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Comparison of demographic, clinical and laboratory characteristics between first and second COVID-19 waves in a secondary care hospital in Qatar: A retrospective study

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Title

Comparison of demographic, clinical and laboratory characteristics between first and second COVID-19 waves in a secondary care hospital in Qatar: A retrospective study

Key words

COVID-19 infection, Coronavirus, SARS-CoV-2, Pandemic, First wave, Second wave

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Abstract

Objective: To compare the patient profiles in Qatar during the first and second waves of the COVID-19 pandemic. **Setting:** A retrospective observational study was conducted comparing the demographic, clinical, and laboratory characteristics of patients with COVID-19 infection admitted to a secondary care hospital in Qatar, during the first and second waves of the pandemic. **Participants:** 1039 patients from the first wave and 991 from the second wave who had pneumonia on chest X-ray and had a laboratory-confirmed SARS-CoV-2 infection by a real-time PCR test of a nasopharyngeal swab specimen were included. The study excluded patients with a normal chest X-ray and those who had a positive COVID-19 antigen test but a negative PCR test. **Outcome:** Length of stay, need for mechanical ventilation, final disposition and mortality were the key outcomes studied **Results:** Upper respiratory symptoms (18.5 % vs. 36.1 %, p 0.001), cough (79.2% vs.87%, p<0.001) and dyspnea (27.5% vs. 38% p<0.001) were more common in the second wave. Second wave patients had significantly higher respiratory rate, lower peripheral oxygen saturation, needed more supplemental oxygen and had higher incidence of pulmonary embolism. More patients received hydroxychloroquine and antibiotics during the first wave and more received steroids, antivirals and interleukin-1 antagonist during the second wave. The second wave had a shorter length of stay (14.58 ±7.75 vs. 12.61 ±6.16), p <0.001) and more patients were discharged home (22% vs. 10% p<0.001). **Conclusions:** Patients who presented during the second wave of Covid-19pandemic appeared to be more ill clinically and based on their laboratory

parameters. However, they required shorter hospitalization and were more likely to be discharged home. This could represent greater expertise in handling such patients that was acquired during the first wave as well as use of more appropriate and combination therapies during the second wave.

Introduction

Coronavirus disease 2019 (COVID-19), first identified in the Wuhan province of China, was declared a global pandemic by the World health organization (WHO) on March 11th, 2020 [1]. To date, it has affected 311,207,461, with more than 5 million deaths worldwide. In Qatar, COVID-19 infection has affected 278,698 individuals with 621 deaths [2]. In Qatar, the first wave began in March 2020 and peaked in May 2020 whereas second wave began in February 2020 and reached its peak in April 2021.

During both pandemic waves, Ras Laffan Hospital, a secondary care hospital, was one of the COVID-19 designated hospitals under Hamad Medical Corporation (HMC). If patients met the admission criteria, they were transferred to Ras Laffan Hospital from non-COVID hospitals and tertiary care COVID facilities. During the first and second waves, respectively, 3650 and 4050 patients with a confirmed SARS-CoV-2 infection were hospitalized and treated at the Ras Laffan hospital.

From the time it was originally discovered in Wuhan, the disease profile, epidemiology, and treatment guidelines for COVID-19 infection had evolved continuously. On the basis of the most recent scientific findings, WHO released and updated diagnostic and treatment guidelines, as well as quarantine guidelines, on a regular basis. Countries around the world revised their management and quarantine standards on a regular basis based on this and locally available data.

In the Middle East region, there is a dearth of published data comparing epidemiology and outcomes of serial waves of the COVID-19 epidemic. As a result, we chose to investigate and compare these in both waves better understand and manage future events.

Objective

The goal of this study was to examine admission characteristics and outcomes in COVID-19-infected hospitalized patients during the first and second waves of the pandemic.

Methods

Study type and setting

A retrospective observational study was conducted at Ras Laffan hospital, Hamad Medical Corporation, Qatar. This hospital was one of the COVID-19 designated hospitals under HMC. The study was conducted from June 2021 to September 2021.

Study participants

Patients admitted between 1stto 30th of May 2020 in the first wave and those admitted between 1st and 15th of March 2021 during the second wave were included in the study. The patients were included if they had pneumonia on chest X-ray and had a laboratory-confirmed SARS-CoV-2 infection by a real-time PCR test of a nasopharyngeal swab specimen. The study excluded patients with a normal chest X-ray and those who had a positive COVID-19 antigen test but a negative PCR test.

Patient and public involvement

No patient involved

Data collection

Using the patients' health care numbers, files from the clinical information system were reviewed. Data was collected on demographics, admission symptoms, co-morbidities, length of stay, laboratory and radiographic results, oxygen requirements, treatment details, complications, and outcomes.

Outcome of the study

The requirement for mechanical ventilation, length of stay, final disposition and mortality were the key outcomes studied along with their clinical and laboratory characteristics.

Statistical analysis

The data were analyzed using IBM SPSS Statistics version 27 (Armonk, NY: IBM Corp) and the level of significance was set at a P value < 0.05. Descriptive statistics were used to summarize demographic, anthropometric, clinical, laboratory, radiological characteristics, and related follow-up outcome measures of these patients. Continuous variables with normal distribution were presented as mean and standard deviation (SD), whereas median and interquartile range (IQR) was used in case of skewed/non-normal data. Categorical variables were presented as frequencies and proportions. The Shapiro-Wilk test was used to test for normality of the data distribution. The statistical P-value for outcomes measured quantitatively and differences between the two independent groups

(first and second COVID-19 waves) were compared using unpaired t or Mann Whitney U tests as appropriate depending on the normality of the data distribution. Associations between two or more qualitative or categorical variables across two independent groups were compared using Pearson Chi-square or Fisher exact test as applicable. Box plots were constructed to depict distribution of age, duration of symptoms, BMI, vital signs, and various parameters related to laboratory profiles across both groups first and second COVID-19 waves.

Results

Baseline demographic characteristics

During the first and second waves, respectively, 3650 and 4050 patients with a confirmed SARS-CoV-2 infection were hospitalized. The study included 1039 patients from the first wave and 991 participants from the second wave. During both waves, the average age of the subjects was similar [44.9 ±9.9 vs. 44.34±9.56]. In both waves, the proportion of patients among various age groups was comparable, with the majority of patients being between the ages of 36 and 50. (52.9 % vs.54.0 %). Males made up 95.2 % of the first wave and 88.5 % of the second wave patients (Table 1).

Clinical characteristics on admission

In the first wave patients had longer duration of symptoms prior to admission compared to second wave (4.88 ± 2.91 vs. 4.57 ±2.50, p 0.010). Upper respiratory symptoms (36.1% vs. 18.5%, p <0.001)), cough (87% vs. 79.2%, p<0.001), and shortness of breath (38% vs. 27.5%, p<0.001)), were significantly higher in the

second wave than the first. We did not find any significant difference in gastrointestinal symptoms between the two waves.

Diabetes mellitus (29.5% vs. 21.9%) and hypertension (26 % vs. 26.5%) were the most common co-morbid conditions observed in both waves; however, frequency of diabetes mellitus was significantly higher in the first wave (p <0.001)

The mean body mass index (BMI) was 27.95 ±4.46 and 28.29 ± 4.83 in the first and second waves, respectively (p= 0.263). Most patients had higher BMI in both the waves, with the majority having a BMI between 25.1 to 30 (48.2% vs. 45%) followed by more than 30 (27.1% vs. 28.5%) (Table-1). The details of distribution of age, duration of symptoms and BMI are plotted in Figure 1 A-C.

Vital signs and oxygen requirement

Patients in the second wave had significantly higher respiratory rate (23±6 vs. 22±5 p<0.001) and significantly lower peripheral oxygen saturation (93±5 vs. 94±4, p<0.001) when compared to the first wave. Furthermore, during the second wave significantly higher number of patients received supplemental oxygen on admission (40.3% vs. 22.9 %, p< 0.001) and also during their stay in the hospital (39.8% vs. 30.3%, p < 0.001) Table- 2 and figure 2 A-H.

Laboratory parameters and chest X-ray findings

The first wave had significantly higher C-reactive protein (50.54 ±53.28 vs. 33.68 ±44.20, p<0.001) and HbA1c values (7.37± 2.04 vs. 6.94± 1.83 p<0.001). The mean values of white blood cell count (6.49 ±2.41 vs. 6.27 ± 2.21, p 0.031), hemoglobin (14.35 ±1.37 vs. 14.16 ± 1.43, p 0.003), and platelet counts (234.99 ±89.44 vs.

225.55 ±82.50, p 0.014) were lower in the second wave than the first. The patients in the second wave, had considerably lower mean albumin levels than the first wave (35.58 ±4.94 vs. 36.97 ±4.83, p<0.001). Patients in the second wave had higher hepatic transaminases and alkaline phosphatase levels than the first wave, although the differences were statistically insignificant. In both waves, the majority of patients had bilateral pneumonia on chest x-ray. Table- 3 and figure 3 A-K.

Treatment received

In the first wave, the usage of amoxicillin/clavulanic acid (60.9% vs.29.3%) and azithromycin/clarithromycin (74.1% vs. 41.9%) and usage of hydroxychloroquine (88.5% vs. 60.3%, p<0.001) was higher.

A significantly higher number of patients in the second wave received steroids (47.7% vs.17.1%, p <0.001), favipiravir (71% vs. 22.1%, p<0.001) or lopinavir/ritonavir (63.6% vs. 35.5%, p<0.001 and anakinra (10.6% vs. 2.7%, p <0.001).

Similar number of patients in both the waves received cephalosporins (74.3% vs. 70.5%, p=0.058) and prophylactic anticoagulation (97.4% vs. 99%).Table - 4.

Complications/ outcome and disposition

In the first and second waves, 5.3% and 6.5 %of patients, respectively, required transfer to a higher center for further care. Among those who were transferred, 28 (2.7%) patients in the first wave and 40 (4%) in the second wave received mechanical ventilation (p= 0.093). In the second wave, the percentage of patients

who developed pulmonary embolism was significantly higher (1.1 % vs. 0.03%, p=0.025), furthermore, a higher proportion of mortality (0.81% (8/991) vs. 0.3% (3/1030)) was recorded in the second wave, however this difference was statistically insignificant (p=0.112).

The majority of patients in the first wave stayed for 15 to 30 days (50.9 % vs. 21.4%), while the majority of patients in the second wave stayed for 8 to 14 days (64.4% vs. 25.15%), table 5. In the second wave, the average length of stay was 1.9 days shorter which was statistically significant (14.58 ±7.75 vs. 12.61 ±6.16, p <0.001).

The majority of the patients in both the waves were transferred to quarantine facilities from the hospital (84.6% vs. 71.1%). In the second wave, however, more patients were discharged to their homes.

Discussion

To our knowledge, this is the first study in the region to compare COVID-19 individuals hospitalized during the first and second waves of the SARS-CoV-2 pandemic. Our findings show a significant variation between the two waves in terms of clinical features, laboratory markers and outcomes.

There was no difference in the average age of the patients between the two waves. In confirmation to our findings, a previous study by Wolfsburg et al. [3] found no difference in the mean age of patients between two waves (65.9 vs. 65.8 years), whereas in contrast to our results a study by Iftimie et al. [4] found that the patients in the second wave were significantly younger than the first wave (58 years vs. 67 years). However, our study sample was much younger in

both waves [44.90 ±9.99 vs. 44.34 ±9.57] than the above two study populations. On admission to the hospital cough, shortness of breath and upper respiratory symptoms were more common in the second wave. The patients in the second wave had more symptoms and were sicker as evidenced by tachypnea and hypoxia and more patients requiring oxygen. We did not observe a significant difference in the prevalence of gastrointestinal symptoms between both the waves. This is in contrast to previous research [4, 5], which reported a higher prevalence of gastrointestinal complaints in the in the second wave.

The most common co-morbidities in both waves of the research population were diabetes mellitus and hypertension. The number of diabetes patients, on the other hand, was much higher in the first wave. When comparing co-morbidities in both the waves, previous research have yielded conflicting outcomes. Iftimie et al. [4] showed no significant differences in co-morbidity between the two waves, however Jarrett et al. [6] and Sargin et al. [7] identified a higher frequency of chronic kidney illness in the second wave than in the first wave.

Despite the fact that the mean BMI did not alter significantly between the two waves, the majority of our research group had a higher BMI in both, suggesting obesity as a probable risk factor for COVID-19 infection. However this needs further studies analyzing the correlation between obesity as a risk factor and Covid-19 infection. Obesity was found in 30% of the whole study population in both waves, according to a study from Switzerland [3]. Another study from the United States [6] found that the second wave had a higher BMI than the first wave (32.58 vs. 29.83).

The study of laboratory measurements revealed that the first wave had higher mean values of CRP and HbA1c, while hypoalbuminemia was significantly higher in the second wave. Furthermore levels of leukocyte and platelet count were lower in second wave than the first wave. The second wave had higher mean levels of hepatic transaminases. The higher HbA1c readings in the first wave are unsurprising given the higher prevalence of diabetes mellitus in the first wave compared to the second wave. The higher hepatic transaminases in the second wave could be due to a variety of factors. One probable reason could be secondary to the side effect of favipiravir, as it was used more frequently in the second wave than in the first wave.

In our study population, the use of steroids was much higher in the second wave [47% vs. 17%]. This is because during the early stage of the first wave scientific literature regarding the benefit of steroids in COVID-19 infection was still in its preliminary stage and its use was limited. The frequency of usage of steroids in published data was still greater (99% [6], 76% [3]) than ours in the second wave. Because the aforementioned two studies included individuals with more severe disease than our research sample, the frequency of steroid administration differed. In terms of prophylactic anticoagulation, practically more than 97% of the patients in both waves received anticoagulation in our research group. This was much greater than the 59% in the first wave and 74% in the second wave reported in a research conducted in the United States [6].

The usage of hydroxychloroquine was significantly higher in the first wave, whereas the use of favipiravir and anakinra was much higher in the second wave, according to our findings. This is because treatment guidelines evolved and

modified from the first wave to the second wave based on published scientific information around the world. Furthermore, use of antibiotics was significantly higher in the first wave than the second wave. There are multiple reasons for this. First, during the first wave azithromycin was more commonly used along with hydroxychloroquine as a treatment for COVID-19 infection. Second, due to lack of experience and expertise in managing the COVID-19 pandemic antibiotics were more commonly prescribed for patients with COVID pneumonia during the first wave; however during the second wave clinicians acquired adequate knowledge and experience and were more confident to treat patients without antibiotics unless indicated.

Despite the fact that patients in the second wave were sicker as evidenced by more symptoms, tachypnea and hypoxia on admission and laboratory parameters, the duration of hospitalization were significantly lower in the second wave. In the present study the average length of stay in the second wave was nearly 2 days less than in the first. This supports the findings of other research [3, 4, 7], which similarly found a shorter length of stay in the second wave. In addition more patients were discharged home in the second wave than transferred to quarantine facility. Possible explanation for this could be the change in discharge/transfer criteria. Secondly, better understanding of the disease course and experience of managing the first wave made the health care professionals more confident in early discharge of patients in the second wave. Finally, better home surveillance of discharged patients, development of better follow up care, and community awareness and education might have also played an important role.

Even while the number of patients who needed to be transferred to a higher center, those who needed mechanical ventilation, had a pulmonary embolism and those who died were all somewhat higher in the second wave than in the first, the difference was not statistically significant. Available published data from two studies, one from Switzerland [3] and another from Turkey [7] found no significant difference in the proportion of patients requiring or at risk for Intensive Care Unit (ICU) admission in both the waves. However, the percentage of patients needing ICU care in the above two studies was higher than our results in both the waves. This could be related to the fact that our study and theirs had different severity of cases and also could be due to the difference in admission criteria in our study and others. Our admission criteria included patients with pneumonia requiring less than 4 L of oxygen at the time of admission, whereas other studies included more severe cases or ICU cases. Others have reported similar results, finding no substantial change in the number of patients requiring mechanical ventilation in both waves [6, 7]. There was no significant change in mortality rates between the two waves in the present study. Previous research comparing mortality rates between the two COVID-19 pandemic waves came up with mixed results. Our findings are consistent with those of Wolfisberg et al.[3] and Sargin et al. [7], who found no difference in mortality rates between the two waves, but Iftimie et al.[4] and Jarrett et al.[6] reported lower mortality in the second wave, in contrast to our findings. Similarly, two studies from the United States found that the second wave had a reduced mortality rate [8, 9]. According to published statistics from Japan based on a public registry reported that the second wave of patients were younger, had fewer underlying co-morbidities, and had lower mortality rates [10].

A few studies from Europe also found lower mortality in the second wave. Chest X-ray severity of pneumonia, in-hospital mortality, and CRP readings were considerably greater in the first wave, according to an Italian study involving 200 Caucasian males over 50 years. They also discovered that the first wave had more patients who required mechanical ventilation [11]. Another study from Spain found that the second wave had younger patients, a shorter duration of stay in the hospital, fewer invasive mechanical ventilation, and decreased mortality [4].

Limitations

There were certain limitations to our research. To begin with, some data on co-morbidity and symptoms may have been overlooked due to the retrospective nature of the study. Second, there might have been selection bias because our research population was mostly male patients as most female COVID-19 patients were admitted to other COVID designated hospitals. As a result, the number of female patients in our study may have been underestimated. Third, because our research sample included only mild to moderate Covid-19 infections, the findings may not be generalized to severe COVID -19 infections. Finally, the relationship between risk variables and outcomes was not examined as it was not the primary goal of our study.

