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Clinical features and laboratory values associated with disease severity in Covid-19 patients: a single center experience

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ABSTRACT

Background: To date, several studies were published about clinical features and laboratory values associated with disease severity in Covid-19 patients. We aimed to show the relationship between disease severity and clinical and laboratory characteristics of the patients as a single center experience.

Material and Method: Clinical features and laboratory data of fifty patients diagnosed with Covid-19 by PCR was evaluated at diagnosis. These patients divided into 2 groups as early and advanced disease. Clinical features and laboratory data were compared in terms of severity of disease.

Results: In all patients, the most common accompanying disease was coronary artery disease. Cough and headache were the most common complaints. Laboratory values showed low lymphocyte count and high CRP levels in all patients. Twenty four patients in early stage and 26 patients in advanced stage were compared in terms of clinical features and laboratory values. In advanced stage, it was observed that body weight, number of comorbid diseases, age, CRP, procalcitonin, BUN, GGT, fibrinogen, D-dimer and ferritin levels of patients were higher whereas height, serum total protein, albumin and potassium levels were lower when compered with early stage patients ($p<0.05$).

Conclusions: Our data showed that older age, having cough, increased number of comorbid diseases, CRP, BUN, GGT, fibrinogen, D-dimer and ferritin and decresed serum total protein, albumin, potassium levels at the time of diagnosis in Covid-19 patients were associated with advanced stage disease.

Keywords: Covid-19, disease severity

INTRODUCTION

Coronaviruses (CoV) are a large family of viruses showing wide clinical variation from common gribal infection to more serious diseases such as the Middle East Respiratory Syndrome (MERS-CoV) and severe Acute Respiratory Syndrome (SARS-CoV). Since December 8, 2019, several cases of pneumonia of unknown etiology have been reported in Wuhan, a city within the Hubei province of China. The disease and the virus that causes it have been named as Covid-19 and SARS-COV-2, respectively and ultimately it was declared as a pandemic disease by WHO on March 11, 2020 (1-3). Most patients eventually made a recovery after careful treatment, but, some developed more severe and even critical illness (4,5). Although early diagnosis and timely treatment of critical cases is very crucial, factors related to disease severity are still unclear.

To date, the severity of the disease has been shown to be related to many clinical futures and laboratory parameters, such as age, presence of co-morbidities, (like diabetes, obesity, heart disease), elevated blood urea nitrogen (BUN), creatinine, procalcitonin, lactate dehydrogenase, D-dimer, C-reactive protein (CRP), neutrophil, lymhocyte counts and pro-inflammatory

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cytokines, such as interleukin-6, respectively (6-8). So, we aimed to show correlation between clinical and laboratory data and the severity of Covid-19 infection in adults as a single center experience.

MATERIAL AND METHOD

Patients

The data of Covid-19 patients diagnosed with polymerase chain reaction (PCR), between June 10, 2020 and june 30, 2020 were analyzed retrospectively.

Fifty Covid-19 patients were included in this study. Early and advenced stage patients included to this study were compared in terms of their age, gender, body surface area, symptoms (for instance fever, cough, sputum, sore throat, diarrhea, headache), leukocytes, neutrophils, hemoglobin, hematocrit, lymphocytes, eosinophils, monocytes, platelets, CRP, BUN, creatinine, total protein, albumin, procalcitonin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), gamma glutamyl transferase (GGT), sodium, potassium, International Normalized Ratio (INR), activated Partial Thromboplastin Time (aPTT), fibrinogen, D-dimer, ferritin, hospitalization time and mortality rates.

Laboratory Analysis

Real-time reverse transcriptase-polymerase chain reaction (PCR) tests for SARS-CoV-2 RNA were performed using nasopharyngeal swabs. Total nucleic acid extraction of nasopharyngeal swabs of viral isolates was performed using a biospeedy and coyote extraction system (Bioeksen ltd and Coyote Bioscience ltd). Real-time PCR (RT-PCR) assays for SARS-CoV-2 RNA detection were performed using Biospeedy Covid-19 RT-qPCR Detection Kit (Bioeksen, Istanbul, Turkey).

