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Psychiatric aspects of healthcare workers during COVID-19 pandemic in Surabaya, Indonesia: prevalence of anxiety, resilience, burnout, and their correlations to stress markers

Margarita M. Maramis[1*], Soetjipto[1], Yunias Setiawati[1], Agustina Konginan[1], Nalini Muhdi[1], Winson Chuanardi[2,3], Yusuf Ibrahim[3], Rosalia A. Malika[3], Sandra C.N. Tang[3], Kadek D. Chandita[3], Natasha A. Tayibnapis[4], Abdul J.A. Hayyan[5], Adde M.P. Chafid[6], Elizeus Hanindito[6], Nancy M. Rehatta[6], Moses G.R. Pandin[7], Tarmono[7], Damayanti Tinduh[5,7], Cita R.S. Prakoeswa[8,9], Fitriah Munawaroh[10]

[1]Department of Psychiatry, Faculty of Medicine, Universitas Airlangga/Dr. Soetomo General Academic Hospital, Surabaya, Indonesia;
[2]Institute of Psychiatry, Psychology, and Neuroscience, King's College London, London, United Kingdom;
[3]Faculty of Medicine, Universitas Airlangga/Dr. Soetomo General Academic Hospital, Surabaya, Indonesia;
[4]Department of Psychiatry, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia;
[5]Department of Physical Medicine and Rehabilitation, Faculty of Medicine, Universitas Airlangga/Dr. Soetomo General Academic Hospital, Surabaya, Indonesia;
[6]Department of Anesthesiology and Reanimation, Faculty of Medicine, Universitas Airlangga/Dr. Soetomo General Academic Hospital, Surabaya, Indonesia;
[7]Research and Development Unit, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia;
[8]Professional Education, Research and HRD, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia;
[9]Department of Dermatology Venereology, Faculty of Medicine, Universitas Airlangga/Dr. Soetomo General Academic Hospital, Surabaya, Indonesia;
[10]Department of Clinical Pathology, Faculty of Medicine, Universitas Airlangga/Dr. Soetomo General Academic Hospital, Surabaya, Indonesia.

*Corresponding author:
Margarita M. Maramis;
Department of Psychiatry, Faculty of Medicine, Universitas Airlangga/Dr. Soetomo General Academic Hospital, Surabaya, Indonesia;
margarit@fk.unair.ac.id

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ABSTRACT

Introduction: The coronavirus disease (COVID-19) pandemic severely affected healthcare services, including causing negative impacts on healthcare workers' mental health. An observational study was conducted at Dr. Soetomo General Hospital aimed to measure the prevalence of anxiety, resilience, burnout and their correlations to stress biomarkers amongst healthcare workers in Surabaya, Indonesia, during the COVID-19 pandemic.

Methods: Participants were residents who managed COVID-19 patients, chosen using random sampling. All participants had a 1-week shift working with COVID-19 patients in an isolation ward. The study used online questionnaires and laboratory data at the shift's beginning and end. Along with collecting sociodemographic characteristics, State-Trait Anxiety Inventory (STAI), Brief Resiliency Scale (BRS), and Maslach Burnout Inventory (MBI) scales were administered online. At the same time, laboratory markers such as Neutrophil to lymphocyte ratio (NLR), Interleukin-6 (IL-6), cortisol, and CD4 values were studied.

Results: 61 participants were included in the study. At the beginning of the shift, 59% of participants had moderate to severe anxiety, and 83.62% had normal to high resilience. The early proportion of the participants having burnout from combined MBI measures was 88.52%. MBI-EE median scores were lower in the married group (6.50 vs. 9.50, p-value=0.030). NLR value was significantly related to STAI-S and BRS (p-value=0.007 and 0.049, respectively).

Conclusions: Most healthcare workers had anxiety and burnout, with normal levels of resilience. Our study found that NLR might be useful as a marker for anxiety and resilience.

