Original Article

Risk factors predicting disease severity and mortality in coronavirus disease 2019 Saudi Arabian patients

Wala M. Al Balwi[1], Nouf AlGhamdi[1], Reem Alshahrani[1], Ihssan H. Abdelrahman[1,2], Sami Mahmoud[3], Ali Al-Hamad[3], Salma Al Hamzah[3], Fahad Al Jraid[3] Maha Al Turki[1,2], Mohammed A. Al Balwi[2,3,4]

[1]Department of Clinical Nutrition, College of Applied Medical Sciences, King Saud Bin Abdulaziz University for Health Sciences, [3]Department of Pathology and Laboratory Medicine, King Abdulaziz Medical City, Ministry of National Guard Health Affairs, [2]King Abdullah International Medical Research Centre, National Guard Health Affairs, [4]Department of Pathology, College of Medicine, King Saud Bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia

Address for correspondence:
Prof. Mohammed A. Al Balwi, Department of Pathology and Laboratory Medicine, MC 1122, King Abdulaziz Medical City, Ministry of National Guard Health Affairs, P.O. Box 22490, Riyadh 11426, Saudi Arabia.
E-mail: balwim@ngha.med.sa

Submission: 18-12-2022
Accepted: 20-02-2023
Published: 25-04-2023

Access this article online

Quick Response Code:

Website: www.thoracicmedicine.org

DOI: 10.4103/atm.atm_435_22

Abstract:

CONTEXT: Coronavirus disease 2019 (COVID-19) became a global pandemic that may be associated with significant associated risk factors.

AIMS: The aim of this study was to evaluate the factors predisposing risk to death in COVID-19 patients.

SETTINGS AND DESIGN: This is a retrospective study that presents the demographic, clinical presentation, and laboratory findings on our patients to determine risk factors contributing to their COVID-19 outcome.

METHODS: We used logistic regression (odds ratios) to examine associations between clinical findings and risk of death in COVID-19 patients. All analyses were done using STATA 15.

RESULTS: A total of 206 COVID-19 patients were investigated, 28 of them died, and 178 survived. Expired patients were older (74.04 ± 14.45 vs. 55.56 ± 18.41 in those who survived) and mainly of male gender (75% vs. 42% in those who survived). The following factors were strong predictors of death: hypertension (OR: 5.48, 95% CI: 2.10–13.59, $P < 0.001$), cardiac disease (OR: 5.08, 95% CI: 1.88–13.74, $P = 0.001$), and hospital admission (OR: 39.75, 95% CI: 5.28–299.12, $P < 0.001$). In addition, blood group B was more frequent in expired patients (OR: 2.27, 95% CI: 0.78–5.95, $P = 0.065$).

CONCLUSIONS: Our work adds to the current knowledge about the factors predisposing to death in COVID-19 patient. In our cohort, expired patients were of older age and male gender plus they were more likely to have hypertension, cardiac disease, and hospital severe disease. These factors might be used to evaluate risk of death in patients recently diagnosed of COVID-19.

Keywords:

Coronavirus disease 2019, mortality, risk factors, Saudi

COVID-19 is caused by a novel coronavirus known as severe acute respiratory syndrome-coronavirus (SARA-CoV-2). COVID-19 was first identified in Wuhan City, China, at the end of 2019 and the disease spread first to neighboring Asian countries and then worldwide.[1] The World Health Organization (WHO) has labeled coronavirus disease 2019 (COVID-19) as a global pandemic accounting for thousands of deaths worldwide.

In March 11, 2020, the WHO declared COVID-19 as a global pandemic with reported cases of 269,112,118 worldwide and a total of 5,307,847 deaths globally.[2] COVID-19 was confirmed in Saudi Arabia in March 2020 and then it has caused thousands of deaths due to drastic morbidity and mortality. Clinically, COVID-19 symptoms may vary from asymptomatic to symptomatic characterized by fever, dry throat, and tiredness and less common symptoms of diarrhea, sore throat, and

How to cite this article: Al Balwi WM, AlGhamdi N, Alshahrani R, Abdelrahman IH, Mahmoud S, Al-Hamad A, *et al*. Risk factors predicting disease severity and mortality in coronavirus disease 2019 Saudi Arabian patients. Ann Thorac Med 2023;18:98-102.

