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Original Article

Clinical Characteristics and Treatment Outcomes of Mild to Moderate COVID-19 Patients at Tertiary Care Hospital, Al Baha, Saudi Arabia: A Single Centre Study



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ABSTRACT

Objective: Since the severity of symptoms affects the treatment option for Coronavirus Disease 2019 (COVID-19) patients, the treatment pattern for mild to moderate non-ICU cases must be evaluated, particularly in the current scenario of mutation and variant strain for effective decision making.

Methods: The objective of retrospective analysis was to assess clinical and treatment outcomes in mild to moderate symptoms in non-ICU patients with COVID-19 who were admitted to major tertiary care hospitals in Al Baha, Saudi Arabia, between April and August 2020.

Results: A total of 811 people were admitted for COVID-19 treatment, age ranging from 14 to 66, diabetes mellitus (31%, n = 248) and hypertension (24%, n = 198) were the most common comorbid conditions. The hydroxychloroquine (HCQ) treated group (G1 n = 466) had an MD of 8 and an IQR of 5–13 for time in hospital with a 4.3% mortality rate, while the non-HCQ group (G2 n = 345) had an MD of 6 and an IQR of 3–11 for time in hospital with a 3.2% mortality rate. A combination of antiviral and antibiotic treatment was found to be effective, other most frequent intervention was analgesics 85.7%, anticoagulant 75%, minerals (Zinc 83% and Vit D3 82%).

Conclusions: The therapy and clinical outcomes from the past will be the guiding factor to treat the COVID variants infection in the future. Patients treated with HCQ had a higher mortality rate, whereas those who were given a non-HCQ combination had a greater clinical outcome profile.

Data Availability: Data available on request due to ethical restrictions. The anonymized data presented in this study are available on request from the corresponding author. The data are not publicly available to maintain privacy and adhere to guidelines of the ethics protocol.

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Introduction

A new form of viral pneumonia case of unknown origin was identified in Wuhan, China, in late December 2019, and was later labelled as novel coronavirus disease [1,33,34]. COVID-19 is still affecting over 213 countries worldwide, including Saudi Arabia, owing

to this spread [2]. COVID-19 patients were categorized into mild, moderate, severe, and asymptomatic categories depending on the severity of the disease. Mild to moderate patients with COVID-19 have mild clinical symptoms that, if left untreated for a long time, can progress to serious cases [3,4]. Furthermore, the incidence of the disease tends to vary across populations due to detectable comorbid conditions, demographical attributes, and immune system responses. Pneumonia is the most common potential manifestation that has the potential to escalate into Acute Respiratory Distress Syndrome (ARDS) [5]. Septic shock, arrhythmias, and multi-organ

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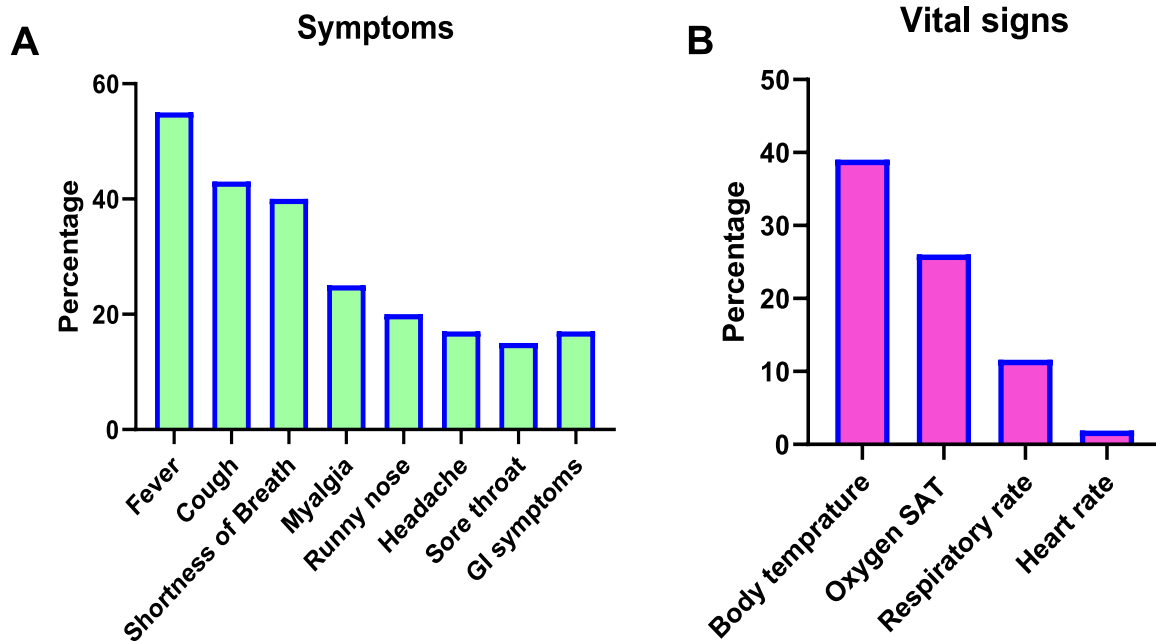


