

RESEARCH  
ARTICLE

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## Diagnostic Value of Platelet Mass Index, Plt/Mpv Ratio and Other Hemogram Parameters in Covid-19 Patients Who Presented to Emergency Department

### ABSTRACT

**Objective:** The objective of this study was to compare platelet mass index, platelets count/mean platelet volume and other hemogram parameters between COVID-19 patients and a control group and to determine the parameters that are significant in discrimination between COVID-19 and healthy control patients without COVID 19.

**Methods:** Data of a total of 80 patients who presented to the emergency department of our hospital with the symptoms suggesting COVID-19 with a polymerase chain reaction (PCR) positive result and 80 healthy controls with a PCR (-) test results were retrospectively analyzed. Patients' laboratory parameters including white blood cells (WBC), neutrophils count, lymphocytes count, monocytes count, neutrophils to lymphocytes ratio (NLR), lymphocytes to monocytes ratio (LMR), platelets (PLT), platelets to lymphocytes ratio (PLR), mean platelet volume (MPV), red blood cell distribution width (RDW), platelet mass index (PMI), red blood cell distribution width/ mean platelet volume (RDW/MPV) and platelet count/ mean platelet volume (PLT/MPV) ratios were analyzed. At the same time a receiver operating characteristic (ROC) analysis was performed for determining laboratory indicators in distinguishing control and COVID-19 positive cases from each other.

**Results:** In our study, WBC, lymphocytes, monocytes, neutrophils, LMR, platelets, PMI and PLT/MPV levels decreased, while PLR and MPV values increased in COVID-19 patients. According to ROC analysis, among the parameters examined in terms of making discrimination between COVID-19 and control groups, LMR, PLR, PMI and PLT/MPV parameters had significant areas under curve. The best cut-off points of the parameter were found as <2.91 for LMR, 117.95 for PLR, 2167.65 for PMI and <25.13 for PLT/MPV.

**Conclusions:** Our study revealed decreased WBC, lymphocytes, monocytes, neutrophils, LMR, platelets, PMI and PLT/MPV levels and elevated PLR and MPV values in COVID-19 patients. We believe that these parameters can be helpful in follow-up of the prognosis of COVID-19 patients and distinguishing these patients from healthy persons without COVID-19.

**Keywords:** COVID-19, Neutrophils, Lymphocytes, Platelets

## Trombosit Kitle İndeksi, Plt/Mpv Oranı ve Diğer Hemogram Parametrelerinin Acil Servise Başvuran Covid-19 Hastalarında Tanısal Değeri

### ÖZET

**Amaç:** Bu çalışmanın amacı, trombosit kitle indeksi, trombosit sayısı / ortalama trombosit hacmi oranı ve diğer hemogram parametrelerini koronavirüs (COVID-19) hastaları ve kontrol grubu arasında kıyaslamak ve COVID-19 hastaları ile COVID-19 olmayan sağlıklı kontrol hastaları ayırımının yapılmasında anlamlı olan parametrelerin saptanmasıdır.

**Gereç ve Yöntem:** Hastanemizin acil servisine COVID-19'u düşündüren semptomlarla başvuran ve polimeraz zincir reaksiyonu (PCR) pozitif olan 80 hasta ile PCR (-) olan 80 kontrol bireyi retrospektif olarak incelenmiştir. Hastaların beyaz kan hücreleri (WBC), nötrofil sayısı, lenfosit sayısı, monosit sayısı, trombosit sayısı, nötrofil/lenfosit oranı (NLR), lenfosit/monosit oranı (LMR), trombosit sayısı, trombosit/lenfosit oranı (PLR), ortalama trombosit hacmi (MPV), kırmızı hücre dağılım genişliği (RDW), trombosit kitle indeksi (PMI), kırmızı kan hücreleri dağılım genişliği / ortalama trombosit hacmi (RDW / MPV) ve trombosit sayısı/ ortalama trombosit hacmi (PLT / MPV) oranları analiz edilmiştir. Aynı zamanda kontrol ve COVID-19'u ayırmada anlamlı parametrelerin belirlenmesi için Receiver Operating Characteristic (ROC) analizi yapıldı.