Conclusions

Patients in the second wave were more symptomatic and unwell than those in the first wave, but they stayed in the hospital for a shorter time and were more likely to be discharged home, according to our data. The most prevalent symptoms in both waves were cough and shortness of breath, although they were much

greater in the second wave. Diabetes mellitus and raised CRP levels were more common in the first wave, but hypoalbuminemia was more prevalent in the second wave. In the first wave, antibiotics and hydroxychloroquine were more commonly utilized, but in the second wave, steroids, antivirals, and interleukin-1 antagonists were more commonly employed. The first wave's experience and lessons acquired by health care professionals, as well as a collaborative team effort involving numerous government agencies and community awareness and engagement, have helped us to manage the second wave more effectively.

Strengths

- First study in the region to compare patient characteristics between the two waves
- All patient variables were compared, including demographics, clinical complaints, vital signs, laboratory indicators, and outcomes.

Limitations

- The relationship between risk factors and outcomes was not investigated.
- Patients with severe COVID-19 were not included

Author's contribution

VN- Study design, data collection, analysis, manuscript writing, editing

NP- Study design, data collection, analysis, manuscript writing, editing

PC- Study design, data analysis, editing

AS- Data collection, analysis

PR- Data collection, analysis

IV-Study design, editing

JM- Analysis, manuscript writing

JS-Data collection, literature review

RH- Data collection, manuscript writing

AB- Data collection, manuscript writing

AA- Data collection, editing

MB- Data analysis, manuscript writing

SA- Data collection, manuscript writing

MA-Data collection, editing

AA- Data collection, literature review

RA- Data collection, literature review

AK- Data analysis, manuscript writing, editing

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Competing interests' statement

The authors declare that they have no competing interest involved

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Data sharing statement

No additional data available

Ethical approval

The study was approved by the Institutional Review Board of medical research center, Hamad, Medical Corporation (Approval no-MRC-01-21-312).

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Table-1. Baseline epidemiological and clinical characteristics of patients during the first and second wave of the COVID – 19 pandemic

Variables	First wave (n=1039 n (%)	Second wave (n=991 n (%)	p- value
Age (In years)			
Mean ±SD	44.90 ±9.99	44.34 ±9.57	0.194
18 - 35	202 (19.4)	192 (19.4)	0.896
36 - 50	550 (52.9)	535(54)	
51 -- 65	265 (25.5)	247 (24.9)	
Above 65	22 (2.1)	17 (1.7)	
Gender			
Male	989 (95.2)	877 (88.5)	<0.001
Female	50 (4.8)	114 (11.5)	
Signs and symptoms			
Asymptomatic	48 (4.6)	94 (9.5)	<0.001
Mean duration of symptoms in days ±SD	4.88 ±2.91	4.57 ±2.50	0.010
Fever	893 (85.9)	870 (87.8)	0.220
Respiratory symptoms	856 (82.4)	709 (71.5)	<0.001
Upper respiratory symptoms	192 (18.5)	358 (36.1)	<0.001
Cough	823 (79.2)	862 (87)	<0.001
Shortness of breath	286 (27.5)	377 (38)	<0.001
Chest pain	43(4.1)	37(3.7)	0.639
GI symptoms	88 (8.5)	66 (6.7)	0.124
Vomiting	50 (4.8)	38 (3.8)	0.280
Diarrhea	49 (4.7)	38 (3.8)	0.327
Co-Morbidities			
Immunosuppression	12 (1.2)	4 (0.4)	0.056
Chemotherapy	6 (0.6)	5 (0.5)	0.823

Diabetes Mellitus	307(29.5)	217 (21.9)	<0.001
Hypertension	270 (26)	263 (26.5)	0.777
Coronary artery disease	41 (3.9)	26 (2.6)	0.095
Chronic kidney disease	17 (1.6)	14 (1.4)	0.681
Cancer	5 (0.5)	5 (0.5)	0.940
Liver disease	3 (0.3)	6 (0.6)	0.283
COPD/Asthma	19 (1.8)	8 (0.8)	0.045
Body mass index (kg/m²)			
Mean ± SD	27.95 ±4.46	28.29 ± 4.83	0.263
< 18.5	1(0.2)	6 (1.1)	0.360
18.6 – 25	102 (24.5)	137 (25.4)	
25.1– 30	201 (48.2)	243 (45)	
>30	113 (27.1)	154 (28.5)	

Results are shown as number of cases and percentages (in parenthesis) or as means with ± standard deviations.
COPD-Chronic obstructive pulmonary disease

Table-2. Showing vital Signs and oxygen requirement

Variables		First wave (n=1039)	Second wave (n=991)	p- value
Temperature C^0 Mean ±SD	On admission	37.3±0.75	37.3± 0.72	0.976
	Maximum	38.1±0.89	38.2±0.88	0.024
p-- value		<0.001	<0.001	
Pulse rate (Beats per minute) Mean ±SD	On admission	89±14	88±13	0.439
	Maximum	102±11	103±11	0.164
p- value		<0.001	<0.001	
Respiratory Rate /min Mean ±SD	On admission	19±2	19±3	0.030
	Maximum	22±5	23±6	<0.001
p- value		<0.001	<0.001	
Spo2 (%)Mean ±SD	On admission	97±2	97±1	0.327
	Lowest	94±4	93±5	<0.001
p- value		<0.001	<0.001	
Patients received supplemental oxygen. Number (%)	On admission	238 (22.9)	399 (40.3)	<0.001
	After admission	315 (30.3)	394(39.8)	<0.001
p- value		<0.001	<0.001	

Table- 3. Showing laboratory parameters and chest X-ray findings

Variables	First wave Mean ±SD	Second wave Mean ±SD	p- value
WBC (10^3/ul)	6.49 ±2.41	6.27 ±2.21	0.031
Hemoglobin (g/dl)	14.35±1.37	14.16 ± 1.43	0.003
Platelet count (10^3/ul)	234.99 ±89.44	225.55 ±82.50	0.014
Albumin (gm/L)	36.97 ±4.83	35.58 ±4.94	<0.001
C-Reactive Protein (mg/L)	50.54 ±53.28	33.68 ±44.20	<0.001
Lactate	1.74 ±0.77	1.73±0.91	0.924
Procalcitonin	0.41 ±1.62	0.30±1.15	0.284
D- Dimer	1.20 ±4.28	1.10±3.84	0.651
Aspartate aminotransferase (AST)	44.14 ±34.47	50.81 ±141.91	0.152
Alkaline phosphatase (ALP)	77.56 ±31.71	78.29±34.96	0.626
Alanine aminotransferase (ALT)	42.74 ±33.28	44.30 ±34.24	0.305
Total Bilurubin	9.97 ±5.73	9.57±6.20	0.143
HbA1c	7.37± 2.04	6.94± 1.83	<0.001
Chest X ray findings			
Unilateral infiltrations	185 (17.8)	236 (23.8)	0.001
Bilateral infiltrations	854 (82.2)	755 (76.2)	

Table -4. Showing the details of treatment received

Treatment	First wave (n=1039) n (%)	Second wave (n=991) n(%)	p-value
Dexamethasone	178 (17.1)	473 (47.7)	<0.001
Anticoagulation	1012 (97.4)	981 (99)	0.007
Favipiravir	230 (22.1)	704 (71)	<0.001
Hydroxychloroquine	920(88.5)	598 (60.3)	<0.001
Lopinavir/ ritonavir	369 (35.5)	630 (63.6)	<0.001
Anakinra	28 (2.7)	105 (10.6)	<0.001
Tocilizumab	21 (2.0)	19 (1.9)	0.866
Amoxicillin/clavulanic acid	633 (60.9)	290 (29.3)	<0.001
Ceftriaxone/ Cefuroxime	772 (74.3)	699 (70.5)	0.058
Azithromycin /Clarithromycin	770 (74.1)	415 (41.9) (6.9)	<0.001
Piperacillin /tazobactum	51 (4.9)	68	0.061

*One patient might have received more than one type of treatment

Table- 5. Showing final outcomes and disposition

Variables	First Wave (n=1030) n (%)	Second wave (n=991) n(%)	p-value
Mechanical ventilation	28 (2.7)	40 (4.0)	0.093
Pulmonary embolism/DVT	3 (0.3)	11 (1.1)	0.025
Death	3 (0.3)	8 (0.8)	0.112
Discharge disposition			
Discharge home	105 (10.1)	222 (22.4)	<0.001
Transfer to quarantine	879 (84.6)	705 (71.1)	
Transfer to higher center	55 (5.3)	64 (6.5)	
Length of stay in days			
Mean ± SD	14.58 ±7.75	12.61 ±6.16	<0.001
0-7	227 (21.8)	126 (12.7)	<0.001
8-14	261 (25.1)	638 (64.4)	
15-30	529 (50.9)	212 (21.4)	
>30	22 (2.1)	15 (1.5)	

Figure legends

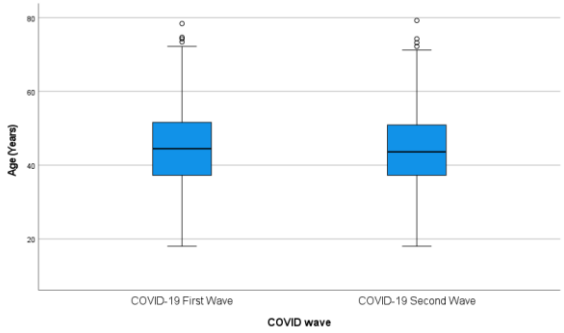
Figure 1.A-C. Box plot showing the distribution of age, duration of symptoms and BMI

Figure 2 A-D. Box plots depicting the vital signs
Figure 2.E-H. Box plots depicting the vital signs

Figure 3. A-F. Box plots depicting distribution laboratory parameters

Figure 3.G-K. Box plots depicting distribution laboratory parameters

A



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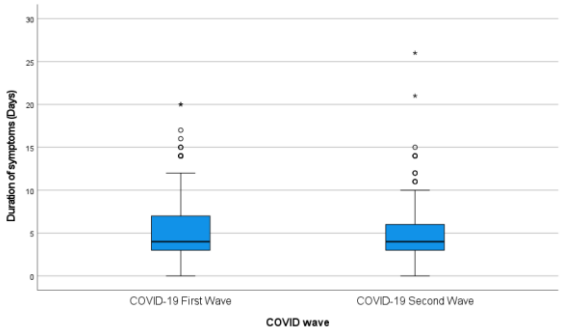

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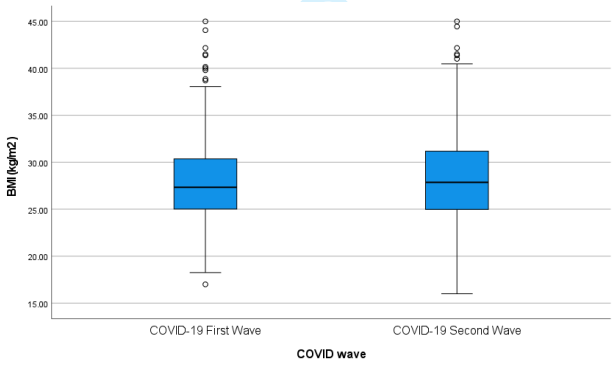


Figure 1.A-C.

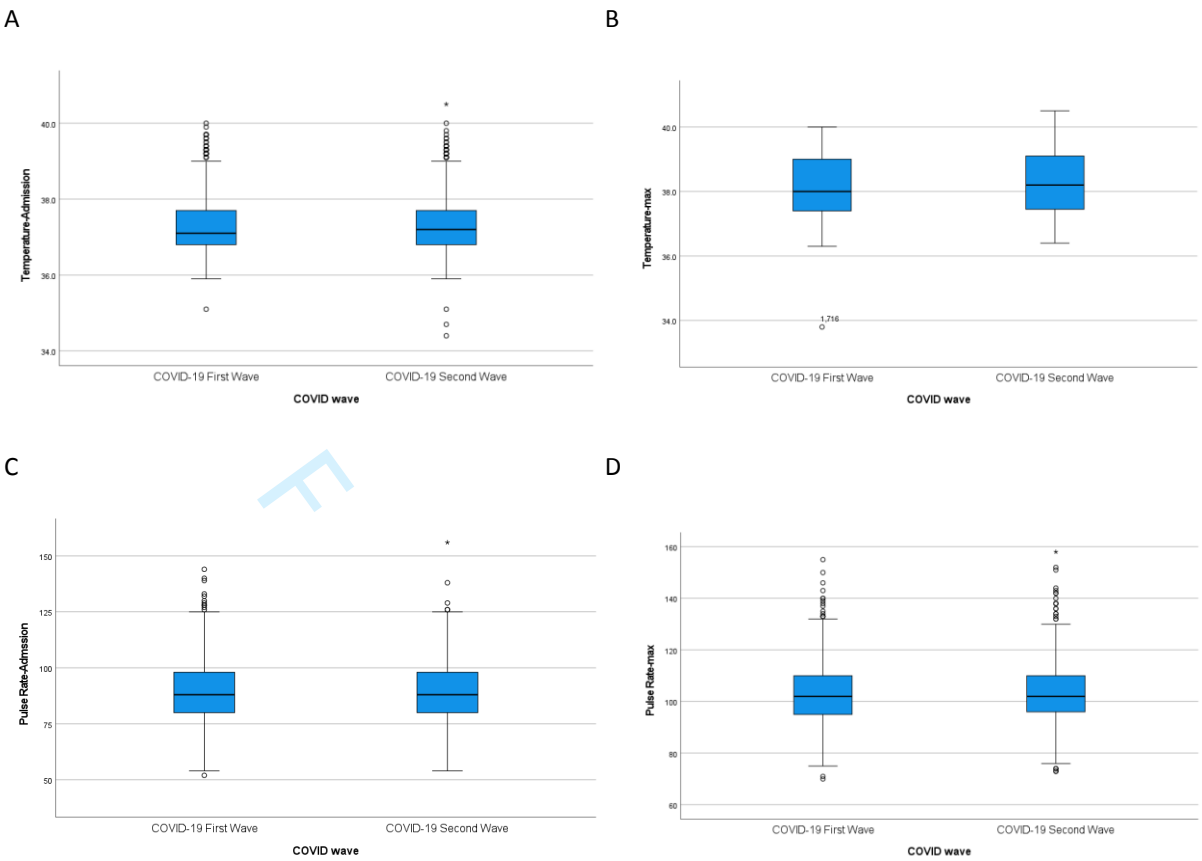
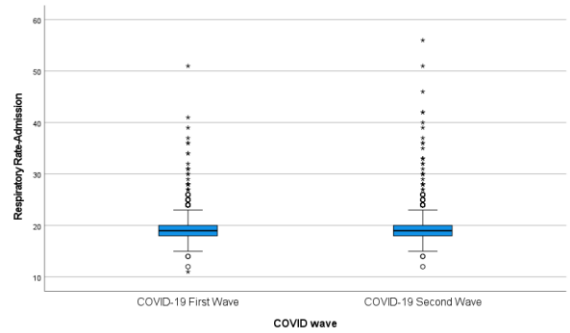


Figure 2 A-D.

E



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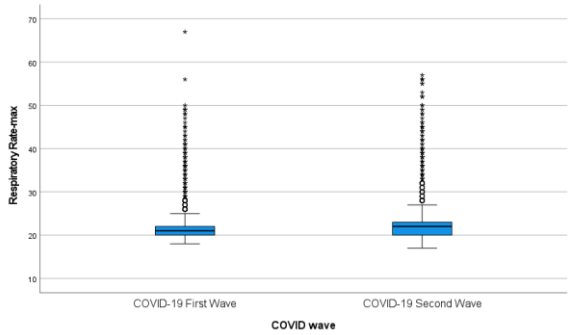

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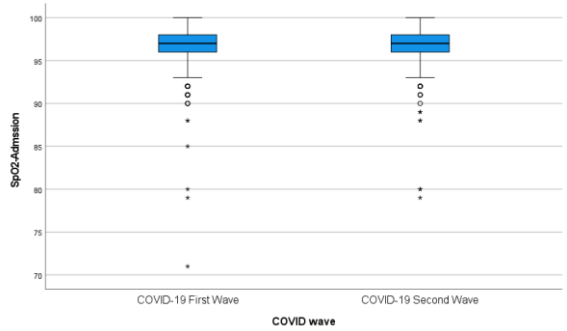