Fig. 1. Shows the (A) Percentage of the patients with the symptoms of COVID-19 and (B) Vital signs.

failure were among the other potentially serious complications reported [6,7]. The white blood cell count that has been reported varies as leukocytosis, lymphopenia and leukopenia, which can predict the COVID-19 patient outcomes [8,9]. Furthermore, there has been no irrefutable clinical evidence that cross immunity will occur due to prior exposure to identical strains of virus [10]. COVID-19 patients presented most probably with, dry cough, fever, and fatigue. Fever is the most common symptom in other infections as well [36]. A less abundant symptoms also reported such as hypogeusia, anosmia, headache and diarrhea. Moreover, the patients may have dyspnea, chest pain and loss of movement [7,11]. The large proportion of infected individuals with COVID-19 are asymptomatic which can transmit SARS-CoV-2 to other individuals and it is the most challenging issue [7].

The current scenario of immunization and vaccination is highly predicated to be end of the pandemic, but mutation, particularly the D614G mutation in the viral S-protein, which is now the most pervasive worldwide, has curtailed this hope [12,13,35]. Despite the fact that many antiviral drugs have been licensed for the care of COVID-19 patients, the lack of a scientifically validated successful treatment indicates that COVID-19 patient management is largely supportive, with the main aim being to reduce mortality [13]. In our previous publication we demonstrated the efficacy of hydroxychloroquine and other medications in the care of COVID-19 ICU patients using a cohort observational method [14]. The current retrospective study aims to evaluate the clinical and treatment outcomes in mild to moderate non-ICU COVID-19 patients in Saudi Arabia.

Materials and methods

Study design

We adopted single center, retrospective cohort study design for this instant study. The study was conducted on the non-ICU patients admitted in the tertiary care hospitals, Al Baha, Saudi Arabia between April 2020 to August 2020. All COVID-19 positive patients tested with RT-PCR test were included in the study. We used the retrospective cohort study design to assess the clinical and treatment outcomes in mild to moderate non-ICU COVID-19 patients in Saudi Arabia.

Data collection

A unified and predesigned data collection form was designed to collect data from non-ICU patient's electronic medical records which have pre-specified data variables. The collected data was only used for the benefits of this study. The demographics, clinical signs or symptoms, comorbidities, therapies received, outcomes and laboratory findings were obtained through data collection form. Moreover, the patients were divided into two groups as well. Group one patients were those who were receiving hydroxychloroquine therapy and group two patients were without hydroxychloroquine therapy. The privacy and integrity of collected data was ensured.

Data analysis

Data analysis was conducted by using the Statistical Package for Social Sciences program version 24 (SPSS-24). The descriptive statistical analysis was used to describe the baseline clinical characteristics and demographical data respectively. The categorical variables are expressed as counts, percentages and 95% confidence interval, on the other hand the continuous variables are expressed as means and standard deviations when data were normal or as interquartile ranges (IQRs) and medians (MDs) otherwise.

Ethical approval

The Scientific and Research Committee at King Fahad Hospital in Al Baha, Saudi Arabia, provided the approval (Protocol number 42193626 dated 09/09/2020) to this study. The details and information gathered is kept confidential. This study do not contain any personal details. This is a secondary analysis of routine monitoring data that has been anonymized.

Results

Demographics

The total 811 COVID-19 non-ICU patients were included in the study. Demographical data has been shown in Table 1 and Fig. 1. The ages of patients range from 14 up to 66 years old respectively. The

Table 1a
Demographics data of study population.

Age	(n = 811)	%	95% CI
14 <	49	6	4.50–7.90
15–25	99	12	10.13 – 14.64
26–35	117	14	13.86 – 20.50
36–45	136	17	14.36 – 19.50
46–55	152	19	16.21 – 21.57
56–65	120	15	12.52 – 17.41
66 >	138	14	14.59 – 19.76
Gender	(n = 811)		
Male	403	49.7	46.26 – 53.13
Female	408	50.3	46.87 – 53.74
Nationality	(n = 811)		
Saudi	681	84	81.29 – 86.33
Non-Saudi	130	16	13.67 – 18.71
Comorbidities	(n = 811)		
Diabetes mellitus	248	31	27.51 – 33.84
Hypertension	198	24	21.58 – 27.49
Pulmonary disease	54	7	5.14 – 8.59
Asthma	18	2.2	1.41 – 3.48
Renal failure	7	1	0.42 – 1.77
Smoking	(n = 811)		
Yes	258	32	28.70 – 35.10
No	533	66	62.39 – 68.91
Outcome	(n = 811)		
Alive	780	96	94.63 – 97.29
Death	31	4	2.71 – 5.37
Presence of clinical symptoms	(n = 811)		
Symptomatic	621	77	73.54 – 79.36
Asymptomatic	190	23	20.64 – 26.46

major age group of patients were 46–55 years old (19%, n = 152). Moreover, the elder patients had age of more than 66 years were (14%, n = 138) respectively. Furthermore, the majority of the patients were females (50.3%, n = 408) and males were (49.7%, n = 403). The major patients were Saudi national (84%, n = 681) and minority of patients were non-Saudi nationals (16%, n = 130). Furthermore, majority of patients were non-smokers (68%, n = 533) and some of them were smokers (32%, n = 258).

