Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Original Article

Demographic, clinical, and laboratory characteristics of patients with COVID-19 during the second and third waves of the pandemic in Egypt

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ABSTRACT

Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel virus that belongs to the coronaviruses and causes coronavirus disease 2019 (COVID-19). In this study, we explored the demographic details, clinical features, and routinely conducted laboratory investigations of patients with COVID-19 during the second and third waves of the pandemic to understand their possible diagnostic and prognostic values in Egypt.

Methods: In this retrospective cohort study, the demographic characteristics, detailed medical history, laboratory findings, and symptoms of all enrolled patients with SARS-CoV-2 were collected from the medical records of Beni Suef University Hospitals between December 15, 2020, and April 15, 2021.

Results: This retrospective study included 473 patients, almost all of whom were elderly. The median age of the patients was 48 years, and those with moderate and severe disease were older than those with mild infections. The proportion of females was higher (63.4%) than males (36.6%). Diabetes mellitus (DM) was the most common comorbidity (17.3%), and fever was the most typical manifestation of COVID-19 (62.6%). Those with severe disease showed a higher C-reactive protein level (CRP) than those with moderate (p-value 0.009) or mild (p-value 0.01) diseases. Serum ferritin levels were significantly higher in patients with severe disease than in those with moderate disease (p-value 0.018). In contrast, D-dimer and serum creatinine were normal and showed no significant difference in all comparisons (p-value overall 0.21).

Conclusion: This study observed several variations in COVID-19 patients' characteristics. The new manifestations included skin rash, bone and low back pains, and rigors. In contrast to females, most males had moderate-to-severe illness. Old age and higher body mass index was associated with increasing severity. D-dimer and complete blood count were normal and could not identify potential COVID-19 patients. Patients who had mild illness were still at risk of developing post-COVID complications.

Introduction

Coronavirus disease 2019 (COVID-19) is a novel outbreak caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The first case of SARS-CoV-2 infection appeared in Wuhan City, Hubei Province, China, and manifested as respiratory illness; the World Health Organization (WHO) reported this case on December 31, 2019 [1]. The WHO conducted a meeting on January 30, 2020, in which the COVID-19 outbreak was declared a global health emergency [2]. The first case of COVID-19 in Egypt was detected on February 14, 2020 [3]. Subsequently, Egypt sought to prevent the spread of COVID-19 infection with a partial ban that started on March 25, 2020 [4]. According to the consultant for health affairs

Abbreviations: AUC, Area under the ROC curve; BMI, Body mass index; CBC, Complete blood count; CKD, Chronic kidney disease; CRP, C-reactive protein; DM, Diabetes mellitus; DVT, Deep vein thrombosis; FBS, Fasting blood sugar; MOHP, Ministry of health and population; OR, Odds ratio; ROC, Receiver operator characteristic; SPSS, Statistical Package for the Social Sciences; WHO, World Health Organization.

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of the president, the second wave in Egypt began on November 26, 2020 [5], while the third wave began at the end of March 2021, with an increased number of cases (>650 cases) [6,7].

The most typical clinical manifestations of COVID-19 are cough, fever, dyspnea, and pneumonia [8]. The WHO classifies cases into mild, moderate, and severe according to the severity of the disease [9]. The diagnosis is confirmed by reverse transcription-polymerase chain reaction (RT-PCR) of nasopharyngeal and oropharyngeal swab samples obtained from patients with symptoms [9]. Hematologic parameters are also changed in patients with COVID-19 infection. Several studies have found that increased D-dimer and abnormal coagulation parameters were associated with poor prognosis [9–11], in addition to fibrin degradation products and baseline platelet concentrations. The demographic details, clinical characteristics, and laboratory findings of patients with COVID-19 showed variation during the second wave as the incidence rate, number of infected patients, and hospitalization rate increased. All variations were different from the characteristics of the first wave [12,13].

Moreover, variations were also noted between the second and third waves [14,15]. Despite the changes in patients' demographic, clinical, and laboratory characteristics with COVID-19 during the different pandemic waves, only a few studies have observed these characteristics in Egypt during the first pandemic wave [4,16]. Furthermore, no previous studies were retrospectively conducted on patients with COVID-19 to determine these characteristics in Egypt during the second and third waves. Therefore, we explored the demographic details, clinical features, and routine laboratory investigations of patients with COVID-19 to establish potential diagnostic and prognostic values of COVID-19 in Egypt.

Material and methods

This retrospective cohort study was conducted in accordance with the STROBE Statement and Checklist for cohort studies [17].

Study design and setting

This study is a single-center retrospective cohort study conducted in Beni Suef University Hospitals in Egypt.

Study population and sample size

The target population included patients who were admitted to Beni Suef University Hospitals with confirmed COVID-19. According to the WHO criteria [18], patients were classified into mild, moderate, and severe groups according to the severity of the disease. For sample size calculations, we performed a retrospective analysis of the hospital medical records and filtered the data according to our inclusion and exclusion criteria and in a way similar to that described in D. Liao et al.'s study [19]. Retrospective studies use statistical power rather than calculating sample sizes [20], and we call these Post hoc power analyses based on determining the main outcome variable; the power of the study is 0.99. The statistical power was calculated using G*power software 3.1.9.4 [21]. based on the following assumptions: main outcome variable and disease severity. Patients were classified into mild, moderate, and severe disease groups. Patients were classified into mild, moderate, and severe disease groups. The main statistical test is Post hoc power analysis: alpha = 0.01, total sample size = 473, effect size = 0.30 (see **Supplementary Fig. 1**).

