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Short Communication

## Risk factors for COVID-19 infection and hospitalization, a population based case-control study from eastern Iran



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### ABSTRACT

**Objectives:** Investigating the factors associated with COVID-19 infection and its severity can be a major element in controlling the pandemics. This study aims to assess risk factors of COVID-19 infection and factors associated with hospitalization of COVID-19 cases.

**Methods:** In this case-control study, 416 confirmed COVID-19 cases based on the polymerase chain reaction test and 535 controls were selected from the urban and rural areas of Sistan-region-East of Iran.

**Results:** Cases had a lower frequency of hypertension than controls (12.3% vs 18.3% respectively,  $P = 0.011$ ). Out of the investigated factors, only age over 50, increased the chance of hospitalization (odds ratio = 5,  $P = 0.007$ ).

**Conclusion:** Although age was expected to be a risk factor, the observed protective effect of hypertension should be considered with caution.

### Introduction

Coronaviruses belong to the large family of the coronaviridae including common cold virus to the agents responsible for severe diseases such as severe acute respiratory syndrome, Middle East Respiratory Syndrome, and COVID-19 [1,2]. According to the available literature, different factors have been reported as risk factors of COVID-19 infection. It should be noted that the impact of these factors is controversial in different studies [3–5].

Sistan area located in the eastern part of Iran with more than 25,000 active COVID-19 cases, has experienced seven peaks of the SARS-CoV-2 pandemics. There is no scientific evidence regarding the main risk factors of COVID-19 infection and its severity in this area. Therefore, this study aimed to assess the factors associated with occurring infection as well as risk factors for hospitalization among a sample of the rural and urban population of the eastern part of Iran.

### Methods

The present study was carried out based on the case-control design. Cases were confirmed patients with COVID-19 infection selected based on the polymerase chain reaction test results collected from the medical and health records. Controls were subjects without evidence of COVID-19 infection randomly selected from the population of the cases' res-

idence area. In the selected rural and urban areas, all confirmed cases identified during the COVID-19 pandemics were selected by the consensus method. Number of controls in each area was the same as cases of that area.

After providing informed consent, required information was collected using a researcher-made checklist by face-to-face interview with the study subjects, their families, health staff of the health houses, and also from the medical records. Confirmed cases were classified as out-patients (asymptomatic and symptomatic cases without history of hospitalization) and hospitalized.

Data were described by percent frequency. Comparing the categorical variables between cases and controls was performed using chi square test. Investigating the association between COVID-19 infection and hospitalization was performed using logistic regression models adjusting for potential confounders. All statistical analyses were performed using Stata version 14 software.

### Results

In this study, 951 subjects from rural and urban regions in three districts of Sistan area (Zabol, Nimrooz, and Zahak) were investigated. These subjects included 416 COVID-19 confirmed cases and 535 controls. It should be noted that 119 cases were excluded from the study because of unreliable information. Out of them, 477 (50%) were male

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**Table 1**  
Demographic and clinical factors in cases and controls/outpatient and hospitalized patients with COVID-19.

COVID-19 cases vs healthy controls from the general population					COVID-19 hospitalized cases vs COVID-19 outpatients					
Demographic and clinical factors		All study subjects			P-value	Demographic and clinical factors		COVID-19 confirmed cases		P-value
		Controls	COVID-19 confirmed cases					Outpatient	Hospitalized	
Gender	Male	n	269	208	0.932	Male	n	187	11	0.467
		%	50.28	50			%	49.34	57.89	
	Female	n	266	208		Female	n	192	8	
		%	49.72	50			%	50.66	42.11	
Age	<60	n	436	359	0.052	<50	n	300	6	<0.0001
		%	81.5	86.3			%	79.16	31.58	
	>60	n	99	57		>50	n	79	13	
		%	18.5	13.7		%	20.84	68.42		
History of diabetes mellitus	yes	n	43	38	0.548	yes	n	31	6	0.001
		%	8.04	9.13			%	8.18	31.58	
History of cancer	yes	n	5	1	0.180	yes	n	1	0	0.823
		%	0.93	0.24			%	0.26	0	
History of hypertension	yes	n	98	51	0.011	yes	n	43	8	<0.001
		%	18.32	12.26			%	11.35	42.11	
History of immunodeficiency	yes	n	0	2	0.108	yes	n	2	0	0.751
		%	0	0.48			%	0.53	0	
History of cardiovascular disease	yes	n	12	9	0.934	yes	n	7	2	0.013
		%	2.24	2.16			%	1.85	10.53	