**Bulgular:** Çalışmamızda WBC, lenfosit, monosit nötrofil, LMR, trombosit, PMI ve PLT/MPV değerleri COVID-19 hastalarında düşmüş, PLR ve MPV değerleri ise yükselmiştir. LMR, PLR, PMI ve PLT/MPV'nin eğri altında kalan alanları anlamlıdır. İncelenen parametreler için en iyi cut-off noktaları; LMR için <2.91, PLR için 117.95, PMI için 2167.65 ve PLT/MPV için <25.13'tür.

**Sonuç:** Çalışmamızda COVID-19 hastalarında WBC, lenfosit, monosit, nötrofil, trombosit, PMI ve PLT/MPV düzeylerinin azaldığı, PLR ve MPV değerlerinin ise azaldığı saptanmıştır. Bu parametreler COVID-19 hastalarının prognozunu izlenmesinde ve bu hastaların, COVID-19 bulunmayan sağlıklı kişilerden ayırt edilmesinde yardımcı olabileceğini düşünmekteyiz.

**Anahtar Kelimeler:** COVID-19, nötrofil, lenfosit, platelet

## INTRODUCTION

At the end of December 2019, pneumonia cases of unknown origin have been increasingly seen in Wuhan province of Hubei state in China. The disease was then declared to be caused by a novel coronavirus named Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The disease was rapidly spread throughout mainland China and then all over the world (1). According to the current data, the early Coronavirus Disease 2019 (COVID-19) cases were associated with a seafood market in Wuhan where wild animals are sold (2). The World Health Organization (WHO) termed this new disease as COVID-19 and declared it as a pandemic on March 12, 2020(3). Today, COVID-19 is continuing to affect all the world as well as Turkey and to cause many deaths and morbidities. As of 03/10/2020, according to the daily report of WHO, there were over 34 million cases and more than 1,000,000 deaths worldwide (4). On the other hand, according to the Turkish Ministry of Health, there were 321,512 cases and 8,325 deaths in Turkey as of 02 October (5).

At present, unfortunately we are not in a position to effectively treat COVID-19, because today no specific antiviral drugs have yet been developed and approved to treat human CoV infections (6-8). Nevertheless, vaccination programs have been launched in several countries at the time of this study. In the literature, first publications about COVID-19 have been predominantly published by Chinese authors (9-15). According to the first studies on COVID-19, the main symptoms of presentation were fever, cough and shortness of breath (16). However as the disease progressed, new symptoms and involvement of cardiac, gastrointestinal and neurologic systems have been increasingly reported.

Although the standard method of diagnosis is polymerase chain reaction (PCR) test, laboratory markers are among the most important indicators for the confirmation of diagnosis of COVID-19. Because the disease has a dynamic process leading to new and unexpected conditions every passing day, laboratory findings are extremely important to evaluate the evolution of COVID-19 and to guide treatment interventions (17). It has been reported that some blood parameters significantly decrease, while the others significantly increase during progression of COVID-19 (18). The laboratory findings, which are observed to change in infectious processes including COVID-19 are widely varied. Several hemogram parameters have been studied so far in COVID-19. However, to our knowledge there is no study investigating diagnostic value of platelet mass index (PMI) and platelets count to mean platelet volume (PLT/MPV) parameters in COVID-19. Therefore, the objective of this study was to compare PMI, PLT/MPV and other laboratory parameters between COVID-19 patients and a

control group and to determine the parameters that are significant in discrimination between COVID-19 and healthy control patients without COVID 19.

## MATERIAL AND METHODS

In this study, data of a total of 80 patients who presented to the emergency department (ED) of our hospital with the symptoms suggesting COVID-19, confirmed with the diagnosis of COVID-19 through PCR (+) test, but had no lung involvement on chest computed tomography (CT) and, who were advised outpatient treatment and quarantine between 15/05/2020 and 15/08/2020 and 80 healthy control patients with a PCR (-) test results who had suspected contact history, but had no any discomfort as the control group were retrospectively analyzed. Accordingly, a total of 80 patients who presented to the ED with symptoms such as fever, dry cough, dyspnea, sore throat and fatigue that suggest COVID-19 and had PCR (+) test result were assigned to PCR (+) group or COVID-19 group (COVID-19 group), and 80 control subject who presented to the ED only with a suspected contact history and had PCR (-) test result to PCR (-) (control group). Patients with complete data were included in the study. Patients with missing data, malignancy, receiving chemotherapy or using steroids were excluded from the study.

