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Relationship of Pentraxin 3 Levels with Severity COVID-19 Patients Treated at Haji Adam Malik Hospital Medan

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Abstract: ***Background**: Coronavirus disease 2019 (COVID-19) is highly contagious and deadly and is associated with organ dysfunction. Pentraxin-3 (PTX3) is a member of the super family of pentraxins and is involved in acute inflammation and the innate immune system. Pentraxin-3 (PTX3) participates in innate resistance to infection and is closely related to the severity of COVID-19. **Methods**: This research is an observational study with cross sectional data collection method. This study took blood samples of 34 patients with moderate and severe COVID 19 patients being treated at the HAM Hospital. Samples were examined only once for Pentraxin 3 in moderate and severe COVID-19 patients. The research was conducted after obtaining ethical approval and informed consent. **Result and Discussion**: 22 male patients (64.7%) and 12 female patients (35.3%) with the youngest 32 years old and the oldest 75 years old. By using the enter method in multivariate analysis, only one independent variable was obtained that could predict the severity of COVID-19 disease, namely the level of pentraxin 3 (p=0.015). The results of the analysis using the ROC curve obtained that the AUC area of pentraxin 3 levels in predicting the severity of COVID-19 disease was 81.4% with p=0.003 and 95%I K 65.6%-97.3%. This shows that pentraxin 3 levels can be used to predict the severity of COVID-19 disease with a good level of ability (AUC > 80%-90%). **Conclusion and Suggestion**: Pentraxin 3 levels can be used as an alternative biomarker to assess the severity of COVID-19, because PTX3 is closely related to the pathogenesis of inflammation and organ dysfunction related to COVID 19.*

Keywords: COVID-19, Pentraxin 3, Severity

1. Introduction

In December 2019, the first mysterious case of pneumonia was reported in Wuhan, Hubei Province. The source of the transmission is still unknown, but the first case was linked to a fish market in Wuhan. Coronavirus Disease 2019 (COVID-19) is an infectious disease caused by *Severe Acute Respiratory Syndrome Coronavirus 2 (*SARS-CoV-2). SARS-CoV-2 is a new type of coronavirus that has never been previously identified in humans. Common signs and symptoms of COVID-19 infection include symptoms of acute respiratory distress such as fever, cough and shortness of breath. The average incubation period is 5-6 days with the longest incubation period being 14 days. In severe cases of COVID-19 it can cause pneumonia, acute respiratory syndrome, kidney failure, and even death.[1, 2]

Pentraxin-3 (PTX3) is a member of the pentraxin super family and is involved in acute and chronic inflammation and innate immunity. PTX3 levels fluctuate with the intensity of the immune-inflammatory response. PTX3 is induced by SARS-CoV-2 in respiratory tract epithelial cells. At the single cell level, COVID-19 monocytes and pulmonary macrophages express pentraxin 3.[3] This study aimed to detect PTX3 serum levels in moderate and severe groups of COVID-19 patients, and analyze the relationship between PTX3 levels and the severity of COVID-19 disease in COVID-19 patients.

2. Purpose

This study aims to determine the relationship between Pentraxin 3 levels and the severity of COVID-19 patients treated at RSUP. H. Adam Malik, Medan.

3. Methods

This research is an observational study with *cross sectional* data collection method. The study was conducted at the Department of Clinical Pathology, USU Medical Faculty / H. Adam Malik Hospital, Medan in collaboration with the Pulmonology Department of USU Medical Faculty / H. Adam Malik Hospital, Medan, from March 2021 to May 2021. The research subjects were patients with moderate and severe COVID-19 degrees. who were treated at H. Adam Malik Hospital, Medan, and had met the inclusion criteria

The sample size in this study was determined as many as 34 samples. The inclusion criteria in this study were all adult patients who were confirmed positive for COVID-19 by RT-PCR, moderate and severe degrees. Pentraxin 3 examination was carried out at the Department of Clinical Pathology, USU Medical Faculty / H. Adam Malik Hospital, Medan using the Chemwell automatic analyzer using the ELISA method. PTX3 examination was carried out on moderate and severe COVID-19 patients.

4. Statistical Analysis

Data analysis was performed using SPSS software (*Statistical Package for Social Sciences*, Chicago, IL, USA) for Windows. The description of the characteristics of the research subjects is presented in tabulated form and described. The relationship between Pentraxin 3 levels and the severity of COVID-19 patients using the *Mann Whitney* test. All statistical tests with p value < 0.05 were considered significant.

