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Original Article

Focusing on Asthma and Chronic Obstructive Pulmonary Disease with COVID-19

Bilun Gemicioglu[1], Hafize Uzun[2], Sermin Borekci[1], Ridvan Karaali[3], Sebuh Kurugoglu[4], Pınar Atukeren[2], Sabri Sirolu[4], Sinem Durmus[2], Ahmet Dirican[5], Mert Ahmet Kuskucu[6], Fehmi Tabak[3]

[1] Istanbul University–Cerrahpasa, Cerrahpasa Faculty of Medicine, Department of Pulmonary Diseases, Istanbul, Turkey
[2] Istanbul University–Cerrahpasa, Cerrahpasa Faculty of Medicine, Department of Medical Biochemistry, Istanbul, Turkey
[3] Istanbul University–Cerrahpasa, Cerrahpasa Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, Istanbul, Turkey
[4] Istanbul University–Cerrahpasa, Cerrahpasa Faculty of Medicine, Department of Radiology, Istanbul, Turkey
[5] Istanbul University–Cerrahpasa, Cerrahpasa Faculty of Medicine, Department of Biostatistic, Istanbul, Turkey
[6] Istanbul University–Cerrahpasa, Cerrahpasa Faculty of Medicine, Department of Microbiology, Istanbul, Turkey

Abstract

Introduction: We aimed to evaluate clinical and laboratory findings of hospitalized asthma and chronic obstructive pulmonary disease (COPD) patients with COVID-19 and demonstrate that they have different symptoms and/or laboratory results and outcomes than COVID-19 patients with comorbidity (CoV-com) and without comorbidity (CoV-alone).

Methodology: The data of the demographic, clinical, laboratory findings of hospitalized CoV-alone, asthma, COPD patients with COVID-19 (CoV-asthma, CoV-COPD, respectively), and CoV-com were analyzed.

Results: Out of 1082 patients hospitalized for COVID-19, 585 (54.1%) had CoV-alone, 40 (3.7%) had CoV-asthma, 46 (4.3%) had CoV-COPD and 411 (38%) had CoV-com. Cough, shortness of breath, fever and weakness were the most common four symptoms seen in all COVID-19 patients. Shortness of breath, myalgia, headache symptoms were more common in CoV-asthma than the other groups ($p < 0.001$, $p < 0.01$, $p < 0.05$ respectively). Sputum was more common in CoV-COPD than other groups ($p < 0.01$). COPD group most frequently had increased values, different from the other groups with CRP>5ng/mL in 91.3%, D-dimer > 0.05mg/dL in 89.1%, troponin > 0.014micg/L in %63.9, INR>1.15 in 52.2%, CK-MB>25U/L in 48.5%, PT>14s in 40.9% of patients ($p < 0.05$, $p < 0.001$, $p < 0.001$, $p < 0.001$, $p < 0.05$, $p < 0.001$, respectively). NT-ProBNP was found to have the highest AUC value and the best differentiating parameter for CoV-asthma from CoV-alone. Typical CT findings were present in 44.4% of CoV-alone, 57.5% of CoV-asthma, 28.3% of CoV-COPD and 38.9% of CoV-com groups. CoV-COPD and CoV-com patients died more frequently than other groups (17.8%, 18.5%).

Conclusions: CoV-asthma and CoV-COPD patients might have different symptoms and laboratory parameters than other COVID-19 patients which can guide the physicians.

Key words: Asthma; COPD; COVID-19 symptoms; biochemical parameters; RT-PCR; Chest CT.

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Introduction

During the coronavirus disease 2019 (COVID-19) pandemic, two major chronic respiratory diseases; asthma and chronic obstructive pulmonary disease (COPD) patients who had risk for COVID-19 were evaluated by various researchers [1,2]. According to a study performed in the UK, asthma was about 14.5% out of admitted 20133 COVID-19 cases and other chronic pulmonary diseases were 17.7% [3]. Richardson *et al.* [4] reported 9% asthma and 5.4% COPD comorbidity in 5700 hospitalized COVID-19 patients in US. On the contrary only 1.5% of the cases reported to have COPD in China [5]. Clinical data of COVID-19 patients with or without a comorbidity displayed fever, cough, fatigue, and shortness of breath when they were admitted to the hospitals [3-7]. Fever, cough, fatigue, and shortness of breath symptoms could also be seen in COPD or in asthma exacerbation with viral or bacterial infections [1,8]. Physicians need to perform other laboratory tests (real-time reverse transcriptase polymerase chain reaction (RT-PCR), hematological and biochemical analysis, radiological

examination) in order to evaluate signs or symptoms to distinguish the exacerbation of asthma and COPD from severe adult respiratory syndrome of coronavirus-2 (SARS CoV-2) infection. But the value of these tests and the differences of these tests from the COVID-19 cases without comorbidity (CoV-alone), in asthma and COPD patients with COVID-19 (CoV-asthma, CoV-COPD, respectively) were not fully studied.

Hematological and biochemical data of COVID-19 patients revealed that patients might have elevated or decreased parameters, usually depending on the comorbidity or the severity of the disease [9]. The detection of patients' RNA with RT-PCR was needed for the accurate diagnosis of COVID-19. However, the sensitivity of the nasopharyngeal swabs varied from 45% to 67% depending on the days since symptom onset [10]. Yet, outside Wuhan, He *et al.* [11] found that RT-PCR and chest computed tomography (CT) results had comparable sensitivity. Chest CT was implied to offer the greatest sensitivity of up to 99% for detecting COVID-19 in a systematic review by Xu *et al.* [12].

The symptoms of COVID-19 patients could be confused with asthma and COPD exacerbation symptoms. False negative PCR results could be encountered to differentiate COVID-19 cases from asthma and COPD exacerbations. The differences of these groups' laboratory parameters and symptoms in CoV-asthma and CoV-COPD patients from the CoV-alone and CoV-com were not studied in detail. The aim of this study was to evaluate the clinical and laboratory findings and outcome of CoV-asthma, CoV-COPD, CoV-alone and CoV-com and reveal the differences and similarities between groups to guide the physicians who provide care for asthma and COPD patients with COVID-19.

Methodology

This study is a single center, retrospective and non-interventional, cross-sectional study focused on the clinical and laboratory data in real life conditions, aiming to observe the adult hospitalized COVID-19 patients, with and without comorbidity, with asthma and with COPD.

Ethical approval of this study was obtained by the Ethics Committee of the Medical Faculty of our University, (05/21/2020; No: 83045809-604.01.02-63860). The study was conducted between 22 May 2020 to 22 August 2020 with recovery of the first 1082 cases data of adult COVID-19 patients hospitalized in the University Hospital and met all inclusion and exclusion criteria.

Patients

The physicians collected all hospitalized patients' data consecutively whose patient's medical record to select the study patients and to avoid bias patients still hospitalized were excluded.

Admission criteria to hospital for COVID-19 cases in this time period were having CT findings suspicious for COVID-19 pneumonia with or without initial RT-PCR positivity finding with COVID-19 symptoms or having positive RT-PCR test with oxygen saturation rate below 90%. CoV-asthma, CoV-COPD, CoV-com and CoV-alone were included in the study. All patients were monitored by a specialist of pulmonary diseases and/or infectious diseases and/or internal medicine. The inclusion criteria were as follows:

- Age of COVID-19 diagnosis: ≥18 years hospitalized and discharged or died.
- Diagnosis of COVID-19 was validated via chest CT findings with PCR positivity or having positive RT-PCR test with oxygen saturation rate below 90%.
- Diagnosis of asthma was validated with a pulmonology specialist physician and with the historical diagnosis in the Governmental System with Global Initiative for Asthma (GINA) 2020 criteria (www.ginasthma.org).
- Diagnosis of COPD was validated with a pulmonology specialist physician and with the historical diagnosis in the Governmental System with the Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2021 criteria (www.goldcopd.org).
- Asthma and COPD patients with and without other comorbidities were enrolled.

