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A new parameter for predict the clinical outcome of patients with COVID-19 pneumonia: The direct/total bilirubin ratio

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Abstract

Aim: An urgent need to define clinical and laboratory parameters to predict progression to the severe and lethal forms of Coronavirus Disease 2019 (COVID-19). To investigate the direct/total bilirubin ratio (D/TBil), as a novel parameter, to predict the poor survival of COVID-19 Pneumonia.

Methods: The clinical characteristics and laboratory parameters of hospitalised COVID-19 pneumonia patients were analysed from 20 March to August 1, 2020, in a tertiary hospital, retrospectively. All remarkable variables were selected for a forward stepwise binary logistic regression analysis to define the independent risk factors for mortality.

Results: 537 (248 women and 289 men) patients were separated into two groups for analysis: survivors vs deceased. The mean age of the deceased group was statistically significantly higher than the survivor group 72 (30-92) years vs 50 (18-97) years ($P < .001$). D/TBil, age, gender, hypertension and neutrophil-to-lymphocyte ratio (NLR) variables contributed significantly to the binary logistic regression model. The mortality risk increased 14.6 times in patients with D/TBil > 0.5, and 2.4 times in patients with NLR > 4.

Conclusion: D/TBil > 0.5 was associated with a novel parameter to poor survival of COVID-19 on admission. Also, the combination of age, gender, the presence of hypertension, D/TBil and NLR contributed significantly to predicting the poor survival of COVID-19.

1 | INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a highly infectious viral respiratory disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). COVID-19 has spread rapidly nearly all around the world and is becoming an important public health condition.[1,2] Patients, infected by SARS-CoV-2, have varied clinical presentations from asymptomatic/mild symptoms to severe illness and mortality.[3]

Early in the outbreak, there was an urgent need to define clinical and laboratory parameters to predict progression to the severe and lethal forms of COVID-19. Also, early recognition of severe patients with COVID-19 would be of vital importance for the management of disease and the use of medical facilities. At present, many studies show that lots of laboratory parameters are utilised to determine and predict the severity of COVID-19, which is hoped to be of major aid to physicians. Also, these laboratory parameters are useful tools for the evaluation of the severity and extent of COVID-19 pneumonia.[4-8] Bilirubin, an endogenous end product of haeme catabolism, has been known as a protective bioactive molecule, has effective antioxidant, anti-inflammatory and other vital physiological functions.[9,10] In vitro studies noticed that bilirubin has quite powerful antiviral activity.[11,12] Previously a study conducted on sepsis noticed that serum bilirubin levels in patients were associated with poor outcomes, such as mortality.[13] Wu et al[14] conducted a study of patients with sepsis, and they noticed that the prognosis was associated particularly with direct bilirubin (DBil) rather than total bilirubin (TBil). Also, they

suggested DBil had a more accurate predictive value than TBil in patients with sepsis.[14] However, the relationship between bilirubin with poor clinical outcomes has not been yet well described in COVID-19 patients.

In this study, we analysed the early clinical presentation, basic laboratory findings and clinical outcomes in our emergency department patients who were hospitalised diagnosed with COVID-19 pneumonia. Our aim was to investigate the direct/total bilirubin ratio (D/TBil), as a novel parameter to predict the poor survival of COVID-19 pneumonia.

What's known

- Early recognition of severe patients with COVID-19 would be of vital importance for the management of disease and the use of medical facilities.
- Bilirubin, an endogenous end product of haeme catabolism, has been known as a protective bioactive molecule, has effective antioxidant, anti-inflammatory and other vital physiological functions.

What's new

- On hospital admission, we identified a novel parameter D/TBil above 0.5 associated with poor clinical outcomes such as mortality in hospitalised patients diagnosed with COVID-19 pneumonia at an early stage. Also, we noticed in our study that combination age, gender, and hypertension, D/TBil and NLR contributed significantly to predicting the poor survival of COVID-19.

