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Impact of comorbidities on hospitalised Syrian patients with COVID-19: a retrospective study

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ABSTRACT

Objectives This study aims to compare the clinical manifestations, laboratory findings, outcomes and overall survival time of patients with COVID-19 with and without comorbidities.

Design Retrospective design.

Setting This study was undertaken at two hospitals in Damascus.

Participants A total of 515 Syrian patients met the inclusion criterion, laboratory-confirmed COVID-19 infection following the Centers for Disease Control and Prevention. Exclusion criteria were suspected and probable cases that were not confirmed with a positive reverse transcription-PCR assay, and patients who self-discharged from the hospital against medical advice.

Primary and secondary outcome measures First, assess the impacts of comorbidities on COVID-19 infection in four areas (clinical manifestations, laboratory findings, severity and outcomes). Second, calculate the overall survival time for patients with COVID-19 with comorbidities.

Results Of 515 patients included, 316 (61.4%) were male and 347 (67.4%) had at least one coexisting chronic disease. Patients with comorbidities compared with no comorbidities were more vulnerable to poor outcomes such as severe infection (32.0% vs 9.5%, p<0.001), severe complications (34.6% vs 9.5%, p<0.001), the need for mechanical ventilation (28.8% vs 7.7%, p<0.001) and death (32.0% vs 8.3%, p<0.001). Multiple logistic regression showed that age ≥65 years old, positive smoking history, having ≥2 comorbidities and chronic obstructive pulmonary disease were risk factors linked to severe COVID-19 infection in patients with comorbidities. Overall survival time was lower among patients with comorbidities (vs no comorbidities), patients with ≥2 comorbidities (vs one comorbidity), and patients with hypertension, chronic obstructive pulmonary disease, malignancy or obesity (vs other comorbidities) (p<0.05).

Conclusion This study revealed that COVID-19 infection had poor outcomes among those with comorbidities. Severe complications, mechanical ventilation usage and death were more prevalent among patients with comorbidities compared with those with no comorbidities.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Data collection issues include disorganised files, subjective records, lost records and illegible handwriting.
⇒ Data gathered included comorbidities, clinical manifestations, laboratory findings and outcomes of hospitalised patients with COVID-19.
⇒ The retrospective design of the study is inferior in evidence compared with prospective studies.
⇒ This study's sample covered two main hospitals in Damascus and Rural Damascus.
⇒ The ethics committee of Damascus Hospital granted the study's approval.

INTRODUCTION

Since COVID-19 was first recognised in December 2019,[1] a collaborative effort focused on understanding the epidemiological, demographic and clinical features of this virus was triggered. COVID-19 continues to spread, infecting over half a billion and killing millions of people worldwide.[2] Despite the thousands of published medical research and their milestones, and somehow overcoming the pandemic, the virus continues to cause unpredictable chaos.[3] One observation quickly noticed by the medical community after the start of the epidemic was that COVID-19 affects people differently, with most cases showing mild symptoms. However, many studies revealed that the presence of comorbidities can be associated with more severe infection cases and clinical complications.[4–6] Approximately one in five individuals is at increased risk of severe COVID-19.[7] After these results were announced around the world, it is not surprising that generalised anxiety and COVID-19-related fear were elevated among individuals with high-risk diseases such as diabetes, hypertension, cardiovascular and chronic respiratory diseases.[8] In light of this crisis, the medical community has agreed that vaccines remain the only way to fight the pandemic; thus, in December 2020, the US Food and Drug Administration issued an emergency use authorisation to facilitate the use and availability of COVID-19

vaccines.[9] Despite the confirmation about the efficacy and safety of COVID-19 vaccines,[10 11] vaccine hesitancy worldwide became a big obstacle in the vaccination process.[12] In Syria, only 9.3% of the population is fully vaccinated,[13] with vaccine hesitancy higher among people with a history of chronic comorbidities.[14] Many studies showed that people with comorbidities had greater odds of developing severe post-vaccination side effects.[15 16] To accurately study the impact of comorbidities on the severity of COVID-19 infection and thus confirm the importance of protecting this vulnerable group, this study was conducted to evaluate the impact of comorbidities on the clinical manifestations, laboratory findings and outcomes of COVID-19-infected patients. The objective was to study the differences in outcomes and overall survival (OS) time among patients with COVID-19 with different types of comorbidities.

METHODS

Study design, settings and participants

This retrospective, multicentre, observational study was conducted at two main hospitals in Damascus and Rural Damascus: Damascus Hospital (Al-Mujtahid) and Al-Mouwasat Hospital. Al-Mouwasat Hospital is affiliated with the Syrian Ministry of Higher Education and Scientific Research, while Damascus Hospital is affiliated with the Syrian Ministry of Health. Damascus Hospital and Al-Mouwasat Hospital were emergency hospitals involved in the isolation and management of patients with COVID-19 during the outbreaks. A total of 515 patients with confirmed COVID-19 diagnoses between 1 September 2021 and 30 September 2021 were enrolled in this study. The third wave of COVID-19 peaked in September 2021.