Exclusion criteria were as follows:

- Patients still hospitalized but not yet discharged from the hospital were excluded.
- Patients with asthma and COPD hospitalized in the non-COVID part of the hospital or without PCR positivity or without typical COVID chest CT findings were excluded.

Procedures and measures

A "Case Report Form" was prepared by the authors. Data included the information written on patients' routine medical records file. The collected previous and current medical history data were included: the referral information; socio-demographics (height, body weight, body mass index, education status and location of primary residence); etiology; medical history (reasons for application, concomitant diseases); risk factors (smoking, occupation); first diagnostic tests during admission to the hospital before COVID-19 treatment

including PCR, complete blood count (CBC), biochemical tests and CT; and the outcome.

Combined pharyngeal and nasopharyngeal swab samples were obtained for RT-PCR assay.

All biochemical parameters, CBC and coagulation tests were measured at Central Biochemistry Laboratory of our Medical Faculty.

The chest CT examinations were reported in accordance with the Radiological Society of North America (RSNA) Consensus Statement on Reporting Chest CT Findings Related to COVID-19 [13].

Medical treatments for COVID-19 were initiated and proceeded with respect to our Ministry of Health guidelines. Underlying treatment of patients with asthma and COPD were written from the patients' medical record and checked from the governmental system.

Statistical analysis

In the biostatistical analysis of the study, the criteria discussed were defined by mean, standard deviation, frequency, and percentage values. Chi-Square and Fisher exact tests were used to compare frequencies and percentages between the groups. For comparison of variable averages with normal distribution; "one-way analysis of variance" (One-Way ANOVA) in comparing more than two group averages and in order to interpret the differences between subgroups in variables with significant differences with ANOVA, the post-hoc "Scheffe" test was also used in binary comparisons of subgroups. If necessary, nonparametric "Kruskal-Wallis one-way analysis of variance" and post hoc Dunn's methods were used in appropriate experimental fictions (depending on the number of subjects and homogeneity control). In the study cases, receiver operating characteristic (ROC) curve analysis was used to investigate the performance of important criteria in determining disease diagnosis. A *p*-value below 0.05 was expressed as significant. All statistical analyses were carried out using the Statistical Product and Service Solutions (SPSS) v. 21.0 (IBM, Armonk, NY, USA) package program.

Results

1136 COVID-19 patients were hospitalized in our hospital during the study time. 54 COVID-19 patients hospitalized who didn't meet inclusion criteria were excluded. A total of 1082 newly diagnosed COVID-19 treatment-naïve adult patients with COVID-19 were included. The patients were categorized into four groups; COVID-19 patients without any comorbidities (N: 585), patients with comorbidities (N: 411), patients

Table 1. Sociodemographic data.

	CoV-alone		CoV-Asthma		CoV- COPD		CoV-Com		P value
N (%)	585	(54)	40	(3.7)	46	(4.3)	411	(38)	
Female N (%)	243	(41.5)	29	(72.5)	15	(32.6)	206	(50.1)	0.000***
Male N (%)	342	(58.5)	11	(27.5)	31	(67.4)	205	(49.9)	
Age (Year) (mean ± SD)	51.8 ± 15.8 (cd***)		56.1 ± 15 (c***)		68.5 ± 9.7 (abd***)		61.7 ± 15.8 (ac***)		0.000***
≥ 65y N (%)	110	(32.8)	13	(32.5)	29	(63)	183	(44.5)	0.000***
Occupation	N	(%)	N	(%)	N	(%)	N	(%)	
Unemployed	38	(20.5)	0	(0.0)	4	(22.2)	28	(19.6)	
Officer	13	(7.0)	1	(10.0)	0	(0.0)	5	(3.5)	
Health worker	18	(9.7)	2	(20.0)	0	(0.0)	14	(9.8)	0.023*
Self employed	61	(33.0)	3	(30.0)	4	(22.2)	47	(32.9)	
House wife	27	(14.6)	4	(40.0)	1	(5.6)	18	(12.6)	
Retired	28	(15.1)	0	(0.0)	9	(50.0)	31	(21.7)	
BMI$_{(kg/m^2)}$ Mean±SD)	27.5 ± 4.6		28.9 ± 5.3		27.3 ± 3.5		28.3 ± 6.4		0.455
BMI > 30 N (%)	43	(24.9)	12	(36.4)	6	(23.1)	40	(34.5)	
Smoking Habit	N	(%)	N	(%)	N	(%)	N	(%)	
Non- Smoker	124	(67.4)	25	(62.5)	5	(12.8)	80	(65.0)	0.000***
Ex-smoker	42	(22.8)	14	(35.0)	23	(59.0)	35	(28.5)	
Smoker	18	(9.8)	1	(2.5)	11	(28.2)	8	(6.5)	
Comorbidity			N	(%)	N	(%)	N	(%)	
Hypertension			15	(37.5)	23	(51.1)	218	(53.0)	0.171
Diabetes			13	(32.5)	29	(64.4)	129	(31.4)	0.000***
Cancer (last 2 years)			2	(5.0)	7	(15.6)	63	(15.3)	0.274
Cardiac insuf			2	(5.0)	6	(13.3)	38	(9.2)	0.417
Other cardiac			4	(10.0)	11	(24.4)	65	(15.8)	0.179
Renal problem			0	(0.0)	6	(13.3)	41	(10.0)	0.079
Others			7	(17.5)	9	(20.0)	178	(43.3)	0.000***

In this table, the superscripts a, b, c and d show significant differences to study groups of CoV-alone, CoV-Asthma, CoV-COPD and CoV-com, respectively, and the following asterisks (*) notation show the significance level of the differences (*p < 0.05, **p < 0.01, ***p < 0.001) in one-way ANOVA result.

with COVID-19 and asthma (N: 40), and patients with COVID-19 and COPD (N: 46).

Sociodemographic and clinical data

Sociodemographic data of the patients' groups were shown in Table 1. Only a female patient in the CoV-asthma group, at the age of 28, had no comorbidity, was neither obese nor a smoker.

Cough, shortness of breath, fever and weakness were most common four symptoms seen in all COVID-19 patients (Table 2).

Hematological and biochemical laboratory results

Hematological and biochemical laboratory parameters of the groups were shown in Table 3.

Hematologic parameters below or above the reference value of the groups at admission to hospital were shown in Table 4.

In CoV-alone patients, a positive moderate correlation was found between the hospitalization time and C-reactive protein (CRP) ($r = 0.502$, $p < 0.001$) and lactate dehydrogenase (LDH) levels ($r = 0.505$, $p < 0.001$). While there was a negative correlation between intensive care unit (ICU) length of stay and albumin ($r = -0.432$, $p < 0.001$), it was found that there was a positive correlation between ICU length of stay and N-terminal brain natriuretic peptide (NT-proBNP) ($r = 0.462$, $p < 0.001$), urea ($r = 0.548$, $p < 0.001$), CRP ($r=0.444$, $p<0.001$), LDH ($r = 0.547$, $p < 0.001$), and D-dimer levels ($r = 0.435$, $p < 0.001$).

In COVID-19 patients with comorbidities, only CRP levels were positively correlated with ICU length of stay ($r = 0.484$, $p<0.001$).

In patients with CoV-COPD, a very strong positive correlation was found between ICU length of stay and NT-proBNP levels ($r = 0.988$, $p < 0.01$).

In CoV-asthma patients, SpO_2 at first admission was negatively correlated with the hospitalization time ($r = -0.573$, $p<0.001$), LDH levels ($r=-0.447$, $p<0.01$) and ICU length of stay ($r = -0.442$, $p < 0.01$). ICU length of stay was also positively correlated with urea ($r=0.518$, $p<0.001$) and CRP levels ($r = 0.654$, $p < 0.001$) in these patients.

