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Association between Clinical, Radiological, and Psychiatric Symptoms in Patients with COVID-19

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Abstract: So far, COVID-19 is still considered a pandemic worldwide with various clinical, radiological, and psychiatric features. The aim of this study is to assess the correlation among these features. We performed an observational study on patients who have been diagnosed with COVID-19 to analyze their clinical symptoms using the simplified Radiographic Assessment of Lung Edema score and Mini International Neuropsychiatric Interview (MINI ICD-10 version). A total of 50 patients with COVID-19 were included in this study. Generally, COVID-19 infection may entail various symptoms, such as dyspnea, cough, fever, anosmia, diarrhea, vomiting, joint pain, and loss of consciousness. Panic disorder (38% of the cases) is significantly related to the clinical symptoms and severity of the disease ($r = 0.29$, $p = 0.032$ versus $r = 0.3$, $p = 0.027$). However, no significant association has been found with the severity of radiological and psychiatric problems. COVID-19 infection also entails various psychiatric problems, with panic disorder being the most common problem related to the symptoms and severity of the disease. Influential variables affecting these conditions may also result from acute illnesses due to COVID-19 symptoms, comorbidities, and environmental factors.

Keywords: clinical symptoms, radiological symptoms, psychiatric symptoms, COVID-19.

新冠肺炎患者的临床、放射学和精神病症状之间的关联

摘要: 迄今为止, 新冠肺炎仍被认为是具有各种临床、放射学和精神病学特征的全球大流行病。这项研究的目的是评估这些功能之间的相关性。我们对经诊断为新冠肺炎的患者进行了一项观察性研究, 以简化的肺水肿放射线照相评估和迷你国际神经精神病学访谈 (迷你心脏疾病-10 版本) 对他们的临床症状进行分析。本研究共纳入 50 例新冠肺炎患者。通常, 新冠肺炎感染可能引起各种症状, 例如呼吸困难, 咳嗽, 发烧, 失眠, 腹泻, 呕吐, 关节痛和意识丧失。恐慌症 (占病例的 38%) 与疾病的临床症状和严重程度密切相关 ($r = 0.29$, $p = 0.032$, $r = 0.3$, $p = 0.027$)。然而, 没有发现与放射和精神病问题的严重程度有显著关联。新冠肺炎感染还带来各种精神病问题, 其中恐慌症是与疾病的症状和严重程度有关的最常见

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问题。影响这些条件的影响变量也可能是由于新冠肺炎症状，合并症和环境因素引起的急性疾病所致。

关键词：临床症状，放射学症状，精神病症状，新冠肺炎。

1. Introduction

Coronavirus disease (COVID-19), an infection caused by a virus called SARS-CoV-2, is a worldwide pandemic that, as of January 2, 2021, has resulted in 1,796,292 deaths out of a total of 82,322,167 confirmed cases [1]. This pandemic has broad clinical manifestations, with the most critical one being acute respiratory distress syndrome [2]. Definitive diagnosis of COVID-19 relies on positive findings of real-time reverse transcription fluorescence-based polymerase chain reaction (RT-PCR) [3]. However, multiple factors, such as the limited and long turnover period of testing and the fact that the symptoms resemble those of common tropical diseases, such as dengue and typhoid fever, cause clinicians to issue delayed decisions regarding timely interventions to reduce the rate of mortality [4, 19]. Hence, rapid and accurate diagnostic tests are usually interpreted more cautiously in COVID-19 cases, especially chest radiological findings.

One of the clinical manifestations in patients who have tested positive for COVID-19 is lower respiratory tract illness along with fever, dry cough, and dyspnea. However, radiological changes in the lungs of individuals with COVID-19-related pneumonia have not yet been fully characterized [5]. Although several studies have pointed out that computed tomography (CT) is a sensitive approach, it cannot always be performed because of the associated radiation risk [6]. The Radiographic Assessment of Lung Edema (RALE) score, which has been proposed by Warren et al., assesses lung involvement and has been used in several studies to define the severity of the radiological findings of COVID-19. A higher RALE score is associated with worse outcomes and is considered a predictor for mortality for patients with COVID-19 [7].

It should also be noted that the mental health problems associated with COVID-19 infection have broad manifestations. One such manifestation that should not be underestimated is mental illnesses, such as delirium [8]. A study in the Netherlands showed that, out of a total of 47 patients, 38% had delirium as a result of severe COVID-19 infection [8-10]. Several research findings have also revealed that patients with COVID-19 exhibit symptoms of anxiety, including posttraumatic stress disorder, depression, and insomnia. Moreover, 22.5% of patients with COVID-19 have claimed to have neuropsychiatric symptoms [11]. In Indonesia, however, no studies have been performed to

assess the correlation among all of these factors. Therefore, the aim of this study is to evaluate the association between the clinical, radiological, and psychiatric symptoms in patients with COVID-19.

