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Evaluation of the Clinical Findings of the Patients Receiving the Diagnosis and Treatment of Covid-19 and the Data Based on the Applied Pain Scores

Covid-19 Tanı ve Tedavisi Alan Hastaların Klinik Bulguları ve Uygulanan Ağrı Skorlarına Bağlı Verilerin Değerlendirilmesi

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Abstract

Aim: The aim is to establish the most suitable treatment modalities for patient follow-ups, by correlating the physiological effect, namely the pain symptom, along with its variations, and the objective pain scale scores and certain biochemical parameters in response to the cellular, tissue, and organ deformation elicited by the Covid-19 virus infection.

Materials and Methods: In the study,Pain symptoms were evaluated with three different scales (FLACC, VAS, WB) and many biochemical parameters during daily follow-ups of patients who were hospitalized in Kafkas University Medical Faculty Research Hospital in Turkey between November 1 and November 16, 2020.

Results: In the study, it was observed that there were significant differences between the VAS hospitalization and VAS discharge scores ($p<0.001$) and between the WB hospitalization and WB discharge scores ($p<0.01$) in patients. Additionally, significant positive correlations were found between VAS hospitalization score and CRP, as well as between VAS hospitalization score and urea and creatinine ($p<0.01$), while a negative correlation was observed between VAS hospitalization score and CA value. Furthermore, a significant difference was detected between VAS discharge score and CRP and urea, with a weak positive correlation being found. These results suggest that pain scores have a significant association with laboratory findings in hospitalized patients.

Conclusion: An association can be observed between pain scores and laboratory parameters, resulting from the impact of a novel viral pathogen with global reach on select biochemical markers. However, additional investigations are required to corroborate these findings.

Keywords: Covid-19, biochemical parameters, pain scales, pain

Öz

Amaç: Covid-19 virüsü enfekte olmuş hastalarda virüsün yarattığı hücre, doku, organ deformasyonuna yanıt olarak oluşan fizyolojik etki yani ağrı semptomunu, çeşitliliğini ve objektif ağrı skala skorları ve biyokimyasal bazı parametrelerle ilişkilendirilerek tedavi rejimlerinin kapsamları, güvenilirlikleri hasta takipleri ile en uygun tedavi yaklaşımlarının belirlenmesini sağlamaktır.

Gereç ve Yöntem: Çalışma 1 Kasım -16 Kasım 2020 tarihleri arasında Türkiye'de Kafkas Üniversitesi Tıp Fakültesi Araştırma Hastanesinde yatarak tedavi gören ve günlük takiplerinde yapılan tetkiklerle, ağrı semptomları üç farklı ölçekle (FLACC, VAS, WB) ve birçok biyokimyasal parametre değerlendirildi.

Bulgular: Hastalarda VAS yatış ile VAS taburcu skorlar arasında ($p< 0.001$) ve WB yatış ile WB taburcu skorları arasında da anlamlı farklılık bulunmuştur ($p<0.01$). Ağrı skorları ile laboratuvar bulguları arasındaki ilişkilerinde VAS yatış skoru ile CRP arasında anlamlı pozitif, VAS Yatış skoru ile üre ve kreatinin arasında anlamlı pozitif ($p<0.01$), VAS yatış ile CA değeri arasında negatif yönlü, VAS taburcu skoru ile CRP ve üre arasında anlamlı pozitif zayıf bir ilişki olduğu görüldü.

Sonuç: Tüm dünyayı etkisi altına alan "yeni bir virüs" tarafından oluşturulan etkiye bağlı ağrı skorları ile bazı biyokimyasal değerler arasında ilişki vardır. Daha ileri çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Covid-19, biyokimyasal parametreler, ağrı skalaları, ağrı

