms in the behavioral domain post-discharge.

Conclusion: COVID-19 infection had a high psychological impact on patients admitted to the hospital, especially ICU patients. Psychological intervention is needed to be a part of treatment in COVID-19 patients, especially during hospitalization.

Keywords: COVID-19, intensive care unit, anxiety score, depression score, M-HADS

ABSTRAK

Pengenalan: Wabak COVID-19 telah menimbulkan malapetaka dan telah menimbulkan rasa tidak selamat dan situasi panik yang teruk. Pesakit dengan COVID-19 mempunyai tahap tekanan psikologi yang berbeza, seperti kebimbangan dan kemurungan, yang mungkin berkaitan dengan prognosis mereka. Kajian ini bertujuan untuk menilai tekanan psikologi dalam kalangan pesakit COVID-19 semasa dan selepas keluar masuk unit rawatan rapi (ICU) dan bukan ICU.

Kaedah: Ini merupakan kajian pemerhatian prospektif terhadap 118 pesakit dewasa yang telah dijangkiti COVID-19 dan dimasukkan ke Hospital Raja Perempuan Zainab II, Kota Bharu, Kelantan antara September 2021 dan Mac 2022. 59 pesakit telah dimasukkan ke ICU (Kumpulan 1) dan 59 pesakit telah dimasukkan ke wad pengasingan COVID-19 (bukan ICU – Kumpulan 2). Kesemua pesakit menerima soal selidik *Malay validated Hospital Anxiety Depression Scale (M-HADS)* sebanyak dua kali, semasa keluar dari ICU atau wad pengasingan COVID-19 dan 1 bulan selepas keluar dari hospital. Kedua-dua skor kebimbangan dan skor kemurungan untuk Kumpulan 1 dan Kumpulan 2 dibandingkan menggunakan *repeated measure ANOVA* dan *linear regression* digunakan untuk mengawal faktor pengasas bersama.

Keputusan: Dalam Kumpulan 1; 13 (22.03%) pesakit tergolong dalam kategori 4b, 41 (69.50%) sebagai kategori 5a dan 5 (8.47%) sebagai kategori 5b, manakala dalam Kumpulan 2; 7 (11.86%) sebagai kategori 2, 7 (11.86%) sebagai kategori 3, 17 (28.81%) sebagai kategori 4a dan, 28 (47.46%) sebagai kategori 4b. Min skor kemurungan berdasarkan kategori COVID-19 semasa discaj; dalam Kumpulan 1, kategori 4b (7.62 ± 2.220), kategori 5a (8.49 ± 2.040), dan kategori 5b (7.40 ± 1.340), manakala dalam Kumpulan 2, kategori 4b (7.21 ± 1.770). Selepas pelepasan; dalam Kumpulan 1, kategori 4b (5.69 ± 1.440), kategori 5a (6.05 ± 1.280), dan kategori 5b (6.40 ± 0.550), manakala dalam Kumpulan 2, kategori 4b (5.71 ± 1.330). Min skor kebimbangan berdasarkan kategori COVID-19 semasa discaj; dalam Kumpulan 1, kategori 4b (9.92 ± 2.060), kategori 5a (11.73 ± 2.950), dan kategori 5b (11.80 ± 1.300), manakala dalam Kumpulan 2, kategori 4b (10.29 ± 1.560). Selepas pelepasan; dalam Kumpulan 1, kategori 4b (8.08 ± 1.800), kategori 5a (9.32 ± 2.330), dan kategori 5b (9.20 ± 1.640), manakala dalam Kumpulan 2, kategori 4b (7.68 ± 1.280). Kelaziman kemurungan semasa pelepasan dalam

