



Bioscientia Medicina: Journal of Biomedicine & Translational Research

Journal Homepage: www.bioscmed.com

Psychosomatic Aspect of the COVID-19 Pandemic

Rahmy Nurdin^{1*}, Arina Widya Murni²

¹Departement of Internal Medicine, Faculty of Medicine, Universitas Andalas, Padang, Indonesia

²Division of Psychosomatic, Department of Internal Medicine, Faculty of Medicine, Universitas Andalas, Padang, Indonesia

ARTICLE INFO

Keywords:

Pandemic
COVID-19
Psychosomatic
Stress

*Corresponding author:

Rahmy Nurdin

E-mail address:

dr.rahmynurdin@gmail.com

All authors have reviewed and approved the final version of the manuscript.

<https://doi.org/10.37275/bsm.v6i13.650>

ABSTRACT

A pandemic is an epidemic of an infectious disease that spreads over a wider area, multiple continents, or the entire world at the same time. Since COVID-19 was declared a pandemic on March 11th, 2020, the world has entered a global emergency phase. The COVID-19 pandemic has changed the way of life and become a stressor in this century. Various factors become stressors during a pandemic. Many people experience negative emotions, such as fear, anxiety, and depression, during the COVID-19 pandemic. When negative emotions are no longer controlled, they will have a negative effect on the autonomic nervous system and cerebral cortex, causing psychosomatic and somatic symptoms. Many studies have shown a significant relationship between perceived stress and psychosomatic complaints. Research has also shown that stress during the COVID-19 pandemic is associated with an increase in psychosomatic symptoms. In the future, negative emotions during a pandemic, if not managed properly, can lead to post-traumatic stress disorder (PTSD). Peoples who are vulnerable to mental disorders due to COVID-19 include people with chronic diseases. Stressors during a pandemic can exacerbate anxiety, depression, and chronic stress in people with chronic diseases, causing exacerbations of chronic diseases, increasing somatic symptoms, and decreasing immune responses, resulting in increased infection and mortality risk.

1. Introduction

A pandemic is an epidemic of an infectious disease that spreads over a large area, for example, several continents, or around the world at the same time. History records that there have been several pandemics. The 19th century saw cholera and flu pandemics. The 20th century saw the Spanish Flu, Asian Flu, and Ebola pandemics, and then in the 21st century, there was an outbreak of SARS and MERS. During a pandemic, everyone experiences emotions, thoughts, and situations that have never been experienced before, which have an impact on the health, economic, social, and security fields. Health impacts, both physical and psychological. The psychological effects of the pandemic occur as a

response to social isolation and lockdown, psychological response to the diagnosis, public response to those who have confirmed symptoms of infection, and after infection.¹⁻³

A case of unknown pneumonia was discovered and reported for the first time in Wuhan, Hubei Province, China, on December 31st, 2019. A new type of coronavirus was identified as the cause of pneumonia. On February 11th, 2020, the World Health Organization (WHO) released the official name of the virus, namely severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and the disease caused by the virus is called Coronavirus Disease 2019 (COVID-19). This disease spread rapidly in various

provinces in China, and along with the movement of people, the disease spread to almost all continents in less than 3 months. WHO officially declared COVID-19 as a pandemic on March 11th, 2020.^{4,5}

The world has entered into a global emergency since COVID-19 was declared a pandemic. The pandemic has changed the habits and way of life of people around the world. Many factors have become stressors during the COVID-19 pandemic, impacting physical and mental health. According to a survey conducted by the Chinese Academy of Social Science, many people experience negative emotions, such as fear, anxiety, and depression, during the COVID-19 pandemic. When the stress level is controlled, it can increase the body's resistance and cause a defense mechanism, but when the stress level and negative emotions are no longer controlled, it will have a negative influence on the autonomic nervous system and cerebral cortex. This can cause psychosomatic and somatic symptoms, which can eventually lead to psychological disorders and mental illness. Psychosomatic disorders are disorders that affect the mind and body simultaneously. The relationship between mind and body depends on the relationship between the central nervous system and the rest of the body, the relationship between emotions, mind, and physical organs, and the relationship between the conscious and subconscious with the body.^{5,6}