headache, rash of skin, and loss of taste or smell.[3] Severe cases of COVID-19 illness may require intensive care unit hospitalization and oxygen treatment. It has been reported that severe COVID-19 cases may associated with acute respiratory distress syndrome, septic shock, acute renal failure, and chronic heart failure.[4]

Although most of the COVID-19 patients especially the elderly may have secondary respiratory infection leading to develop coagulation abnormalities such as thrombocytopenia, hypercoagulation, disseminated intravascular coagulation, and venous thrombosis that increase inflammations, vascular hyperpermeability, multiorgan failure, and eventually death overtime.[5] Worldwide, thousands of studies were conducted to predict the influence factors that may contribute to increase individual susceptibility or not to the severity of COVID-19 disease. Several factors were intensively included in these studies such as factors of age, gender, comorbidities and mortalities, viruses and bacterial infections, various laboratory investigations, and host genetic makeup.[6-8] Recently, correlation reports linked COVID-19 risk and severity to the ABO blood group.[9-11] In this study, we aimed to investigate the risk factors associated with severe mortality among COVID-19 cohort confirmed cases.

Methods

Data collection and patient phenotype

This is a record-based cross-sectional study that included patients from King Abdulaziz Medical Center, Ministry of National Guard Health Affair, Riyadh, Saudi Arabia. All patients with vary asymptomatic, mild or severe presentation which required hospital admission and had reverse transcriptase–polymerase chain reaction (RT-PCR) confirmed COVID-19 according to WHO interim guidance between April 2020 and August 2021. This study was approved by the Institutional Review Board at King Abdullah International Medical Research Center (SP21R/266/05). All patients' data were collected from the patients' electronic files (BestCare system) including detailed demographic information, clinical data, and laboratory investigation findings. Only patients with age more than 16 years old; both gender; confirmed positive RT-PCR COVID-19; and having vitamin D and ferritin laboratory investigations including ABO blood antigen group were recruited. Our patients' blood group was compared to control data from published ABO and Rh blood Saudi Arabian data.[12]

Statistical analysis

Patients' basic descriptive data and clinical presentation, complications, and admission were summarized as frequencies and percentages. Continuous data of the descriptive statistics were presented as mean and standard deviation. Pearson's Chi-square test was used to analyze categorical variables and Student's *t*-test for continuous variables. Univariate analysis was performed against our primary outcome (expiration), and variables significant at $P < 0.05$ were selected for inclusion in our multivariate model. Statistical analysis was performed with STATA version 15.0 software (StataCorp, College Station, TX, USA) with statistical significance defined at values of $P < 0.05$.

Results

Of 8000 patients whose RT-PCR tests were confirmed positive for COVID-19, about 206 (2.6%) patients were selected randomly and enrolled in the final analysis due to the availability of their vitamin D, ferritin, and ABO group laboratory tests. The ages of patients ranged from 16 to 99 years. The mean (±SD) age was 55.5 ± 18.4 years, 110 (53.6%) were female, and 96 (46.4%) were male [Table 1]. The male-to-female ratio was approximately 1:1.2. About 99 (48.1%) patients were hospitalized, in which only 27 (13.1%) patients were expired. Our patients had several comorbidities disorders, including diabetes mellitus, hypertension, dyslipidemia, pulmonary and autoimmune disease, obesity, neurological disease, chronic heart disease, chronic kidney disease, endocrine disease, and other [Table 1].

Table 1 shows the demographics of the total COVID group plus the expired and alive groups. The expired group were older, male gender (75%), hypertensive, suffered more neurological diseases, cardiac and stroke and were admitted to the hospital. Diabetes mellitus (48.5%), hypertension (40.8%), dyslipidemia (35.9%), pulmonary and autoimmune diseases (19.4%), and obesity (9.2%) were the prevalent common comorbidity. All severe comorbidity admitted cases may require oxygen saturation or mechanical ventilation due to respiratory distress complicated with pneumonia and other presentation. The inflammatory marker mean (± SD) levels among patients for ferritin (μg/L) and Vitamin D (nmol/L) were 798.2 ± 1239.3 and 54.4 ± 35.2, respectively.

