ARAŞTIRMA MAKALESİ / *RESEARCH ARTICLE*

Intensive Care Prediction During Treatment of Covid-19 Patients

Covid-19 Hastalarının Tedavisi Sırasında Yoğun Bakım Tahmini

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ABSTRACT

Aim: *We aimed to research the routine examinations, clinical and radiological findings of patients hospitalized with the diagnosis of Covid-19, the clinical course of the patients whose treatments were ongoing, and the markers that could predict the possibility of admission to the intensive care unit.*

Material and Method: *Retrospectively compared the examinations and findings on the day of hospitalization of the patients who were followed up for Covid-19 treatment with the data on the first day of their admission to the intensive care unit.*

Results: *Out of 195 patients treated with the diagnosis of Covid-19 in the service on the first day. Fever, shortness of breath, chest pain, and cough were the most common symptoms. Platelet and lymphocyte ratio was higher in the patients' first days in the service compared to the first days in intensive care, and the change that occurred was statistically significant (p<0.05). A significant difference was found between SOFA score and gender (p<0.05) and between SOFA score and age (p<0.05).*

Conclusion: *Covid-19 patients with comorbid diseases such as advanced age, diabetes, hypertension, heart and respiratory failure, and acute and chronic renal failure carry a higher risk.*

Key words: *intensive care; covid-19; PLR; SOFA score*

ÖZET

Amaç: *Covid-19 tanısıyla hastaneye yatışı yapılan hastaların rutin tetkikleri, klinik, radyolojik bulguları ile tedavisi devam eden hastaların klinik seyrini ve yoğun bakıma alınma ihtimalini önceden gösterebilecek belirteçleri araştırmayı amaçladık.*

Materyal ve Metot: *Covid-19 tedavisi için takip edilen hastaların hastaneye yatış günü muayene ve bulguları retrospektif olarak yoğun bakıma yatışlarının ilk günkü verileriyle karşılaştırıldı.*

Bulgular: *Serviste ilk gün Covid-19 tanısı ile tedavi edilen 195 hastadan. Ateş, nefes darlığı, göğüs ağrısı ve öksürük en sık görülen semptomlardı. Hastaların servisteki ilk günlerinde trombosit ve lenfosit oranı yoğun bakımdaki ilk günlere göre daha yüksek bulundu ve meydana gelen değişim istatistiksel olarak anlamlıydı (p<0,05). SOFA puanı ile cinsiyet arasında (p<0,05), SOFA puanı ile yaş arasında (p<0,05) anlamlı fark bulundu.*

Sonuç: *İleri yaş, diyabet, hipertansiyon, kalp ve solunum yetmezliği hastalıkları, akut ve kronik böbrek yetmezliği gibi komorbid hastalıkları olan Covid-19 hastaları daha yüksek risk taşımaktadır.*

Anahtar kelimeler: *yoğun bakım; covid-19; PLR; SOFA skoru*

Introduction

The Coronaviridae family, which includes different mammalian and animal pathogens, may cause different clinical pictures in humans, ranging from colds to severe respiratory diseases. Coronavirus infection emerged in Wuhan, China, in December 2019 and is called Covid-19 (2019-nCoV), following the Severe Acute Respiratory Syndrome (SARS-CoV) and Middle East Respiratory Syndrome (MERS-CoV), which have been effective worldwide with the millennium and are epidemiologically considered zoonotic infections[1,2]. Coronaviruses can spread rapidly among infected cases and cause a worldwide pandemic[3]. In patients infected with Covid-19, it is difficult to isolate and diagnose the agent since different clinical pictures often occur, and some cases may be asymptomatic.