2 | MATERIALS AND METHODS

Gazi Yasargil Training and Research Hospital as a tertiary hospital designated for diagnosis, management and treatment of new emerging infectious diseases such as COVID-19 in Diyarbakır, Turkey. The institutional ethics board of the Gazi Yasargil Training and Research Hospital, an affiliate of the University of Health Science, reviewed and approved this retrospective study (Decision Date: 24, July 2020, No: 530).

This study enrolled 537 COVID-19 pneumonia patients, who were diagnosed according to WHO interim guidelines from 20, March to 1, August 2020, in the Gazi Yasargil Training and Research Hospital ED. Then the patients were transferred to the intensive care unit (ICU) or medical floor. In addition to characteristic non-contrast chest computed tomography (CT) imaging of pneumonia, all patients required at least one of the following inclusion criteria in order to establish the COVID-19 pneumonia diagnosis: (i) having an epidemiological history; (ii) having symptoms of viral infection: fever, cough, sore throat, rhinorrhoea, shortness of breath, chest pain, muscle ache, nausea vomiting and diarrhoea; (iii) having etiological evidence: reverse transcription polymerase chain reaction (RT-PCR)detection of SARS-CoV-2 nucleic acid positive in throat swabs. All patients were divided into two groups: survivor group and deceased group. The definition of the survivor group—patients were discharged from the hospital; the definition of the deceased group—patients were dead during hospitalisation. We examined the electronic medical records. Sociodemographic information such as age, gender as well as past medical histories such as hypertension, diabetes mellitus, cardiac disease, and chronic obstructive pulmonary disease, chronic kidney disease, malignancy, vitals, clinical symptoms, laboratory results and clinical outcomes were collected. Nasopharyngeal swab samples were collected and used in the RT-PCR assay for the detection of SARS-CoV-2 viral nucleic acid. Laboratory variables were tested with usual methods, including complete blood count (CBC) with differential, albumin, aminotransferases (AST and ALT), lactate dehydrogenase (LDH), C-reactive protein (CRP), blood urea nitrogen, creatinine, direct bilirubin (DBil), total bilirubin (TBil), d-dimer, cardiac troponin I. All patients' laboratory data were collected from their first laboratory test on admission to ED. Also, we calculated the D/TBil, neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR) of all patients. All data were primarily analysed by trained physicians.

2.1 | Statistics analysis

The SPSS version 22.0 (IBM SPSS Statistics for Windows, version 22.0. Armonk, United States of America) was used for statistical analysis. The normality of data was tested by using the Kolmogorov Smirnov test. When conditions for normal distribution were not met, comparisons for two independent groups were performed using Mann–Whitney *U* test and Mantel- Haenszel Ki–Kare test median values (minimum-maximum) for data non-normally distributed in descriptive statistics, frequency and percentage distributions for categorical data were given.

Stepwise, by forward selection, binary logistic regression was performed with COVID-19 outcome of survival or death as independent variables. All significant variables were added to model, but only those that made remarkable contributions remained in the model. In this regression model, D/TBil, age, gender, presence of hypertension, and NLR were used as independent variables to determine significant predictors for COVID-19 mortality. Receiver operating characteristic (ROC) analysis was used to determine the cut-off value of the laboratory parameters in the established model. A P value of < 0.05 was considered significant for all analyses.

3 | RESULTS

537 (248 women and 289 men) patients were included in our study. Patients were separated into two groups for analysis: survivors vs deceased. The deceased group had 101(18.8%) patients and the survivor group had 436 (81.2%) patients. A total of 537 patients were aged 54 years (min-max, 18-97). The mean age of the deceased group was statistically significantly higher than the mean age of the

survivor group 72 (min-max, 30-92) years vs 50 (min-max, 18-97) years ($P < .001$). The prevalence of comorbidities such as hypertension and diabetes in the deceased group was statistically significantly higher than the survivor ($P < .001$ and $P = .003$). Demographic data, presence of comorbidities and outcomes of patients were displayed in Table 1.

