Original Article

Differences In Interleukin-6 and Liver Enzyme Level Based On Clinical Severity of COVID-19 Patients at Dr. M. Djamil General Hospital, Padang

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Abstract

Background: COVID-19 pathogenesis involves the release of proinflammatory cytokines and chemokines, known as a "cytokine storm." Interleukin-6 (IL-6) plays a key role in initiating cytokine storms. Cytokine storm causes multiple organ complications. Liver injury affects 14% to 53% of COVID-19 patients and is manifested by increased liver enzymes. This study evaluated differences in IL-6 and liver enzyme levels based on clinical severity in COVID-19 patients.

Method: A retrospective cross-sectional study was conducted. COVID-19 patients treated at Dr. M. Djamil General Hospital, Padang, from January 1, 2021, to December 31, 2021, and who met the inclusion and exclusion criteria, were the research subjects. The Kruskal-Wallis test was performed to analyze differences in IL-6, SGOT, and SGPT levels based on clinical severity.

Results: Most participants (42.06%) were under 50 years old, half were female (56.15%), obesity was the most common comorbidity (41.39%), and moderate severity was most common (42.06%). The majority of the subjects, 87.47%, had elevated IL-6 levels (≥7 pg/mL). SGOT levels of ≥32 IU/L (46.76%) and SGPT levels of ≥31 IU/L (41.39%) were found in less than half of the subjectsClinical severity was significantly associated with IL-6 levels, resulting in a significant difference in IL-6 levels (P<0.05). The clinical severity of COVID-19 patients at Dr. M. Djamil General Hospital, Padang, resulted in a significant difference in SGOT and SGPT levels (P<0.05).

Conclusion: IL-6 levels differed based on clinical severity in COVID-19 patients. SGOT and SGPT levels also differed by clinical severity.

Keywords: clinical severity, COVID-19, IL-6, liver enzyme

INTRODUCTION

The coronavirus disease 2019 (COVID-19) caused by the Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-2) is a threat to public health globally.[1,2] The spectrum of clinical presentations of the disease ranges from asymptomatic and mild-to-moderate to

severe, life-threatening illness. Coronavirus disease 2019 causes respiratory problems such as pneumonia and can develop into Acute Respiratory Distress Syndrome (ARDS), septic shock and multi-organ dysfunction, including the liver, kidneys, and heart.[2]

Interleukin-6 (IL-6) is the primary initiator of cytokine storms.[3] There has been research to determine the benefits of the initial IL-6 examination as a predictor of the severity of COVID-19 disease. According to Liu et al and Gubernatorova et al, IL-6 levels are an important factor in predicting the progression of COVID-19 infection.[4,5] Herold et al investigated the predictive value of various cytokines and concluded that IL-6 is the best predictor of COVID-19 disease progression, outperforming C-reactive protein (CRP) and other inflammatory markers.[6]

Cytokine storms can lead to complications in organs other than the lungs, such as the heart, kidneys, gastrointestinal tract, and liver.[2,6] Liver injury occurs in 14% to 53% of COVID-19 patients and is characterized by elevated hepatic enzyme levels of serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), and elevated bilirubin.[7]

However, the exact mechanism of liver damage remains unclear. Bourgonje et al concluded that liver damage in COVID-19 can occur through a variety of mechanisms, including hepatotoxicity from antiviral drugs and direct viral infection of liver cells and bile duct cells via angiotensin-converting enzyme 2 (ACE2), which is a SARS-CoV-2 receptor.[8] Another mechanism is hepatic cell ischemia caused by cytokine storms.

McConnell et al first reported a link between IL-6, hyperinflammation, and liver injury in COVID-19 patients, which found that higher IL-6 and coaguolpathy were associated with liver injury in COVID-19 patients.[9] Da et al also stated that liver injury in COVID-19 is related to the severity of COVID-19 and hyperinflammation, specifically an increase in inflammatory markers such as IL-6, C-reactive protein (CRP), lactate dehydrogenase (LDH), and ferritin.[10] Ponziani et al discovered a correlation between abnormal liver function tests and IL-6 levels, proving that COVID-19 liver injury was caused by systemic inflammation.[11]

Based on this background, this study aims to describe the differences in IL-6 and liver enzyme levels based on the clinical severity of COVID-19 patients at Dr. M. Djamil General Hospital, Padang.