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Hence, it is important to perform a detailed physical, radiological, and laboratory examination[4,5]. The most common symptoms in Covid-19 patients were fever, cough, and fatigue. The definitive diagnosis is made with real-time Polymerase Chain Reaction (PCR), and the image of "ground glass opacity" in computed tomography helps the diagnosis[6,7,8]. Most patients with suspected Covid-19 are followed up on an outpatient basis since they do not have severe pneumonia findings. Some patients with negative PCR test results received anti-viral treatment due to ground glass appearance on thorax computed tomography (CT) [9]. While some patients admitted to the hospital are discharged after short-term treatment, some require intensive care due to severe respiratory distress and deterioration[10]. In suspicious cases admitted to the hospital, treatment of acute respiratory failure and hemodynamic support, isolation, and rapid diagnosis are needed. Decision-making processes can guide implementations in the follow-up[11]. This algorithm is important not only for the clinical follow-up and treatment plan of Covid-19 patients but also for healthcare workers and other patients at risk of nosocomial infection[12]. This study investigated the markers that could predict the possibility of the need for an intensive care unit in a tertiary hospital.

Materials and Methods

A retrospective analysis was conducted on admitted and confirmed Covid-19 cases at the Samsun Training and Research Hospital between March 11 – May 30, 2020. The same hospital conducted the study after the Ministry of Health Scientific Committee's approval with the form 2020-05-17T22_26_50, and the Local Ethics Committee dated 05.06.2020 and numbered Non-Interventional Clinical Research/2020/8/1.

Selection of Patients

For patients treated in the hospital with the diagnosis of Covid-19, the clinical picture worsened during their treatment, and patients who were taken into the intensive care unit were included in the study. The hospitalization period of the patients in the service was at least one day. While comparing the service and intensive care parameters of the patients, the parameters on the first day of the service admission were defined as the service period (SP) and the intensive care period (ICP) for the parameters on the first day in the intensive care unit.

Data Collection

Age, gender, hospitalization indication, indication for admission to intensive care unit, co-morbid diseases, CT evaluation, and PCR test result on the first day were obtained from patient records. The patients' routine biochemistry and complete blood count were evaluated according to the results of the first day of admission to the service and the first day of admission to the intensive care unit. The Sepsis-related Organ Failure Assessment (SOFA) was analyzed according to the day they were taken into intensive care.

Statistical Study

The data were analyzed using the statistical software SPSS 24 (Statistical Package for the Social Sciences–IBM®). Descriptive statistics were presented as numbers and percentages for categorical, mean ± standard deviation, or median for numerical variables. The normality of continuous variables was evaluated using the Kolmogorov-Smirnow test and the Shapiro-Wilk test. For comparison of numerical variables between groups, the Mann-Whitney U test was used for two independent groups; one Way Anova test or Kruskal-Wallis Method was used for more than two groups. Bonferroni Test was applied after multiple analyses. While the distribution relationship between categorical variables was analyzed with the Chi-Square test, the t-Test for Two Independent Groups was used to compare numerical data. The results were evaluated at a confidence interval of 95%, with a value of $p<0.05$ considered significant.

Results

Out of 195 patients that were included in our study, 105 (53.8%) were male, and 90 (46.2%) were female (Table 1). The average age of the patients was 69.77±15.73 years; the average age of women was significantly higher than the average age of men ($p<0.05$) (Table 1).

In SP of the patients, fever (n=x, 36.9%), shortness of breath (n=x, 80%), cough (n=x, 25.1%), and chest pain (n=x, 14.9%) were the most common symptoms. When the symptoms were analyzed in the ICP, 12.82% fever, 89.74% shortness of breath, 10.77% chest pain, and 15.9% cough were significant (Table 2).

In patients, 44.62% hypertension (HT), 14.36% Acute renal failure/Chronic renal failure (ARF/CRF), 23.59% heart failure, 15.38% Coronary Artery Disease (CAD), 18.97% Chronic Obstructive Pulmonary Disease

(COPD), 26.67% Diabetes Mellitus (DM), 12.31% cancer and 22.05% Cerebrovascular Disease (CVD) were the most common comorbid diseases (Table 3).

In the study, CT was performed in 95.38% of the patients who received treatment, 81.03% consistent with Covid-19, and 18.97% had non-infectious CT findings (Table 4). In ICP, 25.13% (n=49) patients required intubation (Table 2).

