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Relationship between the Length of Isolation and Swab Results with Degree of Anxiety and Depression Disorders in Patients with Confirmed of Coronavirus Disease 2019

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Abstract

BACKGROUND: The outbreak of coronavirus disease 2019 (COVID-19) has increased the burden of psychological stress.

AIM: This study aims to determine the relationship between the length of isolation, the results of the COVID-19 polymerase chain reaction swab test, the time of reporting, and the level of knowledge with the degree of depression and anxiety in patients with swab results confirmed by SARS-CoV-2.

METHODS: This study is an analytical observational study with a cross-sectional design. After the data were collected, a bivariate statistical analysis was carried out for the Kruskal–Wallis and Spearman Test.

RESULTS: A total of 25 patients with a diagnosis of COVID-19 were included in this study.

CONCLUSION: The study found that the length of isolation, frequency of swab, the time spent focusing on COVID-19, and level of knowledge were not related to the degree of depression and anxiety. However, mental attention and appropriate intervention are an important part of clinical care for those at risk.

Introduction

SARS-CoV-2 or Coronavirus (Coronavirus Disease 2019 [COVID-19]) is a single-stranded, encapsulated RNA virus that produces influenza-like symptoms. The coronavirus outbreak came to attention on December 31, 2019 when China reported to the World Health Organization (WHO) about a cluster of 40 pneumonia cases of unknown etiology in Wuhan City in Hubei Province, China [1], [2]. COVID-19 has spread in sizeable numbers around the world and is seen as a global health problem. This requires attention from public health institutions to increase awareness of this virus [3], [4], [5]. The WHO declared the COVID-19 emergency to be the sixth public health emergency and requires international attention on January 30, 2020. Based on the report on March 24, 2020, the total number of individuals diagnosed with COVID-19 was 372,757 cases with 16,231 deaths in 170 countries/regions. Of these cases, 123 cases were reported in Vietnam. COVID-19 was officially declared by the WHO as a pandemic on March 11, 2020. The treatments and vaccines for COVID-19 are currently being developed. Therefore, prevention and supportive care are highly recommended preventing transmission of COVID-19, especially in countries with weaker health-care systems [6]. Routine surveillance is highly emphasized to prevent transmission of COVID-19 to new locations [4]. The public health response to prevent the spread of COVID-19 has begun at different rates across countries that have been detected [7].

The COVID-19 pandemic causes panic and health problems for the public like previous experiences with Middle-East respiratory syndrome coronavirus (MERS-CoV) [8], [9], [10], [11]. In addition, myths and inaccurate information regarding this pandemic, travel restrictions, and quarantine of tourists can affect the psychological health of the public [8], [12]. This affects public health and quality of life. Health awareness is defined as the ability to seek, understand, and apply health-related information that can help the health-care system and individuals to obtain better quality of care,

lifestyle, disease management, decision-making on therapy, and health outcomes [13].

Improving health awareness is an approach strategy to prevent and control disease [9], [14]. Health professionals need to understand how much patients are aware of their health before providing interventions or education to improve quality of life [15], [16], [17]. People with health problems and need a visit to the clinic are a vulnerable population. The COVID-19 pandemic causes panic and anxiety disorders which further worsen their health outcomes, especially for outpatients with suspected COVID-19 symptoms. It is important to look for protective factors that provide benefits to people's mental health and quality of life. We suspect that people who are exposed to the COVID-19 virus then become patients under monitoring tend to experience depression and anxiety disorders.

Methods of Research

Research design

This study is an analytical observational study with a cross-sectional design to determine the relationship between length of isolation, frequency of swab, and swab test reporting on the degree of depression and anxiety disorders in patients with polymerase chain reaction (PCR) swab confirmed SARS-CoV-2. Depression was assessed by the Hamilton Depression Rating Scale (HDRS) questionnaire and anxiety was assessed by the Hamilton Anxiety Rating Scale (HARS) score. SARS-CoV-2 swab test results were defined as oropharyngeal swab test results using the real time PCR method, which were divided into positive and negative.

Research location and time

The research was conducted by online media/video calls on patients in the COVID-19 treatment room at Sanglah Hospital, Denpasar and the COVID-19 treatment hospital in Bali Province in the period June 2020–August 2020.

The scope of research

This research is within the scope of psychiatric medicine, especially neurotic disorders.