Comorbidities

The patients included in study have different comorbidities as well. The patients with diabetes mellitus were (31%, n = 248), hypertension (24%, n = 198), pulmonary disease (7%, n = 54), asthma (2.2%, n = 18) and renal failure (1%, n = 7) respectively. Shown in [Tables 1a](#) and [1b](#). ([Table 2](#)).

Clinical characteristics and symptoms

The majority of the patients were symptomatic (77%, n = 621), and some of them were asymptomatic (23%, n = 190). Furthermore, the clinical characteristics of the patients were fever (55%), cough

Table 1b
Shows all the comorbidities in patients admitted in hospital.

Age	DM		HTN		Pulmonary disease		Asthma		Renal Failure		Smoking		Symptomatic		Asymptomatic	
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
14 <	0	0	0	1	0	0	0	0	00	00	0	00	08	03	6	17
15–25	2	0	0	0	2	5	1	3	00	00	7	12	24	22	7	17
26–35	3	1	1	0	3	6	1	1	00	00	40	9	48	32	8	13
36–45	15	11	6	10	2	7	0	2	00	01	38	6	55	37	9	19
46–55	31	26	20	16	5	5	3	2	00	01	46	8	45	41	5	27
56–65	20	21	26	24	5	5	3	2	00	00	32	12	78	58	6	21
66 >	74	44	44	50	2	7	0	0	03	02	35	11	92	73	10	23
Total	145	103	97	101	19	35	08	10	03	04	198	60	350	271	53	137
	248		198		54		18		07		258		621		190	
P Value	< 0.0002 **		< 0.0001 **		0.1690		0.1269		0.0153		0.2045		< 0.0001 **		0.3134	

*P-value estimated using one way ANOVA and confirmed utilizing independent-samples Bonferroni test.

Table 2
Length of hospital stay.

	Mean	SD	Median	IQR
All patients	9	± 8.4	7	4–12
14 <	6.5	± 5.2	6	2–10
15–25	7	± 7.1	5	3–11
26–35	8.6	± 6.9	7	4–11
36–45	8.3	± 6.8	6	4–12
46–55	8.9	± 7.9	7	4–11
56–65	10	± 9.2	8	4–13
66 >	11.6	± 11.4	9	4–15

(43%), shortness of breath (61%), myalgia (28%), headache (27%), sore throat (15%) and GI symptoms (17%) respectively. Clinical characteristic details are shown in [Table 3](#), [Figs. 1](#) and [2](#).

Vital signs

The vital signs were recorded in the patients including temperature with MD and IQR of (37, 37–37), heart rate (1.9%) with MD and IQR (81, 70–90), respiratory rate (11.6%) with MD and IQR (24.5, 20–82), Oxygen SAT 26% with MD and IQR (90, 21–94). Vital signs are shown in [Table 3](#), [Figs. 1](#) and [2](#).

Laboratory findings

The laboratory test findings were also assessed which includes several important lab interventions. The WBC count was recorded to be less than $4 \times 10^9/l$ (15.7%, n = 127), normal range was recorded in majority of patients $4–12 \times 10^9/l$ (71%, n = 576) and more than $12 \times 10^9/l$ (13.3%, n = 108). The neutrophils count had MD and IQR (60, 48–72) with majority of cases 38.6% having less than 55% count, 32.4% cases have 55–70% count and 29% have more than 70% count respectively. Lymphocytes had MD and IQR (30, 19–41) with 29% of cases have less than 20% of lymphocytes, major cases 45.1% have 20–40% count and 26% cases have greater than 40% lymphocyte count. D-dimer was also recorded having MD and IQR (661, 403–1170) with 17% of cases having less than 80, 36.7% of cases having 80–583 D-dimer, and majority 46.3% of cases have greater than 583 D-dimer respectively. PTP, APTT, AST, ALT and ALP levels were also assessed with MD and IQR (12, 11–13), (30, 27–33), (25, 18–35), (24, 16–40) and (69, 54–92) respectively. Moreover, the MD and IQR of creatinine along with recorded levels are also shown in [Table 3](#). The levels of basophils and monocytes were also recorded to assess immune response of patients and depicted in [Table 3](#), [Figs. 1](#) and [2](#).

Therapy interventions

The patients were divided into two groups. The one group was receiving therapy of hydroxychloroquine and other group was not

Table 3
Clinical Characteristics and Symptoms.

