(RESEARCH ARTICLE)

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Correlation between HS-troponin I level and Brixia score in COVID-19 patients with diabetes mellitus at ICU of Dr. Moewardi Hospital, Indonesia

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Abstract

COVID-19 can cause disturbances in insulin production and worsen the clinical condition of patients with comorbid diabetes mellitus. In patients with diabetes mellitus, one of the complications is heart disease. Therefore, a study was conducted to determine the relationship between hs-Troponin I levels, which is a biomarker of heart disease, with the severity of COVID-19 patients as measured by the Brixia score in COVID-19 patients with comorbid diabetes mellitus in the ICU (Intensive Care Unit) of Dr. Moewardi Hospital, Surakarta. The study was conducted with a cross-sectional approach, the sample was COVID-19 patients with comorbid diabetes mellitus in the ICU, chosen by purposive sampling method. The dependent variable of this study was the Brixia score, and hs-Troponin I would be the independent variable. Data were analyzed by contingency coefficient test with p<0.05 indicating statistical correlation. 44 patients hospitalized in ICU for COVID-19 were enrolled. The mean age was 61±8 years old. 27% of patients had normal hs-Troponin I levels, and 73% had elevated hs-Troponin I levels. 11% of patients had a low Brixia score, 43% had a moderate score, and 45% had a high score. Data were analyzed, and the result is the value of X2 count=2.804 < X2 table=5.991 which means that there is no relationship between variables. The values of p=0,246 (p>0,05) and r=0,245 showed that there is no significant relationship between hs-Troponin I and Brixia score. Hs-Troponin I level is negatively correlated to Brixia score in COVID-19 patients with diabetes mellitus.

Keywords: COVID-19; Brixia Score; Chest X-Ray; hs-Troponin I; ICU; Diabetes Mellitus

1. Introduction

Coronavirus Disease 2019 (COVID-19) is a disease that is becoming a worldwide pandemic, which first appeared in December 2019 in China. This disease is caused by the SARS-CoV 2 virus, which is similar to its predecessor, SARS-CoV, which causes SARS. In the human body, the SARS-CoV 2 virus will bind to the Angiotensin Converting Enzyme 2 or ACE 2 receptor which is expressed in several organ cells, including the respiratory tract, heart, kidney, liver, digestive tract, and pancreas (1). This is what underlies the alleged cause of organ failure in COVID-19 patients. COVID-19 patients show various symptoms, such as chest pain, loss of smell or anosmia, fever, cough, malaise, and others. In some people, COVID-19 can cause no symptoms at all, but in others, the symptoms can become more severe, especially in people with comorbid or comorbid diseases, one of which is diabetes mellitus (2). One of the clinical manifestations of COVID-19 occurs in the lungs. The severity of COVID-19 can be seen from the chest X-ray, and assessed using the Brixia score.

Diabetes mellitus or DM is a chronic metabolic disease characterized by increased blood sugar levels caused by a lack of insulin secretion, defects in insulin action, or both (3). Diabetes Mellitus can cause several complications, one of which is heart disease. Diagnosis of heart disease can be confirmed by various examinations, one of which is the examination

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of troponin I. Troponin is a complex protein found in heart cells, consisting of three subunits, namely troponin-T, troponin-I, and troponin-C. Of the three types of troponins, troponin-I and troponin-T are used as biomarkers in heart disease because both troponins are specific troponins in the heart muscle (4). Troponin in the blood is produced when a myocardial infarction occurs, where there is a rupture of the cardiac cell membrane and the release of material in the heart cells, including troponin I. Troponin I in sufficient quantities that enters the circulation can be a biomarker of damage to the heart muscle (5). It can be checked by laboratory examination of high sensitivity troponin-I (hs Troponin-I). In a study conducted by Segre et al., 2015, it was stated that troponin concentrations increased in diabetic patients with stable coronary artery disease.

In COVID-19, the SARS-CoV-2 virus can infect pancreatic beta cells due to the presence of ACE2 (Angiotensin Converting Enzyme 2) receptors in the pancreas. According to Beyerstedt, S et al., 2021, in patients with type 2 diabetes, ACE2 expression was found to be increased in the pancreas, liver, and adipose tissue. As a result, pancreatic beta-cell depletion occurs and induces apoptosis (7). This of course causes disruption of the function of pancreatic beta cells in producing the hormone insulin. In addition, in COVID-19 patients there is also an increase in insulin resistance as an inflammatory response, thus exacerbating the clinical condition of COVID-19 patients with comorbid diabetes mellitus (8).

