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Description of clinical manifestations of COVID-19 patients in the isolation treatment room

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***Abstract*---**Cases of patients infected with Covid-19 are still quite high. The emergence of Covid-19 was followed by the emergence of various variants of this disease. The consequences of the emergence of various variants of Covid-19 will be followed by the occurrence of various new clinical manifestations in patients. These clinical manifestations need to be evaluated. This study aims to determine the description of the clinical manifestations of Covid-19 patients. This study was a quantitative descriptive study. The study was conducted from January to February 2021. The sample consisted of 100 patients who were confirmed positive for Covid-19 and underwent treatment at Dr. Kariadi General Hospital, Semarang, Indonesia. The results showed that most common clinical manifestations of Covid-19 patients including increase in D-dimer (97%), lymphopenia (85%), pneumonia (82%), heart to breath (62%), cough (59%), increasing od prothrombin (57%), fever (56%), SpO2 < 90% (at room temperature) / happy hypoxia (43%), tachycardia (39%), fatigue (37 %), nausea (26%), headache (24%), sore throat (16%). The clinical manifestations of

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Covid-19 that are not experienced by many patients in isolation rooms include: ronchi (6%), platelets <100x103 / uL (5%) decrease of smell ability (3%), fibrinogen <200 mg / dl (2%), bradycardia (1%). None of the Covid-19 patients had an integumentary disorder in this study. This study recommends that institutions have to evaluate all clinical manifestations of Covid-19 appropriately and add clinical manifestation of happy hypoxia and tachycardia clinical manifestations to the screening of Covid-19 patients.

***Keywords*---**clinical manifestations, isolation, COVID-19.

Introduction

Coronavirus Disease 2019 (Covid-19) is an infectious disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). This virus can cause severe symptoms such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS) to death of unknown etiology (Burhan et al., 2020). Based on data, it shows that as many as 223 countries have contracted Covid-19. There were 108,006,680 confirmed cases and 2,378,115 deaths or 2.2% (World Health Organisation, 2020). Data from the Indonesian National Covid-19 task force on February 14, 2021, shows positive cases of 1,217,468, recovered 1,025,273, 33,183 deaths, and 161,731 active cases. Three provinces have contributed the many cases, namely DKI Jakarta, West Java, and Central Java (Komite Penanganan Covid-19 dan Pemulihan Ekonomi Nasional, 2020).

The highest Covid-19 case in Central Java Indonesia is Semarang. The city of Semarang updated as of February 14, 2021, the total number of confirmed cases was 29,463, suspected 119, probable 25, probable death 160, died 1612, cured 20,589, and confirmed currently undergoing treatment 397 (Pemerintah Kota Semarang, 2020). The data from Dr. Kariadi General Hospital Semarang on November 30, 2020, showed a total of 3524 patients, 2767 confirmed, 2165 recovered, 499 deaths, and 103 active confirmations who were undergoing treatment (Tim Covid RSUP Dr Kariadi Semarang, 2020).

Severe cases of Covid-19 can lead to pneumonia, acute respiratory syndrome, kidney failure, and even death (Kementerian Kesehatan Republik Indonesia, 2020). The impact of the Covid-19 pandemic on the Indonesian economic sector includes layoffs (termination of employment), the occurrence of PMI Manufacturing Indonesia, decreased imports, increased prices (inflation) as well as losses in the tourism sector which led to a decrease in occupancy (Yamali, 2020). Another impact on the health sector is death. The increasing mortality in Indonesia is influenced by the comorbid possessed by corona virus-positive patients, the elderly, and inadequate health facilities (Ilpaj, 2020).

Efforts that have been made by the Indonesian government include lockdowns, physical distancing, and large-scale social restrictions (Ilpaj, 2020). Also, the government issued guidelines for the treatment or management of Covid-19 and vaccinations. This guideline contains treatment for patients with Covid-19 and clinical information on optimal Covid-19 treatment (National Institutes of Health,

2020). Covid-19 cases continue to increase in number, followed by the appearance of a new variant. This new variant has consequences for new clinical manifestations. These clinical manifestations need to be evaluated. Determining clinical manifestations of Covid-19 can assist health workers in determining interventions for Covid-19 patients. Health workers can determine the prognosis of patients being treated by correctly identifying the clinical manifestations experienced by the patient (World Health Organisation, 2020). Based on the description, the researchers are interested in conducting research related to the description of the clinical manifestations of Covid 19 and exploring more deeply about clinical manifestations of Covid-19 patients at Dr. Kariadi General Hospital Semarang. The general objective is to find out how the clinical manifestations.

Methods

This research uses a descriptive quantitative design this study aims to find out how is the clinical manifestations of Covid-19 patients in isolation rooms. The inclusion criteria in this study included: All patients who were confirmed positive for Covid-19 who were treated at the Dr. Kariadi Semarang. The exclusive criteria in this study were patients undergoing treatment with criteria for suspected and possible Covid 19. The research was conducted in January-February 2021. This research was conducted in the Covid-19 isolation room at Dr. Kariadi General Hospital Semarang, Indonesia which the central government hospital for Covid-19 referrals for screening, testing, cohort, and treatment. The sample consisted of 100 patients who were confirmed positive for Covid-19 and underwent treatment in an isolation room.