In the study, hemogram and biochemistry results in SP and ICP were compared in 2 groups; C-reactive Protein (CRP), white blood cell (WBC), erythrocyte (RBC), hemoglobin (Hb), hematocrit (Hct), platelet (Plt), absolute lymphocyte (Lym), monocyte, eosinophil, basophil, red blood cell volume (RDW), mean platelet volume (MPV), mean values of glucose, urea, and calcium were found to be lower than the results of the first day in service. However, absolute neutrophil (Neu), creatine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), retain kinase (CK), sodium, potassium, and chlorine values were observed to be higher than in the first day in the service. Increases and decreases in mean values of CRP, WBC, RBC, Plt, Lym, Neu, eosinophils, basophils, glucose, urea, AST, potassium, and chlorine were statistically significant ($p<0.05$) (Table 5).

The mean neutrophil/lymphocyte ratio (NLR) was 6.29±3.32 in SP and 8.56±3.26 in SP and ICP. No statistically significant difference was found in the NLR values of the groups ($p>0.05$). The mean platelet/lymphocyte ratio (PLR) was 241.7±58.99 in SP and 226.33±58.32 in ICP. The change in PLR values was found to be statistically significant ($p<0.05$) (Table 6).

In the study, the mean age of the patients with the SOFA score between 0–5 was 68.64±16.74 years, and the mean age of the patients with the SOFA score between 6–11 was 71.88±13.51 years. A statistically significant difference was found between SOFA score and age ($p<0.05$) (Table 7).

The PCR test we used for diagnosis was negative in 31.28%, positive in 59.49%, and not studied in 9.23% (Table 8).

Discussion

Covid-19 disease, which infects millions of people worldwide, affects older people with high comorbidities more and increases hospitalization rates. Due to the hospital's limited service and intensive care bed capacities, a good triage is required for patient admission to both services and intensive care units.

Table 1. *Demographic data*

		SG patients (n: 195)				t Test	P-value
		n	%	Avg ± Std	Min-max		
Age (years)	Female	90	46.2	72.63±15.05	24–92	**2.369**	**0.032***
	Male	105	53.8	67.32±15.95	20–92		
	Total	**195**	**100**	**69.77±15.73**	**20–92**		

Table 2. *Data on SG complaints, CUG patient complaints, and intubation status*

		SG patients (n: 195)		CUG patients (n: 195)		
	V/Y	n	%	n	%	p
Fever	Yes	72	36.92	25	12.82	**0.048***
	No	123	63.08	170	87.18	
Shortness of breath	Yes	156	80.00	175	89.74	**0.007***
	No	39	20.00	20	10.26	
Cough	Yes	49	25.13	31	15.9	**0.001***
	No	146	74.87	164	84.1	
Chest pain	Yes	29	14.87	21	10.77	**0.001***
	No	166	85.13	174	89.23	
Endotracheal intubation	Yes	-	-	49	25.13	
	No	-	-	146	74.87	

Table 3. *Presence of comorbid disease*

		SG patients (n: 195)	
Comorbid diseases	V/Y	n	%
HT	**Yes**	**87**	**44.62**
	No	108	55.38
ABY/KBY	**Yes**	**28**	**14.36**
	No	167	85.64
Heart failure	**Yes**	**46**	**23.59**
	No	149	76.41
CAH	**Yes**	**30**	**15.38**
	No	165	84.62
COPD	Yes	37	18.97
	No	158	81.03
DM	Yes	52	26.67
	No	143	73.33
Cancer	Yes	24	12.31
	No	171	87.69
CVD	Yes	43	22.05
	No	152	77.95

Table 4. *Data of the first day CT results in service*

		Patients who received treatment on the first day in the service (n: 195)	
		n	%
CT	Yes	186	95.38
	No	9	4.62
Compatible with COVID-19	Yes	158	81.03
Non-infectious finding	Yes	28	18.97