H

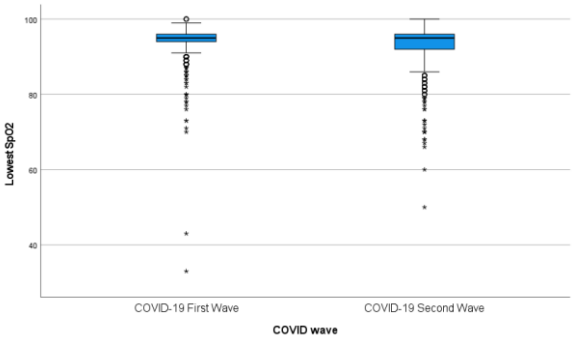


Figure 2 E-H. Boxplots depicting the vital signs

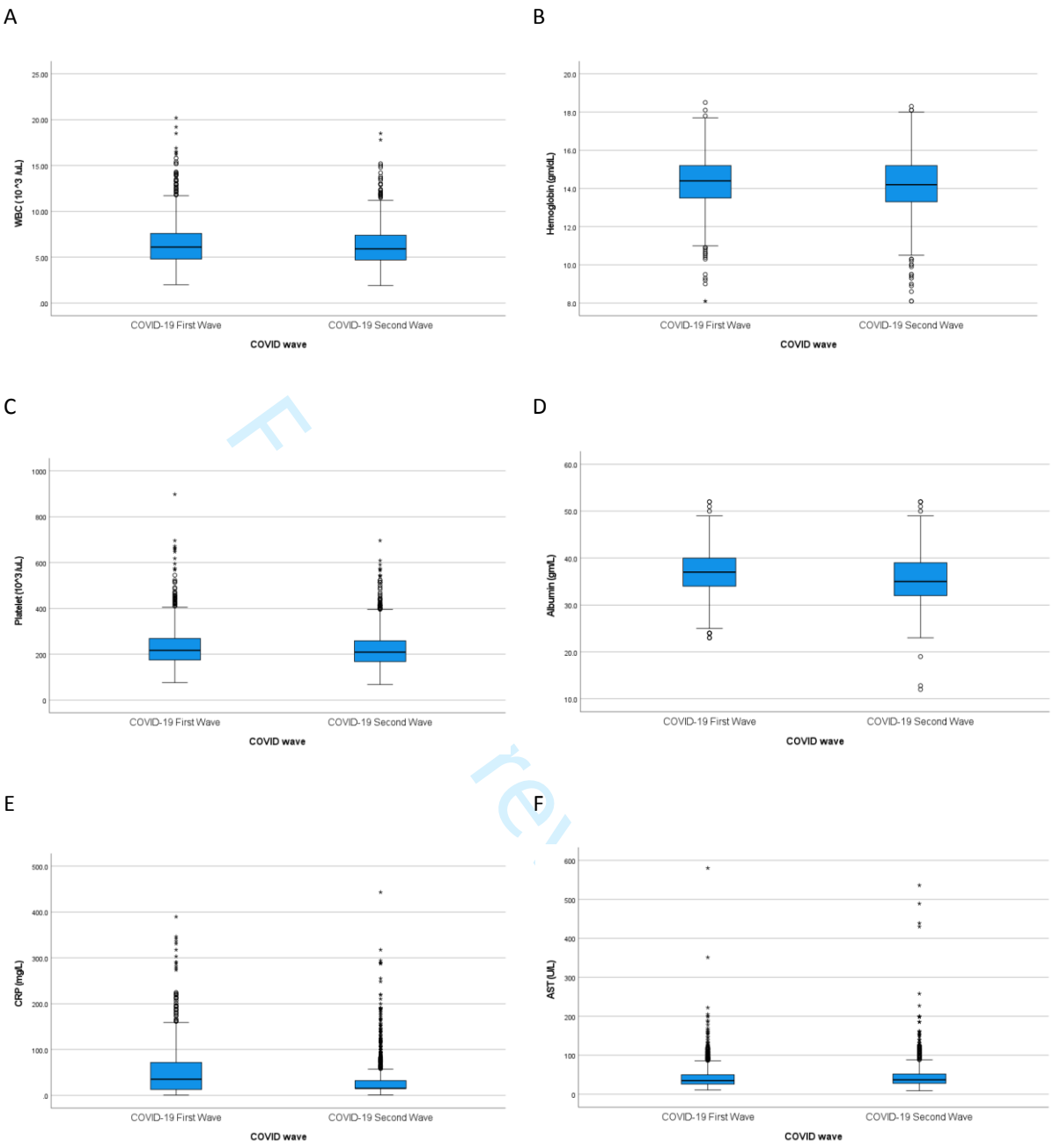
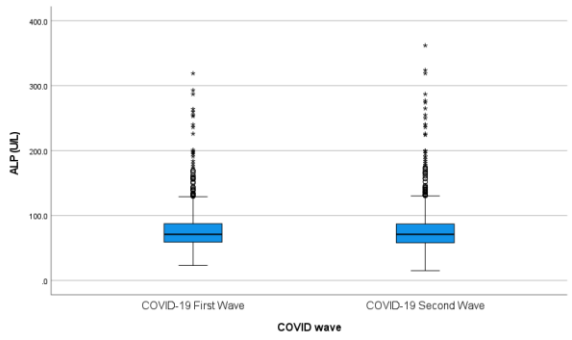

A
WBC (10^3 /uL)
COVID-19 First Wave
COVID-19 Second Wave
COVID wave
B
Hemoglobin (gm/dL)
COVID-19 First Wave
COVID-19 Second Wave
COVID wave
C
Platelet (10^3 /uL)
COVID-19 First Wave
COVID-19 Second Wave
COVID wave
D
Albumin (gm/L)
COVID-19 First Wave
COVID-19 Second Wave
COVID wave
E
CRP (mg/L)
COVID-19 First Wave
COVID-19 Second Wave
COVID wave
F
AST (U/L)
COVID-19 First Wave
COVID-19 Second Wave
COVID wave

Figure 3 A-F.

G



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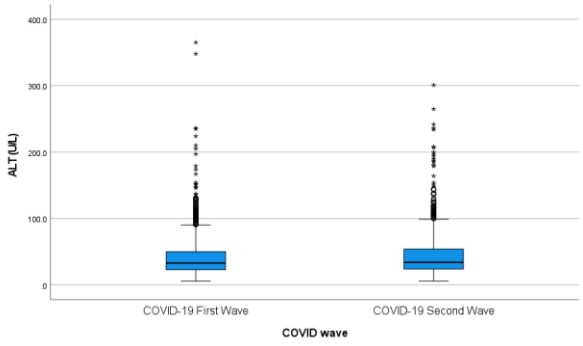

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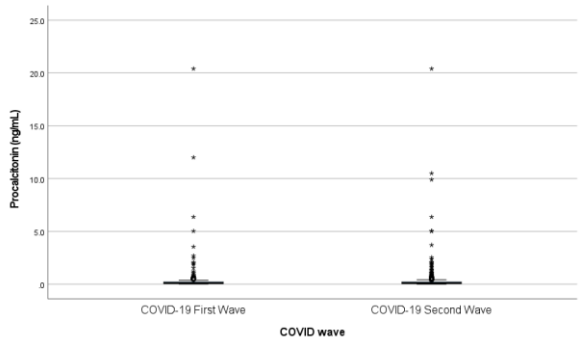

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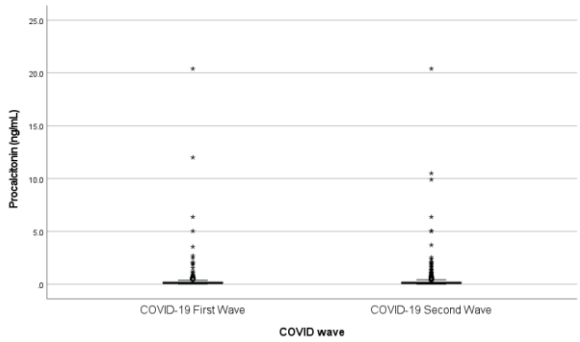

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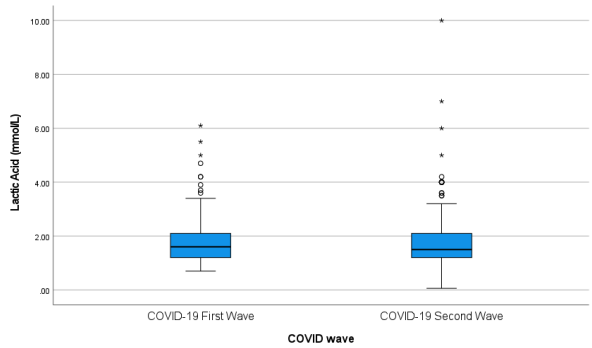

Figure 3 G-K.

Check list

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	4-5
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6-7
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	7
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	NA
Study size	10	Explain how the study size was arrived at	NA
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8-11
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8-11
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	11
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8-11
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	12-16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	16-17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12-16
Generalisability	21	Discuss the generalisability (external validity) of the study results	12-16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Comparison of demographic, clinical and laboratory characteristics between first and second COVID-19 waves in a secondary care hospital in Qatar: A retrospective study

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Secondary Subject Heading:	Global health
Keywords:	COVID-19, EPIDEMIOLOGY, INFECTIOUS DISEASES

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Title

Comparison of demographic, clinical and laboratory characteristics between first and second COVID-19 waves in a secondary care hospital in Qatar: A retrospective study

Key words

COVID-19 infection, Coronavirus, SARS-CoV-2, Pandemic, First wave, Second wave

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Abstract

Objective: To compare the patient profile and outcomes in Qatar during the first and second waves of the COVID-19 pandemic. **Setting:** A retrospective observational study was conducted comparing the demographic, clinical, and laboratory characteristics of patients with COVID-19 infection admitted to a secondary care hospital, during the first and second waves of the pandemic. **Participants:** 1039 patients from the first wave and 991 from the second wave who had pneumonia on chest X-ray and had a confirmed SARS-CoV-2 infection by a real-time PCR test of a nasopharyngeal swab were included. Patients with a normal chest X-ray and those who had a negative PCR test despite a positive COVID-19 antigen test were excluded. **Outcome:** Length of stay, need for mechanical ventilation, final disposition and mortality were the key outcomes studied **Results:** Flu like symptoms (18.5 % in the first wave vs. 36.1 % in the second wave, p 0.001), cough (79.2% vs.87%, p<0.001) and dyspnea (27.5% vs. 38% p<0.001) were more common in the second wave. Second wave patients had significantly higher respiratory rate, lower peripheral oxygen saturation, needed more supplemental oxygen and had higher incidence of pulmonary embolism. More patients received hydroxychloroquine and antibiotics during the first wave and more received steroids, antivirals and interleukin-1 antagonist during the second wave. The second wave had a shorter length of stay (14.58 ±7.75 vs. 12.61 ±6.16), p <0.001) and more patients were discharged home (22% vs. 10% p<0.001). **Conclusions:** Patients who presented during the second wave of Covid-19 pandemic appeared to be more ill clinically and based on their laboratory

parameters.They required shorter hospitalization and were more likely to be discharged home. This could represent greater expertise in handling such patients that was acquired during the first wave as well as use of more appropriate and combination therapies during the second wave.

Strengths

- First study in the region to compare patient characteristics between the two waves
- All patient variables were compared, including demographics, clinical complaints, vital signs, laboratory indicators, and outcomes.

Limitations

- The relationship between risk factors and outcomes was not investigated.
- Patients with severe COVID-19 were not included

Introduction

Corona virus disease 2019 (COVID-19), first identified in the Wuhan province of China, was declared a global pandemic by the World Health Organization (WHO) on 11 March, 2020 [1]. To date, it has affected 521,920,560 with more than 6 million deaths worldwide. In Qatar, COVID-19 infection has affected 367,099 individuals with 677 deaths till May 2022 [2]. On 29 February 2020 Qatar reported its first confirmed case of COVID-19 infection. During the first and second wave maximum number of cases was reported between 16 April 2020 and 20 July 2020 and between 8 February 2021 and 8 June 2021 respectively.

The virus responsible for the COVID-19 infection is Severe acute respiratory syndrome corona virus (SARS-CoV-2) , a novel corona virus belonging to the family Coronaviridae[3].The initial outbreak in China was thought to be originated by zoonotic spread from the seafood markets in the Wuhan province. Afterwards human-to-human transmission was recognized for the community spread of the disease, which rapidly became a global infection leading to the pandemic [4-7].

The mode of transmission of the virus from person to person is via respiratory droplets. Transmission may also occur through fomites such as bed linen, thermometers etc used by the COVID-19 infected patients. Airborne spread has been reported from aerosol generating procedures such as endotracheal intubation, bronchoscopy, open suctioning, tracheostomy, and nebulization [8, 9].

The spectrum of clinical manifestations of COVID-19 infection ranges from asymptomatic infection to symptomatic presentation. A systematic review done before the introduction of the COVID-19 vaccination reported that 33% of COVID -

19 infections are asymptomatic [10]. However these asymptomatic individuals can have radiological findings of ground glass opacities or patchy infiltrations in CT scan [11] . Most common symptoms of presentations are fever, malaise, myalgia, shortness of breath, and dry cough. Gastrointestinal symptoms may also be found in some patients with COVID-19 infection [12, 13].

The severity of symptomatic disease might vary from mild disease which accounts for the majority of the cases to severe or critical illness. Patients with severe disease may have dyspnea, hypoxia or radiological imaging demonstrating more than 50% involvements of lungs whereas; patients with critical disease will have features of shock, respiratory or multi organ failure [14-18]. A report from Centers for Disease Control and Prevention (CDC) from United States on 1.3million cases reported a cumulative incidence of 403.6 cases per 100,000 persons. The incidence was higher among patients more than 80 years of age. Cardiovascular disease (32%) and diabetes mellitus (30%) were the most common co-morbid conditions noted. Overall 14% were hospitalized, 2% were admitted to the ICU and 5% died. The hospitalization and death were 6 times and 12 times respectively higher among patients with underlying co-morbidities than those without [19].

During the first wave the Government of Qatar introduced strict preventive measures starting from March 2020, which included closure of all educational institutions and commercial establishments, closure of public and private offices, restaurants, banning of social gatherings, sports and entertainment activities, ban on international travel and strict home confinement. Wearing face mask in public space was made mandatory. As the number of cases in the first wave began to

recede, the restrictions were lifted in a phased manner from second half of June 2020. During the second wave when the number of cases started to raise the government reintroduced some of the preventive measures to contain the disease starting from February 2021. There was closure of parks, cinemas, sports activities. The public and private offices were allowed work with not more than 50% of capacity and there was ban on social gatherings however there was no complete lockdown.

During both pandemic waves, Ras Laffan Hospital, a secondary care hospital, was one of the COVID-19 designated hospitals under Hamad Medical Corporation (HMC). If patients met the admission criteria, they were transferred to Ras Laffan Hospital from non-COVID hospitals and tertiary care COVID facilities. During the first and second waves, respectively, 3650 and 4050 patients with a confirmed SARS-CoV-2 infection were hospitalized and treated at the Ras Laffan hospital.

From the time it was originally discovered in Wuhan, the disease profile, epidemiology, and treatment guidelines for COVID-19 infection had evolved continuously. On the basis of the most recent scientific findings, WHO released and updated diagnostic and treatment guidelines, as well as quarantine guidelines, on a regular basis. Countries around the world revised their management and quarantine standards on a regular basis based on this and locally available data.

Although the data on first 5000 cases of COVID-19 infection in Qatar have been reported [20], there is a lack of published literature comparing the epidemiology and consequences of repeated waves of the COVID-19 pandemic across the Middle East area, including Qatar. Furthermore, Qatar's population is made up

mostly of people of diverse countries and ethnic backgrounds. Hence, we chose to investigate and compare the characteristics and outcomes in both waves to better understand and manage future events

Objective

The goal of this study was to examine the patient profile and outcomes in COVID-19-infected hospitalized patients during the first and second waves of the pandemic.

Methods

Study type and setting

A retrospective observational study was conducted at Ras Laffan hospital, Hamad Medical Corporation, Qatar. This hospital was one of the COVID-19 designated hospitals under HMC.

Study participants and sample selection

Patients admitted between 1stto 30th of May 2020 in the first wave (n=1039) and those admitted between 1st and 15th of March 2021 during the second wave (n=991) were included in the study. The duration of the recruitment of patients was shorter in the second wave in order to make it comparable and equal number with the first wave. Though we did not use random sampling technique to select patients, it is worth to note that all the patients who met the inclusion criteria within the specified period were included. The patients were included if they had pneumonia on chest X-ray and had a laboratory-confirmed SARS-CoV-2 infection by a real-time PCR test of a nasopharyngeal swab specimen. The study excluded

patients with a normal chest X-ray and those who had a negative PCR test despite a positive COVID-19 antigen test.

Patient and public involvement

No patient involved

Data collection

Using the patients' health care numbers, files from the clinical information system were reviewed. Data was collected on demographics, admission symptoms, co-morbidities, length of stay, laboratory and radiographic results, need for supplemental oxygen, treatment details, complications, and outcomes.

Outcome of the study

The need for mechanical ventilation, length of stay, final disposition and mortality were the key outcomes studied along with their clinical and laboratory characteristics.

Statistical analysis

Descriptive statistics were used to summarize demographic, anthropometric, clinical, laboratory, radiological characteristics, and related follow-up outcome measures of these patients. Continuous variables with normal distribution were presented as mean and standard deviation (SD), whereas median and interquartile range (IQR) was used in case of skewed/non-normal data. Categorical variables were presented as frequencies and proportions. The Shapiro-Wilk test was used to test for normality of the data distribution. The

statistical analysis method for outcomes measured quantitatively and differences between the two independent groups (first and second COVID-19 waves) were compared using unpaired t or Mann Whitney U tests as appropriate depending on the normality of the data distribution. Associations between two or more qualitative or categorical variables across two independent groups were compared using Pearson Chi-square or Fisher exact test as applicable. Box plots were constructed to depict distribution of age, duration of symptoms, BMI, vital signs, and various parameters related to laboratory profiles across both groups (first and second COVID-19 waves). All P values presented were two-tailed, and P values <0.05 was considered as statistically significant. All Statistical analyses were performed using statistical packages SPSS version 27.0 (Armonk, NY: IBM Corp) and Epi-info (Center for Disease Control and Prevention, Atlanta, GA) software.

Results

Baseline demographic characteristics

During the first and second waves, respectively, 3650 and 4050 patients with a confirmed SARS-CoV-2 infection were hospitalized. The study included 1039 patients from the first wave and 991 participants from the second wave. During both waves, the average age of the subjects was similar [44.9 ±9.9 vs. 44.34±9.56]. In both waves, the proportion of patients among various age groups was comparable, with the majority of patients being between the ages of 36 and 50. (52.9 % vs.54.0 %). Males made up 95.2 % of the first wave and 88.5 % of the second wave patients (Table 1).

Clinical characteristics on admission

In the first wave patients had longer duration of symptoms prior to admission compared to second wave (4.88 ± 2.91 vs. 4.57 ±2.50, p 0.010). Flu like symptoms (36.1% in the second wave vs. 18.5% in the first wave, p <0.001)), cough (87% vs. 79.2%, p<0.001), and shortness of breath (38% vs. 27.5%, p<0.001)), were significantly higher in the second wave than the first. We did not find any significant difference in gastrointestinal symptoms between the two waves.

Diabetes mellitus (29.5% vs. 21.9%) and hypertension (26 % vs. 26.5%) were the most common co-morbid conditions observed in both waves; however, frequency of diabetes mellitus was significantly higher in the first wave (p <0.001)

The mean body mass index (BMI) was 27.95 ±4.46 and 28.29 ± 4.83 in the first and second waves, respectively (p= 0.263). Most patients had higher BMI in both the waves, with the majority having a BMI between 25.1 to 30 (48.2% vs. 45%) followed by more than 30 (27.1% vs. 28.5%) (Table-1). The details of distribution of age, duration of symptoms and BMI are plotted in Figure 1 A-C.