The instrument used was the observation sheet adopted from the Covid-19 clinical observation of the Ministry of the Health Republic of Indonesia which contained manifestation symptoms in the respiratory system, digestive system, sensory perception system, integumentary system, hematology & lymphatic system, nervous system, the circulatory system, and the musculoskeletal system. Data is analyzed univariately using frequency distributions. This research complies with research ethics, including anonymity. This study has an ethical permit with an ethical clearance number: 751/EC/KEPK-RSDK/2021, obtained from Dr. Kariadi General Hospital's research ethic committee.

Results

Patient characteristics include age, gender, travel history, contact history, and severity. Based on data of this study, most of the categories of age were adult (69%) and most gender 51% was female. Most confirm Covid-19 patient (94%) not have experience of travel history, the most of respondents (83%) did not have contact to covid-1 patients, most of the respondents (70%) had Covid-19 moderate severity, and most of the respondent (94 %) was obtained positive confirmation status for Covid-19 from PCR examinations. The findings of this study in table 1 indicate that the most common comorbid diseases of Covid-19 patients are hypertension at 27%, followed by diabetes mellitus at, 24% and heart disease at as much as 15%.

Table 1
Respondents' Frequency Distribution Based on Comorbid Characteristics (n =100)

Comorbid	f	%
Tuberculosis	1	1
Diabetes Mellitus	24	24
HIV / Aids	1	1
Autoimmune disease	1	1
Immunosuppressants	3	3
Chronic Kidney Disease (CKD)	6	6
Heart disease	15	15
COPD	0	0
Hypertension	27	27
High cholesterol	2	2
Total	100	100

Table 2 describes the clinical manifestations of Covid-19 based on disorders in various body systems. Research showed that the most dominant clinical manifestations experienced by Covid-19 patients in the respiratory system are pneumonia 82%, shortness of breath 62%, and coughing 59%.

Table 2
Table 2. Clinical Manifestation of Covid-19 Based on Human Organ System (n = 100)

Characteristics	Yes		No	
	f	(%)	f	(%)
Respiratory system				
Cough	59	59	41	41
Sputum Production	12	12	88	88
Hard to breathe	62	62	38	38
Sore throat	16	16	84	84
Cold	9	9	91	91
Hemoptysis	0	0	100	100
Pneumonia	82	82	18	18
Stridor	3	3	97	97
Ronchi	6	6	94	94
Sensory perception system				
Taste disorders	0	0	100	100
Olfactory disturbances	3	3	97	97
Nervous system				
Fever	56	56	44	44
Headache	24	24	76	76
Seizures	0	0	100	10
Hematological and lymphatic systems		85		15

Characteristics	Yes		No	
	f	(%)	f	(%)
Lymphopenia	85	97	15	3
D-dimer increases	97	57	3	43
Prothrombin time increases	57	5	43	95
Platelets <100x103 / uL	5	2	95	98
Fibrinogen <200 mg / d	2		98	
Musculoskeletal system				
Muscle ache	5	5	95	95
Fatigue	37	37	63	63
Digestive system				
Nausea	26	26	74	74
Vomiting	20	20	80	80
Abdominal pain	10	10	90	90
Diarrhea	14	14	86	86
The integumentary system				
Morbiliform	0	0	100	100
Utikaria	0	0	100	100
Rash	0	0	100	100
Lesions	0	0	100	100

Based on table 2, the dominant clinical manifestation in the sensory perception system is an olfactory disturbance (decrease of smell) of as much as 3%. Most of the clinical manifestations in the nervous system are fever (56%) and headache (24%), in the circulatory system is SpO2 <90% (happy hypoxia) as much 43% and tachycardia 39%. Dominant clinical manifestations in the system of the hematology and lymphatic system, are an increase in D-dimer by 97%, lymphopenic an 85%, and an increase in prothrombin time by 57%. The dominant of clinical manifestation the in muscular system is fatigue (37%), and the clinical manifestation in the digestive system is nausea (26%), vomiting (20%) and diarrhea (14%). This study showed, that there is no data on Covid-15 patients who experience clinical manifestations in the integumentary system.

