Dubai Medical Journal

Dubai Med J DOI: 10.1159/000516591 Received: September 17, 2020 Accepted: April 18, 2021 Published online: June 3, 2021

Clinical Profile of Mortality and Treatment Profile of Survival in Patients with COVID-19 Pneumonia Admitted to Dubai Hospital

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Keywords

 $COVID-19 \cdot Corona \cdot SARS-CoV-2 \cdot Clinical \ profile \cdot Steroids \cdot Outcomes \cdot Chloroquine$

Abstract

Background: Most COVID-19 studies conclude old age and coexisting illnesses as mortality determinants owing to different populations or methodologies, or omitting factors affecting outcomes. Methods: We analyzed COVID-19 patients' data (N = 391) of Dubai Hospital between January 1, 2020 and June 30, 2020. Results: Only 19 patients (4.8%) were UAE nationals, while 372 (95.2%) were expatriates. Median age was 48 (interquartile range, 40–56) years; 22% were <40 years, and only 16.6% were female. Cough was the most common symptom (78.7%), fever was 77.4%, and gastrointestinal symptoms were least common (13.8%). Approximately 95% had elevated C-reactive protein (CRP) and D-dimers (79%), lymphocytopenia 47.3%, and thrombocytopenia 13.8%. Mortality was 30% for the total sample and 50% in ICU patients. ICU patients were older than non-ICU (age; 49.6 ± 10.9 vs. 46.7 \pm 12.7 years, p = 0.04). Eighty-five percent of ICU pa-

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Introduction

COVID-19 is a novel beta coronavirus, first identified in Wuhan city, China, with a genetic makeup 96% identical to a bat coronavirus [1, 2]. Epidemiologic investigations and contact tracing of initial cases reveal that the COVID-19 outbreak started from a Wuhan fish market selling various animals such as rabbits, snakes, and bats [3]. COVID-19 is transmitted from human to human through contact, respiratory droplets, and fecal route [4]. Due to the rapid spread and sharp rise in mortality and morbidity, the World Health Organization declared CO-VID-19 as a pandemic in March 2020 [5]. As of August 2020, the World Health Organization reports that the UAE has 60,999 cases with 351 deaths [6]. Limited descriptive data are available for demographics, presenting characteristics and outcomes of the UAE population's hospitalized COVID-19 patients.

Patients with COVID-19 usually present with fever, myalgias, nonproductive cough, and progressive shortness of breath. In moderate to severe cases, signs of organ dysfunction, such as acute respiratory distress syndrome (ARDS), acute kidney injury, pulmonary edema, myocarditis, septic shock, and deaths, can occur [7]. Most COVID-19 studies [8] conclude that old age and coexisting illnesses are mortality determinants. We do not agree with this conclusion as our clinical observation suggests otherwise due to predominantly young patients and the United Arab Emirates [9]. Moreover, we believe other studies might not have adjusted for confounders affecting outcomes. We aimed to answer this question by including many clinical variables affecting outcome in our statistical analysis.

Objectives

We aimed to study the attributes of severe and fatal disease in the unique UAE population and analyze survival determinants in this cohort. Our outcomes of interest were mortality (survival) and length of stay in the ICU and hospital.

Methods

This study is a retrospective, single-center study of all patients' electronic medical records (EMR) with proven COVID-19 pneumonia admitted to Dubai Hospital, United Arab Emirates. We performed detailed statistical subgroup analysis, which may help clinicians, researchers, and authorities optimize future management of COVID-19 pneumonia. We created a list of clinical parameters for our study and extracted the following data from Dubai Hospital EMR system. We included all admitted patients with pneumonia who are PCR-positive for COVID-19 between January 1, 2020 and June 30, 2020 and excluded all patients <18 years. Demographics data included recent travel history, clinical signs, and symptoms on admission. We collected the following laboratory data: white blood cell counts, lymphocyte counts, platelets count, blood chemistries, renal indices, coagulation profile, liver function tests, inflammatory and disease markers including C-reactive protein (CRP), ferritin, procalcitonin, lactate dehydrogenase, creatinine kinase, and D-dimers. Daily levels of important markers affecting clinical decision-making were also recorded to collect a detailed daily profile of average D-dimers, CRP, ferritin, and procalcitonin.

Repeated nasopharyngeal or tracheal swab results have recorded the evidence of seroconversion as per protocol. We recorded the number of days to conversion and the number of swabs performed. Other culture studies include blood cultures. Treatment profiles were recorded to use chloroquine, antivirals, antibacterials, immunosuppressives, plasma therapy, and steroids. We also recorded the use of invasive mechanical ventilation, recruitment maneuvers, prone positioning, continuous renal replacement therapy (CRRT), and extracorporeal membrane oxygenation.