Vital signs and oxygen requirement

Patients in the second wave had significantly higher respiratory rate (23±6 vs. 22±5 p<0.001) and significantly lower peripheral oxygen saturation (93±5 vs. 94±4, p<0.001) when compared to the first wave. Furthermore, during the second wave significantly higher number of patients received supplemental oxygen on admission (40.3% vs. 22.9 %, p< 0.001) and also during their stay in the hospital (39.8% vs. 30.3%, p < 0.001). During the stay in the hospital there was significant variation in the vital parameters of the patients within the group from admission

value to their respective maximum/minimum values (p <0.001) Table- 2 and figure 2 A-H.

Laboratory parameters and chest X-ray findings

The first wave had significantly higher C-reactive protein) (median 35.4, IQR 12.9, 72 vs. median 15.2, IQR 15.2, 32.2, p<0.001 and HbA1c values (7.37± 2.04 vs. 6.94± 1.83 p<0.001). The mean values of white blood cell count (6.49 ±2.41 vs. 6.27 ± 2.21, p 0.031), hemoglobin (14.35 ±1.37 vs. 14.16 ± 1.43, p 0.003), and platelet counts (234.99 ±89.44 vs. 225.55 ±82.50, p 0.014) were lower in the second wave than the first. The patients in the second wave, had considerably lower mean albumin levels than the first wave (35.58 ±4.94 vs. 36.97 ±4.83, p<0.001). Patients in the second wave had higher hepatic transaminases and alkaline phosphatase levels than the first wave, although the differences were statistically insignificant. In both waves, the majority of patients had bilateral pneumonia on chest x-ray. Table- 3 and figure 3 A-K.

Treatment received

In the first wave, the usage of amoxicillin/clavulanic acid (60.9% vs.29.3%) and azithromycin/clarithromycin (74.1% vs. 41.9%) and usage of hydroxychloroquine (88.5% vs. 60.3%, p<0.001) was higher.

A significantly higher number of patients in the second wave received steroids (47.7% vs.17.1%, p <0.001), favipiravir (71% vs. 22.1%, p<0.001) or lopinavir/ritonavir (63.6% vs. 35.5%, p<0.001 and anakinra (10.6% vs. 2.7%, p <0.001).

Similar number of patients in both the waves received cephalosporins (74.3% vs. 70.5%, p=0.058) and prophylactic anticoagulation (97.4% vs. 99%).Table - 4.

Complications/ outcome and disposition

In the first and second waves, 5.3% and 6.5 %of patients, respectively, required transfer to a higher center for further care. Among those who were transferred, 28 (2.7%) patients in the first wave and 40 (4%) in the second wave received mechanical ventilation (p= 0.093). In the second wave, the percentage of patients who developed pulmonary embolism was significantly higher (1.1 % vs. 0.03%, p=0.025), furthermore, a higher proportion of mortality (0.81% (8/991) vs. 0.3% (3/1030)) was recorded in the second wave, however this difference was statistically insignificant (p=0.112).

In the second wave, the average length of stay was 1.9 days shorter which was statistically significant (14.58 ±7.75 vs. 12.61 ±6.16, p <0.001). The majority of patients in the first wave stayed for 15 to 30 days (50.9 % vs. 21.4%), while the majority of patients in the second wave stayed for 8 to 14 days (64.4% vs. 25.15%), table 5.

There was significantly higher percentage of patients who were transferred to quarantine facility in the first wave than the second wave (84.6% vs. 71.1%, p<0.001) where as significantly higher percentage of patients were discharged to their home in the second wave than the first wave (22.4% vs 10.1%, p <0.001).

Discussion

To our knowledge, this is the first study from the state of Qatar to compare COVID-19 individuals hospitalized between the first and second waves of the SARS-CoV-2 pandemic. Our findings show a significant variation between the two waves in terms of clinical features, laboratory markers and outcomes.

There was no difference in the average age of the patients between the two waves. In confirmation to our findings, a previous study conducted in Switzerland by Wolfsburg et al. [21] found no difference in the mean age of patients between two waves (65.9 vs. 65.8 years), whereas in contrast to our results a study by Iftimie et al. from Spain [22] found that the patients in the second wave were significantly younger than the first wave (58 years vs. 67 years). Our research sample, however, was substantially younger in both waves [44.90 9.99 vs. 44.349.57] than the previous two study groups. The young male expatriate workforce makes up the bulk of Qatar's population, which might explain this. We predicted the duration of symptoms prior to admission to be longer in the second wave than in the first because the patients were more apprehensive and sought medical assistance earlier in the first wave than in the second. Furthermore, the knowledge acquired and improved understanding of the COVID-19 disease epidemiology gained from handling the first wave should have given health practitioners the confidence to manage patients with mild to moderate disease at home rather than in the hospital during the second wave. Our findings, on the other hand, revealed that the duration of symptoms before to admission was longer in the first wave than in the second.

On admission to the hospital cough, shortness of breath and upper respiratory symptoms were more common in the second wave. The patients in the second wave had more symptoms and were sicker as evidenced by tachypnea and hypoxia and more patients requiring oxygen. We did not observe a significant difference in the prevalence of gastrointestinal symptoms between both the waves. This is in contrast to previous research [22, 23], which reported a higher prevalence of gastrointestinal complaints in the in the second wave.

The most common co-morbidities in both waves of the research population were diabetes mellitus and hypertension. The number of diabetes patients, on the other hand, was much higher in the first wave. One possible explanation for the lower number of diabetes mellitus patients in the second wave is that health advice given by the WHO as well as published literature showing evidence of diabetes mellitus as a risk factor for having the severe disease made these patients more cautious and isolate themselves, thereby shielding and protecting them from being exposed to infected patients. When comparing co-morbidities in both the waves, previous research have yielded conflicting outcomes. Iftimie et al. [22] showed no significant differences in co-morbidity between the two waves, however Jarrett et al. [24] and Sargin et al. [25] identified a higher frequency of chronic kidney illness in the second wave than in the first wave.

Despite the fact that the mean BMI did not alter significantly between the two waves, the majority of our research group had a higher BMI in both, suggesting obesity as a probable risk factor for COVID-19 infection. However this needs further studies analyzing the correlation between obesity as a risk factor and Covid-19 infection. Obesity was found in 30% of the whole study population in

both waves, according to a study from Switzerland [21]. Another study from the United States [24] found that the second wave had a higher BMI than the first wave (32.58 vs. 29.83).

The study of laboratory measurements revealed that the first wave had higher mean values of CRP and HbA1c, while hypoalbuminemia was significantly higher in the second wave. Furthermore levels of leukocyte and platelet count were lower in second wave than the first wave. The second wave had higher mean levels of hepatic transaminases but the difference was statistically not significant. The higher HbA1c readings in the first wave are unsurprising given the higher prevalence of diabetes mellitus in the first wave compared to the second wave. The higher hepatic transaminases in the second wave could be due to a variety of factors. One probable reason could be secondary to the side effect of favipiravir, as it was used more frequently in the second wave than in the first wave.

In our study population, the use of steroids was much higher in the second wave [47% vs. 17%]. This is because during the early stage of the first wave scientific literature regarding the benefit of steroids in COVID-19 infection was still in its preliminary stage and its use was limited. The frequency of usage of steroids in published data was still greater (99% [24], 76% [21]) than ours in the second wave. Because the aforementioned two studies included individuals with more severe disease than our research sample, the frequency of steroid administration differed. In terms of prophylactic anticoagulation, practically more than 97% of the patients in both waves received anticoagulation in our research group. This was much greater than the 59% in the first wave and 74% in the second wave reported in a research conducted in the United States [24].

The usage of hydroxychloroquine was significantly higher in the first wave, whereas the use of favipiravir and anakinra was much higher in the second wave, according to our findings. This is because treatment guidelines evolved and modified from the first wave to the second wave based on published scientific information around the world. Furthermore, use of antibiotics was significantly higher in the first wave than the second wave. There are multiple reasons for this. First, during the first wave azithromycin was more commonly used along with hydroxychloroquine as a treatment for COVID-19 infection. Second, due to lack of experience and expertise in managing the COVID-19 pandemic antibiotics were more commonly prescribed for patients with COVID pneumonia during the first wave; however during the second wave clinicians acquired adequate knowledge and experience and were more confident to treat patients without antibiotics unless indicated.

Despite the fact that patients in the second wave were sicker as evidenced by more symptoms, tachypnea and hypoxia on admission and laboratory parameters, the duration of hospitalization were significantly lower in the second wave. In the present study the average length of stay in the second wave was nearly 2 days less than in the first. This supports the findings of other research [21, 22, 25], which similarly found a shorter length of stay in the second wave. In addition more patients were discharged home in the second wave than transferred to quarantine facility. Possible explanation for this could be the change in discharge/transfer criteria. Secondly, better understanding of the disease course and experience of managing the first wave made the health care professionals more confident in early discharge of patients in the second wave. Finally, better home surveillance of discharged patients, development of better

follow up care, and community awareness and education might have also played an important role.

Even while the number of patients who needed to be transferred to a higher center, those who needed mechanical ventilation, had a pulmonary embolism and those who died were all somewhat higher in the second wave than in the first, the difference was not statistically significant. Available published data from two studies, one from Switzerland [21] and another from Turkey [25] found no significant difference in the proportion of patients requiring or at risk for Intensive Care Unit (ICU) admission in both the waves. However, the percentage of patients needing ICU care in the above two studies was higher than our results in both the waves. This could be related to the fact that our study and theirs had different severity of cases and also could be due to the difference in admission criteria in our study and others. Our admission criteria included patients with pneumonia requiring less than 4 L of oxygen at the time of admission, whereas other studies included more severe cases or ICU cases. Others have reported similar results, finding no substantial change in the number of patients requiring mechanical ventilation in both waves [24, 25]. There was no significant change in mortality rates between the two waves in the present study. Previous research comparing mortality rates between the two COVID-19 pandemic waves came up with mixed results. Our findings are consistent with those of Wolfisberg et al.[21] and Sargin et al. [25], who found no difference in mortality rates between the two waves, but Iftimie et al.[22] and Jarrett et al.[24] reported lower mortality in the second wave, in contrast to our findings. Similarly, two studies from the United States found that the second wave had a reduced mortality rate [26, 27]. According to published statistics from Japan based on a public registry reported that the

second wave of patients were younger, had fewer underlying co-morbidities, and had lower mortality rates [28].

A few studies from Europe also found lower mortality in the second wave. Chest X-ray severity of pneumonia, in-hospital mortality, and CRP readings were considerably greater in the first wave, according to an Italian study involving 200 Caucasian males over 50 years. They also discovered that the first wave had more patients who required mechanical ventilation [29]. Another study from Spain found that the second wave had younger patients, a shorter duration of stay in the hospital, fewer invasive mechanical ventilation, and decreased mortality [22].

The first wave's experience and lessons acquired by health care professionals, as well as a collaborative team effort involving numerous government agencies and community awareness and engagement, have helped us to manage the second wave more effectively.

Limitations

There were certain limitations to our research. To begin with, some data on co-morbidity and symptoms may have been overlooked due to the retrospective nature of the study. Second, there might have been selection bias because our research population was mostly male patients as most female COVID-19 patients were admitted to other COVID designated hospitals. Third, because our research sample included only mild to moderate Covid-19 infections, the findings may not be generalized to severe COVID -19 infections. Finally, the relationship between risk variables and outcomes was not examined as it was not the primary goal of our study.

Recommendation for future research

Future study should compare the relationship between various risk variables and outcomes over serial COVID-19 waves. Long-term consequences of COVID-19 infection in the first and second waves can also be studied and compared.

Conclusions

Patients in the second wave were more symptomatic and unwell than those in the first wave, but they stayed in the hospital for a shorter time and were more likely to be discharged home, according to our data. The most prevalent symptoms in both waves were cough and shortness of breath, although they were much greater in the second wave. Diabetes mellitus and raised CRP levels were more common in the first wave, but hypoalbuminemia was more prevalent in the second wave. In the first wave, antibiotics and hydroxychloroquine were more commonly utilized, but in the second wave, steroids, antivirals, and interleukin-1 antagonists were more commonly employed. There was no significant difference in the need for mechanical ventilation or mortality rate between the two waves.

Author's contribution

VN- Study design, data collection, analysis, manuscript writing, editing

NP- Study design, data collection, analysis, manuscript writing, editing

PC- Study design, data analysis, editing

AS- Data collection, analysis

PR- Data collection, analysis

IV-Study design, editing

JM- Analysis, manuscript writing

JS-Data collection, literature review

RH- Data collection, manuscript writing

AB- Data collection, manuscript writing

AA- Data collection, editing

MB- Data analysis, manuscript writing

SA- Data collection, manuscript writing

MA-Data collection, editing

AA- Data collection, literature review

RA- Data collection, literature review

AK- Data analysis, manuscript writing, editing

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Competing interests' statement

The authors declare that they have no competing interest involved

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Data sharing statement

No additional data available

Ethical approval

The study was approved by the Institutional Review Board and institutional research committee of medical research center, Hamad, Medical Corporation (Approval no-MRC-01-21-312).

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Table-1. Baseline epidemiological and clinical characteristics of patients during the first and second wave of the COVID – 19 pandemic

Variables	First wave (n=1039 n (%)	Second wave (n=991 n (%)	p- value
Age (In years)			
Mean ±SD	44.90 ±9.99	44.34 ±9.57	0.194
18 - 35	202 (19.4)	192 (19.4)	0.896
36 - 50	550 (52.9)	535(54)	
51 -- 65	265 (25.5)	247 (24.9)	
Above 65	22 (2.1)	17 (1.7)	
Gender			
Male	989 (95.2)	877 (88.5)	<0.001
Female	50 (4.8)	114 (11.5)	
Signs and symptoms			
Asymptomatic	48 (4.6)	94 (9.5)	<0.001
Mean duration of symptoms in days ±SD	4.88 ±2.91	4.57 ±2.50	0.010
Fever	893 (85.9)	870 (87.8)	0.220
Respiratory symptoms	856 (82.4)	709 (71.5)	<0.001
Flu like symptoms	192 (18.5)	358 (36.1)	<0.001
Cough	823 (79.2)	862 (87)	<0.001
Shortness of breath	286 (27.5)	377 (38)	<0.001
Chest pain	43(4.1)	37(3.7)	0.639
GI symptoms	88 (8.5)	66 (6.7)	0.124
Vomiting	50 (4.8)	38 (3.8)	0.280
Diarrhea	49 (4.7)	38 (3.8)	0.327
Co-Morbidities			
Immunosuppression	12 (1.2)	4 (0.4)	0.056
Chemotherapy	6 (0.6)	5 (0.5)	0.823

Diabetes Mellitus	307(29.5)	217 (21.9)	<0.001
Hypertension	270 (26)	263 (26.5)	0.777
Coronary artery disease	41 (3.9)	26 (2.6)	0.095
Chronic kidney disease	17 (1.6)	14 (1.4)	0.681
Cancer	5 (0.5)	5 (0.5)	0.940
Liver disease	3 (0.3)	6 (0.6)	0.283
COPD/Asthma	19 (1.8)	8 (0.8)	0.045
Body mass index (kg/m²)			
Mean ± SD	27.95 ±4.46	28.29 ± 4.83	0.263
< 18.5	1(0.2)	6 (1.1)	0.360
18.6 – 25	102 (24.5)	137 (25.4)	
25.1– 30	201 (48.2)	243 (45)	
>30	113 (27.1)	154 (28.5)	

Results are shown as number of cases and percentages (in parenthesis) or as means with ± standard deviations.
COPD-Chronic obstructive pulmonary disease
For statistical analysis first wave was compared with the second wave. Quantitative data were compared using t test (normal data distribution) and Mann Whitney U test for skew data distribution. Qualitative data were compared using Chi-square test.

Table-2. Showing vital Signs and oxygen requirement

Variables		First wave (n=1039)	Second wave (n=991)	p- value
Temperature C^0 Mean ±SD	On admission	37.3±0.75	37.3± 0.72	0.976
	Maximum	38.1±0.89	38.2±0.88	0.024
p-- value		<0.001	<0.001	
Pulse rate (Beats per minute) Mean ±SD	On admission	89±14	88±13	0.439
	Maximum	102±11	103±11	0.164
p- value		<0.001	<0.001	
Respiratory Rate /min Mean ±SD	On admission	19±2	19±3	0.030
	Maximum	22±5	23±6	<0.001
p- value		<0.001	<0.001	
Spo2 (%)Mean ±SD	On admission	97±2	97±1	0.327
	Lowest	94±4	93±5	<0.001
p- value		<0.001	<0.001	
Patients received supplemental oxygen. Number (%)	On admission	238 (22.9)	399 (40.3)	<0.001
	After admission	315 (30.3)	394(39.8)	<0.001
p- value		<0.001	<0.001	

For statistical analysis first wave was compared with the second wave. Quantitative data were compared using t test (normal data distribution) and Mann Whitney U test for skew data distribution. Qualitative data were compared using Chi-square test.