Inclusion criteria

Inclusion criterion was Damascus Hospital laboratory and Al-Mouwasat Hospital laboratory-confirmed COVID-19 infection following the Centers for Disease Control and Prevention (CDC) published criteria.[17 18]

Exclusion criteria

Exclusion criteria were suspected and probable cases that were not confirmed with a positive reverse transcription-PCR (RT-PCR) assay, and patients who self-discharged from the hospital against medical advice, and therefore, missed their outpatient follow-up.

Data collection

Clinical records and laboratory results were reviewed by the authors. Furthermore, the authors contacted patients via telephone when data from files were incomplete. The data collected included sociodemographic features (age, sex and smoking history); vital signs (temperature, heart rate, respiratory rate, systolic blood pressure and diastolic blood pressure); clinical symptoms (dry cough, dyspnoea, fever, chills, weakness and fatigue, oedema, sore throat, chest pain, headache, runny nose, anosmia, ageusia, arthralgia, myalgia, irritability, confusion, loss of consciousness, nausea, vomiting, diarrhoea, abdominal pain, lethargy, bradyglossia, anorexia and weight loss); comorbidities (hypertension, diabetes mellitus, cardiovascular diseases, chronic obstructive pulmonary disease (COPD), chronic liver disease, chronic kidney disease, gastrointestinal disease, neurological disease, malignancy, autoimmune disease, obesity and recent surgery within the last month); complications (acute respiratory distress syndrome (ARDS), heart failure, acute renal injury, acute liver injury and septic shock); laboratory results on admission (complete blood count, kidney function tests, liver function tests, D-dimer and C reactive protein (CRP)); radiological assessment; RT-PCR results; clinical outcomes (complete recovery, need for oxygen therapy, need for mechanical ventilation and death).

Two investigators separately checked the data collection to confirm the accuracy of the data gathered. Patients were classified into two groups. The first group consisted of patients with COVID-19 with at least one of the following comorbidities: hypertension, diabetes mellitus, cardiovascular diseases, COPD, chronic liver disease, chronic kidney disease, gastrointestinal disease, neurological disease, malignancy, autoimmune disease, obesity and recent surgery within the last month; the second group, patients with COVID-19 without any comorbidity.

Study definitions

Manifestations found on chest X-ray and CT scans were reviewed by an attending physician in the respiratory department. ARDS was diagnosed when someone with a confirmed COVID-19 infection met the Berlin 2012 ARDS diagnostic criteria: (1) acute hypoxaemic respiratory failure; (2) presentation within 1 week of worsening respiratory symptoms; (3) bilateral airspace disease on chest X-ray, CT or ultrasound that is not fully explained by effusions, labour or lung collapse, or nodules; (4) cardiac failure is not the primary cause of acute hypoxaemic respiratory failure.[19] COVID-19 infection severity was divided into three groups: mild, moderate and severe, based on the National Institutes of Health COVID-19 treatment guidelines.[20]

Patient and public involvement

The public was not involved in the study design, conduct of the study or plans to disseminate the results to study participants.

Statistical analysis

Categorical variables were reported as frequencies and percentages (descriptive statistics), and continuous variables were presented as medians with IQR. The Mann-Whitney U test was conducted to compare the age, vital signs on admission and laboratory results between patients with COVID-19 with comorbidities and patients with COVID-19 without comorbidities. The X^2 test and Fisher's exact test were used as appropriate to compare the two groups, patients with COVID-19 with comorbidities and

patients with COVID-19 without comorbidities, against sociodemographic features, clinical manifestations, complications and outcomes. The X^2 test was also used to compare patients with COVID-19 with different comorbidities (hypertension, diabetes mellitus, cardiovascular disease, COPD, malignancy and obesity) against severe infection, complications (ARDS, heart failure, acute renal injury, acute kidney injury and septic shock), mechanical ventilation and death. Multivariable logistic regression was performed to detect factors associated with severe COVID-19 infection (vs no severe COVID-19 infection), and selected factors included age (≥65 years vs <65 years), sex (male vs female), smoking history (positive smoking history vs negative smoking history), number of comorbidities (≥2 comorbidities vs one comorbidity) and type of comorbidities (hypertension vs diabetes mellitus, cardiovascular diseases, COPD, chronic liver disease, chronic kidney disease, gastrointestinal disease, neurological disease, malignancy, autoimmune disease, obesity and recent surgery within the last month; diabetes vs hypertension, cardiovascular diseases, COPD, chronic liver disease, chronic kidney disease, gastrointestinal disease, neurological disease, malignancy, autoimmune disease, obesity, and recent surgery within the last month; and COPD vs hypertension, diabetes mellitus, cardiovascular diseases, chronic liver disease, chronic kidney disease, gastrointestinal disease, neurological disease, malignancy, autoimmune disease, obesity, and recent surgery within the last month). For survival analysis, the set time from the presence of symptoms until death or the last follow-up (30 September 2021) was used. The Kaplan-Meier survival curves were conducted and differences in survival rate were analysed by log-rank test. All statistical analyses were performed using the SPSS statistics V.25.0. A statistically significant p value was set at <0.05.