Table 2 shows univariate and multivariate analysis for factors that predicted expiration due to COVID. Hypertension, cardiac disease, and hospitalization were the three main factors predicted expiration of our COVID patients. The logistic regression analysis with single variate factors showed significant predicting death once comparing lived and died patients with male mean aged (SD) (74.0 ± 14.5 years, $P < 0.0001$) and female aged (52.7 ± 17.1 years, $P < 0.001$), respectively. Furthermore, hypertension (OR = 5.48, 95% CI = 2.10–13.59; $P < 0.001$), chronic heart

Table 1: Patient's descriptive demographics data

Data	Alive, *n* (%)	Expired, *n* (%)	Total, *n* (%)	*P*
Age (year), mean±SD	52.65±17.14	74.04±14.45	55.56±18.41	<0.001
BMI (kg/m^2), mean±SD	30.99±10.43	28.53±8.46	30.65±10.20	NS
Vitamin D (nmol/L), mean±SD	54.62±34.00	52.73±42.65	54.37±35.15	NS
Ferritin (µg/L), mean±SD	709.27±1132.68	1322.6±1672.67	798.22±1239.26	0.02
Male gender	75 (42.10)	21 (75.00)	96 (46.60)	0.001
Diabetes	84 (47.19)	16 (57.14)	100 (48.54)	NS
Hypertension	63 (35.40)	21 (75.00)	84 (40.80)	<0.001
Dyslipidemia	64 (36.00)	10 (35.70)	74 (35.90)	NS
Obesity	17 (9.55)	2 (7.14)	19 (9.22)	NS
CKD	10 (5.62)	4 (14.30)	14 (6.80)	NS
Liver disease	5 (2.81)	1 (3.57)	6 (2.91)	NS
Neurological disease	18 (10.10)	7 (25.00)	25 (12.10)	0.025
Stroke	3 (1.69)	3 (10.7)	6 (2.91)	0.008
Cardiac disease	13 (7.30)	8 (28.6)	21 (10.20)	0.008
Cancer/leukemia	5 (2.81)	3 (10.70)	8 (3.88)	0.044
Pulmonary/AI	35 (17.70)	5 (17.90)	40 (19.40)	NS
Thyroid disease	12 (6.74)	1 (3.57)	13 (6.31)	NS
Hospital admission	72 (40.50)	27 (96.40)	99 (48.10)	<0.001

BMI=Body mass index, CKD=Chronic kidney disease, AI=Autoimmune disease, SD: Standard deviation, NS=Nonsignificant

disease (OR = 5.08, 95% CI = 1.88–13.82; $P = 0.001$), and hospital admission (OR = 39.75, 95% CI = 5.28–299.12, $P < 0.001$) were significant between live and expired patients. All three factors were significant in multivariate analysis [Table 2]. There was no significant evidence that patients with others factors including ferritin and Vitamin D levels; however, ferritin levels were higher in expired patients ($P = 0.02$).

No significant association was found between the distribution of blood groups in total COVID compared to controls, except for blood group AB+, which was increased in the COVID group compared to controls ($P = 0.023$). The expired group showed increased blood group B + representation 31.82% vs. 17% in control ($P = 0.065$) [Table 3].

Table 2: Univariate and multivariate analyses for risk factors predicting death of coronavirus disease 2019 patients

Variables	Univariate			Multivariate		
	OR	*P*	95% CI	OR	*P*	95% CI
Hypertension	5.48	<0.001	2.10-13.59	12.4	0.005	2.16-71.04
Cardiac disease	5.08	0.001	1.88-13.74	13.46	0.003	2.47-73.28
Hospital admission	39.75	<0.001	5.28-299.12	51.37	0.004	3.64-723.23

OR=Odds ratio, CI=Confidence interval

Table 3: Blood group distribution between coronavirus disease 2019 total, expired and controls[12]