A meta-analysis stated that the cTnI value increased significantly in severe COVID-19 (9). From this background, researchers are interested in examining the relationship between hs-troponin I levels and the assessment of the Brixia score in COVID-19 patients with comorbid diabetes mellitus in the ICU of Dr. Moewardi Hospital Surakarta.

2. Material and methods

The observational study with a cross-sectional approach was conducted at the Radiology installation, Dr. Moewardi Hospital in January 2020-June 2022. The subjects of this study were COVID-19 patients hospitalized in ICU with diabetes mellitus comorbid. A number of 44 patients had their thorax x-ray and hs-Troponin I level checked. The dependent variable of this study was Brixia score, and hs-Troponin I would be the independent variable. Brixia score is a chest x-ray assessment, that will be divided into 3 categories, namely mild (score 0-8), moderate (score 7-12), and severe (score 13-18). Hs-Troponin I is a biomarker of heart disease, with the cut-off used in this study being 34ng/L for men and 16ng/L for women. Brixia score was measured by dividing the thorax x-ray photos into 6 and scoring each part by 0-3. Hs-troponin I levels were obtained from the medical record.   The relationship between hs-Troponin I level and Brixia score was analyzed by contingency coefficient test.

3. Results

3.1. Sample Characteristics

This study involved 44 COVID-19 patients who were treated in the ICU of Dr. Moewardi Hospital in the period from January 2020-June 2022.

Table 1 showed the categorical data including gender, age, hs-Troponin I levels, and Brixia score. It showed that most of the objects were male (73%). The age distribution showed that most patients were in the age group of 51-60 years old (38%) and 61-70 years old (38%). 73% of patients had increased hs-Troponin I. Most of their Brixia score was severe (45%), followed by moderate (43%).

Table 2 showed that the mean age of the patients was 61 years old (Mean= 61; SD= 8), the mean hs-Troponin I level was 5671.77 ng/L (Mean= 5671.77; SD= 11990.05), and the mean Brixia score was 12 (Mean= 12; SD= 4).

Table 1 Sample characteristics in categorical data

Category	n	%
Gender		
Male	32	73%
Female	12	27%
Age		
≤50 years old	5	11%
51-60 years old	17	38%
61-70 years old	17	38%
>70 years old	6	13%
hs-Troponin I level		
Normal	12	27%
Increase	32	73%
Brixia Score		
Mild	5	11%
Moderate	19	43%
Severe	20	45%

Table 2 Sample characteristics in continuous data

Variables	n	Mean	SD	Min	Max
Age (year)	44	61	8	39	80
Hs-Troponin I levels (ng/L)	44	5671.77	11990.05	3	40000
Brixia score	44	12	4	2	18

3.2. Data Analysis

Table 3 showed that patients with increased hs-Troponin I level have a tendency to have severe Brixia score, and patients with normal hs-Troponin I level are likely to have moderate Brixia score.

Table 3 Cross-tabulation of hs-Troponin I with Brixia score

hs-Troponin I level (ng/L)	Brixia score			Total
	Mild	Moderate	Severe	
Increase (>34 for male, >16 for female)	3	12	17	32
Normal	2	7	3	12
Total	5	19	20	44

Based on table 4, it is known that there is no significant relationship between hs-Troponin I and Brixia score. So hs-Troponin I level is negatively correlated to Brixia score in COVID-19 patients with diabetes mellitus.

Table 4 Coefficient contingency analysis of the relationship between hs-Troponin I level and Brixia score

Variables	r	p-value
Hs-Troponin I	0.245	0.246

4. Discussion

This study involved 44 people, most of them were male (73%). These characteristics are in accordance with a systematic review and meta-analysis compiled by Abate et al., (2020), which stated that the prevalence of symptomatic COVID-19 was more found in men than women.

The results of the sample based on age showed the highest age distribution at the age of 51-60 and 61-70 years with an average of 61 years. This result is not much different from the results of Elhadi et al., (2021), which was conducted on COVID-19 patients in the ICU, which stated that the majority of patients were over 60 years old with an average age of 69 years.