Inclusion criteria

We included patients admitted to the hospitals between December 15, 2020, and April 15, 2021. Patients were diagnosed according to the WHO interim guidance based on a SARS-CoV-2-positive nasopharyngeal swab by RT-PCR. We included patients aged ≥18 from both the sexes with mild, moderate, and severe COVID-19.

Exclusion criteria

Patients with missing data were transferred to other medical facilities with unknown outcomes and those aged <18 years old were excluded.

Data collection

Demographic characteristics, detailed medical history, laboratory findings, and symptoms of all enrolled patients positive for SARS-CoV-2 infection were collected from the medical records of hospitals between December 15, 2020, and April 15, 2021. We handled and managed the data in a spreadsheet before starting the analysis. Data on demographic characteristics, previous medical history, and laboratory findings, including hematologic and biochemical parameters (complete blood count [CBC], liver function tests, kidney function test, C-reactive protein [CRP], fasting blood glucose, ferritin, and D-dimer), were collected. The diagnosis of COVID-19 was based on the history of epidemiologic exposure and clinical manifestations. The diagnosis was confirmed when positive results were obtained on performing SARS-CoV-2 RT-PCR test (see **Supplementary Table 1**). According to the COVID-19 protocol of the Egyptian Ministry of Health [22,23], the primary treatment for mild, moderate, and severe cases are based on antiviral drugs, immune modulators, anti-inflammatory drugs, analgesics, and multivitamins (see Appendix 1). After the patients were discharged from the hospital, their mean follow-up duration was approximately 13.5 days, which changed according to the patients' severity of disease.

Statistical analysis

The collected data were summarized and presented using suitable tables and graphs. Continuous nonnormally distributed variables are presented as median and interquartile range, and categorical variables are presented as numbers and percentages. Statistical significance was evaluated using the Kruskal–Wallis test for continuous variables and a chi-square test (χ^2) or Fisher's exact test for categorical variables as appropriate. We performed post hoc pairwise comparisons among groups using the Bonferroni adjustment method after significant effects have been found. The association between the variables was tested using Spearman correlation analysis, followed by multinomial logistic regression analysis, including all factors showing significance ($p < 0.05$). Multinomial logistic regression models were conducted to determine the association between the predictor and dependent variables. The optimal CRP cutoff point was evaluated using the receiver operator characteristic (ROC) curve. The dependent variable (severity grade) was classified as mild (reference category), moderate, or severe. Therefore, the multinomial regression model was used to compare mild vs. moderate and mild vs. severe disease probabilities. A p-value of ≤0.05 was considered statistically significant. We conducted statistical analyses using the Statistical Package for the Social Sciences (SPSS) software (version 26.0) [24].

Ethical approval

This study was an observational cohort study that recruited human participants and thus conducted according to the ethical principles of the Declaration of Helsinki. The study was ethically approved by the ethical research committee of the Faculty of

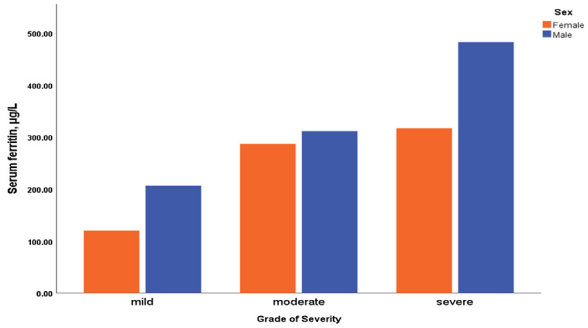

Fig. 1. Distribution of serum ferritin among sexes by grade of severity.

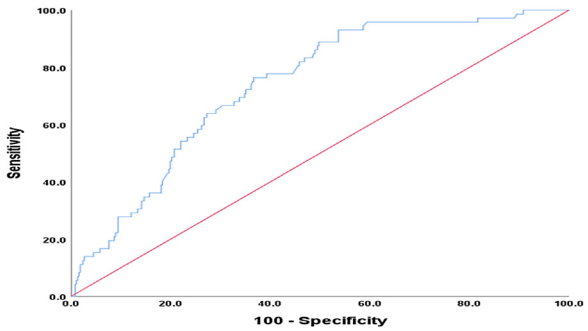

Fig. 2. Receiver operator characteristic curve for C-reactive protein to predict severe cases.

Medicine, Beni Suef University, Beni Suef, Egypt (ethical approval number: FMBSUREC/09052021/Eid) (see **Supplementary Fig. 2**). In addition, informed oral consent was obtained from the patients or relatives for their medical reports.