Kumpulan 1; adalah ringan (52.54%) dan sederhana (10.17%) dengan skor min kemurungan ialah (8.20 ± 2.049) , jika tidak, dalam Kumpulan 2; ringan (40.68%), dan sederhana (1.69%) dengan skor min kemurungan (6.98 ± 1.624) . Kelaziman kemurungan selepas pelepasan dalam Kumpulan 1; adalah ringan (1.69%) dan 98.31% lagi tiada kemurungan dengan skor min kemurungan ialah (6.00 ± 1.273) , jika tidak, dalam Kumpulan 2; tiada kemurungan (100%), dengan skor min kemurungan (5.54 ± 1.250) . Prevalens kebimbangan semasa keluar, Kumpulan 1; adalah ringan (25.42%), sederhana (61.02%), dan teruk (6.78%) dengan skor min kebimbangan adalah (11.34 ± 2.752) , sebaliknya, dalam Kumpulan 2; ringan (45.76%), dan sederhana (38.98%) dengan min skor kebimbangan (9.53 ± 2.104) . Kelaziman kebimbangan selepas pelepasan dalam Kumpulan 1; adalah ringan (40.68%), dan sederhana (27.12%) dengan skor kebimbangan min adalah (8.97 ± 2.197) , jika tidak, dalam Kumpulan 2; ringan (33.90%), dan sederhana (1.69%) dengan skor min kemurungan (7.20 ± 1.540) . Jantina ($p\text{-value} = 0.033$), tahap pendidikan ($p\text{-value} = 0.018$), dan tahap oksigen ($p\text{-value} = 0.008$) dikaitkan dengan kemurungan semasa pelepasan, dan umur ($p\text{-value} < 0.001$) dikaitkan dengan kemurungan selepas pelepasan. Sokongan sosial ($p\text{-value} = 0.010$), tahap oksigen ($p\text{-value} = 0.010$), dan modaliti rawatan ($p\text{-value} = 0.027$) dikaitkan dengan kebimbangan semasa pelepasan, dan ketepuan oksigen ($p\text{-value} = 0.005$), dan rawatan modaliti (nilai $p = 0.090$) dikaitkan dengan kebimbangan selepas pelepasan. Kelaziman PTSD; 10.17% mempunyai gejala ringan dalam domain psikologi, jika tidak, tiada pesakit mempunyai gejala dalam domain tingkah laku selepas keluar.

Kesimpulan: Jangkitan COVID-19 memberi impak psikologi yang tinggi dalam kalangan pesakit yang dimasukkan ke hospital terutamanya pesakit ICU. Intervensi psikologi diperlukan untuk menjadi sebahagian daripada rawatan pesakit COVID-19 terutamanya semasa dimasukkan ke hospital.

Kata kunci: COVID-19, unit rawatan rapi, skor kebimbangan, skor kemurungan, M-HADS

CHAPTER 1: INTRODUCTION

1.1 Introduction

Since December 2019, the outbreak of COVID-19 caused by severe acute respiratory syndrome, has widely and rapidly spread worldwide. Reported death was increasing every day. As of April 2022, more than 500,186,525 confirmed cases and at least 6,190,349 deaths have been reported in 216 countries, according to World Health Organization (WHO). Specific in Malaysia, till April 2022, more than 4,370,000 confirmed cases and at least 35,397 deaths.

Some of the COVID-19 patients will develop severe respiratory distress syndrome, leading to Intensive Care Unit (ICU) admission. Treatment in the intensive care unit was very stressful for patients and resulted in long-term psychological morbidity.

Depression is characterized by low mood or loss of interest for more than two weeks with a range of other symptoms.

Anxiety is a normal emotion that may become persistent and inappropriate. 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. But there was a lack of studies specifically related to COVID-19 patients in ICU.

These negative psychological morbidities can have a long-term impact on subsequent recovery and patient quality of life. Several studies suggested that early intra ICU psychological intervention may help ICU patients recover from the stressful experience, scanning through the literature review this topic was widely studied in the developed country over years. However, it gains little concern among Asians and the Malaysian population.