Symptoms	(n=811)	%	95% CI
Fever	442	55	51.06 – 57.90
Cough	349	43	39.67 – 46.47
Shortness of Breath	325	40	36.76 – 43.49
Myalgia	202	25	22.05 – 28.00
Runny nose	158	20	16.90 – 22.35
Headache	135	17	14.24 – 19.37
Sore throat	117	15	12.18 – 17.01
GI symptoms	84	17	8.44 – 12.64
Vital Signs	(n=811)	%	95% CI
Temperature (Median, IQR)	37, 37-37		
Cases < 38	317	39	35.79 – 42.29
Heart rate (Median, IQR)	81, 70-90		
Cases < 100	16	1.9	1.22 – 3.18
Respiratory rate (median, IQR)	24.5, 20-82		
Cases < 24	94	11.6	9.57 – 13.98
Oxygen SAT (median, IQR)	90, 21-94		
Cases with SAT > 90%	211	26	23.12 – 29.14
Lab results	(n=811)	%	
WBC (median, IQR)	6, 4-8		
< 4	127	15.7	13.32 – 18.32
4 – 12	576	71	67.81 – 74.04
< 12	108	13.3	
Neutrophils (median, IQR)	60, 48-72		
> 55%	313	38.6	35.31 – 41.99
55 – 70%	263	32.4	29.30 – 35.73
< 70%	235	29	25.96 – 32.19
Lymphocytes (median, IQR)	30, 19-41		
> 20%	234	28.9	25.84 – 32.07
20-40%	366	45.1	41.74 – 48.57
< 40%	211	26	23.12 – 29.14
D-dimer (median, IQR)	661, 403-1170		
> 80	137	17	14.47 – 19.63
80-583	298	36.7	33.50 – 40.12
< 583	376	46.3	42.96 – 49.80
PTP (median, IQR)	12, 11-13		
> 12	466	57	54.03 – 60.82
12-14.6	278	34	31.09 – 37.61
< 14.6	67	8	6.56 – 10.36
APTT (median, IQR)	30, 27-33		
> 27	189	23	20.52 – 26.34
27-44	577	71	67.93 – 74.16
< 44	45	5.5	
AST (median, IQR)	25, 18-35		
> 15	83	10.3	8.33 – 12.51
15-41	582	71.7	68.57 – 74.75
< 41	146	18	15.51 – 20.80
ALT (median, IQR)	24, 16-40		
> 0	0	0	0
0-43	621	76.6	73.54 – 79.36
< 43	190	23.4	20.64 – 26.46
ALP (median, IQR)	69, 54-92		
> 40	59	7.2	5.68 – 9.27
40-129	655	80.8	77.91 – 83.33
< 129	97	12	9.90 – 14.38
Creatinine (median, IQR)	68, 54-85		
> 41.2	82	10.1	8.22 – 12.38
41.2-52.4	115	14.2	11.95 – 16.75
< 52.4	614	75.7	72.64 – 78.53
BUN (median, IQR)	4, 3-6		
> 2.5	60	7.4	5.79 – 9.41

Table 3 (continued)

2.5-6.3	573	70.6	67.43 – 73.68
< 6.3	178	22	19.24 – 24.93
Eosinophils (median, IQR)	1, 0-2		
> 1	428	53	49.33 – 56.19
1-4	321	39.6	36.27 – 42.99
< 4	62	7.6	6.01 – 9.68
Basophils (median, IQR)	0, 0-1		
> 0.5	430	53	49.58- 56.43
0.5-1	284	35	31.81 – 38.37
< 1	97	12	9.90 – 14.38
Monocytes (median, IQR)	8, 6-10		
> 2	27	3.3	2.30 – 4.80
2 - 8	395	48.7	45.28 – 52.14
< 8	389	48	44.54 – 51.41
HB (median, IQR)	14, 13-15		
> 12	127	16	13.32 – 18.32
12 – 16	575	71	67.68 – 73.92
< 16	109	13	11.26 – 15.96

receiving any hydroxychloroquine therapy. The group one (G1 n = 466) had MD 8 and IQR 5–13 for time in hospital along with 4.3% mortality rate. However, on the other hand group two (G2 n = 345) had MD 6 and IQR 3–11 for time in hospital along with 3.2% mortality rate. The P value was estimated for both time of hospital stay and mortality rates by using *t*-test and implementing Mann-Whitney U test for utilizing independent samples. The length of hospital stay for various age groups are shown in Table 4a and therapy outcomes shown in Table 4b and Fig. 3.

Treatment therapy

Antiviral/antimalarial/antibiotic medication was given to the patients alone or in combination with analgesics/antacids/anticoagulant/antithrombotic/ corticosteroids / vitamins/minerals based on the symptoms listed in Table 3. The patients (n = 6) were provided with antiviral treatment having mortality rate of 17% and odd ratio of 5.12, 0.59–45.6. Furthermore, the patients treated with antimalarial (n = 125), antibiotics (n = 133) therapy having mortality rate of 3% and 4% respectively along with odd ratios 0.8, 0.28–2.3 for antimalarial and 0.98, 0.37–2.6 for antibiotics. However, many patients were treated with combination therapies as well the mortality rates along with P-values and Odd ratios are shown in Table 5. Moreover, some patients (n = 173) categorized as asymptomatic with mild symptoms or no symptoms were treated with only analgesics/antacids/vitamins/minerals without any antiviral, antibiotic, or antimalarial treatments.

Drug category

The different drug categories were provided for the treatment of patients. The important drug categories provided to the patients are shown in Table 6 provided as supplement. The analgesics 85.7%, anticoagulant 75%, antimalarial (Hydroxychloroquine 57.5%), minerals (Zinc 83%), Vit. D3 82%, antibiotics (Ceftriaxone 43% and Azithromycin 35%), corticosteroids (Methylprednisolone 18% and Dexamethasone 14%), antivirals (Favipiravir 6.5%, Oseltamivir 14%, Lopinavir/Ritonavir 2% and Ribavirin 2%) antithrombotic 22% and immunomodulators (Interferon beta – 1B 1%) were the most important drug categories provided as the treatment interventions to the patients.