Determination of data source

The target population is all patients in the COVID-19 wards. The affordable population is all patients in isolation rooms at Sanglah Hospital and hospitals where COVID-19 treatment in Bali Province is hospitalized from June 2020 to August 2020. Inclusion criteria: All patients in isolation rooms at Sanglah Hospital and hospitals where COVID-19 treatment who were hospitalized from June 2020 to August 2020 and were willing to be the research sample. The exclusion criteria were patients in the COVID-19 isolation room who had experienced mental disorders (psychiatry) before the swab results were confirmed for SARS-CoV-2 and patients with impaired consciousness.

Sampling technique

The sampling method is purposive sampling, where the researcher determines the sampling with special characteristics that are in accordance with the research objectives so that it is expected to be able to answer research problems.

Data analysis

Descriptive analysis aims to describe the characteristics of the research subject and the overall research variables. In this study, the normality test of the analytical method data was carried out with the Kolmogorov–Smirnov test. If $p > 0.05$, then the data are normally distributed. In this study, the bivariate Kruskal–Wallis test was used to determine the relationship between the length of isolation, the frequency of undergoing swab, and the time of reporting with depression and anxiety. Spearman correlation test was used to determine the relationship between the level of knowledge with the degree of depression and anxiety. Data analysis was carried out using the Program Statistics for Social Sciences version 21 program. (SPSS Inc., USA). The significance level (α) of this study was set at a probability value (p) of < 0.05 with a 95% confidence interval.

Results

A total of 25 COVID-19 patients were included in this study. In this study, the patient's age ranged from 23 to 70 years, with a median value of 54 years. The sample is dominated by men (56%) with jobs in the health sector (52%). The highest proportion for sample swab was twice (32%), while for isolation was 14 days (48%). The maximum the time spent focusing on COVID-19 is 1–2 h (44%). The most of the samples were married (84%). The level of knowledge has a median of 5 which means good. The patients' HARS scores ranged from 0 to 28 while the HDRS scores ranged from 1 to 32 in this study. For more details, see Table 1.

From the bivariate analysis using the Kruskal–Wallis test, it was found that the length of isolation was not associated with the degree of depression and anxiety in patients with confirmed

Table 1: Sample Characteristics

Variables	N=25
Age (year), median (min-max)	54 (23–70)
Sex	
Men	14 (56%)
Women	11 (44%)
Occupation	
Tourism	1 (4%)
Lecturer	1 (4%)
Health worker	13 (52%)
Student	1 (4%)
Others	9 (36%)
Number of swabs	
Once	4 (16%)
Twice	9 (36%)
3 times	8 (32%)
>3 times	4 (16%)
Length of isolation	
<14 days	8 (32%)
14 days	12 (48%)
15–27 days	1 (4%)
28 days	2 (8%)
>28 days	2 (8%)
Reporting time	
<1 h	9 (36%)
1–2 h	11 (44%)
>3 h	5 (20%)
Marital status	
Married	21 (84%)
Single	4 (16%)
Knowledge level, median (min-max)	5 (baik) (2–6)
HARS, median (min-max)	6 (0–28)
HDRS	6 (1–32)

SARS-CoV-2 (p = 0.910 and p = 0.901, respectively). This is shown in Tables 2 and 3.

Table 2: The relationship between the length of isolation and the degree of depression in patients with PCR swab confirmed SARS-CoV-2

		n	HDRS	p value
Length	< 14 days	21	6 (1–32)	0.941
of isolation	< 14 days	4	7 (2–13)	

In line with this, the frequency of undergoing swab tests was also not associated with the degree of depression (p = 0.187) and anxiety (0.794). This is shown in Tables 4 and 5.

Table 3: The relationship between the length of isolation and the degree of anxiety in patients with PCR swab confirmed SARS-CoV-2

		n	HARS	p value
Length	< 14 days	21	6 (0–28)	0.766
of isolation	< 14 days	4	10 (2–20)	

In addition, the time of reporting was also not related to the degree of depression (p = 0.715) and anxiety (p = 0.54) in patients with confirmed SARS-CoV-2. This is shown in Tables 6 and 7.

Furthermore, Spearman correlation analysis showed that there was no relationship between the patient's level of knowledge and the degree of depression (r = −00.73 and p = 0.73) and anxiety (r = 0.001 and p = 0.995). This is shown in Tables 8 and 9.

Table 4: The relationship between the frequency of undergoing PCR swab tests and the degree of depression in patients with PCR swab confirmed SARS-CoV-2

		n	HDRS	p value
Number	1 time	4	7.5 (3–23)	0.187
of swab test	2 times	9	8 (3–23)	
Number	3 times	8	5.5 (1–11)	
	> 3 times	4	2.5 (1–9)	

Table 5: The relationship between the frequency of undergoing PCR swab tests and the degree of anxiety in patients with PCR swab confirmed SARS-CoV-2

		n	HARS	p value
Number	1 time	4	8 (4–28)	0.794
of swab test	2 times	9	6 (2–27)	
	3 times	8	10 (0–23)	
	> 3 times	4	4 (2–21)	

Discussion

This study found that the length of isolation, frequency of swab, the time spent focusing on COVID-19, and level of knowledge were not related to the degree of depression and anxiety. This is different from some existing studies.