According to the results of haematologic parameters performed on admission, the deceased group compared with the survivor group had more significan increases in white blood cell count (WBC), neutrophil, lymphocyte, NLR, PLR (all of $P < .001$) and more significant decreases in haemoglobin (HGB) and haematocrit (HCT) levels ($P = .014$ and $P = .008$). Also according to the results of biochemical and the other parameters performed on admission, the deceased group compared with the survivor group had more significant increases in DBil, D/TBil, aspartate aminotransferase (AST), LDH, CRP, blood urea nitrogen, creatinine, d-dimer, cardiac troponin I ($P < .001$, respectively) and a more significant decrease in albumin level ($P < .001$). Laboratory parameters performed on the admission of patients were displayed in Table 2.

Logistic regression analysis was performed with demographic data, presence of comorbidity and laboratory parameters for estimating the probability of our patients dying of COVID-19 in this study. We noticed that D/TBil, age, gender, hypertension and NLR variables contributed significantly to the binary logistic regression model (Table 3). The cut-off value for the independent variables such as D/TBil and NLR in the model was determined using ROC analysis (Table 4). The D/TBil cut-off value of 0.5 was differentiated between deceased and survivor groups (area under the curve (AUC): 0.858, 75.8% sensitivity, 85.8% specificity) and NLR cut-off value of 4.03 was differentiated between deceased and survivor groups (AUC: 0.729, 68% sensitivity, 65.8% specificity). In our model, the mortality risk increased 14.6 times in patients with D/TBil value greater than 0.5, and the mortality risk increased 2.4 times in patients with NLR value greater than 4 (Table 3). According to our model, when D/TBil is used as a stand-alone explanatory variable for estimating the likelihood of in COVID-19 patients having an outcome of survival or death, the explanatory rate was 24.9%. The total explanatory rate of all explanatory variables in our model was 37.8% (Table 3).

According to the comparison of D/TBil value of our patients with age-standardised mortality rates in our model, if patients had D/TBil value > 0.5 with above 50 years of age, the mortality rate was 63.1%, and if patients had D/TBil value < 0.5 with above 50 years of age, the mortality rate was 12.6%. On the other hand, if patients had D/TBil value > 0.5 with under 50 years of age, the mortality rate was 21%, and if patients had D/TBil value < 0.5 with under 50 years of age, the mortality rate was 0%. According to our model, in the above 50 years old patients, had D/TBil value > 0.5, was increased the mortality risk 11.83 times (Table 5).

TABLE 1 Demographic data, presence of comorbidities and outcomes of survivor and deceased groups

	All Patients	Survivor	Deceased	
	n:537	n:436 (%81.2)	n:101 (%18.8)	*P*
Age median (min-max)	54 (18-97)	50 (18-97)	72 (30-92)	<.001
Sex, n (%)				.048
Female	248 (%46.2)	210 (%48.2)	38 (%37.6)	
Male	289 (%53.8)	226 (%51.8)	63 (%62.4)	
Hospitalisation, n (%)				<.001
Medical floor	332 (%61.8)	332 (%76.1)	0 (0.0)	
ICU	89 (%16.6)	40 (%9.2)	49 (%48.5)	
Transfer from medical floor to ICU	116 (%21.6)	64 (%14.7)	52 (%51.5)	
Underlying comorbidities, n (%)				
Hypertension	155 (%28.9)	92 (%21.1)	63 (%62.4)	<.001
Diabetes	93 (%17.3)	65 (%14.9)	28 (%27.7)	.003
COPD-asthma	65 (%12.1)	48 (%11)	17 (%16.8)	.13
Coronary artery disease/heart failure	59 (%11)	42 (%9.6)	17 (%16.8)	.056
Length of hospital stay days	11.18 (1-90)	10.5 (4-42)	14.1 (1-90)	.073
Median (min-max)				

Note: COPD, chronic obstructive pulmonary disease; ICU, intensive care unit. Categorical variables shown as n (%), Median (min, max) shown for variables with non-normal distributions, Min: minimum, Max: maximum.