Blood group	Controls, *n* (%)	COVID total, *n* (%)	Not expired, *n* (%)	Expired, *n* (%)
A	2840 (28.57)	22 (23.08)	16 (23.19)	6 (27.27)
B	1690 (17.00)	14 (14.29)	7 (10.14)	7 (31.82)**
AB	402 (4.04)	8 (8.79)*	8 (11.59)	0
O	5007 (50.38)	47 (49.45)	38 (55.07)	9 (40.91)
Total	9939 (100.00)	91 (100.00)	69 (100.00)	22 (100.00)

*2.29 (0.95-4.76), *P*=0.023, **2.27 (0.78-5.95), *P*=0.065. COVID: Coronavirus disease 2019

Discussion

Our study findings revealed that in our cohort of COVID-19 patients, there was an excess of females; however, in the expired group, three quarter of them were male. The mean age of the total group was in the fifth decade, but the expired group were older (in the seventh decade of age). The majority of expired patients were hospitalized compared to <50% of the nonexpired patients; this was in alliance with the international reporting.[13] We showed that expired patients had higher levels of ferritin; ferritin was reported as a promising predictor of mortality in COVID-19 cases.[14] Cytokine storm is a systemic inflammatory response to infections and drugs leading to excessive activation of immune cells, hyperferritinemia, and pro-inflammatory cytokines production.[15] Therefore, ferritin may not only be a marker of inflammation but may play a role in cytokine storm.

Low vitamin D status was reported to be associated with pneumonia and upper respiratory tract infections, secondary to the weakness of immune system, and elevated inflammatory cytokines in COVID-19 patients.[16] In this study, Vitamin D deficiency showed no association with disease susceptibility or severity, despite, that Vitamin D deficiency was a common health observation among Saudi Arabian adult population with varies reported prevalence estimated between 28% and 75%.[17] Data are not available on whether the patients in this study were on vitamin D supplement.

This study identified hypertension, chronic heart disease, and diabetes mellitus as the most significant predictors of expiration among the different studied factors. Previous research on COVID-19 patients showed increased mortality risk with the presence of hypertension, diabetes mellitus, and cardiovascular diseases.[13] A more recent single-institute study from Saudi Arabia showed an association between diabetes mellitus and COVID-19 severity and outcomes.[18]

Gil-Manso *et al*.[9] showed that patients with blood group O showed a persistent specific immune response against SARS-CoV-2, while non-O needed longer time to clear the virus; thus, blood group appears to be protective. Pereira *et al*.[11] reviewed the published literature on the blood group associations with COVID-19 severity and found that overall, blood type A is the most associated with COVID-19 severity and mortality, while blood group O was a protective factor for the disease progression. A study from our hospital recently showed that blood group B was associated with severity, while blood group O was protective;[19] our results here are in agreement with Jawdat *et al*.,[19] whether this association with blood group B and disease severity is a specific finding to Saudis or it is the blood group O and protection from severe disease is the link needs to be studied further.

Recently, we used the same cohort to investigate risk of death in COVID-19 patients. We identified age, age/body mass index, hypertension, cardiac disease, and hospital admission as risk factors for death in COVID-19 patients.[20]

Our study revealed predictive factors for developing severe COVID-19 that can be used by physicians to identify high-risk COVID-19 cases and determine appropriate measurement to achieve the best possible clinical outcomes. Our sample size is relatively small to make strong conclusion about predictors of mortality in COVID-19 patients. However, our findings are in agreement with published data.

Data sharing

The data associated with this manuscript are available upon request.

Ethical approval

This study was approved by the Institutional Review Board (IRB) at King Abdullah International Medical Research Canter (SP21R/266/05).