1.2 Study Rationale

COVID-19 is a new pandemic disease that was very rapidly outbreak worldwide. There were several studies had been done related to the psychological impact of the COVID pandemic era. Most of the studies related to healthcare workers. Only a few studies had been done among non-ICU COVID-19 patients, but up to date, none of the studies for COVID-19 ICU patients.

Therefore, by doing this study, data from this study can be used to create or plan a proper early intervention to support psychological COVID-19 patients from the initial phase of the disease that involves a multidisciplinary team including primary team such as medical and supportive team anesthesiology and psychiatry team. Involvement from a multidisciplinary team such as a counselor and psychiatrist in managing the COVID-19 patient may later improve the outcome of the patient.

Up to date, specifically in Malaysia, no study has been carried out to look for psychological assessment in COVID-19 patients during and post ICU and non-ICU discharge.

1.3 Literature Review

Psychological Patient Intensive Care Unit (ICU)

Advanced in medicine, medical therapy results in a greater survival rate among ICU patients. However, treatment in the intensive care unit is very stressful for 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 for some time (Rattray et al, 2010).

Depression is characterized by low mood or loss of interest for more than two weeks with a range of other symptoms (Wade et al, 2012). Anxiety is a normal emotion that may become persistent and inappropriate (Wade et al, 2012). The prevalence of anxiety ranges from 12% to 43% (Scragg et al, 2001), and depression, ranges from 10-30% (Scragg et al, 2001). These psychological morbidities persist up to one-year post ICU discharge.

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. reported younger patient has higher anxiety score. However, Scretg et el. reported no strong association between age and depression and anxiety following ICU treatment (Scragg et al, 2001). A study showed that women have higher anxiety and depression score (Rattray et al, 2010). Unemployment is significantly associated with anxiety post ICU discharge.

Mechanical ventilation during ICU admission was associated with these psychological morbidities after ICU discharge (Myhren et al, 2010). Rattray et al. reported there was no association between severity of illness (APACHE II score) and length of ICU stay with depression and anxiety post ICU discharge. Scragg et al. also reported there was no association between length of ICU stay with depression and anxiety post ICU discharge.

This negative psychological morbidity can have a long-term impact on subsequent recovery and patient quality of life. The quality of life in a patient after ICU admission was found to be worst in prolonged mechanically ventilated patients, severe trauma, or sepsis patients (Oeyen et al, 2010). Studies suggested that early intra-ICU psychological intervention may help ICU patients recover from stressful experiences (Rattray et al, 2008). Daily sedation withdrawal also offers benefits to the recovery of ICU patients (Rattray et al, 2008).

All reported study above was related to general cases admitted to ICU. Almost none of it was reported in a COVID-19 psychological assessment. Therefore, many studies need to be done to collect data regarding psychological assessment in positive COVID-19 patients especially, in ICU.

COVID-19

COVID-19, similarly to SARS, is a beta-coronavirus that can be spread to humans through intermediate hosts such as a bat, human-to-human transmission has been observed via virus-laden respiratory droplets. It was very infective, with one person infected, it can infect another 4 people.

Severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) pneumonia is a newly recognized illness that has spread around the world and recorded many deaths. As of June 2020, more than 8700000 confirmed cases and at least 460000 deaths have been reported in 216

countries, according to World Health Organization (WHO). The clinical spectrum of COVID-19 pneumonia ranges from mild to critically ill cases.

As the number of cases climbed up at a great speed, panic prevailed among the general population, and the capacity of local fever clinics was soon overwhelmed. The mass media/newspaper/ blogs have been updating the information about the rapid rise in cases leading to admission to hospital, being kept in the isolation ward, requiring oxygen support, being admitted to Intensive Care Unit (ICU), associated mortality and fate of the dead bodies (packaging/ filled up graveyards/ crematorium). All this news has led to significant fear, anxiety, uncertainty, and restlessness in the general population. Given the high infectivity and reported consequences of infections, including mortality, COVID-19 is known to have significant negative mental health outcomes, not only in those who are diagnosed with the infection and their family members but also in the general public (Wang et al, 2020).