METHOD

This was a retrospective cross-sectional study. The study was carried out at Dr. M. Djamil General Hospital, Padang, from April 2022 to November 2022. COVID-19 patients treated at Dr. M. Djamil General Hospital, Padang, between January 1 and December 31, 2021, who had IL-6, SGOT, and SGPT test results, complete medical records including age, gender, and comorbidities, and were aged ≥18 years, were included. Exclusion criteria included patients with autoimmune diseases

(rheumatoid arthritis, systemic lupus erythematosus/SLE, rheumatic heart disease, primary Sjogren's syndrome, fibrous bone dysplasia, juvenile idiopathic arthritis/JIA, and uveitis), chronic inflammation (Erdheim's disease, Chester, Behcet's syndrome, systemic sclerosis, large cell arteritis), malignancy (ovarian cancer, colorectal cancer, prostate cancer, breast cancer, bone cancer, hematologic cancers, pancreatic, lung, liver, and lymphatic cancers, hepatoma), post-organ transplantation, hepatitis, chronic liver disease.

RESULT

There were 447 subjects in this study. Table 1 shows the characteristics of COVID-19 patients treated at RSUP Dr. M. Djamil Padang. Most subjects (42.06%) were less than 50 years old, half were female (56.15%), obesity was the most common comorbidity (41.39%), and most patients had moderate disease severity (42.06%). Elevated IL-6 levels (>7 pg/mL) were found in 87.47% of subjects. SGOT levels of ≥32 IU/L (46.76%) and SGPT levels of ≥31 IU/L (41.39%) were found in less than half of the subjects.

The initial analysis was carried out by using Kolmogorov-Smirnov to test the normality of the data on IL-6, SGOT, and SGPT levels based on the clinical severity of the COVID-19 patient. The non-parametric Kruskal-Wallis statistical test was performed for further analysis because the data were not normally distributed.

Table 1. Characteristics of COVID-19 Patients Treated at Dr. M. Djamil General Hospital, Padang

Variable	n	%
Gender		
Female	251	56.15
Male	196	43.85
Age		
<50	188	42.06
50-59	112	25.05
60-69	90	20.13
≥70	57	12.75
Comorbid		
Obesity	185	41.39
Hypertension	55	12.30
Diabetes Mellitus	51	11.40
Cardiovascular	23	5.14
Chronic Kidney	17	3.80
Disease		
Chronic Pulmonary	10	2.23
Cerebrovascular	21	4.69
Clinical Degree		
Mild	24	5.37
Moderate	188	42.06
Severe	96	21.48
Critically ill	139	31.10
IL-6		
<7 pg/mL	56	12.53
≥7 pg/mL	391	87.47
SGOT		
<32 IU/L	238	53.24
≥32 IU/L	209	46.76
SGPT		
<31 IU/L	262	58.61
≥31 IU/L	185	41.39

Note: IL-6=interleukin 6; SGOT=serum glutamic oxaloacetic transaminase; SGPT=serum glutamic pyruvic transaminase

Table 2 shows that patients with critical clinical severity have a higher level of IL-6 (92.20 pg/mL) than patients with severe clinical (75.30 pg/mL), moderate clinical (17.10 pg/mL), and mild clinical (11.90 pg/mL). IL-6 levels differed significantly across severity groups ($P<0.05$).

Table 2. IL-6 Level Differences Based on Clinical Severity of COVID-19 Patients Treated at Dr. M. Djamil General Hospital, Padang

Clinical Severity	IL-6 Levels [Median (Min-Max)]	P
Mild	11.90 (3.50 – 272.70)	0.0001*
Moderate	17.10 (1.05 – 3617.00)	
Severe	75.30 (2.49 – 3287.00)	
Critical	92.20 (1.50 – 3287.00)	

Note: *P<0.05 significant with Kruskal-Wallis test

Table 3 shows that SGOT levels are higher at critical and severe clinical severity (39.00 IU/L) than at moderate (24.00 IU/L) and mild (21.00 IU/L). The findings revealed a significant difference in SGOT levels based on the clinical severity of COVID-19 patients at Dr. M. Djamil General Hospital, Padang (P<0.05). SGPT level in critical clinical cases was higher (31.0 IU/L) than in severe clinical cases (28.50 IU/L), but mild clinical levels were higher (22.50 IU/L) than moderate clinical (20.00 IU/L). SGPT levels also showed significant differences across clinical severity levels (P<0.05).