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Pirzada A, Mokhtar AT, Moeller AD. COVID-19 and myocarditis: What do we know so far? CJC Open 2020;2:278-85.
2. Cucinotta D, Vanelli M. WHO declares COVID-19 a pandemic. Acta Biomed 2020;91:157-60.
3. Kim GU, Kim MJ, Ra SH, Lee J, Bae S, Jung J, *et al.* Clinical characteristics of asymptomatic and symptomatic patients with mild COVID-19. Clin Microbiol Infect 2020;26:948.e1-3.
4. Esposito L, Cancro FP, Silverio A, Di Maio M, Iannece P, Damato A, *et al.* COVID-19 and acute coronary syndromes: From pathophysiology to clinical perspectives. Oxid Med Cell Longev 2021;2021:4936571.
5. Biswas I, Khan GA. Coagulation disorders in COVID-19: Role of toll-like receptors. J Inflamm Res 2020;13:823-8.
6. Samadizadeh S, Masoudi M, Rastegar M, Salimi V, Shahbaz MB, Tahamtan A. COVID-19: Why does disease severity vary among individuals? Respir Med 2021;180:106356.
7. Zirpe K, Pote P, Deshmukh A, Gurav SK, Tiwari AM, Suryawanshi P. A retrospective analysis of risk factors of COVID-19 associated mucormycosis and mortality predictors: A single-Center study. Cureus 2021;13:e18718.
8. Wong CK, Wong JY, Tang EH, Au CH, Wai AK. Clinical presentations, laboratory and radiological findings, and treatments for 11,028 COVID-19 patients: A systematic review and meta-analysis. Sci Rep 2020;10:19765.
9. Gil-Manso S, Miguens Blanco I, Motyka B, Halpin A, López-Esteban R, Pérez-Fernández VA, *et al.* ABO blood group is involved in the quality of the specific immune response anti-SARS-CoV-2. Virulence 2022;13:30-45.
10. Ratiani L, Sanikidze TV, Ormotsadze G, Pachkoria E, Sordia G. Role of ABO blood groups in susceptibility and severity of COVID-19 in the Georgian population. Indian J Crit Care Med 2022;26:487-90.
11. Pereira E, Felipe S, de Freitas R, Araújo V, Soares P, Ribeiro J, *et al.* ABO blood group and link to COVID-19: A comprehensive review of the reported associations and their possible underlying mechanisms. Microb Pathog 2022;169:105658.
12. Alzahrani M, Jawdat D, Alaskar A, Cereb N, Hajeer AH. ABO and Rh blood group genotypes in a cohort of Saudi stem cell donors. Int J Immunogenet 2018;45:63-4.
13. Singh AK, Gillies CL, Singh R, Singh A, Chudasama Y, Coles B, *et al.* Prevalence of co-morbidities and their association with mortality in patients with COVID-19: A systematic review and meta-analysis. Diabetes Obes Metab 2020;22:1915-24.
14. Ahmed S, Ansar Ahmed Z, Siddiqui I, Haroon Rashid N, Mansoor M, Jafri L. Evaluation of serum ferritin for prediction of severity and mortality in COVID-19- A cross sectional study. Ann Med Surg (Lond) 2021;63:102163.
15. Behrens EM, Koretzky GA. Review: Cytokine storm syndrome: Looking toward the precision medicine era. Arthritis Rheumatol 2017;69:1135-43.
16. Munshi R, Hussein MH, Toraih EA, Elshazli RM, Jardak C, Sultana N, *et al.* Vitamin D insufficiency as a potential culprit in critical COVID-19 patients. J Med Virol 2021;93:733-40.
17. Tuffaha M, El Bcheraoui C, Daoud F, Al Hussaini HA, Alamri F, Al Saeedi M, *et al.* Deficiencies under plenty of sun: Vitamin D status among adults in the kingdom of Saudi Arabia, 2013. N Am J Med Sci 2015;7:467-75.
18. Alguwaihes AM, Al-Sofiani ME, Megdad M, Albader SS, Alsari MH, Alelayan A, *et al.* Diabetes and Covid-19 among hospitalized patients in Saudi Arabia: A single-centre retrospective study. Cardiovasc Diabetol 2020;19:205.
19. Jawdat D, Hajeer A, Massadeh S, Aljawini N, Abedalthagafi MS, Alaamery M. Correlation between ABO blood group phenotype

and the risk of COVID-19 infection and severity of disease in a Saudi Arabian Cohort. J Epidemiol Glob Health 2022;12:85-91.

20. Al Balwi W, Al Turki M, Memish ZA, Fakhoury HM, Al Balwi M, Hajeer AH. Age/BMI is a stronger predictor of death in COVID-19 patients than age alone: A pilot study. J Epidemiol Glob Health 2022;12:548-51.