RESULTS

Sociodemographic features, clinical manifestations, complications and outcomes of patients with COVID-19

A total of 515 patients with COVID-19 were included in this study. The median age was 60 years, and the range was between 16 and 95 years. There were 316 (61.4%) men and 199 (38.6%) women. One hundred ninety-two (37.3%) patients were current or previous smokers. Of 347 (67.4%) patients with comorbidities, 196 (56.6%) have hypertension, 149 (42.9%) have diabetes mellitus, 102 (29.4%) have a cardiovascular disease, 43 (12.4%) have a renal disease, 42 (12.1%) are obese, 35 (10.1%) have COPD, 34 (9.8%) have malignancies, 29 (8.4%) have a neurological disease, 23 (6.6%) have an autoimmune disease, 14 (4.0%) have a haematological disease, 13 (3.7%) have a gastrointestinal and liver disease, and 13 (3.7%) had surgery within the last month. One hundred eighty-nine (36.7%) reported having two or more comorbidities. The median (IQR) number of comorbidities for the population was 1 (2) comorbidity, ranging from 0 to 7 comorbidities. Patients with comorbidities were older (median=65 years) compared with patients with no comorbidities (median=52 years). Also, patients with comorbidities had a higher positive smoking history (40.6%) compared with those with no comorbidities (30.4%). Patients with comorbidities had higher respiratory rate on admission (median=28 breaths/min) in comparison with patients without comorbidities (p=0.009). The most common symptoms among patients with COVID-19 were dry cough (380, 73.8%), weakness and fatigue (374, 72.6%), fever (357, 69.3%) and dyspnoea (357, 69.3%). The predominant clinical presentation among patients with COVID-19 with comorbidities was dyspnoea (267, 76.9%), followed by dry cough (250, 72.0%), fever (242, 69.7%), and weakness and fatigue (242, 69.7%). On the other hand, weakness and fatigue (132, 78.6%) was the most common clinical symptom among patients with COVID-19 without comorbidities. Patients with comorbidities were more likely to suffer from dyspnoea (76.9%) compared with patients without comorbidities (53.6%) (p<0.001) (table 1).

Regarding COVID-19 severity, most patients had moderate disease (203, 39.4%). Patients without comorbidities were more likely to experience mild disease (98, 58.3%). One hundred twenty-seven (24.6%) patients developed severe COVID-19, and severe infection was more common among patients with at least one comorbidity (111, 32.0%) compared with those without comorbidities (16, 9.5%) (p<0.001). A comparison of COVID-19 infection severity between patients with different comorbidities showed that patients who had surgery during the last month were more likely to develop severe infection (9, 69.2%), followed by patients with malignancies (22, 64.7%) and COPD (20, 57.1%). A total of 457 (88.7%) patients required oxygen support. Patients with comorbidities were more vulnerable to poor outcomes including severe complications compared with patients without comorbidities (34.6% and 9.5%, respectively; p<0.001). Patients with comorbidities were associated with the need for mechanical ventilation (28.8%) compared with patients without comorbidities (7.7%) (p<0.001). Patients with comorbidities were more likely to develop COVID-19-related complications including ARDS (109, 31.4%), heart failure (92, 26.5%), acute renal injury (17, 4.9%) and shock (14, 4.0%) compared with patients without comorbidities (p<0.001, p<0.001, p=0.002 and p=0.007, respectively). At the time of the last follow-up, 125 (24.3%) patients had died. Patients with at least one comorbidity had a higher mortality percentage (32.0%) compared with patients without comorbidities (8.3%) (p<0.001). Patients who had surgery within the last month had higher reported COVID-19-related death (4, 30.8%) compared with all other comorbidities (table 1).

Laboratory and radiological findings

The most common chest CT findings were bilateral peripheral patchy consolidation (435, 84.5%) and ground-glass opacity (183, 35.5%). Laboratory tests revealed that patients in the comorbidity group had a significantly lower

Table 1 Sociodemographic features, clinical manifestations, complications and outcomes of patients with COVID-19 with and without comorbidities