Keywords: COVID-19, health personnel, anxiety, biomarkers, burnout.
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INTRODUCTION

Cases of novel coronavirus (2019-nCoV), later known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), causing the disease called coronavirus disease (COVID-19) pneumonia began in Wuhan, China, in December 2019.[1] World Health Organization (WHO) officially declared COVID-19 outbreak as a pandemic on March 11th, 2020.[2] Indonesia reported the first COVID-19 case on March 2nd, 2020, and the number of cases kept rising until then. East Java ranked second highest in performed cases, just under the Capital District of Jakarta.[3] The rise of COVID-19 cases resulted in hospital overload in Surabaya, including Dr. Soetomo General Hospital as the biggest referral and teaching hospital in eastern Indonesia.[4]

Healthcare professionals directly involved in the diagnosis, treatment, and care of patients with COVID-19 are at risk of experiencing psychological distress and other mental health symptoms due to this urgent circumstance. The rising number of confirmed and suspected cases, the voluminous workload, the exhaustion of personal protective equipment, the extensive media attention, the scarcity of specialized medications, and the perception of inadequate

assistance may all add to the mental strain of these healthcare professionals. Healthcare professionals' negative psychological responses to the SARS pandemic in 2003 have been documented in earlier research.[5]

According to studies, these healthcare professionals experienced high stress, anxiety, and depressive symptoms, which may have long-term psychological repercussions. They also felt uncertain and stigmatized, reported reluctance to work or resignation thoughts, and feared spreading the disease to their family, friends, and co-workers. Similar worries regarding the emotional well-being, psychological adjustment, and recovery of healthcare professionals caring for and treating COVID-19 patients are increasingly emerging.[5,6]

The anxiety of contracting and passing the infection to the families, the pain of losing patients and colleagues, also the pressure to make difficult triage decisions affected healthcare workers' mental well-being. Healthcare systems globally worked at more than their maximum capacity for many months, adding physical and psychological exhaustion.[7,8] A study reported that 75% of healthcare workers were distressed, one-third had insomnia, and half were depressed.[5] This study aimed to assess the mental health aspects using psychological markers, contributing factors based on the demographic data of the frontline healthcare workers facing the COVID-19 pandemic at Dr. Soetomo General Hospital Surabaya, and their correlations to the biological markers.

METHODS

Study Design

The study was an observational study done in May-June 2020, which could be considered the early stages of the first wave of the COVID-19 pandemic in Indonesia. Participants were residents in the anesthesiology and internal medicine department at Dr. Soetomo General Hospital Surabaya, who managed COVID-19 patients in isolation wards. The exclusion criteria were residents that did not fill in the questionnaires completely, had comorbidities (diabetes, hypertension, heart disease or autoimmune disorders), residents that were infected with COVID-19, currently or previously diagnosed with psychosis, and the ones that refused to participate.

Data Collection

After their 1-week shifts, the residents were instructed to self-isolate in facilities provided by the hospital. Online questionnaires were filled out by each participant at the beginning and after the end of the shift. Demographic factors data collected were gender, age, marital status, residency department, and enrollment year. State-Trait Anxiety Inventory (STAI), Brief Resilience Scale (BRS), and Maslach Burnout Inventory (MBI) were used as the examination tools for the psychological markers. State anxiety (STAI-S) is the present subjective feeling of fear and tension, also the occurrence of autonomic nervous activation responding to dangerous or threatening conditions. In this study, we focused on using STAI-S, which describes how the individual feels under the current situation. STAI-S contains 20 statements, with the score interpretation ranging from 20-80. A score between 20-37 means having low or no anxiety, 38-44 indicates medium anxiety and 45-80 suggests high anxiety.[9] The brief resiliency scale (BRS) was published by Smith et al. in 2008 and has been proven valid and reliable. Resilience is defined as the capability to return to a previous functional level after dealing with stress. BRS consists of six questions, with three positive statements and three negative statements. Participants choose one of the five responses to the statements, ranging from "strongly disagree" to "strongly agree". There are three categories of results: low resilience (score 1.00-2.99), normal resilience (3.00-4.30), and high resilience (4.31-5.00).[10]

