Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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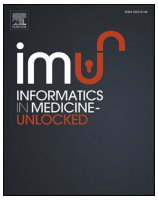

Predictors of COVID-19 severity and hospitalization: A survey-based study from Jordan

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ABSTRACT

Objectives: To explore the possible predictors of severe illness and hospitalization due to COVID-19 among Jordanians.

Method: The study was cross-sectional, survey-based and was conducted from March to July of 2021. Individuals who had recovered from COVID-19 (n = 2148) were recruited in the study. Participants were categorized according to the severity of COVID-19 infection and hospitalization. The study sample was stratified according to age, gender, body mass index (BMI), comorbidities, family income, smoking status, and ABO blood groups. Risk factors were investigated using the Chi-square test and multivariate logistic regression analyses.

Results: Severe illness and hospitalization were associated with older age, males, individuals with comorbidities, higher BMI, and lower-income. No significant differences were found in the incidence of severe illness or hospitalization frequency between the ABO groups or between smokers and non-smokers. Multivariate logistic regression analyses predicted male gender, being older than 40, having a BMI of over 30, having 3 or more comorbidities, and low family income as risk factors for severe COVID-19 outcomes.

Conclusion: Age was the strongest predictor for severe COVID-19 outcome, followed by having 3 or more comorbidities and to a lesser extent male gender and obesity. These results could help target at-risk groups with infection prevention measures including prioritizing primary COVID-19 vaccines, as well as booster doses.

1. Introduction

Coronavirus disease 2019 (COVID-19) was first identified in Wuhan, China in December 2019. The etiology was recognized as the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. The virus has rapidly spread worldwide and caused a pandemic responsible for more than 505 million confirmed cases and over 6 million deaths as of April 22, 2022 [2]. The clinical manifestations and outcomes of SARS-CoV-2 infection vary widely between individuals and range from asymptomatic to fatal. It is estimated that asymptomatic infections make up approximately 35% of SARS-CoV-2 infections and are expected to contribute to the spread of the virus in communities [3]. Most symptomatic COVID-19 cases are mild to moderate in severity. The most common symptoms of mild-moderate cases are cough, fever, and fatigue [4]. The rate of severe cases requiring hospitalization varies between countries and is estimated to occur in 10–20% of symptomatic infections [5]. The main clinical manifestation of severe infection is pneumonia with hypoxemia (SpO2 < 92%), which may progress to life-threatening complications, including acute respiratory distress syndrome and multi-organ failure [4,6].

Since the early days of the pandemic, it was clear that SARS-CoV-2 infection has a disproportionate impact on different groups of the population. For this reason, several potential risk factors have been studied to identify the predictors of severe COVID-19, hospitalization, and death. Age is known to be a major predictor of disease severity [5]. Most hospitalizations and deaths associated with COVID-19 occur in the elderly group [7]. In addition, reports have indicated that the risk of severe disease and death is influenced by other factors, including gender, smoking, comorbidities, ABO blood group, ethnicity, and body mass index (BMI) [8–10].

Jordan is one of the hardest-hit countries by the pandemic. Since the first case was identified in early March 2020, Jordanian health authorities have recorded more than 1.7 million confirmed cases of COVID-19 and 14,066 deaths as of June 3, 2022, placing the country among the top 50 in the world in terms of the number of confirmed cases [11]. The Jordanian population is characterized by several features that make it

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distinct from other populations. It is estimated that 60% and 94% of the population are under 30 and 60 years of age, respectively [12]. The smoking rate in Jordan is one of the highest in the world [13]. Furthermore, about half of Jordanian residents suffer from low socio-economic status. Hence, we hypothesized that the unique characteristics of the Jordanian population would influence predictors of COVID-19 severe outcomes. In this study, we explored several potential risk factors for severe COVID-19 outcomes among the Jordanian population.