Disease Severity

Patients were divided into 4 stage according to their clinical status. Stage 1; asymptomatic (without any symptoms), stage 2; symptomatic without lung involvement, stage 3; symptomatic with lung involvement, stage 4; acute respiratory distress syndrome, intubation, multiorgan failure (9,10). Stage 1, 2 patients were accepted as early stage and 3,4 patients were accepted as advanced stage patients.

Statistical Analysis

Data analysis was performed using IBM SPSS v26 software. Descriptive statistics were used to summarize data. Variables assessed for normal distribution with the Kolmogorov Smirnov test. Categorical data were presented as number-percentages, and numerical data were presented as median, minimum, and maximum. Differences between categorical variables were analyzed with the Chi-Square test, and numeric variables were compared with the Mann-Whitney U test. A two-sided p-value ≤0.05 was considered statistically significant.

The study was approved by the research ethics committee (date/reference number: 30-06-2020/892). All analyses were performed in accordance with the principles of the Declaration of Helsinki.

RESULT

Fifty patients were included in the study. When the comorbid diseases of the patients were evaluated, most common accompanying disease was coronary artery disease and second was hypertension. Cough and headache were the most common complaints in hospital admissions. Laboratory values showed low lymphocyte count and high CRP levels (**Table 1**).

Twenty four patients in early stage and 26 patients in advanced stage were compared in terms of clinical features and laboratory values (**Table 2**). In advanced stage, it was observed that body weight, number of comorbid diseases, age, CRP, procalcitonin, BUN, GGT, fibrinogen, D-dimer and ferritin levels of patients were higher whereas height, serum total protein, albumin and potassium levels were lower when compered with early stage patients ($p<0.05$).

DISCUSSION

In our study clinical and laboratory features evaluated in Covid-19 patients were compatible with the literature. Rodriguez-Morales et al. (6) performed a systematic literature review with meta-analysis, using three databases to assess clinical, laboratory, imaging features, and outcomes of Covid-19 confirmed cases. They showed that fever (88.7%), cough (57.6%) and dyspnea (45.6%) were the most prevalent manifestations. Cough and headache were the most common symptoms in our study. Three patients included in our trial had dyspnea. They reported that the mean age of patients across 18 studies was 51.97 (46.06–57.89), and male sex was 55.9 (51.6–60.1). Patients presented comorbidities were 36.8% of all cases. Most prevalent comorbid diseases were hypertension (18.6%), cardiovascular disease (14.4%), and diabetes (11.9%). In our study, the median age was 44 years, the ratio of women to men was equal, and the most common comorbid disease was coronary artery disease. Gürbüz P. reported that obesity has been obtained to be an independent and important risk factor for Covid-19 process in nearly all researches (11). Higher BMI but not significantly was evaluated in advanced disease in our study.

Table 1. Clinical features and laboratory values of all the patients

Characteristics and labratory values (normal range)			All patients median (min-max)
Total number of patients			50
Median age			44 (18-88)
Gender (Number/percent)	Female		25 (50)
	Male		25 (50)
Height (centimeter)			162 (153-185)
Weight (kilogram)			70 (50-110)
Body surface area (/m²)			1.77 (1.47-2.1)
Number of comorbid disease	Hypertension (HT)		4
	Coronary artery disease (CAD)		5
	Diabetes mellitus (DM)		1
	Asthma/chronic obstructive pulmonary disease (COPD)		2
	DM+HT		2
	COPD+HT		2
	CAD+HT		3
	Number of all comorbid disease		25
Symptoms (number, (%))	Fever		23 (46)
	Cough		34 (68)
	Sputum		11 (22)
	Throat ache		7 (14)
	Diarrhea		15 (30)
	Headache		34 (68)
Stage (number, (%))	Early	Stage I	1 (2)
		Stage II	23 (46)
	Advanced	Stage III	24 (48)
		Stage IV	2 (4)
Complete blood count (median)	Leukocyte (4-10 x10³/µL)		5.19 (2.83-20.36)
	Neutrophil (2-6 x10³/µL)		3.27 (0.86-18.81)
	Hemoglobin (13.6-17.2 gr/dL)		13.95 (8.5-17.9)
	Hematocrit (39-50%)		40.75 (25.6-52.7)
	Lymphocyte (1.3-3.5 x10³/µL)		1.28 (0.39-2.53)
	Monocyte (0.3-0.9x10³/µL)		0.47 (0-1.16)
	Eosinophil (0-0.5x10³/µL)		0.02 (0-0.6)
	Platelet (150-400x10³/µL)		210 (116-389)
C-reactive protein (0-0.35 mg/dL)			0.56 (0-15.7)
BUN (5.1-16.8 mg/dL)			31 (13-98)
Creatinine (0.57-1.25 mg/dL)			0.75 (0.43-1.81)
Total protein (6.4-8.3 g/dL)			7 (5.62-8.7)
Albumin (3.5-5 gr/dL)			4.2 (2.59-5.04)
Procalcitonin (0-0.5 ng/mL)			0.05 (0.01-3.51)
AST (5-34 U/L)			27 (11-89)
ALT (0-55 U/L)			21 (7-93)
ALP (40-150U/L)			78 (11-210)
GGT (9-64 U/L)			19 (8-189)
Sodyum (136-145 mmol/L)			138 (126-142)
Potasyum (3.5-5.1 mmol/L)			4.1 (3.4-5.4)
INR (0.8-1.2)			1.2 (0.92-2.80)
APTT (23-35 sn)			24.78 (18.6-58)
Fibrinogen (150-350 mg/dL)			295 (2.48-743)
D-dimer (0-0.55 mg/L)			0.17 (0-3.98)
Ferritin (22-322 ng/mL)			105.5 (7.69-1475)
Lenght of stay in hospital (day)			5 (1-17)
Mortality (number/percent)			2 (4)