Maslach Burnout Inventory (MBI) is divided into dimensions of burnout such as emotional exhaustion (EE), depersonalization (DP), and personal accomplishment (PA).[11] The 22-item questionnaire evaluates these domains of burnout, containing 9 items for emotional exhaustion (MBI-EE), 5 items for depersonalization (MBI-DP), and 8 items for personal accomplishment (MBI-PA). Each item is rated using a Likert scale, measuring the experience of the participants, ranging from never (0) to every day (6). The MBI-EE score can be interpreted as severe burnout for a total score ≥30, moderate burnout for 18-28, and low burnout for ≤17. The MBI-DP score comprises severe burnout for a total score ≥ 12, moderate burnout for 6-11, and low burnout for ≤5. The MBI-PA is considered severe burnout for a total score of ≤ 33, moderate burnout of 34-39, and low burnout for ≥40.[12]

In regard to biological markers, participants' saliva samples were collected in the morning between 7 to 9 a.m. Using the passive drooling method, unstimulated saliva samples were collected from each participant. The participants were asked to tilt their heads forward, allowing the saliva to pool on the floor of the mouth, then it was collected into the sterile collecting tube (Salimetrics, Carlsbad, CA, USA). The participants should not eat or drink anything at least 1 hour prior to the saliva collection. Also, the participants were instructed to brush their teeth and wash their oral cavities with sterilized water. Samples were kept cold using a cooler box and transported to the laboratory. In the laboratory, samples were centrifuged at 1700xg at 4°C for 10 minutes within one hour after collection, Samples were aliquoted and stored at -80°C for further analysis of cortisol level.

Determination of salivary cortisol was performed using a cortisol enzyme immunoassay kit (Salimetrics, State College, PA, USA). Samples (25 µL) were treated according to the manufacturer's instructions. A microplate reader measured the optical density of the samples and standards at a wavelength of 450 nm (Human Diagnostics, Germany).

Neutrophil to lymphocyte ratio (NLR), CD4 and Interleukin-6 (IL-6) were measured using a blood sample. 5 ml blood samples were collected from the median cubital vein using a standardized venipuncture technique in a serum separator tube (SST) for Interleukin 6 and an EDTA tube for CD4 analysis. Blood samples were centrifuged at 2500 rpm for 15 minutes. The serum was then aliquoted and stored at -80°C. Quantification of Interleukin-6 used commercial ELISA kit (Elabscience® Biotechnology Inc.) according to the manufacturer's

instructions. A microplate reader measured the samples' optical density and standards (Human Diagnostics, Germany). The samples' concentration was calculated according to the relevant standard curve. CD4 was analyzed by flow cytometry using the BD FACS Calibur Flowcytometry system (BD Bioscience, USA) according to the manufacturer's instructions.

Data Analysis

In the matter of statistical analysis, it was performed with SPSS software. Univariate analysis was performed to evaluate the proportion and median of each variable. Bivariate analysis with Mann-Whitney U Test was carried out to assess the differences among group and Spearman Test. We also use Kruskal-Wallis and Wilcoxon tests. The data were considered to have a significant correlation if the value level of significance was <0.05.

RESULTS

Characteristics of the patients

The sociodemographic data of the respondents can be seen in Table 1. Most respondents were male (80.33%) and recently enrolled in the residency program (47.54% registered in 2019). There were more anesthesiology residents compared to their colleagues from internal medicine (57.38% vs 42.62%). Most of them were already married (65.57%).