Data of the patients were obtained from the hospital medical records and retrospectively analyzed. The diagnosis of COVID-19 pneumonia was confirmed according to the case definition established by WHO with positive PCR test results through naso-pharyngeal swab samples (19).

Patients' demographic characteristics such as age and gender, clinical symptoms and laboratory parameters including white blood cells (WBC), neutrophils count, lymphocytes count, monocytes count, neutrophils to lymphocytes ratio (NLR), lymphocytes to monocytes ratio (LMR), platelets, platelets to lymphocytes ratio (PLR), mean platelet volume (MPV), red blood cell distribution width (RDW), platelet mass index (PMI), RDW/MPV and PLT/MPV ratios were measured and analyzed. All laboratory parameters were studied with automated laboratory methods using commercial kits in line with the instruction of the manufacturer.

At the same time a receiver operating characteristic (ROC) curve analysis was performed for determining laboratory indicators in distinguishing control and COVID-19 positive cases from each other. Accordingly the optimal cut-off points to predict COVID-19 and sensitivity, specificity, positive predictive value and negative predictive value were also calculated.

**Ethical Considerations:** Ethical consent was obtained from the Harran University Clinical Research Ethics Committee for the study (Date:17/08/2020 decision number:

HRU/20.14.13). Since this study included retrospective evaluations, informed consent was not deemed necessary. This study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

**Statistical Analysis:** Data obtained in this study was statistically analyzed using Statistical Package for Social Sciences (SPSS) version 17.0 (IBM Corporation, Armonk, NY, USA) statistical software. Normality of the data was analyzed using Kolmogorov-Smirnov test. Descriptive statistics were expressed as mean  $\pm$  standard deviation for continuous variables and median interquartile range (IQR) when appropriate. Whereas categorical data were expressed as numbers and percentages. Differences between the Control and COVID-19 groups were compared using Student's t test, while Mann-Whitney U test was used in the comparison of continuous variables that did not meet parametric test assumption. Categorical variables were analyzed with Continuity corrected Chi-square ( $\chi^2$ ) test. The optimal cut-off points of laboratory measurements to determine the existence of COVID-19 were investigated in ROC analyses as giving the maximum sum of sensitivity and specificity for the significant test. Sensitivity, specificity, positive, and negative predicted values with 95% confidence interval for each significant laboratory measurement to discriminate the patients with COVID-19 were also calculated.  $P < 0.05$  values considered statistically significant.

## RESULTS

In our study, PCR (+) group consisted of 80 patients and PCR (-) group 80 control subjects. The mean age was  $46.9 \pm 17.2$  years in PCR (+) group and  $45.9 \pm 9.3$  years in PCR (-) group. No

statistically significant difference was found between both groups in terms of age ( $p = 0.681$ ). Of patients in PCR (+) group, 53 (66.3%) were male and 27 (33.7%) female, while of subjects in the control group, 58 (72.35%) were male and 22 (27.5%) female. No significant difference was observed between the two groups in terms of gender distribution ( $p = 0.493$ ).

When the studies laboratory parameters were evaluated; WBC was significantly lower in the PCR (+) group compared to PCR (-) group ( $p < 0.001$ ). Similarly neutrophils count was significantly lower in PCR (+) group compared to PCR (-) group ( $p < 0.001$ ). Lymphocytes count was statistically significantly lower in PCR (+) group compared to PCR (-) group ( $p < 0.001$ ). Monocytes count also was significantly lower in PCR (+) group compared to PCR (-) group ( $p < 0.001$ ).

LMR ratio was statistically significantly lower in PCR (+) group compared to PCR (-) group ( $p < 0.001$ ). Again, platelets count was significantly lower in PCR (+) group compared to PCR (-) group ( $p < 0.001$ ). On the other hand, PLR ratio was statistically significantly higher in PCR (+) group compared to PCR (-) group ( $p < 0.001$ ). Similarly MPV value was statistically significantly higher in PCR (+) group compared to PCR (-) group ( $p = 0.025$ ). PMI ratio was significantly lower in PCR (+) group compared to PCR (-) group ( $p < 0.001$ ). Again, PLT/MPV ratio was statistically significantly lower in PCR (+) group compared to PCR (-) group ( $p < 0.001$ ). No statistically significant difference was found between the two groups in terms of the other studied parameters. Demographic features and laboratory findings of the groups are given in Table 1.