	All patients (N=515)	Patients with comorbidities (n=347)	Patients without comorbidities (n=168)	P value
Age (years), median (IQR)	60 (21)	65 (19)	52 (12)	<0.001
Sex				
Male	316 (61.4)	210 (60.5)	106 (63.1)	0.573
Female	199 (38.6)	137 (39.5)	62 (36.9)	
Smoking history	192 (37.3)	141 (40.6)	51 (30.4)	0.024
Vital signs on admission, median (IQR)				
Temperature on admission (°C)	38 (1)	38 (1)	38 (1)	0.989
Heart rate (beats/min)	94 (21)	95 (25)	93 (16)	0.316
Respiratory rate (breaths/min)	28 (8)	28 (10)	26 (8)	0.009
Systolic pressure (mm Hg)	120 (29)	120 (30)	123 (10)	0.594
Diastolic pressure (mm Hg)	80 (10)	80 (10)	77 (10)	0.605
Clinical manifestation				
Dry cough	380 (73.8)	250 (72.0)	130 (77.4)	0.197
Dyspnoea	357 (69.3)	267 (76.9)	90 (53.6)	<0.001
Fever	357 (69.3)	242 (69.7)	115 (68.5)	0.766
Chills	119 (23.1)	80 (23.1)	39 (23.2)	0.968
Weakness and fatigue	374 (72.6)	242 (69.7)	132 (78.6)	0.035
Oedema	11 (2.1)	11 (3.2)	0 (0.0)	0.019
Sore throat	73 (14.2)	37 (10.7)	36 (21.4)	0.001
Chest pain	66 (12.8)	52 (15.0)	14 (8.3)	0.034
Headache	115 (22.3)	63 (18.2)	52 (31.6)	0.001
Runny nose	71 (13.8)	24 (6.9)	47 (28.0)	<0.001
Anosmia (loss of smell)	36 (7.0)	18 (5.2)	18 (10.7)	0.021
Ageusia (loss of taste)	34 (6.6)	16 (4.6)	18 (10.7)	0.009
Arthralgia	122 (23.7)	70 (20.2)	52 (31.0)	0.007
Myalgia	137 (26.6)	76 (21.9)	61 (36.3)	0.001
Irritability	9 (1.7)	6 (1.7)	3 (1.8)	1.000
Confusion	52 (10.1)	46 (13.3)	6 (3.6)	0.001
Loss of consciousness	24 (4.7)	19 (5.5)	5 (3.0)	0.207
Nausea	29 (5.6)	21 (6.1)	8 (4.8)	0.552
Vomiting	65 (12.6)	43 (12.4)	22 (13.1)	0.822
Diarrhoea	58 (11.3)	40 (11.5)	18 (10.7)	0.784
Abdominal pain	33 (6.4)	22 (6.3)	11 (6.5)	0.928
Lethargy	33 (6.4)	28 (8.1)	5 (3.0)	0.027
Bradyglossia	13 (2.5)	12 (3.5)	1 (0.6)	0.070
Anorexia	103 (20.0)	64 (18.4)	39 (23.2)	0.204
Weight loss	21 (4.1)	10 (2.9)	11 (6.5)	0.049
Disease severity				
Mild	185 (35.9)	87 (25.1)	98 (58.3)	<0.001
Moderate	203 (39.4)	149 (42.9)	54 (32.1)	0.019
Severe	127 (24.6)	111 (32.0)	16 (9.5)	<0.001
Oxygen therapy	457 (88.7)	306 (88.2)	151 (89.9)	0.568
Mechanical ventilation	113 (21.9)	100 (28.8)	13 (7.7)	<0.001

Continued

Table 1 Continued

	All patients (N=515)	Patients with comorbidities (n=347)	Patients without comorbidities (n=168)	P value
Complications	136 (26.4)	120 (34.6)	16 (9.5)	<0.001
ARDS	124 (24.1)	109 (31.4)	15 (8.9)	<0.001
Heart failure	103 (20.0)	92 (26.5)	11 (6.5)	<0.001
Acute renal injury	17 (3.3)	17 (4.9)	0 (0)	0.002
Acute liver injury	4 (0.8)	4 (1.2)	0 (0)	0.309
Septic shock	14 (2.7)	14 (4.0)	0 (0)	0.007
Outcomes				
Alive at the time of last follow-up	390 (75.7)	236 (68.0)	154 (91.7)	<0.001
Death	125 (24.3)	111 (32.0)	12 (8.3)	

ARDS, acute respiratory distress syndrome.

lymphocyte count (1.0×10^9/L) compared with patients without comorbidities (1.4×10^9/L) (p<0.001). Higher levels of CRP and D-dimer were found among patients with comorbidities (55.1 mg/L and 0.8 mg/L) compared with patients without comorbidities (24.0 mg/L and 0.6 mg/L; p<0.001 and p=0.05, respectively). Low platelet count, low haemoglobin levels, and high levels of aspartate aminotransferase (AST), creatinine, and blood urea were linked with patients with COVID-19 with comorbidities compared with patients without comorbidities (p<0.001) (table 2).

Complications and outcomes of patients with COVID-19 by types of comorbidities

Comparing the outcomes of COVID-19 with different types of comorbidities (hypertension, diabetes mellitus, cardiovascular diseases, COPD, malignancies and obesity) showed that patients with malignancies were more vulnerable to poor outcomes including severe infection (22, 64.7%) and need for mechanical ventilation (19, 55.9%) than those with other comorbidities (p=0.002 and p=0.001, respectively). Also, patients with COPD were associated with severe complications (22, 62.9%), including ARDS (21, 60.0%), heart failure (19, 54.3%) and death (20, 57.1%) compared with those with other comorbidities (p=0.002, p=0.003, p=0.016 and p=0.018) (table 3).

Multivariate logistic regression analysis for factors associated with severe COVID-19 infection in patients with comorbidities

Multiple logistic regression analysis showed that age ≥65 years old (vs <65 years; OR: 2.344, p=0.000), positive smoking history (vs negative smoking history; OR: 1.786, p=0.011), having ≥2 comorbidities (vs 1 comorbidity; OR: 2.584, p=0.004) and COPD (vs other comorbidities; OR: 2.708, p=0.011) were risk factors linked to severe COVID-19 infection in patients with comorbidities. Patients with diabetes mellitus (vs other comorbidities; OR: 1.235, p=0.436) did not show significant differences (table 4).