We tried to compare the psychological and biological markers of the respondents at the beginning of their shifts concerning different demographic factors. From the MBI-EE results, there was a significant difference between married and not married groups, with a lower score means

Table 1. Demographic data

Variable	n	%
Age (Range)	24-36	
Gender		
Male	49	80.33
Female	12	19.67
Department		
Anesthesiology	35	57.38
Internal Medicine	26	42.62
Enrollment Year		
2016 or before	5	8.20
2017	11	18.03
2018	16	26.23
2019	29	47.54
Marital Status		
Not Married	21	34.43
Married	40	65.57

Table 2. Markers and demographic factor based on gender

	Total Median (IQR)	Male Median (IQR)	Female Median (IQR)	p-value
Psychological markers				
STAI-S	40.00 (32.50-46.00)	40.00 (33.00-44.50)	37.00 (30.50-50.00)	0.683
BRS	3.67 (3.17-4.00)	3.67 (3.33-4.00)	3.42 (3.04-4.00)	0.505
MBI-EE	7.00 (3.50-14.00)	7.00 (4.00-13.50)	11.50 (3.00-16.25)	0.637
MBI-DP	7.00 (4.00-12.50)	7.00 (4.00-13.00)	6.00 (2.00-7.75)	0.111
MBI-PA	33.00 (27.00-39.00)	33.00 (27.00-37.50)	33.50 (23.75-39.75)	0.892
Biological markers				
NLR	1.91 (1.64-2.73)	1.90 (1.66-2.73)	1.95 (1.59-2.69)	0.921
Cortisol	0.47 (0.30-0.66)	0.48 (0.30-0.66)	0.41 (0.28-0.69)	0.885
IL-6	233.77 (8.06-727.53)	177.21 (7.86-727.53)	270.41 (10.58-782.81)	0.899
CD4	614 (508-788)	609 (508-785)	738.50 (447.25-862.75)	0.644

Table 3. Markers and demographic factor based on department

	Department Median (IQR)		p-value
	Anesthesiology	Internal Medicine	
Psychological markers			
STAI-S	40.00 (36.00-44.00)	38.50 (31.75-47.75)	0.635
BRS	3.67 (3.00-4.00)	3.42 (3.17-4.17)	0.947
MBI-EE	7.00 (4.00-13.00)	8.00 (3.00-15.00)	0.930
MBI-DP	7.00 (5.00-12.00)	7.00 (2.00-13.00)	0.496
MBI-PA	33.00 (27.00-39.00)	34.50 (28.75-40.00)	0.277
Biological markers			
NLR	2.00 (1.66-2.77)	1.83 (1.58-2.58)	0.393
Cortisol	0.48 (0.32-0.71)	0.37 (0.26-0.64)	0.240
IL-6	80.18 (7.40-679.21)	379.28 (17.58-752.23)	0.287
CD4	609 (511-774)	633 (506.75-870.25)	0.600

Table 4. Markers and demographic factor based on enrolment year

	2016 or before Median (IQR)	2017 Median (IQR)	2018 Median (IQR)	2019 Median (IQR)	p-value
Psychological markers					
STAI-S	49.00 (39.00-58.00)	40.00 (32.00-49.00)	37.00 (25.50-41.00)	40.00 (33.00-48.50)	0.070
BRS	3.50 (3.00-3.92)	3.50 (3.00-3.67)	4.00 (3.71-4.13)	3.33 (3.09-4.00)	0.057
MBI-EE	16.00 (4.00-29.50)	7.00 (2.00-8.00)	6.00 (3.25-9.75)	8.00 (3.00-16.00)	0.255
MBI-DP	13.00 (8.50-22.50)	6.00 (0.00-8.00)	6.00 (4.25-7.00)	8.00 (3.50-14.00)	0.038*
MBI-PA	31.00 (27.00-37.00)	29.00 (23.00-40.00)	34.50 (23.25-39.75)	33.00 (28.50-36.00)	0.750
Biological markers					
NLR	1.94 (1.64-2.43)	1.89 (1.65-2.12)	2.11 (1.60-2.96)	1.91 (1.62-2.71)	0.910
Cortisol	0.58 (0.41-0.86)	0.51 (0.29-0.71)	0.37 (0.26-0.55)	0.48 (0.30-0.70)	0.253
IL-6	679.21 (128.09-1315.47)	6.86 (2.11-46.55)	397.55 (13.10-1223.22)	315.80 (37.05-687.50)	0.024*
CD4	590 (486.50-830.50)	594 (460-708)	648 (521.50-804.25)	65 (513.50-819.50)	0.516

