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Coronavirus Pandemic

The outcomes of severe COVID-19 pneumonia managed with supportive care in Palestine: an experience from a developing country

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Abstract

Introduction: About 14% of COVID-19 patients experience severe symptoms and require hospitalization. Managing these patients could be challenging for limited-resource countries, such as Palestine. This study aimed to evaluate hospitalized severe COVID-19 patients' treatment outcomes managed with supportive care and steroids.

Methodology: This was a single-center observational retrospective cohort study that enrolled COVID-19 patients admitted to the "Martyrs medical military complex- COVID Hospital" in Palestine. The managing physicians manually collected data through chart reviews, including patients' characteristics, complications, outcomes, and different management modalities. Continuous and categorical variables between those who were discharged alive and who died were compared using t-test and Chi-squares test, respectively.

Results: Overall, 334 patients were included in this study. Median (IQR) age was 62 (11) years, 49.1% were males, and 29.6% were ICU status patients. The median (IQR) PaO_2/FiO_2 ratio was 76 (67), and 67.6% of these patients had moderate to severe acute respiratory distress syndrome, and 4.8% of the patients received invasive mechanical ventilation. Most of the patients (78.7%) had at least one comorbidity, and 18.3% developed at least one complication. The overall mortality was 12.3% (95% CI 8.9-16.2%), and the median (IQR) length of hospital stay was 11 (8) days. Age (aOR 1.05, $p = 0.08$), smoking (aOR 4.12, $p = 0.019$), IMV (aOR 27.4, $p < 0.001$) and PaO_2/FiO_2 ratio (aOR 1.03, $p < 0.001$) were found to predict higher mortality.

Conclusions: Supportive care for patients with severe COVID-19 pneumonia in a Palestinian hospital with limited resources was associated with in-hospital mortality of 12.3%.

Key words: Supportive care; steroids; mortality rate; severe COVID-19; risk factors; Palestine.

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Introduction

Since the first COVID-19 case was discovered in China in late 2019, and as of January 6, 2021, the pandemic has had more than 84 million confirmed cases and had claimed more than 1.8 million lives worldwide [1]. COVID-19 presentation is unpredictable; symptoms range from being asymptomatic to fatal. The majority experienced fever, cough, or shortness of breath, 36% had muscle aches, and 34% reported headaches [2]. While reports from China showed that 81% of COVID-19 cases were mild, 14% were severe and required hospitalization, and 5% were critical [3]. Patients may present with lower respiratory symptoms and develop pneumonia, sepsis and septic shock, or thromboembolism. The disease may progress to respiratory or multi-organ failure, including acute kidney injury (AKI) and cardiac injury, or eventually, death [4]. Supportive care is the mainstay of treatment, while other therapies are used inconsistently, depending on existing literature over time and the available resources in different countries. The management of COVID-19 patients depends on the severity of the disease. For severe and hospitalized cases, the standard of care is close monitoring, supportive care, including oxygen escalation therapies as needed and corticosteroids based on the recovery trial [5], and finally, if available, remdisivir is given to shorten recovery time as shown in the ACTT-1 trial [4,6]. However, such remdesivir findings were not replicated in the solidarity trial [7]. Many countries also adopted

convalescent plasma after reviewing patient registry data from the Mayo Clinic [8]. For our cohort in Palestine, the mainstay of therapy for hospitalized COVID-19 patients was dexamethasone and supportive care because neither remdesivir nor convalescent plasma were available.

There is limited evidence regarding other therapies, including antivirals, antimicrobials, immune-based therapy, vitamins, and minerals. The national institute of health guidelines did not support these therapies [4]; hence were not in our protocol. Higher dexamethasone dose (20 mg dexamethasone IV for 5 days followed by 10 mg IV for additional 5 days or till discharge) had been reported to be effective in patients with moderate to severe Acute respiratory distress syndrome (ARDS) and COVID-19, as shown in the CODEX trial [9]. Some retrospective studies suggested better outcomes when intermediate low molecular weight heparin (LMWH) dosage was used for deep vein thrombosis (DVT) prophylaxis compared to standard prophylactic LMWH dosage [10]. An ongoing randomized controlled trial, Anti-thrombotic for Adults Hospitalized With COVID-19 (ACTIV-4), will hopefully provide guidance regarding the best DVT prophylaxis strategy for hospitalized COVID-19 patients [11]. Recent studies have shown potential benefit from Tocilizumab in hospitalized COVID-19 patients [5,12,13].