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INTRODUCTION

Pain during respiratory tract infections caused by bacteria and viruses is one of the most important reasons that lead the patient to the doctor. Pain dimensions can be evaluated with unidimensional and multidimensional scales (1,2). The concept of pain, which is a universal experience, is defined by the International Association for the Study of Pain (IASP) as "sensory and emotional experience that is associated with or during tissue damage or potential tissue damage" (3). Since Covid-19 is a neurotropic virus, it can be a source of neurogenic-neuropathic pain, and it can also cause nociceptive and nociplastic pain with the release of various mediators as a result of tissue damage. Apart from these, it can also be a source of central and functional pain your damage; central nervous system symptoms (headache, epilepsy, delirium, cerebrovascular, encephalitis) inflammatory processes and peripheral nervous system symptoms (anosmia, agousis, acute myelitis, Guillain Barré syndrome, polyneuritis) are due to immune-mediated mechanisms, while musculoskeletal symptoms atony, paresis, myalgia) may be directly related (4). Considering the evaluation of data related to the biochemical findings and applied pain scores of COVID-I9 patients, in a retrospective observational study conducted in China, it is stated that 36.4% of the causes of pain are neurological, and in another study, neurological symptoms that cause pain are higher, especially in the elderly.(5,6). In Italy, it has been stated that the pain in hospitalized patients with Covid-19 is especially headache, and these have different characteristics of acute onset (7). Again, in a meta-analysis involving 1558 patients and six studies in China, chronic obstructive pulmonary disease, cardiovascular disease, diabetes and hypertension were found to be the most important independent risk factors, respectively (5). The prevalence of pain in hospitalized patients was found to be 37%. In studies examining the prevalence of pain, it has been reported that the main causes of acute pain are head and lower extremity pain, and chronic pain is low back pain (1). There are very few studies on biochemical findings that will contribute to the determination of the severity and degree of the disease with the findings that may be created by a "new virus" COVID-19 in study. The objective of this study is to identify the most appropriate treatment approaches for patient follow-ups by examining the physiological impact of pain symptoms, their variations, and objective pain scale scores, as well as certain biochemical parameters in response to cellular, tissue, and organ deformation induced by Covid-19 virus infection. To achieve this objective, the medical records of 189 patients in the Covid service at Kafkas University Medical Faculty Research Hospital and the intensive care unit were retrospectively analyzed. The average pain scores of patients were determined using the Face, Legs, Movement, Crying, Consolation, Behavioral Scale (FLACC), Visual Analog Scale (VAS), Faces Scale (FS=WB) scales, and the correlation between the disease and multiple other diseases and biochemical parameters were investigated.

MATERIAL and METOD

Material

In the study, records of 189 patients in the Covid service and intensive care unit of Kafkas University Medical Faculty Research Hospital between November 1 and November 16, 2020 were reviewed retrospectively. Considering the guidelines of the World Health Organization (WHO), SARS-CoV-2 RNA detection was performed by polymerase chain reaction (PCR=PCR) test in patients diagnosed with Covid-19 in accordance with the Declaration of Helsinki, regardless of whether they had a symptom or not. Approval of the Turkish Ministry of Health with the date and number of 15.04.20217 80576354-050-99762) was obtained from the Non-Interventional Clinical Research Ethics Committee of the Faculty of Medicine of Kafkas University. The patients who were hospitalized and evaluated in their daily follow-ups, including pain symptoms, were used with 3 different scales such as FLACC, VAS, WB. Asymptomatic patients who were diagnosed with Covid-19 and did not show signs of chest radiographs or chest tomography and did not have pneumonia were followed up with outpatient treatment. Age, gender, etiological factors and Ferritin, D-Dimer, WBC (Leukocyte count), HGB (Hemoglobin) (Hgb), HCT (Hematocrit), RDV (Red cell Distribution Width) (Erythrocyte count), NEU (Neutrophil), LYM (Lymphocyte Count), MON (Monocytes), BAS (Basophil), EOS (Eosinophil), NEU% (% Neutrophil), LYM% (% lymphocyte), MON %(% Monocytes), BAS% (% Basophil), EOS % (% Eozonophil), PCT (Platelet Crit), MPV (Mean Platelet Volume), PLT (Platelet count), PDW (Platelet Distribution Width), Troponine, laboratory values were studied. PT(SN) (Protronbine), PT% (%Protronbine), PT (INR)(Prothrombine time), Activated PTT (Partial Thromboplastin Time) were measured.