Discussion

Based on the data of this study, most of the categories of age were adult (69%). Age is a risk factor for Covid-19 to infect someone more severely (WHO, 2020). Age also affects the recovery period for someone infecwith ted the Covid-19 (Kalantari et al., 2020). Statistical analysis showed that mortality increased significantly in the age group> 60 years. Mortality was significantly associated with old age. Based on the results of the current study, the prevalence of Covid-19 at a lower age (0–9 years) is lower and the mortality rate is higher in the elderly (Li et al., 2021). The adult age group has a more dynamic lifestyle with a high level of socialization. Young employees, for example, like to gather and discuss to complete a job in the office. Then, when working hours are over, one way to unwind and get tired is to visit the nearest cafe or restaurant. In essence,

activities that used to be routine during normal times are now at risk of transmission during a pandemic. Also, there is an assumption who are younger are more resistant to Covid-19, but this also contributes to the number of infections among the productive age Another suitable study was conducted in Iran, where 784 samples of nasopharyngeal/oropharyngeal swabs from patients with suspected Covid-19 symptoms from 24 February to 24 March 2020 were examined used the RT-PCR method. The results showed that the highest disease occurred in the 50–59 years age group, while the lowest was in the 0–9 years age group. The highest number of positive samples in terms of Covid-19 among suspected individuals was for patients aged> 80 years (89%), and the highest mortality rate was in the 70-79 years (31%) and> 80 years age range (Kalantari et al., 2020).

In this study, most of the Covid-19 patients gender 51%weree female. Gender affects clinical presentation, duration and severity of symptoms, and outcome of therapy in Covid-19 infection. This difference explains the vulnerability of men to Covid-19. One hundred twenty-seven patients had symptoms of Covid-19 and tested positive for Covid-19 (women 42.52%) at the Wuhan union hospital. In that retrospective analysis, it was found that men infected with Covid-19 reported more symptoms than women infected with Covid-19. Gender differences may be a factor in maintaining Covid-19 immunity in response to treatment, men, and women show statistically significant differences in relevance to cytokine production associated with more significant symptom development (Li et al., 2021).

Most of the respondents (70%) had Covid-19 moderate severity. Severity is the severity or severity of cases experienced by patients who are confirmed positive for Covid-19 (Burhan et al., 2015). The results showed that respondents who had moderate severity were 70%, while critical severity was 14%, and severe severity was 16%. The treatment received by patients can vary according to the level of severity (Pranita, 2020). Moderate severity is the dominant characteristic. Patients of moderate severity had a fever and respiratory symptoms, and pneumonia on radiological examinations of the lungs. The next dominant characteristic is severe severity. The severe severity of the patient is a condition of respiratory distress with a respiratory rate ≥ of 30 x / minute, SpO2 ≤ 93%, and PaO2 / FiO2 ≤ 300 mmHg. Patients with mild severity were not treated in isolation treatment rooms, so there were no respondents with mild severity (Nugraha & Handayani, 2020).

Comorbidity is a condition in which the patient already has a pre-existing disease, is chronic, and will aggravate the course of the Covid-19 disease. The results of the study that predominantly Covid-19 patients had comorbid hypertension 27%, diabetes mellitus 24%, and heart disease 15%. Supporting research based on existing data, comorbid hypertension and diabetes mellitus, male gender, and active smoking are risk factors for SARS-CoV-2 infection (Susilo et al., 2020). Significant risk associations were observed for age over 60 years, female gender, and various pre-existing disease conditions such as diabetes, kidney disease, liver disease, and heart disease. Asthma and diabetes were the dominant major comorbidities among patients, and patients with pre-existing diabetes developed the disease compared to other patients who were not diagnosed with a disease. Therefore, the elderly, women, and sufferers of comorbidities such as diabetes

mellitus, heart disease, kidney disease, and liver disease are the populations most vulnerable to contracting Covid-19 (Alam et al., 2021).

The most dominant clinical manifestations experienced by Covid-19 patients in this study. n the respiratory system are pneumonia 82%, shortness of breath 62%, coughing 59%, and 16% sore throat 16%. The results of other studies also showed that most patients infected with SARS-CoV-2 show symptoms in the respiratory system such as coughing, sneezing, and shortness of breath (Susilo et al., 2020). The incubation period for Covid-19 is between 3-and 14 days. It is marked by the levels of leukocytes and lymphocytes that are still normal or slightly decreased, and the patient has not felt any symptoms. Subsequently, the virus begins to spread through the bloodstream, especially to organs that express *Angiotensin-converting enzyme 2* (ACE2) in the lungs and the patient begins to experience mild symptoms. Four to seven days from the onset of symptoms, the patient's condition begins to worsen as marked by the onset of spasms, decreased lymphocytes, and worsening of lung lesions/pneumonia. If this phase is not resolved, Acute Respiratory Distress Syndrome (ARDS), sepsis, and other complications can occur. The S protein in SARS-CoV-2 facilitates the entry of the coronavirus into the target cells. Viral depends on the ability of the virus to bind to ACE2 in the lungs, namely extracellular membrane receptors expressed on epithelial cells, and on priming protein S to cellular proteases, namely transmembrane serine protease / TMPRSS2 (Handayani et al., 2020). TMPRSS2 is an endothelial cell surface protein that is involved in the viral entry and spread of coronaviruses including severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes Covid-19. Blocking TMPRSS2 could potentially be an effective clinical therapy for Covid-19 (Shabir, 2021). The virus then enters the cytoplasm, after coding occurs, the polyproteins are broken down by proteases, and chymotrypsin is activated. The resulting complex promotes the production of RNA via replication and transcription, grown into the lumen of the endoplasmic reticulum. The virions are then released from the infected cells by exocytosis. The released virus can infect target cells and cause the main symptoms and signs of Covid-19.