This study aimed to evaluate the in-hospital mortality rate, hospital length of stay (LOS), complications, and treatment outcomes of hospitalized severe COVID-19 patients. We also investigated our practice's impact, which were supportive care and steroids managed entirely by internal medicine physicians and general practitioners in a hospital with limited resources.

Methodology

Study design and population

A single-center observational retrospective cohort study was conducted between June and December 2020 in the Martyrs Medical Military Hospital, a government-own care facility for managing COVID-19 patients in the Northern part of West Bank in Palestine. This referral hospital for severe COVID-19 cases is managed by internal medicine specialists and general practitioners. It had 25 beds and 7 intensive care unit (ICU) beds, 7 high flow oxygen therapy devices, 5 non-invasive positive pressure devices, and 7 ventilators.

Inclusion criteria included being adult patients, hospitalization for more than 24 hours, and severe COVID-19 diagnosis. COVID-19 diagnosis was confirmed when reverse transcription-polymerase chain reaction was positive. Patients were excluded if they did not meet the above criteria. All aspects of the study protocol, including access and use of patients' clinical information, complied with the world medical association code of ethics. Institutional Review Boards (IRB) approval was obtained from the Palestinian Ministry of Health.

Data Collection

We did a paper charts review and collected data from hospital records on patients' demographics, comorbidities, COVID-19 complications, and management. These included baseline characteristics; age, gender, smoking status, diabetes, cardiovascular disease (CVD), asthma or chronic obstructive pulmonary disease (COPD), cancer, and chronic kidney disease (CKD) based on KDIGO definition [14] and baseline complications like; acute kidney injury (AKI) according to RIFLE criteria [15], and acute coronary syndrome (ACS) including unstable angina, STEMI, and NSTEMI according to the fourth universal definition of myocardial infarction [16]. Oxygen saturation on admission and the worst Po2/Fio2 ratio during the hospital stay data were collected. Further, we recorded the proportion of patients who needed low flow oxygen therapy (LFOT), high flow oxygen therapy (HFOT), non-invasive positive pressure ventilation (NIPPV), the use of invasive mechanical ventilation (IMV), and the hospital length of stay (LOS). Prophylactic versus therapeutic anticoagulation and regular versus high dose dexamethasone data were recorded.

Clinical definitions

Severe COVID-19 was defined as severe pneumonia with clinical signs, such as fever, cough, dyspnea, fast breathing with any of the following: respiratory rate > 30 breaths/min; severe respiratory distress; or SpO2 < 90% on room air [17]. Acute respiratory distress syndrome (ARDS) and its classifications (mild, moderate, and severe) were defined according to the Berlin definition [18].

Patients were considered ICU status if they were admitted to the ICU or they met ICU admission criteria and received ICU level care (HFOT, NIPPV, or IMV) and monitoring outside the ICU on medical floors due to lack of ICU beds. ICU admission criteria included hemodynamic instability or worsening acute respiratory failure necessitating escalation of oxygen therapies from LFOT; nasal cannula, simple facemask, non-rebreather mask (NRB) to HFOT, NIPPV, or IMV.

Oxygen therapy was escalated in patients from NRB to HFOT to NIPPV. If all of these measures failed to improve oxygenation to > 90% and patients continued to have increased breathing difficulty, intubation and IMV were considered with the patients' consent.