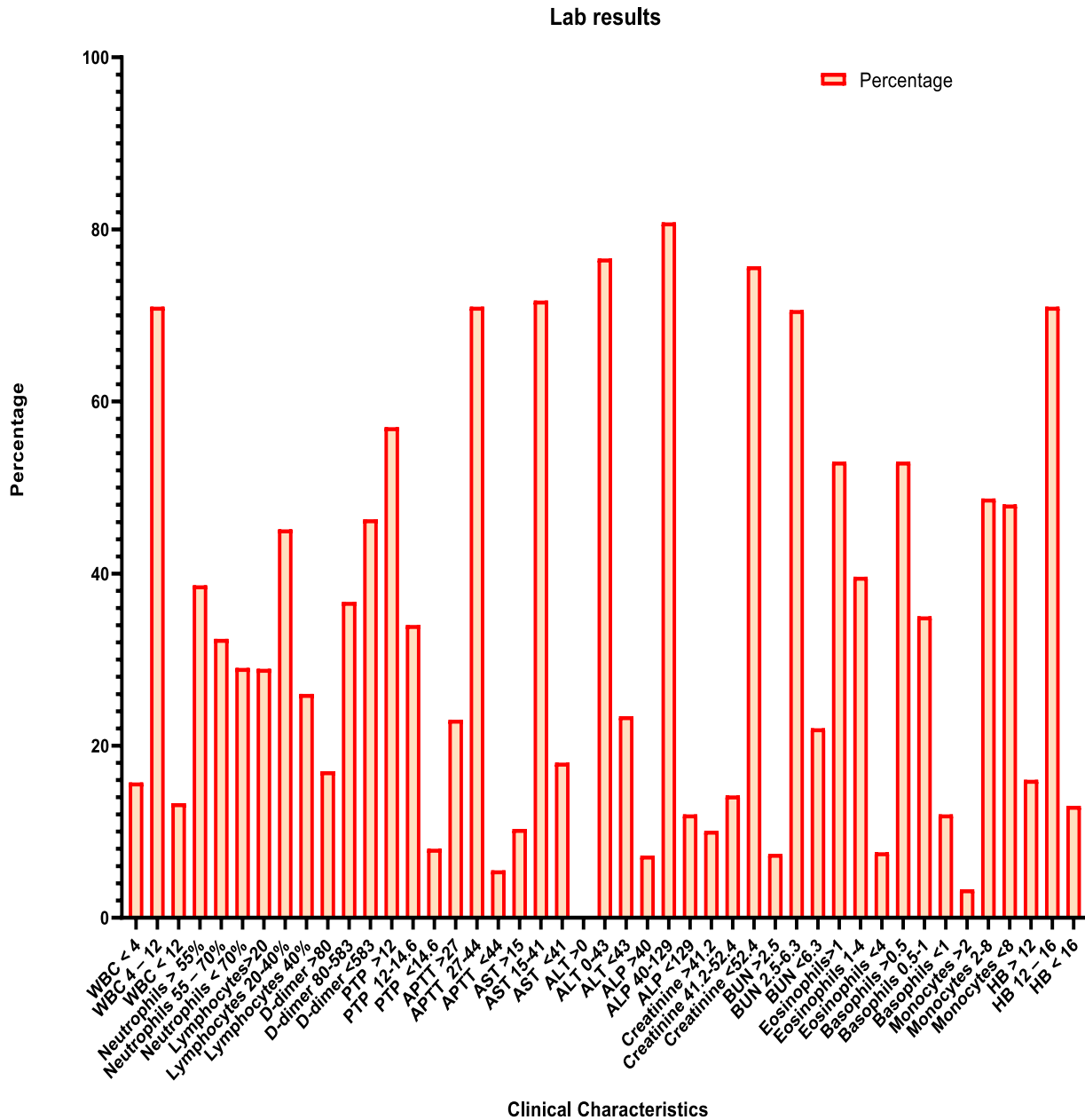


Fig. 2. Shows percentage of clinical characteristics of patients.

Table 4a
Treatment Therapy.

Outcome	G1 (n = 466)				G2 (n = 345)				P-value
	Mean	SD	Median	IQR	Mean	SD	Median	IQR	
Time in hospital	9.9	8.4	8	5–13	7.8	8.3	6	3–11	< 0.001 *
Mortality rate (Death)	N		%		N		%		0.422
	20		4.3		11		3.2		

Group 1 (G1): Patient's treatment regimens include Hydroxychloroquine.
Group 2 (G2): Patient's treatment regimens DO NOT include Hydroxychloroquine.