The results of this study showed that 3% of Covid-19 patients experience disturbances in the sensory perception system in the form of olfactory nerve disorders (decreased ability to smell) and none of them have impaired taste function. This finding is different from previous research in that anosmia was noted in 73% of patients before the Covid-19 diagnosis and was the initial symptom in 26.6% (Kaye et al., 2020). Anosmia or decreased ability to smell are the main manifestations of suspected Covid-19. SARS-CoV-2-related anosmia may be a new viral syndrome specific to Covid-19 and can be mediated by intranasal inoculation of SARS-CoV-2 into the olfactory neural circuitry (Han et al., 2020). Anosmia (loss of sense of smell) and dysgeusia (alteration of the sense of taste) have been reported in association with the Covid-19 pandemic. Dysgeusia may be related to alteration in the perception of taste due to loss of the sense of olfaction. Anosmia can be a presenting symptom of Covid-19, consistent with other emerging international reports. Anosmia may be critical in the timely identification of individuals infected with SARS-CoV2 who may be unwittingly transmitting the virus (Kaye et al., 2020). Less direct damage by the virus and less inflammation either due to virus characteristics or previous immunity could

explain less damage to the olfactory epithelium and/or central nervous system. Systemic and local inflammation in the olfactory epithelium, apoptosis of the olfactory receptor neurons and sustentacular cells, changes in the olfactory cilia and odor transmission, injury of microglial cells, effect on the olfactory bulb, epithelial olfactory injury, as well as damage of olfactory receptor neurons and olfactory stem cells neurons have been described as possible mechanisms (Rodriguez-Sevilla et al., 2022).

This study showed, that most clinical manifestations of Covid-19 patients in the nervous system are fever (56%) and headache (24%). Regular high fever in Covid-19 is considered to be an indicator of severe infection. In a study of 201 patients in Wuhan, high fever (>39°C) was associated with a higher likelihood of acute respiratory distress syndrome (Wu et al., 2020). The viral phase of the illness in Covid-19 is likely a manifestation of the body's immune response to the viral replication to augment immunity. If the viral infection does not resolve in due course, the disease process is complicated by the viral triggered state of dysregulated inflammation described as cytokine storm or secondary hemophagolymphocytosis, heralded by unremitting fever (Mehta et al., 2020).

Regarding the manifestation of headaches in Covid-19 patients, the result of this study is different from previous studies of 1968 participants with or without COVID-19 infection who reported headache attacks during the pandemic. Among them 714 (36.3%) had migraine and 1077 (54.7%) participants were diagnosed with tension-type headaches (Uygun et al., 2020). The underlying mechanisms of headache related to COVID-19 are not clear. A direct invasion of trigeminal nerve endings in the nasal or oral cavity by the virus seems one of the most reasonable mechanisms underlying headache close relation between headache and anosmia/ageusia. Some coronaviruses were shown to be neurotropic and former SARS-CoV has been observed in the human brain (Uygun et al., 2020). The mechanism of headache is also possible due to an inflammatory reaction. Neurological disorders in Covid-19 patients can be mediated by the systemic inflammatory state that occurs in Covid-19. Increased cytokines can cause microglia cells in the central nervous system to secrete pro-inflammatory cytokines that interfere with the work and resistance of the nervous system, causing fever and headache, or dizziness (Zhang et al., 2020).

The results of our study showed that Covid-19 patients experienced clinical manifestations in the circulatory system. 43% of them experienced decreased SpO2 (<90%), which is called happy hypoxia, 39% experienced tachycardia, 10% experienced cyanosis and 11% of them experienced pallor. The dominant characteristic in the circulatory system is happy hypoxia. This can be explained by the hypothesis of the involvement of neurological factors. In hypoxic conditions, the body will activate the carotid body chemoreceptors, and afferent signals are transmitted through the nucleus tractus solitarius. This results in increased respiratory rate, pulse/tachycardia, and a sensation of dyspnea. Covid-19 infects the brain via the olfactory bulb and olfactory nerves, via the trans-synaptic spread, eventually reaching the brain stem and the nucleus of the tractus solitarius. Inflammation of the nucleus solitary tract by viral invasion triggers afferent hypoxic stimulation from the carotid body which is not transmitted effectively to the solitary tract nucleus, resulting in an impaired

efferent respiratory response. This explains why Covid-19 patients show nearly normal breathing in the presence of severe hypoxia (Dewi & Utama, 2021).
Tachycardia is the next dominant characteristic in the cardiovascular and circulatory system as much as 39%. Cardiac manifestations etiology seems to be multifactorial, comprising direct viral myocardial damage, hypoxia, hypotension, enhanced inflammatory status, ACE2-receptors downregulation, drug toxicity, endogenous catecholamine adrenergic status, among others (Kochi et al., 2020). The condition of tachycardia cannot be separated from the role of the heart organ. A previous study showed that the pathophysiology involved in cardiovascular manifestations is thought to be a combination of various aspects. SARS-Cov-2 was found in the myocardial tissue at several autopsies. The results of pathological examinations in other patients also showed inflammatory cell infiltrates in the absence of SARS-CoV-2 in the myocardial tissue. The first mechanism that is thought to be involved is direct damage to heart tissue by a virus. It is mediated by ACE2 which is expressed in high concentrations in cardiac tissue. Another mechanism involved is an inflammatory condition that causes hyperpermeability and spasms which then results in microvascular damage. The systemic inflammation that occurs in Covid-19 can also play a role in myocardial tissue damage, a mechanism for the heart to compensate for tachycardia (Prakoeswa, 2020).