Stress caused by the pandemic situation causes not only psychological changes but also affects physiological (somatic), causing psychosomatic symptoms. A large number of studies have shown a significant relationship between perceived stress and psychosomatic complaints. Zidkova et al. showed a relationship between the COVID-19 pandemic and an increase in psychosomatic symptoms (3.2%-17.3% of respondents) and the occurrence of negative emotions (9.9%-33.3% of respondents). Negative emotions that occur during the pandemic, such as fear, anxiety, and depression, if not treated properly, can cause psychosomatic disorders and, in the future, can cause post-traumatic stress disorder (PTSD) and can become a serious mental illness. Chang and Park found a

PTSD prevalence of 20.3% in people who had suffered from COVID-19.⁷⁻¹⁰

Based on the description above, the authors do a literature review that describes the psychosomatic aspects of the COVID-19 pandemic. This literature review aims to see the impact of the COVID-19 pandemic on mental health, which focuses on psychosomatic aspects as a branch of science that discusses diseases that involve the body and mind, especially in high-risk groups of people. Also, as a reminder of the importance of the role of doctors in comprehensive patient management, not only physical treatment but also psychosomatic symptoms that can occur. Therefore, psychosomatic approaches and treatment are important to apply.

COVID-19 pandemic

Definition of pandemic

An outbreak is a term to describe the occurrence of the spread of disease over a large area and in many people. The definition of an epidemic in Indonesia based on law No. 4/1984 is the same as an epidemic, which is the outbreak of an infectious disease in a community whose number of sufferers increases significantly beyond the usual situation at a certain time and area, and also can cause catastrophe. An outbreak on a larger scale is called a pandemic. The word pandemic comes from the Greek words "pan" which means all, and "demos" which means people. Based on the dictionary of epidemiology, a pandemic is defined as an epidemic of an infectious disease that spreads widely throughout the world or a wider area, crosses international boundaries, and usually affects humans in large numbers.^{2,11}

Pandemic impact

Pandemics have an impact on various aspects of life. The pandemic has had an impact on health, the economy, society, and security. Pandemics cause high morbidity and mortality in the world. On the economic front, the pandemic causes economic instability. Travel restrictions and market closures have disrupted food supplies and daily necessities. The pandemic also

has an impact on global security. The issue of biological weapons, resulting in infection, can also weaken a country's military.²

The impact of the pandemic in the health sector is not only on physical health as a result of the disease but also affects mental health. An outbreak or pandemic can be a stressor and cause stress to society. Fear and anxiety about an illness, plus stressors due to the impact of the pandemic on the economy, politics, and lifestyle changes. Al-Rabiaah et al. reported the results of the epidemic's impact on medical students. It was found that all respondents experienced anxiety, minimal anxiety (77%), mild anxiety (18.4%), and moderate anxiety (4.6%), and found a correlation between stress levels with the incidence of a generalized anxiety disorder (GAD).^{12,13}

COVID-19 pandemic

The COVID-19 pandemic began with the discovery of unknown pneumonia cases, which were first reported on December 31, 2019, in Wuhan, Hubei Province, China. In a short time, the cases spread to various provinces in China and then spread to various countries. This pneumonia was later identified as caused by a new type of coronavirus (novel coronavirus). WHO released the official name of the new virus on February 11, 2020, namely severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and the disease it causes is called Coronavirus Disease 2019 (COVID-19). SARS-CoV-2 can be transmitted from human to human. In less than three months, this disease has infected more than 126,000 people in 123 countries in Asia, Europe, America to Africa. WHO officially declared COVID-19 as a pandemic on March 12th, 2020.^{4,5}

Stress and the immune system

Stress is a condition that is a psychobiological consequence of the failure of living organisms to respond effectively to any physical or emotional threat, whether the stressor is an actual threat or an imaginary threat. A stressor is defined as a stimulus that the brain perceives as a threat and causes a

dysphoric state, and physiologically increases the production of noradrenaline and adrenaline for the fight-or-flight mechanism. Stressors can be in the form of pain, perception of threat, and the compulsion to do activities that are not by the circadian rhythm. Stressors are perceived by the brain as stressful conditions and affect all homeostatic functions, from the cardiovascular to the immune system. Stressful life events and the negative emotions that result from stress can interfere with the immune response by interfering with interactions between the central nervous system (CNS), endocrine system, and immune system.¹⁴⁻¹⁶

