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Original Article

Predisposing risk factors for COVID-19 infection: A case-control study

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Abstract

Background: The Covid-19 epidemic in 2019 has created many public health problems. Literature that focuses on the risk factors of this issue is limited especially in developing countries. This study proposed to examine the risk factors of COVID-19 infection in the west area of Iran.

Methods: This case-control study was conducted from February to April 2020 in Nahavand county, western Iran. Cases were all patients who were coronavirus positive and, the controls included people who had clinical signs consistent with COVID-19, but their test results were negative. Two controls were selected for every case. Multivariate logistic regression was applied to evaluate the effects of epidemiological aspects on the incidence of COVID-19.

Results: Significant risk factors for COVID-19 infection based on the multivariable logistic regression model were male gender (OR=1.82, P=0.0.15), age group over 60 years (OR=2.04, P=0.017), living in urban areas (OR=1.79, P=0.018), being married (OR=2.08, P=0.022), having history of contact with the corona patients (OR=5.61, P=0.009), and comorbidities (OR=1.78, P=0.031).

Conclusion: This study highlighted the factors associated with the occurrence of COVID-19 infection. These findings may help guide recommendations for the protection of high-risk groups.

Keywords: Coronavirus; Covid-19; Epidemiology; Incidence; Iran.

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In December 2019, an outbreak of coronavirus infection with the unknown source (COVID-19) first emerged in Wuhan, China, resulting in more than 80,000 confirmed cases in this country and being transported to an increasing number of countries (1). World Health Organization (WHO) reports global public health emergency over the COVID-19 outbreak on January 30, 2020. Therefore, the coronavirus infection nearby to severe acute respiratory syndrome (SARS) and the Middle East respiratory syndrome (MERS) has become a global emergency and a crucial health issue for humans (2). The issue was so important that the emergence of COVID 19 has attracted global attention and, the WHO has announced COVID-19, a public health emergency of international concern (PHEIC). Declaring a PHEIC is an important note at the most influential level, for the global community to launch a globally coordinated attempt to prevent the outbreak, needs a powerful public health response, high-level political responsibility, and enough funding (3). Preventing the spread of the coronavirus requires identifying contributing risk factors in the occurrence of the disease. Primary epidemiological and clinical investigations represented that the majority of the cases were males, middle-aged, or elder individuals, with a mean incubation period of 5.2 days (range 0-14 days), and a serial interval of 7.5 days (95% CI 2-17 days) (4, 5).

The general symptoms were fever, cough, and weakness. The majority of the patients revealed the abnormalities of chest CT-findings (6). Despite the worldwide spread, the epidemiological and clinical patterns of COVID-19 remain largely unclear. Literature typically focuses on the risk factors since this issue is limited in developing countries. This research proposed to determine the risk factors of coronavirus infection in the west area of Iran.

Methods

Study design and patients: This case-control study was conducted from February to April 2020 in Nahavand County, the west of Iran (Nahavand county is located in the southwest of Hamadan province). We retrospectively examined the medical records of patients who were admitted into the Nahavand county hospitals and health centers, from February 24 – April 21, 2020. In this study, 126 cases and 252 controls were evaluated. Throat samples were obtained from all susceptible people (those with fever, cough, and shortness of breath). Then, the prepared samples were examined by the reverse transcription-polymerase chain reaction (RT-PCR) test. If the test result was positive, the person would be considered as a case, otherwise, it would be evaluated as a control. So, the case group was all patients diagnosed as COVID-19.

The control group included patients who had clinical symptoms consistent with the COVID-19 but had a negative test result, these subjects were selected at random from the medical records by an investigator (MS), who was not involved in statistical analysis. The control group was selected from the hospital where the cases were hospitalized. It should be noted that we selected two controls for each case. The Research Committee of Hamadan University of Medical Sciences approved the whole study (No. IR.UMSHA.REC.1399.166). Furthermore, all participants were selected voluntarily, and oral informed consent was taken from each of them.

Epidemiological investigation and data collection: Interviews with cases and controls were conducted using a questionnaire by a trained examining physician between February and April 2020. Information collected included demographic data (age, gender, and place of residence), personal medical history, coexisting conditions, occupation description, History of contact with travelers in contaminated areas, and travel history to contaminated areas.

Data analysis: Descriptive statistics were reported as number and percentage for categorical variables and mean (SD) for continuous variables across the patient's background. We used univariable logistic regression analysis to evaluate the influence of possible risk factors on the occurrence of coronavirus infection at the 95% significance level ($P<0.05$). All statistical analyses were performed using the Stata software Version 14 (Stata Corp, College Station, TX, USA).