Discussion

COVID-19 is a global pandemic that has been sweeping the world since December 2019. This study was the single-centre retrospective cohort study that was conducted to summarizing the demographics, clinical characteristics and outcomes of mild to moderate COVID-19 patients admitted in tertiary care hospitals in Saudi Arabia. The

clinical features of COVID-19 are highlighted in this study was done on all age groups. Certain studies suggested that age is the primary risk factor for the severity of COVID-19 disease, as it has been mentioned in some studies that over the age of 50 is known to be at high risk, whilst others claim that over the age of 60 is at high risk [15,16]. In our findings, male and female covid 19 patients were identified in almost equal proportions, but three studies from Riyadh

Table 4b
Percentage of mortality in male and female patients, with age.

n = 811					
	Total	Death	Percentage Mortality	95% CI	P value
Male	403	19	4.71%	2.33–6.65	P < 0.001 **
Female	408	12	2.94%	1.76–4.21	
n = 811					
	Age	Death	Percentage Mortality	95% CI	0.2321 (> 0.05)
Male	< 50	1	0.36%	0.02–0.58	
	50–70	7	12%	9.12–14.21	
	> 70	11	16%	14.34–18.41	
Female	60–70	5	1%	0.48–1.42	
	> 70	7	5.83%	3.63–7.52	

*P-value estimated using t-tests and confirmed utilizing independent-samples Mann-Whitney U test.

city hospitals reported more male patients than female patients. This difference is due to the characteristic of a metropolitan city with a large percentage of male foreigner population [17–19]. The COVID-19 have incubation period of 1–14 days and majority of studies conducted reported that the patients presented with cough, fever, sputum, dyspnoea and fatigue [16,20,21]. Recently, the median incubation period of SARS-CoV-2 reported in Saudi Arabia is 6 days [21]. In our study the most common symptoms of COVID-19 were fever, cough and dyspnoea which has been compared with the percentage of another similar single centre study conducted in Wuhan (China). The patients with fever 52.3%, cough 70.40% and dyspnoea 18.39% respectively [22]. When compared to other most afflicted nation, the majority of Saudi Arabians had mild-moderate symptoms [23]. It has been noted that in our study the majority of patients presented with dyspnoea. Moreover, the GI symptoms were

also present in our patients. Furthermore, the comorbidities also contributed into the risk factor for COVID-19 infection. In our study the high number of patients were diabetic, it has been cited in the study that diabetes contributes in COVID-19 infection due to elevated ACE-2 receptors and furin proprotein [24,25]. The study reported 8% COVID-19 fatality rate in patients with diabetes [26]. Moreover, the risk for ICU admissions with diabetic comorbidity is 14.2% higher than the individuals who are without diabetes [27]. The comorbidity of hypertension was also present in patients included in our study. We need to be vigilant frequently because in Italy the 73.8% of deceased patients had hypertension [15]. HCQ use by COVID-19 patients hospitalized in the United States did not increase the probability of survival, according to a major study published in the United States [11]. Our findings are consistent with observations in the literature that the use of an HCQ-containing regimen for the care of COVID-19 patients did not have therapeutic benefits [28]. Our data shows that the patients treated HCQ had a higher mortality rate, whereas those who were given a non-HCQ combination had a greater clinical outcome profile. In a study conducted at King Salman Hospital (KSH) in Riyadh, Saudi Arabia, patients treated with HCQ had a lower death rate than those who were not [18]. This study does not specify if it was taken alone or in conjunction with another medicine. The data in our study clearly show that taking HCQ with antiviral and antibacterial drugs increased mortality when compared to taking HCQ alone. This is in line with other studies that have been published [14,28]. Alsuwaidan et al. found that HCQ improved fever symptoms in COVID-19 patients with no comorbidities, however they did not look at mortality rates [29]. Alotaibi et al. compared favipiravir to HCQ in COVID-19 patients and found that favipiravir patients had slightly greater mortality, which differs from our findings. This could be attributed to the higher percentage of comorbidity in the investigated patients. In contrast, they identified a

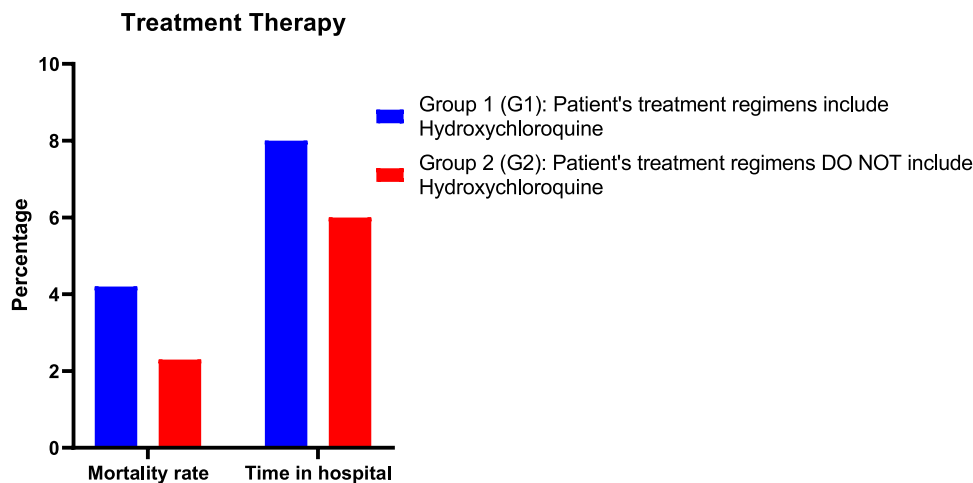


Fig. 3. Represents percentage of mortality and hospital stay time in patients treated with hydroxychloroquine and non-hydroxychloroquine.