TABLE 2 Laboratory parameters of patients on admission ED

	Survivor			Deceased				Total		
	Median	Min.	Max.	Median	Min.	Max.	*P*	Median	Min.	Max.
Wbc (4 * 10^3 - 10 * 10^3/mm^3) (*10^3)	7.6	1	42.7	9.9	1.1	57.1	**<.001**	8	1	57.1
Neu (2 * 10^3 - 7 * 10^3/mm^3) (*10^3)	5.5	0.3	28.9	7.7	0.7	41.3	**<.001**	5.9	0.3	41.3
Lym (0.8 * 10^3 - 4 * 10^3/mm^3) (*10^3)	1.5	0.1	6.9	1.7	0.3	46	**<.001**	1.6	0.1	46
Nlr	4.2	0.4	27.8	8,2	0,3	34.1	**<.001**	5	0.3	34.1
Plt (150 * 10^3-450 * 10^3/mm^3) (*10^3)	227.1	71	671	213.9	48	684	.052	224.4	48	684
Plr	173.6	22.6	936.4	243	5	1385.7	**<.001**	187.7	5	1385.7
Haemoglobin (11-16 gr/dL)	13.5	1.8	18.5	12.9	6.4	19.2	**.014**	13.4	1.8	19.2
Haematocrit (37%-54%)	41.9	17	55	39.8	3.8	61.6	**.008**	41.5	3.8	61.6
Calcium (8.8-10.6 mg/dL)	8.7	7.5	10.8	8.6	6.4	10.9	.092	8.6	6.4	10.9
Albümin (34-48 g/L)	41.6	22	54	33.6	7	51	**<.001**	40	7	54
ALT (0-41 U/L)	30.7	6	442	38.2	7	473	.516	32.2	6	473
AST (0-40 U/L)	35.3	4	1441	59.4	8	1129	**<.001**	40.2	4	1441
C-reactive protein (0-5 mg/L)	51.1	0,3	350	126.4	2	297	**<.001**	66.2	0.3	350
Direkt Bilirubin (0-0.3mg/dL)	0.23	0	1.9	0.39	0.1	3.6	**<.001**	0.26	0	3.6
Direct/total bilirubin	0.39	0.05	0.83	0.56	0.2	1	**<.001**	0.43	0.05	1
Chlorine (98-107 mmol/L)	103.2	79	114	103.9	91	146	.680	103.3	79	146
Kreatinin (0.72-1.25 mg/dL)	0.95	0.23	9.99	1.5	0.58	12.82	**<.001**	1	0.23	12.82
LDH (135-225 U/L)	285.3	14	1544	406.3	159	1327	**<.001**	309.3	14	1544
K (3.5-5.1 mmol/L)	4	2.93	6.74	4.2	2.99	6.62	.103	4.1	2.93	6.74
Sodium (134-146 mEq/L)	137	127	150	136.5	125	175	**.005**	136.9	125	175
Urea (16-48mg/dL)	31.2	9	247	66.9	13	223	**<.001**	38.4	9	247
D-Dimer (0-243 ng/mL)	364.2	35	4195	1438.1	93	43 993	**<.001**	565,1	35	43 993
Troponin (0-0.16 ng/mL)	0.13	0.03	5.4	0.33	0.01	14.19	**<.001**	0.17	0.01	14.19

Note: Bold *P* values was considered statistically significant ($P < 0.05$).

Alt, alanine aminotransferase; Ast, aspartate aminotransferase; K, potassium; LDH, lactate dehydrogenase; Lym, Lymphocyte; Neu, neutrophil; NLR, neutrophil to lymphocyte ratio; PLR, platelet lymphocyte ratio; Plt, platelet; WBC, white blood cell.