Table 2 Comparison of laboratory findings between patients with comorbidities and patients without comorbidities

Laboratory findings, median (IQR)	All patients (N=515)	Patients with comorbidities (n=347)	Patients without comorbidities (n=168)	P value
Leucocyte count (10^9/L)	11.4 (7.0)	11.0 (8.6)	11.8 (4.8)	0.558
Neutrophil count (10^9/L)	9.1 (6.2)	9.1 (7.4)	9.3 (4.3)	0.857
Lymphocyte count	1.1 (1.3)	1.0 (1.1)	1.4 (1.6)	<0.001
Haemoglobin (g/L)	127 (30)	120 (40)	131 (20)	<0.001
Platelets (10^9/L)	244 (113)	220 (125)	289 (80)	<0.001
ALT (U/L)	23 (16)	23 (17)	21 (13)	0.110
AST (U/L)	30 (19)	33 (20)	24 (13)	<0.001
Creatinine (mg/dL)	1.2 (1)	1.3 (1)	1.1 (0)	<0.001
Blood urea (mg/dL)	47 (41)	57 (52)	40 (16)	<0.001
CRP (mg/L)	44 (59)	55.1 (82)	24 (19)	<0.001
D-dimer (mg/L)	0.7 (2)	0.8 (3)	0.6 (1)	0.05

ALT, alanine transaminase; AST, aspartate aminotransferase; CRP, C reactive protein.

Table 3 Complications and outcomes of patients with COVID-19 by types of comorbidities*

	Hypertension (N=196)	Diabetes mellitus (N=149)	Cardiovascular diseases (N=102)	COPD (N=35)	Malignancies (N=34)	Obesity (N=42)	P value
Severe infection	68 (34.7)	53 (35.6)	36 (35.3)	20 (57.1)	22 (64.7)	20 (47.6)	0.002
Complications	76 (38.8)	54 (36.2)	39 (38.2)	22 (62.9)	19 (55.9)	26 (61.9)	0.002
ARDS	69 (35.2)	50 (33.6)	34 (33.3)	21 (60.0)	19 (55.9)	22 (52.4)	0.003
Heart failure	60 (30.6)	43 (28.9)	30 (29.4)	19 (54.3)	13 (38.2)	20 (47.6)	0.016
Acute renal injury	12 (6.1)	8 (5.4)	2 (2.0)	3 (8.6)	3 (8.8)	0 (0.0)	0.242
Acute liver injury	1 (0.5)	1 (0.7)	1 (1.0)	0 (0.0)	1 (2.9)	0 (0.0)	0.678
Septic shock	8 (4.1)	5 (3.4)	5 (4.9)	2 (5.7)	3 (8.8)	5 (11.9)	0.263
Mechanical ventilation	62 (31.6)	44 (29.5)	32 (31.4)	18 (51.4)	19 (55.9)	23 (54.8)	0.001
Outcomes							
Death	73 (37.2)	54 (36.2)	37 (36.3)	20 (57.1)	19 (55.9)	23 (54.8)	0.018

*Multiple test corrections were not applied.
ARDS, acute respiratory distress syndrome; COPD, chronic obstructive pulmonary disease.

Survival analysis

The Kaplan-Meier curve revealed that patients with COVID-19 with at least one comorbidity have significantly lower OS time compared with patients with COVID-19 without comorbidities (mean=19.7 (18.6–20.8) vs 27.1 (26.1–28.0), p<0.000) (figure 1A and online supplemental table 1). Furthermore, patients with ≥2 comorbidities (vs 1 comorbidity), and patients with hypertension (vs other comorbidities), malignancies (vs other comorbidities) and obesity (vs other comorbidities) were found to have significantly shorter OS periods (figure 1B,C and figure 1E–G; online supplemental tables 2 and 3 and online supplemental tables 5–7). Patients with diabetes mellitus (vs other comorbidities) did not show a significant difference (figure 1D and online supplemental table 4).

DISCUSSION

This first study describes the impacts comorbidities have on the infection severity among Syrian patients with COVID-19. In our study, we found that chronic disease was more prevalent with increasing age. Previous studies have proven the relationship between ageing and chronic diseases.[21 22]

Positive smoking history was linked to patients with comorbidities compared with those without comorbidities. Several studies found that tobacco is a well-known risk factor for early morbidity and mortality worldwide.[23 24] Regarding vital signs on admission, patients with comorbidities had a significantly higher respiratory rate than those without comorbidities. This finding was consistent with a previous study conducted in China.[25]

Table 4 Multivariable logistic regression analysis on risk factors associated with severe COVID-19 infection in patients with comorbidities*