NT-proBNP levels were found to be elevated in CoV-asthma patients rather than CoV-alone patients, and NT-proBNP were significant in differentiating CoV-asthma patients from CoV-alone patients according to ROC analysis. The NT-proBNP value higher than 1092.1 pg/mL indicates that the patient has CoV-asthma rather than COVID-19 alone, with 71% sensitivity and 87.50% specificity.

PCR and Computed tomography (CT) findings

At hospital admission PCR positivity rate of CoV-alone, CoV-asthma and CoV-COPD and CoV-com groups were 51.1%, 47.5%, 32.6% and 45.3%, respectively, in the total group positivity rate was 48%**.** The second PCR tests added very few positivity rates; +8.2% for CoV-alone, +5.0% for CoV-asthma, +8.7% for CoV-COPD and +9.0% for CoV-com group. For the total group, the added value is 8.4%.

CT findings at admission to hospital were shown in Table 5.

Treatments and clinical outcomes

COVID-19 treatment and clinical outcomes are shown in Table 6.

Table 2. Clinical Data Results at admission to hospital.

	CoV-alone N:585		CoV-asthma N:40		CoV-COPD N: 46		CoV-Com N:411		P Value
Symptoms N (%)	N	(%)	N	(%)	N	(%)	N	(%)	
Fever and/or chills	200	(34.2)	16	(40.0)	10	(21.7)	123	(29.9)	0.138
Cough	215	(36.8)	19	(47.5)	17	(37.0)	154	(37.5)	0.604
Shortness of breath	131	(22.4)	23	(57.5)	20	(43.5)	130	(31.6)	0.000***
Weakness. fatigue	109	(18.6)	10	(25.0)	11	(23.9)	72	(17.5)	0.523
Sputum	15	(2.6)	2	(5.0)	6	(13.0)	18	(4.4)	0.003**
Headache	38	(6.5)	5	(12.5)	1	(2.2)	13	(3.2)	0.015*
Taste/smell disturb	6	(1.0)	1	(2.5)	0	(0.0)	5	(1.2)	0.729
Myalgia	41	(7.0)	9	(22.5)	2	(4.3)	27	(6.6)	0.002**
Nasal congestion	1	(0.2)	0	(0.0)	0	(0.0)	3	(0.7)	0.495
Diarrhea / Vomiting	40	(6.8)	1	(2.5)	2	(4.3)	23	(5.6)	0.596
$Pulse_{(rate/min)}$ (mean±SD)	88.5 ± 16.5		87.4 ± 15.2		90.8 ± 23.1		90.5 ± 21.7		0.606
$SBP_{(mmHg)}$ (mean±SD)	127.4 ± 10.3(c*)		127.3± 11.6(c*)		142.3 ± 5.2 (a*)		128.5 ± 30.3		0.001***
$DBP_{(mmHg)}$ (mean±SD)	80.3 ± 5.2		78.0 ± 6.2		86.8 ± 8.7(d*)		73.7 ± 25.9(c*)		0.002**

SBP: systolic blood pressure; DBP: diastolic blood pressure. In this table, the superscripts a, b, c and d show significant differences to study groups of CoV-alone, CoV-Asthma, CoV-COPD and CoV-com, respectively, and the following asterisks (*) notation show the significance level of the differences (*p<0.05, **p<0.01, ***p<0.001) in one-way ANOVA result.

Table 3. Hematological and biochemical parameters of the subjects included in the study.

Variables	CoV-alone		CoV-Asthma		CoV- COPD		CoV-Com		*p*
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
SpO_2 (%) (FM)	94.1	4.30	94.26	3.81	92.57	7.08	92.97 ^{a*}	6.50	0.236
SpO_2 (%) (LM)	91.83 $^{c**\ d***}$	5.18	91.00	4.74	88.16 ^{a**}	9.16	89.66 ^{a***}	7.36	0.000***
$WBC_{(\times10^9/L)}$	7.26^{cd***}	3.80	6.89	2.88	10.60^{a***}	5.12	9.07^{a***}	6.49	0.000***
$RBC_{(\times10^6/\mu L)}$	4.67 ^{cd***}	0.59	4.54	0.66	4.12^{a***}	0.79	4.32 ^{a***}	0.81	0.000***
$HGB_{(g/dL)}$	13.32^{cd***}	1.81	12.78	1.69	11.62 ^{a***}	2.12	12.33 ^{a***}	2.31	0.000***
$Hct_{(\%)}$	38.98 ^{cd***}	5.27	38.64	4.76	35.45 ^{a***}	6.21	36.07 ^{a***}	6.48	0.000***
$PLT_{(\times10^4/\mu L)}$	219.04 ^{c**}	85.53	205.91^{c**}	74.96	277.01^{abd**}	163.0	223.71^{c**}	105.71	0.164
$Neut_{(\times10^9/L)}$	4.74 ^{cd***}	3.48	4.79^{c**}	2.34	7.94 ^{a***b**}	4.18	6.11^{a***}	5.30	0.000***
$Lymph_{(\times10^9/L)}$	1.50	0.79	1.34	0.73	1.42	0.77	1.48	1.48	0.819
$Mono_{(x10^3/\mu L)}$	0.58 ^{cd***}	0.34	0.52	0.26	1.06 ^{a*}	1.38	0.76^{a*}	1.57	0.004***
$EOS_{(x10^3/\mu L)}$	0.07	0.21	0.11	0.27	0.08	0.09	0.07	0.12	0.541
NLR	4.47 ^{cd**}	6.22	4.24	2.96	8.09^{a**}	7.25	6.08 ^{a**}	7.68	0.000***
PLR	180.13 ^{c*}	112.55	191.36	126.03	242.08 ^{a*}	161.53	202.09	166.96	0.049*
$Glucose_{(mg/dL)}$	119.99 ^{d***}	42.06	120.79	38.10	135.74	60.82	139.56^{a***}	54.40	0.000***
$Urea_{(mg/dL)}$(FM)	32.29 ^{cd***}	22.36	33.55 ^{cd*}	22.31	56.39 ^{a***b*}	49.86	49.22 ^{a***b*}	41.03	0.000***
Creatinine $_{(mg/dL)}$	0.96 ^{d***}	0.62	0.92	0.26	1.40	1.08	1.38 ^{a***}	1.56	0.000***
Total $Protein_{(g/dL)}$	7.16	0.73	7.13	0.64	6.82	0.78	7.02	0.86	0.027*
$Albumin_{(g/dL)}$	4.13 ^{cd***}	0.57	4.10 ^{c*}	0.45	3.66 ^{a***b*}	0.61	3.85 ^{a***}	0.66	0.000***
$Tot.Bilirubin_{(mg/dL)}$	0.56	0.68	0.41	0.22	0.58	0.48	0.76	1.89	0.020*
Direct $Bilirubin_{(mg/dL)}$	0.23	0.44	0.14	0.08	0.25	0.35	0.37	1.55	0.371
Uric $Acid_{(mg/dL)}$	4.73 ^{cd***}	1.46	4.81^{c*}	2.23	6.21^{a***b*}	3.01	5.65^{a***}	2.57	0.000***
$CRP_{(mg/L)}$, (FM)	48.94^{d***}	64.01	45.47	48.82	77.44	81.42	74.14 ^{a***}	84.70	0.000***
$Na_{(mmol/L)}$	137.67	3.64	138.16	3.78	135.89	6.92	137.06	5.13	0.027*
$K_{(mmol/L)}$	4.34 ^{c**}	0.50	4.41	0.64	4.75^{a**}	0.75	4.46	0.81	0.001***
$Cl_{(mmol/L)}$	99.00	3.84	99.34	3.35	97.84	7.41	98.42	5.12	0.199
$Ca_{(mg/dL)}$	8.92	0.63	9.03	0.62	8.80	0.62	8.83	0.82	0.531
$AST_{(U/L)}$	34.07	33.69	33.63	23.27	49.60	77.62	38.54	47.66	0.695
$ALT_{(U/L)}$	32.70	39.95	25.24	17.34	34.45	60.45	30.96	43.68	0.659
$LDH_{(U/L)}$, (FM)	278.25^{d***}	141.94	298.03	153.52	314.48	188.73	367.45 ^{a***}	409.54	0.003***
$GGT_{(U/L)}$	46.00	62.75	29.81	24.87	59.63	82.19	60.49	106.25	0.183
$CK_{(U/L)}$	192.48	537.10	157.38	221.16	148.64	198.21	175.07	510.72	0.943
$CK\text{-}MB_{(U/L)}$	28.72	25.25	33.59	38.25	36.30	25.75	45.89	91.54	0.020*
$Ferritin_{(ng/mL)}$, (FM)	389.83^{d***}	581.55	247.66	381.26	355.94	423.64	624.83^{a***}	1122.53	0.000***
Troponin $T_{(\mu g/L)}$	NN	0.03	0.02	0.03	0.06	0.15	0.04	0.09	0.000***
$PT_{(s)}$	13.25 ^{cd***}	2.97	13.12	1.48	14.72	4.04	14.71 ^{a**}	6.14	0.000***
PT activity $_{(\%)}$	85.41 ^{c*d**}	17.48	85.99	16.55	75.33 ^{a*}	21.26	78.72 ^{a**}	21.65	0.000***
INR	1.11^{d**}	0.25	1.10	0.12	1.24	0.35	1.25 ^{a**}	0.55	0.000***
$APTT_{(s)}$	25.29 ^{d**}	4.09	25.30	3.62	27.46	4.84	27.11^{a**}	7.72	0.018*
$Fibrinogen_{(mg/dL)}$, (FM)	458.35	170.90	450.89	145.87	461.23	173.27	478.52	173.05	0.323
D-$Dimer_{(mg/dL)}$,(FM)	1.87 ^{d*}	6.70	1.74	5.55	2.52	3.50	3.22 ^{a*}	6.53	0.000***
$Pro\text{-}BNP_{(pg/mL)}$	2302.26	6784.6	4955.27	11306.6	10687.2	13923.7	6748.71	10115.4	0.000***
$Urea_{(mg/dL)}$ (HM)	42.26 ^{cd***}	33.91	50.18 ^{c*d*}	35.33	82.28$^{a***\ b*}$	74.64	74.17 $^{a***\ b*}$	60.50	0.000***
Creatinine$_{(mg/dL)}$, (HM)	1.11^{b***}	0.80	6.90^{acd***}	25.59	1.72^{b***}	1.62	2.02 ^{b***}	3.99	0.000***
$CRP_{(mg/L)}$, (HM)	75.46 ^{c**d***}	83.56	83.43	85.52	131.84^{a**}	97.84	118.99 ^{a***}	108.41	0.000***
$LDH_{(U/L)}$, (HM)	395.27 ^{d***}	260.87	396.55	210.77	484.74	347.12	580.12 ^{a***}	550.57	0.000***
$Ferritin_{(ng/mL)}$, (HM)	550.29 ^{cd***}	671.32	397.68	528.43	632.13	598.74	1006.09^{a***}	2512.25	0.000***
Fibrinogen $_{(mg/dL)}$, (HM)	556.25	186.80	545.93	163.05	626.36	166.36	588.09	188.72	0.011**
D-$Dimer_{(mg/dL)}$, (HM)	3.84 ^{d***}	9.67	6.92	17.89	6.34	12.60	7.98^{a***}	12.70	0.000***