Our patients' supportive care included close monitoring, oxygen therapy, and awake prone position as tolerated by the patients, dexamethasone, and conservative fluid therapy. A higher than usual enoxaparin dose (40 mg twice daily or 60 mg daily) for venous thromboembolism prophylaxis and dexamethasone (6 mg IV daily for ten days) in all admitted patients. We also used therapeutic enoxaparin dose (1 mg/kg twice daily) and high dose dexamethasone regimen (20 mg for five days followed by 10 mg for five days) in all ICU patients with COVID-19 pneumonia. A high D-dimer > 1200 ng/mL (whenever available) and therapeutic LMWH dose for clinical suspicion of venous thromboembolism and low bleeding risk were considered.

This study's outcome of interest was in-hospital mortality of COVID-19 patients. The study population was classified into two groups: discharged alive or dead. We included all patients who died in the hospital as COVID-19 related death regardless of the immediate cause of death. We did not follow up with patients after discharge, and our outcomes were limited to the hospital stay.

Statistical analysis

All statistical analyses were done with IBM SPSS Statistics for Windows, Version 20.0 (IBM Corp., Armonk, NY: IBM Corp). Continuous variables were expressed as mean ± standard deviation (S.D.) or median (interquartile range (IQR)). Counts and percentages described categorical variables. We

Table 1. Baseline characteristics of the COVID-19 patients with in-hospital mortality (n = 334).

Characteristic	Total	Dead (n = 41)	Alive (n = 293)	p-Value*
Age (median (IQR))	62 (13)	62 (12)	63 (17)	0.005**
Gender				
Male	164 (49.1)	22 (13.4%)	142 (86.6%)	0.533
Female	170 (50.9)	19 (11.2%)	151 (88.8%)	
Smoker				
Yes	94 (28.1)	13 (13.8%)	81 (86.2%)	0.588
No	240 (71.9)	28 (11.7%)	212 (88.3%)	
Comorbidities				
Yes	263 (78.7)	38 (14.4%)	225(85.6%)	0.02
No	71 (21.3)	3 (4.2%)	68 (95.8%)	
Diabetes				
Yes	182 (45.5)	27 (14.8%)	155 (85.2%)	0.119
No	152 (54.5)	14 (9.2%)	138 (90.8%)	
Hypertension				
Yes	200 (59.9)	27 (13.5%)	173 (86.5%)	0.405
No	134 (40.1)	14 (10.4%)	120 (89.6%)	
Cardiovascular disease				
Yes	97 (29)	19 (19.6%)	78 (80.4%)	0.009
No	237 (71)	22 (9.3%)	215 (90.7%)	
Lung disease				
Yes	29 (8.7)	3 (10.3 %)	26 (89.7%)	0.74
No	305 (91.3)	38 (12.5%)	267 (87.5%)	
Cancer				
Yes	19 (5.7)	3 (15.8%)	16 (84.2%)	0.631
No	315 (94.3)	38 (12.1%)	277 (87.9%)	
CKD				
Yes	30(9)	5 (16.7%)	25 (83.3%)	0.442
No	304(91)	36 (11.8%)	268 (88.2%)	
***PaO₂/FiO₂* ratio** (median (IQR))	76 (67)	61 (31)	85 (72)	<0.001**
ARDS				
Mild	108 (32.3)	2 (1.9%)	106 (98.1)	<0.001
Moderate	121 (36.2)	3 (2.5%)	118 (97.5%)	
Severe	105 (31.4)	36 (34.3%)	69 (65.7%)	

* Chi-square test; ** Mann Whitney U test; ACS: acute coronary syndrome; AKI: acute kidney injury; IMV: invasive mechanical ventilation; LFOT: Low Flow O2 Therapy; HFOT: High Flow O2 Therapy; NIPPV: Non-invasive positive pressure ventilation.