Table 2. Comparison of laboratory values and clinical features of early and advanced stage patients

Characteristics and labratory values (normal range)			Early stage median (min-max)	Advanced stage median (min-max)	p
Total number of patients			24	26	-
Median Age (year)			27.5 (18-52)	57.5 (27-88)	<0.001
Gender	Female (number/percent)		10 (41.7)	15 (57.7)	0.396
	Male (number/percent)		14 (58.3)	11 (42.3)	
Height (centimeter)			166 (158-185)	160 (153-180)	0.047
Weight (kilogram)			69.0 (55-82)	80.5 (50-110)	0.035
Body Surface area (/m²)			1.76 (1.56-2.02)	1.87 (1.47-2.1)	0.213
Number of comorbid diseases	Hypertension (HT)		1	3	-
	Coronary artery disease (CAD)		-	5	-
	Diabetes mellitus (DM)		-	1	-
	Asthma/chronic obstructive pulmonary disease (COPD)		1	1	-
	DM+HT		-	2	-
	COPD+HT		1	1	-
	CAD+HT		-	3	-
	Number of all comorbid diseases		3	22	p<0.043
Symptoms (number, (%))	Fever		9 (37.5)	14 (53.8)	0.382
	Cough		10 (41.7)	24 (92.3)	<0.001
	Sputum		2 (8.3)	9 (34.6)	0.057
	Throat ache		6 (25)	1 (3.8)	0.055
	Diarrhea		8 (33.3)	7 (26.9)	0.853
	Headache		16 (66.7)	18 (69.2)	1.000
Stage (number, (%))	Early	Stage I	1 (4.2)	-	-
		Stage II	23 (95.8)	-	-
	Advanced	Stage III	-	24 (92.3)	-
		Stage IV	-	2 (7.7)	-
Complete blood count	Leukocyte (4-10 x10³/µL)		5.54 (3.25-9.09)	5.13 (2.83-20.36)	0.398
	Neutrophil (2-6 x10³/µL)		3.33 (1.63-6.84)	3.26 (0.86-18.81) 0.614	0.614
	Hemoglobin (13.6-17.2 gr/dL)		14.3 (10.5-17.2)	13.65 (8.5-17.9)	0.244
	Hematocrit (39-50%)		41.25 (35.2-52.2)	40.25 (25.6-52.7)	0.541
	Lymphocyte (1.3-3.5 x10³/µL)		1.21 (0.61-2.53)	1.39 (0.39-2.32)	0.778
	Monocyte (0.3-0.9x10³/µL)		0.49 (0.00-1.12)	0.43 (0.32-1.16)	0.122
	Eosinophil (0-0.5x10³/µL)		0.05 (0.00-0.60)	0.01 (0.00-0.21)	0.058
	Platelet (150-400x10³/µL)		221 (152-389)	196 (116-309)	0.062
C-reactive protein (0-035 mg/dL)			0.26 (0.01-1.84)	2.27 (0.00-15.7)	<0.001
BUN (5.1-16.8 mg/dL)			27 (15-38)	36 (13-98)	0.005
Creatinine (0.57-1.25 mg/dL)			0.72 (0.43-1.25)	0.8 (0.55-1.81)	0.083
Total protein (6.4-8.3 g/dL)			7.35 (6.3-8.7)	6.7 (5.62-8.2)	0.033
Albumin (3.5-5 gr/dL)			4.3 (3.8-5.0)	3.8 (2.59-4.7)	<0.001
Procalcitonin (0-0.5 ng/mL)			0.042 (0.02-0.26)	0.063 (0.1-3.51)	0.046
AST (5-34 U/L)			25 (11-73)	28.5 (14-89)	0.052
ALT (0-55 U/L)			21.5 (7-86)	20.5 (9-93)	0.351
ALP (40-150U/L)			81.5 (11-210)	77 (42-120)	0.331
GGT (9-64 U/L)			15.5 (8-189)	27 (10-130)	<0.001
Sodyum (136-145 mmol/L)			138 (134-142)	138 (126-142)	0.747
Potassium (3.5-5.1 mmol/L)			4.18 (3.30-5.08)	3.98 (3.1-5.4)	0.040
INR (0.8-1.2)			1.08 (0.97-1.97)	1.13 (0.92-2.80)	0.524
APTT (23-35 sn)			22.7 (18.6-26.5)	24.05 (20-58)	0.056
Fibrinogen (150-350 mg/dL)			251 (2.5-356)	371 (50.9-743)	<0.001
D-dimer (0-0.55 mg/L)			0.08 (0-0.56)	0.28 (0.05-3.98)	<0.001
Ferritin (22-322 ng/mL)			57 (7.7-268)	169 (33-1475)	0.002
Lenght of stay in hospital (day)			5 (1-17)	10 (1-16)	0.037
Mortality (number,%)			0 (0)	2 (7.7)	0.491