**Table 1.** The comparisons of demographic characteristics and laboratory measures

	Control (n=80)	COVID-19 (n=80)	P-value
Age (years) *	45.9 $\pm$ 9.3	46.9 $\pm$ 17.2	0.681
Male factor	58 (72.5%)	53 (66.3%)	0.493
Female	22 (27.5%)	27 (33.7%)	
WBC **	9.71 (8.52-11.14)	5.62 (4.64-6.79)	<0.001
Neutrophil **	5.46 (4.62-6.93)	3.44 (2.37-4.67)	<0.001
Lymphocyte **	3.01 (2.32-3.78)	1.59 (1.13-2.11)	<0.001
Monocyte *	0.73 $\pm$ 0.24	0.55 $\pm$ 0.26	<0.001
NLR **	1.74 (1.28-2.59)	2.08 (1.36-3.46)	0.143
LMR **	4.26 (3.31-5.36)	3.23 (2.35-4.98)	<0.001
Platelet **	269.5 (240.5-305.0)	210.0 (177.5-226.2)	<0.001
PLR **	89.0 (73.4-113.6)	131.1 (105.3-186.8)	<0.001
MPV *	10.1 $\pm$ 1.07	10.4 $\pm$ 0.74	0.025
RDW **	13.0 (12.3-13.7)	13.0 (12.3-13.7)	0.852
PMI **	2749.8 (2339.0-3103.1)	2135.1 (1909.6-2695.7)	<0.001¶
RDW/MPV	1.27 (1.18-1.43)	1.25 (1.17-1.35)	0.224¶
PLT/MPV	27.4 (22.6-31.6)	20.8 (16.6-25.7)	<0.001¶

\* Data were expressed as mean  $\pm$  SD, \*\* Descriptive statistics were shown as median (25<sup>th</sup> – 75<sup>th</sup>) percentiles, † Student's t test, ‡ Continuity corrected  $\chi^2$  test, ¶ Mann Whitney U test.

WBC: white blood cell, NLR: neutrophils to lymphocytes ratio, LMR: lymphocytes to monocytes ratio, PLR: platelets to lymphocytes ratio, MPV: mean platelet volume, RDW: red cell distribution width, PMI: platelet mass index, PLT: platelet count

A ROC analysis was performed to determine laboratory values that are significant in distinction between PCR (+) and PCR (-). Accordingly, among the parameters examined in terms of making

discrimination between COVID-19 and control groups, LMR, PLR, PMI and PLT/MPV parameters had significant areas under curve (for all  $p < 0.001$ ) (Table 2).

**Table 2.** The ROC analysis results of laboratory indicators in distinguishing healthy controls and COVID-19 (+) patients from each other

	AUC	95% CI	P-value
<b>NLR</b>	0.567	0.478-0.656	0.143
<b>LMR</b>	0.664	0.579-0.749	<b>&lt;0.001</b>
<b>PLR</b>	0.757	0.682-0.831	<b>&lt;0.001</b>
<b>PMI</b>	0.715	0.634-0.795	<b>&lt;0.001</b>
<b>RDW/MPV</b>	0.556	0.466-0.645	0.224
<b>PLT/MPV</b>	0.737	0.659-0.814	<b>&lt;0.001</b>

AUC: Area under the ROC curve, CI: Confidence interval.

