



ORIGINAL ARTICLE

Alterations with PCR Positivity at Admission and Predictive Factors of Prolonged Hospital Stay in COVID-19

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Abstract

Introduction: The aim of the present study is to investigate the baseline predictive factors of prolonged hospital stay and to compare the patient characteristics according to polymerase chain reaction (PCR) positivity.

Methods: Between March 11 and June 1, 2020, 234 patients hospitalized in a non-intensive care unit clinic with a diagnosis of COVID-19 were included retrospectively. The duration of hospitalization were classified as ≤ 7 days and > 7 days. Furthermore, according to real-time PCR (RT-PCR) of nasopharyngeal swab positivity, patients were divided into two Groups.

Results: Of all the 234 patients, the mean age was 54 ± 13 and 167 (71%) was male. Thirty-six (36%) were PCR positive (+) at the first swab samples. Hospital stay was longer than 7 days in 122 (52%) of the patients. Ten patients (4.3%) died within 60-days. PCR-positive cases had lower baseline leukocytes ($p=0.002$), C-reactive protein ($p=0.001$) values, whereas hemoglobin ($p=0.001$) and albumin levels ($p<0.0001$) were detected in PCR-positive patients. While demographics and mortality were similar, hospital stay longer than 7 days were detected in a higher rate in PCR-positive patients ($p=0.025$). The analysis on hospital stay proved that, apart from PCR positivity rate, baseline aspartate aminotransferase (AST) level prolongs hospital stay in COVID-19 patients.

Discussion and Conclusion: This study demonstrates significant differences in patients with and without PCR positivity. Higher baseline AST levels and first PCR positivity prolongs hospital stay. Studies including larger patient groups would be better determine and enhance in this regard.

Keywords: Aspartate aminotransferase; Coronavirus; PCR test.

Coronavirus disease-2019 (COVID-19), which is caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), has caused a pandemics with a high morbidity and mortality rate across the world^[1,2].

The course of the disease proceeds on a wide spectrum: from asymptomatic real-time-polymerase chain reaction

(PCR) positivity to serious pneumonia and acute respiratory distress syndrome (ARDS). The follow-up and treatment protocol is carried out according to the National Health Ministry and World Health Organization (WHO). Still, there is not sufficient scientific information on the course of the disease^[3]. Mortality, however, increases with viral load^[4].

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During the onset of the disease, despite the presence of radiological findings, the literature specifies that 30–60% PCR positivity is found although there is no clear determination on PCR positivity. In symptomatic cases, with serial PCR follow-ups, this ratio can reach to levels of 90%^[5,6]. Studies exist on the relationship among PCR positivity, clinical deterioration, and mortality^[7].

With the spread of the infection and the increase in the number of patients who need to be followed up in the hospital, the health institutions are overloaded, and this situation has reached life-threatening dimensions^[8]. Urgent interventions were required to meet the demand in the hospital, and the patient circulation was tried to be ensured by discharging the patients needing hospitalization earlier^[9]. A meta-analysis on length of hospital stay in COVID-19 patients revealed that hospital stay is ranged between 5 and 29 days. This duration was independent from the study date^[10,11].

The objective of this study is to investigate the baseline predictive factors of prolonged hospital stay and to compare the characteristics of the patients according to PCR positivity.

Materials and Methods

The present study is a single-center, retrospective study designed in a chest diseases training and research hospital. The scientific research grant on which this study is based has been approved by Training and Research Hospital clinical research ethical committee (protocol no: 2020-04 date: August 06, 2020), the science committee of the Hospital and the General Directorate of health services of National Health Ministry of Türkiye. Our study was conducted in accordance with the Declaration of Helsinki. Informed consent form regarding data use was obtained from all patients included in the study.

Between March 11 and June 1, 2020, 234 hospitalized patients with COVID-19 in our non-ICU clinic in compliance with the WHO interim guidance have been examined retrospectively. According to hospital stay duration, patients were grouped as hospitalized ≤ 7 days and longer than 7 days. Furthermore, the characteristics of the patients were investigated according to PCR positivity, patients were divided into two groups as: PCR (+) and PCR (–). The demographic data of the patients, their medical histories, laboratory findings, and real-time polymerase chain reaction (RT-PCR) results have been collected from hospital database record system. The laboratory data have been maintained from the initial blood tests exercised during

hospitalization in our hospital. The hemogram data of the patients included in this study have been analyzed through Sysmex XT4000i appliance and their biochemical tests have been examined in the hospital laboratory using Beckman Coulter AU2700 appliance.