Table 3. Differences in Liver Enzyme Levels Based on Clinical Severity of COVID-19 Patients Treated at RSUP DR. M Djamil Padang

Clinical Severity	SGOT[a]	P	SGPT[a]	P
Mild	21.50 (13-49)	0.0001*	22.50 (8-95)	0.0001*
Moderate	24.00 (7-220)		20.50 (5-213)	
Severe	39.00 (11-439)		28.50 (3-402)	
Critical	39.00 (5-3103)		31.00 (6-1753)	

Note: *P<0.05 significant with Kruskal-Wallis test; [a]Median (Min-Max); IL-6=interleukin 6; SGOT=serum glutamic oxaloacetic transaminase; SGPT=serum glutamic pyruvic transaminase

DISCUSSION

According to the study's findings, women were treated more frequently than men (56.15% versus 43.8 %). The higher number of female cases may reflect regional COVID-19 distribution in West Sumatra, where females outnumber males 54.2% to 45.1%.[12] The findings of this study are similar to those of Mardewi's study in Bali, where women is more women than men (53.9% vs. 46.1%).[13] In Liu et al's study of 69 severe cases of COVID-19, there were 52.17% more women than men.[14] Kuehn's study also found a higher prevalence of COVID-19 in women (70%), but a higher death rate from COVID-19 in men.[15]

Another study, conducted in Germany by Doerre et al, reported that the incidence of COVID-19 was higher in working-age women. Higher contact rates may explain the greater number of female COVID-19 cases. Doerre's contact matrices research discovered a pattern in which women have a higher presentation of contact with COVID-19 cases (13-26%), but as age increases, especially in the 50-69 year range, men have a 9%-14% higher contact presentation. Due to a greater number of contacts, young and middle-aged women contribute to an increase in the incidence of infection.[16]

The findings of this study are inversely proportional to those of a study conducted in Ontario, Canada, which found that COVID-19 events were more common in men. These differences may be due to gender roles, behavior, and

occupational exposure that put men at a higher risk of COVID-19 infection. Men are more likely to work in fields that require them to work outside the home and interact with a large number of people. Furthermore, men are more likely to engage in risky behaviors such as smoking and drinking alcohol. Smoking is associated with higher ACE2 expression in type 2 pneumocytes and alveolar macrophages, resulting in a higher prevalence of COVID-19 in this subgroup.[17]

Women are thought to be less susceptible to COVID-19 than men due to differences in innate immunity, steroid hormones, and sex chromosomal factors. When compared to men, the immune regulatory gene encoded by the X chromosome in women causes inflammation and lower viral loads. T cells and TLR7 were found to be higher in women who had a better immune response.[18]

The majority of patients in this study were 18-49 years old (42.06%), followed by 50-59 years (25.05%), 60-69 years (20.13%) and 70 years (12.75%). The findings of this study are based on the discovery that people under the age of 50 have a twofold higher likelihood of close contact with COVID-19 cases. According to the Centers for Disease Control (CDC), social interaction, workplaces, and community transmission all play a role in the sharp increase in COVID-19 cases among young adults. Individuals aged 18–29 are more vulnerable due to lower adherence to handwashing, mask use, and social distancing.[19]

The findings of this study are consistent with research conducted by Malmgren et al in Washington in 2021, which discovered that the young adult age group (20-39 years) has the highest incidence of COVID-19. COVID-19 incidence decreased in the older age group and increased in the 20-39 year age group after the peak (March 22, 2020), rising from 20% to 40% of total cases.[19] Another study conducted by Yu in South Korea in 2020 found that the age group 20-39 years had the highest incidence of COVID-19 (37%), followed by the age group 40-59 years (31%).[20]

In contrast to the findings of this study, Dhama et al found that the elderly, particularly those with comorbidities, are more vulnerable to COVID-19. Preliminary COVID-19 studies revealed that there were more cases in the 49-55-year-old age group, indicating that the elderly, particularly those with comorbidities, are more vulnerable to COVID-19.[21]

Preliminary COVID-19 research found that the 49-55 age group had the highest number of cases. Subsequent studies with a larger sample size revealed that the prevalence of COVID-19 is higher in people over 60 than in younger people. Specific risk factors for the geriatric population include age-related decline in the physiological function of various organs, including the respiratory system, and impaired mucociliary clearance of foreign particles or microorganisms. Furthermore, aging has been linked to a

decline in the physiological functions of various vital organs as well as innate and adaptive immune defenses.[21]