**Table 2**  
Multivariate analysis for assessing the factors associated with COVID-19 infection and hospitalization.

Getting infection or hospitalization	Demographic and clinical factors	Odds ratio	95% confidence interval
Factors associated with COVID-19 infection	Female gender	1.03	0.79, 1.34
	Diabetes mellitus	1.52	0.92, 2.51
	hypertension	0.64	0.42, 0.98
	Cardiovascular disease	1.08	0.44, 2.68
	Age>60	0.99	0.98, 1
Factors associated with COVID-19 hospitalization	History of diabetes mellitus	2.14	0.65, 7.05
	History of hypertension	2.59	0.80, 8.32
	History of cardiovascular disease	2.82	0.46, 17.48
	Female gender	0.34	0.11, 1.04
	Age >50	5	1.55, 16.12

and the mean (SD) age of the subjects was 40.12 (18.84) years. As demonstrated in Table 1, frequencies of demographic factors as well as history of co-morbidities such as diabetes mellitus, cancer, immunodeficiency and cardiovascular diseases were the same among cases and controls. However, frequency of having hypertension was significantly higher among controls than cases (18.3% vs 12.3% respectively,  $P = 0.011$ ). According to the multivariate analyses, controlling the effect of potential confounders, Just having hypertension had a significant association with COVID-19 infection (odds ratio (OR) = 0.64,  $P = 0.41$ ) (Table 2).

Table 1 also shows that COVID-19 hospitalized cases compared with outpatient cases had significantly higher age (age >50: 68.4% vs 20.8% respectively,  $P < 0.0001$ ), as well as higher history of co-morbidities such as diabetes mellitus (31.58% vs 8.18% respectively,  $P = 0.001$ ), hypertension (42.11% vs 11.35% respectively,  $P < 0.0001$ ) and cardiovascular diseases (10.53% vs 1.85% respectively,  $P = 0.013$ ). After adjustment for potential confounders, just the OR for older age remained statistically significant (OR = 5,  $P = 0.007$ ).

## Discussion

In this research, the only unexpected result was lower frequency of hypertension among COVID-19 cases than controls. Results of a survey carried out in Iran by Araban et al. [6] showed that COVID-19 cases had higher rates of hypertension (1.2%), cardiovascular diseases (14.8%), and diabetes mellitus (12.4%) than the cases in our study region. However, they just performed a descriptive study without any comparison

between COVID-19 cases and controls. Another study conducted by Alizadehsani et al. [7] in Tehran – the capital of Iran- showed just age as a risk factor for COVID-19 and other co-morbidities did not have any influence on getting infection and disease. Unlike the results of most previous studies, in our study, history of hypertension caused 36% reduction in the chance of COVID-19. Such different results can be due to various factors such as different definitions of hypertension and different selection of cases and controls as well as various confounders in those studies. However, in agreement with our results, Shibata et al. and Shiffrin et al. reported that some antihypertensive medications such as angiotensin receptor blockers and angiotensin-converting enzyme inhibitors can up-regulate the angiotensin-converting enzyme 2 receptors which is responsible in facilitating the COVID-19 cell entry [8,9]. Moreover, an ecologic study carried out among the Japanese population [10] showed a negative association between antihypertensive treatment and COVID-19 prevalence which is partially in parallel with the results of the present study.

Comparing outpatient and hospitalized patients regarding different risk factors showed more expected results. Our univariate analyses showed that hospitalized COVID-19 cases were older than outpatients and had higher frequency of co-morbidities such as diabetes mellitus, cardiovascular diseases, and hypertension. It should be noted that, adjusted associations controlling the effect of potential confounders, we just found that age older than 50, caused a five times increase in the chance of hospitalization. Similar to our findings, Adham et al. [11] reported significant associations between age and chronic diseases with hospitalization among patients with COVID-19 in Ard-

abil, Iran. Kinoshita et al. [10] reported age of more than 60, obesity, gout, psychiatric disease and diabetes mellitus as risk factors for hospitalization among patients with COVID-19 while just the effect of age was proved in the present study. Finally, contrast to the current results, diabetes mellitus, cardiovascular disease and immunodeficiency and also male gender were introduced as risk factors for hospitalization of Mexican children under 18 [10]. The age of the participants could be a reason for the different results between that study and the present research.