RT-PCR tests of SARS-CoV-2 are performed in validated microbiology laboratories of our center and Istanbul Cerrahpaşa Medical Faculty. Swab samples had been secured from upper respiratory tracts during the first application of the patients to the hospital and transferred by viral transport medium to the laboratory. Complete RNA Extraction has been obtained through Genmark RNA isolation kit and the method of Genom previously described as the appropriate method for SARS-CoV-2 in the example of respiration lasting 2 h^[12].

Statistical Methods

The data were analyzed by SPSS statistic 21.0 (SPSS Inc., Chicago, USA). Continuous variables were expressed as median and interquartile range. The normal distribution hypothesis was tested with the Kolmogorov-Smirnov test. The differences between the two groups were analyzed using the Mann-Whitney U test. Categorical variables were expressed as frequency rates and percentages (%). χ^2 tests were performed to test for differences in proportions of categorical variables between two or more groups. The significance level was accepted as <0.05 in all statistical analyses.

Results

Of all the 234 patients, the mean age was 54 ± 13 and 167 (71%) was male. The first PCR test was detected positive in 81 (36%) patients and 122 (52%) were hospitalized longer than 7 days. 60-day mortality was recorded in 10 (4.3%) patients.

Age and genders were similar between PCR (+) and (–) patients. The baseline leukocytes (6.9 ± 2.5 vs. 8.6 ± 4.9 , $p=0.002$), and C-reactive protein (CRP) (52.7 ± 44.5 vs. 83.6 ± 74.1 , $p=0.001$) levels were lower, whereas hemoglobin (13.9 ± 1.4 vs. 13.3 ± 1.8 , $p=0.001$) and albumin (41.1 ± 4.7 , vs. 38.6 ± 4.5 , <0.0001) levels were higher in PCR-positive group. 60-day mortality was similar between the groups, prolonged hospital stay rate was more frequent in PCR (+) patients (62% vs. 47%, $p=0.025$) (Table 1).

The comparison of patients according to hospital stay revealed similar age and gender rates between hospitalization 7 days or shorter and longer than 7 days. Baseline leukocytes, hemoglobin, lemphocytes, procalcitonin, albumin,

Table 1. Clinical characteristics of the patients according to PCR positivity

	All patients (n=234)	PCR (+) (n=81)	PCR (-) (n=153)	P
Age	54±13	52.2±11.8	54.8±13.9	0.161
Male gender, n (%)	167 (71%)	54 (67%)	113 (74%)	0.357
WBC count (×10 ⁹ /L)	7.9±4	6.9±2.5	8.6±4.9	0.002
Hemoglobin (g/dL)	13.5±1.7	13.9±1.4	13.3±1.8	0.012
Lymphocytes (×10 ⁹ /L)	1.5±0.7	1.6±0.7	1.5±0.5	0.148
Procalcitonin (mug/L)	0.2±1.1	0.07±0.08	0.29±1.3	0.160
Albumin (g/dL)	39.4±4.7	41.1±4.7	38.6±4.5	<0.0001
LDH (U/L)	357±149	358±133	357±156	0.950
AST (U/L)	41.2±22	41±15	41±25	0.983
CRP (mg/L)	73.3±66.5	52.7±44.5	83.6±74.1	0.001
SpO ₂ (%)	94.5±15	96±22.5	94±19.3	0.370
D-dimer (ng/mL)	1.5±4.1	0.8±1.4	1.9±5	0.062
Troponin (ng/mL)	14.6±12.5	4.7±4.2	20.2±15.6	0.391
Fibrinogen (mg/mL)	477±107	459.2±99	488±111	0.081
D-dimer/Fibrinogen	3.7±9.4	2.0±2.9	4.7±9.1	0.289
60-day mortality, n (%)	10 (4.3)	1 (1.3)	9 (6)	0.170
>7 days hospital stay, n (%)	122 (52)	50 (62)	72 (47)	0.025

AST: Aspartate aminotransferase; CRP: C-reactive protein; LDH: Lactate dehydrogenase; WBC: White blood cell.

lactate dehydrogenase, CRP, troponin, and fibrinogen levels did not correlate with hospital stay. Baseline aspartate aminotransferase (AST) levels (45±28 vs. 37±22, p=0.013) and PCR positivity rates (41% vs. 25%, p=0.025) were higher in

patients requiring prolonged hospital stay (Table 2).