The samples in this study had laboratory tests for hs-Troponin I. The grouping of hs-Troponin I levels was based on a cut-off of 34ng/L for men and 16ng/L for women (12). The total sample whose levels were above the cut-off was 32 people, while the remaining 12 people had normal hs-Troponin I levels. This shows that in COVID-19 patients with comorbid diabetes mellitus, there is a tendency for episodes of cardiovascular disease to occur. This is because diabetes mellitus is a predisposing factor for cardiovascular disease. Diabetes mellitus can cause diabetic cardiomyopathy and atherosclerotic cardiovascular disease, which leads to heart failure (13).

Assessment of brixia in the sample was carried out by dividing the patient's chest X-ray into 6 parts, then scoring 0-3. A total of 20 samples (45%) got a score of 13-18, 19 patients (43%) got a score of 7-12, and 5 patients (11%) patients (43%) got a score of 0-6. These results indicate that the brixia score in most of the samples is high or moderate.

Analysis of the data in this study showed the results of X2 count 2.804. When compared with X2which is 5.991, then X2count is less than X2which shows no correlation between hs-Troponin I levels and the severity of COVID-19 in patients with diabetes mellitus. The results were p=0.246 (p>0.05), which indicated that there was no statistically significant relationship. This is not in accordance with the hypothesis of this study, namely that there is a relationship between hs-Troponin I levels and the severity of COVID-19 in comorbid diabetes mellitus patients.

Differences in the results of this study with hypotheses can be caused by several things. First, it can be caused by the absence of data regarding the type of drug and the regularity of the patient taking medication may affect the results of this study. Drugs with a mechanism of lowering blood sugar levels can cause hypoglycemia. As is well known, hypoglycemia increases mortality in the event of a cardiovascular episode. In addition, there are classes of drugs such as sodium-glucose cotransporter 2 inhibitors (SGLT2i) which can increase protection against cardiovascular disease. The mechanism of SGLT2i drugs is with SGLT2 so that it inhibits glucose reabsorption in the renal tubules. Another effect of this inhibition is to increase urinary excretion, thereby reducing circulating glucose levels (14). In addition to these effects, SGLT2i also has an effect on weight loss, blood pressure, and lipid profile, thereby reducing risk factors for cardiovascular events (15).

The next variable that becomes a confounder in this study is whether or not Diabetes Mellitus is controlled. Both hyperglycemia and hypoglycemia have adverse effects on the cardiovascular system. Chronic high sugar levels and fluctuating sugar levels are triggers for the emergence of an inflammatory response. The presence of inflammation and oxidative stress in DM patients can trigger atherogenesis or plaque buildup in the arteries, thereby increasing the likelihood of cardiovascular episodes. In addition, if severe hypoglycemia occurs, it will trigger adrenergic activation, oxidative stress, and arrhythmias. Hypoglycemia in DM patients increases mortality when a cardiovascular episode occurs (16). This shows that whether or not DM is controlled will affect the risk of heart disease, which also affects the levels of hs-Troponin I.

De Jong (17) states that the duration of diabetes mellitus is associated with an increased risk of cardiovascular disease in both men and women. Increasing the duration of diabetes mellitus for 5 years will increase the risk of heart disease by 20% in men and women. In another study that examined the relationship between the duration of diabetes mellitus and coronary heart disease, it was also stated that the risk of coronary heart disease was 1.38 times higher in patients with diabetes mellitus duration of more than 10 years (18). This suggests that the duration of DM will affect the risk of

heart disease, which also affects the levels of hs-Troponin I. The mechanism by which DM increases the risk of heart disease is still unknown certainly, but several studies have found that diabetes can increase the expression of the IIB/IIIA glycoprotein receptor and von willebrand factor that can help platelet activation (19).

In sum, the difference between the results of this study to the hypothesis may be caused by: there is no data on the type of drug the patient is taking, whether or not Diabetes Mellitus is controlled, and there is no data on the length of time the patient has diabetes. In addition, it could also be due to the absence of data on the timing of the hs-Troponin I examination related to the time specificity of the increase in troponin I levels since the onset of symptoms. Therefore, it is suggested to the next study to take these factors into consideration.

5. Conclusion

Hs-Troponin I level is negatively correlated to Brixia score in COVID-19 patients with diabetes mellitus.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

This study has no conflicts of interest.

Statement of ethical approval

The ethical clearance approval letter was issued by the Research Ethics Committee at Dr. Moewardi Hospital, Surakarta, No. 466/IV/HREC/2022.

Statement of informed consent

 Informed consent was obtained from all individual participants included in the study.

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