4 | DISCUSSION

The contagiousness of COVID-19, arising in Wuhan, China, has been an important public health condition all over the world. Early recognition of severe patients with COVID-19 is very important for the management of disease and the use of medical facilities. Laboratory tests are useful tools for the evaluation of the severity and extent of COVID-19 pneumonia.[4-7] In our study, we retrospectively analysed the clinical characteristics and laboratory parameters in 537 hospitalised patients diagnosed with COVID-19 pneumonia with definitive clinical outcome and we found that D/TBil, as a novel predict parameter, showed good prognostic values for outcome prediction of COVID-19 pneumonia.

Interestingly, we found that the D/TBil, as a novel predicted parameter, was an effective biochemical parameter for predicting poor outcomes. Moreover, we identified D/TBil above 0.5 as associated with poor clinical outcomes such as mortality in hospitalised patients diagnosed with COVID-19 pneumonia.

Bilirubin, an endogenous end product of haeme catabolism, has been known as a protective bioactive molecule, has effective

TABLE 3 Binary logistic regression analysis results and model analysis summary

					95% CI for	EXP(B)		Cox & Snell R
B			*P*	OR	Lower	Upper	−2 Log likelihood	Square
Step 1	D/TBil	3.059	<.001	21.3	12.298	36.89	343.63	0.249
	Constant	−1.179	<.001	0.308				
Step 2	Age	0.073	<.001	1.076	1.054	1.098		
	D/TBil	2.665	<.001	14.363	7.802	26.445	276.267	0.343
	Constant	−5.703	<.001	0.003				
Step 3	Gender	1.074	.002	2.926	1.503	5.694		
	Age	0.08	<.001	1.083	1.059	1.107	265.496	0.357
	D/TBil	2.766	<.001	15.897	8.416	30.025		
	Constant	−6.23	<.001	0.002				
Step 4	Gender	1.329	<.001	3.779	1.867	7.647		
	Age	0.071	<.001	1.073	1.049	1.098		
	D/TBil	2.785	<.001	16.206	8.408	31.236	254.926	0.37
	HT	1.117	<.001	3.054	1.545	6.039		
	Constant	−5.603	<.001	0.004				
Step 5	Gender	1.341	<.001	3.823	1.863	7.847		
	Age	0.066	<.001	1.068	1.044	1.093		
	D/TBil	2.685	<.001	14.662	7.521	28.584	.248.22	0.378
	NLR	0.896	<.001	2.451	1.231	4.88		
	HT	1.176	<.001	3.241	1.615	6.501		
	Constant	−5.428	<.001	0.004				

Note: D/TBil, direct/total bilirubin; HT, hypertension; NLR, neutrophil to lymphocyte ratio.

TABLE 4 ROC analyse for D/TBil and NLR

	Cut-off	Sensitivity	Specificity	LR+	LR−	Area	95% Confidence interval	*P*
D/TBil	0.4647	81.8	72.7	2.99	0.25	0.858	0.817-0.9	<.001
	0.5030	75.8	85.8	5.32	0.28			
	0.6111	36.4	95.9	8.80	0.66			
	0.7054	9.1	99.1	9.90	0.91			
NLR	1.795	94.1	14.7	1.10	0.40	0.729	0.67-0.789	<.001
	4.032	68.3	65.8	1.99	0.48			
	5.44	56.4	79.8	2.79	0.54			
	15.0	19.8	97.2	7.07	0.82			