Table- 3. Showing laboratory parameters and chest X-ray findings

Variables	First wave Mean ±SD (Median, IQR)	Second wave Mean ±SD (Median, IQR)	p- value
WBC (10^3/ul)	6.49 ±2.41 (6.10, 4.80-7.60)	6.27 ±2.21 (5.90, 4.70-7.40)	0.031
Hemoglobin (g/dl)	14.35±1.37 (14.40, 13.50-15.22)	14.16 ± 1.43 (14.20, 13.3-15.2)	0.003
Platelet count (10^3/ul)	234.99 ±89.44 (217, 175-269)	225.55 ±82.50 (209, 168-259)	0.014
Albumin (gm/L)	36.97 ±4.83 (37, 34-40)	35.58 ±4.94 (35, 32-39)	<0.001
C-Reactive Protein (mg/L)	50.54 ±53.28 (35.35, 12.90-72.02)	33.68 ±44.20 (15.2, 15.20-32.20)	<0.001
Lactate	1.74 ±0.77 (1.60, 1.20-2.10)	1.73±0.91 (1.50, 1.20-2.10)	0.924
Procalcitonin	0.41 ±1.62 (0.11, 0.06-0.21)	0.30±1.15 (0.11, 0.06-0.21)	0.456
D- Dimer	1.20 ±4.28 (0.44, 0.32-0.68)	1.10±3.84 (0.42, 0.30-0.63)	0.139
Aspartate aminotransferase (AST)	44.14 ±34.47 (35, 26-50)	50.81 ±141.91 (37, 28-52)	0.020
Alkaline phosphatase (ALP)	77.56 ±31.71(71, 59-87.5)	78.29±34.96 (71, 58-87)	0.626
Alanine aminotransferase (ALT)	42.74 ±33.28 (32.9, 23-50.55)	44.30 ±34.24 (34, 24-54)	0.267
Total Bilurubin	9.97 ±5.73 (8.30, 7-12)	9.57±6.20 (8.0, 6.0-11.0)	0.143
HbA1c	7.37± 2.04 (6.60, 5.90- 8.40)	6.94± 1.83 (6.20, 5.80- 7.3)	<0.001
Chest X ray			

findings			
Unilateral infiltrations	185 (17.8)	236 (23.8)	0.001
Bilateral infiltrations	854 (82.2)	755 (76.2)	

IQR-Interquartile range

Median and IQR were exclusively required for skewed data however to make it unified format we presented it for all the parameters

For statistical analysis first wave was compared with the second wave. Quantitative data were compared using t test (normal data distribution) and Mann Whitney U test for skew data distribution. Qualitative data were compared using Chi-square test.

Table -4. Showing the details of treatment received

Treatment*	First wave (n=1039) n (%)	Second wave (n=991) n(%)	p-value
Dexamethasone	178 (17.1)	473 (47.7)	<0.001
Anticoagulation	1012 (97.4)	981 (99)	0.007
Favipiravir	230 (22.1)	704 (71)	<0.001
Hydroxychloroquine	920(88.5)	598 (60.3)	<0.001
Lopinavir/ ritonavir	369 (35.5)	630 (63.6)	<0.001
Anakinra	28 (2.7)	105 (10.6)	<0.001
Tocilizumab	21 (2.0)	19 (1.9)	0.866
Amoxicillin/clavulanic acid	633 (60.9)	290 (29.3)	<0.001
Ceftriaxone/ Cefuroxime	772 (74.3)	699 (70.5)	0.058
Azithromycin /Clarithromycin	770 (74.1)	415 (41.9) (6.9)	<0.001
Piperacillin /tazobactum	51 (4.9)	68	0.061

*One patient might have received more than one type of treatment

For statistical analysis first wave was compared with the second wave. P-values computed using Pearson Chi-square test.

Table- 5. Showing final outcomes and disposition

Variables	First Wave (n=1030) n (%)	Second wave (n=991) n(%)	p-value
Mechanical ventilation	28 (2.7)	40 (4.0)	0.093
Pulmonary embolism/DVT	3 (0.3)	11 (1.1)	0.025
Death	3 (0.3)	8 (0.8)	0.112
Discharge disposition			
Discharge home	105 (10.1)	222 (22.4)	<0.001
Transfer to quarantine	879 (84.6)	705 (71.1)	
Transfer to higher center	55 (5.3)	64 (6.5)	
Length of stay in days			
Mean ± SD	14.58 ±7.75	12.61 ±6.16	<0.001
0-7	227 (21.8)	126 (12.7)	<0.001
8-14	261 (25.1)	638 (64.4)	
15-30	529 (50.9)	212 (21.4)	
>30	22 (2.1)	15 (1.5)	

For statistical analysis first wave was compared with the second wave. Quantitative data were compared using t test for normal data distribution and Mann Whitney U test for skew data distribution. Qualitative data were compared using Chi-square test.

Figure legends

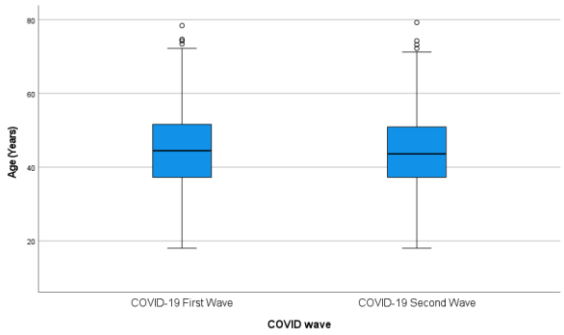
Figure 1.A-C. Box plot showing the distribution of age, duration of symptoms and BMI

Figure 2 A-D. Box plots depicting the vital signs
Figure 2.E-H. Box plots depicting the vital signs

Figure 3. A-F. Box plots depicting distribution laboratory parameters

Figure 3.G-K. Box plots depicting distribution laboratory parameters

A



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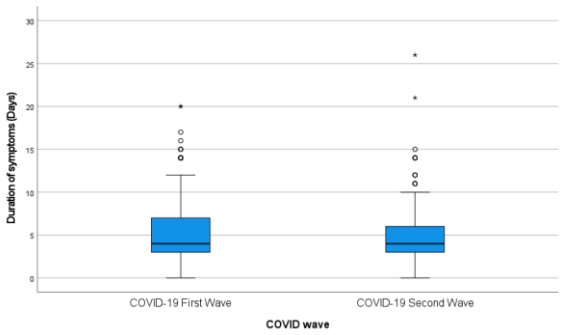

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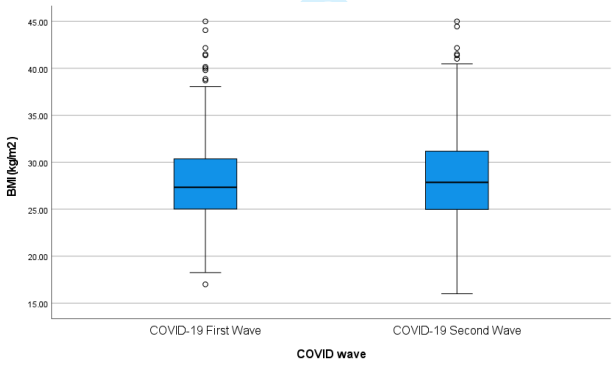


Figure 1.A-C.

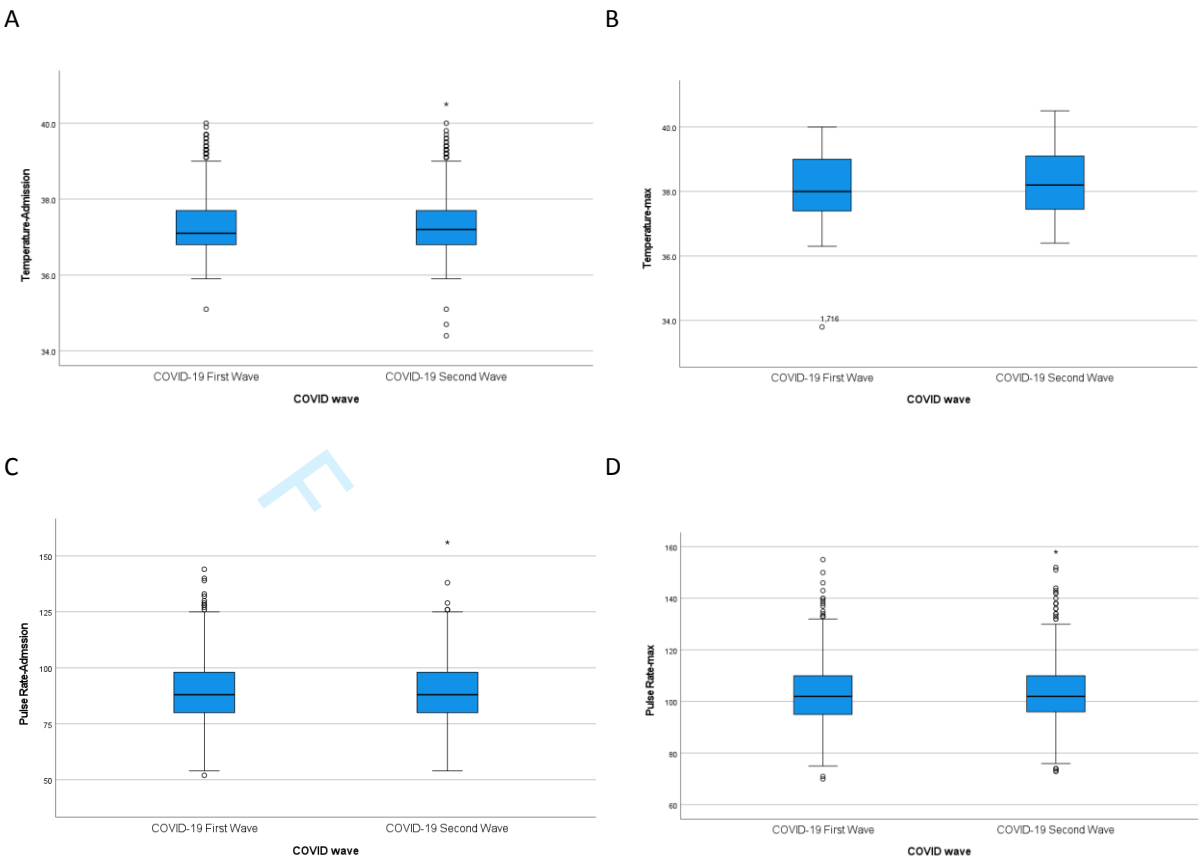


Figure 2 A-D.

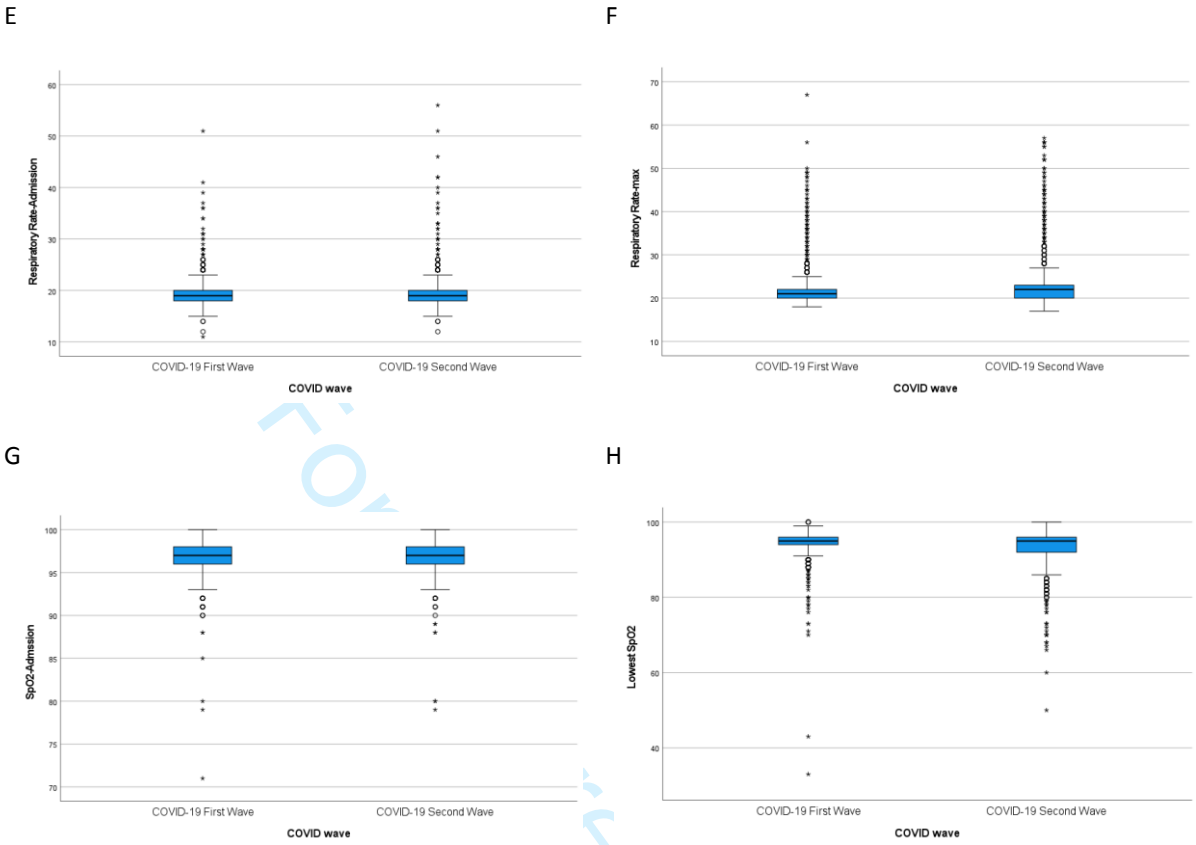


Figure 2 E-H. Boxplots depicting the vital signs

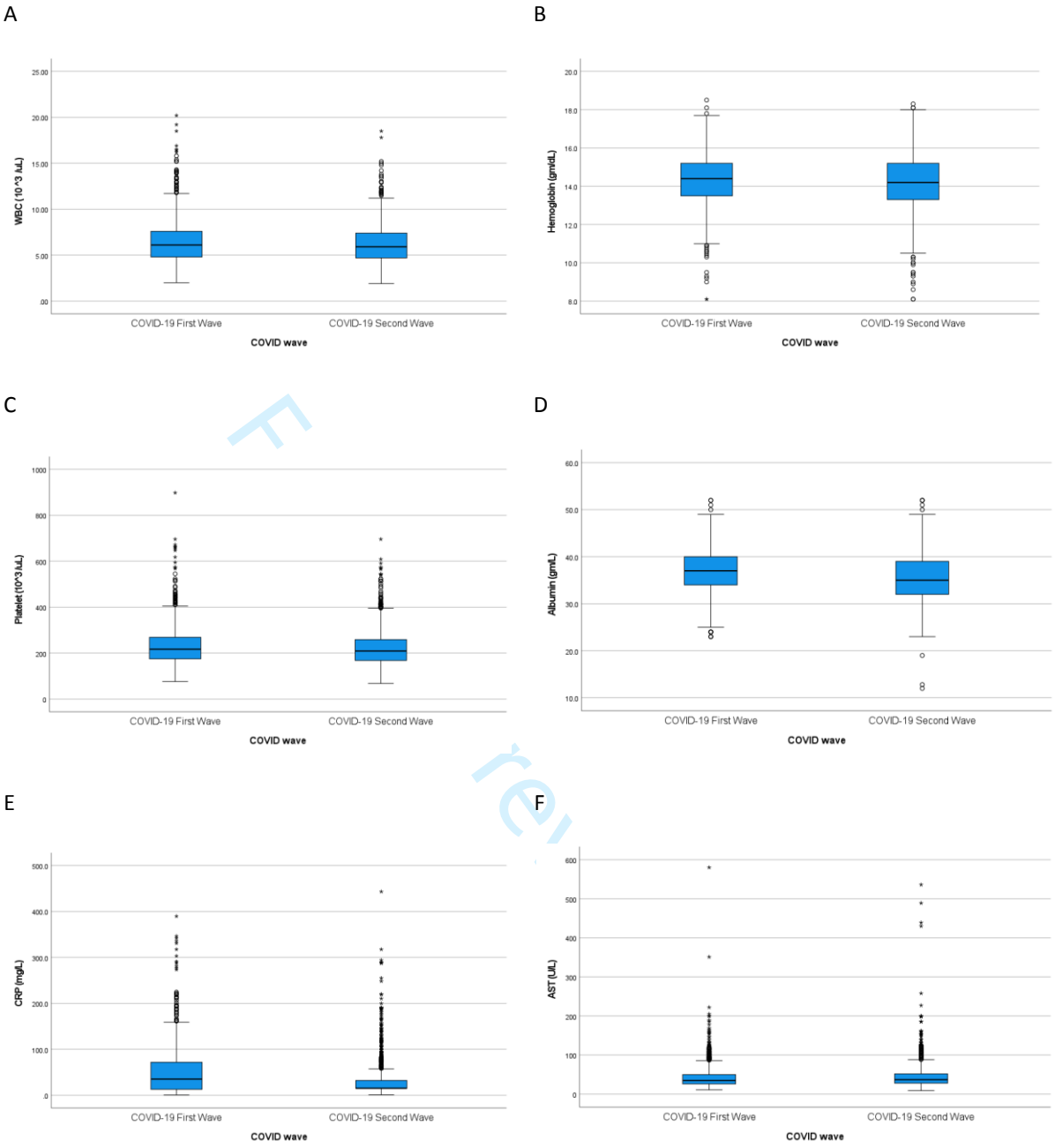
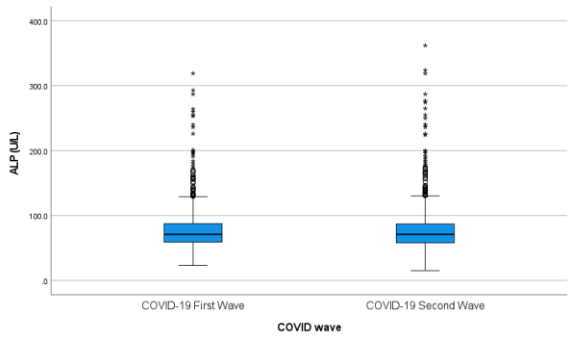

A
WBC (10^3 /uL)
COVID-19 First Wave
COVID-19 Second Wave
COVID wave
B
Hemoglobin (gm/dL)
COVID-19 First Wave
COVID-19 Second Wave
COVID wave
C
Platelet (10^3 /uL)
COVID-19 First Wave
COVID-19 Second Wave
COVID wave
D
Albumin (gm/L)
COVID-19 First Wave
COVID-19 Second Wave
COVID wave
E
CRP (mg/L)
COVID-19 First Wave
COVID-19 Second Wave
COVID wave
F
AST (U/L)
COVID-19 First Wave
COVID-19 Second Wave
COVID wave

Figure 3 A-F.