Definitions, clinical characteristics, and signs and symptoms were categorized as present or absent, for example, fever and cough. Laboratory characteristics were categorized in some cases (lymphopenia for count <1,500 cells per cubic milliliters) or continuous numerical variables (WBC, CRP, ferritin, D-dimer, and procalcitonin). Diagnosis of diseases, ARDS, pneumonia, acute kidney failure, acute heart failure, and rhabdomyolysis was extracted from EMR as charted by clinicians taking care of the patients. All laboratory tests included PCR confirmation of COV-ID-19 and were performed at the Dubai Hospital Laboratory.

Statistical Analyses

Continuous variables were expressed as medians with interquartile range when not normal distribution and mean \pm standard deviation for normal distribution. Categorical variables were presented as counts and percentages. Patients who survived were compared to patients who did not survive. Categorical variables were compared by the χ^2 test, while continuous outcome variables were evaluated by the Mann-Whitney test. Subgroup analyses were also performed: critical versus noncritical, mechanically ventilated versus not ventilated, and different treatment groups (anticoagulants, chloroquine, steroids, and anticoagulation). Multiple logistic regression analyses were performed to determine survival predictors. First, univariate analysis was conducted, and then those variables that were found to be significant were included in the final logistic regression analysis. All analyses were performed with SPSS version 26 (IBM Corp., Armonk, NY, USA).

Results

Demographic and clinical characteristics of our study sample (N, 391) with COVID-19 pneumonia who were admitted to Dubai Hospital are shown in Tables 1–2. Only 19 patients (4.8%) were UAE nationals, while 372

Clinical feature	All patients, n (%)	Mortality	<i>p</i> value*		
	(<i>N</i> = 391)	died = 119 alive = 272			
Female	65 (16.6)	13 (10.9)	52 (19.1)	0.045	
Expatriates	379 (96.9)	119 (100)	260 (95.5)	0.020	
Fever	333 (85.1)	105 (88.2)	228 (83.8)	0.259	
Cough	308 (78.7)	98 (82.3)	212 (77.9)	0.322	
Dyspnea	279 (71.3)	94 (78.9)	185 (68)	0.027	
Gastric symptoms	54 (13.8)	15 (12.6)	39 (14.3)	0.648	
Diabetes	158 (40.4)	48 (40.3)	110 (40.4)	0.984	
Hypertension	89 (22.7)	31 (26)	58 (21.3)	0.305	
CAD	27 (6.9)	12 (10)	15 (5.5)	0.101	
Renal disease	50 (12.7)	21 (17.6)	29 (10.6)	0.057	
Immunodeficiency	19 (4.8)	7 (5.8)	12 (4.4)	0.534	
History of travel	12 (3)	0	12 (4.4)	0.020	
Known exposure	44 (11.2)	11 (9.2)	33 (12.1)	0.406	
Clinical variables, n (%)					
Inpatient fever	300 (76.7)	101 (84.8)	199 (73.1)	0.012	
Tachycardia	259 (66.2)	100 (84)	159 (58.4)	< 0.001	
Hypotension	129 (32.9)	70 (58.8)	59 (21.6)	< 0.001	
Hypoxia	255 (65.2)	107 (89.9)	161 (59.1)	< 0.001	
Mechanical vent	200 (51.1)	104 (87.3)	96 (35.2)	< 0.001	
Vasopressors	186 (47.5)	102 (85.7)	84 (30.8)	< 0.001	
CRRT	71 (18.1)	50 (42)	21 (7.7)	< 0.001	
Bacterial infection	121 (30.9)	64 (53.7)	57 (20.9)	< 0.001	
Bacteremia	94 (24)	53 (44.5)	41 (15)	< 0.001	
Lymphopenia	185 (47.3)	66 (55.4)	119 (43.7)	0.033	
Treatment, n (%)					
Chloroquine	324 (82.8)	99 (83.1)	225 (82.7)	0.909	
Lopinavir/ritonavir	107 (27.3)	51 (42.9)	56 (20.5)	< 0.001	
Favipiravir	301 (76.9)	85 (71.4)	216 (79.4)	0.084	
Steroids	226 (57.8)	87 (73.1)	139 (51.1)	< 0.001	
Tocilizumab	45 (11.5)	22 (18.4)	23 (8.4)	0.004	
ECMO	12 (3)	7 (5.8)	5 (1.8)	0.033	
Sedatives	208 (53.1)	113 (94.9)	95 (34.9)	< 0.001	
Narcotics	178 (45.5)	94 (78.9)	84 (30.8)	< 0.001	
Paralytics	199 (50.8)	104 (87.3)	95 (34.9)	< 0.001	
Anticoagulation	350 (89.5)	114 (95.7)	236 (86.7)	0.007	
GI prophylaxis	352 (90)	113 (94.9)	239 (87.8)	0.031	