2. Methods

2.1. Data Collection

We performed an observational study with a prospective cross-sectional design on 50 patients aged 18–80 who have been diagnosed with COVID-19 using RT-PCR and hospitalized at Rumah Sakit Khusus Infeksi Universitas Airlangga Hospital, Surabaya, Indonesia. We included inpatients with all types of disease severity (mild, moderate, and severe), males and females, with and without comorbidity. We excluded patients who have been intubated and those with dementia from the study. We first recorded the symptoms of the patients during the first time they were hospitalized. We also took note of their vital signs, laboratory test results, and chest X-ray results. To assess their psychiatric symptoms, we used the Mini International Neuropsychiatric Interview (MINI ICD-10 version). While using level 3 personal protective equipment, we used a written form in the isolation room to ask the patients directly about their psychiatric problems. We also performed a psychiatric assessment two to five days after the start of hospitalization.

All the study sample underwent chest X-ray on the first day of admission to the emergency room. We also assessed the severity score of COVID-19-related pneumonia using the simplified RALE score. Generally, the RALE score assesses lung involvement on a scale from 0 to 4 as follows: 0, no lung involvement; 1, less than 25% lung involvement; 2, 25%–50% lung involvement; 3, 50%–75% lung involvement; 4, more than 75% lung involvement. The results are then divided into four categories: normal (score: 0), mild (score: 1-2), moderate (score: 3–5), and severe (score: 6–8) [7].

This study was approved by the ethical committee of the Universitas Airlangga Hospital, Surabaya, Indonesia (letter no. 154/KEP/2020), and is in line with the Declaration of Helsinki (Ethical Principles for Medical Research Involving Human Subjects) version 2013.

2.2. Statistical Analysis

We analyzed the data using IBM SPSS Statistics

version 24.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics included categorical variables reported as a number (percentage) and continuous variables reported as a mean (standard deviation). For missing data, we used listwise deletion or univariable and multivariable analysis. Categorical variables are shown as a number (%), and continuous variables are shown as a mean (standard deviation) or median (range) based on data distribution. We also analyzed the correlations between clinical, radiological, and psychiatric problems using bivariate correlation statistics (Spearman and Kendall tau). We then performed a data analysis using tables and graphics to assess the incidence of psychiatric symptoms from predominant factors among patients with COVID-19, and we used the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement checklist for our report.

3. Results

A total of 50 patients fulfilled the inclusion criteria for this study (26 females, 24 males; mean age: 37.2 ± 12.43 years). Most of the participants were living in the area of Surabaya (88%), with approximately 56% of them holding a bachelor's degree. We categorized disease severity into five degrees: asymptomatic, mild, moderate, severe, and critical [12]. We also considered COVID-19 infection as a factor that affects the mental health of inpatients. We then evaluated the relationship between disease severity and radiological imaging and the mental health of COVID-19-positive patients. Table 1 shows the demographic characteristics of the

research subjects (see Supplementary Material).

3.1. Psychosocial Characteristics of COVID-19 Patients

We used psychosocial characteristics according to the guidelines for the Mini-International Neuropsychiatry Interview Mental Disorders Assessment Instrument. We have 30% (n=15) of patients who experienced depressive episodes, 24% (n=12) who experienced recurrent depressive episodes, 8% who were at risk of suicide (n=4), 38% who had panic disorder (n=19), 16% who had obsessive-compulsive disorder (n=10), and 32% who had a general anxiety disorder (n=16).

3.2. Factors Associated with Mental Illness among Patients with COVID-19

Statistical analysis shows that, in the study population, female patients tend to experience episodes of generalized anxiety disorder (10/16) and panic attacks (12/19).

Patients aged <60 years old are more prone to suffer from mental disturbances. Well educated graduate patients experience episodes of depression (10/15), panic disorder (12/19), and generalized anxiety disorder (13/16).

Patients who are still working have an incidence of major depression (12/15), panic attacks (13/19), and generalized anxiety disorder (14/16). In occupational subgroup analysis, healthcare workers experience many episodes of depression (9/15), panic (14/19), and anxiety (14/16) (Table 2).