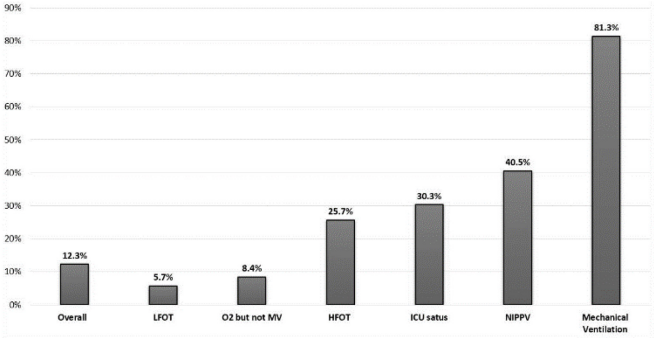
explored data for normality using the Kolmogorov–Smirnov test. Continuous variables with normal distribution between those who were discharged alive and those who died were compared using a t-test. In contrast, variables with non-normal distribution were compared using the Mann-Whitney U test. Chi-squares test compared categorical variables between the two groups, with subgroup analysis comparing ICU vs. non-ICU patients.

We conducted a multivariate analysis using binary logistic regression to assess the relationship between risk factors and to predict in-hospital mortality. Variables included in the model were selected based on previously identified predictors in the literature as age, gender, smoking status, hypertension, CVD, P.F. ratio, and the need for IMV (19–24). We computed the chi-square (x^2 = 105.1, df = 7, p < 0.001) Hosmer-Lemeshow (p = 0.823) and Nagelkerke pseudo-*R-squared* (0.514) goodness-of-fit statistics, which showed the model a good fit to describe the data. A two-sided P-value of < 0.05 was considered statistically significant.

Results

Overall, 334 confirmed cases of severe COVID-19 were reviewed. Table 1 summarizes the basic characteristics of our cohort. The median (IQR) age was 62 (11) years, and the females were 50.9%. Hypertension, diabetes, CVD, and lung diseases were reported in 59.9%, 54.5%, 29%, and 8.7% of the patients, respectively. All patients required oxygen therapy and met the ARDS criteria. The median (IQR) PaO_2/FiO_2 (P.F.) ratio was 76 (67), and mild, moderate, and severe ARDS was observed in 32.3%, 36.2%, and 31.4% of the patients, respectively.

Figure 1. Overall, ICU admissions and Mechanical ventilation COVID-19 patients' mortality rates.



LFOT: Low Flow O2 Therapy; HFOT: High Flow O2 Therapy; NIPPV: Non-invasive positive pressure ventilation.

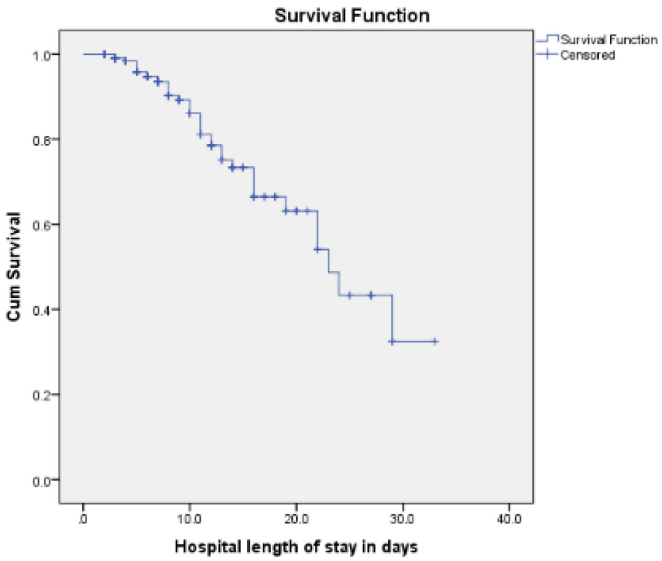
About 30.0% were ICU patients, 4.8% needed IMV, 13.2%, HFOT, and 8.4% required NIPPV. About 18% of the patients developed complications, including ACS (7.5%) and AKI (6.3%), and the median (IQR) hospital LOS was 11 (8) days, as shown in Table 2. The overall mortality rate was 12.3% (95% CI 8.9-16.2%) among hospitalized patients and 30.3% (95% CI 21.5-40.3%) in ICU status patients. The mortality rate was 5.8% (95% CI 3.2-9.5%), 14% (95% CI 5.2-27.4%), 28.6% (95% CI 18.2-48.7%), and 81.3% (95% CI 54.3-95.9) in patients who needed LFOT, HFOT, NIPPV and IMV, respectively (Figure 1). Figure 2 presents the survival analysis of hospitalized COVID-19 patients.