Table 1.	Sample	characteristics	(categorical	variables)

CAD, coronary artery disease; CRRT, continuous renal replacement therapy; ECMO, extracorporeal membrane oxygenation. * χ^2 to compare categorical variables.

patients (95.2%) were expatriates. The patients' median age was 48 (interquartile range, 40–56) years; 22% of the patients were younger than 40 years. Only 16.6% were female. Eighty-five percent of the patients reported a fever history at home, and 77.4 percent had a fever on admission. The most common symptom was cough (78.7%), and the least common were gastrointestinal complaints (13.8%). Among the overall population, 40% had diabetes, 23% had hypertension, and only 6% had heart disease. Patients admitted to the ICU were older than those not admitted in the ICU (49.6 \pm 10.9 vs. 46.7 \pm 12.7 p = 0.04). Moreover, diabetes (43 vs. 39%) and hypertension (25 vs. 21%) were more common among patients admitted to the ICU than those not admitted to the ICU. Among patients admitted to the ICU, 85% required invasive mechanical ventilation, 78% required vasopressors, and 30% required CRRT on admission. In contrast, none needed in the group were admitted to the medical ward.

Continuous variable	Median (IQR)	Median (IQR)			
	(<i>N</i> = 391)	died = 119	alive = 272		
Age, years	48 (40-56)	49 (42–56)	47.5 (41.5–53.5)	0.004	
BMI, kg/m ²	27.3 (24–31)	30 (26.2–33.73)	27 (23.95-30.05)	0.005	
Oxygen, L/m	6 (0-15)	10 (3.25–16.75)	15 (12.5–17.5)	0.001	
Ferritin, ng/mL	1,102 (478–1,804)	1,434 (661.5-2206.5)	1,362 (630-2,094)	0.017	
D-dimer, µg/mL	1.01 (0.52-3.08)	1.54 (0-3.13)	1.09 (0-2.51)	0.001	
CRP, mg/L	106 (57–188)	118.7 (53.4–184)	134.9 (66.5-203.2)	0.001	
Procalcitonin, ng/mL	0.27 (0.11-0.89)	0.36 (0-0.91)	0.34 (0.45-0.635)	0.001	
PH (ABG)	7.38 (7.28-7.43)	7.39 (7.31-7.46)	7.42 (7.35-7.48)	0.418	
PCO2, torr	37.3 (31.3-47.3)	36.8 (30.55-43.05)	36.8 (28.8-44.7)	0.827	
PO2, torr	62.6 (47-88.5)	62.6 (46.9-78.25)	61.8 (41.45-82.15)	0.559	
Bicarbonate, mmol/L	21.6 (18.9–24)	22.1 (19.2–25)	22.3 (20.1-24.5)	0.402	
Magnesium, mg/dL	2.04 (1.9-2.2)	2.07 (1.89-2.25)	2.03 (1.84-2.21)	0.467	
Platelets, ×1,000/µL	203 (155-263)	173 (129–217)	209 (158-260)	0.181	
APACHE 2 score	16 (13–21)	17 (12.5–21.5)	15 (12–18)	0.017	
Outcomes	Median (IQR)	Median (IQR)	Median (IQR)	<i>p</i> value	
Days in ICU	14 (5.0–23)	11 (4–18)	18 (6.5–29.5)	0.003	
Days on MV	11 (5.0–21)	11 (4–18)	14 (5–23)	0.184	
LOS hospital	19 (9.0–33)	14 (7–21)	32 (14.5-49.5)	0.001	

Table 2. Sample characteristics (continuous variables)

CRP, C-reactive protein; APACHE, Acute Physiology and Chronic Health Evaluation. * Mann-Whitney U test is used to compare variables.

On admission, lymphocytopenia was present in 47.3% and thrombocytopenia in 13.8% of hospitalized patients. Most of the patients (>95%) had elevated levels of CRP and D-dimers (79%). Multiple swabs for COVID-19 PCR were performed (mean =5 swabs). Patients took a long time for seroconversion as documented by COVID-19 PCR swab for ICU patients compared to non-ICU patients (15 vs. 13 days p = 0.01).