*$p < 0.05$

Table 5. Markers and demographic factor based on marital status

	Not Married Median (IQR)	Married Median (IQR)	p-value
Psychological markers			
STAI-S	40.00 (36.50-43.00)	39.50 (31.25-48.50)	0.710
BRS	3.67 (3.25-4.00)	3.59 (3.04-4.00)	0.994
MBI-EE	9.00 (6.00-19.50)	6.50 (3.00-11.00)	0.030*
MBI-DP	8.00 (5.50-13.50)	7.00 (3.25-12.75)	0.235
MBI-PA	32.00 (27.50-36.50)	34.00 (27.00-39.75)	0.489
Biological markers			
NLR	2.00 (1.74-2.82)	1.86 (1.58-2.48)	0.139
Cortisol	0.51 (0.31-0.67)	0.43 (0.28-0.66)	0.412
IL-6	208.01 (7.61-634.28)	239.56 (8.64-793.06)	0.665
CD4	591 (465.50-771.50)	620.5 (520-806.25)	0.324

*$p < 0.05$

in the married group. There were no significant differences in psychological markers between different genders or departments. The biological title with significant differences between demographic groups was IL-6, especially between groups of varying enrollment years, although the trend was vague. Other biological markers were not influenced by demographic factors based on gender (Table 2), department (Table 3), enrolment year (Table 4), and marital status (Table 5).

Table 6 showed that the majority had low or no state anxiety (41.09% and 52.45%, respectively), although the total proportion of moderate to severe anxiety was 59% at the beginning of the shift. More than half had normal resilience (83.62%). At the beginning of the change, from the MBI-EE scores, a larger number of the respondents were categorized as having low burnout (85.24%). The MBI-DP results found that the majority had

Table 6. Classification of the psychological status of the respondents

	Beginning of Shift n (%)	Beginning of Self-Isolation n (%)
STAI-S		
Low or no Anxiety	25 (41.09)	32 (52.45)
Medium Anxiety	20 (32.78)	12 (19.67)
High Anxiety	16 (27.13)	17 (27.88)
BRS		
Low resilience	5 (8.19)	6 (9.83)
Normal resilience	51 (83.62)	46 (75.40)
High resilience	5 (8.19)	9 (14.77)
MBI-EE		
Low burnout	52 (85.24)	51 (83.60)
Moderate burnout	7 (11.47)	7 (11.47)
Severe burnout	2 (3.29)	3 (4.93)
MBI-DP		
Low burnout	20 (32.78)	24 (39.34)
Moderate burnout	24 (39.34)	19 (31.11)
Severe burnout	17 (27.88)	18 (29.55)
MBI-PA		
Low burnout	13 (21.31)	11 (18.03)
Moderate burnout	16 (26.22)	16 (26.22)
Severe burnout	32 (52.45)	34 (55.75)

Table 7. Markers at the beginning of shift vs. the beginning of self-isolation

	The Beginning of Shift Median (IQR)	The Beginning of Self Isolation Median (IQR)	p-value
Psychological markers			
STAI-S	40.00 (32.50-46.00)	35.00 (30.00-46.00)	0.289
BRS	3.67 (3.17-4.00)	3.67 (3.25-4.09)	0.375
MBI-EE	7.00 (3.50-14.00)	8.00 (4.50-12.50)	0.803
MBI-DP	7.00 (4.00-12.50)	7.00 (2.00-12.50)	0.546
MBI-PA	33.00 (27.00-39.00)	32.00 (22.50-39.00)	0.380
Biological markers			
NLR	1.91 (1.64-2.73)	1.86 (1.40-2.40)	0.103
Cortisol	0.47 (0.30-0.66)	0.38 (0.27-0.55)	0.007*
IL-6	233.77 (8.06-727.53)	4.65 (2.16-9.60)	<0.001*
CD4	614 (508-788)	606 (505-782.50)	0.873