Table 5. *SG and CUG hemogram and biochemistry results*

	SG (n: 195)		CUG (n: 195)			
	Avg.	std.	Avg.	std.	T	P-value
CRP	68.75	84.32	53.88	91.28	11.387	**0.041****
WBC	10.81	5.84	10.75	6.19	25.819	**0.032****
RBC	4.05	0.80	3.86	0.87	70.797	**0.001****
HB	11.66	2.64	11.13	2.66	61.760	0.345
HCT	34.69	7.15	33.03	7.59	67.724	0.471
Platelet	251.39	116.81	235.39	116.00	30.053	**0.008****
Neutrophil	8.50	5.45	8.91	5.89	21.787	**0.005****
Lymphocyte	1.35	1.18	1.04	0.65	16.021	**0.001****
Monocytes	0.67	0.44	0.66	0.46	4.841	0.933
Eosinophil	0.09	0.26	0.07	0.22	10.798	**0.042****
Basophils	0.05	0.07	0.04	0.05	2.912	**0.004****
RDW	16.16	3.10	15.92	3.86	1.465	0.198
MPV	8.51	1.08	8.63	1.46	25.310	0.099
Glucose	166.27	91.74	144.79	73.03	18.196	**0.001****
Urea	72.40	55.56	77.31	56.02	12.877	**0.040****
Creatinine	1.72	2.64	1.74	2.16	10.403	0.762
Ast	42.47	46.06	84.46	345.67	14.012	**0.030****
Alt	30.51	40.96	56.82	222.69	6.067	0.099
Amylase	73.77	73.33	93.09	176.97	3.653	0.119
Creatine kinase (CK)	210.85	482.84	265.79	611.35	9.161	0.109
Calcium (Ca)	9.24	9.45	8.35	1.35	6.964	0.195
Sodium (Na)	134.35	20.58	136.77	15.30	7.980	0.168
Potassium (K)	4.37	1.00	4.23	0.86	1.387	**0.048****
Chlor (Cl)	99.09	20.36	102.20	12.24	5.819	**0.033****

Table 6. *NLR and PLR analysis values in SG and CUG*

	SG	CUG	
	Avg. ± SD	Avg. ± SD	P
NLR	6.29±3.32	8.56±3.26	0.773
PLR	241.7±58.99	226.33±58.32	**0.001****

Avg. ± SD: Mean ± standard deviation; NLR: Neutral lymphocyte ratio; PLR: Lymphocyte/Platelet ratio.

Table 7. *Comparison of CUG age-SOFA score*

		Age (years)		
		Avg ± Std	t Test	P-value
SOFA score	0–5 (n: 127)	68.64±16.74	4.523	**0.001***
	6–11 (n: 68)	71.88±13.51		

Table 8. *Data of PCR results*

		SG patients (n: 195)	
		n	%
PCR result	Negative	61	31.28
	Positive	116	59.49
	No	18	9.23

Thousands of patients infected with Covid-19 are followed up in hospital services in our country. While the follow-up and treatment of these patients are being carried out, it is tough to predict patients whose general conditions get worse and who may need intensive care. While many studies in the literature analyze the demographic characteristics, clinical course, and prognosis of Covid-19 patients, we aimed to see the indicators that could predict the need for intensive care treatment. While the indication of admission to intensive care at an appropriate time allows effective use of limited intensive care beds, it significantly reduces the mortality and morbidity of patients. Hence we tried to correlate the early triage or progression of the patients with the presence of symptoms and comorbid diseases, physical, imaging, and radiological findings on admission.

In a study conducted by Li et al., among the reasons affecting the risk of death from Covid-19, three important factors were identified: male gender, age above 60 years, and presence of comorbid diseases (diabetes mellitus, hypertension, chronic respiratory failure, cancer, and cardiovascular diseases)[13]. In our study, the average age

of patients who required intensive care was seventy in both genders, and the male gender was more common. The patients' ages and existing comorbid diseases who needed intensive care were similar to other studies.

The SOFA score was significant in showing mortality and morbidity in COVID-19 patients. In a study, patients with SOFA score ≥3 had high mortality[14]. Besides, a significant correlation was found between SOFA score and gender ($p<0.05$) and between SOFA score and age ($p<0.05$)[13]. Bhatraju et al. reported that the mortality rate of COVID-19 patients over the age of 65 is higher than the rest[15]. We found the mean age of patients with high SOFA scores who required intensive care higher. This can be attributed to the presence of comorbid diseases. Hence, it can be considered that patients with Covid-19 are more commonly affected systemically if they have comorbid diseases.