Among the patients admitted to the ICU, extracorporeal membrane oxygenation was utilized in 13 patients, among whom 6 of them survived (46%); MV is required in 85%, vasopressors were required in 79%, sedation in 88%, and muscle paralysis in 84% patients. Survivors have less proportion on sedatives (p = 0.01). Paralytics use was not statistically different between survivors and nonsurvivors. CRRT was utilized in 30% of patients for renal impairment. Survivors were less likely to be treated with CRRT than nonsurvivors (18 vs. 42% p = 0.01). More than half of the patients had evidence of secondary bacterial infections during ICU stay. There was no significant difference in the prevalence of bacterial infections between survivors and nonsurvivors. However, bacteremia was more common in nonsurvivors than survivors (44.5 vs.

15%, *p* 0.022). Only 12% underwent tracheostomy; 80% of those who had tracheostomy survived, compared to 44% who did not have a tracheostomy. Comparison of treatment profiles of survivors versus nonsurvivors is presented in Tables 1–2.

Mortality was 30% for the total sample (N 391) and 50% for those admitted to the ICU (N 240). Among the mechanically ventilated (N = 200) patients, more than half (52%) died.

The median duration of hospitalization was 19 (IQR 9–33) days, ICU stays 14 (IQR 5–23) days, and ventilator days 11 (IQR 5–21) days. Analysis of outcome measures of LOSICU, LOSH, and ventilator days by the Mann-Whitney test showed that survivors spent more days in the ICU (median [IQR] 18 [6.5–29.5] vs. 11 [4–18], *p* value 0.003) and in the hospital (32 [14.5–49.5] vs. 14 [7–21], *p* value 0.001) than nonsurvivors. Ventilator days were not statistically different between the 2 groups (14 [5–23] vs. 11 [4–18], *p* value =0.18). Multiple logistic regression analysis determined age, inpatient fever, use of oxygen, mechanical ventilation, and steroids as predictors of mortality (Table 3). We constructed a Kaplan-Meier plot for the impact of steroids on LOS (Fig. 1).

Table 3. Multiple	logistic	regression -	predictors	of mortality
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Variable	В	<i>p</i> value	Odds ratio	95% CI for odds ratio	
				lower	upper
Female gender	0.096	0.913	1.100	0.197	6.131
Dyspnea	0.158	0.816	1.171	0.310	4.423
Inpatient fever	2.070	0.039	7.922	1.115	56.289
Tachycardia	0.175	0.793	1.192	0.323	4.399
Hypotension	-0.312	0.587	0.732	0.238	2.254
Ventilation	2.530	0.027	12.548	1.342	117.306
Vasopressors	-1.464	0.198	0.231	0.025	2.148
Dialysis	-0.086	0.880	0.917	0.299	2.815
Bacterial infection	0.189	0.785	1.208	0.311	4.691
Bacteremia	0.210	0.765	1.234	0.312	4.877
Lymphopenia	-0.284	0.569	0.753	0.284	1.998
Lopinavir/ritonavir	-0.708	0.141	0.493	0.192	1.264
Steroids	2.229	0.011	9.293	1.658	52.083
Tocilizumab	-1.113	0.061	0.328	0.103	1.051
ECMO	0.277	0.782	1.320	0.185	9.408
Sedatives	-2.484	0.332	0.083	0.001	12.606
Narcotics	0.333	0.663	1.395	0.311	6.256
Paralytics	-0.208	0.923	0.812	0.012	54.282
Anticoagulation	-2.697	0.252	0.067	0.001	6.786
GI prophylaxis	-0.944	0.551	0.389	0.017	8.705
Age, years	0.054	0.038	1.056	1.003	1.112
BMI	-0.003	0.863	0.997	0.959	1.036
Oxygen	-0.099	0.019	0.906	0.834	0.984
Ferritin	0.000	0.134	1.000	1.000	1.001
D-dimer	-0.006	0.815	0.994	0.945	1.046
CRP	0.000	0.890	1.000	0.995	1.006
Procalcitonin	-0.014	0.799	0.986	0.884	1.100
APACHE-2 score	0.004	0.923	1.004	0.923	1.092

CRP, C-reactive protein; APACHE, Acute Physiology and Chronic Health Evaluation; ECMO, extracorporeal membrane oxygenation.

Discussion

Our sample predominantly includes young, male expatriates of the UAE, admitted in Dubai Hospital with COVID-19 pneumonia and with pre-existing medical illnesses. Our median sample age was 48 years, which is different from the Italian population (>70 years) and American patients (67 years) [10, 11]. Obesity was a predictor of mortality in American patients [11], while our sample's mean BMI was 27, and it was not a predictor of mortality. Percent of expatriates was not known for the American or European population, while our sample includes 95% expatriates.