Stress or negative emotions can affect the immune system through two mechanisms, physiological mechanisms and behavioral (psychosocial) mechanisms. Physiologically, stress is associated with the activation of several systems, including the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic nervous system. Activation of these two pathways results in increased levels of certain hormones in the blood, cortisol and catecholamines (epinephrine and norepinephrine). Stress is associated with changes in the number of circulating white blood cells and the number of antibodies in the body. Cortisol secretion plays an important role in the regulation of physiological and behavioral responses in stressful situations. Cortisol increased after strenuous physical exercise and after receiving a task with a heavy mental load. Increased levels of cortisol and epinephrine cause a decrease in circulating white blood cell levels, as well as a decrease in lymphocyte proliferation and NK cell activity.¹⁴⁻¹⁷

Stress disrupts the regulation of humoral and cellular immune responses against pathogens, increasing the risk of infectious disease. There is a relationship between psychological stress and susceptibility to the common cold. Stress causes a decrease in antibody response to vaccines and prolongs wound healing. It has long been known that stress suppresses host resistance to infection and increases the incidence of infection. Negative emotions, including anxiety and depression, can

modulate antibody and T-cell responses to antiviral vaccination, leading to suppression of the immune response. Under stressful conditions, the suppressive activity of the immune system can decrease, which can eventually lead to the activation of latent viruses. Various studies have shown that there is an increase in cortisol levels in COVID-19. It is suspected that cortisol levels can differentiate the severity of COVID-19 risk. Patients with critical symptoms have higher cortisol levels. In a study by Ramezani et al., severe COVID-19 found infection with high levels of serum cortisol and high HADS scores.^{15,18}

Psychosomatic aspects of the COVID-19 pandemic

Deep emotional trauma in society can be caused by an inability to cope with a large-scale human disaster. These include natural disasters, human-made tragedies, war conflicts, social crises, global pandemic diseases, and others. Around 16% of the global population will experience mental health disorders due to disasters, and it is estimated that 12%-47.4% will last a lifetime. Disasters will result in various limitations in getting mental health care, the consequences of which are not managed or inadequate management of disorders related to social stress will affect individuals and families as well as the general population, reduce work productivity, unemployment, homelessness, marital and child care problems, violence household, drug abuse, and suicide. The COVID-19 pandemic is a global disaster facing the world community today.¹²

Acute psychological impact

Fear is a human adaptive defense mechanism, which is a basic need for survival and involves the preparation of several biological processes to respond to life-threatening events. However, when fear is chronic and disproportionate, it becomes dangerous and can lead to the development of various psychiatric disorders. During a pandemic, fear increases anxiety and stress levels in otherwise healthy individuals and increases symptoms in those with pre-existing psychiatric disorders. Past pandemics have shown

that mental health involvement can last a long time, and its prevalence is higher than the infection itself. During the Ebola outbreak, 2013-2016, fear-related behaviors had an epidemiological impact on both individuals and communities during each phase of the outbreak, causing distress and psychiatric symptoms in the population.

According to Inchausti et al., there are three groups of people who are at risk for psychological morbidity during and after the COVID-19 pandemic. The first group is health workers as the frontline in handling patients and pandemics, especially those who work with inpatients, who routinely carry viruses, who carry out high-risk procedures; the second is individuals who have the potential to experience new mental health disorders due to being diagnosed with COVID-19, loss of family or loved ones due to this disease, or the effects of long-lasting social distancing; The third is individuals who previously had a psychopathological condition, may be exacerbated by isolation. According to Xiang et al., groups that are also at risk of experiencing psychological disorders during the pandemic are elderly people, immunocompromised patients, patients with previous psychological disorders, family members of confirmed patients, and residents in red zone areas. The Indonesian Ministry of Health, in its guidebook, has determined groups that must receive mental health assistance, including suspected cases, confirmed cases of COVID-19, patients' families, and also vulnerable groups. Groups that are at risk for mental health impacts due to COVID-19 infection are the elderly, people with chronic diseases, children and pregnant women, physical disabilities, people with mental problems, people with mental disorders, and frontline workers.^{6,19,20}

The risk of being infected with COVID-19 causes a wide range of psychological problems, such as panic disorder, anxiety, and depression, among populations in countries with a high prevalence of the virus. Sorokin et al. found that 35% of respondents experienced anxiety related to COVID-19. Anxiety occurs because of isolation. High-risk groups

experiencing anxiety include people who have previously experienced affective disorders, young people (≤ 20 years), unemployed, single, have a higher education level, and are female. Research by Yao et al. in China concludes that this pandemic is provoking parallel epidemics of anxiety and depression reactions.^{21,22}