Table 2. Clinical characteristics of the patients according to duration of hospital stay

	≤7 day (n=112)	>7 day (n=122)	p
Age	53±14	54±13	0.582
Gender			
Male/Female (%)	79/33 (71/29)	88/34 (72/28)	0.885
WBC count (×10 ⁹ /L)	8.0±4.1	8.0±4.1	0.869
Hemoglobin (g/dL)	13.4±1.7	13.6±1.6	0.607
Lymphocytes (×10 ⁹ /L)	1.5±0.6	1.6±0.9	0.798
Procalcitonin (mug/L)	0.12±0.44	0.29±1.45	0.265
Albumin (g/dL)	39.7±4.9	39.2±4.5	0.506
LDH (U/L)	349±163	366±134	0.408
AST (U/L)	37±22	45±28	0.013
CRP (mg/L)	69±66	77±66	0.330
SpO ₂	94±20	95±3	0.365
D-dimer (ng/mL)	1.6±4.7	1.4±3.4	0.639
Troponin (ng/mL)	24.5±183	6.0±5.9	0.265
Fibrinogen (mg/mL)	471±98	483±114	0.400
D-dimer/Fibrinogen	4.7±13	3±7.5	0.468
PCR (+)/(-) patients	31/81 (25/75%)	50/72 (41/59%)	0.025

AST: Aspartate aminotransferase; CRP: C-reactive protein; LDH: Lactate dehydrogenase; WBC: White blood cell.

Discussion

The present study has demonstrated that there are several alterations in characteristics of the patients according to PCR results. PCR positivity prolongs hospital stay compared to PCR negative patients.

The scientific community in general and clinicians in particular around the world have been busy with controlling the pandemics since December 2019 with intense efforts at research and experiments. While many unknowns still remain and research is ongoing on many fronts, some pathophysiological and clinical knowledge of the SARS-CoV-2 which causes both asymptomatic infection and severe respiratory problems such as ARDS has been secured. The deterioration of the disease is thought to be instigated based on the following: viral load, host defense mechanisms, mast cell activation, and the activation of hypercoagulability cascade^[13-15]. The results of this study support that clinical improvement lasts longer in patients with first PCR positivity. In the study of Mardani et al.,^[14] PCR positivity rate was 35%. Baseline neutrophils, CRP, LDH, AST, and serum urea levels were detected significantly higher in patients with first PCR positivity. In addition, leukocytes and serum albumin levels were significantly lower in PCR-positive cases. The current study also found lower leukocytes in PCR-posi-

tive cases. In contrast, lower CRP levels were demonstrated in PCR-positive patients.

Today, baseline liver functions in COVID-19 patients have gained attention. Moreover, the medical treatment may cause drug-induced liver injury^[15]. The present study has shown that higher levels of AST predicts longer hospital stay. In line with our finding, Gu et al.^[16] have found that baseline AST levels are positively correlated with hospital stay. Baseline AST and alanine aminotransferase levels had been reported significantly higher in patients requiring intensive care unit treatment. We believe further studies may enlighten the underlying reason of prolonged hospital stay is related to either more intense systemic inflammation or the side effects of the medical treatment during hospital treatment.

Conclusion

Several characteristics differ between PCR-positive and negative cases. The first PCR positivity and higher levels of AST are the predictive factors prolonging hospital stay. This study demonstrates significant differences in patients with and without PCR positivity. Higher baseline AST levels and first PCR positivity prolong hospital stay. Studies including larger patient groups would be better determine and enhance in this regard.

Ethics Committee Approval: The scientific research grant on which this study is based has been approved by Training and Research Hospital clinical research ethical committee (protocol no: 2020-04 date: August 06, 2020), the science committee of the Hospital and the General Directorate of health services of National Health Ministry of Türkiye. Our study was conducted in accordance with the Declaration of Helsinki.

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Conflict of Interest: None declared.

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