*$p < 0.05$

Table 8. Correlations between biological markers and psychological markers

r	STAI-S	BRS	MBI-EE	MBI-DP	MBI-PA	NLR	Cortisol	IL-6	CD4
STAI-S		-0.586**	0.459**	0.565**	-0.355**	0.343**	0.047	0.026	-0.251
BRS			-0.332**	-0.323*	0.335**	-0.253*	-0.155	-0.078	0.192
MBI-EE				0.777**	-0.324*	0.086	0.158	-0.059	-0.005
MBI-DP					-0.305*	0.235	0.216	0.040	-0.026
MBI-PA						-0.046	0.023	0.116	0.006
NLR							-0.044	0.150	-0.304*
Cortisol								0.101	0.071
IL-6									0.030

*$p < 0.05$
**$p < 0.01$

moderate burnout (39.34%). The MBI-PA results revealed that over half (52.45%) had severe burnout. The data showed that a greater number of the participants had severe burnout in terms of personal accomplishment.

From Table 7, the median score of STAI-S pointed to medium anxiety at the beginning of the shift, and the score shifted to low or no pressure after the change, although this was not statistically significant. The BRS median score for both phases resulted in normal resilience. All MBI median scores did not have substantial differences between the beginning of the shift and self-isolation, pointing to low burnout for emotional exhaustion, moderate burnout for depersonalization, and severe burnout for personal accomplishment. Interestingly, we found a significant decrease of biomarkers cortisol and IL-6 median levels from respondents at the beginning of self-isolation compared to the beginning of the shift.

Table 8 shows the correlations between biological and psychological markers measured during the beginning of the shift. NLR values were positively correlated with the STAI-S score (moderate relationship) while inversely correlated with the BRS score (weak connection). All the psychological markers were moderate to strongly related to each other. BRS was positively correlated with MBI-PA, yet both were inversely correlated with other psychological traits. Among the biological markers, NLR was inversely correlated to CD4.

DISCUSSION

This study tried to investigate the mental health aspects of residents facing the stress of caring for COVID-19 patients during the pandemic. From our findings, at least half of the respondents suffered from medium to high anxiety, based on the STAI-S scores. Giusti et al. found in their study that only 29% of Italian health professionals had scores below the cut-off for clinical anxiety.[6] A study in Israel found that 34.8% of healthcare workers from a COVID-19 treating hospital had severe anxiety, scoring ≥45 for STAI-S, higher compared to our study.[13] With the additional weight of the COVID-19 pandemic, which brought in more patients to care for, the pressure faced by healthcare workers within this period of time increased. This is worsened by inadequate testing, insufficient personal protective equipment (PPE) and medical supplies, and the extended rotation period.[14,15]

There seemed to be more respondents having low or no state anxiety after their shifts (52.45%). A possible explanation for this may be that anxiety is an emotional state that has anticipatory nature by preparing for upcoming potential risks or threats. Uncertainty and uncontrollability of the future are disruptive and can trigger excessively heightened negative emotional effects.[16,17] The inability to regulate these emotions can induce anxiety.[18] Very little was known about the virus and disease Since our study was conducted in the early stages of the pandemic. These created uncertainties and unpredictability of the condition, causing further anxiety, especially for healthcare workers caring

for COVID-19 patients.

At the beginning of the shift, the proportion of the participants having burnout from combined MBI measures was 54 out of 61 people (88.52%), then decreased to 52 people (85.24%) after the shift. More than half of our respondents had moderate to severe burnout when scored using MBI-DP and MBI-PA scales, while most scored low using the MBI-EE scale (83.62-85.24%). A study about burnout levels of Polish healthcare workers during the pandemic found fewer people having low burnout using the MBI-EE scale (28.37%), but more people having low burnout using MBI-DP and MBI-PA scales (59.15% and 41.25%, respectively).[19] Being a resident is stressful due to long and demanding working schedules. The predisposing factors for residents to experience burnout are lack of sleep, problems with co-workers, patient responsibilities, and inability to manage time and adjust to the new environment. Inheriting neuroticism and having an introverted personality make individuals at a higher risk of burnout.[20]

There was no significant difference in MBI scores between the two examination points. This may be due to the short duration of the shift (1 week), thus giving little room for significant changes. Another explanation is that the second test, after the shifts, was done not immediately after the shifts but 1-2 days after, which may allow participants some resting periods. It is also noted that the overall resilience of the residents was mostly normal, which might account for the result.