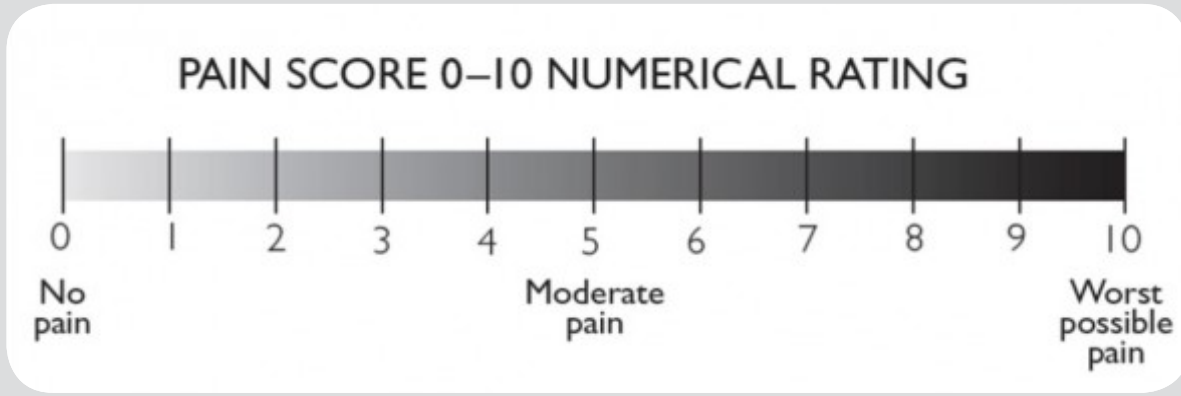

Figure 1. Pain rating scale (3)

Method

Thorax CT was performed for each patient, PCR test was performed, and those who were positive and those with Covid-19 symptoms had vital functions were hospitalized and Covid-19 treatment was started. The pain assessment scales 0-10 numerical pain assessment scales, which were administered to the patients on hospitalization and discharge days, were used.

Statistical Analysis

Descriptive statistics (mean, standard deviation, minimum, maximum, percentage values) of the data were calculated. Mann Whitney U test for two independent groups and Kruskall Wallis test for more than two independent groups were used as nonparametric test for the comparison of non-normally distributed parameters between groups. The results were found to be statistically significant at a 95% confidence interval, $p<0.05$.

RESULTS

The female patients were 68 (36.2%), 120 patients (63.8%) were male, and 96.8% of all patients had tumors; 80.9% had diabetes, 79.0% had hypertension, 87.7% had CH, 81.4% had reflux, 61.7% had cough and 98.4% had no fever.

It is seen that there are variables that have a very strong relationship between laboratory values, as well as variables that are unrelated to each other. The correlation between the variables is shown in Figure 2. As the correlation value between the variables approaches 1, the severity of the relationship between the variables increases. In Figure 2, the variables with a strong and positive relationship between them are shown in dark blue, and the variables with a negative and strong relationship between them are shown in dark red.

DISCUSSION

The Covid-19 epidemic has become an epidemic that threatens global health, weakens the global economy and destabilizes societies around the world (8,9). According to the recommendations published by the International Federation of Clinical Chemistry COVID 19 working group, biochemical and hematological tests; It is stated that it will be useful in the diagnosis of tissue-organ damage related to infection, in identifying the patient with a low risk of severe disease, in determining the patient with a poor prognosis, and in monitoring the course of the disease (10). It was tried to reveal whether there is a relationship with the level of for this purpose, CRP, CK, ALP, AST, ALT, EOS, HGB, HCT, LYM, Troponine T, Urea, creatinine, CA and LDL parameters were evaluated primarily.

Studies have shown that 75.8% of COVID-19 patients admitted to the emergency department have low albumin, 58.3% high C Reactive Protein (CRP), 57.0% high lactate dehydrogenase (LDH), 210 U/L for LDH. L was determined as 35 U/L cutoff value for aspartate aminotransferase (AST) (11). The result of many studies

Table 1. Descriptive statistics of variables

Age	Number(n)	%
< 35 yş	9	4.8
35 - 49	14	7.4
50 - 64	49	26.1
>= 65	116	61.7
Total	188	100.0
Gender		
Female	68	36.2
Male	120	63.8
Total	188	100

Table 2. Descriptive statistics of diseases

Tumor	**Number**	**%**
Not presence	182	96.8
Presence	6	3.2
Total	188	100.0
Diabetes		
Not presence	152	80.9
Presence	36	19.1
Total	188	100.0
HT		
Not presence	147	79.0
Presence	39	21.0
Total	186	100.0
KH		
Not presence	165	87.8
Presence	23	12.2
Total	188	100.0
Reflux		
Not presence	153	81.4
Presence	35	18.6
Total	188	100.0
Cough		
Not presence	116	61.7
Presence	72	38.3
Total	188	100.0
Fever		
Not presence	185	98.4
Presence	3	1.6
Total	188	100.0

