ORIGINAL ARTICLE

Determining the Predictors of Covid-19 Disease Based on Data from Fars Province

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Abstract

Background: The coronavirus disease 2019 (COVID-19) is rapidly spreading worldwide and becoming a pandemic. Since the diagnostic tests are relatively expensive, simple diagnostic tests are valuable for quarantining individuals suspicious of COVID-19. This study is designed to predict the potential contributing factors of COVID-19 diagnosis.

Methods: It was a referral-based historical cohort study. 363358 individuals referred to the health centers from February to November 2020 in Fars province were entered in the study. The collected data before the lab test were symptoms, underlying diseases, some conditions, risk factors, and demographic information. The Reverse transcriptase polymerase chain reaction test was performed to identify the COVID-19 virus. Chi-square and T-tests were used to compare the variables. A logistic regression test was used to identify predictor variables.

Results: Positive COVID-19 test was reported for 119,324 (% 34.9) participations. The positive group result was compared with that of the negative group (n=244,034). The studied symptoms were significant in positive patients. According to the odds ratio (OR), smell disorder (OR=3.80, $P<0.001$), taste disorder (OR=3.17, $P<0.001$), and fever (OR=2.65, $P<0.001$) were common. However, diarrhea, chest pain and dyspnea showed the lowest odds ratio. According to the results, DM (OR=1.46, $P<0.001$), HTN (OR=1.42, $P<0.001$), and CVD (OR=1.27, $P<0.001$) were common in patients with positive COVID-19 tests. Cases whose Body Mass Index (BMI) was more than 40 (excessive obesity) showed a higher odd (OR=1.45, $P<0.001$) for being positive.

Conclusion: According to the results, the symptoms and underlying diseases are effective factors in predicting COVID-19 disease. Identifying these factors for Covid-19 disease helps health policymakers to make quick decisions and take timely action.

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Introduction

As a second 21st-century epidemic, the novel coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), so-called COVID-19, causes severe acute respiratory syndrome in patients. After discovering the COVID-19 virus, it spread rapidly from Wuhan city (China) to all around the world, eventually labeled as a pandemic by the World Health Organization (WHO).[1] Although COVID-19 is similar to well-known respiratory infections in symptoms, its transmission ability is notably higher than H1N1 influenza and SARS.[2, 3] Since COVID-19 and other respiratory infections exhibit similar clinical manifestations, non-clinical or asymptomatic infected patients may play a leading role in extending the duration of the epidemic.[4, 5] So, recognizing the factors that make populations prone to COVID-19 and implementing strong interventions are also beneficial for minimizing the impact of this pandemic, leading to its control. Numerous studies have shown that age and gender can predispose people to the disease. As a risk factor for diseases, age plays an essential role in the severity and mortality of infectious diseases.[6, 7] It is important to note that COVID-19 can also affect young people.[7] However, young people are less likely to be infected by COVID-19.[8] Gender is another determinant of this disease. Studies have shown that women are more likely to be infected by COVID-19, but the manifestations of this disease are higher in men.[9] On the other hand, several diseases and risk factors, such as diabetes mellitus (DM), hypertension (HTN), cardiovascular diseases (CVD), chronic kidney diseases (CKD), and excessive obesity (BMI>40), as well as smoking, are considered as significant risk factors for COVID-19.[10, 11] These factors increase the risks of COVID-19 incidence. Moreover, the signs and symptoms of COVID-19 differ from person to person and between countries. Despite the numerous research efforts, there are still many controversies surrounding this issue, and several symptoms have been reported in different areas. The common signs and symptoms include; fever, cough, and tiredness, whereas uncommons consist of dyspnea or difficulty breathing, muscle aches, sore throat, runny nose, headache, chest pain, nausea, vomiting, and diarrhea.[12, 13] The widespread prevalence of COVID-19 has negatively affected the ability of the health care systems to provide an efficient service; importantly many of the medical staff have been infected by COVID-19.[14, 15] Pandemic diseases markedly increase the demand for diagnostic testing and medical equipment.[16, 17] The simple screening methods for prompt isolating of people suspected of COVID-19 are essential, particularly when healthcare workers are under pressure of successive waves of infectious diseases. To screen people in different regions, uncovering predictive signs in positive COVID-19 patients is highly important. Therefore, the current study was designed to predict the potential contributing factors of COVID-19 diagnosis.