5. Results

This study was followed by 34 COVID-19 patients who were hospitalized at Haji Adam Malik General Hospital

Medan from March 2021-May 2021 and met the inclusion criteria. The characteristics of the research subjects are presented in table 5.1. There were 22 male subjects (64.7%) and 12 female subjects (35.3%). The mean age was 54.91 years with the youngest age being 32 years and the oldest being 75 years.

There were 25 comorbid subjects (73.5%) and 9 people without comorbid (26.5%). Based on table 5.2, there are 11 people (32.4%) with moderate degrees and 23 people (67.6%) with severe degrees. The subjects who died were 17 people (50%).

Table 5.1: Characteristics of Research Subjects

Characteristics of Research Subjects	n = 34
Gender, n (%)	
Man	22 (64.7)
Woman	12 (35.3)
Age, years	
Average (SD)	54.91 (11.52)
Median (Min – Mak)	56 (32 – 75)
Comorbid, n (%)	
There is	25 (73.5)
There is no	9 (26.5)

Table 5.2: Severity and Mortality of Research Subjects

	n = 34
Severity, n (%)	
Severe	23 (67.6)
Moderate	11 (32.4)
Mortality, n (%)	
Life	17 (50)
Die	17 (50)

The results of the examination of pentraxin 3 levels are shown in table 5.3. The mean of pentraxin 3 was 8.74 ng/mL (SD = 58.4 ng/mL) with the lowest level of 2.01 ng/mL and the highest level of 29.64 ng/mL.

Table 5.3: Pentraxin 3 levels

Pentraxin 3, ng/mL	n = 34
Average (SD)	8.74 (5.84)
Median (Min – Max)	7.27 (2.01 – 29.64)

Table 5.4: Relationship of Sex, Age, Comorbidities, Pentraxin 3 with the Severity of COVID-19 Disease

Variable	Severity		p
	Severe (n=23)	Moderate (n=11)	
Gender, n (%)			
Man	17 (77.3)	5 (22.7)	0.138 [a]
Woman	6 (50)	6 (50)	
Age, years			
Average (SD)	56.48 (11.81)	51.64 (10.67)	0.258 [b]
Median (Min – Mak)	59 (32-75)	50 (35-68)	
Comorbid, n (%)			
Yes	19 (76)	6 (24)	0.111 [a]
No	4 (44.4)	5 (55.6)	
Pentraxin 3, ng/mL			
Average (SD)	10.38 (6.25)	5.3 (2.73)	0.003 [c]
Median (Min – Max)	9 (4.07-29.64)	5.05 (2.01-11.6)	

[a] Fischer's Exact, [b] T Independent, [c] Mann Whitney

From table 5.4 the results of the analysis using Fischer's exact test show an insignificant relationship between gender and the severity of COVID-19 disease (p = 0.138). Using the Independent T test showed that there was no significant relationship between age and the severity of COVID-19 disease (p = 0.258). The results of the analysis using Fischer's exact test showed an insignificant relationship between comorbidities and the severity of COVID-19 disease (p = 0.111). Using the Mann Whitney test, it was found that there was a significant relationship between pentraxin 3 levels and the severity of COVID-19 disease (p = 0.003).

The results of the analysis using the ROC curve (figure 5.1) obtained that the AUC area of pentraxin 3 levels in predicting the severity of Covid-19 disease was 81.4% with p = 0.003 and 95% CI 65.6%-97.3%. This shows that pentraxin 3 levels can be used to predict the severity of Covid-19 disease with a good level of ability (AUC > 80%-90%).

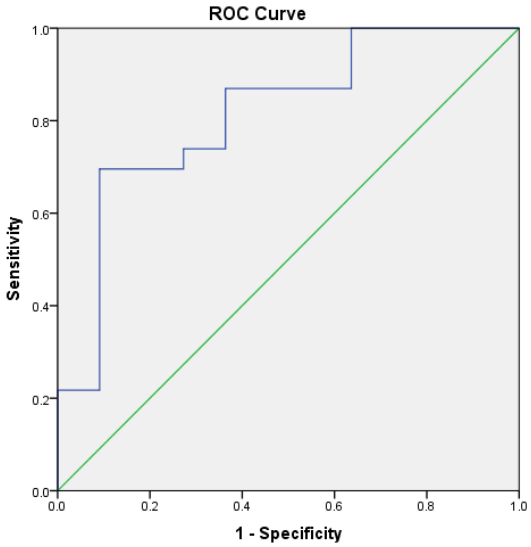

Figure 5.1: ROC Curve of Pentraxin 3 Levels as a Predictor of the Severity of Covid-19 Disease

The best *cut off* value in this study for the severity of COVID-19 based on pentraxin 3 levels was 7.27 ng/mL with a sensitivity of 69.6% and a specificity of 90.9%. Based on the value of the ROC graph, it shows that the examination of pentraxin 3 levels in determining the degree of severity has a high specificity value.