Table 5
Drug Category.

Treatment therapy	n	Alive	Died	P value	Odd ratio (95% CI)
Antiviral therapy ^a	6	5 (83%)	1 (17%)	0.209	5.12, 0.59–45.6
Antimalarial therapy ^a	125	121 (97%)	4 (3%)	0.805	0.8, 0.28–2.3
Antibiotics therapy ^a	133	128 (96%)	5 (4%)	0.976	0.98, 0.37–2.6
Antiviral+ Antimalarial therapy ^a	11	10 (91%)	1 (9%)	0.350	2.57, 0.32–20.7
Antiviral+ Antibiotics therapy ^a	33	30 (91%)	3 (9%)	0.127	2.68, 0.78–9.3
Antimalarial + Antibiotics therapy ^a	212	204 (96%)	8 (4%)	0.966	0.98, 0.43–2.23
Antiviral+ Antimalarial+ Antibiotics therapy ^a	118	111 (94%)	7 (6%)	0.196	1.76, 0.74–4.18
Others ^b	173	171 (83%)	2 (17%)	0.042	4.07, 0.96–17.23

^a supplemented with analgesics/antacids/anticoagulant/antithrombotic/ corticosteroids / vitamins/minerals as per the symptoms.

^b without any antiviral, antibiotics, antimalarial drugs but supplemented with analgesics/ antacids/corticosteroids/vitamins/minerals as per the symptoms.

greater rate of mortality in HCQ patients than in our studied patients with lower comorbidity condition [30]. Vitamin D insufficiency has been reported in COVID-19 patients, and it has been linked to severity and death [19,31]. The lack of measurement of vitamin D deficiency was a limitation in our study. All three studies [19,31,32] concluded that vitamin D supplementation reduced hospital stay and mortality, and our investigation confirmed the same results.

Conclusion

In this single center study, mostly death rate was seen in HCQ treated patients, although other variables may be contributed in mortality, an association between these groups and comorbidity needs to be identified. Comorbidity played a significant role in the increased death rate in COVID – 19 infected patients. Interestingly, in Saudi Arabia, the effects were not as severe, and there were fewer deaths compared to other major affected countries. Our findings indicate that combination therapy had favorable outcomes, but whether this approach is applicable in future outbreaks from COVID variants remain to be proven.

Conflicts of Interest

The authors declare no conflict of interest.

Author's contribution

M.Ab. and S.A.I. developed conceptualization. M.Az., B.B., A.H. data collection, statistical analysis and writing. J.A.M. and Sa. A. data curation. S.A. writing, editing, critical review and finalizing.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.jiph.2022.02.001](https://doi.org/10.1016/j.jiph.2022.02.001).