antioxidant, anti-inflammatory and other vital physiological functions.[9,10] Frank et al[12] suggested that bilirubin not merely protects against inflammation; in addition to it, it has also powerful antiviral properties that can be useful for fighting COVID-19 in their in vitro study. Another in vitro study, Santangelo et al[11] showed the antiviral activity of total bilirubin in their study. They also noticed that indirect bilirubin is quite powerful at inhibiting viral infectivity after 24 h of infection.[11] Chai et al[15] reported that angiotensin-converting enzyme 2 (ACE2) was too much expressed in type II alveolar epithelial cells as well as in bile duct cells and had a significant act in intervening COVID-19 infection. According to previous studies on COVID-19, ACE2 expression in cholangiocytes could directly damage the bile ducts and a potency mechanism of infection by the virus using ACE2 as host cell receptors. Also, high TBil may be associated with SARS-CoV-2-induced bile duct cell damage rather than direct hepatic cell damage caused by the virus.[16,17] Sun et al[18] suggested that SARS-CoV-2 connects to hepatic and biliary epithelial cells through the ACE2 receptors for active viral replication and that caused direct cytotoxicity. Also, they reported that other possible mechanisms of COVID-19-associated liver injury develop with immune-mediated damage, hypoxic damage caused by the disease and drug-induced liver injury. In addition, elevated serum bilirubin can induce oxidative stress and reduce cell survival.[19,20] According to the literature, bilirubin is considered

TABLE 5 The comparison of D/TBil ratio with age-standardised for COVID-19 survival

Age				Deceased	Survivor	OR (CI)
>50	D/TBil	>0.5	n	65	38	
			%	63.1	36.9	
		<0.5	n	24	166	
			%	12.6	87.4	
	Total		n	89	204	11.83 (6.58-21.25)
			%	30.4	69.6	
<50	D/TBil	>0.5	n	6	22	
			%	21.4	78.6	
		<0.5	n	0	208	
			%	0	100	
	Total		n	6	230	
			%	2.5	97.5	
Total	D/TBil	>0.5	n	71	60	
			%	54.2	45.8	
		<0.5	n	24	374	
			%	6	94	
	Total		n	95	434	18.40 (10.77-31.55)
			%	18	82	

a potent antiviral, and increased bilirubin levels may play an active role in the COVID-19 process.

According to a multicentre retrospective study, Fu et al[21] suggested that abnormal TBil on admission was related to poor outcomes in COVID-19 patients. Patel et al[13] noticed that elevation of serum bilirubin levels in patients with sepsis was associated with poor outcomes, such as mortality. In a previous study conducted on patients with sepsis, Zhai et al[22] found that a mild increase in bilirubin levels on ICU admission was related to a remarkable increase in acute respiratory distress syndrome (ARDS) and mortality risks. Also, they suggested that serum bilirubin was an early and sensitive biochemical marker for predicting sepsis-related ARDS.[22] Wu et al[14] conducted a study of patients with sepsis, and they noticed that the prognosis was associated particularly with DBil rather than TBil. Also, they suggested that DBil had a more accurate predictive value than TBil in patients with sepsis.[14] Our study is compatible with the literature. Additionally, our study showed that D/TBil can be used as an independent parameter for estimating the likelihood of COVID-19 patients' outcome of survival or death. According to the literature and the findings in our study, bilirubin is a useful tool to evaluate the severity and extent of COVID-19 pneumonia.

In our study, patients in the deceased group were older than the survivor group and had more underlying comorbidities such as hypertension and diabetes. Dong et al[23] suggested that age and comorbidity can be associated with increased mortality and poor outcomes in patients diagnosed with COVID-19 pneumonia. Advanced age and presence of diabetes were previously noticed to be remarkably correlated with raised incidence, the severity of disease, likewise the risk of mortality in COVID-19.[24,25] Zhou et al[25] reported that the infection-related mortality rate, especially the possible cause of the association between viral infections with age, is perhaps because of weakened cellular immune function and longer term inflammation in the elderly people. Our study showed that patients, who were above 50 years old and D/TBil values > 0.5, had poor survival in COVID-19 pneumonia. As reported in a previous study, patients with coexisting comorbidities such as diabetes, hypertension, malignancies and cardiovascular disease were at higher risk for severe COVID-19.[26] Recent research has revealed that most cases of coronavirus were patients with chronic illnesses, suggesting that this condition may be related to an increased risk of disease severity or death.[27] Similarly to the literature, we noticed in our study that age, gender and hypertension contributed significantly to predicting the poor survival of COVID-19.