Results

We identified 378 subjects with clinical symptoms compatible with COVID-19 infection. Of these, 64.55% (244) were females and 35.45% (134) were males; 54.76% (207) were residents in urban areas and 45.24% (171) of them were residing in rural areas. 147(38.89%) subjects were under the 40 years of age group, 93 (24.60%) in the 40-59 years, and 138 (36.51%) were in the 60 years age group. The mean age was 54.8618.89 years (range 13 and 95 years) in cases and 52.6922.15 (range 2 and 95 years) in controls. Characteristics of case and control subjects are shown in Table 1.

Based on the information presented in table 1, There was a meaningful discrepancy in age, sex, marital status, residency (rural and urban), marital status, comorbidities (including coronary heart disease (CHD), diabetes, hypertension, respiratory disease, mental disorder, stroke renal failure, and other diseases), and history of contact with the travelers in contaminated areas between cases and controls. Therefore, we could observe the association between the acquisition of COVID-19 and significant risk factors. Also, we could find no correlation between the incidence of COVID 19 infection and pregnancy and a history of traveling to the contaminated areas. Generally, 33 deaths occurred in the study period that their information is presented by men and women in Table 1.

The association between the incidence of COVID-19 and predictors are presented in Table 2 using crude and adjusted OR estimates. Based on unadjusted OR estimates, the incidence of COVID 19 in men was 2.19 times higher than women e ($P=0.001$). The risk of incidence of COVID-19 in urban areas was 1.89 times higher than in rural areas. The OR estimate of COVID-19 infection was 2.39 in the 40-59 years age group compared to the those under 40 years of age ($P=0.003$). Also, the adjusted associations were statistically significant. In addition, the OR estimate of the incidence of COVID-19 was 2.26 in subjects who had comorbidities compared to those who did not have comorbidities ($P=0.001$).

Table 1. Characteristics of case and control

Characteristics	Cases (n=126) n (%)	Controls (n=252) n (%)	P-value
Sex			
Male	60 (47.62)	74 (29.37)	0.001
Female	66 (52.38)	178 (70.63)	
Age group			
<40	33 (26.19)	114 (45.24)	0.002
40-59	38 (30.16)	55 (21.83)	
≥60	55 (43.65)	83 (32.94)	
Region			
Urban	44 (34.92)	127 (50.40)	0.004
Rural	82 (65.08)	125 (49.60)	
Marital status			
Single	18 (14.29)	96 (38.10)	0.001
Married	108 (85.71)	156 (61.90)	
Travel history to contaminated areas			
Yes	12 (9.52)	18 (7.14)	0.419
No	114 (90.48)	234 (92.86)	
History of contact with the patient			0.001
Yes	13 (10.32)	5 (1.98)	
No	113 (89.68)	247 (98.02)	
Pregnant			
Yes	3 (2.38)	10 (3.97)	0.425
No	123 (97.62)	242 (96.03)	
Comorbidities			
Yes	78 (61.90)	69 (27.38)	0.001
No	48 (38.10)	183 (72.62)	
Death			
Yes	15 (11.90)	18 (11.25)	0.863
No	111 (88.10)	142 (88.75)	

Table 2. Risk factors for COVID-19 infection

Variable	Crude OR§	95% CI§§	p-value	Adjusted OR ǂ	95% CI	p-value
Sex						
Female	Ref			Ref		
Male	2.19	1.41-3.40	0.001	1.82	1.12-2.95	0.015
Age groups (yr)						
0-39	Ref			Ref		
40-59	2.39	1.35-4.21	0.003	1.97	1.06-3.68	0.033
+60	2.28	1.37-3.83	0.002	2.04	1.14-3.65	0.017
Place of residence						
Rural	Ref			Ref		
Urban	1.89	1.04-2.51	0.005	1.79	1.10-2.91	0.018
Marital status						
Single	Ref			Ref		
Married	3.69	2.11-6.46	<0.001	2.08	1.11-3.91	0.022
Travel history to contaminated areas						
No	Ref			Ref		
Yes	1.37	0.64-2.94	0.421	0.79	0.29-2.10	0.633
History of contact with the patient						
No	Ref			Ref		
Yes	5.68	1.99-16.32	0.001	5.61	1.51-9.42	0.009
Pregnant						
No	Ref			Ref		
Yes	1.69	0.46-6.27	0.430	1.69	0.18-3.57	0.776
Comorbidities						
No	Ref					
Yes	2.26	1.41-3.61	0.001	1.78	1.05-2.99	0.031

§OR, odds ratio. §§ CI, confidence interval. ǂ Odds ratio adjusted for all other variables in the table

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The most effective predictor of COVID-19 infection was the history of contact with the corona patient. The risk of occurrence of COVID-19 in cases who had contact with patients was 5.68 times higher than people who don't have this contact (P=0.001). When adjusted for other variables, the association remains strong (OR=5.61). Of the 387 participants, 102 (26.98%) of them had comorbidities with corona disease. The frequency distribution of type of disease by cases and controls are shown in figure 1. The proportion of diabetes was higher in cases than controls (25 versus 12.9% for diabetes).