Univariate analysis revealed 14.4% death of those with comorbidities (p-value= 0.02), and 19.6% of those with CVD died (p-value: 0.009). Those who died had a significantly lower P.F. ratio of 79.7 ± 42.3 compared to 167.4 ± 67.2 discharged alive (p-value < 0.001) (Table 1).

Complications like ACS and AKI were significantly associated with increased mortality (p-value = 0.013, 0.001), respectively. Mortality was significantly higher among ICU patients (29.6%) and patients who needed IMV. Regarding some treatment modalities, patients who needed high dose dexamethasone (22.4%) or therapeutic dose enoxaparin (19.1%) had significantly higher mortality rates (Table 2).

Among ICU patients, 16.2% were ventilated, and the P.F. ratio was significantly lower than non-ICU patients (99.3 ± 53.8 vs. 180.8± 62.7, p-value < 0.001). Among severe ARDS patients, 64.8% were from ICU,

Figure 2. Kaplan–Meier estimates of in-hospital 30-days mortality.



only 12.4% were on IMV, and 29.5% used NIPPV. The mortality rate among severe ARDS and IMV users were, respectively, 34.3% and 81.3%. Multivariable logistic regression analysis showed that age (p-value = 0.008), smoking (p-value = 0.019), IMV (p -value < 0.001) and PF ratio (p-value < 0.001) increase mortality risk (Table 3). Among the significant factors, PaO_2/FiO_2 ratio, the need for mechanical ventilation, and smoking are the most predictors of mortality among ICU patients, as indicated by the AUC. The AUC was calculated as 0.87(0.81-0.92) for the PaO_2/FiO_2 ratio, 0.65(0.55-0.76) for mechanical ventilation, and 0.52 (0.43-0.62) for smoking (Table 3, Figure 3).

Discussion

This is a retrospective cohort of 334 hospitalized patients with severe COVID-19 disease who were admitted to a small hospital with limited resources. All patients in our cohort received evidence-based supportive care, including dexamethasone. All patients were treated with high dose venous thromboembolism prophylaxis, and ICU patients received therapeutic anticoagulation. All patients received dexamethasone 6 mg IV daily or P.O. for ten days, and ICU patients received high dose dexamethasone. None of the patients received remdesivir, convalescent plasma, or immune-based therapies.

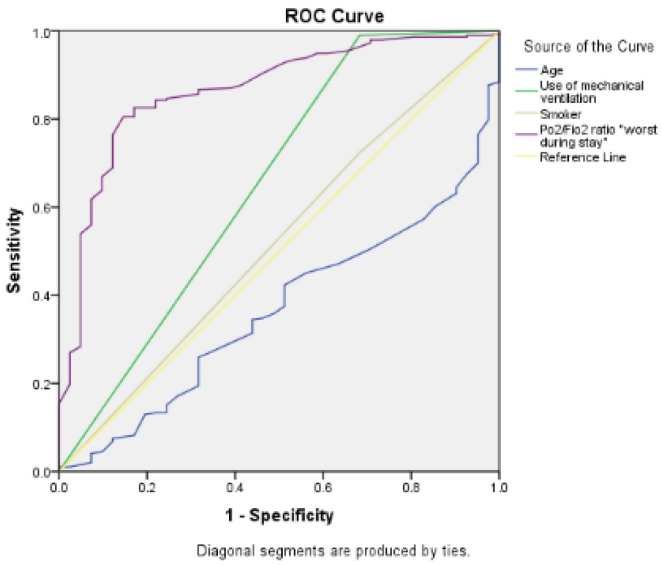
Table 2. Clinical characteristics and outcomes of the COVID-19 patients with in-hospital mortality (n=334).