G



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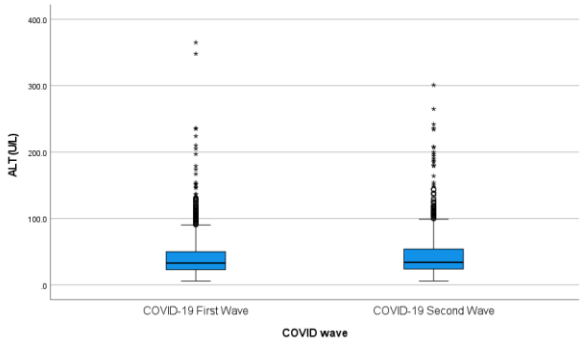

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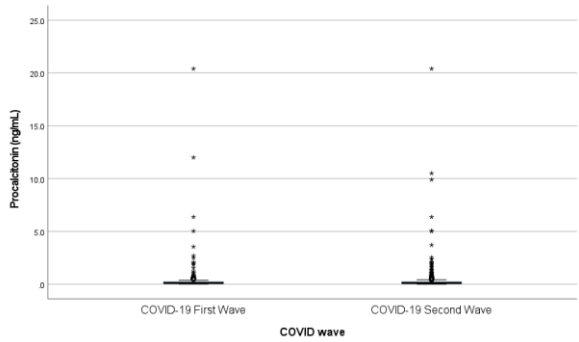

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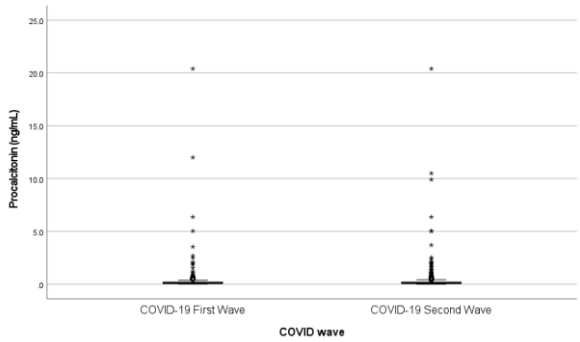

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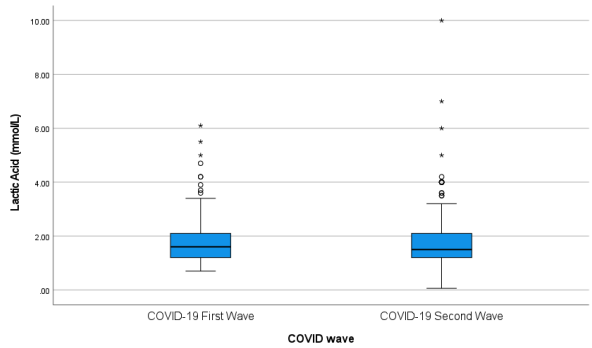

Figure 3 G-K.

Check list

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	4-5
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6-7
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	7
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	NA
Study size	10	Explain how the study size was arrived at	NA
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8-11
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8-11
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	11
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8-11
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	12-16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	16-17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12-16
Generalisability	21	Discuss the generalisability (external validity) of the study results	12-16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Comparison of demographic, clinical and laboratory characteristics between first and second COVID-19 waves in a secondary care hospital in Qatar: A retrospective study

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Primary Subject Heading:	Infectious diseases
Secondary Subject Heading:	Global health
Keywords:	COVID-19, EPIDEMIOLOGY, INFECTIOUS DISEASES

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Title

Comparison of demographic, clinical and laboratory characteristics between first and second COVID-19 waves in a secondary care hospital in Qatar: A retrospective study

Key words

COVID-19 infection, Coronavirus, SARS-CoV-2, Pandemic, First wave, Second wave

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Abstract

Objective: To compare the patient profile and outcomes in Qatar during the first and second waves of the COVID-19 pandemic. **Setting:** A retrospective observational study was conducted comparing the demographic, clinical, and laboratory characteristics of patients with COVID-19 infection admitted to a secondary care hospital, during the first and second waves of the pandemic. **Participants:** 1039 patients from the first wave and 991 from the second wave who had pneumonia on chest X-ray and had a confirmed SARS-CoV-2 infection by a real-time PCR test of a nasopharyngeal swab were included. Patients with a normal chest X-ray and those who had a negative PCR test despite a positive COVID-19 antigen test were excluded. **Outcome:** Length of stay, need for mechanical ventilation, final disposition and mortality were the key outcomes studied **Results:** Flu like symptoms (18.5 % in the first wave vs. 36.1 % in the second wave, p 0.001), cough (79.2% vs.87%, p<0.001) and dyspnea (27.5% vs. 38% p<0.001) were more common in the second wave. Second wave patients had significantly higher respiratory rate, lower peripheral oxygen saturation, needed more supplemental oxygen and had higher incidence of pulmonary embolism. More patients received hydroxychloroquine and antibiotics during the first wave and more received steroids, antivirals and interleukin-1 antagonist during the second wave. The second wave had a shorter length of stay (14.58 ±7.75 vs. 12.61 ±6.16), p <0.001) and more patients were discharged home (22% vs. 10% p<0.001). **Conclusions:** Patients who presented during the second wave of Covid-19 pandemic appeared to be more ill clinically and based on their laboratory

parameters.They required shorter hospitalization and were more likely to be discharged home. This could represent greater expertise in handling such patients that was acquired during the first wave as well as use of more appropriate and combination therapies during the second wave.

Strengths

- First study in the region to compare patient characteristics between the two waves
- All patient variables were compared, including demographics, clinical complaints, vital signs, laboratory indicators, and outcomes.

Limitations

- The relationship between risk factors and outcomes was not investigated.
- Patients with severe COVID-19 were not included

Introduction

Corona virus disease 2019 (COVID-19), first identified in the Wuhan province of China, was declared a global pandemic by the World Health Organization (WHO) on 11 March, 2020 [1]. To date, it has affected 521,920,560 with more than 6 million deaths worldwide. In Qatar, COVID-19 infection has affected 367,099 individuals with 677 deaths till May 2022 [2]. On 29 February 2020 Qatar reported its first confirmed case of COVID-19 infection. During the first and second wave maximum number of cases was reported between 16 April 2020 and 20 July 2020 and between 8 February 2021 and 8 June 2021 respectively.

The virus responsible for the COVID-19 infection is Severe acute respiratory syndrome corona virus (SARS-CoV-2) , a novel corona virus belonging to the family Coronaviridae[3].The initial outbreak in China was thought to be originated by zoonotic spread from the seafood markets in the Wuhan province. Afterwards human-to-human transmission was recognized for the community spread of the disease, which rapidly became a global infection leading to the pandemic [4-7].

The mode of transmission of the virus from person to person is via respiratory droplets. Transmission may also occur through fomites such as bed linen, thermometers etc used by the COVID-19 infected patients. Airborne spread has been reported from aerosol generating procedures such as endotracheal intubation, bronchoscopy, open suctioning, tracheostomy, and nebulization [8, 9].

The spectrum of clinical manifestations of COVID-19 infection ranges from asymptomatic infection to symptomatic presentation. A systematic review done before the introduction of the COVID-19 vaccination reported that 33% of COVID -

19 infections are asymptomatic [10]. However these asymptomatic individuals can have radiological findings of ground glass opacities or patchy infiltrations in CT scan [11] . Most common symptoms of presentations are fever, malaise, myalgia, shortness of breath, and dry cough. Gastrointestinal symptoms may also be found in some patients with COVID-19 infection [12, 13].

The severity of symptomatic disease might vary from mild disease which accounts for the majority of the cases to severe or critical illness. Patients with severe disease may have dyspnea, hypoxia or radiological imaging demonstrating more than 50% involvements of lungs whereas; patients with critical disease will have features of shock, respiratory or multi organ failure [14-18]. A report from Centers for Disease Control and Prevention (CDC) from United States on 1.3million cases reported a cumulative incidence of 403.6 cases per 100,000 persons. The incidence was higher among patients more than 80 years of age. Cardiovascular disease (32%) and diabetes mellitus (30%) were the most common co-morbid conditions noted. Overall 14% were hospitalized, 2% were admitted to the ICU and 5% died. The hospitalization and death were 6 times and 12 times respectively higher among patients with underlying co-morbidities than those without [19].

During the first wave the Government of Qatar introduced strict preventive measures starting from March 2020, which included closure of all educational institutions and commercial establishments, closure of public and private offices, restaurants, banning of social gatherings, sports and entertainment activities, ban on international travel and strict home confinement. Wearing face mask in public space was made mandatory. As the number of cases in the first wave began to

recede, the restrictions were lifted in a phased manner from second half of June 2020. During the second wave when the number of cases started to raise the government reintroduced some of the preventive measures to contain the disease starting from February 2021. There was closure of parks, cinemas, sports activities. The public and private offices were allowed work with not more than 50% of capacity and there was ban on social gatherings however there was no complete lockdown.

During both pandemic waves, Ras Laffan Hospital, a secondary care hospital, was one of the COVID-19 designated hospitals under Hamad Medical Corporation (HMC). If patients met the admission criteria, they were transferred to Ras Laffan Hospital from non-COVID hospitals and tertiary care COVID facilities. During the first and second waves, respectively, 3650 and 4050 patients with a confirmed SARS-CoV-2 infection were hospitalized and treated at the Ras Laffan hospital.

From the time it was originally discovered in Wuhan, the disease profile, epidemiology, and treatment guidelines for COVID-19 infection had evolved continuously. On the basis of the most recent scientific findings, WHO released and updated diagnostic and treatment guidelines, as well as quarantine guidelines, on a regular basis. Countries around the world revised their management and quarantine standards on a regular basis based on this and locally available data.

Although the data on first 5000 cases of COVID-19 infection in Qatar have been reported [20], there is a lack of published literature comparing the epidemiology and consequences of repeated waves of the COVID-19 pandemic across the Middle East area, including Qatar. Furthermore, Qatar's population is made up

mostly of people of diverse countries and ethnic backgrounds. Hence, we chose to investigate and compare the characteristics and outcomes in both waves to better understand and manage future events

Objective

The goal of this study was to examine the patient profile and outcomes in COVID-19-infected hospitalized patients during the first and second waves of the pandemic.

Methods

Study type and setting

A retrospective observational study was conducted at Ras Laffan hospital, Hamad Medical Corporation, Qatar. This hospital was one of the COVID-19 designated hospitals under HMC.

Study participants and sample selection

Patients admitted between 1stto 30th of May 2020 in the first wave (n=1039) and those admitted between 1st and 15th of March 2021 during the second wave (n=991) were included in the study. The duration of the recruitment of patients was shorter in the second wave in order to make it comparable and equal number with the first wave. Though we did not use random sampling technique to select patients, it is worth to note that all the patients who met the inclusion criteria within the specified period were included. The patients were included if they had pneumonia on chest X-ray and had a laboratory-confirmed SARS-CoV-2 infection by a real-time PCR test of a nasopharyngeal swab specimen. The study excluded

patients with a normal chest X-ray and those who had a negative PCR test despite a positive COVID-19 antigen test.

Patient and public involvement

No patient involved

Data collection

Using the patients' health care numbers, files from the clinical information system were reviewed. Data was collected on demographics, admission symptoms, co-morbidities, length of stay, laboratory and radiographic results, need for supplemental oxygen, treatment details, complications, and outcomes.

Outcome of the study

The need for mechanical ventilation, length of stay, final disposition and mortality were the key outcomes studied along with their clinical and laboratory characteristics.

Statistical analysis

Descriptive statistics were used to summarize demographic, anthropometric, clinical, laboratory, radiological characteristics, and related follow-up outcome measures of these patients. Continuous variables with normal distribution were presented as mean and standard deviation (SD), whereas median and interquartile range (IQR) was used in case of skewed/non-normal data. Categorical variables were presented as frequencies and proportions. The Shapiro-Wilk test was used to test for normality of the data distribution. The

statistical analysis method for outcomes measured quantitatively and differences between the two independent groups (first and second COVID-19 waves) were compared using unpaired t or Mann Whitney U tests as appropriate depending on the normality of the data distribution. Associations between two or more qualitative or categorical variables across two independent groups were compared using Pearson Chi-square or Fisher exact test as applicable. Within each group of COVID-19 wave, vital signs and oxygen requirement measured on and after admission were compared using paired t test and McNemar's Chi-square test. Box plots were constructed to depict distribution of age, duration of symptoms, BMI, vital signs, and various parameters related to laboratory profiles across both groups (first and second COVID-19 waves). All P values presented were two-tailed, and P values <0.05 was considered as statistically significant. All Statistical analyses were performed using statistical packages SPSS version 27.0 (Armonk, NY: IBM Corp) and Epi-info (Center for Disease Control and Prevention, Atlanta, GA) software.

Results

Baseline demographic characteristics

During the first and second waves, respectively, 3650 and 4050 patients with a confirmed SARS-CoV-2 infection were hospitalized. The study included 1039 patients from the first wave and 991 participants from the second wave. During both waves, the average age of the subjects was similar [44.9 ±9.9 vs. 44.34±9.56]. In both waves, the proportion of patients among various age groups was comparable, with the majority of patients being between the ages of 36 and

50. (52.9 % vs.54.0 %). Males made up 95.2 % of the first wave and 88.5 % of the second wave patients (Table 1).

Clinical characteristics on admission

In the first wave patients had longer duration of symptoms prior to admission compared to second wave (4.88 ± 2.91 vs. 4.57 ±2.50, p 0.010). Flu like symptoms (36.1% in the second wave vs. 18.5% in the first wave, p <0.001)), cough (87% vs. 79.2%, p<0.001), and shortness of breath (38% vs. 27.5%, p<0.001)), were significantly higher in the second wave than the first. We did not find any significant difference in gastrointestinal symptoms between the two waves.

Diabetes mellitus (29.5% vs. 21.9%) and hypertension (26 % vs. 26.5%) were the most common co-morbid conditions observed in both waves; however, frequency of diabetes mellitus was significantly higher in the first wave (p <0.001)

The mean body mass index (BMI) was 27.95 ±4.46 and 28.29 ± 4.83 in the first and second waves, respectively (p= 0.263). Most patients had higher BMI in both the waves, with the majority having a BMI between 25.1 to 30 (48.2% vs. 45%) followed by more than 30 (27.1% vs. 28.5%) (Table-1). The details of distribution of age, duration of symptoms and BMI are plotted in Figure 1 A-C.

Vital signs and oxygen requirement

Patients in the second wave had significantly higher respiratory rate (23±6 vs. 22±5 p<0.001) and significantly lower peripheral oxygen saturation (93±5 vs. 94±4, p<0.001) when compared to the first wave. Furthermore, during the second wave significantly higher number of patients received supplemental oxygen on

admission (40.3% vs. 22.9 %, p< 0.001) and also during their stay in the hospital (39.8% vs. 30.3%, p < 0.001). During the stay in the hospital there was significant variation in the vital parameters of the patients within the group from admission value to their respective maximum/minimum values (p <0.001) Table- 2 and figure 2 A-H.

Laboratory parameters and chest X-ray findings

The first wave had significantly higher C-reactive protein) (median 35.4, IQR 12.9, 72 vs. median 15.2, IQR 15.2, 32.2, p<0.001 and HbA1c values (7.37± 2.04 vs. 6.94± 1.83 p<0.001). The mean values of white blood cell count (6.49 ±2.41 vs. 6.27 ± 2.21, p 0.031), hemoglobin (14.35 ±1.37 vs. 14.16 ± 1.43, p 0.003), and platelet counts (234.99 ±89.44 vs. 225.55 ±82.50, p 0.014) were lower in the second wave than the first. The patients in the second wave, had considerably lower mean albumin levels than the first wave (35.58 ±4.94 vs. 36.97 ±4.83, p<0.001). Patients in the second wave had higher hepatic transaminases and alkaline phosphatase levels than the first wave, although the differences were statistically insignificant. In both waves, the majority of patients had bilateral pneumonia on chest x-ray. Table- 3 and figure 3 A-K.

Treatment received

In the first wave, the usage of amoxicillin/clavulanic acid (60.9% vs.29.3%) and azithromycin/clarithromycin (74.1% vs. 41.9%) and usage of hydroxychloroquine (88.5% vs. 60.3%, p<0.001) was higher.

A significantly higher number of patients in the second wave received steroids (47.7% vs.17.1%, p <0.001), favipiravir (71% vs. 22.1%, p<0.001) or

lopinavir/ritonavir (63.6% vs. 35.5%, p<0.001 and anakinra (10.6% vs. 2.7%, p <0.001).

Similar number of patients in both the waves received cephalosporins (74.3% vs. 70.5%, p=0.058) and prophylactic anticoagulation (97.4% vs. 99%).Table - 4.

Complications/ outcome and disposition

In the first and second waves, 5.3% and 6.5 %of patients, respectively, required transfer to a higher center for further care. Among those who were transferred, 28 (2.7%) patients in the first wave and 40 (4%) in the second wave received mechanical ventilation (p= 0.093). In the second wave, the percentage of patients who developed pulmonary embolism was significantly higher (1.1 % vs. 0.03%, p=0.025), furthermore, a higher proportion of mortality (0.81% (8/991) vs. 0.3% (3/1030)) was recorded in the second wave, however this difference was statistically insignificant (p=0.112).

In the second wave, the average length of stay was 1.9 days shorter which was statistically significant (14.58 ±7.75 vs. 12.61 ±6.16, p <0.001). The majority of patients in the first wave stayed for 15 to 30 days (50.9 % vs. 21.4%), while the majority of patients in the second wave stayed for 8 to 14 days (64.4% vs. 25.15%), table 5.