In a meta-analysis conducted on 1500 patients, HT, DM, COPD, cardiovascular disease, and CVD were identified as independent risk factors in patients with Covid-19 infection. However, they found no effect on cancer, liver, and kidney disease[16]. The most common comorbid diseases we found in patients were DM, HT, Heart failure, and SVH. These comorbidities are frequently encountered in the elderly population and may increase the risk of admission to the intensive care unit. Comorbid diseases similar to the literature were observed to accompany the clinical pictures in our study. The correlation of comorbid diseases between the groups was not analyzed because the comparisons between the first day of hospitalization and the first day of intensive care could be seen as a study limitation.

Covid-19 tends to cause more severe health problems in those with comorbid diseases and the elderly. According to the report that was prepared by Wu et al., while 81% of elderly patients were mild, 14% severe, and 5% were critical; the mortality rate was reported to be between 2.5–5%[17].

In the study of Guan et al.[18], the rates regarding the severity of the disease were also very close, supporting Wu et al.[17]. They reported 80% of cases as mild to moderate, 13% as severe (dyspnea, respiratory rate ≥30/min, oxygen saturation ≤93%, $PaO_2/FiO_2<300$ and more than 50% lung within 24–48 hours involvement), 6% as critically ill (respiratory failure, septic shock, and multiple organ failure). Fever, shortness of breath, cough, and chest pain were the most common symptoms. While the symptom of shortness of breath increased significantly in patients who were taken into intensive care, the changes in other symptoms were also significant. They were seen as factors that accelerated the admission to intensive care.

In a meta-analysis of asymptomatic Covid-19 patients, Kronbichler et al.[9] reported radiological findings of lung involvement in 62.2% of the cases. The data show that the radiological imagings were valuable. In our study, the most common complaint seen in patients treated in the service on the first day was shortness of breath. CT was performed in 95.38% of these patients, non-infectious findings were observed in 19% of the patients, and radiological findings compatible with Covid-19 were observed in 81%. Approximately 25% of the patient's required endotracheal intubation during intensive care treatment. Furthermore, although some of our patients had negative PCR tests, they were diagnosed and treated with the detection of "ground glass appearance." Radiological diagnosis can prevent delay in treatment as PCR tests can produce false negative results due to non-standard techniques, kit, and test equipment errors. Since some of our patients were brought from external institutions as PCR positive, treatment was initiated in these patients without the test being studied.

Considering the results of hemogram and biochemistry, the values did not return to normal limits on the first day in the intensive care unit suggests that the clinical picture mainly affects the prognosis, not the laboratory results. In other words, the admission of patients to intensive care during the early period of hospitalization can be attributed to the severity of their clinical symptoms and the limited time of initiation of treatment. Another detail is that the duration of hospital admission after the onset of symptoms has an impact on prognosis, as well.

The prognostic value of NLR and PLR values in infectious diseases has been shown in many studies, and it is known that they may have prognostic significance even in advanced-stage cancers[19,20]. NLR and PLR values were also evaluated in Covid-19 patients since it is obvious that the hemogram parameters, which were routinely assessed and frequently controlled during the initial diagnosis, can be used to determine the severity of the disease at a lower cost. Studies show that the NLR value is significantly associated with Covid-19 disease severity and even mortality in male patients[21,22]. This study found no significant correlation between NLR and the seriousness of Covid-19 disease, which may be explained by the low sample size of our research. On the contrary, the PLR level was found to have a significant predictive significance. Qu et al. concluded that the PLR value

could be associated with cytokine storm in patients requiring lengthy hospitalization. This supports our findings and may suggest that the PLR value may show the need for an intensive care unit[23].

The main limitation of our study is the small sample size and the single-center design.

Conclusion

Hospitalization and treatment should not be delayed in elderly patients with comorbid diseases and suspected Covid-19 to reduce the need for intensive care treatment.

We believe that close monitoring of symptoms such as fever and dyspnea, careful analysis of thoracic CTs, and selective admission to the intensive care unit according to hemogram and PLR values can significantly reduce mortality and morbidity of this patient cohort.

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