Results

Baseline demographic and clinical characteristics

This retrospective study included 476 patients. Three patients were excluded: two with inadequate data in their hospital records and <18 years old. Almost all patients were older, and the median age was 48 years old. Patients with moderate and severe disease were older than those with mild disease. The proportion of females was higher (63.4%) than males (36.6%). However, males developed moderate and severe illnesses more frequently than did females. Approximately 8.5% of the patients were smokers. Diabetes mellitus (DM) was the most common comorbidity (17.3%), followed by hypertension (HTN) (16.7%) and hepatitis C virus (HCV) (7.5%). The most common clinical manifestations of COVID-19 were fever (62.6%), followed by cough (52.7%), bony pain (39.8%), dyspnea (36%), rigors (27.3%), and abdominal pain (26.8%). All baseline demographic and clinical characteristics are listed in Table 1.

Hematologic parameters of patients with COVID-19

The hematologic and coagulation parameters are presented in Table 2. Neutrophil count, lymphocyte count, neutrophil/lymphocyte (N/L) ratio, CRP, alanine aminotransferase (ALT), aspartate aminotransferase (AST), platelet, fasting blood sugar (FBS), and serum ferritin (all $p < 0.001$) and monocyte ($p < 0.05$) were significantly different in all comparisons.

Regarding the laboratory findings in Table 2, the patients with severe infection showed significantly higher CRP than those with moderate and mild illness. Serum ferritin was significantly higher in patients with severe disease than in those with moderate disease (mainly males) (see Fig. 1), and FBS was also considerably higher in patients with severe disease than those with moderate and mild illness. Basal O_2 was significantly lower in patients with severe disease ($p < 0.001$), while heart rate was considerably higher in patients with severe disease ($p < 0.001$) (see Table 2).

The optimum cutoff value for CRP to predict severe disease was 17.4 mg/L using a ROC curve with a sensitivity of 76.4% and a specificity of 63.4%. The area under the ROC curve (AUC) for severe cases was 0.73 (see Fig. 2). The accuracy of D-dimer to diagnose was poor (AUC = 0.56) with a cutoff value (0.77), and the accuracy of serum ferritin to diagnose severe cases was fair (AUC = 0.75) with a cutoff value (165.86), and they were at the normal range; this means that there were severe cases with normal serum ferritin and normal D-dimer.

Correlations between grade of severity and other factors

A low positive correlation was noted between body mass index (BMI), sex, DM, HTN, ischemic heart disease, HCV, liver cirrhosis, chronic kidney disease (CKD), cough, sweating, ALT, AST, FBS, segmented neutrophils %, N/L ratio, heart rate, and grade of severity. A low negative correlation was noted between diarrhea, abdominal pain, anosmia, dysgeusia, rhinorrhea, platelet, lymphocyte percentage (%), and grade of severity as well as the association between the grade of severity. A moderately positive correlation was established between age, serum ferritin, CRP, duration of O_2 treatment per day, time of follow-up per day, and grade of severity (see Table 3). All factors showing significance ($p < 0.05$) were evaluated using the multinomial logistic regression model (see Table 4).

Determinants of severity with a multinomial logistic regression model

The multinomial regression analysis revealed that age, BMI, sex, DM, HTN, HCV, liver cirrhosis, CKD, diarrhea, abdominal pain, anosmia, dysgeusia, cough, rhinorrhea, sweating, ALT, AST, CRP, FBS, serum ferritin, segmented %, lymphocyte %, N/L ratio, basal O_2, and heart rate were significant predictors of severe grade (see Table 4).

The odds ratio (OR) for age was 1.07 (95% confidence interval [CI], 1.05–1.08), meaning that older patients had a higher chance of developing the more severe disease than younger patients. The OR for BMI was 1.2 (95% CI, 1.12–1.3), meaning that patients with higher BMI had a higher chance of developing more severe disease than patients with lower BMI. The OR of female patients was 0.48 (95% CI, 0.28–0.82), meaning that female patients had a lesser chance of developing severe symptoms than male patients. The OR for DM, HTN, HCV, liver cirrhosis, and CKD were 0.13 (95% CI, 0.07–0.25), 0.15 (95% CI, 0.07–0.29), 0.10 (95% CI, 0.04–0.27), 0.11 (95% CI, 0.028–0.44), and 0.09 (95% CI, 0.009–0.89), respectively, meaning that patients without these comorbidities had a lesser chance of developing more severe disease than patients with these comorbidities. The OR for diarrhea, abdominal pain, anosmia, dysgeusia, and rhinorrhea were 2.47 (95% CI, 1.16–5.23), 2.53 (95% CI, 1.26–5.06), 2.91 (95% CI, 1.27–6.69), 2.24 (95% CI, 1.016–4.96), and 2.42 (95% CI, 0.99–5.94), respectively, meaning that patients without these symptoms had a lower chance of developing more severe disease than patients with these symptoms. Those patients with symptoms such as cough (OR, 0.44; 95% CI, 0.25–0.75) and sweating (OR, 0.29; 95% CI, 0.11–0.76) had a lower chance of developing more severe disease than those without these symptoms. The OR for laboratory findings ALT, AST, FBS, CRP, serum ferritin, segmented %, and N/L ratio were 1.16 (95% CI, 1.10–1.24), 1.15 (95% CI, 1.09–1.21), 1.012 (95% CI, 1.008–1.017), 1.022 (95% CI, 1.015–1.029), 1.006 (95% CI, 1.004–1.008), 1.05 (95% CI, 1.02–1.07), and 1.28 (95% CI, 1.13–1.45), respectively, meaning that patients

Table 1
Baseline demographic and clinical characteristics of the patients (n = 473).