Table 6: The relationship between reporting time and the degree of depression in patients with PCR swab confirmed SARS-CoV-2

		N	HDRS	p value
Reporting	< 1 h	9	7 (1–13)	0.715
time	1–2 h	11	6 (1–8)	
	> 2 h	5	5 (4–32)	

This may be because: [1] In our study, we did not select the degree of COVID-19 nor did we include adjustment disorder as one of the diagnoses in which many COVID-19 sufferers also experience adjustment disorders. [2] Personality traits and coping mechanisms may also influence the development of depression and anxiety. [3] Not all isolated patients are willing to be involved in the sample, so the number of samples is not large. Research by Kong *et al*. found that isolation was associated with anxiety and depression in COVID-19 patients. In this study, it was stated that social support was an important key to the development of symptoms of depression and anxiety.

Table 7: The relationship between the time of reporting and the degree of anxiety in patients with PCR swab confirmed SARS-CoV-2

		N	HARS	p value
Reporting	< 1 h	9	6 (2–20)	0.54
time	1–2 h	11	5 (0–27)	
	> 2 h	5	11.5 (2–28)	

Patients with low social support are associated with the severity of depression and anxiety symptoms. Several existing studies indicate that patients need more social support, which includes physical and psychological support provided by family members, friends, medical workers, and other relevant institutions in coping mechanisms for this problem [18].

Table 8: The correlation between the level of knowledge and the degree of depression in patients with confirmed PCR swab results

	Depression degree
Knowledge level	r = −00.73
	p = 0.73
	n = 25

Other studies have also revealed that social isolation and loneliness are associated with poor mental health outcomes. In the COVID-19 pandemic, many isolated patients feel useless and alone because of the lack of direct assistance from family and friends. In clinical practice, medical personnel in China try to stay in touch with patients and try various kinds of support to help isolated patients build trust. Meanwhile in Thailand, medical personnel try to teach physical relaxation techniques including singing and dancing to help overcome depression/anxiety that develops as a result of isolation. This doctor-patient relationship is expected to encourage patients to maintain a positive mindset [19].

Table 9: The correlation between the level of knowledge with the degree of anxiety in patients with confirmed PCR swab results

	Anxiety degree
Knowledge level	r = 0.001 p = 0.995 n = 25

In this study, it was found that the level of education has a very low correlation with the level of anxiety and depression. This is different from the results of research conducted by Wang. In a study conducted by Wang, it was found that the level of knowledge is an influential factor in the development of symptoms of anxiety and depression in patients with confirmed COVID-19 infection. In addition, infections that occur in family members are other factors that affect a person's vulnerability to anxiety and depression. The high level of concern for family members and the lack of family support (isolation) exacerbates the patient's pessimism about this disease [20].

In this study, it was found that the length of stay was not associated with the degree of anxiety and depression. The results of this study are different from research conducted by Shoar S. Shoar S in his research found that anxiety and depression were associated with a longer duration of hospitalization and non-adherence to the treatment. Early prevention of health problems plays an important role in clinical outcomes and a better quality of life.

One of the various factors that influence the degree of depression and anxiety cause differences in the results of this study with several existing studies is the presence of cytokine storm syndrome (CSS). "CSS" or "Cytokine release syndrome" were found to increase blood plasma levels of pro-inflammatory cytokines such as interleukin-6 (IL-6), tumor necrosis factor-a (TNF-a), IL-8, IL-10, and IL-2R. Inflammatory cytokines including IL-6, IL-10, IL-1B, IL-2, and the chemo attractant monocyte protein 1 were significantly increased in patients with COVID-19 [21].

Several existing studies indicate that 63–70.3% of patients with COVID-19 exhibit lymphopenia, and it is believed that the virus affects T lymphocytes, particularly CD4 and CD8 T-cells (Liu *et al*., 2020b). The lymphopenia observed in patients with severe COVID-19 was associated with a decrease in absolute T-cell counts, especially CD8 T-cells, and an increase in the levels of pro-inflammatory cytokines including TNF-a, IL-6, IL-8, and interferon (IFN-γ) which were seen significantly in these patients with lung disease and poor outcome. Research conducted by Liu *et al*. showed that patients with severe COVID-19 experienced increased concentrations of the cytokines IL-6, IL-10 and IL-2, and IFN. In addition, the previous studies examining SARS and MERS have also shown increased neutrophil counts, suggesting the possibility that the intensity of the inflammatory response in COVID-19 is similar and related to disease severity [21].