There was significantly higher percentage of patients who were transferred to quarantine facility in the first wave than the second wave (84.6% vs. 71.1%, p<0.001) where as significantly higher percentage of patients were discharged to their home in the second wave than the first wave (22.4% vs 10.1%, p <0.001).

Discussion

To our knowledge, this is the first study from the state of Qatar to compare COVID-19 individuals hospitalized between the first and second waves of the SARS-CoV-2 pandemic. Our findings show a significant variation between the two waves in terms of clinical features, laboratory markers and outcomes.

There was no difference in the average age of the patients between the two waves. In confirmation to our findings, a previous study conducted in Switzerland by Wolfsburg et al. [21] found no difference in the mean age of patients between two waves (65.9 vs. 65.8 years), whereas in contrast to our results a study by Iftimie et al. from Spain [22] found that the patients in the second wave were significantly younger than the first wave (58 years vs. 67 years). Our research sample, however, was substantially younger in both waves [44.90 9.99 vs. 44.349.57] than the previous two study groups. The young male expatriate workforce makes up the bulk of Qatar's population, which might explain this. We predicted the duration of symptoms prior to admission to be longer in the second wave than in the first because the patients were more apprehensive and sought medical assistance earlier in the first wave than in the second. Furthermore, the knowledge acquired and improved understanding of the COVID-19 disease epidemiology gained from handling the first wave should have given health practitioners the confidence to manage patients with mild to moderate disease at home rather than in the hospital during the second wave. Our findings, on the

other hand, revealed that the duration of symptoms before to admission was longer in the first wave than in the second.

On admission to the hospital cough, shortness of breath and upper respiratory symptoms were more common in the second wave. The patients in the second wave had more symptoms and were sicker as evidenced by tachypnea and hypoxia and more patients requiring oxygen. We did not observe a significant difference in the prevalence of gastrointestinal symptoms between both the waves. This is in contrast to previous research [22, 23], which reported a higher prevalence of gastrointestinal complaints in the in the second wave.

The most common co-morbidities in both waves of the research population were diabetes mellitus and hypertension. The number of diabetes patients, on the other hand, was much higher in the first wave. One possible explanation for the lower number of diabetes mellitus patients in the second wave is that health advice given by the WHO as well as published literature showing evidence of diabetes mellitus as a risk factor for having the severe disease made these patients more cautious and isolate themselves, thereby shielding and protecting them from being exposed to infected patients. When comparing co-morbidities in both the waves, previous research have yielded conflicting outcomes. Iftimie et al. [22] showed no significant differences in co-morbidity between the two waves, however Jarrett et al. [24] and Sargin et al. [25] identified a higher frequency of chronic kidney illness in the second wave than in the first wave.

Despite the fact that the mean BMI did not alter significantly between the two waves, the majority of our research group had a higher BMI in both, suggesting obesity as a probable risk factor for COVID-19 infection. However this needs

further studies analyzing the correlation between obesity as a risk factor and Covid-19 infection. Obesity was found in 30% of the whole study population in both waves, according to a study from Switzerland [21]. Another study from the United States [24] found that the second wave had a higher BMI than the first wave (32.58 vs. 29.83).

The study of laboratory measurements revealed that the first wave had higher mean values of CRP and HbA1c, while hypoalbuminemia was significantly higher in the second wave. Furthermore levels of leukocyte and platelet count were lower in second wave than the first wave. The second wave had higher mean levels of hepatic transaminases but the difference was statistically not significant. The higher HbA1c readings in the first wave are unsurprising given the higher prevalence of diabetes mellitus in the first wave compared to the second wave. The higher hepatic transaminases in the second wave could be due to a variety of factors. One probable reason could be secondary to the side effect of favipiravir, as it was used more frequently in the second wave than in the first wave.

In our study population, the use of steroids was much higher in the second wave [47% vs. 17%]. This is because during the early stage of the first wave scientific literature regarding the benefit of steroids in COVID-19 infection was still in its preliminary stage and its use was limited. The frequency of usage of steroids in published data was still greater (99% [24], 76% [21]) than ours in the second wave. Because the aforementioned two studies included individuals with more severe disease than our research sample, the frequency of steroid administration differed. In terms of prophylactic anticoagulation, practically more than 97% of the patients in both waves received anticoagulation in our research group. This

was much greater than the 59% in the first wave and 74% in the second wave reported in a research conducted in the United States [24].

The usage of hydroxychloroquine was significantly higher in the first wave, whereas the use of favipiravir and anakinra was much higher in the second wave, according to our findings. This is because treatment guidelines evolved and modified from the first wave to the second wave based on published scientific information around the world. Furthermore, use of antibiotics was significantly higher in the first wave than the second wave. There are multiple reasons for this. First, during the first wave azithromycin was more commonly used along with hydroxychloroquine as a treatment for COVID-19 infection. Second, due to lack of experience and expertise in managing the COVID-19 pandemic antibiotics were more commonly prescribed for patients with COVID pneumonia during the first wave; however during the second wave clinicians acquired adequate knowledge and experience and were more confident to treat patients without antibiotics unless indicated.

Despite the fact that patients in the second wave were sicker as evidenced by more symptoms, tachypnea and hypoxia on admission and laboratory parameters, the duration of hospitalization were significantly lower in the second wave. In the present study the average length of stay in the second wave was nearly 2 days less than in the first. This supports the findings of other research [21, 22, 25], which similarly found a shorter length of stay in the second wave. In addition more patients were discharged home in the second wave than transferred to quarantine facility. Possible explanation for this could be the change in discharge/transfer criteria. Secondly, better understanding of the

disease course and experience of managing the first wave made the health care professionals more confident in early discharge of patients in the second wave. Finally, better home surveillance of discharged patients, development of better follow up care, and community awareness and education might have also played an important role.

Even while the number of patients who needed to be transferred to a higher center, those who needed mechanical ventilation, had a pulmonary embolism and those who died were all somewhat higher in the second wave than in the first, the difference was not statistically significant. Available published data from two studies, one from Switzerland [21] and another from Turkey [25] found no significant difference in the proportion of patients requiring or at risk for Intensive Care Unit (ICU) admission in both the waves. However, the percentage of patients needing ICU care in the above two studies was higher than our results in both the waves. This could be related to the fact that our study and theirs had different severity of cases and also could be due to the difference in admission criteria in our study and others. Our admission criteria included patients with pneumonia requiring less than 4 L of oxygen at the time of admission, whereas other studies included more severe cases or ICU cases. Others have reported similar results, finding no substantial change in the number of patients requiring mechanical ventilation in both waves [24, 25]. There was no significant change in mortality rates between the two waves in the present study. Previous research comparing mortality rates between the two COVID-19 pandemic waves came up with mixed results. Our findings are consistent with those of Wolfisberg et al.[21] and Sargin et al. [25], who found no difference in mortality rates between the two waves, but Iftimie et al.[22] and Jarrett et al.[24] reported lower mortality in the second

wave, in contrast to our findings. Similarly, two studies from the United States found that the second wave had a reduced mortality rate [26, 27]. According to published statistics from Japan based on a public registry reported that the second wave of patients were younger, had fewer underlying co-morbidities, and had lower mortality rates [28].

A few studies from Europe also found lower mortality in the second wave. Chest X-ray severity of pneumonia, in-hospital mortality, and CRP readings were considerably greater in the first wave, according to an Italian study involving 200 Caucasian males over 50 years. They also discovered that the first wave had more patients who required mechanical ventilation [29]. Another study from Spain found that the second wave had younger patients, a shorter duration of stay in the hospital, fewer invasive mechanical ventilation, and decreased mortality [22].

The first wave's experience and lessons acquired by health care professionals, as well as a collaborative team effort involving numerous government agencies and community awareness and engagement, have helped us to manage the second wave more effectively.

Limitations

There were certain limitations to our research. To begin with, some data on co-morbidity and symptoms may have been overlooked due to the retrospective nature of the study. Second, there might have been selection bias because our research population was mostly male patients as most female COVID-19 patients were admitted to other COVID designated hospitals. Third, because our research sample included only mild to moderate Covid-19 infections, the findings may not

be generalized to severe COVID -19 infections. Finally, the relationship between risk variables and outcomes was not examined as it was not the primary goal of our study.

Recommendation for future research

Future study should compare the relationship between various risk variables and outcomes over serial COVID-19 waves. Long-term consequences of COVID-19 infection in the first and second waves can also be studied and compared.

Conclusions

Patients in the second wave were more symptomatic and unwell than those in the first wave, but they stayed in the hospital for a shorter time and were more likely to be discharged home, according to our data. The most prevalent symptoms in both waves were cough and shortness of breath, although they were much greater in the second wave. Diabetes mellitus and raised CRP levels were more common in the first wave, but hypoalbuminemia was more prevalent in the second wave. In the first wave, antibiotics and hydroxychloroquine were more commonly utilized, but in the second wave, steroids, antivirals, and interleukin-1 antagonists were more commonly employed. There was no significant difference in the need for mechanical ventilation or mortality rate between the two waves.

Author's contribution

VN- Study design, data collection, analysis, manuscript writing, editing

NP- Study design, data collection, analysis, manuscript writing, editing

PC- Study design, data analysis, editing

AS- Data collection, analysis

PR- Data collection, analysis

IV-Study design, editing

JM- Analysis, manuscript writing

JS-Data collection, literature review

RH- Data collection, manuscript writing

AB- Data collection, manuscript writing

AA- Data collection, editing

MB- Data analysis, manuscript writing

SA- Data collection, manuscript writing

MA-Data collection, editing

AA- Data collection, literature review

RA- Data collection, literature review

AK- Data analysis, manuscript writing, editing

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Competing interests' statement

The authors declare that they have no competing interest involved

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Data sharing statement

No additional data available

Ethical approval

The study was approved by the Institutional Review Board and Medical Research Center-institutional research committee of Hamad Medical Corporation (Approval # MRC-01-21-312).

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Table-1. Baseline epidemiological and clinical characteristics of patients during the first and second wave of the COVID – 19 pandemic

Variables	First wave (n=1039) n (%)	Second wave (n=991) n (%)	p- value
Age (in years)			
Mean ±SD	44.90 ±9.99	44.34 ±9.57	0.194**
18 - 35	202 (19.4)	192 (19.4)	0.896*
36 - 50	550 (52.9)	535 (54)	
51 -65	265 (25.5)	247 (24.9)	
Above 65	22 (2.1)	17 (1.7)	
Gender			
Male	989 (95.2)	877 (88.5)	<0.001*
Female	50 (4.8)	114 (11.5)	
Signs and symptoms			
Asymptomatic	48 (4.6)	94 (9.5)	<0.001*
Mean duration of symptoms in days ±SD	4.88 ±2.91	4.57 ±2.50	0.010**
Fever	893 (85.9)	870 (87.8)	0.220*
Respiratory symptoms	856 (82.4)	709 (71.5)	<0.001*
Flu like symptoms	192 (18.5)	358 (36.1)	<0.001*
Cough	823 (79.2)	862 (87)	<0.001*
Shortness of breath	286 (27.5)	377 (38)	<0.001*
Chest pain	43(4.1)	37(3.7)	0.639*
GI symptoms	88 (8.5)	66 (6.7)	0.124*
Vomiting	50 (4.8)	38 (3.8)	0.280*
Diarrhea	49 (4.7)	38 (3.8)	0.327*
Co-Morbidities			

Immunosuppression	12 (1.2)	4 (0.4)	0.056*
Chemotherapy	6 (0.6)	5 (0.5)	0.823*
Diabetes Mellitus	307(29.5)	217 (21.9)	<0.001*
Hypertension	270 (26)	263 (26.5)	0.777*
Coronary artery disease	41 (3.9)	26 (2.6)	0.095*
Chronic kidney disease	17 (1.6)	14 (1.4)	0.681*
Cancer	5 (0.5)	5 (0.5)	0.940*
Liver disease	3 (0.3)	6 (0.6)	0.283*
COPD/Asthma	19 (1.8)	8 (0.8)	0.045*
Body mass index (kg/m²)			
Mean ± SD	27.95 ±4.46	28.29 ± 4.83	0.263**
< 18.5	1(0.2)	6 (1.1)	0.360*
18.6 – 25	102 (24.5)	137 (25.4)	
25.1– 30	201 (48.2)	243 (45)	
>30	113 (27.1)	154 (28.5)	

*Pearson Chi-square test. **Unpaired t test.
Categorical and quantitative data expressed as frequencies and percentages (in parenthesis) and as mean ± SD.
In all statistical comparative analysis performed, second wave was considered as a reference group.
COPD: Chronic obstructive pulmonary disease

Table-2. Showing vital Signs and oxygen requirement

Variables		First wave (n=1039)	Second wave (n=991)	p- value*
Temperature ^{0}C Mean ±SD	On admission	37.3±0.75	37.3± 0.72	0.976
	Maximum	38.1±0.89	38.2±0.88	0.024
p-value**		<0.001	<0.001	
Pulse rate (Beats per minute) Mean ±SD	On admission	89±14	88±13	0.439
	Maximum	102±11	103±11	0.164
p- value**		<0.001	<0.001	
Respiratory Rate /min Mean ±SD	On admission	19±2	19±3	0.030
	Maximum	22±5	23±6	<0.001
p- value**		<0.001	<0.001	
Spo2 (%) Mean ±SD	On admission	97±2	97±1	0.327
	Lowest	94±4	93±5	<0.001
p- value**		<0.001	<0.001	
Patients received supplemental oxygen, number (%)	On admission	238 (22.9)	399 (40.3)	<0.001
	After admission	315 (30.3)	394(39.8)	<0.001
p- value***		<0.001	<0.001	

*Unpaired t test. **Paired t test. *** McNemar's Chi-Square test

In all statistical comparative analysis performed, second wave was considered as a reference group.

Table- 3. Showing laboratory parameters and chest X-ray findings

Variables	First wave Mean ±SD (Median, IQR)	Second wave Mean ±SD (Median, IQR)	p- value
WBC (10^3/ul)	6.49 ±2.41 (6.10, 4.80-7.60)	6.27 ±2.21 (5.90, 4.70-7.40)	0.031*
Hemoglobin (g/dl)	14.35±1.37 (14.40, 13.50-15.22)	14.16 ± 1.43 (14.20, 13.3-15.2)	0.003*
Platelet count (10^3/ul)	234.99 ±89.44 (217, 175-269)	225.55 ±82.50 (209, 168-259)	0.014*
Albumin (gm/L)	36.97 ±4.83 (37, 34-40)	35.58 ±4.94 (35, 32-39)	<0.001*
C-Reactive Protein (mg/L)	50.54 ±53.28 (35.35, 12.90-72.02)	33.68 ±44.20 (15.2, 15.20-32.20)	<0.001**
Lactate	1.74 ±0.77 (1.60, 1.20-2.10)	1.73±0.91 (1.50, 1.20-2.10)	0.924*
Procalcitonin	0.41 ±1.62 (0.11, 0.06-0.21)	0.30±1.15 (0.11, 0.06-0.21)	0.456**
D- Dimer	1.20 ±4.28 (0.44, 0.32-0.68)	1.10±3.84 (0.42, 0.30-0.63)	0.139**
Aspartate aminotransferase (AST)	44.14 ±34.47 (35, 26-50)	46.81 ±40.14 (37, 28-52)	0.020**
Alkaline phosphatase (ALP)	77.56 ±31.71(71, 59-87.5)	78.29±34.96 (71, 58-87)	0.626*
Alanine aminotransferase (ALT)	42.74 ±33.28 (32.9, 23-50.55)	44.30 ±34.24 (34, 24-54)	0.267**
Total Bilurubin	9.97 ±5.73 (8.30, 7-12)	9.57±6.20 (8.0, 6.0-11.0)	0.143*
HbA1c	7.37± 2.04 (6.60, 5.90- 8.40)	6.94± 1.83 (6.20, 5.80- 7.3)	<0.001*
Chest X ray findings			
Unilateral	185 (17.8)	236 (23.8)	0.001***

infiltrations			
Bilateral infiltrations	854 (82.2)	755 (76.2)	

*Unpaired t test. **Mann Whitney U test. ***Pearson Chi-Square test
IQR-Interquartile range
In all statistical comparative analysis performed, second wave was considered as a reference group.

Table -4. Showing the details of treatment received

Treatment†	First wave (n=1039) n (%)	Second wave (n=991) n (%)	p-value*
Dexamethasone	178 (17.1)	473 (47.7)	<0.001
Anticoagulation	1012 (97.4)	981 (99)	0.007
Favipiravir	230 (22.1)	704 (71)	<0.001
Hydroxychloroquine	920(88.5)	598 (60.3)	<0.001
Lopinavir/ ritonavir	369 (35.5)	630 (63.6)	<0.001
Anakinra	28 (2.7)	105 (10.6)	<0.001
Tocilizumab	21 (2.0)	19 (1.9)	0.866
Amoxicillin/clavulanic acid	633 (60.9)	290 (29.3)	<0.001
Ceftriaxone/ Cefuroxime	772 (74.3)	699 (70.5)	0.058
Azithromycin /Clarithromycin	770 (74.1)	415 (41.9)	<0.001
Piperacillin /tazobactum	51 (4.9)	68 (6.9)	0.061

*Pearson Chi-square test.
In all statistical comparative analysis performed, second wave was considered as a reference group.
†Some patients might have received more than one type of treatments.