Quarantine impact

This pandemic has made cities in various countries have to quarantine. The term quarantine means segregating and restricting the movement of people who have potentially been exposed to an infectious disease to ensure they get better and to lower their risk of transmitting it to others. In contrast to isolation, which means the separation of people who have been diagnosed with an infectious disease from healthy people. In history, quarantine was first carried out in the world when there was a leprosy epidemic in Venice, Italy, in 1127. Three hundred years later, a quarantine was also carried out in England because of a plague outbreak. Quarantine is an unpleasant experience. In previous outbreaks, quarantine has been reported to have caused anger and even suicidal ideation. Reduced interpersonal contact as a result of isolation and quarantine can trigger mental disorders such as anxiety and depression or exacerbate existing mental illnesses.^{12,23}

According to WHO, the main psychological impact of the pandemic is increasing levels of stress and anxiety. This is mainly due to the effects of quarantine and changes in daily life routines. Quarantine makes people separated from their families feel lonely, financially insecure, and stigmatized. Several studies mention that the stressors during the quarantine period include the length of time, fear of infection, frustration, boredom, inadequate supply of needs, and inadequate information. Stressors after the quarantine period are financial loss and stigma. Brooks et al. reported that the psychological effects of quarantine could include PTSD, confusion, and anger. Limcaoco et al. conducted a study of 1091 respondents in 41 countries undergoing quarantine and lockdown and

found an increase in anxiety levels, as well as affective and cognitive changes.²⁴⁻²⁷

Psychosomatic disorders related to the COVID-19 pandemic

Research in several countries shows that levels of anxiety and depression during the pandemic increased compared to the time before the pandemic. Many people experience negative emotions, such as fear, anxiety, and depression, during the COVID-19 pandemic. When the stress level is controlled, the body's resistance increases and causes a defense mechanism, but when the stress level is out of control, it will have a negative effect on the autonomic nervous system and the cerebral cortex. This can cause psychosomatic and somatic symptoms, which can eventually lead to psychological disorders and mental illness.⁶

Psychosomatic disorder is a psychological condition that leads to physical symptoms, often without any medical explanation. Mind and body have a single identity. Therefore the interaction between body and mind disease is natural. The relationship between mind and body depends on the relationship between the central nervous system and the rest of the body, the relationship between emotions, the mind and the physical organs, and the relationship between the conscious and subconscious and the body. The etiology of psychosomatic symptoms is not yet clear. However, there are several explanations, molecularly, that there is a role for genetic modification and epigenetics, childhood trauma and other traumatic life events, the aging process, and the existence of situations of uncertainty. A pandemic is a traumatic event. It is proven that there is an increase in stress levels during the pandemic.²⁸

The human body's reaction to stress can be classified into three different categories consisting of emotional, behavioral, and psychological. The physiological response cycle that develops after stress could potentially explain the relationship between stress and somatic complaints and even disease. Stress usually causes activation of the sympathetic

nervous system and the hypothalamic-pituitary-adrenal (HPA) axis, followed by many physiological changes, such as increased blood pressure, tachycardia, immune suppression, and insulin resistance. HPA axis activation is known to influence inflammatory processes in tissues, which may contribute to pain perception by influencing different levels of pain transmission pathways. Similarly, increased levels of cortisol and corticotropin-releasing hormone (CRH), after activation of the HPA axis, have been reported to affect hormone production levels. The circadian rhythm is also regulated by the HPA axis and the autonomic nervous system. Changes in biological rhythms can cause psychosomatic complaints.^{19,29}

Long-term psychological impact

During the 2003 severe acute respiratory syndrome (SARS) outbreak, Antoinette et al. reported that stress levels in SARS survivors remained persistently high and higher than in control subjects one year after the outbreak ended and that psychological distress was at an alarming level. They also found that after one year of the outbreak, healthcare workers who survived had higher stress levels than non-medical workers. The study concludes that the long-term implications of infectious disease outbreaks should not be ignored. The long-term effect of the outbreak on mental health is the risk of developing the post-traumatic disorder (PTSD) in the future.