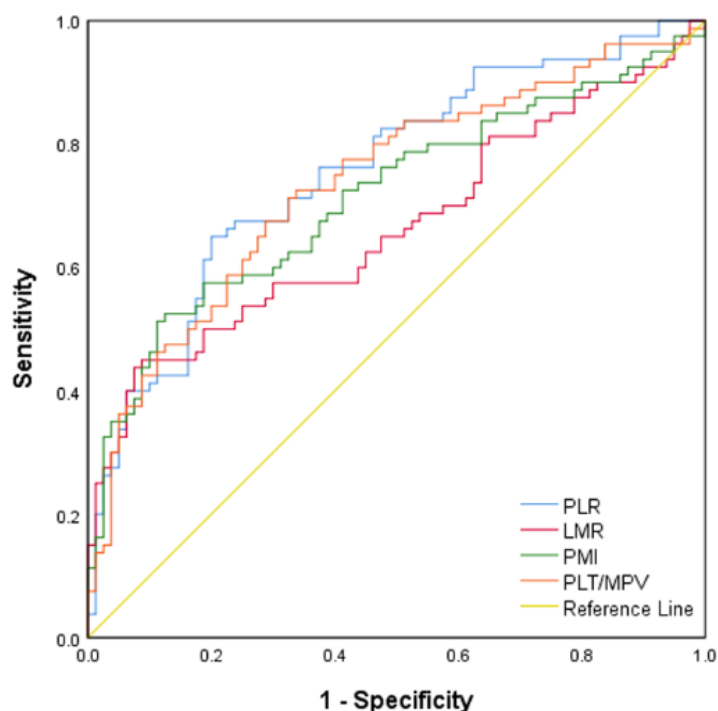
The best cut-off points of the parameters that were significant in distinction between PCR (+) and PCR (-) were found as <2.91 for LMR, 117.95 for PLR, 2167.65 for PMI and <25.13 for PLT/MPV. Sensitivity, specificity, positive predictive value

and negative predictive value of these four parameters in making discrimination between PCR (+) and PCR (-) at 95% confidence interval are shown in Table 3 and Figure 1.

**Table 3.** The optimal cut-off points for statistically significant laboratory measurements according to the ROC analysis and diagnostic performances and 95% CI levels in distinguishing controls and COVID-19 positives from each other

	LMR	PLR	PMI	PLT/MPV
<b>Cut-off point</b>	<2.91	>117.95	<2167.65	<25.13
<b>Sensitivity</b>	43.8 (32.9-54.6)	65.0 (54.5-75.4)	52.5 (41.6-63.4)	71.3 (61.3-81.2)
<b>Specificity</b>	92.5 (86.7-98.3)	80.0 (71.2-88.8)	87.5 (80.2-94.5)	67.5 (57.2-77.8)
<b>PPV</b>	85.4 (74.5-96.2)	76.5 (66.4-86.5)	80.8 (70.1-91.5)	68.7 (58.7-78.6)
<b>NPV</b>	62.2 (53.5-70.9)	69.6 (60.2-79.0)	64.8 (55.8-73.8)	70.1 (59.9-80.3)

PPV: Positive predictive value, NPV: Negative predictive value.



**Figure 1.** Sensitivity, specificity, positive predictive value and negative predictive value of the parameters that were significant as a result of ROC analysis.

## DISCUSSION

Real-Time Reverse Transcription Chain Reaction (RT-PCR) remains the gold standard for the diagnosis and management of COVID-19, although it takes time and the prevalence of false negative results is high (20,21). Several hemogram parameters including white blood cell (WBC), neutrophils count, lymphocytes count and platelets count have been reported to change in COVID-19 patients (10,21,22). Accumulating evidence from studies that will be conducted on this issue will help a rapid diagnosis process and provide contribution to the management.

In the present study where we investigated various blood parameters in COVID-19 and control group; WBC, neutrophils, lymphocytes, monocytes, lymphocytes/monocytes, platelets, PMI and PLT/MPV levels were significantly lower in COVID-19 group compared to the control group. On the other hand, platelet/lymphocytes and MPV values were significantly higher in COVID-19 group.

Although blood picture differs in COVID-19 patients, the most common laboratory findings include normal/low lymphocytes count, unbalanced coagulation, and elevated levels of C-reactive protein (CRP), lactate dehydrogenase, aminotransferase and ferritin. In a study by Guan et al. with 1099 patients, the most common findings was reported as lymphocytopenia by 82.1% (12). Zhou et al. found a correlation between low basal lymphocytes level and poor prognosis in 191 patients (23).

Lymphocyte plays an important role in maintaining hemostasis, an inflammatory response throughout the body and decreased lymphocytes count may cause reduction in immunity. Lymphocytopenia is common in acute infections and is of paramount importance in COVID-19 infections (24). Studies from China and the USA reported low lymphocytes count and coagulation disorder in fatal COVID-19 patients (23-25). In a study from Rome, Italy lymphocyte count was found to be low in 60% and limited in 32% of COVID-19 patients (26). In our study, lymphocytes count was one of the parameters lower in COVID-19 patients compared to the control group ( $p < 0.001$ ).