WBC: white blood cell; RBC: red blood cell; ALT: alanine aminotransferase; AST: aspartate aminotransferase; CK: creatine kinase; CK-MB: creatine kinase-MB; CRP: C-reactive protein; LDH: lactate dehydrogenase; GGT: gamma-glutamyl transferase; TIBC: Total iron binding capacity; NT-proBNP: N-terminal pro-Brain natriuretic peptide; Na: sodium; K: potassium; Cl: chlorine; Ca: calcium; RBC: red blood cell; Hb: haemoglobin; EOS: eosinophil; NLR: Neutrophil - lymphocyte ratio; PLT: Platelet; PLR: Platelet-lymphocyte ratio; MLR: monocyte–lymphocyte ratio; FPR: fibrinogen-platelet ratio; FNR: fibrinogen-neutrophil ratio; PT: prothrombin time; APTT: activated partial thromboplastin time; INR: international normalized ratio; FM: First measurement; LM: Lowest measurement; HM: Highest measurement. In this table, the superscripts a, b, c and d show significant differences to study groups of CoV-alone, CoV-Asthma, CoV-COPD and CoV-com, respectively, and the following asterisks (*) notation show the significance level of the differences (*p < 0.05, **p < 0.01, ***p < 0.001) in one-way ANOVA result.

Table 4. Hematologic parameters below or above the reference value of the groups at admission to hospital.