A survey from the Chinese Academy of Social Science found that negative emotions during a pandemic, such as fear, anxiety, and depression, can cause significant physical and mental disorders. If this does not get proper treatment, it can cause psychosomatic disorders and can cause PTSD, in the future and can become a serious mental disorder. Psychosomatic symptoms may develop after a traumatic event. For example, the incidence of somatic symptoms is reported to be high in war-exposed civilians, military veterans, and emergency workers. Shevlin et al. found that the pattern of association between COVID-19-related anxiety and the incidence of somatic symptoms in the UK remained significant,

even though various variables were controlled for, such as age, gender, income, previous fault problems, and generalized anxiety disorder (GAD).^{28,29}

Psychological impact on chronic disease patients

The Indonesian Ministry of Health, in the guidebook for mental health and psychosocial support during the COVID-19 pandemic, has determined groups that are vulnerable to mental health impacts due to COVID-19 infection, people with chronic diseases, are one of them. Based on the Centers for Disease Control and Prevention (CDC), chronic diseases that can aggravate the symptoms of COVID-19, including cardiovascular disease, chronic kidney disease, cancer, chronic lung disease, diabetes mellitus, human immunodeficiency virus (HIV), people receiving transplant therapy, people receiving immunosuppressant therapy, and autoimmune diseases. The prevalence of comorbid mental disorders such as depression, anxiety, and chronic stress has long been known to be high in people with chronic illnesses. People with chronic illness feel isolated, uncertain about the future, and feelings of guilt due to physical and psychosocial limitations due to their illness, being weighed down by the burden of the COVID-19 pandemic. The consequences can exacerbate chronic illness and create a vicious cycle. Patients with chronic diseases have higher stress levels due to feelings of fear because they have a high risk of worsening clinical outcomes of COVID-19.^{12,19,30}

Lockdown or quarantine during the COVID-19 pandemic has an effect on routine life and disease management in patients with chronic diseases. Based on several studies in previous outbreaks, it was found that the depression rate of people with chronic diseases who were undergoing quarantine was higher than the general population. The COVID-19 pandemic is increasing the frequency and severity of sleep disturbances due to stress. Sleep disturbances increased by 30%-40% in the general population during the pandemic and doubled in people with chronic disease. One night of sleep deprivation has

been shown to decrease the number and function of neutrophils in healthy men.^{12,14,31}

People with chronic illnesses tend to have increased anxiety and disappointment during the COVID-19 pandemic for a variety of reasons. Several studies have investigated the impact of COVID-19 on patients with chronic disease. Wu and Mc Goonan. analyzed 72314 cases in China, getting a case fatality ratio (CFR) in patients with heart disease of 10.5%, diabetes at 7.3%, chronic lung disease at 6.3%, and hypertension at 6% compared to the general population at 2.3%. The risk of complications and mortality is also increased in patients who receive immunosuppressant or immunomodulatory therapy. The pandemic can also result in delays in services for chronic disease patients. This can be a stressor for chronic disease patients, so people with chronic diseases are classified as vulnerable groups to experience mental health disorders during the pandemic. Quarantine during the COVID-19 pandemic also affects chronic disease patients with the incidence of distress, anxiety, depression, and somatization. Louvardi et al. found that 163 chronic diseases (pulmonary, autoimmune, cardiovascular, endocrine) in Greece had higher levels of distress and somatization than 943 healthy individuals, but there was no difference in levels of anxiety and depression.^{32,33}

The SAR-CoV-2 infection has a close relationship with the cardiovascular system. This virus can affect the cardiovascular system through several mechanisms: direct damage to the myocardium, systemic inflammation, disruption of the myocardial supply-demand ratio, plaque rupture and coronary thrombosis, side effects of various therapies, and electrolyte imbalance. Patients who previously had comorbid cardiovascular disease were three times more at risk of developing severe clinical symptoms and requiring intensive care if they had COVID-19. The clinical situation can be exacerbated by stress due to being affected by a pandemic or being infected with COVID-19. The impact of stress on the cardiovascular system also occurs during a pandemic concerning

pandemic-related stress. Psychopathological manifestations can lead to excessive secretion of catecholamines, which can lead to myocardial electrical instability and poor outcome in patients with cardiovascular disease. During a pandemic, people experience the fear of getting sick and dying. Negative feelings related to systemic inflammation and endothelial dysfunction, coupled with an unhealthy lifestyle. Acute and subacute stress activates the adrenergic system and increases the inflammatory response, and causes endothelial dysfunction leading to the formation of atherosclerotic plaques. Stress also triggers cardiac arrest, associated with changes in the neurohormonal, hemodynamic, and coagulation systems that can lead to plaque rupture, platelet activation, and coronary constriction.³⁴