References

- Wang C, Horby PW, Hayden FG, Gao GF. A novel coronavirus outbreak of global health concern. *Lancet* 2020;395:470–3.
- Ebrahim S, Memish Z. Saudi Arabia's measures to curb the covid-19 outbreak: temporary suspension of the Umrah pilgrimage. *J Travel Med* 2020;20.
- Chen Z, Tian Y, Liu L, An J. Production of a monoclonal antibody against non-structural protein 3 of dengue-2 virus by intrasplenic injection. *Hybridoma* 2008;27:467–71.
- Yang Y, Hu X, Xiong L, et al. Clinical characteristics of hospitalized mild/moderate COVID-19 patients with a prolonged negative conversion time of SARS-CoV-2 nucleic acid detection. *BMC Infect Dis* 2021;21:1–8.
- Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395:497–506.
- Chen T, Wu D, Chen H, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. *BMJ* 2020;368.
- Arentz M, Yim E, Klaff L, et al. Characteristics and outcomes of 21 critically ill patients with COVID-19 in Washington State. *JAMA* 2020;323:1612–4.
- Yang J, Zheng Y, Gou X, et al. Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis. *Int J Infect Dis* 2020;94:91–5.
- Tan L, Wang Q, Zhang D, et al. Lymphopenia predicts disease severity of COVID-19: a descriptive and predictive study. *Signal Transduct Target Ther* 2020;5:33.
- Severance EG, Bossis I, Dickerson FB, et al. Development of a nucleocapsid-based human coronavirus immunoassay and estimates of individuals exposed to coronavirus in a US metropolitan population. *Clin Vaccin Immunol* 2008;15:1805–10.
- Fu L, Wang B, Yuan T, et al. Clinical characteristics of coronavirus disease 2019 (COVID-19) in China: a systematic review and meta-analysis. *J Infect* 2020;80:656–65.
- Malik JA, Mulla AH, Farooqi T, et al. Targets and strategies for vaccine development against SARS-CoV-2. *Biomed Pharm* 2021;111254.
- Mishra SK, Tripathi T. One year update on the COVID-19 pandemic: where are we now? *Acta Trop* 2020;105778.
- Alghamdi S, Barakat B, Berrou I, et al. Clinical efficacy of hydroxychloroquine in Patients with COVID-19: findings from an observational comparative study in Saudi Arabia. *Antibiotics* 2021;10:365.
- Onder G, Rezza G, Brusaferro S. Case-fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. *JAMA* 2020;323:1775–6.
- Liu K, Chen Y, Lin R, Han K. Clinical features of COVID-19 in elderly patients: a comparison with young and middle-aged patients. *J Infect* 2020;80:e14–8.
- Alguwaihes AM, Al-Sofiani ME, Megdad M, et al. Diabetes and Covid-19 among hospitalized patients in Saudi Arabia: a single-centre retrospective study. *Cardiovasc Diabetol* 2020;19:205.
- Sheshah E, Sabico S, Albakr RM, et al. Prevalence of diabetes, management and outcomes among Covid-19 adult patients admitted in a specialized tertiary hospital in Riyadh, Saudi Arabia. *Diabetes Res Clin Pr* 2021;172:108538.
- Alguwaihes AM, Sabico S, Hasanato R, et al. Severe vitamin D deficiency is not related to SARS-CoV-2 infection but may increase mortality risk in hospitalized adults: a retrospective case-control study in an Arab Gulf country. *Aging Clin Exp Res* 2021;33:1415–22.
- Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020;395:1054.
- Alsafayan YM, Althunayyan SM, Khan AA, et al. Clinical characteristics of COVID-19 in Saudi Arabia: a national retrospective study. *J Infect Public Health* 2020;13:920–5.
- Shu L, Wang X, Li M, et al. Clinical characteristics of moderate COVID-19 patients aggravation in Wuhan Stadium Cabin Hospital: a 571 cases of retrospective cohort study. *J Med Virol* 2021;93:1133–40.
- Yezli S, Khan A. COVID-19 social distancing in the Kingdom of Saudi Arabia: bold measures in the face of political, economic, social and religious challenges. *Travel Med Infect Dis* 2020;37:101692.
- Rao S, Lau A, So H-C. Exploring diseases/traits and blood proteins causally related to expression of ACE2, the putative receptor of SARS-CoV-2: a Mendelian randomization analysis highlights tentative relevance of diabetes-related traits. *Diabetes Care* 2020;43:1416–26.
- Fernandez C, Rysä J, Almgren P, et al. Plasma levels of the proprotein convertase furin and incidence of diabetes and mortality. *J Intern Med* 2018;284:377–87.
- Yang J, Zheng Y, Gou X, et al. Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis. *Int J Infect Dis* 2020;94:91–5.
- Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected Pneumonia in Wuhan, China. *JAMA* 2020;323:1061–9.
- Alahmari AA, Khan AA, Elganainy A, et al. Epidemiological and clinical features of COVID-19 patients in Saudi Arabia. *J Infect Public Health* 2021;14:437–43.
- Alsuwaidan S, Memish ZA, Alaklobi F, et al. The utilization of hydroxychloroquine to reduce the main signs and symptoms of COVID-19 patients, a cross-sectional study. *Annu Med Surg* 2021;70:102867.
- Alotaibi M, Ali A, Bakhshwin D, et al. Effectiveness and safety of favipiravir compared to hydroxychloroquine for management of Covid-19: a retrospective study. *Int J Gen Med* 2021;14:5597–606.
- Al-Daghri NM, Amer OE, Alotaibi NH, et al. Vitamin D status of Arab Gulf residents screened for SARS-CoV-2 and its association with COVID-19 infection: a multi-centre case-control study. *J Transl Med* 2021;19:166.
- Sabico S, Enani MA, Sheshah E, et al. Effects of a 2-week 5000 IU versus 1000 IU vitamin D3 supplementation on recovery of symptoms in patients with mild to moderate Covid-19: a randomized clinical trial. *Nutrients* 2021;13(7):2170. <https://doi.org/10.3390/nu13072170>
- Farooqi T, Malik JA, Mulla AH, Al Hagbani T, Almansour K, Ubaid MA, et al. An overview of SARS-COV-2 epidemiology, mutant variants, vaccines, and management strategies. *J Infect Public Health* 2021 <https://doi.org/10.1016/J.JIPH.2021.08.014>.
- Malik JA, Maqbool M. COVID-19: An overview of current scenario. *CELLMED* 2020;10:211–8 <https://doi.org/10.5667/CELLMED.2020.0021>.
- Malik JA, Ahmed S, Mir A, Shinde M, Bender O, Alshammari F, et al. The SARS-CoV-2 mutations versus vaccine effectiveness: New opportunities to new challenges. *J Infect Public Health* 2022;15:228–40 <https://doi.org/10.1016/J.JIPH.2021.12.014>.
- Alzahrani MA, Sadoma HHM, Mathew S, Alghamdi S, Malik JA, Anwar S. Retrospective Analysis of Antimicrobial Susceptibility of Uropathogens Isolated from Pediatric Patients in Tertiary Hospital at Al-Baha Region, Saudi Arabia. *Healthcare* 2021;9:1564.