Our study showed that clinical manifestations of Covid-19 patients in the system of the hematology and lymphatic systems are an increase in D-dimer by 97%, lymphopenia at 85% and an increase in prothrombin time as much as 57%, platelets <100,000 / uL as much 5% and Fibrinogen <200 mg / dL 2%. Covid-2019 is associated with a strikingly high prevalence of coagulopathy and venous thromboembolism that may contribute to respiratory deterioration. Monitoring coagulation variables is important, as abnormal coagulation tests are related to adverse outcomes and may necessitate adjuvant antithrombotic interventions. In the initial phase of the infection, D-dimer and fibrinogen levels are increased, while activated partial prothrombin time, prothrombin time (Iba et al., 2020). Coagulopathy is a common feature of SARS-CoV-2 infection, and an increase in d-dimer is the most common finding. One of the larger initial studies found abnormally elevated d-dimer levels in 260 of 560 cases (46.4%) with a prevalence of 43% in non severe patients compared with 60% in critically ill ICU patients (Guan et al., 2020). The hematological examination is important to monitor disease progression, especially in the early stages of the Covid-19 disease journey. The predominant manifestation of the hematologic and lymphatic systems is an increase in D-dimers. Previous studies also showed that Covid-19 patients with the normal value of D-dimer were 40% while the abnormal result of D-dimer was 60% (Permana et al., 2021).

D-dimers are protein fragments that can help the blood clotting process. D-dimer is simply a laboratory test parameter that gives an idea of the presence or absence of clots in the blood. Normal values of D-dimer are 0-300 ug/ml. High D-dimer levels can predict the death of Covid-19 patients, because the higher the level, the greater the risk of the patient experiencing blockages due to blood clots. In Covid-19 patients, blood clots are prone to occur due to viral infection itself. SARS-CoV-2 virus infection causes systemic inflammation and excessive cytokine storms in the patient's body. Cytokine storms are the release of too many cytokines (cell-

stimulating biological compounds). As a result, the immune system damages the body. Systemic inflammation, this condition is any sign of inflammation that appears in the body due to infection. Both of these can eventually lead to activation of coagulation and thick blood or hypercoagulation (Guan et al., 2020; Iba et al., 2020; Permana et al., 2021).

The next dominant manifestation in the system of the hematology and lymphatic systems is lymphopenia. Based on the results of the lymphocyte examination, the lymphocyte value decreased as much as 43,4% of patients (Permana et al., 2021) Lymphopenia is a condition where the lymphocyte level is ≤ 1100 cells / μL. T lymphocytes have functioned as effector cells and regulatory cells. Lymphocytes as effector cells can recognize antigens (CD4 and T helper) and eliminate cells infected by infectious agents. Lymphocytes as regulatory cells help the work of B lymphocytes and suppress excessive cytotoxic T action. This depends on the stimuli that the lymphocyte cells get. Studies that support the results of lymphopenia occur in 75% of patients who are often accompanied by eosinopenia. The drastic increase in the production of pro-inflammatory cytokines such as interleukin-6 (IL-6) is thought to play a role in the mechanism of lymphopenia in Covid-19 (Prakoeswa, 2020).

Clinical manifestations of hematological disorders in the form of increased prothrombin time were also found in this study, experienced by 57% of Covid-19 patients. The previous study in Wuhan investigated the prognostic value of coagulation parameters in patients with COVID-19 based on at least 5 wk of follow-up. Prolonged prothrombin time at admission was found to be a strong predictor of a poor outcome in Covid-19 patients as well as age, respiration rate, and FDP concentration, which were also found to contribute to the risk of death in Covid-19 patients (Wang et al., 2020). Tang et al also reported increased d-dimers and fibrin degradation products along with mildly to moderately increased prothrombin times (PTs) and activated partial thromboplastin times (aPTT) in COVID-19. Of note is they reported that 71.4% of non survivors fulfilled the criteria of sepsis-induced coagulopathy, while 0.6% of the survivors met the criteria (Tang et al., 2020). The PT is a measure of the integrity of the extrinsic and final common pathways of the coagulation cascade that consists of tissue factors and factors VII, II, V, X, and fibrinogen. The elevation of PT international normalized ratio in infectious disease is usually accompanied by low factor levels of VII, IX a, and X. This is associated with bleeding risk and relates to thrombosis in the patients with infectious disease (Walborn et al., 2018).