The majority of patients (87.47%) had IL-6 levels of ≥7 pg/ml. Interleukin-6 is a cytokine that appears during the early stages of infection, particularly in the mucosa.[22] The biological effects of IL-6 production have been linked to both pro- and anti-inflammatory effects, emphasizing IL-6's importance in the activation and regulation of immune responses. Controlling monocyte differentiation into macrophages by regulating macrophage colony-stimulating factor, increasing B-cell IgG by regulating IL-21 expression, negative regulation of dendritic cell maturation through activation of the STAT3 signaling pathway, and enhancing Th2 response by inhibiting Th1 polarization are all biological activities influenced by IL-6 production.[22,23]

The combination of IL-6 and transforming growth factor beta induces the differentiation of naive CD4 cells into Th17 cells, which play an important role in mucosal defense against pathogens. The synergistic interaction of IL-6, IL-7, and IL-15 can also induce CD8 T cell differentiation. The effect of viruses on the body is to make the adaptive immune system release interferon; however, in the case of the SARS-CoV-2 infection, interferon release is delayed. This delay causes the viral load to rise, resulting in the uncontrolled release of inflammatory cytokines like IL-6. This overexpression can result in tissue damage to infected organs and worsen clinical outcomes.[22,23]

The findings of this study are comparable to those of Ananda et al in Palembang, who divided patients into two groups based on IL-6 levels, normal and high. This study discovered that only 16.1% of COVID-19 patients had normal IL-6 levels, while the majority (83.9%) had high IL-6 levels (100 pg/ml).[24] Another study, conducted in 140 COVID-19 patients by Liu et al, discovered that 67.9% of patients had IL-6 levels greater than 7 pg/mL.[4]

Liver enzymes showed an increase in SGOT (>32 IU/L) in 46.76% of patients and an increase in SGPT (>31 IU/L) in 41.39% of patients in this study. Several mechanisms have been proposed to explain the pathobiology of COVID-19 liver injury. The SARS-CoV-2 virus can bind to ACE2 on cholangiocytes, resulting in a systemic inflammatory response and liver damage. Other mechanisms that can cause hepatocyte injury include cytokine storms caused by hyperinflammation and metabolic disturbances caused by hypoxia.[25]

Other research suggests that several etiologies, including direct hepatic injury, inflammatory response, congestive hepatopathy, hepatic ischemia, drug-induced liver injury (DILI), and muscle damage, may contribute to elevated liver enzymes in SARS-CoV-2 patients. The findings of this study are similar to those of Hwaiz et al, who found that 40% of COVID-19 patients had elevated SGOT levels and 34.7% had elevated SGPT levels.[25] Another study, conducted in 2022 in India by Harisha et al, discovered higher

incidences of SGOT and SGPT, at 40.2% and 65.5%, respectively.[26]

The three most common comorbidities in this study were obesity (41.39%), hypertension (12.30%), and diabetes mellitus (11.40%). The findings of this study are consistent with the demographic information provided by the CDC for COVID-19 patients. The study, which included 180 COVID-19 patients who were hospitalized, discovered that 89.3% of them had comorbidities, with obesity, hypertension, and diabetes mellitus being the most common.[27] The findings of this study are also supported by reports from two Spanish hospitals' intensive care units, which identified obesity as the most common co-morbidity, accounting for 48% of all cases.[28]

Obesity has four mechanisms that increase the risk of SARS-CoV-2 infection and place patients in a severe clinical stage. First, because it increases ACE-2 expression, adipose tissue can serve as a reservoir for virus production, allowing SARS-CoV-2 to enter cells. Second, obesity is associated with impaired immune function, which prevents viral replication. Third, obesity increases inflammation, which affects the lung parenchyma and bronchi. Fourth, obesity can reduce lung capacity and reserves, making ventilation more difficult.[29]

In contrast to the findings of this study, Karyono et al in Indonesia reported in 2020 that hypertension (52.1%), diabetes mellitus (33.6%), and cardiovascular disease (20.9%) were the three most common comorbidities among confirmed COVID-19 patients. The most common cause of COVID-19 infection has been identified as hypertension. People with high blood pressure, according to the theory, have more RAAS inhibitors like ACE-2, which are linked to an increased susceptibility to COVID-19.[30] Diabetes and COVID-19 may be caused by SARS-CoV-2-induced chronic inflammation, increased coagulation activity, a weakened immune response, or direct pancreatic damage. Diabetes makes people more susceptible to bacterial, fungal, parasitic, and viral infections.[31]