Table 3. Descriptive statistics of pain scores and comparisons of pain scores

Variable	n	Avarage	Sd	Median	Min	Max	p
VAS hospitalisation	185	8.12	1.63	9	2	10	p<0.001
VAS discharged	184	5.29	1.79	5	1	10	
WB hospitalisation	184	6.64	1.62	6	2	10	p<0.001
WB discharged	183	4.29	1.65	4	1	10	

P<0.05 Wilcoxon-igned rank teste

on Covid-19 patients is decrease in blood lymphocyte and fibrinogen levels and liver-kidney function tests, troponin I, D-Dimer, lactate dehydrogenase, prothrombin time, creatinine kinase, C-reactive protein, ferritin, interleukin-6 increase. may guide the clinician as predictors of poor prognosis (12). Although most patients

Table 4. Distribution of pain scores in CoRads groups

	CoRads					
	1	2	3	4	5	
Pain score	median (min- max)					p
VAS hospitalisation	9 (2-9)	9 (9-10)	9 (5-10)	9 (7-10)	8 (4-10)	0,11
VAS discharged	5.5 (2-6)	7 (6-8)	6 (3-9)	6 (4-8)	5 (1-10)	0,13
WB hospitalisation	8 (2-8)	8 (6-8)	8 (4-8)	8 (4-8)	6 (4-10)	0,86
WB discharged	4 (2-6)	6 (4-6)	6 (2-6)	4 (2-6)	4 (2-10)	0,50

P<0.05, Kruskall- Wallis teste

Table 5. Pain scores by FLACC hospitalization and FLACC discharge status

	FLACC hospitalisation			**FLACC** discharge		
	1	2		1	2	
Pain scores	median (min- max)		p	median (min- max)		p
VAS hospitalisation	5 (2-8)	9 (5-10)	0,00	8 (2-10)	9 (6-10)	0,00
VAS discharged	3 (1-5)	6 (2-10)	0,00	5 (1-8)	7 (5-10)	0,00
WB hospitalisation	4 (2-6)	8 (4-10)	0,00	6 (2-10)	8 (6-10)	0,00
WB discharged	2 (1-4)	4 (2-10)	0,00	4 (1-6)	6 (4-10)	0,00

P<0.05, Mann Whitney U test

have high levels of CRP, elevations of ALT, AST, CK, and D-Dimer are less common in the initial phase of the disease, in severe cases, compared to non-serious cases. more prominent laboratory abnormalities have been demonstrated (12,13). As in other studies, the severity of the disease can be predicted as the determining factors of oxygen saturation, respiratory rate, lung x-ray/tomography findings, as well as blood C-reactive protein (CRP),

Table 6. Correlations between VAS and WB scores and laboratory findings

Pain Score		EOS	HGB	HCT	LYM	WBC	CRP	LDH	Troponin	AST	ALT	Üre	Creatinin	CA
VAS hospitalisation	r	-0,02	-0,14	-0,14	-0,04	0,07	0,201*	0,05	0,14	-0,03	-0,14	0,259*	0,230*	-0,160*
	p	0,82	0,06	0,06	0,64	0,32	0,01	0,48	0,06	0,68	0,06	0,00	0,00	0,03
VAS discharged	r	0,03	-0,06	-0,08	-0,01	0,09	0,157*	0,05	0,12	0,00	-0,05	0,199*	0,11	-0,10
	p	0,68	0,44	0,30	0,91	0,25	0,04	0,50	0,12	1,00	0,48	0,01	0,16	0,18
WB hospitalisation	r	-0,06	-0,168*	-0,180*	-,155*	-0,01	0,15	0,01	0,12	-0,09	-,181*	0,251*	0,159*	-0,12
	p	0,46	0,02	0,02	0,04	0,84	0,05	0,93	0,11	0,23	0,02	0,00	0,03	0,11
WB discharged	r	-0,03	-0,11	-0,13	-0,11	0,07	0,157*	0,00	0,15	-0,10	-0,14	0,211*	0,09	-0,05
	p	0,73	0,14	0,08	0,14	0,38	0,04	0,95	0,05	0,19	0,07	0,00	0,24	0,51

P<0 5

coagulation tests, procalcitonin, lactate dehydrogenase and creatine kinase (CK) results and pain intensity. degree is that there may be predictable parameters about the severity of the disease. It suggests that COVID-19 infection may be associated with cellular immunodeficiency, coagulation activation, myocardial injury, liver and kidney damage (6,12,13).