As the SARS-CoV-2 outbreak progresses, recent studies conducted with COVID-19 patients noticed that useful blood biomarkers, which were found to be associated with the severity and prognosis of COVID-19 pneumonia.[4-7] In our study, we analysed hematologic, biochemical and inflammatory biomarker test results and noticed some biomarker abnormalities that were found between deceased and survivor groups, which may enable significant recognition for poor prognosis. In our study, we found that NLR was the most effective haematological parameter for predicting poor outcomes. Also, we noticed that the combination of D/TBil and NLR parameters contributed significantly to predicting the poor survival of COVID-19. The NLR was a widely used biomarker for evaluating the gravity of bacterial infections and predicting the prognosis of patients with pneumonia.[28,29] In recent studies, it has been determined that haematological parameters such as NLR and

PLR are remarkably increased in COVID-19 patients.[30,31] Based on these findings, we suggested that haematological parameters that are particularly correlated with inflammatory parameters are the effective in-clinic outcome, especially developing bacterial super-infections, and direct important parameters affecting the outcome.

4.1 | Limitations

This study had several limitations. Our study was conducted in a single centre with a relatively small patient group. We are incapable of examining the mechanisms of our findings because of the retrospective condition of our study. Also, we used demographic data, the presence of comorbidity and laboratory parameters to determine the prognosis of COVID-19. However, we did not include imaging features for lung involvement of COVID-19 pneumonia to determine the prognosis of COVID-19. Although our study was retrospective, we did not use a specific cut-off in time to define in-hospital mortality. We paid attention to the in-hospital mortality situation at any time rather than the duration of the mortality in fatal pandemic. Additional prospective, long-term and large-scale studies are needed to verify the reliability of the D/TBil as an independent prediction parameter for poor survival in COVID-19 patients.

5 | CONCLUSIONS

On hospital admission, we identified a novel parameter D/TBil above 0.5 as associated with poor clinical outcomes such as mortality in hospitalised patients diagnosed with COVID-19 pneumonia at an early stage. Also, we noticed in our study that combination of age, gender, and hypertension, D/TBil, and NLR contributed significantly to predicting the poor survival of COVID-19.

ETHICS, CONSENT AND PERMISSIONS

All patients gave their consent to participate in the study.

CONSENT TO PUBLISH

The authors have obtained consent to publish from the participant (or legal parent or guardian for children) to report individual patient data.

DATA AVAILABILITY STATEMENT

The authors declare that materials described in the manuscript, including all relevant raw data, will be freely available to any scientist wishing to use them for non-commercial purposes, without breaching participant confidentiality. Moreover, the authors ensure that their datasets are presented in the main manuscript.

DISCLOSURES

All authors certify that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received or pending), are the following: None.

AUTHOR CONTRIBUTIONS

Study concept and design: SA and MÖ; Methodology: SA and MÖ; Data analysis and interpretation: SA and MÖ; Drafting of the manuscript: SA and MÖ; Critical revision of the manuscript: SA and MÖ; Statistical analysis: SA and MÖ All authors read and approved the final version of the manuscript.

AUTHORSHIP STATEMENT

SA and MÖ were responsible for the study design study supervision, data analysis and manuscript writing. The authors confirm that all listed authors meet the authorship criteria and that all authors are in agreement with the content of the manuscript.

ETHICAL APPROVAL

This study was approved by the ethics committee of Gazi Yaşargil Education and Research Hospital with the decision numbered 530 and dated July 24, 2020. Written informed consent was obtained from all participants at each stage of the study.

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