Methods

Setting and Sampling

In this referral base historical cohort study, 363358 individuals referred to the health centers of Fars province (south of Iran) from February to November 2020; they were all entered in the study. Individuals entered the study were patients introduced to the COVID-19 test. After sampling, the participants received a tracking code and their information was recorded in the corona lab system. Patients referred to the hospital were excluded from the study due to the high probability of being positive. Symptoms, underlying diseases, some conditions, and risk factors like pregnancy, smoking, BMI>40 (excessive obesity), and demographic information were gathered before testing and registered into the COVID-19 lab database. These data include: gender, age, occupation, nationality, date of symptoms onset , date of referral, date of hospitalization, date of sampling, contact with positive patients during the last two weeks, and review of simultaneous factors, including pregnancy, chronic diseases, and results of the tests. The reverse transcriptase polymerase chain reaction (RT-PCR) test was done for all people, and its result merged with previous data.

Statistical Analysis

Quantitative data were described with mean and standard deviation, and qualitative data were described with numbers and percentages. The normality of data was also confirmed by checking the kurtosis and skewness indices. For continuous and categorical variables, Chi-square and T-tests were used to test the statistical significance of differences between negative and positive groups. In this study, logistic regression was used to identify the predictors of the positive test in suspicious people. First, simple logistic regression was performed, and then the significant variables were entered into multiple logistic regression. The data were analyzed using SPSS, version 16 (SPSS Inc., Chicago, IL, USA). The $P<0.05$ was considered a significant level.

Ethical Consideration

This study was reviewed and approved by the Research Review Board of the Ethics Committee of Shiraz University of Medical Sciences (Code: IR.SUMS.REC.1399.317). The questionnaires were anonymous, without any identifying information.

Results

Demographic Information

In this historical cohort study, 363,358 people were sampled, of which 119,324 (34.9%) had positive COVID-19 tests. This group was compared with a group whose test result was negative (n=244,034). Table 1 lists the demographic information of the two groups. The dominant age group was 35- 49 years (34.8%), followed by males as dominant gender group (58.7%), and the most prevalent nationality was Iranian (97.6%). According to the results, there was a statistically significant difference between the two groups in terms of age ($P<0.001$), gender ($P<0.001$), job ($P<0.001$), and nationality ($P<0.001$).

Symptoms

Table 2 summarizes the results of the presence of symptoms and their duration. Symptoms were mostly seen in positive patients. According to OR in the simple

Table 1: Demographic information of individuals with positive PCR test and negative PCR test

Variables		Group		P value
		Negative (n=244,034)	Positive (n=119,324)	
Age, Mean±SD (years)		38.74±15.09	40.37±15.28	<0.001
<5		1,944 (78.7)	526 (21.3)	<0.001
5 to 9		3,094 (76.3)	960 (23.7)	
10 to 19		11,619 (69.2)	5,176 (30.8)	
20 to 34		76,899 (65.6)	40,249 (34.4)	
35 to 49		80,540 (63.1)	42,189 (36.9)	
50 to 64		34,716 (58.7)	20,336 (41.3)	
65+		13,895 (58.7)	9,761 (41.3)	
Gender	Male	134,558 (66.5)	67,733 (33.5)	<0.001
	Female	88,487 (63.2)	51,591 (36.8)	
Nationality	Iran	217,877 (64.9)	117,666 (35.1)	<0.001
	Afghan	3,514 (76.0)	1,107 (24.0)	
	Other	1,654 (75.0)	551 (25.0)	
Job	Unemployment	4,484 (63.4)	2,588 (36.6)	<0.001
	Health workers without contact	4,453 (71.6)	1768 (28.4)	
	A health worker with contact	7,357 (72.6)	2,771 (27.4)	
	Administrate Health worker	3,452 (77.5)	1,003 (22.5)	
	Housewife	37,305 (58.6)	26,362 (41.4)	
	Student	11,975 (69.7)	5,204 (30.3)	
	General driver	5,907 (79.2)	1,552 (20.8)	
	Military/Soldier	8,783 (62.7)	5,214 (37.7)	
	Employee	39,608 (70.8)	16,349 (29.2)	
	Children	3,168 (78.2)	882 (21.8)	
	Others	88,820 (62.3)	53,757 (37.3)	
Province	Fars	221,231 (65.0)	118,872 (35.0)	<0.001
	Others	1,814 (80.1)	452 (19.9)	
City	Shiraz	140,740 (66.8)	72,088 (33.9)	<0.001
	Other cities of Fars	80,614 (63.3)	46,814 (36.7)	
	Cities of other provinces	1,691 (80.0)	422 (20.0)	