	Total (n = 473)	Mild (n = 259)	Moderate (n = 140)	Severe (n = 74)	P Value			
	overall	Mild Vs. Moderate	Mild Vs. severe	Moderate Vs. severe				
Age (years)	48 (32–60)	37 (50–28)	60 (65–48)	60(70–53)	<0.001	<0.001	<0.001	0.1
BMI (kg/m^2)	25 (27.75–22)	24 (27–21)	25.1 (28.75–23)	26(30–24)	<0.001	<0.001	<0.001	0.12
Gender								
Female	300 (63.4%)	180 (60%)	81 (27%)	39(13%)	0.008	0.02	0.007	0.47
Male	173 (36.6%)	79 (45.7%)	59 (34.1%)	35(20.2%)				
Comorbidity								
Smoking	40(8.5%)	25(62.5%)	9(22.5%)	6(15%)	0.54			
Malignancy	4(0.8%)	0	3(75%)	1(25%)	0.07			
CHF	4(.9%)	1(25%)	2(50%)	1(25%)	0.48			
DM	81(17.3%)	23(28.4%)	27(33.3%)	31(38.3%)	<0.001	0.003	<0.001	<0.001
HTN	78(16.7%)	20(25.6%)	32(41%)	26(33.3%)	<0.001	<0.001	<0.001	0.04
BA	10(2.1)	5(50%)	4(40%)	1(10%)	0.74			
IHD	20(4.3%)	6(30%)	9(45%)	5(25%)	0.07			
HCV	35(7.5%)	7(20%)	13(37.1%)	15(42.9%)	<0.001	0.004	<0.001	0.02
Liver Cirrhosis	18(3.8%)	3(16.7%)	8(44.4%)	7(38.9%)	<0.001	0.008	<0.001	0.3
CKD	9(1.9%)	1(11.1%)	5(55.6%)	3(33.3%)	0.03	0.013	0.01	0.84
Hypothyroidism	4(0.9%)	2(50%)	2(50%)	0	0.55			
RhA	5(1.1%)	3(60%)	1(20%)	1(20%)	0.88			
Clinical Manifestations								
Diarrhea	96(20.5%)	66(68.8%)	21(21.9%)	9(9.4%)	0.007	0.015	0.01	0.58
Abdominal Pain	125(26.8%)	79(63.2%)	35(28%)	11(8.8%)	0.02	0.24	0.007	0.08
Anosmia	82(17.6%)	60(73.2%)	15(18.3%)	7(8.5%)	0.001	0.002	0.009	0.78
Dysgeusia	80(17.2%)	55(68.8%)	17(21.3%)	8(10%)	0.02	0.02	0.04	0.77
Fever	293(62.6%)	153(52.2%)	87(29.7%)	53(18.1%)	0.13			
Rigors	127(27.3%)	77(60.6%)	30(23.6%)	20(15.7%)	0.17			
Dyspnea	167(36%)	70(41.9%)	59(35.3%)	38(22.8%)	<0.001	0.002	<0.001	0.19
Chest Pain	61(13.1%)	32(52.5%)	21(34.4%)	8(13.1%)	0.65			
Sore Throat	74(15.8%)	46(62.2%)	18(24.3%)	10(13.5%)	0.35			
Vomiting	77(16.5%)	49(63.6%)	17(22.1%)	11(12%)	0.19			
Headache	113(24.2%)	80(70.8%)	25(22.1%)	8(7.1%)	<0.001	0.004	0.001	0.18
Dizziness	76(16.3%)	52(68.4%)	14(18.4%)	10(13.2%)	0.02	0.009	0.19	0.42
Fatigue	79(17%)	42(53.2%)	23(29.1%)	14(17.7%)	0.82			
Bony Pain	186(39.8%)	112(60.2%)	50(26.9%)	24(12.9%)	0.12			
Cough	246(52.7%)	113(45.9%)	86(35%)	47(19.1%)	<0.001	0.001	0.002	0.71
Skin Rash	13(2.8%)	5(38.5%)	5(38.5%)	3(23.1%)	0.48			
Rhinorrhea	62(13.5%)	45(72.6%)	11(17.7%)	6(9.7%)	0.008	0.007	0.04	0.92
Sweeting	25(5.5%)	10(40%)	6(24%)	9(36%)	0.06			

Notes: Data are presented as median (interquartile range) or number (percentage). We did not perform group comparisons for variables with overall p-values > 0.05. Instead, categorical variables were analyzed using the χ^2 test or Fisher's exact test, and the Kruskal–Wallis test was used for continuous variables. P-values $\leq$ 0.05 were considered statistically significant.
Abbreviations: BMI, body mass index; CHF, congestive heart failure; DM, diabetes mellitus; HTN, hypertension; BA, bronchial asthma; IHD, ischemic heart disease; HCV, hepatitis c virus; CKD, chronic kidney disease; and RhA, rheumatoid arthritis.

with higher laboratory findings had a higher chance of developing more severe disease than those with lower laboratory findings. The OR for lymphocyte percentage was 0.95 (95% CI, 0.92–0.97), meaning that those patients with a higher lymphocyte percentage had a lesser chance of developing more severe disease than those with a lower lymphocyte percentage.