Parameters		CoV-alone		CoV-Asthma		CoV-COPD		CoV-Com		p
		Count	%	Count	%	Count	%	Count	%	
NLR	NLR>0.6	570	(98.4)	40	(100.0)	46	(100.0)	397	(97.3)	0.323
	NLR<0.6	9	(1.6)	0	(0.0)	0	(0.0)	11	(2.7)	
PLR	PLR<286.92	501	(86.5)	36	(90.0)	33	(71.7)	334	(81.9)	0.015*
	PLR>286.92	78	(13.5)	4	(10.0)	13	(28.3)	74	(18.1)	
PLR	PLR>44.57	572	(98.8)	39	(97.5)	45	(97.8)	393	(96.3)	0.083
	PLR<44.57	7	(1.2)	1	(2.5)	1	(2.2)	15	(3.7)	
Glucose	Glucose<109 mg/dL	148	(51.9)	18	(47.4)	16	(38.1)	55	(29.7)	0.000***
	Glucose>109 mg/dL	137	(48.1)	20	(52.6)	26	(61.9)	130	(70.3)	
Urea	Urea<49 mg/dL	529	(90.9)	34	(85.0)	30	(65.2)	280	(68.5)	0.000***
	Urea>49 mg/dL	53	(9.1)	6	(15.0)	16	(34.8)	129	(31.5)	
Creatinine	Creatinine<1.2 mg/dL	511	(87.7)	35	(87.5)	28	(60.9)	291	(71.1)	0.000***
	Creatinine>1.2 mg/dL	72	(12.3)	5	(12.5)	18	(39.1)	118	(28.9)	
Total protein	Total protein<8.3 g/dL	275	(97.9)	35	(97.2)	40	97.6)	177	(97.8)	0.995
	Total protein>8.3 g/dL	6	(2.1)	1	(2.8)	1	(2.4)	4	(2.2)	
Albumin	Albumin<5.2 g/dL	292	(99.7)	37	(100.0)	43	(100.0)	195	(100.0)	0.816
	Albumin>5.2 g/dL	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	
T.bilirubin	T.bilirubin<1.2 mg/dL	288	(95.4)	38	(100.0)	41	(93.2)	179	(89.5)	0.022*
	T.bilirubin>1.2 mg/dL	14	(4.6)	0	(0.0)	3	(6.8)	21	(10.5)	
D.bilirubin	D.bilirubin<0.3 mg/dL	264	(87.7)	35	(92.1)	37	(84.1)	157	(78.5)	0.023*
	D.bilirubin>0.3 mg/dL	37	(12.3)	3	(7.9)	7	(15.9)	43	(21.5)	
Uric acid	Uric acid<7 mg/dL	251	(93.7)	31	(83.8)	33	(80.5)	131	(77.5)	0.000***
	Uric acid>7 mg/dL	17	(6.3)	6	(16.2)	8	(19.5)	38	(22.5)	
CRP	CRP<5 mg/L	134	(23.0)	9	(22.5)	4	(8.7)	66	(16.1)	0.012*
	CRP>5 mg/L	449	(77.0)	31	(77.5)	42	(91.3)	344	(83.9)	
Na	Na<145 mmol/L	305	(99.0)	38	(100.0)	44	(97.8)	195	(96.5)	0.176
	Na>145 mmol/L	3	(1.0)	0	(0.0)	1	(2.2)	7	(3.5)	
K	K<5.1 mmol/L	293	(95.1)	34	(89.5)	37	(84.1)	179	(89.5)	0.019*
	K>5.1 mmol/L	15	(4.9)	4	(10.5)	7	(15.9)	21	(10.5)	
Cl	Cl<107 mmol/L	303	(99.3)	38	(100.0)	41	(93.2)	191	(97.0)	0.015*
	Cl>107 mmol/L	2	(0.7)	0	(0.0)	3	(6.8)	6	(3.0)	
Ca	Ca<10.2 mmol/L	289	(99.0)	37	(97.4)	42	(100.0)	189	(98.4)	0.706
	Ca>10.2 mmol/L	3	(1.0)	1	(2.6)	0	(0.0)	3	(1.6)	
AST	AST<40 U/L	458	(78.7)	31	(77.5)	31	(67.4)	318	(77.8)	0.368
	AST>40 U/L	124	(21.3)	9	(22.5)	15	(32.6)	91	(22.2)	
ALT	ALT<41 U/L	465	(79.8)	35	(87.5)	39	(84.8)	342	(83.4)	0.326
	ALT>41 U/L	118	(20.2)	5	(12.5)	7	(15.2)	68	(16.6)	
LDH	LDH<250 U/L	324	(56.0)	23	(57.5)	22	(47.8)	195	(48.0)	0.078
	LDH>250 U/L	255	(44.0)	17	(42.5)	24	(52.2)	211	(52.0)	
GGT	GGT<60 U/L	216	(80.6)	31	(86.1)	29	(76.3)	134	(76.1)	0.466
	GGT>60 U/L	52	(19.4)	5	(13.9)	9	(23.7)	42	(23.9)	
CK	CK<190 U/L	204	(82.6)	28	(82.4)	30	(83.3)	136	(86.1)	0.819
	CK>190 U/L	43	(17.4)	6	(17.6)	6	(16.7)	22	(13.9)	
CK-MB	CK-MB<25 U/L	142	(67.6)	20	(62.5)	17	(51.5)	77	(54.2)	0.048*
	CK-MB>25 U/L U/L	68	(32.4)	12	(37.5)	16	(48.5)	65	(45.8)	
Ferritin	Ferritin<400 ng/mL	378	(67.6)	31	(81.6)	32	(71.1)	241	(61.8)	0.039*
	Ferritin>400 ng/mL	181	(32.4)	7	(18.4)	13	(28.9)	149	(38.2)	
Troponin	Troponin<0.014 µg/L	200	(84.7)	25	(83.3)	13	(36.1)	79	(50.6)	0.000***
	Troponin>0.014 µg/L	36	(15.3)	5	(16.7)	23	(63.9)	77	(49.4)	
PT	PT<14 s	243	(84.4)	31	(83.8)	26	(59.1)	137	(72.5)	0.000***
	PT>14 s	45	(15.6)	6	(16.2)	18	(40.9)	52	(27.5)	
INR	INR<1.15	225	(78.1)	28	(75.7)	21	(47.7)	123	(65.1)	0.000***
	INR>1.15	63	(21.9)	9	(24.3)	23	(52.3)	66	(34.9)	
APTT	APTT<32 s	274	(95.1)	37	(100.0)	37	(84.1)	164	(87.2)	0.001***
	APTT>32 s	14	(4.9)	0	(0.0)	7	(15.9)	24	(12.8)	
Fibrinojen	Fibrinojen<350 mg/dL	150	(28.1)	7	(18.9)	9	(20.0)	91	(23.3)	0.216
	Fibrinojen>350 mg/dL	384	(71.9)	30	(81.1)	36	(80.0)	300	(76.7)	
D-dimer	D-dimer<0.5 mg/dL	241	(42.6)	18	(46.2)	5	(10.9)	102	(25.4)	0.000***
	D-dimer>0.5 mg/dL	325	(57.4)	21	(53.8)	41	(89.1)	300	(74.6)	

NLR: Neutrophil - lymphocyte ratio; PLR: Platelet-lymphocyte ratio; CRP: C-reactive protein; ALT: alanine aminotransferase; AST: aspartate aminotransferase; CK: creatine kinase; CK-MB: creatine kinase-MB; LDH: lactate dehydrogenase; GGT: gamma-glutamyl transferase; PT: prothrombin time; APTT: activated partial thromboplastin time. The unit of these parameters are given in Table 3. *p<0.05; **p<0.01; ***p<0.001.

Length of stay in hospital and in intensive care unit (ICU) was remarkably higher in CoV-COPD group than the others ($p < 0.001$, $p < 0.01$ respectively).

Underlying treatment of asthma group at admission to hospital consisted of 25 patients (62%) on inhaled corticosteroid (ICS)/long-acting β2-agonist (LABA) (one of them also received one biologic or placebo), 5 patients (12.5%) on ICS and as needed short acting beta agonist (SABA) and 10 patients (25%) on as needed SABA. COPD patients underlying treatments were very different than asthma; 15 (30.6%) used LABA/ long-acting muscarinic antagonist (LAMA), 7 (15.2%) used ICS/LABA, 10 (21.7%) used ICS/LABA/LAMA, 5 (10.9%) SABA/ short acting muscarinic antagonists (SAMA) and 10 (30.6%) LAMA.

Discussion

The results revealed that 3.7% of hospitalized COVID-19 adult patients were asthma patients and 4.3% were COPD patients. Cough was the one most common of the three symptoms seen in all groups. Shortness of breath was the most common symptom for CoV-asthma and CoV-COPD groups. The augmentation of these symptoms might be in asthma and COPD exacerbations. COPD group had most frequently increased CRP, D-dimer, troponin, INR, CK-MB and PT values than the reference range and different than the other groups ($p < 0.05$, $p < 0.001$, $p < 0.001$, $p < 0.001$, $p < 0.05$, $p < 0.001$ respectively). NT-proBNP was found to have the highest AUC value and the best differentiating parameter for CoV-asthma from CoV-alone. PCR positivity is gold standard but may not be positive in half of the COVID-19 patients. Different CT patterns and worst outcome seen in CoV-COPD were also important findings of our study.

Sociodemographic and clinical data

Mean age was over 50 in all groups. But CoV-COPD group had a higher mean age, higher smoking rate and contained a higher male percentage than the

Table 5. Computed Tomography Findings at admission to hospital*.

N (%)	CoV-alone		CoV-Asthma		CoV- COPD		CoV-Com		p value
Multifocal N (%)	347	(76.9)	26	(81.3)	20	(76.9)	225	(77.3)	0.991
Ground glass opacities	377	(97.4)	27	(96.4)	22	(100.0)	244	(98.8)	0.533
Crazy paving pattern	180	(46.5)	15	(55.6)	12	(54.5)	131	(53.0)	0.356
Consolidation	201	(51.9)	10	(37.0)	8	(36.4)	169	(68.4)	0.000***
Halo sign	156	(40.3)	10	(37.0)	7	(31.8)	98	(39.8)	0.870
Reverse halo sign	60	(15.5)	4	(14.8)	1	(4.5)	47	(19.0)	0.287
Pleural effusion	34	(8.8)	1	(3.7)	5	(22.7)	48	(19.4)	0.000***
Lymphadenopathy	45	(11.6)	4	(14.8)	8	(36.4)	76	(30.8)	0.000***
Tromboembolia	4	(1.0)	0	(0.0)	0	(0.0)	1	(0.4)	0.916
Emphysema	48	(12.5)	2	(7.4)	9	(40.9)	45	(18.4)	0.000***
Typical COVID*	260	(44.4)	23	(57.5)	13	(28.3)	160	(38.9)	0.000***

*Only patients having CT in the hospital system were analyzed by two radiology specialists. **Typical COVID CT sign; Multifocal GGO of rounded morphology with or without consolidation or visible intra lobular lines ("crazy-paving"), reverse halo sign or other findings of organizing pneumonia (20). *p < 0.05, **p < 0.01, ***p < 0.001.