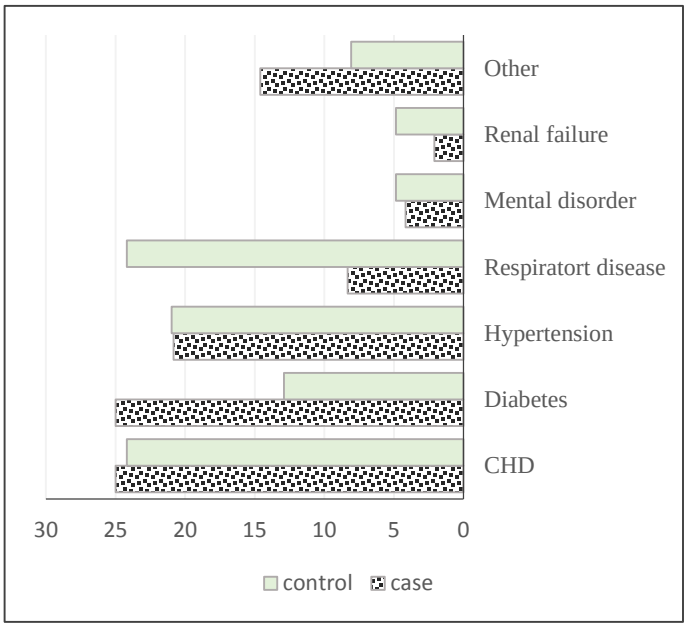

Figure 1. Frequency distribution of comorbidies with COVID-19 by case and control

Discussion

This study proposed to determine the risk factors associated with the incidence of Covid-19 in the west of Iran. The epidemiological and demographic features of the cases and controls were obtained from the clinical records. In particular, the male gender, elderly over 60 years, having an underlying disease, and history of contact with the corona patient were associated with higher odds of COVID-19 related incidence.

The current study verified that increased age was associated with the occurrence of COVID-19. This result is concordance with the previous paper which demonstrated a higher incidence rate between the elderly populations (7, 8). Elderly people, because they have a less capable immune response to infectious challenges, are more susceptible to infection. On the other hand, based on previous researches, aging has been expressed as an important independent risk factor for mortality in SARS and MERS. Initial studies in macaques treated with SARS-CoV discovered that the production of inflammatory factors and deficiency in control of viral replication is higher in the more adult macaques than in the younger adults. (9).

According to the information presented in this article, more than 50% of the patients in this research were residents in urban areas. The collection of cases in urban regions may happen because of factors correlated with access to healthcare or inadequate or poor surveillance and monitoring in rural regions (10). Data analysis showed that the chance of incidence of COVID-19 in men was 2.19 times higher than women. The higher incidence among the men population in the research could be attributed to an obviously higher proportion of approved COVID-2019 cases of males compared to females in Nahavand County (11). On the other hand, this decreased sensitivity of women to viral infections can be attributed to the protection from sex hormones and the X chromosome, which perform an essential role in innate and adaptive inviolability (5).

On another aspect, a higher incidence rate of CoV in men might be due to higher social interactions in workplaces. National office for statistics reported that men included 81 percent of the workforce in Iran during 2018-19; while more than 50 percent of them are employed in service occupations. Therefore, there is a higher possibility for men to obtain CoV infection due to higher social interactions in work environments (12).

Another interesting finding of this research is that having an underlying disease increases the chance of occurrence of COVID-19 (4). Based on the previous case series in 2020, the incidence of underlying diseases such as hypertension and subsequent hospitalization in the invasive care unit and death has been reported in patients with COVID-19 (13). According to the research of first this year, severe acute respiratory syndrome coronavirus contaminates the lungs by the angiotensin-converting enzyme II receptor (14). More research is required to determine the mechanism of COVID-19. Also, clinical investigations are needed to verify whether angiotensin-converting enzyme inhibitors and angiotensin receptor blockers could stay profitable for cases with COVID-19. According to the information presented in this article, 38.10% of cases and 21.43% of controls had comorbidities. Jing Yang et al. (15) conducted a meta-analysis in 2020 to

determine the prevalence of comorbidities in patients with COVID 19. Based on their finding existence of chronic diseases such as hypertension, diabetes, respiratory system disease, cardiovascular disease, and their susceptibility conditions may be associated with the pathogenesis of COVID-19. Chronic diseases participate in some standard characteristics with infectious disorders, such as the pro-inflammatory state, and the attenuation of the natural immune answer (16).