There are very limited literature reviews on this psychological experience of patients with COVID-19 during their hospitalization. One study (n=144) reported significant anxiety (34%) and depression (28%) at admission to isolation wards (Kong et al, 2020), the other (n=26) study reported higher anxiety and depressive score on HAM-A and HAM-D respectively after one week of hospitalization, which decreased after comprehensive psychological intervention (Yang et al, 2020). Another study (n=57) found the prevalence of depression to be around 30% in newly recovered COVID-19 patients (Zhang et al, 2020).

But there is still a lack of study-related psychological experience for COVID-19 patients that admitted/discharged from the ICU. Thus, this study is very important to get further data for psychological assessment in COVID-19 patients that were admitted/discharged from ICU. From this study, further action and intervention can be developed to help COVID-19 patients, especially in ICU.

COVID-19 and Non COVID-19 Infection

Studies have proven that ICU admission is associated with psychological distress and all patients admitted to ICU should have the issues addressed regardless of COVID-19 status. But until this moment, there was no single study related to a psychological assessment regarding COVID-19 patients in ICU. Therefore, a comparison between psychological distress between COVID-19 patients and non-COVID-19 patients in ICU cannot be done.

One study for non-ICU COVID-19 patients (n=144) reported significant anxiety (34%) and depression (28%) at admission to isolation wards (Kong et al, 2020) compared to the prevalence of anxiety ranging from 12% to 43% (Scragg et al, 2001) and for depression, ranges from 10-30% (Scragg et al, 2001) for non-COVID-19 patients in ICU. From this data, we may conclude that ICU COVID-19 patients may have higher psychological distress compared to non-COVID-19 ICU patients since non-ICU COVID-19 patients had shown almost similar psychological distress to non-COVID-19 ICU patients.

Several factors may contribute to psychological distress in COVID-19 patients compared to non-COVID-19 patients. There was a difference in pathophysiology of Acute Respiratory Distress Syndrome (ARDS) between COVID-19 and non-COVID-19 patients. From Up to date, when the COVID-19 virus enters the human body, it interacts with ACE 2 receptors and releases its RNA inside the epithelial cells where it replicates and released for further infection to neighboring cells and spread from the nasal passage to the alveolar area of the lung. Most COVID-19 patients developed ARDS by changing vessel integrity, supporting a pro-coagulative condition, inducing vascular inflammation, and reconciling inflammatory infiltrative. But ARDS in non-COVID-19 infection, is a consequence of alveolar injury-producing diffuse alveolar damage. Therefore, a conclusion may be made that, ventilation and perfusion (V/Q) mismatch in COVID-19 infection due to increased death space due to pulmonary vessel microthrombi and V/Q mismatch in non-COVID-19 patients was due to increase shunting result from severe alveolar damage.

Managing ARDS in COVID-19 patients and non-COVID-19 patients had some similarities but had huge differences. The similarity for both ARDS patients, studies were shown that lung protective strategies, prone position, and usage of muscle relaxation will improve morbidity and mortality.

From the RECOVERY trial study, the use of dexamethasone resulted in lowered 28-day mortality among those who were receiving either invasive mechanical ventilation or oxygen alone (Peter Horby et al, 2021) in COVID-19 patients. In hospitalized COVID-19 patients with hypoxia and systemic inflammation, tocilizumab improved survival and other clinical outcomes. These benefits were seen regardless of respiratory support and were added to the benefits of systemic corticosteroids (Peter Horby, 2021).

In terms of mechanical ventilatory support, one study found no statistically detectable difference between patients undergoing early versus late intubation in terms of morbidity, namely duration of MV, ICU length of stay, and renal replacement therapy. These findings referring to severe respiratory failure associated with COVID-19 are not in line with findings from observational studies on ARDS not associated with COVID-19.