In this study, the most severe clinical severity of COVID-19 was found to be moderate (42.06%), followed by critical (31.10%). The findings of this study are consistent with the characteristics of patients found in a study conducted by Liu in Beijing in 2020, which discovered that the majority of patients (49.53%) had moderate degrees, followed by critical degrees (23.08%).[32] This study's findings differ from those of Li et al in Wuhan, China, who reported that 49.1% of patients in the severe category were treated at Tongji Hospital from January 26 to February 5, 2020. This disparity in findings could be attributed to the fact that Wuhan experienced its highest peak of the COVID-19 outbreak from mid-January to early February, with familial clusters and a high prevalence of COVID-19 in older adults.[33]

The prevalence of mild clinical symptoms in COVID-19 patients was found to be 5.4% in this study. According to the COVID-19 management guidelines,

COVID-19 patients with mild clinical symptoms receive outpatient treatment followed by independent isolation, but patients with mild COVID-19 require hospitalization if comorbidities or coincidences exist.[2]

According to the findings of this study, IL-6 levels were higher in patients with critical clinical conditions than in patients with severe, moderate, and mild conditions. There is a significant difference in IL-6 levels between COVID-19 patients treated at Dr. M. Djamil General Hospital, Padang, based on clinical severity. The higher the clinical severity, the higher the IL-6 level tends to be.

Monocytes and macrophages produce IL-6 in the early stages of infection. Interleukin 6 plays a critical role in the cytokine storm in COVID-19. Interleukin-6 is a pro-inflammatory molecule that can activate inflammatory cells and other mediators in the lungs, causing parenchymal damage and dyspnea. High levels of IL-6 prevent NK cells from releasing perforin and granzyme B, preventing infected cells from dying and resulting in continuous antigen stimulation. Increased IL-6 levels are followed by an increase in immune cell proliferation, which causes the release of proinflammatory cytokines and chemokines. This is referred to as a "cytokine storm." A cytokine storm causes lung damage, which leads to ARDS and multi-organ dysfunction.[34]

Coome et al discovered that serum IL-6 levels were significantly higher in patients with severe COVID-19 in a meta-analysis study.[35] According to available data, elevated levels are significantly associated with negative outcomes such as intensive care, ARDS, and death. Serum IL-6 levels in these COVID-19 patients were nearly three times higher than in those without complications. According to Chen et al, a cut-off value of 55 pg/mL could indicate a severe course of the disease, whereas in other studies, a cut-off value of 80 pg/mL could indicate mortality.[36]

A retrospective analysis of IL-6 levels in serum samples of 68 infected patients conducted by Sun et al in 2020 discovered that IL-6 levels were significantly higher in patients with severe COVID-19 symptoms than mild symptoms, and that of the 40 seriously ill patients, 8 developed a critical degree of COVID-19 and experienced respiratory failure. Interleukin-6 levels were significantly higher in these eight patients than in 32 other critically ill patients, with IL-6 levels in one patient increasing up to 23 times after developing a critical illness.[37] These findings were nearly identical to those found in this study, where the highest IL-6 value was found in one patient in the critical clinical degree group, with an IL-6 value of 3287 pg/mL.

This study also discovered that 70.8% of mild clinical COVID-19 patients had an increase in IL-6 7 pg/mL, with the highest IL-6 level being 272.70 pg/mL. In the study by Gao et al, IL-6 levels in mild clinical COVID-19 were also elevated. Age, gender, the immune system, and

comorbidities are all factors that influence these conditions.[38]

Sun et al's study confirmed that IL-6 is closely related to infection severity, but it also demonstrated that IL-6 plays an important role in the occurrence of COVID-19 lung injury. Interleukin-6 can rapidly activate pathogenic T cells during COVID-19 infection, causing them to produce GM-CSF, IL-6, and other factors. GM-CSF then activates CD14+ and CD16+ inflammatory monocytes, increases IL-6 production, and initiates a positive feedback loop, causing diffuse damage to alveolar and pulmonary capillary endothelial cells. Large amounts of exudate can clog the airways, resulting in pneumonia and ARDS.[37]

This study reported that SGOT and SGPT levels differed depending on the clinical severity of COVID-19 patients. There is a trend toward higher SGOT and SGPT levels as clinical severity rises. In this study, SGOT levels were 39.00 IU/L and SGPT levels were 31.00 IU/L in the clinically critical group. In mild- moderate cases, the majority of patients with clinically critical degrees had increased SGOT, namely 60.4% and 51.1% of 139 patients, respectively, whereas only a few patients had abnormal SGOT and SGPT values.