The dominant clinical manifestations of the muscular system in Covid-19 patient were fatigue of as much as 37% and muscle pain of as much as 5%. The concept of fatigue has been used to describe a presumed tendency for people naturally to become tired of the rules and guidance they should follow to prevent the spread of Covid-19. Fatigue is an impaired ability to perform a mental or physical task as a result of depleted mental or physical resources. This is well studied in endurance sports and tasks that require sustained mental effort (Michie et al., 2020). Fatigue syndrome may result from damage to olfactory sensory neurons, causing an increased resistance to cerebrospinal fluid (CSF) outflow, and further leading to congestion of the glymphatic system with subsequent toxic build-up within the central nervous system (CNS).There has been concern about possible long-term

sequelae resembling myalgic encephalomyelitis / chronic fatigue syndrome in COVID-19 patients. Clarifying the mechanisms underlying such a “post-COVID-19 fatigue syndrome” is essential for the development of preventive and early treatment methods for this syndrome (Wostyn, 2021).

The results showed that Covid-19 patients experienced clinical manifestations of the digestive system were nausea as much as 26%, vomiting as much as 20%, diarrhea as much as 14%., and abdominal pain as much as 10%. The SARS-CoV-2 virus is known to bind closely to the ACE-2 receptor. ACE-2 receptors are abundant in epithelial cells in the liver and glandular cells in the spinal and gastric epithelium. This viral infection process can damage the liver and affect the work of the intestinal epithelial cells. Damage to the intestinal epithelium causes malabsorption, leading to manifestations of nausea, vomiting, and diarrhea (Prakoeswa, 2020). The presence of gastrointestinal manifestations is also associated with increased duration of treatment and worsening of the patient. Analysis of 82 patients who died in Wuhan China showed 78% of patients had significant liver damage with increased AST and ALT associated with the duration of disease progression from diagnosis to death (Kumar et al., 2020).

Our study showed the incidence of diarrhea in Covid-19 patients was as much as 14%. Clinical studies show an incidence rate of diarrhea ranging from 2% to 50% of cases. It may precede or trail respiratory symptoms. A pooled analysis revealed an overall percentage of diarrhea onset of 10.4% (D’amico et al., 2020). the studies provided additional evidence that coronaviruses may infect the gastrointestinal tract because high co-expression of ACE2 and TMPRSS2 was detected in enterocytes, the esophagus, and lungs (D’amico et al., 2020; Kawase et al., 2012). SARS-CoV uses the angiotensin-converting enzyme 2 (ACE2) and the serine protease TMPRSS2 for S protein priming. ACE2 and TMPRSS2 are not only expressed in the lung, but also in the small intestinal epithelia. ACE2 is expressed furthermore in the upper esophagus, liver, and colon. SARS-CoV-2 binding affinity to ACE2 is significantly higher (10–20 times) compared with SARS-CoV. Several reports indicate viral RNA shedding in stool is a detectable longer period than in nasopharyngeal swabs (D’amico et al., 2020).

The results showed that there were no clinical manifestations of the integumentary system in all respondents. Skin manifestations are rarely found in COVID-19 patients but there are 2 cases reported in China that show skin manifestations. Skin manifestations found in COVID-19 patients in several cases include morbilliform rash, urticaria, a rash with pokie, a rash with purpura, papulovesicular lesions, chilblain, and livedoid lesions (Rukmana, 2020). The skin manifestations found in Covid-19 patients in some cases include morbilliform rash, urticaria, rash with plexus, rash with purpuric, papulovesicular lesions, chilblain, and livedoid lesions. Another study also showed that Covid-19 patients with skin manifestations were also not found (Prakoeswa, 2020). The lack of tests and the number of Covid-19 cases that manifested clinical skin causes researchers unable to determine the relationship between the type of lesion and Covid-19 cases. The results of other studies suggest that the relationship between clinical skin manifestations and Covid-19 is not clear (Rukmana, 2020).

Nurses, doctors and health workers must correctly identify each of the clinical manifestations experienced by Covid-19 patients. Appropriate evaluation of each clinical manifestation of Covid-29 patients is needed to determine the appropriate action.

Research limitations

The data of this study were only obtained based on the documentation of the patient's medical records without direct examination and observation. This research was also only conducted in one location.

Conclusion

The dominant clinical manifestations in the respiratory system were pneumonia (82%), shortness of breath (62%), and coughing (59%). Clinical manifestations in the sensory perception (decrease of smell function) only 3% experienced by patients. The clinical manifestations of the nervous system are fever (56%) and headaches (24%). The clinical manifestations of the circulatory system are a decrease of SpO2 <90% (43%) and tachycardia (39%). The clinical manifestations of the hematological and lymphatic systems were an increase in D-dimer by 97%, lymphopenia by 85%, and an increase in prothrombin time by 57%. The dominant clinical manifestations of the muscular system were fatigue (37%) and muscle pain (5%). The dominant clinical manifestations of the digestive system were nausea (26%), vomiting (20%), and diarrhea (14%). There were no clinical manifestations of the integumentary system in all respondents. Appropriate evaluation of each clinical manifestation of Covid-29 patients is needed to determine the appropriate action.