In the present study, platelets count was significantly lower in COVID-19 patients compared to the control subjects. Therefore COVID-19 patients are more likely to have lymphopenia and thrombocytopenia. In a publication from Hong Kong lymphopenia was reported in 98% and thrombocytosis in 49% of COVID-19 patients (27).

In a study by Qin et al., NLR ratio was found to be higher in patients with severe COVID-19 than in those with mild disease (28). In our study no significant difference was found between PCR (+) and PCR (-) groups in terms of NLR. However,

in the study by Qin et al., all patients included in the study had severe or mild COVID-19 disease. We could conclude that even if NLR can not distinguish COVID-19 and non-COVID-19, at least it has a prognostic value in determining severity of the disease.

In our study, neutrophils count was significantly lower in the PCR (+) group compared to PCR (-) group. Evidence in the literature suggests that neutrophil count increases as the disease progresses. Increased neutrophils count cause a risk for the development of acute respiratory distress syndrome (ARDS) during disease and death (25). In a meta-analysis, it was found with multivariate analysis that PLR ratio is an independent predictor of prolonged hospitalization in a period where platelets peak. It was proposed that high PLR ratio may indicate a more prominent cytokines storm as a result of increased platelet activation (29).

WBC value was found to be significantly lower in COVID-19 patients compared to healthy individuals (30). Similarly, in our study WBC was statistically significantly lower in the PCR (+) group compared to PCR (-) group. Again in a study by Pan et al., MPV value was significantly increased in COVID-19 patients. Consistently with the literature, in our study MPV value was significantly higher in PCR (+) group compared to PCR (-) group. In the study by Pan et al., monocytes count was significantly lower in COVID-19 patients compared to the healthy controls (30). Similarly in the present study monocytes count was significantly lower in PCR (+) group compared to PCR (-) group.

In our study, we performed ROC analysis in order to determine blood parameters that will make distinction between COVID-19 group and control group. According to the results of this analysis, among the studied parameters areas under curve values of LMR, PLR, PMI and PLT/MPV parameters were found to be significant. Sensitivity, specificity, positive predictive value and negative predictive value of these four parameters in discrimination of COVID-19 and non-COVID-19, and the best cut-off points for these parameters are given in table 3.

Sensitivity and specificity ratios that result from these cut-off values may be influenced by the number of patients included in the study and by demographic features of the patient population. The use of these values we especially determined for PMI and PLT/MPV in clinic: a cut-off value with a high specificity provides a comfortable observation before further investigations and early consultation in suspected COVID-19 patients who presented to ED with complaints such as fever, cough and dyspnea; on the other hand, a test result above a cut-off value of high sensitivity can predict further investigation and early consultation for the patient.

Studies in the literature on this issue have analyzed a wide spectrum of blood parameters, biochemical parameters and enzymes. However, to our knowledge, there is still no study in the literature to investigate PMI and PLT/MPV parameters in terms of COVID-19 disease.

**Study Limitations:** First, this study has a retrospective design. In addition, it was conducted in a single center. On the other hand, the number of participants was relatively high. Perhaps we could analyze other parameters at the same time. However, given the abundance of parameters that could be studied, the study would be more complex to interpret and healthy conclusions would not be drawn. Therefore many studies have focused on different parameters. The most commonly studied parameters are lymphocytes, neutrophils, platelets, monocytes and WBC. We believe that the results we obtained from this study will be guiding for

further studies to be conducted on this issue.

### CONCLUSION

Discharge of COVID-19 patients should not be considered an endpoint for monitoring and precautionary measures. The way to full recovery may be long for COVID-19 patients and especially critical patients. In addition, the possibility of re-infection should be evaluated in patients who recovered from the disease. Regular control visits are necessary for monitoring possible changes in blood parameters and biochemical parameters and to assess potential complications in future. For this purpose blood parameters could provide practical methods. In our study, WBC, lymphocytes, monocytes, neutrophils, LMR, platelets, PMI and PLT/MPV levels decreased, while PLR and MPV values increased in COVID-19 patients. Our findings should be supported by further multicenter comprehensive studies.

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