Table 6. COVID-19 treatment and clinical outcomes.

COVID treatment and outcome N (%)	CoV-alone N: 585		CoV-Asthma N: 40		CoV- COPD N:46		CoV-Com N:411		p value
Hydroxychloroquine	473	(81.0)	33	(82.5)	40	(88.9)	336	(81.8)	0.623
Ritonavir+Lopinavir	26	(4.5)	1	(2.5)	1	(2.2)	18	(4.4)	0.842
Oseltamivir	280	(47.9)	27	(67.5)	19	(42.2)	224	(54.5)	0.019*
Favipiravir	277	(47.4)	20	(50.0)	28	(62.2)	222	(54.0)	0.082
Tocilizumab	66	(11.3)	7	(17.5)	6	(13.3)	41	(10.0)	0.487
Systemic Corticosteroid	24	(4.1)	3	(7.5)	4	(8.9)	49	(11.9)	0.000***
Azithromycin	344	(58.9)	30	(75.0)	26	(57.8)	258	(62.8)	0.164
Enoxaparin	373	(63.9)	29	(72.5)	36	(80.0)	293	(71.3)	0.020*
Nasal O_2	311	(53.3)	30	(75.0)	34	(75.6)	247	(60.1)	0.001***
O_2 with reservoir	12	(2.1)	3	(7.5)	3	(6.7)	20	(4.9)	0.028*
High flow O_2	7	(1.2)	1	(2.5)	0	(0.0)	5	(1.2)	0.774
Intensive care unit admission	47	(8.0)	6	(15.0)	13	(28.9)	102	(24.8)	0.000***
Intubation	17	(2.9)	2	(5.0)	8	(17.8)	41	(10.0)	0.000***
Home discharged	535	(91.6)	33	(86.8)	30	(64.4)	301	(73.2)	0.000***
Other unit discharged	26	(4.5)	4	(10.5)	8	(17.8)	34	(8.3)	0.000***
Death	23	(3.9)	1	(2.6)	8	(17.8)	76	(18.5)	0.000***

*p < 0.05, **p < 0.01, ***p < 0.001.

other groups. Higher age, male gender and smoking were demonstrated as major risk factors in COVID-19 [7,9]. All patients in CoV-COPD group had at least one other comorbidity and more than half had diabetes and/or hypertension. These comorbidities were present for CoV-com group and also were demonstrated as major comorbidities of COVID-19 in other studies [4,5,7,9]. Having comorbidity or obesity or being smoker/ex-smoker and/or aging were present in 95.5% of the CoV-asthma group. Only one patient at the age of 28 who was female had no comorbidity, no obesity, no smoking but in regard to the underlying treatment it was revealed that she used salbutamol when needed. Using ICS might decrease the risk of COVID-19 as reported by Liu *et al.* [14].

The most common symptoms in admission to the hospital, in CoV-alone group were cough and fever, in CoV-asthma group were shortness of breath, cough and fever, in CoV-COPD group were shortness of breath and cough, in CoV-com group were cough, shortness of breath and fever in our study. These results demonstrate that the difficulty of diagnosis of COVID-19 in asthma and COPD patients as they usually had these symptoms when they were uncontrolled or had an exacerbation of their diseases. This problem has already been pointed [1,15]. For the differential diagnosis, performing PCR is important but may be negative at the first visit. Physicians should know if a patient has COVID-19 before performing spirometry or nebulized treatments or non-invasive ventilation that produces aerosols [15-17]. Higher levels of fatigue, myalgia and headache seen in our asthma patients may point to COVID-19 rather than asthma exacerbation and this must be evaluated with future research. The difference of sputum percentage seen in CoV-COPD patients from the other groups was clinically non-significant as it is one of the major symptoms of COPD. CoV-COPD patients had significantly lower level of SpO_2, higher level of SBP than the other groups. More severe disease and worse outcome in COPD and COVID-19 patients were also demonstrated in other studies [1,18].

Hematological and biochemical findings

Researchers demonstrate that COVID-19 patients have abnormalities in some hematological and biochemical parameters depending on the stage and severity of the diseases [19]. The worst outcome was seen in CoV-COPD group and had increased CRP, D-dimer, troponin, INR, CK-MB, and PT values than the reference range. Physicians who think that their COPD patient may have COVID-19 must ask for PCR and also request these biochemical parameters that may guide them as a diagnostic tool for COVID-19. Elevated levels of these biochemical results may warrant multiple PCR tests or thorax CT if the first PCR test remains negative.

We found that there was a positive correlation between ICU length of stay and NT-proBNP, urea, CRP, LDH, and D-dimer levels in CoV-alone patients. Fan et al. [20] identified LDH as a discriminator between ICU and non-ICU patients in their series of COVID-19 patients from Singapore. Increased LDH is common in COVID-19 patients in the ICU setting and indicates a poor outcome in other studies [20-22]. Liu et al [22] mentioned that COVID-19 patients with lymphopenia, higher urea, LDH at admission pointed poor outcomes, particularly for older patients and those with comorbid conditions. In the current study, unlike other groups, increased NT-proBNP levels are directly related to the increase in ICU and indicate a poor outcome in CoV-COPD patients. In CoV-com patients only CRP levels were positively correlated with ICU length of stay.

COVID-19 is a systemic infection with significant impacts on the hematopoietic system and hemostasis. Yang et al. [23] demonstrated that elevated age and neutrophil-lymphocyte ratio (NLR) can be considered as independent prognostic biomarkers for indicating the poor clinical outcomes in COVID-19 patients. Lymphopenia can be considered to be a cardinal laboratory sign, and is potentially prognostic [22,24]. Qin *et al.* [19] reported that there is an increase in NLR in patients with severe disease compared to those without. In the current study, we found that platelet, white blood cell count, monocytes, neutrophils, NLR, platelet-lymphocyte ratio (PLR) as inflammatory parameters were higher in CoV-COPD patients than CoV-alone patients. It was concluded that especially hematologic-inflammatory indices such as NLR and PLR might be useful markers for monitoring CoV-COPD patients.

Only 5% of CoV-asthma patients had cardiac insufficiency but NT-proBNP was found to have the highest AUC value and the best differentiating parameter for CoV-asthma from CoV-alone. This finding might guide physicians who provide care for asthma patients during the COVID-19 pandemic and must be evaluated in further research.

PCR and CT findings

Our initial PCR positivity rate was lower than other researchers' reports (25,26). These percentages were the initial PCR results at admission to hospital. However, it was important for the first distinguishing

diagnosis from the exacerbation of asthma and COPD. Negative initial RT-PCR test in asthma and COPD patients might be attributed easily to the exacerbation of these diseases.

Our findings of CT were similar to other researchers' findings [6,25,27]. Most common imaging findings in chest CT were ground glass opacities (GGOs), whether isolated or coexisting with consolidations, in bilateral and sub-pleural distribution in a systematic review comprising 4410 cases [27]. Many radiological findings didn't differ significantly in CoV-alone, CoV-asthma and CoV-COPD groups in our study. The prevalence of emphysema was, unsurprisingly, higher in CoV-COPD patients (17.4%) than the other groups. Zhang *et al.* [28] also found that severe COVID-19 patients with COPD had different patterns on the CT when compared to patients without comorbidity.

Treatments and clinical outcome

Medical treatments were used in accordance with the Ministry of Health guidelines in that time period.

CoV-COPD patients more frequently used favipiravir and enoxaparin, they were admitted to ICU and intubated more frequently than the other groups. Death rate was also higher than the other groups. Poor outcome of COPD patients has already been demonstrated in other studies [1,18].