Table 2 Factors predominant to psychological aspect among COVID-19 patients

Predominant Factor	Episode Depression		Panic Disorder		General Anxiety Disorder	
	n	%	n	%	n	%
Sex						
- Male	5/15	33	7/19	37	6/16	37.5
- Female	10/15	67	12/19	63	10/16	62.5
Working during pandemic						
Still working	12/15	80	13/19	68	14/16	87.5
Not working	3/15	20	6/19	32	2/16	12.5
Working Status						
Healthcare Worker	9/15	60	14/19	73	11/16	68
Non-Healthcare Worker	6/15	40	5/19	27	5/16	32
Symptoms						
Dyspnea	3/15	20	6/19	31.5	5/16	31
Fever	4/15	26	8/19	42	7/16	43.75
Cough	9/15	60	12/19	63	10/16	62.5
Education						
Well educated	10/15	67	12/19	63	13/16	81.25
Low educated	5/15	33	7/19	37	3/16	18.75
Comorbid						
Diabetes Mellitus	1/15	6.67	2/19	10.5	2/16	12.5
Hypertension	0	0	2/19	10.5	1/16	6.25

COVID-19 also seems to affect the mental health of patients. Patients with the symptoms of a cough seem to have more complaints of mental illness from

depression (9/15), panic (12/19), and anxiety (5/16), as do patients with comorbidity merely to have a mental illness episode (Fig. 1).

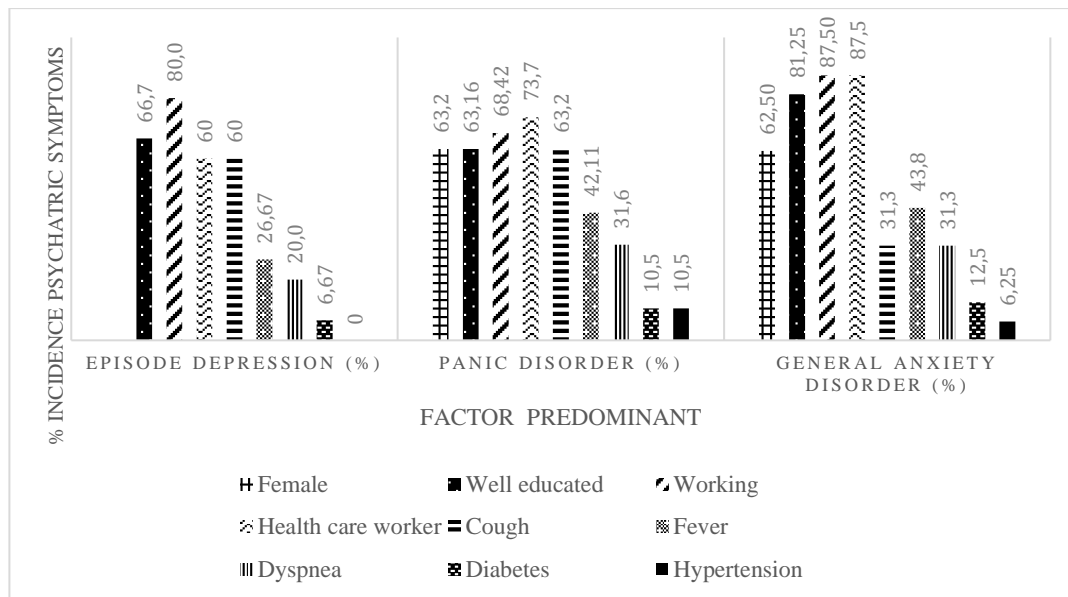


Fig. 1 Incidence psychiatric symptoms among characteristic of patients

Mental disorders that accompany COVID-19 patients are associated with several acute medical conditions. The more symptoms COVID-19 patients experience, the more prone they are to significant panic disorders ($p=0.032$). Although, in this study, we did not find a significant association between oxygen

saturation, oxygen supplementation, and inflammatory markers, patients with moderate-to-severe chest x-rays had panic disorder (10/50). Besides, the more serious the patient's illness, the greater the risk of panic disorder is ($p=0.027$) (Table 3).

Table 3 Correlation psychiatric symptoms and clinical symptom, RALE score, and severity of COVID-19

Psychiatric symptoms	Clinical symptoms		RALE score		Severity COVID-19	
	r	pValue	r	pValue	r	p-Value
Episode Depression	0.06	0.64	-0.15	0.24	-0.06	0.65
Recurrence depression	0.01	0.94	-0.86	0.51	-0.05	0.74
Suicide risk	0.01	0.96	-0.18	0.15	-0.21	0.11
Panic disorder	0.29	0.032*	0.2	0.12	0.3	0.027*
Obsessive compulsive	0.015	0.91	0.06	0.65	0.021	0.87
General anxiety disorder	0.188	0.16	0.06	0.67	0.13	0.33

We reviewed the socio-demographic side; depressive episodes occur mostly in female patients with an undergraduate educational background, living in the center of a city, still working, and being hospitalized.