		95% CI for OR		
	OR	Lower	Upper	P value
≥65 years old (vs <65)	2.344	1.480	3.713	<0.001
Male (vs female)	0.938	0.593	1.482	0.782
Positive smoking history (vs negative history)	1.786	1.142	2.795	0.011
≥2 comorbidities (vs 1 comorbidity)	2.584	1.364	4.897	0.004
Hypertension (vs diabetes mellitus, cardiovascular diseases, COPD, chronic liver disease, chronic kidney disease, gastrointestinal disease, neurological disease, malignancy, autoimmune disease, obesity and recent surgery within the last month)	0.782	0.426	1.433	0.426
Diabetes (vs hypertension, cardiovascular diseases, COPD, chronic liver disease, chronic kidney disease, gastrointestinal disease, neurological disease, malignancy, autoimmune disease, obesity and recent surgery within the last month)	1.235	0.726	2.101	0.436
COPD (vs hypertension, diabetes mellitus, cardiovascular diseases, chronic liver disease, chronic kidney disease, gastrointestinal disease, neurological disease, malignancy, autoimmune disease, obesity and recent surgery within the last month)	2.708	1.258	5.829	0.011

*The accuracy rate for the model is 76.9%.
COPD, chronic obstructive pulmonary disease.

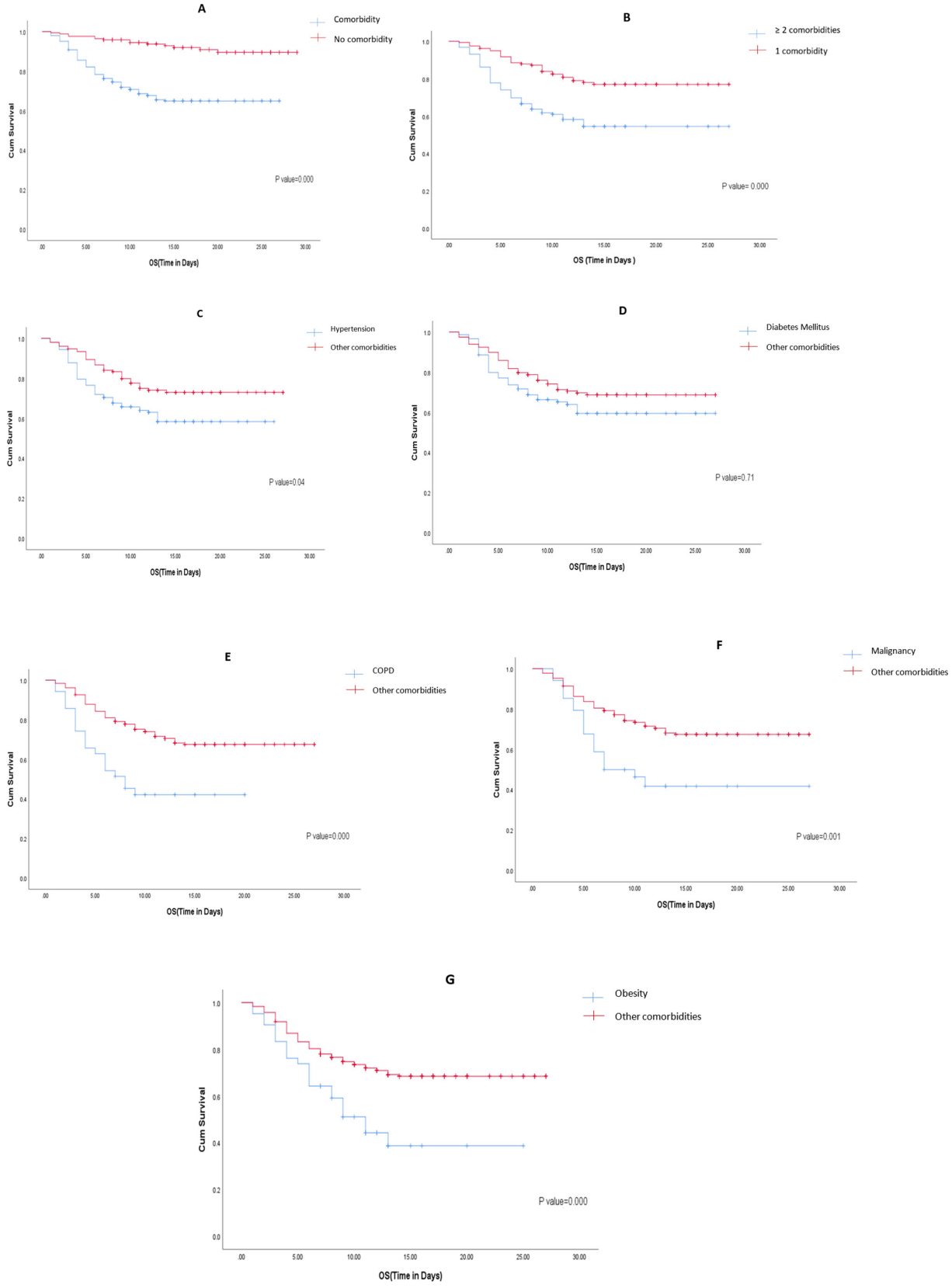

Figure 1 Kaplan-Meier plot of OS comparing patients with COVID-19 by comorbidities. COPD, chronic obstructive pulmonary disease; OS, overall survival.