2. Conclusion

A pandemic is a global threat that has an impact on physical and psychological health. There are three groups at risk for psychological morbidity during and after the COVID-19 pandemic; the first is a health worker, the second is a person infected with COVID-19 or a family member with COVID-19, the third is a person with a previous mental disorder, a person with a chronic illness and the elderly. Pandemics can cause acute or chronic psychological impacts. Acute psychological effects can be in the form of anxiety, depression, panic disorder, and psychosomatic disorders. The long-term psychological impact can lead to PTSD and eventually lead to severe mental disorders. Patients with chronic diseases as one of the risk groups can get an impact reducing their immune response if they experience stress related to the pandemic or because they are confirmed to have COVID-19. So, it affects disease exacerbations and clinical deterioration. Therefore, comprehensive management is important in managing the COVID-19 pandemic, not only in handling physical disorders but also psychological disorders. And special attention also needs to be given to patients with chronic diseases to prevent the adverse effects of stress on their disease.

3. References

1. Qiu W, Rutherford S, Mao A, Chu C. The pandemic and its impact. *Health, Culture and Society Journal*. 2017; 9(10): 3–11.
2. Ornell F, Schuch JB, Sordi AO, Kessler FHP. Pandemic fear and COVID-19: mental health burden and strategies. *Brazilian Journal of Psychiatry*. 2020; 42(3): 232–5.
3. Kumar S, Arafat Y, Kabir R, Sharma P, Saxena SK. Coping with mental health challenges during COVID-19. In Saxena SK. *Coronavirus Disease 2019 (COVID-19): epidemiology, pathogenesis, and therapeutics*. 2020. Germany. Springer. 199–213.
4. Zhang N, Wang L, Deng X, Liang R, Su M, et al. Recent advances in the detection of respiratory virus infection in humans. *Journal of medical virology*. 2020; 92(4): 408–17.
5. Susilo A, Rumende M, Pitoyo CW, Santoso WD, Yulianti M, et al. Coronavirus disease 2019: Review of recent literature. *Jurnal Penyakit Dalam Indonesia*. 2020; 7(1): 45–68.
6. Xiang YT, Yang Y, Li W, Zhang L, Cheung T, et al. Timely mental health care for the 2019 novel coronavirus outbreaks is urgently needed. *Lancet Psychiatric*. 2020; 7: 228–9.
7. Wang C, Pan R, Wan X, Tan Y, Xu L, et al. Immediate psychological responses and associated factors during in the Initial stage of 2019 Corona Virus Disease (COVID-19) epidemic among di general population in China. *Int J Environ Res Public Health*. 2020; 17.
8. Zidkova R, Malinakova K, Van Dijk JP, Tavel P. The occurrence of the psychosomatic symptoms during the coronavirus pandemic. *Proceeding the 3rd international electronic conference on environmental research and public health*. 2020; 1–6.
9. Murni AW. Comprehensive therapy for handling the COVID-19 outbreak. *Proceedings of the 20th periodic scientific meeting of internal medicine. Bagian IPD FKUA*. 2020; 134–45.
10. Chang MC, Park D. Incidence of post-traumatic stress disorder after coronavirus disease. *Healthcare*. 2020; 8(373): 1–7.
11. Law No. 4 of 1984. *Outbreaks of infectious diseases*.
12. Cossie K, Popovic S, Sarlija M, Kesedzie I. Impact of human disaster and COVID-19 pandemic on mental health: the potential of digital psychiatry. *Psychiatria Danubian*. 2020; 31(1): 25–31.
13. Al-Rabiaah A, Temsah MH, Al-Eyadhy AA, Hasan GM, Al-Zaamil F, et al. Middle east respiratory syndrome- coronavirus (MERS-CoV) associated stress among medical students at a university teaching hospital in Saudi Arabia. *Journal of infection and public health*. 2020; 13(5): 687–91.
14. Morey JN, Boggero IA, Scott AB, Segerstrom SC. Current direction in stress and human immune function. *Current opinion in psychology*. 2015. 1(5): 13–7.
15. Seiler A, Fagundes CP, Christian LM. The impact of everyday stressors on the immune system and health. In Chouler A, *Stress challenges and immunity in space*. 2nd ed. Springer. 2020; 71–92.
16. Sharsavarani AM, Abadi EAM, Khalkoran H. stress: facts and theories through literature review. *International Journal of Medical Review*. 2015; 2(2): 230–41.
17. Stephen MA, Wand G. Stress and the HPA axis: Role of glucocorticoid in alcohol dependence. *Alcohol research: a current review*. American Psychological Association. 2016; 468–83.
18. Ramezani M, Leila S, Kariamialavijeh E, Razaei O, Hajiesmaeli M, Pakdaman H. The role of anxiety and cortisol in outcomes of a patient with COVID-19. *Basic and Clinical Neuroscience*. 2020; 11(2): 179–83.
19. Directorate General of Disease Prevention and Control of the Ministry of Health of the Republic of Indonesia. *Guidelines for mental health and psychosocial support in a pandemic*. 2020. Jakarta. Kemenkes RI.