Characteristic	Total	Dead (n = 41)	Alive (n = 293)	p-Value*
Complications[¥]				
Yes	61 (18.3%)	26 (42.6%)	35 (57.4%)	< 0.001
No	273 (81.7%)	15 (5.5%)	258 (94.5%)	
ACS				
Yes	25 (7.5%)	7 (28.0%)	18 (72.0%)	0.013
No[†]	309 (92.5%)	34 (11.0%)	275 (89.0%)	
AKI				
Yes	21 (6.3%)	11 (52.4%)	10 (47.6%)	< 0.001
No	313 (93.7%)	30 (9.6%)	283 (90.4%)	
Needed high Dexamethasone regimen				
Yes	98 (29.3%)	22 (22.4%)	76 (77.6%)	< 0.001
No	236 (70.7%)	19 (8.1%)	217 (91.9%)	
Dexamethasone 6mg				
Yes	320 (95.5%)	39 (12.2%)	281 (87.8%)	0.815
No	14 (4.2%)	2 (14.3%)	12 (85.7%)	
Enoxaparin use				
Therapeutic dose	98 (29.3%)	27 (19.1%)	114 (80.9%)	0.001
Prophylactic dose	236 (70.7%)	14 (7.3%)	179 (92.7%)	
LFOT				
YES	242(72.5%)	14(5.8%)	228 (94.2%)	< 0.001
No	92(27.5%)	27 (29.3%)	65 (70.7%)	
ICU status				
YES	99 (29.6%)	30 (30.3%)	69 (69.7%)	< 0.001
No	235 (70.4%)	11 (4.7%)	224 (95.3%)	
Needed HFOT				
Yes	44 (13.2%)	6 (14%)	37 (86%)	0.719
No	264 (79%)	35 (12%)	256 (88%)	
Needed NIPPV				
Yes	28 (8.4%)	8 (28.6%)	20 (71.4%)	0.06
No	297 (88.9)	33 (10.8%)	273(89.2%)	
Mechanical Ventilation				
Yes	16 (4.8%)	13 (81.3%)	3 (18.8%)	< 0.001
No	318 (95.2%)	28 (8.8%)	290 (91.2%)	
ICU LOS in days (median (IQR))	9 (9)	8.5 (12)	9 (8)	0.129**
Hospital LOS in days (median (IQR)	11 (8)	10.5 (1)	11 (9)	< 0.001**

[¥] Complication include: AKI, ACS or other like, stroke, gastrointestinal bleeding, etc; *Chi-Squared test; **Mann-Whitney U test; ACS: acute coronary syndrome; AKI: acute kidney injury; LFOT: Low Flow O2 Therapy; HFOT: High Flow O2 Therapy; NIPPV: Non-invasive positive pressure ventilation.

Our cohort of patients is similar to the cohort in the Solidarity trial's control arm and the treatment arm of the recovery trial with one exception; these trials included patients who did not require oxygen at all while all patients in our cohort required oxygen support and have sever COVID-19 pneumonia. The overall hospital mortality in our cohort was 12.3%, which was less than that reported in the control arm of the solidarity trial (14.2%) and the dexamethasone arm of the recovery trial (24.5%) after excluding patients who did not use oxygen [5,7]. The hospital mortality was also less than reported mortality (17% to 23.4%) in some European, American, and Chinese studies for all hospitalized COVID-19 patients, regardless of oxygen use [19–24]. ICU mortality for our cohort was 30.3%, which was comparable to global rates of 8%, 23.6%, 24.3%, 25.6%, 29.2%, and 37.7% in U.K., USA, Germany, Italy, Spain, and China, respectively [25]. Internal medicine specialists managed our cohort using limited resources, suggesting that supportive care including steroids seemed to be effective across different hospital and ICU care delivery models. It is challenging to compare mortality and other outcomes of COVID-19 patients in different trials given the heterogeneity in these clinical trials. It is also key to control for the severity of illness and modalities of treatments used in these trials. We reviewed clinical trials from nearby countries and found substantial differences in patients' cohorts included. In a published trial from Hamad Medical Center in Qatar, the hospital and ICU mortality were 0.28% and 11.1%, respectively [26]. It was reported that 94.2% of non-ICU patients and 6.5% of ICU patients did not require oxygen therapy at all. Also, 41.7% of ICU patients required only LFOT and won't have met the ICU admission criteria in our cohort. Only 0.5% of non-ICU patients and 65% of ICU patients received corticosteroids, in contrast to all patients in our study. Most ICU patients received antiviral therapies and Tocilizumab while none of these therapies was used in our cohort. Another trial reported outcomes of 768 COVID-19 patients from