2. Methods

2.1. Study design

This study is part of the Jordan COVID-19 project (JCP). This project was approved by the Institutional Review Board at Jordan University of Science and Technology (Ref. 3/139/2021, dated 30.03.2021). The project recruited Jordanians who recovered from COVID-19 (≥18 years old). The study was conducted from March to July of 2021 and participants were recruited from the whole of Jordan. The study sample was recruited by a total of 10 research assistants distributed over all governorates of Jordan. To minimize selection bias, the study population was stratified based on age, sex, and history of hospitalization due to COVID-19. Then, the number of participants required in each stratum was estimated before the study sample was recruited. Participants who had received COVID-19 vaccination before contracting the disease were excluded from the study. Participants were interviewed in person or over the phone and questionnaires were filled in by the research assistant or, in some cases, by the participants according to their preference. The questionnaire was constructed using Google Forms™ and validated by a group of selected experts in the field. The questionnaire was piloted on a sample of the population and feedback from the participants was used to revise the questions and the content of the questionnaire. Responses from the pilot study were not included in the final analysis. The questionnaire covered different aspects including demographics, symptoms, hospitalization, and information about COVID-19 disease infection and testing. The first section of the questionnaire obtained online consent from the participants and confirmed recovery from COVID-19. The questionnaire and raw data will be available upon request from the corresponding author.

2.2. COVID-19 severity classification

Each participant was categorized into one of four COVID-19 severity groups based on clinical manifestations and disease history. Disease severity was used as a dependent variable in various statistical analyses in conjunction with potential disease risk factors. The four disease severity groups are asymptomatic, mild, moderate, and severe COVID-19. This classification was based on criteria presented by Parasher A. (2021) [6]. Cases showing symptoms such as fever, sore throat, malaise, body aches, nausea, etc., but without symptoms of pneumonia were classified as mild COVID-19. Cases of pneumonia (persistent fever and cough) without hypoxemia were classified as moderate COVID-19. Cases of confirmed severe pneumonia with hypoxemia were classified as severe COVID-19. Individuals who experienced asymptomatic, mild, or moderate COVID-19 were considered to have non-severe COVID-19. In addition to using disease severity as the dependent variable in the analyses, hospitalization status was included as an additional dependent variable and was correlated with potential disease risk factors.

2.3. Body mass index calculation and categorization

The questionnaire collected information about the participants' weight and height. The BMI was then calculated by dividing the weight (Kg) by the square of the height (meters). BMI values were used to classify each participant into one of four categories according to the World Health Organization (WHO) classification: underweight (<18.5 kg/m^2), normal (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2), and obese (>30 kg/m^2).

2.4. Comorbidities

The questionnaire collected information on the following comorbidities: cardiovascular diseases, diabetes mellitus, chronic respiratory diseases, kidney diseases, liver diseases, cancer, immunodeficiencies, autoimmune diseases, and anemia. Participants were stratified into four groups based on the number of comorbidities (0, 1, 2, ≥3).

2.5. Statistical analysis

Data were analyzed using the Statistical Package for the Social Sciences version 26 (IBM Inc., Armonk, New York, United States). Baseline descriptive characteristics of the study population were presented as mean ± SD for age and BMI variables and as numbers and percentages for categorical variables. The association of potential disease risk factors was investigated first by stratifying the sample according to each factor and then assessing differences in the proportions of severe vs. non-severe COVID-19 or hospitalized vs. non-hospitalized among the strata of each factor. The Chi-square test was used to test the significance of the differences in proportions between groups. Participants with missing blood groups were excluded from the corresponding analyses. To compensate for other possible risk factors, two multivariate logistic regression analyses were performed with severe illness as the output of the first and hospitalization as the output of the second. Collinearity between the independent variables was ruled-out before running the logistic regression analysis. No evidence of collinearity was found by Pearson's correlation or by the tolerance and variance inflation factor indices. P values less than 0.05 were considered statistically significant.

3. Results

3.1. Study population

A total of 2148 participants were recruited in the study. Of those, 58.0% were female. The mean age of the sample was 40.2 ± 15.5 years, whereas the mean BMI was 28.17, which falls in the overweight category according to the WHO classification. A total of 362 (17%) participants were current smokers, and 496 (23%) reported having at least one comorbidity. Severe COVID-19 and hospitalizations were reported by 12.1% and 10.2% of participants, respectively. Data for the blood group

Table 1
Baseline characteristics of the study population.

Characteristic	Value: N, %
Number of participants	2148
Sex	
Men	903, 42%
Women	1245, 58%
Smoking use	362, 17.0%
Blood group	
A	822, 38.3%
B	330, 15.4%
AB	205, 9.5%
O	749, 34.9%
Unknown	42, 2.0%
Individuals with chronic diseases	496, 23%
Disease severity	
Asymptomatic	197, 9.2%
Mild	1306, 60.8%
Moderate	385, 17.9%
Severe	260, 12.1%
Admitted to hospital	219, 10.2%
Income (1$ USA = 0.71 JD)	
Low (<650 JD)	1156, 53.8%
Moderate-high (≥650 JD)	992, 46.2%

of 42 participants were not provided. Table 1 presents the baseline characteristics of the participants.