In regard to the underlying treatments of patients; Wang L et al found that using SABA was associated with hospitalization in asthma and COVID patients after multivariate analysis [29]. One quarter of CoV-asthma patients used SABA as needed only without ICS, 75% had treatments with ICS or ICS/LABA. Using SABA without ICS was not yet recommended in GINA as it increases the risk of exacerbation (www.ginasthma.org). But these patients didn't use oral steroid during their hospitalization as they didn't have asthma exacerbation at the same time. None of them used regular oral corticosteroids that can alter immune response to viral infections. There was one CoV-asthma patient from a phase 3 study using a biologic or placebo.

Treatment of COPD patients showed that they were from different groups of the GOLD Guideline (www.goldcopd.org). They were also very severe COPD patients on triple therapies.

The worst outcome was in CoV-COPD group as 28.9% of CoV-COPD patients admitted to ICU and 17.8% died. The Global Alliance Against Chronic Respiratory Diseases (GARD) editorial described chronic respiratory diseases as important causes of death and advised special collaboration and partnership, sharing resources and experiences, which are essential to control the pandemic [30].

Limitations of this Study

First, the study population included only hospitalized patients within a certain time period of one center, while the study population of asthma and COPD groups was small. Second, asthma and COPD patients did not have spirometry results as we did not recommend doing routine pulmonary function tests during the COVID-19 pandemic, especially for COVID-19 patients [16]. However, their diagnoses were checked by the national health system data written by the physicians. Also, we didn't have a control group of asthma and COPD patients with exacerbation without COVID-19 to compare with the study groups; CoV-asthma and CoV-COPD.

Conclusions

Cough, shortness of breath, fever and weakness were most common four symptoms seen in all COVID-19 patients. Shortness of breath, myalgia, and headache symptoms were more common in CoV-asthma than the other groups. Sputum was more common in CoV-COPD than other groups.

For COPD patients suspected of having COVID-19, physicians must ask for a PCR test and also requesting CRP, D-dimer, troponin, INR, CK-MB and PT levels might guide them for the differential diagnosis between COVID-19 and exacerbation of their diseases.

NT-proBNP was found to have the highest AUC value and the best differentiating parameter for CoV-asthma from COV-alone.

The outcome of CoV-COPD was remarkably worse than the other groups.

Authors' Contribution

Designed the study: BG, HU, SB, RK, SK, SS, SD, PA, AD, MAK, FT. Performed the study: BG, HU, SB, RK, SK, SS, SD, PA, AD, MAK, FT. Contributed important reagents / collected data: BG, HU, SB, RK, SK, SS, SD, PA, AD, MAK, FT. Analyzed data: AD, SD, BG, HU. Concept, supervision, literature search: BG, HU. Drafted, wrote, reviewed and approved the submission of the manuscript: BG, HU, SB, RK, SK, SS, SD, PA, AD, MAK, FT.

References

1. Leung JM, Niikura M, Yang CWT, Sin DD (2020) COVID-19 and COPD. Eur Respir J 13: 2002108.
2. Morais-Almeida M, Pité H, Aguiar R, Ansotegui I, Bousquet J (2020) Asthma and the Coronavirus Disease 2019 Pandemic: A Literature Review. Int Arch Allergy Immunol 181: 680-688.

3. Docherty AB, Harrison EM, Green CA, Hardwick HE, Pius R, Norman L, Holden KA, Read JM, Dondelinger F, Carson G, Merson L, Lee J, Plotkin D, Sigfrid L, Halpin S, Jackson C, Gamble C, Horby PW, Nguyen-Van-Tam JS, Ho A, Russell CD, Dunning J, Openshaw PJ, Baillie JK, Semple MG; ISARIC4C investigators (2020) Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. BMJ 22: m1985.
4. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW; the Northwell COVID-19 Research Consortium, Barnaby DP, Becker LB, Chelico JD, Cohen SL, Cookingham J, Coppa K, Diefenbach MA, Dominello AJ, Duer-Hefele J, Falzon L, Gitlin J, Hajizadeh N, Harvin TG, Hirschwerk DA, Kim EJ, Kozel ZM, Marrast LM, Mogavero JN, Osorio GA, Qiu M, Zanos TP (2020) Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. JAMA 22: 2052-2059.
5. Guan WJ, Liang WH, Zhao Y, Liang HR, Chen ZS, Li YM, Liu XQ, Chen RC, Tang CL, Wang T, Ou CQ, Li L, Chen PY, Sang L, Wang W, Li JF, Li CC, Ou LM, Cheng B, Xiong S, Ni ZY, Xiang J, Hu Y, Liu L, Shan H, Lei CL, Peng YX, Wei L, Liu Y, Hu YH, Peng P, Wang JM, Liu JY, Chen Z, Li G, Zheng ZJ, Qiu SQ, Luo J, Ye CJ, Zhu SY, Cheng LL, Ye F, Li SY, Zheng JP, Zhang NF, Zhong NS, He JX; China Medical Treatment Expert Group for COVID-19 (2020) Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. Eur Respir J 14: 2000547.
6. Rodriguez-Morales AJ, Cardona-Ospina JA, Gutiérrez-Ocampo E, Villamizar-Peña R, Holguin-Rivera Y, Escalera-Antezana JP, Alvarado-Arnez LE, Bonilla-Aldana DK, Franco-Paredes C, Henao-Martinez AF, Paniz-Mondolfi A, Lagos-Grisales GJ, Ramírez-Vallejo E, Suárez JA, Zambrano LI, Villamil-Gómez WE, Balbin-Ramon GJ, Rabaan AA, Harapan H, Dhama K, Nishiura H, Kataoka H, Ahmad T, Sah R; Latin American Network of Coronavirus Disease 2019-COVID-19 Research (LANCOVID-19). Electronic address: https://www.lancovid.org (2020) Clinical, laboratory and imaging features of COVID-19: A systematic review and meta-analysis. Travel Med Infect Dis 34: 101623.
7. Yang J, Zheng Y, Gou X, Pu K, Chen Z, Guo Q, Ji R, Wang H, Wang Y, Zhou Y (2020) Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis. Int J Infect Dis 94: 91-95.
8. Castillo JR, Peters SP, Busse WW (2017) Asthma Exacerbations: Pathogenesis, Prevention, and Treatment. J Allergy Clin Immunol Pract 5: 918-927
9. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, Liu L, Shan H, Lei CL, Hui DSC, Du B, Li LJ, Zeng G, Yuen KY, Chen RC, Tang CL, Wang T, Chen PY, Xiang J, Li SY, Wang JL, Liang ZJ, Peng YX, Wei L, Liu Y, Hu YH, Peng P, Wang JM, Liu JY, Chen Z, Li G, Zheng ZJ, Qiu SQ, Luo J, Ye CJ, Zhu SY, Zhong NS; China Medical Treatment Expert Group for Covid-19 (2020) Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med 30: 1708-1720.
10. Zhao J, Yuan Q, Wang H, Liu W, Liao X, Su Y, Wang X, Yuan J, Li T, Li J, Qian S, Hong C, Wang F, Liu Y, Wang Z, He Q, Li Z, He B, Zhang T, Fu Y, Ge S, Liu L, Zhang J, Xia N, Zhang Z (2020) Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019. Clin Infect Dis 19: 2027-2034.
11. He JL, Luo L, Luo ZD, Lyu JX, Ng MY, Shen XP, Wen Z (2020) Diagnostic performance between CT and initial real-time RT-PCR for clinically suspected 2019 coronavirus disease (COVID-19) patients outside Wuhan, China. Respir Med 168: 105980.
12. Xu B, Xing Y, Peng J, Zheng Z, Tang W, Sun Y, Xu C, Peng F. (2020) Chest CT for detecting COVID-19: a systematic review and meta-analysis of diagnostic accuracy. Eur Radiol 30: 5720-5727.
13. Simpson S, Kay FU, Abbara S, Bhalla S, Chung JH, Chung M, Henry TS, Kanne JP, Kligerman S, Ko JP, Litt H (2020) Radiological Society of North America Expert Consensus Statement on Reporting Chest CT Findings Related to COVID-19. Endorsed by the Society of Thoracic Radiology, the American College of Radiology, and RSNA - Secondary Publication. J Thorac Imaging 35: 219-227.
14. Liu S, Zhi Y, Ying S (2020) COVID-19 and Asthma: Reflection During the Pandemic. Clin Rev Allergy Immunol 59: 78-88.
15. Bousquet J, Jutel M, Akdis CA, Klimek L, Pfaar O, Nadeau KC, Eiwegger T, Bedbrook A, Ansotegui IJ, Anto JM, Bachert C, Bateman ED, Bennoor KS, Berghea EC, Bergmann KC, Blain H, Bonini M, Bosnic-Anticevich S, Boulet LP, Brussino L, Buhl R, Camargos P, Canonica GW, Cardona V, Casale T, Chinthrajah S, Akdis M, Chivato T, Christoff G, Cruz AA, Czarlewski W, Del Giacco S, Du H, El-Gamal Y, Fokkens WJ, Fonseca JA, Gao Y, Gaga M, Gemicioglu B, Gotua M, Haahtela T, Halpin D, Hamelmann E, Hoffmann-Sommergruber K, Humbert M, Ilina N, Ivancevich JC, Joos G, Khaitov M, Kirenga B, Knol EF, Ko FW, Koskinen S, Kowalski ML, Kraxner H, Kudlay D, Kuna P, Kupczyk M, Kvedariene V, Abdul Latiff AH, Le LT, Levin M, Larenas-Linnemann D, Louis R, Masjedi MR, Melén E, Mihaltan F, Milenkovic B, Mohammad Y, Morais-Almeida M, Mullol J, Namazova L, Neffen H, Nunes E, O'Byrne P, O'Hehir R, O'Mahony L, Ohta K, Okamoto Y, Onorato GL, Panzner P, Papadopoulos NG, Passalacqua G, Patella V, Pawankar R, Pham-Thi N, Pigearias B, Popov TA, Puggioni F, Regateiro FS, Rolla G, Rottem M, Samolinski B, Sastre J, Schwarze J, Sheikh A, Scichilone N, Soto-Quiros M, Soto-Martinez M, Sova M, Nicola S, Stelmach R, Suppli-Ulrik C, Taborda-Barata L, To T, Tomazic PV, Toppila-Salmi S, Tsiligianni I, Usmani O, Valiulis A, Ventura MT, Viegi G, Vontetsianos T, Wang Y, Williams S, Wong GWK, Yorgancioglu A, Zernotti M, Zidarn M, Zuberbier T, Agache I (2021) ARIA-EAACI statement on asthma and COVID-19. Allergy 76: 689-697.
16. Gemicioğlu B, Börekçi Ş, Görek Dilektaşı A, Ulubay G, Azap Ö, Saryal S (2020) Turkish Thoracic Society Experts Consensus Report: Recommendations for Pulmonary Function Tests During and After COVID 19 Pandemic. Turk Thorac J 21: 193-200.
17. Flick H, Arns BM, Bolitschek J, Bucher B, Cima K, Gingrich E, Handzhiev S, Hochmair M, Horak F, Idzko M, Jaksch P, Kovacs G, Kropfmüller R, Lamprecht B, Löffler-Ragg J, Meilinger M, Olschewski H, Pfleger A, Puchner B, Puelacher C, Prior C, Rodriguez P, Salzer H, Schenk P, Schindler O, Stelzmüller I, Strenger V, Täubl H, Urban M, Wagner M, Wimberger F, Zacharasiewicz A, Zwick RH, Eber E (2020) Management of patients with SARS-CoV-2 infections and of patients with chronic lung diseases during the COVID-19 pandemic (as of 9 May 2020): Statement of the Austrian Society of Pneumology (ASP). Wien Klin Wochenschr 32: 365-386.