Table 5.5: Accuracy of Pentraxin 3 levels on the severity of COVID-19

	Level Severity		Sensitivity	Specificity	PPV	NPV
	Heavy	Currently				
Pentraxin 3						
7.27	16	1	69.6%	90.9%	94.1%	58.8%
< 7.27	7	10				

By using the cut off value of Pentraxin 3 of 7.27 ng/mL to predict the severity of Covid-19 disease, the sensitivity value is 69.6%, specificity is 90.9%, *positive predictive value is* 94.1%, *negative predictive value is* of 58.8%, the accuracy of Pentraxin 3 levels with a *cut off* value of 7.27 is 76.5%.

6. Discussion

From the characteristics of the research subjects, the number of patients who became the sample was 34 patients. It

consisted of 22 people (64.7%) male and 12 people (35.3%) female. This is in line with the research conducted by *Karyono D., et al (*2020) in Indonesia with n = 27, 696 it was found that men (54.6%) were infected with the COVID-19 virus more than women (45.4%).[4] Several *studies* show similar findings where more men are infected with COVID-19 than women. Women are known to be more resilient in terms of viral infections.[5]

The median age of patients infected with COVID-19 from this study was 56 years with ages ranging from 32 to 75 years. This is in line with a study conducted by *Zhang JJ, et al (*2020) where out of 140 patients diagnosed with COVID-19, the median age of the patients was 57 years, ranging from 25 to 87 years.[6]

The risk of patients who have comorbidities to get COVID-19 is greater than patients who do not have comorbidities. Namely, patients with comorbid as many as 25 people (73.5%) and without comorbid as many as 9 people (26.5%). This is in line with the research conducted by *Chen N, et al (*2020) in which about half of the total research sample (n = 99) namely 50 people (51%) have chronic diseases (*underlying diseases).*[7]

From the results of the analysis of the relationship between gender and the severity of the disease, the relationship between the two is not significant. This is in line with research conducted by *Raimondi F, et al (*2021) where women who are hospitalized are less likely to die from Covid-19; however, once severe disease occurs, the risk of death is similar to that of men.[8]

The results of other analyzes in this study said that there was no significant relationship between age and the degree of COVID-19 disease. This is in contrast to a study in China where COVID-19 mostly infects older people due to a lack of immune system as a result of the aging process. Furthermore, most older people have multiple comorbidities that make them more susceptible to contracting COVID-19.[9]

The results of the analysis showed a non-significant relationship between comorbidities and the severity of COVID-19 disease. These results are not in line with the meta-analysis study conducted by *Cheng, et al (*2021) which stated that from 22 studies involving 3286 patients with confirmed COVID-19, chronic comorbidities could contribute to the severity of patients. According to the study, old age with 2 or more comorbidities significantly impacts the care of COVID-19 patients.[10]

Comorbidities may also be associated with reduced immune function. Also, polypharmacy and comorbidity are closely related to each other. Because innate immunity is greatly decreased in comorbid conditions and because patients are taking more drugs concurrently, adverse drug reactions along with decreased immunity can be expected in these patients which can ultimately increase the risk of death.[11]
Meanwhile, the level of pentraxin 3 on the severity of COVID-19 in this study was said to have a significant relationship between the two. Where the average level of pentraxin 3 with severe severity is 10.38 ng/mL while the average level of pentraxin 3 with moderate severity is much lower at 5.3 ng/mL. This is in line with the study conducted by *Brunetta, et al (*2021) where in this study an increase in the concentration of pentraxin 3 was found in 96 patients who detected COVID-19. Pentraxin 3 was a strong independent predictor of 28-day mortality in multivariate analysis, better than conventional markers of inflammation. Thus, pentraxin 3 concentrations can serve as a strong prognostic indicator of short-term mortality in COVID-19 patients.[3]

So that in this study, based on ROC curve analysis, the best *cut-off* value for pentraxin 3 levels for predicting the severity of COVID-19 was 7.27 ng/mL.

7. Conclusion

Incidence by gender in COVID-19 patients was more male than female with a mean age of 54.91 years. And found a significant relationship between pentraxin 3 levels with the severity of COVID-19 disease

8. Suggestion

With significant results from Pentraxin 3 levels, the predictive value of Pentraxin 3 on the severity of COVID-19 patients is very high. So it can be recommended to do a Pentraxin 3 examination in COVID-19 patients treated at the RSUP. H. Adam Malik, Medan to be able to determine the degree of severity.

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