20. Inchausti F, Macbeth A, Ohayon IH, Dimaggio G. Psychological intervention and COVID-19: what we know so far and what we can do. *Research Gate*. 2020; 1–21.
21. Sorokin MY, Kasyanov SD, Rukavishnikov GV, Makarevich OV, Neznanov NG, et al. Structure of anxiety associated with the COVID-19 pandemic in the Russian-speaking sample: result from an online survey. *MedRxiv*. 2020; 1–12.
22. Yao H, Chen JH, Xu YF. Patients with mental health disorders in the COVID-19 epidemic. *Lancet Psychiatry*. 2020; 7(4): 21.
23. Wu P, Fang Y, Guan Z, Fan B, Kong J, et al. The psychological impact of the SARS epidemic on hospital employees in China: exposure, risk perception, and altruistic acceptance of risk. *La Revue Canadienne de Psychiatrie*. 2009; 54(5): 302–11.
24. WHO. Mental health and psychosocial considerations during the COVID-19 outbreak. Geneva. 2020.
25. Limcaoco RSG, Mateos EM, Fernandez JM, Roncero C. Anxiety, worry, and perceived stress in the world due to the COVID-19 pandemic, March 2020. Preliminary result. *medRxiv*. 2020; 1–12.
26. Khan S, Siddique R, Li H, Ali A, Shereen MA, et al. Impact of coronavirus outbreaks on psychological health. *Journal of global health*. 2020; 10(1): 1–6.
27. Brooks SK, Webster RK, Smith LE, Woodland L, Wessely S, et al. The psychological impact of quarantine and how to reduce it: a rapid review of the evidence. *The Lancet*. 2020; 1–9
28. Gica S, Kavakli M, Durduran Y, Ak M. The effect of the COVID-19 pandemic on psychosomatic complaints and investigation of the mediating role of intolerance to uncertainty, biological rhythm change and perceived COVID-19 threat in this relationship: A web-based community survey. *Psychiatric and Clinical Psychopharmacology*. 2020; 30(2): 89–96.
29. Shevlin M, Nolan E, Owczarek M, McBride O, Murphy J, et al. COVID-19 related anxiety predicts somatic symptoms in UK population. *British Journal of Health Psychology*. 2020; 1–8.
30. Wankowicz P, Szylińska A, Rotter I. The impact of the COVID-19 pandemic on psychological health and insomnia among people with chronic disease. *Journal of Clinical Medicine*. 2020; 10: 1–8.
31. Saqib MAN, Siddiqui S, Qasim M, Jamil MA, Rafique I, et al. Effect of COVID-19 lockdown on a patient with chronic disease. *Diabetes and metabolic syndrome: clinical research and reviews*. 2020; 14: 1621– 623
32. Wu, McGoogan JM. A characteristic and important lesson from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72314 cases from the Chinese Center for disease control and prevention. *JAMA*. 2020; 323(13): 1239–42.
33. Lovardi M, Pelekasis P, Chrousos GP, Darviri C. Mental health in chronic disease patients during the COVID-19 quarantine in Greece. *Palliative and supportive care*. Cambridge University Press. 2020; 394–9.
34. Mattioli AV, Nasi M, Cocchi C, Farinetti A. COVID-19 outbreak: impact of the quarantine-induced stress on cardiovascular disease risk burden. *Future Cardiology*. 2020; 1–4.