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References

Alam, M. R., Kabir, M. R., & Reza, S. (2021). Comorbidities might be a risk factor for the incidence of COVID-19: Evidence from a web-based survey. Preventive Medicine Reports, 21, 101319.

Burhan, E., Susanto, A. D., Nasution, S. A., Ginanjar, E., Pitoyo, C. W., Susilo, A., Firdaus, I., Santoso, A., Juzar, D. A., Arif, S. K., Lolong, N. G. ., Wulung, Damayanti, Wiyono, T. W. H., Prasenohadi, Isbaniah, F., Handayani, D., Soedarsono, Harsini, … Katu, S. (2015). Pengaruh pendidikan kesehatan secara individual tentang pembatasan asupan cairan terhadap pengatahuan tentang pembatan cairan IDWG (Interdialitic Weight Gain) pada pasien hemodialisis. Jurnal Online Mahasiswa, 2(2).

Burhan, E., Susanto, A. D., Nasution, S. A., Ginanjar, E., Pitoyo, C. W., Susilo, A., Firdaus, I., Santoso, A., Juzar, D. A., Arif, S. K., Wulung, N. G. ., Damayanti, T., Wiyono, W. H., Prasenohadi, Isbaniah, F., Handayani, D.,

Soedarsono, H., Sugiri, J. R., Afiatin, … IDAI, T. C.-19. (2020). Protokol Tatalaksana COVID-19 (1st ed., Vol. 1). PDPI, PERKI, PAPDI, PERDAKIN, IDAI.

D'amico, F., Baumgart, D. C., Danese, S., & Peyrin-Biroulet, L. (2020). Diarrhea during COVID-19 infection: pathogenesis, epidemiology, prevention, and management. Clinical Gastroenterology and Hepatology, 18(8), 1663–1672.

Dewi, D. A. P., & Utama, W. T. (2021). 'Happy' Hipoksemia pada pasien COVID-19. Medical Profession Journal of Lampung, 10(4), 677–684.

Fakhrul Rozi Yamali1, R. N. P. (2020). Dampak Pandemi Covid-19 Terhadap Ekonomi Indonesia. Medcom,Id, 4(2), 1. https://doi.org/10.33087/ekonomis.v4i2.179

Guan, W., Ni, Z., Hu, Y., Liang, W., Ou, C., He, J., Liu, L., Shan, H., Lei, C., & Hui, D. S. C. (2020). Clinical characteristics of coronavirus disease 2019 in China. New England Journal of Medicine, 382(18), 1708–1720.

Han, A. Y., Mukdad, L., Long, J. L., & Lopez, I. A. (2020). Anosmia in COVID-19: mechanisms and significance. Chemical Senses, 45(6), 423–428.

Handayani, D., Hadi, D. R., Isbaniah, F., Burhan, E., & Agustin, H. (2020). Penyakit virus Corona 2019. Jurnal Respirologi Indonesia, 40(2), 119–129.

Iba, T., Levy, J. H., Levi, M., Connors, J. M., & Thachil, J. (2020). Coagulopathy of coronavirus disease 2019. Critical Care Medicine.

Kalantari, H., Tabrizi, A. H. H., & Foroohi, F. (2020). Determination of COVID-19 prevalence with regards to age range of patients referring to the hospitals located in western Tehran, Iran. Gene Reports, 21, 100910.

Kawase, M., Shirato, K., van der Hoek, L., Taguchi, F., & Matsuyama, S. (2012). Simultaneous treatment of human bronchial epithelial cells with serine and cysteine protease inhibitors prevents severe acute respiratory syndrome coronavirus entry. Journal of Virology, 86(12), 6537–6545.

Kaye, R., Chang, C. W. D., Kazahaya, K., Brereton, J., & Denneny III, J. C. (2020). COVID-19 anosmia reporting tool: initial findings. Otolaryngology–Head and Neck Surgery, 163(1), 132–134.

Kementerian Kesehatan Republik Indonesia. (2020). Pedoman dan Pencegahan Coronavirus (COVID- 19). Pedoman Dan Pencegahan Coronavirus (COVID- 19), 4, 1–214. https://doi.org/10.33654/math.v4i0.299

Kochi, A. N., Tagliari, A. P., Forleo, G. B., Fassini, G. M., & Tondo, C. (2020). Cardiac and arrhythmic complications in patients with COVID-19. Journal of Cardiovascular Electrophysiology, 31(5), 1003–1008.

Komite Penanganan Covid-19 dan Pemulihan Ekonomi Nasional, K. (2020). Data Sebaran Covid-19 Di Indonesia. Beranda.

Kumar, V. C. S., Mukherjee, S., Harne, P. S., Subedi, A., Ganapathy, M. K., Patthipati, V. S., & Sapkota, B. (2020). Novelty in the gut: a systematic review and meta-analysis of the gastrointestinal manifestations of COVID-19. BMJ Open Gastroenterology, 7(1), e000417.