We found that the median BRS score in our study is 3.67, similar to the average score (3.6) found in a survey of healthcare workers in the United States during the pandemic.[21] Higher resilience was related to older age, which may come from more experience facing life challenges and adapting better towards stress.[22] Higher resilience was linked with lower levels of anxiety and burnout. Other studies also revealed similar results, showing an inverse relationship between anxiety and resilience.[23,24] Resilience supposedly helps maintain mental well-being and cope with anxiety and depression, thus resulting in a better quality of life for healthcare workers in an epidemic.[25,26] Meanwhile, anxiety was found to correlate positively with burnout. Like our study, Çelmeçe and Menekay found a positive correlation between anxiety and burnout.[27]

Married residents had lower levels of emotional exhaustion compared to their single colleagues. Several studies agreed with this finding,[28–30], yet another study found a different conclusion.[27] Living with a couple is thought to provide social support and security, preventing burnout. Gender did not seem to be related to our study's psychological markers. Studies in Turkey stated that women healthcare workers were more anxious than men.[27,31] Duarte et al. also reported that females were associated with higher personal burnout than males.[32] The reasoning behind this is probably due to females' multiple responsibilities in their social and family lives, putting them more at risk of higher psychological distress among females.[30,33]

There was no difference in the psychological markers between anesthesiology and internal medicine residents in our study. Before the pandemic, Rodriguez et al. described in their research that a high prevalence of burnout was reported in the anesthesiology specialty. At the same time, burnout was moderate in internal medicine.[34] Burnout syndrome was more frequent in urgency and surgical residencies compared to other clinical things.[35]

The study indicated that NLR was positively related to anxiety and negatively to resilience. Some research has suggested that NLR elevation was found in several psychiatric diagnoses, including anxiety disorder.[36] The increase in NLR was thought to be linked with inflammatory processes shared across disorders. Hodes et al. reported that higher leukocytes circulated in mice more susceptible to stress than resilient mice in a study.[37] Repeated exposure to social stress is thought to increase neutrophil and monocyte circulating levels, possibly producing subsequent anxious and depressive behaviors.[38]

NLR in our study was also found to be inversely correlated with CD4. A study using mice described T cells' role in helping individuals adapt and cope with acute psychological stress. In contrast, CD4+ CD25+ regulatory T cells limit this adaptive immune response and can cause maladaptation to trauma.[39] Balderas-Vazquez et al. described that depressed patients have decreased CD4 lymphocytes, and the decrease corresponded with the severity of depression.[40] CD4 T helper cells and lymphocytes were higher in physicians with higher personal accomplishment scores using MBI. This finding may explain how the sense of reward and gratification from work may help improve the immune defense of healthcare workers.[41]

Cortisol and IL-6 in our study significantly decreased after the 1-week shift. Other studies found that patients with severe burnout produced more salivary cortisol.[42,43] Repeated exposure to stressors without sufficient recovery may cause prolonged hypothalamic-pituitary-adrenocortical (HPA) axis and further lead to higher circulating levels of glucocorticoids. However, the long-term strain on the HPA axis is suggested to cause hypoactivity and lower salivary cortisol response, especially in patients with more severe burnout.[44] Previous studies found that the level of IL-6 was related to acute stress symptoms and related with depression. In a study using mice, IL-6 released was higher in mice more susceptible to social stress, which could later infiltrate the blood-brain barrier, alter astrocytes or microglia, and cause neuroinflammation.[45] Since our study participants were mostly resilient, they could use their resting time to use coping mechanisms and decrease anxiety after their shifts, which might explain the cortisol and inflammatory marker decrease.