Our study's survival rate was 70%, which is like recent studies [12], and higher than that in earlier studies with insufficient data about follow-up [1, 13, 14]. Survival among those requiring invasive mechanical ventilation

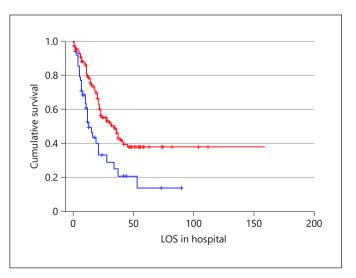


Fig. 1. Kaplan Meier plot for effect of steroids on length of stay.

was 48%, which is less than that other studies [9, 15]. One reason could be that previous studies had incomplete follow-up data as they were published with the ongoing pandemic.

Among the mechanically ventilated patients, those treated with steroids had better survival than those not treated with steroids (52 vs. 36%, p = 0.04). Similar results were reported by the RECOVERY trial [16]. Among patients with nonsevere disease and those not requiring mechanical ventilation, treatment with steroids adversely affected survival (61 vs. 79%, p = 0.01). A recent trial from Brazil did not detect any survival benefit from steroids [15]. Treatment with steroids has been documented to be a predictor of mortality in mild disease [16].

Steroid dosages and duration was variable – hydrocortisone from 200 to 400 mg/day or methylprednisolone 40–80 mg/day or dexamethasone 12–32 mg/day. Duration ranges from single dose on admission to more than 2 weeks course. The choice of steroid, dose, and duration was at the discretion of the treating physician.

Treatment with chloroquine was similar between survivors and nonsurvivors (82.7 vs. 83.1%, p = 0.6), which are like results reported by Cavalcanti et al. [17]. However, survivors were less frequently treated with lopinavir-ritonavir (20.5 vs. 42.9%, p = 0.01). Among mechanically ventilated patients, survival with lopinavir-ritonavir was also worse (40 vs. 55%, p = 0.04). A recent trial also showed no survival advantage with lopinavir-ritonavir treatment [18]. Prior studies [19] found multiple factors predicting mortality, such as age and comorbid conditions, which we did not predict; most likely, our population and methodology were different. We also adjusted for numerous confounding factors known to determine mortality. Arbitrary exclusion of many such confounders in our hypothetical model also provided us similar predictors of mortality; therefore, the omission of confounding factors may have played a role in other studies.

Patients requiring vasopressors and CRRT reflect the severity of organ dysfunction; therefore, finding these factors as determinants of survival for COVID-19 pneumonia is no surprise. Similar results were documented by other studies [20]. CRP, ferritin, and D-dimers were significantly lower in patients who survived, and they were not predictors of survival, as suggested by other studies [20]. This difference in results is most likely due to differences in methodology, statistical modeling, and different inclusion of confounding factors.

Our study has the following weaknesses. This study is a retrospective, single-center, community hospital study; therefore, results may not apply to other populations. To our knowledge, no research has documented the clinical profile of patients who had died from COVID-19 pneumonia in the Middle East with the inclusion of all relevant clinical predictors as we did. Other studies found many predictors of survival, including steroids. Well-designed, prospective, multicenter trials with large sample size, preferably with the inclusion of all critical clinical factors affecting survival, are urgently needed to determine a better management strategy.

Conclusion

Patients affected by COVID-19 were predominantly young, expatriate males with pre-existing conditions of diabetes and hypertension. Outcomes with chloroquine, antivirals, and anticoagulation were not different between survivors and nonsurvivors. The majority admitted suffered severe ARDS requiring invasive mechanical ventilation and renal replacement therapy. Markers of disease activity, ferritin, CRP, and D-dimers were higher in patients who died. Multiple logistic regression analyses determined steroid treatment to be a predictor of mortality.

Statement of Ethics

Ethical approval was provided by DSREC-07/2020_10/approved on July 13, 2020 (according to Local Ethical Committee guidelines, for retrospective medical records chart review observational studies; no consent from patients are required).

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

The authors did not receive any funding.

Author Contributions

R.N.: conceived the research idea, proposal writing, data collection, data analysis, and manuscript writing. I.A. and A.E.: conceived the idea, proposal writing, and review of final manuscript. C.D. and N.A.: idea conception and data collection. M.K.: data collection. M.A., M.J., A.N., S.T., S.S., M.H., M.K., I.B., A.E., L.S., S.K., and R.A.: idea conception and data collection.

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