Figure 3. ROC curve for PaO_2/FiO_2 ratio, mechanical ventilation, age, and smoking score in predicting in-hospital mortality.



King Saud Medical City in Saudi Arabia [27]. The hospital and ICU mortality were 11.5% and 25.3%, respectively. Among the 768 patients included in the analysis, 178 were isolated in home or hotel settings. The authors did not report the percentage of patients who required oxygen therapy. Also, 32.7% of patients had ARDS compared to all patients in our cohort. A recently published systematic review and meta-analysis of observational studies reported on ICU mortality of hospitalized COVID-19 patients [28]. ICU mortality in middle eastern and north African countries was reported at 61.9%. Among the studies included was a study that included 113 hospitalized patients in Iran [29]. Hospital and ICU mortality were 3.9% and 45% respectively. Most of these patients (61%) did not require oxygen support, all received antiviral therapies, and only 4.4% received corticosteroids. The meta-analysis also included a study that reviewed outcomes in 1096 patients who were admitted to a hospital in Kuwait [30]. The hospital and ICU mortality were 0.28% and 40%, respectively. Most of non-ICU patients

Table 3. Multivariable binary regression analysis of factors associated with in-hospital mortality.

Characteristic	Adjusted OR (95% CI)	Adjusted p-value	AUC (95%CI)
Age (mean ± SD)	1.05 (1.01-1.09)	0.008	0.37 (0.29-0.44)
PaO_2/FiO_2 ratio	1.03 (1.02-1.04)	<0.001	0.87(0.81-0.92)
Gender (male)	2.12 (0.74-6.29)	0.176	-------
Smoker	4.12 (1.27-13.83)	0.019	0.52 (0.43-0.62)
Hypertension	1.34 (0.5-3.57)	0.56	-------
Cardiovascular disease	1.74 (0.69-4.41)	0.244	-------
IMV	27.4 (5.83-128.5)	< 0.001	0.65(0.55-0.76)

P/F ratio: PO2/FIO2 ratio; ACS: acute coronary syndrome; AKI: acute kidney injury; IMV: invasive mechanical ventilation; The reference variable for gender is male, for the rest, it was yes.

(97%) did not received oxygen support, 13.7% received antivirals and only ICU patients (3.8%) received corticosteroids. Another study that was included is from Yemen and included 49 ICU patients, where 18 received NIPPV and 27 received IMV, and reported ICU mortality was 67% [31].

In-hospital mortality in our cohort was higher in patients with lower P.F. ratio and who required escalating oxygen therapies. Higher mortality was observed among recipients of IMV in our cohort (81.3%) than the reported mortality of patients in the control arm of the solidarity trial or the dexamethasone arm of the recovery trial (29.3%) [5,7]. We believe this was related to a higher threshold to escalating care to invasive mechanical ventilation in our cohort, which resulted in selection bias.

The high threshold for intubation in our institution is multifactorial. It is attributed to the availability of HFOT and NIPPV, a limited number of ventilators, and lack of critical care and anesthesia expertise, in addition to the family decision not to use IMV, against medical advice, with the belief that their relatives will die if they elect IMV, which served as a self-fulfilling prophecy. Only 16 patients (4.8%) in our cohort ended up on IMV, compared to (11.4%) in the control arm of the solidarity trial and (20.2%) in the dexamethasone arm of the recovery trial, after excluding patients who did not use oxygen, and compared to 80% in ARDS patients regardless of etiology [5,7,32]. This selection bias is evident when we compare ARDS mortality in our cohort to reported mortality in other studies.