Table- 5. Showing final outcomes and disposition

Variables	First Wave (n=1030) n (%)	Second wave (n=991) n(%)	p-value
Mechanical ventilation	28 (2.7)	40 (4.0)	0.093*
Pulmonary embolism/DVT	3 (0.3)	11 (1.1)	0.025*
Death	3 (0.3)	8 (0.8)	0.112*
Discharge disposition			
Discharge home	105 (10.1)	222 (22.4)	
Transfer to quarantine	879 (84.6)	705 (71.1)	
Transfer to higher center	55 (5.3)	64 (6.5)	<0.001*
Length of stay in days			
Mean ± SD	14.58 ±7.75	12.61 ±6.16	<0.001 **
0-7	227 (21.8)	126 (12.7)	
8-14	261 (25.1)	638 (64.4)	
15-30	529 (50.9)	212 (21.4)	
>30	22 (2.1)	15 (1.5)	<0.001*

*Pearson Chi-Square test. **Unpaired t test.

In all statistical comparative analysis performed, second wave was considered as a reference group.

Figure legends

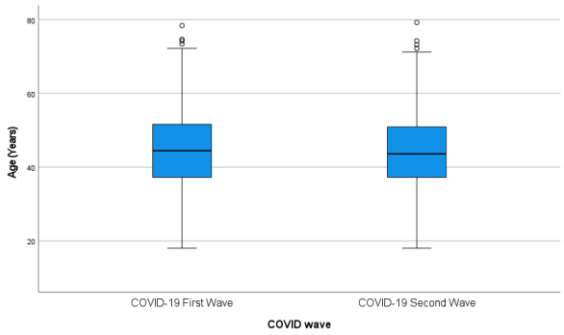
Figure 1.A-C. Box plot showing the distribution of age, duration of symptoms and BMI

Figure 2 A-D. Box plots depicting the vital signs
Figure 2.E-H. Box plots depicting the vital signs

Figure 3. A-F. Box plots depicting distribution laboratory parameters

Figure 3.G-K. Box plots depicting distribution laboratory parameters

A



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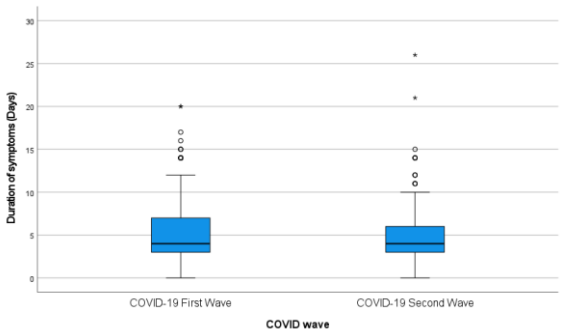

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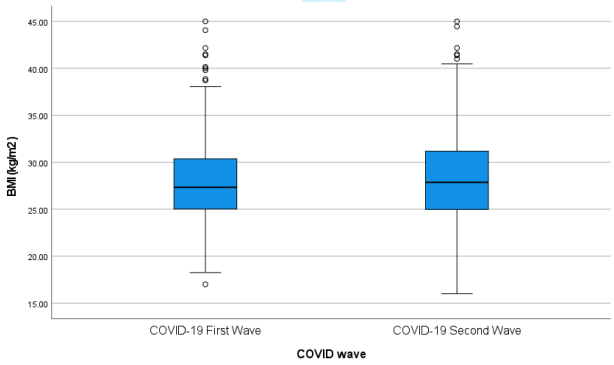


Figure 1.A-C.

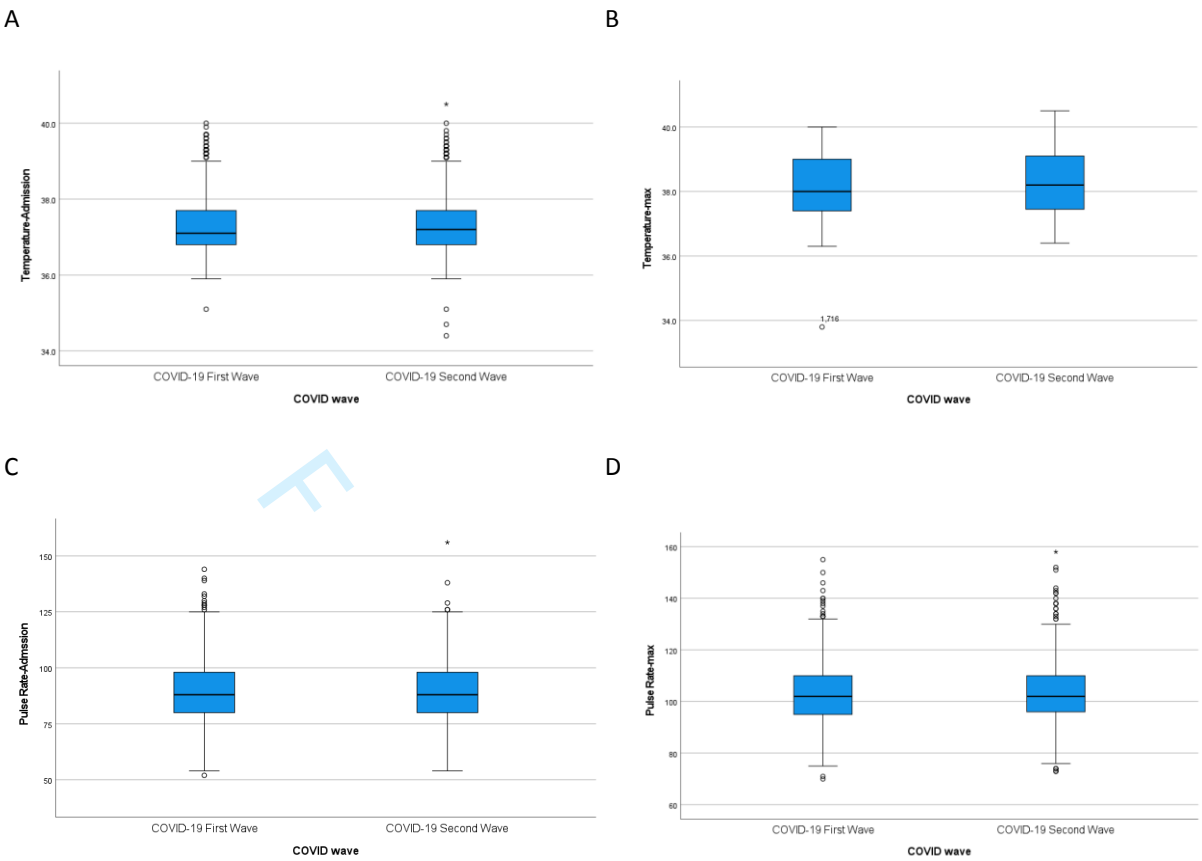


Figure 2 A-D.

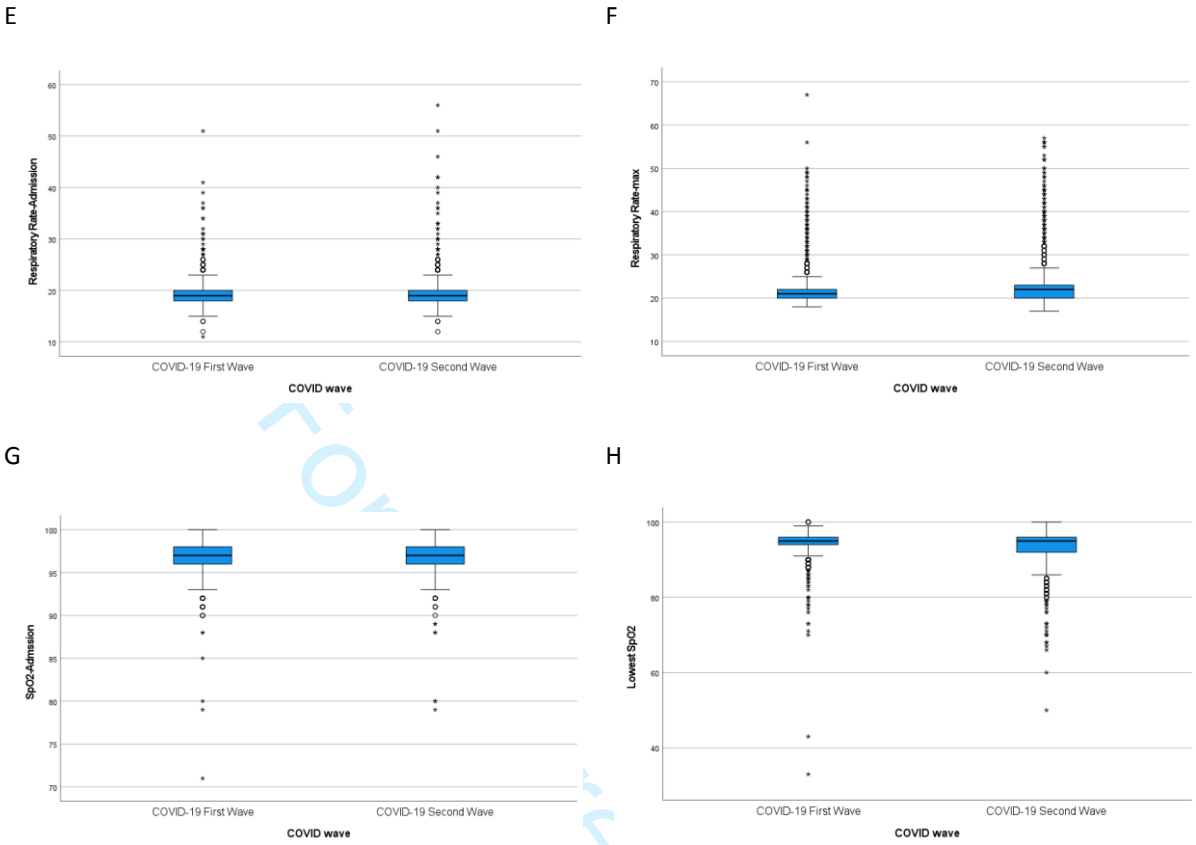


Figure 2 E-H. Boxplots depicting the vital signs

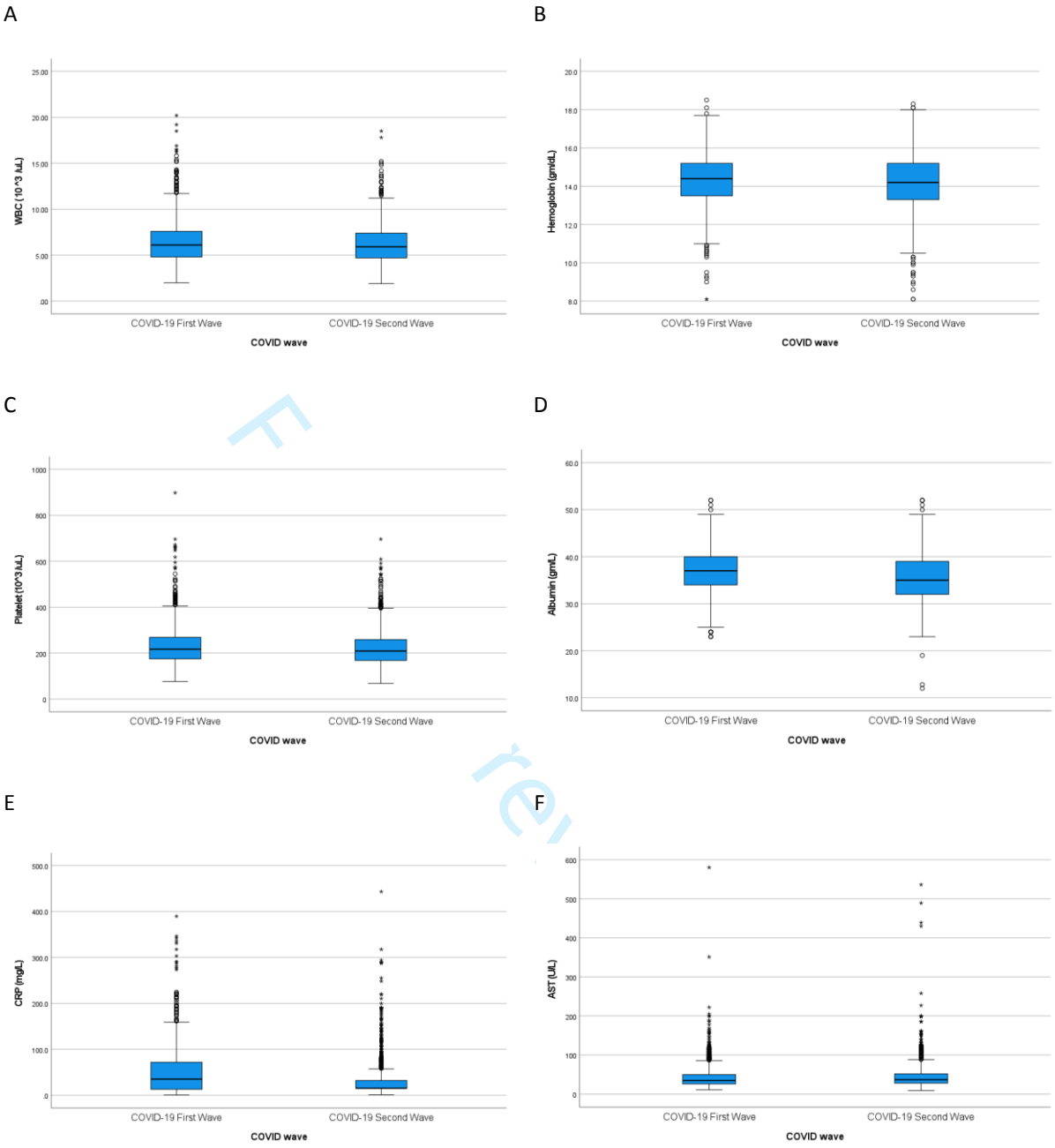
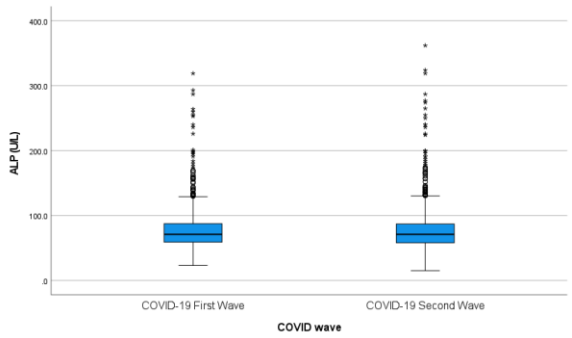

A
WBC (10^3 /uL)
COVID-19 First Wave
COVID-19 Second Wave
COVID wave
B
Hemoglobin (gm/dL)
COVID-19 First Wave
COVID-19 Second Wave
COVID wave
C
Platelet (10^3 /uL)
COVID-19 First Wave
COVID-19 Second Wave
COVID wave
D
Albumin (gm/L)
COVID-19 First Wave
COVID-19 Second Wave
COVID wave
E
CRP (mg/L)
COVID-19 First Wave
COVID-19 Second Wave
COVID wave
F
AST (U/L)
COVID-19 First Wave
COVID-19 Second Wave
COVID wave

Figure 3 A-F.

G



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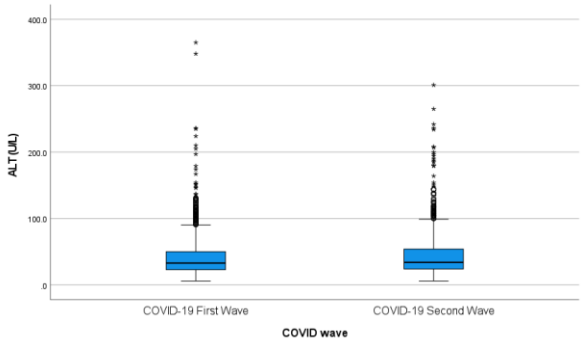

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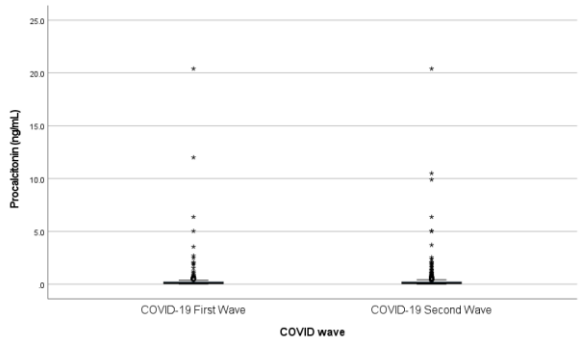

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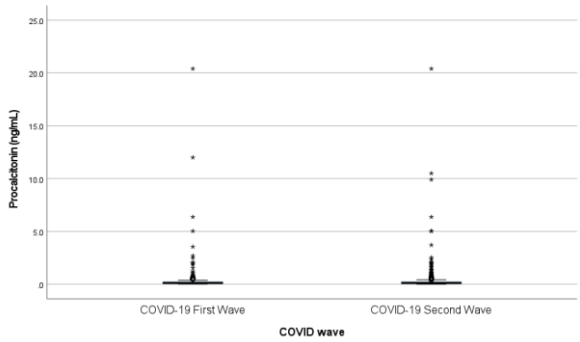

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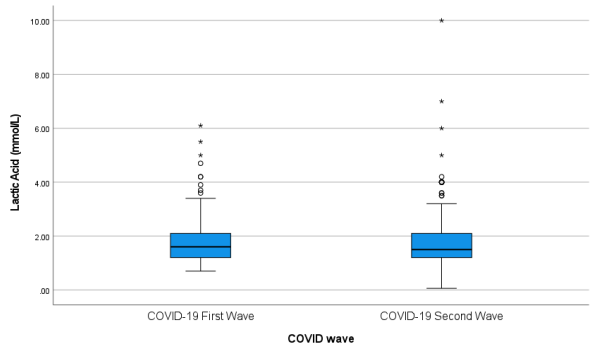

Figure 3 G-K.

Check list

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	4-5
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6-7
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	7
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	NA
Study size	10	Explain how the study size was arrived at	NA
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8-11
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8-11
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	11
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8-11
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	12-16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	16-17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12-16
Generalisability	21	Discuss the generalisability (external validity) of the study results	12-16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.