In this study, controls were selected from the population without a positive polymerase chain reaction test as well as those without a history of common symptoms of COVID-19 from the beginning of the pandemic. Therefore, some of these subjects might have asymptomatic infection. The explanation for this limitation is that most of the study samples were selected before the Omicron pandemic and asymptomatic cases during this period were lower than the Omicron-dominant period. Thus, false-negative controls seem to be negligible.

In conclusion, our study showed that demographic and clinical factors cannot be risk factors of COVID-19 infection and disease, but older age increases the risk of hospitalization. The protective effect of hypertension in developing COVID-19 infection should be investigated by further prospective population-based studies.

#### Declarations of competing interest

The authors have no competing interests to declare.

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#### Ethics approval and consent to participate

The present study was approved by Zabol University of Medical Science ethical committee (IR.ZBMU.REC.1400.015). All ethical principles of the Helsinki ethical declaration have been met and written informed consent were obtained from all the participants.

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#### Author contributions

MM and MM acquired data, performed the statistical analyses, interpreted data, and drafted and revised the manuscript for important intellectual content and approved the final version. SS and HM interpreted data, reviewed the analyses and approved the final version. All authors have read and approved the manuscript.

#### Consent for publication

Not applicable.

#### Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

#### References

- [1] Cascella M, Rajnik M, Cuomo A, Dulebohn SC, Features Di Napoli R. *Evaluation and Treatment Coronavirus (COVID-19)*. Treasure IslandFL: StatPearls Publishing; 2020.
- [2] Liu Z, Magal P, Seydi O, Webb G. Understanding unreported cases in the COVID-19 epidemic outbreak in Wuhan, China, and the importance of major public health interventions. *Biology* 2020;9:50. doi:10.3390/biology9030050.
- [3] Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020;382:1708–20. doi:10.1056/NEJMoa2002032.
- [4] Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020;395:1054–62. doi:10.1016/S0140-6736(20)30566-3.
- [5] Shahbazi F, Solgi M, Khazaei S. Predisposing risk factors for COVID-19 infection: a case-control study. *Caspian J Intern Med* 2020;11:495–500. doi:10.22088/cjim.11.0.495.
- [6] Araban M, Karimy M, Koohestani H, Montazeri A, Delaney D. Epidemiological and clinical characteristics of patients with COVID-19 in Islamic Republic of Iran. *East Mediterr Health J* 2022;28:249–57. doi:10.26719/emhj.22.008.
- [7] Alizadehsani R, Alizadeh Sani Z, Behjati M, Roshanzamir Z, Hussain S, Abedini N, et al. Risk factors prediction, clinical outcomes, and mortality in COVID-19 patients. *J Med Virol* 2021;93:2307–20. doi:10.1002/jmv.26699.
- [8] Shibata S, Arima H, Asayama K, Hoshida S, Ichihara A, Ishimitsu T, et al. Hypertension and related diseases in the era of COVID-19: a report from the Japanese Society of Hypertension Task Force on COVID-19. *Hypertens Res* 2020;43:1028–46. doi:10.1038/s41440-020-0515-0.
- [9] Schiffrin EL, Flack JM, Ito S, Muntner P, Webb RC. Hypertension and COVID-19. *Am J Hypertens* 2020;33:373–4. doi:10.1093/ajh/hpaa057.
- [10] Kinoshita M, Sato K, Vellingiri B, Green SJ, Tanaka M. Inverse association between hypertension treatment and COVID-19 prevalence in Japan. *Int J Infect Dis* 2021;108:517–21. doi:10.1016/j.ijid.2021.05.071.
- [11] Adham D, Habibzadeh S, Ghobadi H, Jain SA, Abbasi-Ghahramanloo A, Moradi-Asl E. Epidemiological characteristics and mortality risk factors among COVID-19 patients in Ardabil, Northwest of Iran. *BMC Emerg Med* 2021;21:67. doi:10.1186/s12873-021-00463-x.