COVID -19 pneumonia patients often have bilateral infiltrates and are hypoxic with a P.F. ratio < 300, making ARDS a likely diagnosis in most of them. All patients were labeled and managed as ARDS in our cohort. Although we did not report Acute Physiologic Assessment and Chronic Health Evaluation (APACHE) or Sequential Organ Failure Assessment (SOFA) acuity scores, we believe it is very high. All our patients met the Berlin criteria for ARDS, and one-third had severe ARDS.

In our cohort, the in-hospital mortality of severe ARDS patients was 34.3%, compared to 46.1% in a worldwide study that evaluated 30,000 patients [32]. Additionally, 87.6% of severe ARDS patients in our cohort did not receive IMV, and the mortality in these patients was 27.2% compared to 81.3% in the remaining recipients (12.4%) of IMV. We observed higher mortality in the high doses of dexamethasone group and full anticoagulation with enoxaparin. This was attributed to selection bias, given that these regimens were only offered based on the severity of illness. The LOS in patients who were discharged alive was comparable to the median recovery time in the treatment arm of the ACTT-1 trial, despite excluding remdesivir in this study [6].

The predictors of mortality were the need for IMV, smoking status, and age with adjusted Odd Ratio (95% CI) of 27.4 (5.83-128.5), 4.12 (1.27-13.83), 1.05 (1.01-1.09), respectively. As expected, a low P.F. ratio predicted mortality and guided the managing team to escalate oxygen therapy and adopt strategies like high-dose dexamethasone and full anticoagulation [22,24]. Age was an independent predictor of mortality in which older ages are at higher risk for death, which was reported in many previous studies [19–23]. We also found that some patients had AKI during their stay, and some developed ACS; these events strongly predicted mortality, as shown in Table 2. A possible mechanism of an underlying endothelitis triggered by the virus was hypothesized, as frequently reported in the literature [24,33]. Other comorbidities previously identified were not significant in this study, like diabetes [22,23], chronic lung disease, COPD, and cancer [19]. Simultaneously, the male gender was not associated with high mortality compared to previous studies [19,20,22,23]. A prediction model based on the above factors can be easily computed within a low resource-center and may help physicians triage their patients according to available resources.

Our study has several limitations. First, outcomes in this study were limited to the hospital stay, and patients were not followed up after discharge; therefore, 28 days and 90 days' mortalities are not available. Second, we did not collect data on inflammatory markers used in literature [19–21,24], to guide immune-based therapies since it was not used in our hospital. There was no substantial evidence to support such a practice until recent trials that showed potential benefit from Tocilizumab [5,12,13]. Third, this was a single-center study, which limits its generalizability. Thus, illness severity and patients' characteristics in our cohort were comparable to other centers worldwide. Fourth, we did not use remdesivir, which was not available in our hospital and in Palestine in general. Literature about remdesivir is conflicting; therefore, we hope that our study will add to the body of literature that lack of remdesivir use did not affect time to recovery, as shown in our cohort.

Conclusions

In conclusion, the relatively low overall in-hospital mortality in our cohort (12.3%) supports our evidence-based practice of supportive care and corticosteroids in

countries with limited resources. This study had found that gender, smoking, need for IMV, were all independent predictors for mortality. Finally, when medical intensivists are not available, critically ill COVID-19 patients can be safely managed by internal medicine specialists equipped with evidence-based protocols.

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Authors' contributions

Y.E., MH, and Z.N. participated in conceiving the idea and study design, supervised data collection, data analysis, manuscript writing. A.A., D.S., IA, MN, R.R., and S.R. performed the material preparation, data collection, and analysis. All authors interpreted the results. Z.N., IA, A.A., and R.R. wrote the first draft of the manuscript, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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