In a conclusion, it may not be feasible to compare the psychological condition of COVID-19 patients with non-COVID-19 patients. It may be feasible to compare the psychological condition of ICU and non-ICU COVID-19 patients.

1.4 Study Objectives

1.4.1 General

- To assess psychological distress among COVID-19 patients during and post ICU and non ICU discharge.

1.4.2 Specific

- To determine the difference between the prevalence of depression and anxiety among COVID-19 patients during and post ICU and non ICU discharge.
- To determine the association of depression and anxiety among COVID-19 patients during and post ICU discharge with clinical factors and socio-demographic.
- To determine the prevalence of Posttraumatic Stress Disorder among COVID-19 patients post ICU and non ICU discharge.

1.4.3 Null Hypothesis

- There is no significant difference between the prevalence of depression and anxiety among COVID-19 patients during and post ICU and non ICU discharge.
- There is no significant association between depression and anxiety among COVID-19 patients during and post ICU discharge with clinical factors and socio-demographic.
- There is no significant Posttraumatic Stress Disorder (PTSD) among COVID-19 patients post ICU and non ICU discharge.

1.4.4 Alternative Hypothesis

- There is a significant difference between the prevalence of depression and anxiety among COVID-19 patients during and post ICU and non ICU discharge.
- There is a significant association between depression and anxiety among COVID-19 patients during and post ICU discharge with clinical factors and socio-demographic.
- There is significant Posttraumatic Stress Disorder (PTSD) among COVID-19 patients post ICU and non ICU discharge.

CHAPTER 2: STUDY PROTOCOL

2.1 Research Methods and Methodology

2.1.1 Research Design

Prospective Cohort Single-Center Observational Study

2.1.2 Study Period

September 2021 – March 2022

2.1.3 Study Population

COVID-19 patients who were admitted to the Isolation COVID-19 ward and Intensive Care Unit Hospital Raja Perempuan Zainab 2 from September 2021 until March 2022.

2.1.4 Study Area

Intensive Care Unit and COVID-19 Isolation COVID-19 ward, Hospital Raja Perempuan Zainab 2, Kota Bharu, Kelantan.

2.2 Subject Criteria

2.2.1 Inclusion Criteria

- Adult age > 18 years old
- Confirmed COVID-19 positive (via reverse transcriptase-polymerase chain reaction, RT-PCR)
- Able to understand Malay validated Hospital Anxiety Depression Score (M-HADS) and Malay validated Impact of Event Scale-Revised (IES-R)
- Admitted to a general ward and Intensive Care Unit > 24 hours
- All COVID-19 patients from categories 1 to 5

2.2.2 Exclusion Criteria

- Refuse to participate.
- Underlying mental disorder/ head injury
- Patient that required mechanical ventilation for more than 7 days or required more than 1 intubation.

2.2.3 Withdrawal Criteria

- Due to the observational nature of the study, the protocol does not define any withdrawal/discontinuation criteria. Patients electing to withdraw from the study may do so at any point. Withdrawal participants will be replaced with another participant until the targeted number of participants is achieved.

2.3 Sample Size Estimation

2.3.1 For objectives 1 and 2: To determine the difference between the incidence of depression and anxiety among COVID-19 patients during and post ICU and non-ICU discharge.

By using GPower 3.1 software, repeated measure: ANOVA approach, the sample size was calculated 3 times

	Within factors	Between factors	Within-between interaction
Effect size (f)	0.25	0.25	0.25
α error	0.05	0.05	0.05
Power	0.8	0.8	0.8
Number of groups	2	2	2
Number of measurements	2	2	2
Sample size	1 group = 34 Total = 68	Total = 98	1 group = 34 Total = 68
Anticipate drop-up rate (%)	20	20	20
Corrected sample size	82	118	82

Up to date, there was no available data in the literature review that study about the difference between the incidence of depression and anxiety among COVID-19 patients during and post ICU and non-ICU discharge.