Additionally, metabolic diseases may lead to weak immune function by weakening macrophage and lymphocyte function, which may cause individuals more susceptible to disease complications (17). In 2014, Hong et al. in Korea conducted a prospective case-control study on seasonal influenza to determine the factors that increase the risk of incidence of flu and its adverse consequences. The results of their research showed that chronic cardiovascular disease and diabetes were associated with increased complications of influenza, and diabetes as an independent risk, increase the risk of severe seasonal influenza more than 3.5 times (19). Moreover, a study investigated the potential predictors for subjects with MERS-CoV infection, discovering diabetes, smoking, and cardiovascular disease were too significantly associated with MERS-CoV disease (20).

There are a few limitations to our study. First, clinical data are uncollected in this research, so, we suggest that this information be investigated in similar studies. Second, we only assessed symptomatic cases. While asymptomatic cases were not included in this research, perhaps the different risk factors were involved in the occurrence of disease in these cases. Third, the data were collected retrospectively in all retrospective surveys; recall bias was an important concern. Despite this limitation, in this study, corona patients were selected from all hospitals in order to reduce the selection bias. On the other hand, the study was conducted shortly after the epidemic, thus minimizing the information bias to which retrospective studies are otherwise susceptible.

In conclusion, this study introduced several effective predictors for the incidence of COVID-19 among patients who were hospitalized with a diagnosis of corona infection. The most important of which was the male gender, elder age group, living in urban areas, history of contact with the COVID-19 patients, and the existence of comorbidities. These predictors may be useful for the protection of high-risk groups.

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References

1. Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med 2020; 382: 727-33.
2. Wu C, Chen X, Cai Y, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med 2020; 180: 1-11.
3. Dong Y, Mo X, Hu Y, et al. Epidemiology of COVID-19 among children in China. Pediatrics 2020; 145: e20200702.
4. Bai Y, Yao L, Wei T, et al. Presumed asymptomatic carrier transmission of COVID-19. JAMA 2020; 323: 1406-7.
5. Shahbazi F, Khazaei S. Socio-economic inequality in global incidence and mortality rates from cronavirus disease 2019: an ecological study. New Microbes New Infect 2020; 38: 100762.
6. Liao J, Fan S, Chen J, et al. Epidemiological and clinical characteristics of COVID-19 in adolescents and young adults. Innovation 2020; 1:100001. Available at: https://doi.org/10.1016/j.xinn.2020.04.001
7. Choi KW, Chau TN, Tsang O, et al. Outcomes and prognostic factors in 267 patients with severe acute respiratory syndrome in Hong Kong. Ann Intern Med 2003; 139: 715-23.
8. Hong KH, Choi JP, Hong SH, et al. Predictors of mortality in Middle East respiratory syndrome (MERS). Thorax 2018; 73: 286-9.
9. 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.
10. Xu RH, He JF, Evans MR, et al. Epidemiologic clues to SARS origin in China. Emerg Infect Dis 2004; 10: 1030-7.
11. Alipio M, Pregoner JD. Epidemiological characteristics of an outbreak of Coronavirus Disease 2019 in the Philippines. Available at SSRN 3568934. 2020. DOI: 10.1101/2020.04.12.20053926
12. Hooper GL, Quallich SA. Health seeking in men: a concept analysis. Urol Nurs 2016; 36: 163-72.
13. Xie J, Wang H, Kang Y, et al. The epidemiology of sepsis in chinese icus: a national cross-sectional survey. Crit Care Med 2020; 48: e209-18.
14. Zhao Y, Zhao Z, Wang Y, et al. Single-cell RNA expression profiling of ACE2, the putative receptor of Wuhan 2019-nCov. BioRxiv 2020. Available at: https://www.biorxiv.org/content/10.1101/2020.01.26.919985v1.full.pdf
15. Yang J, Zheng Y, Gou X, et al. Prevalence of comorbidities in the novel Wuhan coronavirus (COVID-19) infection: a systematic review and meta-analysis. Int J Infect Dis 2020; 94: 91-5.
16. Odegaard JI, Chawla A. Connecting type 1 and type 2 diabetes through innate immunity. Cold Spring Harb Perspect Med 2012; 2: a007724.
17. Dooley KE, Chaisson RE. Tuberculosis and diabetes mellitus: convergence of two epidemics. Lancet Infect Dis 2009; 9: 737-46.
18. Guo L, Wei D, Zhang X, et al. Clinical features predicting mortality risk in patients with viral pneumonia: the MuLBSTA score. Front Microbiol 2019; 10: 2752.
19. Hong KW, Cheong HJ, Choi WS, et al. Clinical courses and outcomes of hospitalized adult patients with seasonal influenza in Korea, 2011–2012: Hospital-based Influenza Morbidity & Mortality (HIMM) surveillance. J Infect Chemother 2014; 20: 9-14.
20. Alraddadi BM, Watson JT, Almarashi A, et al. Risk factors for primary Middle East respiratory syndrome coronavirus illness in humans, Saudi Arabia, 2014. Emerg Infect Dis 2016; 22: 49-55.