The OR for basal O_2 was 0.98 (95% CI, 0.97–0.99), meaning that patients with higher basal O_2 had a lesser chance of developing more severe disease than lower basal O_2. The OR for heart rate was 1.05 (95% CI, 1.03–1.08), meaning that patients with a higher heart rate had a higher chance of developing more severe disease than those with a lower heart rate.

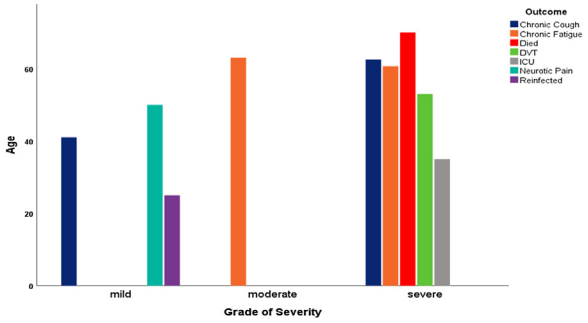

Fig. 3. Distribution of age among outcomes of patients by grade of severity.

Clinical complications and mortality rate

Six death events occurred during hospitalization; all six patients (100%) had severe disease. In addition, clinical follow-up complications, such as deep vein thrombosis (DVT), appeared in one patient (0.2%) with severe illness after hospital discharge despite oral anticoagulation therapy. Moreover, persistent polyneuropathic pain appeared in one patient (0.2%) with mild disease, chronic cough appeared in three patients (0.6%; one with mild disease and two with severe illness), and chronic fatigue occurred in five patients (1.1%; two with moderate disease and three with severe disease) (see Fig. 3).

Discussion

COVID-19 emerged in December 2019 in Wuhan. Unfortunately, the published data from Egypt currently only present the patient characteristics of the first wave of the pandemic. Therefore, the disease characteristics, severity, mortality, risk factors, and associated comorbidities remain unclear [25], especially in Egypt. The current

Table 2
Laboratory findings of the patients (n = 473).

	Missing data	Total(n = 473)	Mild (n = 259)	Moderate (n = 140)	Severe (n = 74)	P Value			
						overall	Mild Vs Moderate	Mild Vs severe	Moderate Vs severe
Creatinine, mg/dL	0	0.87(1−0.66)	0.8(1−0.66)	0.87(1−0.66)	0.9(1.1−0.7)	0.1			
ALT, U/mL	0	27(31−25)	27(29−25)	29(33−25.25)	30(33.25−26)	<0.001	<0.001	<0.001	0.26
AST, U/mL	0	31(34−28)	30(33−28)	33(35−29)	33(38−29)	<0.001	<0.001	<0.001	0.42
FBS, mg/dL	0	97(105−88)	92(102−87)	98(107−88)	104.5(202.5-89)	<0.001	0.01	<0.001	0.008
INR	0	1.08(1.13−1.04)	1.08(1.12−1.04)	1.085(1.14−1.05)	1.085(1.15−1.03)	0.09			
CRP, mg/L	19	12(42.7−3.7)	5.68(16.5−1.98)	23.06(52.9−7.62)	41.69(87.67−17.5)	<0.001	0.01	0.01	0.009
D-dimer, mg/L	91	0.34(0.65−0.2)	0.34(0.6−0.21)	0.36(0.68−0.17)	0.39(0.98−0.21)	0.21			
Serum Ferritin, μg/L	175	169.83(312.7−76.9)	99.82(208.45−49.01)	243.12(376.46−101.06)	321(594.7−176.51)	<0.001	<0.001	<0.001	0.018
Hemoglobin, gm/Dl	61	12.5(13.5−11.5)	12.5(13.32−11.5)	12.6(13.5−11.5)	12.4(13.5−11.2)	0.67			
RBCs, × 10Î2/L	66	4.6(4.95−4.29)	4.63(4.96−4.34)	4.5(4.85−4.24)	4.6(5.12−4.15)	0.14			
HCT, %	66	39.4(42.4−36.1)	39.3(42.27−36.35)	39.4(42.3−36.2)	39.35(43.05−34.55)	0.82			
MCV, fL	65	86.4(90.17−82)	85.95(90.2−81.7)	85.95(90.05−82.52)	85.9(90.37−80.15)	0.64			
MCH, pg	65	27.7(29.07-26.6)	27.6(29-26.5)	28(29.4-26.92)	27.45(28.95−26.7)	0.12			
MCHC, g/dL	65	31.9(32.8−30.8)	31.8(32.6−30.52)	32.05(33.1−30.92)	31.8(3287−30.9)	0.11			
Platelet, 10Ŷ/L	62	234(283−188)	248(299−200.5)	223(261.5−169)	216(265−171.5)	<0.001	0.94	0.002	<0.001
WBCs, 10Ŷ/L	23	7.2(9.62−5.4)	7.4(9.6−5.6)	7.1(10.13−5.15)	6.4(9−5.25)	0.39			
Staff Neutrophils, %	24	2(3−2)	2(2.3−2)	2(2−2)	2(3−2)	0.23			
Segmented Neutrophils, %	26	59(69−51)	57(68−49)	59(69−54)	64(73−58)	<0.001	0.04	<0.001	0.01
Lymphocyte Percentage, %	25	30(38−21)	33(40−22.25)	30(36−21)	25(32−17.5)	<0.001	0.01	<0.001	0.059
Neutrophil-to-Lymphocyte Ratio	46	2.06(3.42−1.43)	1.82(3.09−1.31)	2.07(3.38−1.56)	2.64(4.26−1.94)	<0.001	0.04	<0.001	0.01
Monocyte Percentage, %	28	6(7−5)	6(7−5)	6(7−5)	5(6.75−4)	0.02	0.016	0.011	0.63
Eosinophil Percentage, %	27	2(2−2)	2(2−2)	2(2−2)	2(2−2)	0.12			
Basophil Percentage, %	29	0	0	0	0	0.61			
Other indices									
Basal O_2	94	96(98−93)	98(99−96)	96(97−94)	89(92−80)	<0.001	<0.001	<0.001	<0.001
Heart Rate	150	98(106−88)	94(100.25−88)	98(102−88)	104(110−93)	<0.001	0.38	<0.001	0.001
Duration of O_2 Treatment, Days	204	0	0	0	1(10−0)	<0.001	0.26	<0.001	<0.001
Duration of Steroid Treatment, Days	32	4(7−3)	3(4−0)	7(10−5)	10(14−6)	<0.001	<0.001	<0.001	0.008
Duration of Follow Up	33	10(18−8)	10(11−7)	15(20−10)	21.5(30−16.5)	<0.001	<0.001	<0.001	<0.001