Considering COVID-19 clinical manifestations, the most common symptoms among all patients with COVID-19 were dry cough, followed by weakness and fatigue, fever and dyspnoea. This was similar to other studies reported by the Sakarya University Training and Research Hospital, the European Centre for Disease Prevention and Control,

and a systematic review.[26–28] Weakness and fatigue was the most frequent clinical presentation of COVID-19 infection in patients without comorbidities. This was in line with a previous study from Turkey,[29] where dyspnoea was found to be the most common symptom among patients with comorbidities in Egypt.[30] Dyspnoea was linked to patients with comorbidities compared with those without comorbidities. This was consistent with a study conducted in Bangladesh.[31] Regarding disease severity, patients without comorbidities were more likely to experience mild disease, and this was reported by previous studies in China and Nigeria.[32 33] On the other hand, severe cases were related to patients with comorbidities, and this was consistent with a study conducted in China and a literature review.[34 35] The need for mechanical ventilation was linked to patients with comorbidities. A previous study from the USA revealed a similar finding.[36]

We found that patients with pre-existing comorbidities are more likely to suffer from COVID-19 complications and have a high mortality rate compared with those without comorbidities. According to the CDC, a person with one or more chronic medical conditions is more likely to experience severe COVID-19 infection and have poor outcomes.[37] Several studies have linked poor COVID-19 outcomes, including complications, and higher mortality rates with the presence of pre-existing chronic diseases.[38–41] Regarding laboratory findings, significantly higher blood urea, creatinine, AST, CRP and D-dimer levels, and lower haemoglobin levels, platelet count and lymphocyte count were linked to patients with comorbidities. A study conducted at the Memorial Healthcare System showed that patients with lymphocytopenia had a significantly higher comorbidity profile compared with those without lymphocytopenia.[42] Previous studies revealed that comorbidities were more frequent among patients with elevated D-dimer and CRP levels.[43 44] Another study from China demonstrated that the blood levels of leucocyte count and neutrophil count and the serum concentrations of CRP were higher in patients with increased leucocyte count and chronic diseases.[45] It is recognised that patients with underlying chronic disease experience chronic systemic inflammation in their body and express more ACE2.[46] These may induce a higher systemic inflammatory response when infected with COVID-19 compared with patients without an underlying chronic disease. A lower haemoglobin level in hospitalised patients with COVID-19 was linked to the presence of underlying chronic diseases according to an Iranian study.[47] Hypertension followed by diabetes mellitus and cardiovascular disease were the most common comorbidities in this study. Similar frequencies were reported in an Italian study and a Spanish study.[48 49] Data showed that recent surgery within 1 month before COVID-19 infection was linked to higher disease severity and mortality. A cohort study in Italy reported that mortality following surgery was significantly higher for those with COVID-19 infection compared with control patients without COVID-19.[50] The reason may be the over-reaction of the immune system as a result of an aggressive inflammatory response and release of excessive proinflammatory cytokines 'cytokines storm', leading to multiorgan failure and effects on endothelial cells resulting in clot formation and infarctions.[51 52] This interaction between the virus and the immune system could clarify the deterioration of the postoperative course. Furthermore, most of this study's participants are elderly patients with underlying chronic diseases, which may add additional risk to postoperative morbidity and mortality. Patients with COVID-19 with a history of underlying malignancy were significantly associated with severe disease and the need for mechanical ventilation compared with those with other types of comorbidities. A previous study conducted by the same authors showed that patients with cancer are at high risk of severe complications and mortality due to COVID-19.[53] Systematic reviews showed the same results.[54–56] This present study suggested that ARDS and heart failure were more likely to occur among patients with COVID-19 with COPD. In addition, they had the highest mortality in comparison with those with other types of comorbidities. The significant impact COPD has on COVID-19-infected patients has been observed in systematic reviews and retrospective studies.[57–61] A study from China suggested that COVID-19-infected patients with pre-existing COPD are more vulnerable to acute exacerbation of COPD and subsequent respiratory failure, which is the main culprit for unfavourable clinical outcomes.[62] COVID-19 uses the ACE2 as the cellular entry receptor.[63] A previous study showed that ACE2 expression on the epithelial cells in the lower airways was significantly higher among subjects with COPD versus those without COPD. This can explain the increased risk of severe COVID-19 in this population.[64] Furthermore, this study revealed that elderly patients ≥65 years old, patients with positive smoking history, patients with two or more comorbidities, and patients with COPD had greater odds of experiencing severe COVID-19 infection. Several studies from China and Australia and two systematic reviews reported the same factors.[4 65–67] This study showed that the OS time of patients with COVID-19 with comorbidities was lower than that of patients without comorbidities. A retrospective cohort study reported that the presence of comorbidities among hospitalised patients with COVID-19 would reduce the survival rate among these patients.[68] Furthermore, the OS time was lower among patients with two or more comorbidities compared with patients with only one comorbidity. Other previous studies illustrated that a history of multiple comorbidities was linked to an increased death rate among patients with COVID-19.[61 63 69] This current study revealed that hypertension, obesity, malignancy and COPD were related to a lower survival rate among patients with COVID-19. A study reported a lower probability of survival time among the hypertensive group compared with the non-hypertensive group.[70] Another study in Nigeria demonstrated that the risk of death was fourfold higher among the hypertensive group compared with the normotensive group.[71] A previous systematic