Li, X., Liu, L., Yang, Y., Yang, X., Wang, C., Li, Y., Ge, Y., Shi, Y., Lv, P., & Zhou, H. (2021). Gender-associated difference following COVID-19 virus infection: implications for thymosin alpha-1 therapy. International Immunopharmacology, 90, 107022.

Mehta, P., McAuley, D. F., Brown, M., Sanchez, E., Tattersall, R. S., & Manson, J. J. (2020). COVID-19: consider cytokine storm syndromes and immunosuppression. The Lancet, 395(10229), 1033–1034.

Michie, S., West, R., & Harvey, N. (2020). The concept of "fatigue" in tackling covid-19. BMJ, 371, m4171. https://doi.org/10.1136/bmj.m4171

National Institutes of Health, N. (2020). Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. Disponible en: https://covid19treatmentguidelines.nih.gov/. Nih, 2019, 130.

Nugraha, E. M., & Handayani, I. G. A. K. R. (2020). Kemenkes nomor hk. 01.07/menkes/382/2020 sebagai pembuka jalan perekonomian Indonesia dalam masa new normal. Seminar Nasional & Call for Papers 2020, 39.

Pemerintah Kota Semarang, P. (2020). Dashboard Data Covid Kota Semarang.

Permana, A., Yari, C. E., & Aditya, A. K. (2021). Gambaran D-Dimer dan limfosit pada pasien terkonfirmasi Covid-19 di RS Haji Jakarta. Anakes: Jurnal Ilmiah Analis Kesehatan, 7(1), 62–71.

Prakoeswa, F. R. S. (2020). Dasamuka Covid-19. Medica Hospitalia: Journal of Clinical Medicine, 7(1A), 231–240.

Rodriguez-Sevilla, J. J., Güerri-Fernádez, R., & Recasens, B. B. (2022). Is there less alteration of smell sensation in patients with Omicron SARS-CoV-2 variant infection? Frontiers in Medicine, 9, 1–6.

Rukmana, D. M. (2020). Manifestasi kulit pada pasien COVID-19. Medical Profession Journal of Lampung, 10(3), 437–442.

Salma Matla Ilpaj, N. N. (2020). Analisis Pengaruh Tingkat Kematian Akibat Covid-19 Terhadap Kesehatan Mental Masyarakat di Indonesia. 3.

Shabir, O. (2021). What is TMPRSS2. https://www.news-medical.net/health/What-is-TMPRSS2.aspx

Susilo, A., Rumende, C. M., Pitoyo, C. W., Santoso, W. D., Yulianti, M., Herikurniawan, H., Sinto, R., Singh, G., Nainggolan, L., & Nelwan, E. J. (2020). Coronavirus disease 2019: Tinjauan literatur terkini. Jurnal Penyakit Dalam Indonesia, 7(1), 45–67.

Tang, N., Li, D., Wang, X., & Sun, Z. (2020). Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. Journal of Thrombosis and Haemostasis, 18(4), 844–847.

Tim Covid RSUP Dr Kariadi Semarang, C. (2020). Data Covid RSUP Dr Kariadi Semarang.

Uygun, Ö., Ertaş, M., Ekizoğlu, E., Bolay, H., Özge, A., Kocasoy Orhan, E., Çağatay, A. A., & Baykan, B. (2020). Headache characteristics in COVID-19 pandemic-a survey study. The Journal of Headache and Pain, 21(1), 1–10.

Walborn, A., Williams, M., Fareed, J., & Hoppensteadt, D. (2018). International normalized ratio relevance to the observed coagulation abnormalities in warfarin treatment and disseminated intravascular coagulation. Clinical and Applied Thrombosis/Hemostasis, 24(7), 1033–1041.

Wang, L., He, W.-B., Yu, X.-M., Hu, D.-L., & Jiang, H. (2020). Prolonged prothrombin time at admission predicts poor clinical outcome in COVID-19 patients. World Journal of Clinical Cases, 8(19), 4370.

WHO. (2020). Rapid hospital readiness checklist: Interim Guidance.

World Health Organisation. (2020). Draft landscape of COVID-19 candidate vaccines. World Health Organisation, June, 3.

Wostyn, P. (2021). COVID-19 and chronic fatigue syndrome: Is the worst yet to come? Medical Hypotheses, 146, 110469. https://doi.org/https://doi.org/10.1016/j.mehy.2020.110469

Wu, C., Chen, X., Cai, Y., Zhou, X., Xu, S., Huang, H., Zhang, L., Zhou, X., Du, C., & Zhang, Y. (2020). Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Internal Medicine, 180(7), 934–943.

Zhang, H., Penninger, J. M., Li, Y., Zhong, N., & Slutsky, A. S. (2020). Angiotensin-converting enzyme 2 (ACE2) as a SARS-CoV-2 receptor: molecular mechanisms and potential therapeutic target. Intensive Care Medicine, 46(4), 586–590.