3.2. Risk factors for severe COVID-19 and hospitalization

To examine the impact of age on disease severity and hospitalization due to COVID-19, participants were divided into 5 age groups as shown in Table 2. Significantly higher proportions of severe COVID-19 and hospitalization were seen in the older groups ($p < 0.001$) (Table 2). For example, 37.9% of participants over the age of 60 years experienced severe illness compared to 4.0% of participants in the 18–30 years age group. Similarly, the hospitalization rate was higher for participants older than 60 years (34.5%) than those within the 18–30 years age group (2.0%). Significantly higher frequencies of severe illness and hospitalization were observed in males compared to females (17.7% vs. 8.0%, $p < 0.001$ and 16.5% vs. 5.6%, $p < 0.001$, respectively) (Table 2).

Next, the effect of comorbidities on disease severity and hospitalization was investigated. The sample was divided into groups based on the presence/number of comorbidities (Table 2). Higher ratios of severe illness and hospitalizations were found in the groups with comorbidities than in the non-comorbidities group. Furthermore, a significant increase in the frequency of severe illness and hospitalizations was observed with an increase in the number of comorbidities ($p < 0.001$). The participants were then stratified into four groups based on their BMI (Table 2). The groups with higher BMI values had significantly higher frequencies of severe illness and hospitalization than the groups with lower BMI values ($p < 0.001$) (Table 2).

The study population was then divided into two groups based on the monthly income of the family (Table 2). A significantly higher frequency of severe illness was found in the low-income group (<650 JD/month) compared to the moderate/high-income group (>650 JD/month) (15.0% vs 8.8%, $p < 0.001$). Similarly, hospitalization rates were significantly higher in the low-income group than in the moderate/high income group (12.7% vs 7.3%, $p < 0.001$).

The rates of severe illness and hospitalizations did not differ according to ABO blood groups ($p > 0.05$), or smoking status ($p > 0.05$) (Table 2).

Variables were further analyzed by multivariate logistic regression to control for the confounding factors. Following adjustment, male gender, having a BMI of more than 30, having 3 or more comorbidities, and being older than 40 years, predicted higher risk for severe illness and hospitalization (Table 3). On the other hand, ABO blood groups and smoking were not among the risk factors for severe illness or hospitalization. Surprisingly, smoking was inversely correlated with the risk of severe illness [OR = 0.515 (95% CI: 0.334–0.796)], but not with hospitalization. The discrepancy between univariate and multivariate analyses could be attributed to the fact that most cigarette smokers in the study sample (82.0%) were males (Supplementary Table 1). Since the male gender is one of the predicted risk factors for disease severity, this could mask the effect of smoking in the results of univariate analyses.

4. Discussion

In this study, we explored demographic and clinical predictors for COVID-19 severe illness and hospitalization among Jordanian adults. Our study showed that age was the strongest predictor for severe COVID-19 outcome followed by having 3 or more comorbidities and obesity. The strength of the current study is that it described the predictors of disease severity and hospitalization of COVID-19 using a relatively large sample of subjects recovered from COVID-19. Therefore, the study provides a comprehensive understanding of the risk factors for severe outcomes in Jordan and in other countries with similar socioeconomic and racial characteristics. This could provide helpful information for health policymakers, to enable the targeting of at-risk groups with more stringent infection prevention measures including prioritizing these groups for primary COVID-19 vaccination and possibly booster doses of vaccine.

Old age is an established risk factor for severe disease in the literature [5]. It was consistently the strongest predictor of severe disease outcomes in the examined population. The odds ratio for hospitalization is greater than 9 for the >60 years age group compared to the 18–30 years age group. This finding is consistent with several studies in other countries such as China and the USA [5,9,14,15]. Having multiple comorbidities was also an independent predictor of severe outcomes, which is in line with most previous studies [8,15]. In a study from Saudi Arabia, diabetes mellitus was a strong predictor of COVID-19 hospitalization [16]. In agreement with the current study, Ko et al. reported a higher risk of hospitalization for COVID-19 patients with 3 or more comorbidities [8].

In agreement with the study findings, obesity was reported by other groups to increase the risk of severe or critical COVID-19 outcomes [14, 17–19]. For example, a high prevalence of obesity was found among

Table 2
Rates of severe COVID-19 and hospitalization according to age, gender, and BMI.