In another study, more advanced age (32.0 (26.0-39.3); 54.0 (38.3-59.3), p<0.001) in the inpatient group, blood values higher lactate dehydrogenase (LDH) (195.0 (156.5-225.3); 248.5 (200.3-334.5), p<0.001) and higher NLR (1.56 (1.08-2.62); 2.60 (1.65-4.90), p<0.001) were seen. Accordingly, advanced age, high LDH and high NLR values in Covid-19 patients require inpatient treatment (14).

It has been observed that patients with Covid-19 have become dependent/semi-dependent in performing some activities of daily living due to pain in varying degrees and accompanying systemic symptoms. It is seen that patients can change the time to stand up according to the degree of their activities being affected. Knowing the severity of the pain that affects the activities of the patients ensures that the interventions are made and the patients are discharged early. For this, the intensity of the pain must be measured accurately.

Considering the data obtained in our study; while it may be possible that patients' own descriptions and scale score determinations may be affected by their psychological moods related to the symptoms of the disease, the categorical data in the FLACC measurement is more likely to allow the determination of more objective data depending on the physical examination findings. Although there are not enough articles evaluating pain profiles, studies show that there is a significant parallelism between pain and clinical and biochemical findings (16,17). It has been reported that the rate in patients with myalgia, head, throat and chest pain is 28.5%, 14.9%, 14.0%, 12.3%, respectively.

CONCLUSION

Based on our findings, it can be posited that pain is not a prominent symptom in Covid-19 patients, but it may be a determining factor in patients with mild to moderate symptoms. Our analysis reveals a positive, strong, and statistically significant relationship (p<0.001) between the VAS admission and VAS discharge, as well as WB admission and WB discharge variables, with correlation coefficients of 0.823, 0.734, and 0.744, respectively. Furthermore, there is a significant association between VAS discharge and WB hospitalization and discharge (p<0.001), with a correlation coefficient of 0.660 between VAS variable and WB hospitalization, and 0.765 between WB discharge. Additionally, a strong and significant correlation (p<0.001) was found between WB hospital-

Table 7: Laboratory findings by FLACC hospitalization status

	FLACC hospitalisation	**Ort ± SD**	**Median (min-Maks)**	**p**
EOS	1	0,1316± 0.22	0,1 (0-1)	0.906
	2	0,1257±0,36	0,1 (0-3,70)	
HGB	1	14,98±1,97	15,08 (9,6 -18,409)	0.234
	2	14,64±1,71	14,660(9,7-18-60)	
HCT	1	44,81±6,17	45,4 (31,60-60,70)	0.170
	2	43,45±4,64	43,55 (31,9-57)	
LYM	1	1,56±0,69	1,7 (0,61-3,30)	0.659
	2	1,445±0,58	1,3 (0,37-4,30)	
WBC	1	5,99±1,53	5,5 (3,60-9,60)	0.457
	2	6,27±2,96	5,7 (2,5-20,5)	
CRP	1	3,04±5,91	1,03 (0,07-25,24)	0.016
	2	4,02±5,27	2,2 (0,06-34,12)	
LDH	1	268,68±72,66	258 (188-455)	0.169
	2	308,84±125,11	282 (108-814)	
Troponin T	1	23,1±52,46	11 (3-239)	0.786
	2	18,26±28,44	12 (3-269)	
AST	1	25,05±10,59	25 (15-63)	0.062
	2	31,06±20,16	26 (11-161)	
ALT	1	25,68±9,74	21 (14-47)	0.646
	2	30,92±52,14	20,5 (5-526)	
Ure	1	36,15±11,38	33 (23-62)	0.05
	2	48,96±25,42	41 (16-152)	
Creatinin	1	0,91±0,23	0,9 (0,53-1,60)	0.250
	2	1,11±0,95	0,98 (0,38-10,07)	
CA	1	9,12±0,65	9,1 (8-10)	0.192
	2	9,05±0,71	9 (7,5-12,50)	

*p<0.05

ization and WB discharge variables, with a correlation coefficient of 0.807. The correlation analysis is presented in Figure 1.

While a weak negative correlation (p=0.02, p=-0.168) was observed between the WB hospitalization score and HGB, a similar negative correlation was found between WB hospitalization score and HCT (p=0.02, p=-0.180). Moreover, a weak negative correlation (p=0.04, r=-0.155) was found between the LYM value and the WB hospitalization score, and a weakly significant negative correlation was identified between the WB hospitalization score and the ALT value (p=0.02, r=-0.181). On the other hand, a significant, positive weak correlation was observed between WB hospitalization and re and creatinine values (p<0.01, r=0.251; p=0.03, r=0.159). Furthermore, we tested the existence of a significant and positive weak correlation between WB discharge score and CRP and urea values (p=0.04, r=0.157; p<0.01, r=0.211).