Notes: Data are presented as median (interquartile range) or n (percentage). We did not perform group comparisons for variables with overall p-values > 0.05. Instead, categorical variables were analyzed using the χ^2 test or Fisher's exact test, and the Kruskal–Wallis test was used for continuous variables. P-values ≤ 0.05 were considered statistically significant.
Abbreviations: ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; FBG, fasting blood glucose; INR: The International Normalized Ratio; CRP: C-reactive protein; RBCs, red blood cells; HCT: Hematocrit; MCV: Mean Corpuscular Volume; MCH: Mean Corpuscular Hemoglobin; MCHC: Mean Corpuscular Hemoglobin Concentration; WBCs, white blood cells; and O_2, Oxygen.

Table 3
Correlations between Grade of Severity and other factors (n = 473).

Grade of severity	Grade of severity with other factors Correlation Coefficient	P-value
Age	0.516	<0.001
BMI	0.271	<0.001
Sex	0.143	0.002
Comorbidity		
Smoking	−0.03	0.39
Malignancy	0.09	0.052
CHF	0.05	0.25
DM	0.287	<0.001
HTN	0.283	<0.001
BA	0.005	0.92
IHD	0.102	0.02
HCV	0.228	<0.001
Liver cirrhosis	0.163	<0.001
CKD	0.121	0.009
Hypothyroidism	−0.006	0.89
RhA	−0.005	0.91
Symptoms		
Diarrhea	−0.14	0.002
Abdominal pain	−0.12	0.01
Anosmia	−0.16	<0.001
Dysgeusia	−0.12	0.006
Fever	0.08	0.082
Cough	0.181	<0.001
Skin rash	0.05	0.23
Rhinorrhea	−0.139	0.003
Sweating	0.098	0.03
Hematologic		
Creatinine	0.08	0.07
ALT	0.250	<0.001
AST	0.260	<0.001
FBS	0.221	<0.001
INR	0.08	0.07
CRP	0.422	<0.001
D.Dimer	0.07	0.12
Serum ferritin	0.455	<0.001
Hemoglobin	0.001	0.97
RBC	−0.07	0.14
HCT	−0.01	0.8
MCV	0.009	0.85
MCH	0.05	0.27
MCHC	0.081	0.1
Platelet	−0.205	<0.001
WBCS	−0.05	0.22
Staff%	0.04	0.36
Segmented%	0.200	<0.001
Lymphocyte percentage, %	−0.189	<0.001
Neutrofil to Lymphocte Ratio	0.206	<0.001
Monocyte percentage, %	−0.07	0.12
Eosinophil percentage, %	0.02	0.57
Basophil percentage, %	−0.04	0.35
Others		
Basal O2	−0.51	<0.001
Heart Rate	0.192	0.001
Duration of O2 treatment, days	0.511	<0.001
Duration of Steroid treatment, days	0.676	<0.001
Duration of follow up	0.597	<0.001

Note: P- and R-values were derived from the Spearman correlation test. P-values ≤ 0.05 were considered statistically significant.
Abbreviations: BMI, body mass index; CHF, *congestive heart failure;* DM, diabetes mellitus; HTN, hypertension; BA, bronchial asthma; IHD, ischemic heart disease; HCV, hepatitis c virus; CKD, chronic kidney disease; RhA, rheumatoid arthritis; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; FBG, fasting blood glucose; INR: The International Normalized Ratio; CRP: C-reactive protein; RBCs, red blood cells; HCT: Hematocrit; MCV: Mean Corpuscular Volume; MCH: Mean Corpuscular Hemoglobin; MCHC: Mean Corpuscular Hemoglobin Concentration; WBCs, white blood cells; and O_2, Oxygen.

study examined the disease characteristics during the second and third waves of the pandemic.