Weiliang Cao et al. (7) compared patients that aged between 21~50, 51~65, over 66 years who were accounted for 44.5%, 35.1%, 18.8%, respectively. Fever (89.8%) and cough (67.2%) were common clinical symptoms. The rate of patients with sore throats (14.1%) was rare. White blood cell counts in the normal range of overall patients, but severe group patients were increased significantly ($p<0.01$). Lymphocytes of overall patients were decreased. ALT and AST levels were in the normal range of overall patients, but were elevated in the severe group. Serum creatinine and BUN levels of all patients were in the normal range. CRP level of all patients were increased markedly, which was significantly higher in severe disease group ($p<0.01$). In our study, patients in advanced stage were found to be statistically older. The most common symptoms were cough and fever,whereas the least common was chest pain. There was no significant difference in both leukocyte and lymphocyte counts between disease stages. Higher serum GGT and BUN levels were noted especially in advanced stage patients. Creatinine levels were increased, but could not reach to statistically significance. CRP level was increased in all patients. It was significantly increased in advanced stage disease compared to early stage. Gao et al. (8) reported that a comparison of the hematological parameters between the mild and severe groups showed significant differences in interleukin-6 (IL-6), D-dimer, glucose, thrombin time, fibrinogen, and CRP ($p<0.05$) (8). We could not eveluate interleukin-6 level in our study. In our study, D-Dimer, fibrinogen and CRP levels were statistically higher in advanced stage disease. Moreover, potassium levels, which was not evaluated in these two studies, was significantly lower disease and the length of hospital stay was longer in advanced stage in our study. Although no mortality was observed in early stage patients, 2 patients died due to infection in advanced stage group. The present study has several limitations. The study was retrospective and had a small sample size. For this reason, we did not associate clinical data with disease prognosis.

CONCLUSION

Our data showed that older age, having cough, increased number of comorbid diseases, CRP, BUN, GGT, fibrinogen, D-dimer and ferritin and decresed serum total protein, albumin, potassium levels at the time of diagnosis in Covid-19 patients were associated with advanced stage disease.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was approved by the research ethics committee (date/reference number: 30-06-2020/892).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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