The following hypotheses explain the mechanism of COVID-19-induced liver injury: First, the replication of the SARS-CoV-2 virus in the liver causes direct cytotoxicity.[11,43] SARS-CoV-2 RNA is found in stool and blood samples, proving hepatic exposure to the virus in approximately 2-10% of COVID-19 patients.[10] Although ACE2 expression was higher in cholangiocyte cells, increases in gamma-glutamyl transferase and alkaline phosphatase as biomarkers of cholangiocyte cell injury have been reported in a few studies.[39]

The second is immune-mediated liver damage as a result of COVID-19's systemic inflammatory response syndrome (SIRS), hypoxia as a result of respiratory failure, vascular changes as a result of coagulopathy, or endothelial or cardiac congestion as a result of right heart failure.[40] Ponziani et al discovered a link between abnormal liver function tests and IL-6 levels, demonstrating that liver injury is a result of systemic inflammation in COVID-19.[11]

According to this study, there is a trend toward higher IL-6, SGOT, and SGPT levels as the clinical stage of COVID-19 patients advances. McConnel et al described the relationship between IL-6 and liver injury as follows: an increase in IL-6 causes IL-6 signaling in the liver sinusoidal endothelial cell (LSEC) via the Janus kinase (JAK) or the signal transducer and activator of transcription (STAT), resulting in an increase in pro-coagulant and pro-inflammatory genes, which activate the thrombosis pathway and cause hypercoagulopathy. Hypercoagulopathy results in vascular changes that can harm hepatocyte cells.[9]

According to the findings of various studies, there is a correlation between the severity of COVID-19 and the degree of liver dysfunction. The findings of this study are consistent with those of Hwaiz et al,

who discovered that the majority of patients with abnormal liver enzyme levels received a course of COVID-19 with more severe signs and symptoms (31 out of 48 cases).[25] Patients with a severe case of COVID-19 have more liver dysfunction.[39]

According to Huang et al, 62% of the 13 patients treated in the intensive care unit had an increase in AST, compared to 25% of the 28 patients treated in the usual room.[41] According to reports, COVID-19 clinical severity and advanced age predispose to more severe liver damage. This necessitates more stringent clinical monitoring and consideration when administering therapy to certain individuals who are at risk of liver injury.[42]

In COVID-19 patients, the prevalence of elevated hepatic enzyme levels ranges from 2.5% to 76.3%.[40] Boregowda et al found that patients with severe COVID-19 had significantly higher liver enzyme levels than patients with mild COVID-19 in a meta-analysis study. A pooled analysis also revealed that the non-survival group had significantly higher serum hepatic enzyme activity than the surviving group.[43]

Higuera et al reported an increase in hepatic enzyme levels of 16-62% in COVID-19 patients in another study. Patients with severe COVID-19 have abnormal liver enzyme levels.[44] According to one study, 52% of patients who died had elevated SGOT levels, with an average serum concentration of 45 UI/L.[45]

In their study, Lei et al discovered that in COVID-19, there was an increase in SGOT levels first, followed by an increase in SGPT levels.[46] Previous research has also found that in severe clinical situations, SGOT increases more frequently than SGPT.[41] Because SGOT enzymes can be found in disorders of other organs such as the heart, skeletal muscles, kidneys, brain, pancreas, and white and red blood cells, they are not specific for liver injury.[47]

An increase in SGOT correlates with an increase in neutrophils and a decrease in lymphocytes in COVID-19, according to ordinal regression analysis. This finding implies that immune-mediated inflammation may play a significant role in the development of liver injury in clinically severe COVID-19 patients. More research is needed to determine the mechanism underlying the increase in initial AST in COVID-19 patients.[46]

COVID-19 patients in this study were found to have comorbidities such as hypertension, cardiovascular disease, chronic kidney disease, chronic lung disease, and cerebrovascular disease. More research is needed to determine whether other extrahepatic conditions, such as cardiovascular disease, also cause the increase in SGOT and SGPT. This is one of the study's limitations. This study also has limitations, such as the fact that it is a retrospective study based on data collected from patient medical records and that the distribution of patients in this study at different clinical levels is uneven.

CONCLUSION

Significant differences exist in IL-6, SGOT, and SGPT levels based on COVID-19

clinical severity. IL-6, SGOT, and SGPT levels were higher in critically ill patients than in those with milder illnesses.

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