4. Discussion

Various studies have proclaimed the relationship between mental illness and COVID-19. Our study correlates the degree of clinical complaints according to WHO criteria and the degree of radiological examination severity. This study indicates that COVID-19 patients have an incidence of depressive episodes of around 30% (15 people) and panic disorder 38% (19 people).

The incidence of mental disorders such as depression and panic disorder in patients diagnosed with COVID-19 is relatively high compared to the non-COVID-19 population. However, the explanation for the mechanism of mental illnesses in COVID-19 patients is still unclear [11]. Therefore, it is crucial to

understand the factors and characteristics of COVID-19 patients who experience mental illness.

The disease COVID-19, with its rapid transmission, has caused fear and anxiety. COVID-19 patients also tend to experience discrimination, so that these patients tend to suffer from depression, anxiety, trauma, suicidal thoughts, and panic attacks [13]. COVID-19 has been described as having a relationship with mental illness. This condition occurs during the acute stage of and after the disease for people exposed to the virus either directly and indirectly [14].

In agreement with the findings of Mazza et al. study, female patients experienced episodes of depression ($\chi^2 = 15.13$, $p < 0.001$) and anxiety ($\chi^2 = 42.15$, $p = < 0.001$). In terms of various risk factors related to psychopathology, Mazza et al. have found the females and patients with positive previous psychiatric diagnoses [15]. Nevertheless, as seen in our study, patients aged 40-60 years old have higher depression and sleep disturbances levels, similar to

previous studies suggesting a worse psychological impact of COVID-19 pandemic in younger people [13].

Episodes of mental illness among healthcare workers are often encountered both due to workload and social stigma. The findings of the Saraswathi et al. study found that healthcare workers, such as undergraduate medical students and resident interns, have symptoms of depression, anxiety, and stress during COVID-19 [16, 17].

Our study shows that patients with a higher-level educational background diagnosed with COVID-19, experience quite large mental illness episodes of depression, panic disorder, and generalized anxiety disorder. According to the literature during the COVID-19 pandemic, the well-educated population has a higher risk of anxiety and depression. Based on recent research, there is a significant relationship between education level and depression level. This correlation is due to a high level of self-awareness. Additionally, environmental conditions such as positive diagnoses in family members or friends add to concerns. Patients with low-health status are vulnerable to contracting new diseases [13].

The manifestation of SARS-CoV2 infection on mental illnesses can be caused by an immune response and psychological stress to social isolation. The immune response to coronaviruses induces various cytokines, affecting the severity of the patient's complaints. Various cytokines, such as IL-4 and IL-10, were secreted by T helper-II cells. Those cytokines act as a marker of the severity of inflammation in COVID-19 cases. Cytokine intrusion, especially IL-1 β , IL-6, IL-10, IFN- γ , TNF- α , and Transforming Growth Factor- β (TGF- β), is thought to influence mental illnesses. Interaction between immune systems and psychopathological mechanisms underpinning psychiatric disorders occurs through various pathways. These mechanisms can be related to neuroinflammation, blood-brain-barrier disturbance, or peripheral immune cell perturbation into the central nervous system. It also depends on interference neurotransmitter, hypothalamic-pituitary-adrenal (HPA) dysfunction axis, microglia, and indoleamine 2,3-dioxygenase (IDO) [15].

Based on our research, although many factors affect mental health, especially in COVID-19 patients; early prevention, prompt diagnosis, and therapy are essential. Some research evidence supports the fact that anxiety and depression are associated with length of treatment and therapy adherence. As long as the COVID-19 pandemic continues, a strategy is needed to form psychological support for hospitalized patients with COVID-19 [18].

This study is a single-centered investigation conducted cross-sectionally in which we did not evaluate mental disorders before COVID-19 and the effects of family support. The data collection of this research was carried out on one occasion, not

representing mental conditions that might change with time. Therefore, this study was unable to provide a causal relationship between mental health and sociodemographic variables. The sample study is limited in the number of patients, so we need to enlarge the focus group.

5. Conclusion

COVID-19 patients experience episodes of mental disorders with various features. Panic disorder is the biggest problem that occurs in COVID-19 patients. Influential variables can come from acute conditions due to SARS-CoV2 infection, complaints, comorbidities, and environmental factors. The main thing to acknowledge is that patients need psychological intervention during the COVID-19 pandemic.

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Supplementary Material

Table 1. Characteristic of samples study can be downloaded at DOI: [10.6084/m9.figshare.14216765](https://doi.org/10.6084/m9.figshare.14216765)

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