The relationship between the development of depression and anxiety disorders and activation of the inflammatory response has been seen in several animal and human models and has been the focus of attention in recent studies. High C-reactive protein (CRP) levels are found in about 25% of patients with depressive disorders. In addition to high CRP, the pro-inflammatory IL-6 has been associated with depressive symptoms such as depressed mood, increased appetite, sleep irregularity, low energy, and inability to focus and concentrate. An association was also found between elevated levels of inflammatory markers, particularly IL-6 and suicide in patients suffering from chronic inflammatory diseases, such as inflammatory bowel disease. Where these patients tend to show an increase in suicide rates. The association between IL-6 signaling, depression, and suicide is important in managing clinical symptoms of depression and suicide. Suicide could be an additional sign of high CRP levels seen in inflammatory activity that can be used for immunotherapy for patients with depression and suicidal behavior. It can also help evaluate the effectiveness of immunotherapy for depression and suicidal ideation and behavior [22]. Raison demonstrated in his research that infliximab, a TNF alpha, is effective in depressed and suicidal patients who had high CRP levels before the treatment [22], [23].

One of the first cytokines studied by many researchers, namely, the relationship between cytokines and depression, is IFN-a. It serves as a model for cytokine-induced depression. Approximately 30–50% of patients treated with IFN-a meet the criteria for depression. When the IFN-a cytokine is used for the treatment of infectious diseases such as hepatitis-C and cancer, a behavioral syndrome similar to depression develops in patients, responding to antidepressants. Symptoms associated with depressive disorders include anhedonia, feelings of guilt, suicidal thoughts, and anxiety, as well as cognitive symptoms such as loss of concentration, memory impairment, difficulty in finding words, and confusion. Additional neurovegetative symptoms of depression include fatigue, loss of

energy, abnormal sleep and appetite, and psychomotor retardation. Some patients may exhibit somatic complaints. These symptoms are seen in medically healthy people when the inflammatory system is being activated and in patients with cardiovascular disease, cancer, rheumatological diseases, gastrointestinal diseases, and post-viral infections. IFN-a is a potent inducer of pro-inflammatory cytokines, not only IL-6 but also IL-1β and TNF-a. This causes IFN-a to be associated with changes in serotonin metabolism and has an effect on corticotropin-releasing hormone function by causing an increase in the adrenocorticotropic hormones and cortisol [23], [24].

With the present development of research in the field of COVID-19, it is hoped that a broader explanation of the various factors that can contribute to depression is expected. Several other existing studies have demonstrated an association between depression/anxiety and cytokines such as IL-6, so additional studies are needed to examine the effects of other IL involved in the cytokine storm reaction, to gain further understanding of this process. Cytokine storms are a direct part of the infectious process and their correlation with serotonin and dopamine. Having understood this fact, it is important to maintain a multidisciplinary approach in dealing with the psychological effects of this pandemic. The treatment regimens that focus on reducing the effects of the virus from a cytokine point of view can be effective during the acute phase of the disease. Selective serotonin reuptake inhibitors treatment and other effective standard of care once the acute inflammatory process have subsided and the patient has recovered, especially those with symptoms of anxiety/depression are important.

Research weaknesses

1) This study is from one hospital center, the study sample is not representative of all patients with COVID-19 in Bali, so it can limit the generalizability of the results.
2) Researchers only collect data during hospitalization (admission). Hence, it is not possible to conduct further research on mental changes after being discharged from the hospital.
3) This cross-sectional study was unable to determine a causal relationship between mental health (anxiety or depression) and sociodemographic and clinical variables.

Conclusion

Hospitalized patients with COVID-19 experience symptoms of anxiety and depression. Although in this study, the length of isolation, frequency of swab, length of following the news, and level of knowledge were not significant factors related to the degree of anxiety/depression in patients with confirmed SARS-CoV-2, medical workers are still expected to pay more attention to the mental health of patients with COVID-19, and psychological assistance as well as timely intervention is needed for patients during an pandemic. Further studies need to determine other factors that play a role in influencing the degree of anxiety and depression in patients with confirmed COVID-19, such as cytokine storm syndrome needs to be investigated in the future. Further studies need to consider whether spiritual and local cultural influences can affect the mental resilience of COVID-19 patients, determine the severity of COVID, and immediately carry out mental health screening on all patients who are confirmed to be COVID-19.

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