Criteria		Total number	Severe COVID-19 n (%)	P-value	Hospitalization n (%)	P value
Age group (years)	18–30	710	29 (4.0)	**< 0.001**	14 (2.0)	**< 0.001**
	31–40	493	33 (6.7)		25 (5.1)	
	41–50	387	51 (13.2)		40 (10.3)	
	51–60	297	48 (16.2)		50 (16.8)	
	>60	261	99 (37.9)		90 (34.5)	
Gender	Male	903	160 (17.7)	**< 0.001**	149 (16.5)	**< 0.001**
	Female	1245	100 (8.0)		70 (5.6)	
Comorbidities (number)	0	1652	143 (8.7)	**< 0.001**	113 (6.8)	**< 0.001**
	1	199	28 (14.1)		25 (12.6)	
	2	153	40 (26.1)		33 (21.7)	
	≥3	144	49 (34.0)		48 (33.3)	
BMI Groups	<18.5	59	2 (3.4)	**< 0.001**	0 (0.0)	**< 0.001**
	18.5–24.9	664	38 (6.4)		26 (3.9)	
	25–29.9	786	94 (12.0)		82 (10.4)	
	≥30	639	126 (19.7)		111 (17.4)	
Blood group	A	822	99 (12.0)	0.823	78 (9.5)	0.863
	B	330	40 (12.1)		30 (9.1)	
	AB	205	26 (12.7)		23 (11.2)	
	O	749	81 (10.8)		74 (9.9)	
Smoking status	No	1786	226 (12.7)	0.083	182 (10.2)	0.986
	Yes	362	34 (9.4)		37 (10.2)	
Income (JD)	<650	1156	173 (15.0)	**< 0.001**	147 (12.7)	**< 0.001**
	≥650	992	87 (8.8)		72 (7.3)	

The Chi-square test was used to calculate p values.

Table 3
Multivariate logistic regression results predicting risk factors of severe COVID-19 and hospitalization.

Variable	Category	Severe COVID-19		Hospitalization	
		P-value	Adjusted odds ratio (95% CI)	P-value	Adjusted odds ratio (95% CI)
Gender	Female		Reference		Reference
	Male	**< 0.001**	2.134 (1.564–2.911)	**< 0.001**	2.534 (1.789–3.589)
Blood group	A		Reference		Reference
	B	0.903	1.027 (0.671–1.57)	0.900	0.969 (0.597–1.574)
	AB	0.935	1.021 (0.619–1.685)	0.619	1.147 (0.667–1.973)
	O	0.762	1.054 (0.75–1.48)	0.150	1.315 (0.906–1.908)
BMI group	18.5–24.9		Reference		Reference
	<18.5	0.914	1.085 (0.248–4.736)	0.997	0 (0–0)
	25–29.9	0.145	1.387 (0.893–2.153)	0.079	1.577 (0.949–2.62)
	≥30	**0.003**	1.942 (1.259–2.996)	**0.002**	2.212 (1.343–3.644)
Number of comorbidities	0		Reference		Reference
	1	0.744	1.083 (0.672–1.744)	0.713	1.1 (0.662–1.828)
	2	0.063	1.558 (0.977–2.485)	0.313	1.3 (0.781–2.163)
	≥3	**< 0.001**	2.635 (1.682–4.13)	**< 0.001**	3.163 (1.991–5.026)
Age groups	18–30		Reference		Reference
	31–40	0.212	1.407 (0.823–2.407)	0.077	1.852 (0.935–3.669)
	41–50	**0.001**	2.345 (1.397–3.939)	**< 0.001**	3.24 (1.685–6.231)
	51–60	**0.002**	2.342 (1.353–4.053)	**< 0.001**	4.275 (2.211–8.264)
	>60	**< 0.001**	6.329 (3.76–10.652)	**< 0.001**	9.783 (5.15–18.584)
Smoking status	Nonsmoker		Reference		Reference
	Smoker	**0.003**	0.515 (0.334–0.796)	0.101	0.691 (0.444–1.075)
Income (JD)	≥650		Reference		Reference
	<650	**0.001**	1.637 (1.211–2.211)	**0.001**	1.76 (1.262–2.456)

COVID-19 patients requiring mechanical ventilation [17]. In addition, obesity is believed to be an important factor in shifting severe COVID-19 to younger age groups [20]. Although the exact mechanism is not fully understood, several factors could play a role in the increased risk of severe COVID-19 in obese individuals. For example, obesity is known to induce low-grade systemic inflammation that can impair immune responses against infection [21]. Moreover, Obese individuals have reduced lung capacity which renders them more likely to have reduced lung function [22].