According to Mann Whitney U test results, CRP levels differ significantly according to FLACC hospitalization status (p=0.016). When the FLACC Admission score was 1, the median value for CRP was 1.03 (0.07-25.24); When the FLACC hospitalization score was 2, the median CRP value was 2.2 (0.06-34.12). Urea values also show a significant difference in Flacc hospitalization (p=0.05). Urea median value was 33 (23-62) when Flacc hospital-

Table 8: Laboratory findings by Flacc discharge status

	Flacc Disharged	Avarage	Median (Min-Maks)	p
EOS	1	0,105± 0,12	0,1 (0-1)	0.632
	2	0,16±0,53	0,1 (0-3,7)	
HGB	1	14,78±1,7	14,98 (9,6-18,6)	0.065
	2	14,5±1,84	14,61 (10,30-18,36)	
HCT	1	44±4,93	43,9 (31,6-60,70)	0.035
	2	43,06±4,85	43,4 (33,70-52,10)	
LYM	1	1,5±0,61	1,3 (0,60-4,30)	0.185
	2	1,39±0,57	1,3 (0,37-3)	
WBC	1	5,95±2,51	5,3 (2,5-15,10)	0.095
	2	6,7±6,1	3,18 (2,80-20,50)	
CRP	1	3,37±4,69	1,47 (0,06-25,24)	0.042
	2	4,73±6,3	2,36 (0,24-34,12)	
LDH	1	304,21±125,12	279 (108-814)	0.871
	2	300,21±109,86	275 (141-582)	
Troponin T	1	16,57±27,73	11 (3-239)	0.063
	2	23,17±40,45	13 (3-269)	
AST	1	31,28±20,32	26 (13-161)	0.049
	2	28,21±16,88	24 (11-108)	
ALT	1	28,17±19,49	21 (5-114)	0.030
	2	33,48±75,6	18 (8-526)	
Ure	1	42,54±18,8	38 (16-112)	0.002
	2	54,7±30,17	42,5 (20-152)	
Creatinine	1	1,09±1,07	0,93 (0,5-10,07)	0.122
	2	1,05±0,39	1 (0,38-2,38)	
CA	1	9,04±0,55	9 (7,8-10,20)	0.209
	2	9,1±0,91	8,9 (7,5-12,50)	

*p<0.05

ization was 1, and urea median value was 41 (16-152) when FLACC hospitalization was 2. Here, there is a significant difference between the HCT value and the Flacc discharge status, and when the FLACC discharge score is 1, the HCT median value is 43.9 (31.6-60.7); When the FLACC discharge score was 2, the median HCT value was 43.4 (33.70-52.10). CRP values differ significantly according to FLACC discharge status (p=0.042). When the FLACC Discharge score is 1, the median CRP value is 1.47 (0.006- 25.24); When the FLACC discharge score was 2, the median CRP value was 2.36 (0.24-34.12). While AST values differ significantly according to Flacc discharge status (p=0.04), when FLACC discharge score is 1, the median AST value is 26 (13-161); When the FLACC discharge score was 2, the median AST value was calculated as 24 (11-108). ALT also differs significantly according to FLACC discharge status (p=0.030). Again, Urea showed a significant difference according to the Flacc discharge status (p=0.002), while the median value of urea was 38 (16-112) when the FLACC discharge score was 1, and the median value of urea was 42.5 (20-152) when the FLACC discharge score was 2.

For the orthopedics and traumatology specialist, the pain in COVID-19 patients is a process that only concerns neuroanatomical and neurophysiological, joint, muscle, tendon, bone and cartilage tissues, while the

psychological dimension of this process is extremely important for the physician who sees pain as the sum of physical, mental and social factors. The correct interpretation of symptoms and the use of categorical measurement methods in pain measurement and evaluation are valuable for diagnosis and treatment regimens. The findings obtained in this study are very important in terms of giving clinicians and biochemists some clues about the prognosis and mortality of the disease, considering the Covid-19-pain-biochemical parameters relationship as a whole. For this reason, in order to finalize the treatment in viral infections, it may be recommended to carry out specific studies that reveal the metabolism of the virus-iron interaction and the parameters affected by the infection, and to focus on studies to reduce iron.

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