The current study revealed that patients with moderate and severe COVID-19 were older than those with mild COVID-19. In agreement **with our findings, Liao** et al. [19], Ghweil et al. [4], and Liu et al. [26] reported that elderly patients with COVID-19 were more likely to have acute and severe COVID-19 compared with middle-aged people with COVID-19. This age-dependent variation in the severity of COVID-19 could be explained by decreased cell-mediated immune function and reduced humoral immune function [27]. The proportion of infected females was higher than infected males, which agrees with the findings of two previous studies [28,29]. Two previous studies presented results on sex-specific differences in the severity of COVID-19, which were similar to our work; almost all of the previous work has demonstrated that the number of infected males was higher than that of the infected females [4,19,30–33]. However, the percentage of females was higher, but males developed moderate and severe illness more frequently than females, which is in agreement with the findings of the present study and the previous literature [4,19,30–33]. Approximately 8.5% of the patients were smokers, and smoking has been previously related to higher expression of angiotensin-converting enzyme 2 (ACE2), a receptor for SARS-CoV-2 [34]. A previous systematic review that included five studies reported that smoking is most likely associated with the negative progression and adverse outcomes of COVID-19 [35].

In contrast, the results of our study showed no association between smoking and COVID-19 severity. Our study reported that the incidence of SARS-CoV-2 infection was associated with underlying comorbidities, the most common of which was DM, followed by HTN, as described in most previous literature [4,19,28–30,36,37]. In line with our findings, Marhl et al. [38] reported a higher risk of COVID-19 among patients with diabetes due to the association between the dysregulation of ACE2. The higher risk of COVID-19 among patients with diabetes physiologically maybe because of liver dysfunction and chronic inflammation [38]. In addition, Singh et al. [39] reported that the incidence rate and severity of COVID-19 increased in patients with diabetes.

Moreover, the majority of joint clinical presentations of COVID-19 were fever, followed by cough, as identified in our study and previous studies {Formatting Citation}. Skin rash was the slightest common manifestation of COVID-19, and dermatological manifestations have been increasingly reported in the last few months [40,41]. Our laboratory findings showed that CRP and serum ferritin levels were significantly higher in patients with severe disease than in those with moderate disease, which is in agreement with the results of previous studies [4,28,30,37]. These findings can be explained because CRP is an acute-phase protein that serves as an early marker of COVID-19 infection [42]. The optimum cutoff value for CRP to predict severe disease was 17.4 mg/L using the ROC curve with a sensitivity of 76.4% and a specificity of 63.4%. The AUC for the painful condition was 0.73. Indeed, a pooled analysis of more than ten studies showed that non-survivors with COVID-19 had a significantly higher ferritin level than survivors with COVID-19 [43]. D-dimer, serum creatinine, lymphocyte count, platelet count, staff neutrophils, segmented neutrophils, lymphocytes, monocytes, eosinophils, and basophils, on the other hand, were normal and not significantly different across all comparisons. Moreover, the N/L ratio was standard, which agrees with the findings of Fan et al. [31], which reported that most patients had a standard CBC test. Only patients with severe disease had death events, and approximately six hospitalized patients with severe illnesses died. The survivors of severe disease complained of DVT, chronic cough, and chronic fatigue, and some had to remain under supervision in the intensive care unit. The strengths of our study are its large sample, as we include 473 patients and the fact that our research is the first to discuss the demographic, clinical characteristics and routine laboratory investigations of patients with COVID-19 during the second and third waves of the pandemic in Egypt. The main limitation of this study is the potential for selection bias given its single-center

Table 4
Determinants of Grade of severity with a multinomial logistic regression model (n = 473).