Our study showed that male gender is a predicted risk factor for severe illness and hospitalization. Similarly, this finding was reported in other countries such as the UK and the USA [14,18,19]. In Lebanon, among COVID-19 diabetic patients, severe disease was also associated with male gender [23]. This could be attributed to differences in the expression of the essential molecules for virus entry into host cells, namely ACE2 and TMPRSS2, between the two gender groups [24]. In addition, differences in the strength of the innate and adaptive immune responses between females and males provide another candidate mechanism [25].

The analysis showed that low family income (less than 650 JD or 915 USD/month) is an independent risk factor for severe illness and hospitalization. This finding is in line with that reported in the USA [26]. Several factors could contribute to the increased risk of severe illness in the low-income groups of the population. For example, low income hinders access to high-quality health care. In addition, malnutrition is more likely to occur in low-income groups, which could negatively affect the strength of the immune system and increase the risk of comorbidities. Finally, low-income individuals are less likely to work from home. Hence they are more likely to get a higher dose of viral particles at the time of exposure, which increases their risk of more severe disease [27].

Previous studies have reported links between the ABO blood group and susceptibility to SARS-COV-2 infection [28,29]. Having blood type A was reported to increase susceptibility while having blood type O was reported to provide protection. However, the effect of the ABO blood group on the course of the disease following infection is highly controversial. Some groups have provided evidence that certain ABO blood groups influence infection outcomes, yet no consensus has been reached. For example, having blood type A was reported to increase the risk of severe illness and death by some and, in contrast, to have a protective effect by others [10,30,31]. On the other hand, our study, as well as those of others, found no significant effect by the ABO blood groups on the risk of severe outcomes of COVID-19 [32–34].

Smoking increases susceptibility to infection and the severity of influenza and other viral respiratory tract infections [35,36]. Therefore, smoking has been suggested to be a risk factor for severe COVID-19. However, the effect of smoking on the severity of COVID-19 illness remains a matter of debate. Smoking has been shown to be associated with a higher risk of infection and severe outcomes by many groups [37,38]. In contrast, others have reported no, or an inverse association between smoking and the progression of COVID-19 [14,39]. For example, a systemic review of 13 studies from China reported that the prevalence of smoking among hospitalized COVID-19 patients was significantly lower than the prevalence of smoking in the general Chinese population [39]. A prospective cohort study of 5279 patients with COVID-19 in the USA reported no correlation between current cigarette smoking and severe outcomes [14]. Herein, smoking was not a risk factor for severe COVID-19 or hospitalization in the Jordanian population. In fact, the logistic regression results showed a protective effect of smoking. However, these results should be interpreted with caution as this analysis did not consider the frequency of smoking as a factor and included former smokers within the non-smoker group.

Our study provided the first assessment of the possible risk factors among Jordanian COVID-19 patients based on a relatively large sample size. A previous report from Jordan with a small sample size (n = 133) investigated the clinical predictors of complications, such as admission to the intensive care unit (ICU) and respiratory failure, among hospitalized Jordanian COVID-19 patients [40]. In this study, clinical factors such as fever, dyspnea, and abnormal neutrophil count were among the risk factors for admission to the ICU. This provides important early insight into the predictors of ICU admission among COVID-19 patients. However, the findings cannot be extrapolated to all COVID-19 cases due to the nature of the population (i.e., hospitalized COVID-19 patients only).

Our study has some caveats and limitations that should be acknowledged. First, since the data was self-reported and not validated by any other methods, the accuracy of the responses could be affected by recall bias, overestimation, or dishonesty. In addition, the study was able to recruit former COVID-19 individuals who had recovered. However, fatal COVID-19 cases could not be included in the study sample.

Moreover, the ABO blood group data were missing for 42 participants. Variation in the response rates between different age, gender, clinical or socioeconomic groups of the population could result in the over-representation of some groups and under-representation of others. Finally, the study sample was collected from the general Jordanian population without stratification according to geographical regions. Since the level of healthcare varies slightly between the different Jordanian geographical regions, this might influence the hospitalization rates between the regions. Therefore, future studies are needed to provide a clearer picture for the effect of the risk factors reported herein and to provide a better understanding of the mechanisms by which these factors influence the severity of COVID-19.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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