18. Lippi G, Henry BM (2020) Chronic obstructive pulmonary disease is associated with severe coronavirus disease 2019 (COVID-19). Respir Med 167: 105941.
19. Qin C, Zhou L, Hu Z, Zhang S, Yang S, Tao Y, Xie C, Ma K, Shang K, Wang W, Tian DS (2020) Dysregulation of immune response in patients with COVID-19 in Wuhan, China. Clin Infect Dis 71: 762-768.
20. Fan BE, Chong VCL, Chan SSW, Lim GH, Lim KGE, Tan GB, Mucheli SS, Kuperan P, Ong KH (2020) Hematologic parameters in patients with COVID-19 infection. Am J Hematol 95: E131-E134.
21. Ruan Q, Yang K, Wang W, Jiang L, Song J (2020) Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med 46: 846-8.
22. Liu J, Liu Z, Jiang W, Wang J, Zhu M, Song J, Wang X, Su Y, Xiang G, Ye M, Li J, Zhang Y, Shen Q, Li Z, Yao D, Song Y, Yu K, Luo Z, Ye L (2020) Clinical predictors of COVID-19 disease progression and death: Analysis of 214 hospitalised patients from Wuhan, China. Clin Respir J 15: 293-309.
23. Yang AP, Liu JP, Tao WQ, Li HM (2020) The diagnostic and predictive role of NLR, d-NLR and PLR in COVID-19 patients. Int Immunopharmacol 84: 106504.
24. Vieira LMF, Emery E, Andriolo A (2020) COVID-19: laboratory diagnosis for clinicians. An updating article. Sao Paulo Med J 138: 259-266.
25. Ai T, Yang Z, Hou H, Zhan C, Chen C, Lv W, Tao Q, Sun Z, Xia L (2020) Correlation of Chest CT and RT-PCR Testing for Coronavirus Disease 2019 (COVID-19) in China: A Report of 1014 Cases. Radiology 296: E32-E40.
26. He JL, Luo L, Luo ZD, Lyu JX, Ng MY, Shen XP, Wen Z (2020) Diagnostic performance between CT and initial real-time RT-PCR for clinically suspected 2019 coronavirus disease (COVID-19) patients outside Wuhan, China. Respir Med 168: 105980.
27. Ojha V, Mani A, Pandey NN, Sharma S, Kumar S (2020) CT in coronavirus disease 2019 (COVID-19): a systematic review of chest CT findings in 4410 adult patients [published online ahead of print, 2020 May 30]. Eur Radiol 30: 6129-6138.
28. Zhang N, Xu X, Zhou LY, Chen G, Li Y, Yin H, Sun Z (2020) Clinical characteristics and chest CT imaging features of critically ill COVID-19 patients. Eur Radiol 30: 6151-6160.
29. Wang L, Foer D, Bates DW, Boyce JA, Zhou L (2020) Risk factors for hospitalization, intensive care and mortality among patients with asthma and COVID-19. J Allergy Clin Immunol 146: 808-812.
30. To T, Viegi G, Cruz A, Taborda-Barata L, Asher I, Behera D, Bennoor K, Boulet LP, Bousquet J, Camargos P, Conceiçao C, Gonzalez Diaz S, El-Sony A, Erhola M, Gaga M, Halpin D, Harding L, Maghlakelidze T, Masjedi MR, Mohammad Y, Nunes E, Pigearias B, Sooronbaev T, Stelmach R, Tsiligianni I, Tuyet Lan LT, Valiulis A, Wang C, Williams S, Yorgancioglu A (2020) A Global Respiratory Perspective on the COVID-19 Pandemic: Commentary and Action Proposals. Eur Respir J. 23:56(1) 2001704.

Corresponding author

Prof. Dr. Bilun Gemicioglu
İ.Ü.C. Cerrahpasa Tip Fakültesi, Göğüs Hastaliklari Anabilim Dali 34303 İstanbul, Turkey.
Mobile: +905322876373
Fax: +90 212 3512409
E-mail: bgemici@istanbul.edu.tr; bilung@gmail.com

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