	Grade of severity and predictors			
	Moderate		Severe	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Age	1.07(1.05–1.08)	<0.001	1.09(107–1.11)	<0.001
BMI	1.10(1.03–1.17)	0.001	1.2(1.12–1.3)	<0.001
Sex				
Female	0.6(0.39–0.92)	0.02	0.48(028–0.82)	0.008
Male	ref		ref	
Comorbidity				
DM				
NO	0.4(0.22–0.74)	0.003	0.13(0.07–0.25)	<0.001
Yes	ref		ref	
HTN				
NO	0.28(0.15–0.51)	<0.001	0.15(0.07–0.29)	<0.001
Yes	ref		ref	
IHD				
NO	0.34(0.12–0.99)	0.045	0.32(0.09–1.10)	0.07
Yes	ref		ref	
HCV				
NO	0.27(0.10–0.70)	0.007	0.10(0.04-0.27)	<0.001
Yes	ref		ref	
Liver cirrhosis				
NO	0.19(0.05–0.74)	0.017	0.11(0.028–0.44)	0.002
Yes	ref		ref	
CKD				
NO	0.10(0.01–0.91)	0.04	0.09(0.009–0.89)	0.04
Yes	ref		ref	
Symptoms				
Diarrhea				
NO	1.95(1.13–3.35)	0.016	2.47(1.16–5.23)	0.018
Yes	ref		ref	
Abdominal pain				
NO	1.32(0.82–2.10)	0.24	2.53(1.26–5.06)	0.009
Yes	ref		ref	
Anosmia				
NO	2.55(1.39–4.70)	0.003	2.91(1.27–6.69)	0.012
Yes	ref		ref	
Dysgeusia				
NO	1.96(1.09–3.54)	0.02	2.24(1.016–4.96)	0.045
Yes	ref		ref	
Cough				
NO	0.49(0.32–0.74)	0.001	0.44(0.25–0.75)	0.003
Yes	ref		ref	
Rhinorrhea				
NO	2.54(1.27–5.10)	0.008	2.42(0.99–5.94)	0.05
Yes	ref		ref	
Sweating				
NO	0.92(0.32–2.6)	0.88	0.29(0.11–0.76)	0.011
Yes	ref		ref	
Hematologic				
ALT	1.12(1.06–1.18)	<0.001	1.16(1.10–1.24)	<0.001
AST	1.11(1.06–1.16)	<0.001	1.15(1.09–1.21)	<0.001
FBS	1.006(1.001–1.010)	0.012	1012(1.008–1.017)	<0.001
CRP	1.01(1.009–1.022)	<0.001	1.022(1.015–1.029)	<0.001
Serum ferritin	1.005(1.003–1.007)	<0.001	1.006(1.004–1.008)	<0.001
Platelet	0.99(0.990–0.997)	<0.001	0.99(0.98–0.99)	0.003
Segmented%	1(0.99–1.03)	0.07	1.05(1.02–1.07)	<0.001
Lymphocyte percentage, %	0.98(0.96–1)	0.055	0.95(0.92–0.97)	<0.001
N/L Ratio	1.13(1.006–1.27)	0.04	1.28(1.13–1.45)	<0.001
others				
Basal O2	0.99(0.98–1.001)	0.08	0.98(0.97–0.99)	<0.001
Heart Rate	1.015(0.99–1.33)	0.11	1.05(1.03–1.08)	<0.001

Note: P-values $\leq$ 0.05 were considered statistically significant.
Abbreviations: BMI, body mass index; DM, diabetes mellitus; HTN, hypertension; IHD, ischemic heart disease; HCV, hepatitis c virus; CKD, chronic kidney disease; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; FBG, fasting blood glucose; CRP: C-reactive protein; and O_2, Oxygen.

nature and the missing data as some results of laboratory investigations of some patients.

Conclusion

In conclusion, we observed many variations in COVID-19 patients' characteristics. Regarding the clinical features, fever remained the most common symptom as in the first wave. The new manifestations included skin rash, bony pain, low back pain, and rigors. In particular, the number of females was higher than the number of males; however, most males had a moderate and severe illness, which contrasted with females. Old age, higher BMI was associated with increasing severity. The subjects diagnosed with DM, HTN, HCV, liver cirrhosis, and CKD tended to have higher

disease severity. The severity of COVID-19 can be suggested to be associated with ALT, AST, FBS, CRP, serum ferritin, segmented %, and N/L ratio. The unexpected variation in the laboratory characteristics of patients with COVID-19 as D-dimer and CBC were normal and can't identify potential COVID-19 patients. Post-COVID sequalae (long-haulers) as chronic fatigue, polyneuropathic pains, chronic cough could happen even in patients who experienced the mild disease.

Our main recommendations are for the health system to firmly use RT-PCR to detect COVID-19 infection in addition to hematologic and biochemical parameters. We are also asking for not depending mainly on hematologic and biochemical parameters alone to detect COVID-19 or develop it. Researchers should conduct multicenter studies to elucidate the short- and long-term health effects associated with COVID-19. Our last recommendation is to encourage and facilitate COVID-19 vaccination to prevent this pandemic's spread and its related long-term complications.

Appendix 1

Treatment of COVID-19 Patients

According to the COVID-19 protocol of the Egyptian Ministry of Health [20,21], mild cases were advised for strict home isolation, received oral hydroxychloroquine 400 mg twice in the first day, then 200 mg twice for six days in addition to oral paracetamol, and multivitamins. Moderate cases required hospital admission in intermediate care. They received lopinavir/ritonavir (2 tabs 200/50) every 12 h, oral anticoagulants, and steroids (if the patient has severe dyspnea respiratory rate >24). Severe cases were admitted in the intensive care unit (ICU) and received methylprednisolone 1–2 mg/kg/day or tocilizumab 4–8 mg/kg/dose (maximum two doses 12–24 h apart after the failure of steroid therapy), enoxaparin 1 mg/kg twice daily, and remdesivr 200 mg on the first day then 100 mg daily for nine days together with other supportive and symptomatic measures. Empiric antimicrobials to treat all likely pathogens were given within one hour of ICU admission. Mechanical ventilation was needed in critically ill severe cases [20,21]. After hospital discharge, the mean follow-up was about 13.5 days, which changed according to the severity of the patients.

Appendix 2 Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.jiph.2021.08.009.

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