To the best of our knowledge, there has yet to be a study that comprehensively measured both psychological and biological markers for healthcare workers during the COVID-19 pandemic, comparing conditions before and after shifts, especially in Indonesia. Unfortunately, our study used a small sample size and only represented some healthcare workers. The data was also obtained from the self-reported questionnaire. The conditions during self-isolation needed to be more strictly monitored, which might lead to the heterogeneity of results. In addition, it was difficult to know whether the mental

health concern arose from work-related or non-work-related stress. There was no data that compared the mental state of the residents before and during the pandemic. The 1-week duration of the shift may be too short to cause significant changes in the psychological state of the residents. There was also a possibility that the degree of the problems could have been more considered, as this study was done during the early outbreak of COVID-19 in Indonesia.

CONCLUSION

Most healthcare workers had anxiety and burnout, with normal levels of resilience. NLR might be a candidate for stress biomarkers, also the most inexpensive and easily obtained. The study evaluated the impact of the COVID-19 pandemic on frontline mental health and could contribute to implementing prevention measures for severe burnout and anxiety. Further studies are required to assess the long-lasting psychological effects of COVID-19 on healthcare workers.

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CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

AUTHOR CONTRIBUTION

Margarita M. Maramis, Soetjipto, Yunias Setiawati, Agustina Konginan, Nalini Muhdi, Abdul J.A. Hayyan, Adde M.P. Chafid, Moses G.R. Pandin, Tarmono, Damayanti Tinduh, Elizeus Hanindito, Nancy M. Regatta, Cita R.S. Prakoeswa arranged the concept of the study. Design of the study was designed by: Margarita M. Maramis, Soetjipto, Yunias Setiawati, Agustina Konginan, Nalini Muhdi, Abdul J.A. Hayyan, Adde M.P. Chafid, Damayanti Tinduh, Elizeus Hanindito, Nancy M. Regatta, Cita R.S. Prakoeswa. The clinical study was conducted by Abdul J.A. Hayyan, Adde M.P. Chafid, Yusuf Ibrahim, Rosalia A. Malika, and Margarita M. Maramis. Data acquisition was completed by Abdul J.A. Hayyan, Adde M.P. Chafid, Yusuf Ibrahim, Rosalia A. Malika, and Winson Chuanardi. Margarita M. Maramis, Abdul J.A. Hayyan, Adde M.P. Chafid, and Winson Chuanardi conducted data analysis. Winson Chuanardi, Yusuf Ibrahim, Rosalia A. Malika, Natasha A. Tayibnapis, Sandra C.N. Tang, and Kadek D. Chandita performed the manuscript preparation. Manuscript editing was conducted by Margarita M. Maramis, Soetjipto, Yunias Setiawati, Agustina Konginan, Nalini Muhdi, Winson Chuanardi, Yusuf Ibrahim, Rosalia A. Malika, Natasha A. Tayibnapis, Sandra C.N. Tang, Kadek D. Chandita, Fitriah Munawaroh. A manuscript review was conducted by Margarita M. Maramis, Soetjipto, Yunias Setiawati, Agustina Konginan, Nalini Muhdi, Winson Chuanardi, Yusuf Ibrahim, Rosalia A. Malika, Natasha A. Tayibnapis, Sandra C.N. Tang, Kadek D. Chandita, Fitriah Munawaroh. The guarantor of the study, namely Margarita M. Maramis, Soetjipto, Yunias Setiawati, Agustina Konginan, Nalini Muhdi, Moses G.R. Pandin, Tarmono, Damayanti Tinduh, Elizeus Hanindito, Nancy M. Regatta, Cita R.S. Prakoeswa, Fitriah Munawaroh.

ETHICAL CONSIDERATION

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. The ethics committee of Dr. Soetomo General Hospital approved all procedures involving human subjects/patients. (Ethical Clearance No. 0006/KEPK/V/2020).

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