review reported a high mortality rate was evident among obese patients admitted with COVID-19 compared with non-obese patients admitted with COVID-19.[72 73] A multicentre retrospective study conducted in Syria by the same authors reported that patients with cancer infected with COVID-19 receiving anticancer treatment had a lower OS.[53] Patients with diabetes mellitus did not show significant differences in OS when compared with other comorbidities. A previous study in Bangladesh found the same result.[74] However, many other studies linked patients with COVID-19 with diabetes to a significantly lower OS.[75 76]

Limitations

The main limitation of the study is the issues encountered with data collection, including disorganised files, subjective records and illegible handwriting. To mitigate these issues, patients were contacted for the completion of data collection. Additionally, the system would benefit from electronic files for easier access and storage to eradicate most of the current study's flaws. Another limitation is the possibility of lost records and the withdrawal of some patients, who were transferred to another hospital or private hospital for management. Conducting a prospective multicentre study on a national level should be the next step in overcoming these problems and providing better evidence.

CONCLUSION

This retrospective observational study showed that patients with COVID-19 with comorbidities were correlated with poor COVID-19 outcomes, including severe infection, need for ventilation support, higher mortality and lower OS time. Therefore, patients with comorbidities are highly vulnerable and must be protected against the virus. Patients with comorbidities, who are eligible for the COVID-19 vaccine, must be encouraged to sign up and receive the COVID-19 vaccine.

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Ethics approval This study was approved by the Institutional Review Board (IRB) at the Syrian Private University (SPU). The IRB at SPU did not provide us with a number/ID. All participants confirmed their written consent by answering a yes/no question. Participation in the study was voluntary and participants were assured that anyone who was not inclined to participate or decided to withdraw after giving consent would not be victimised. All information collected from this study was kept strictly confidential.

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Supplementary

Table 1. Mean survival time by comorbidity group and no comorbidity group and the Log Rank test for comparison.

	Mean[a]			
			95% Confidence Interval	
Status	Estimate	Std. Error	Lower Bound	Upper Bound
comorbidity	19.691	.572	18.570	20.813
No comorbidity	27.073	.495	26.104	28.043
Overall	22.976	.470	22.055	23.896

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	38.367	1	.000

Table 2. Mean survival time by patients with ≥2 comorbidities and patients with one comorbidity and the Log Rank test for comparison.

	Mean[a]			
			95% Confidence Interval	
status	Estimate	Std. Error	Lower Bound	Upper Bound
≥2 comorbidities	17.313	.843	15.660	18.965
One comorbidity	22.482	.700	21.109	23.855
Overall	19.691	.572	18.570	20.813

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	21.297	1	.000

Table 3. Mean survival time by patients with hypertension and patients with other types of comorbidity and the Log Rank test for comparison.

	Mean[a]			
			95% Confidence Interval	
Status	Estimate	Std. Error	Lower Bound	Upper Bound
Hypertension	17.638	.777	16.115	19.160
Other comorbidities	21.549	.768	20.045	23.054
Overall	19.691	.572	18.570	20.813

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	8.339	1	.004

Table 4. Mean survival time by patients with Diabetes mellitus and patients with other types of comorbidity and the Log Rank test for comparison.

	Mean[a]			
			95% Confidence Interval	
Status	Estimate	Std. Error	Lower Bound	Upper Bound
Diabetes Mellitus	18.498	.924	16.686	20.309
Other comorbidities	20.548	.723	19.131	21.965
Overall	19.691	.572	18.570	20.813

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	3.267	1	.071

Table 5. Mean survival time by patients with COPD and patients with other types of comorbidity and the Log Rank test for comparison.

	Mean[a]			
			95% Confidence Interval	
Status	Estimate	Std. Error	Lower Bound	Upper Bound
COPD	10.975	1.347	8.335	13.614
Other comorbidities	20.350	.586	19.201	21.965
Overall	19.691	.572	18.570	20.813

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	16.849	1	.000

Table 6. Mean survival time by patients with Malignancy and patients with other types of comorbidity and the Log Rank test for comparison.

	Mean[a]			
			95% Confidence Interval	
Status	Estimate	Std. Error	Lower Bound	Upper Bound
Malignancy	14.503	1.908	10.764	18.242
Other comorbidities	20.255	.591	19.097	21.414
Overall	19.691	.572	18.570	20.813

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	11.331	1	.001

Table 7. Mean survival time by patients with Obesity and patients with other types of comorbidity and the Log Rank test for comparison.

	Mean[a]			
			95% Confidence Interval	
Status	Estimate	Std. Error	Lower Bound	Upper Bound
Obesity	13.623	1.583	10.521	16.725
Other comorbidities	20.413	.593	19.251	21.575
Overall	19.691	.572	18.570	20.813

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	12.760	1	.000