Data were presented as mean±SD for age and number (%) for other categorical data. Some data may be missed. PCR: Polymerase Chain Reaction. SD: Standard Deviation

model, smell disorder (OR=3.80, 95% CI: 3.67-3.94), taste disorder (OR=3.17, 95% CI: 3.0-3.31), and fever were (OR=2.65, 95% CI: 2.60 -2.70) more frequently observed and were ranked 1 to 3, respectively. While diarrhea (OR=1.21, 95% CI: 1.17-1, 26), chest pain (OR=1.35, 95% CI: 1.30-1.40), and dyspnea (OR=1.36, 95% CI: 1.33-1.39) showed the lowest odds ratio. On the other hand, more symptoms were associated with a higher chance of being positive. In multiple models, nausea and taste disorder were insignificant (P>0.05). Unlike the simple model, diarrhea (OR=0.73, 95% CI: 0.70-0.76), chest pain (OR=0.85, 95% CI: 0.81-0.88), and dyspnea (OR=0.91, 95% CI: 0.89-0.94) had a protective effect on the test result. In this regard, the three important symptoms were smell disorder (OR=3.21, 95%CI: 3.06-3.36), fever (OR=2.70, 95%CI: 2.12-2.21), and cough (OR=1.77, 95%CI: 1.79-1.80).

Underlying Diseases/Conditions and Some Risk Factors

Underlying diseases and symptoms were compared between two groups and summarized in table 3. The result of simple and multiple models are also summarized in this table. According to the simple model, DM (OR=1.46, 95%CI: 1.41-1.51), HTN (OR=1.42, 95%CI 1.39-1.48), and CVD (OR=1.27 95%CI: 1.22-1.32) were higher in positive patients. Patients with excessive obesity (OR=1.45, 95%CI: 1.30-1.62) also had more chancesof being positive. In this study, pregnant women had a higher chance of being positive compared to non-pregnant women (OR=1.20, 95%CI: 1.10-1.30). Interestingly, smokers were less likely to be positive (OR=0.85, 95%CI: 0.80-0.90). Furthermore, the number of underlying health conditions increased the risk of being positive (P<0.001). In the multiple regression model, all variables, except CKD, were significant (P<0.05). Table 3 shows detail of these adjusted results 3. In both simple and multiple logistic regression models, cancer, respiratory diseases, and HIV were insignificant (P>0.05).

Discussion

Upon being identified, COVID-19 was rapidly labeled as a pandemic by WHO. In the early phases, when treatment options were unavailable, COVID-19 affected numerous populations worldwide. Although the number of vaccinated individuals is increasing, the incidence rate of COVID-19 is still high in most parts of the world. Because COVID-19 diagnostic resources are limited,

Table 2: Predictor symptom of positive PCR test in suspicious individual based on simple and multiple logistic regression.

Symptoms		Group		Crude OR (95% CI)	P value	Adjusted OR (95% CI)	P value
		Negative	Positive				
Chest pain	Yes	7,302 (57.9)	5,307 (42.1)	1.35 (1.30-1.40)	<0.001	0.85 (0.81-0.88)	<0.001
	No	211,607 (65.1)	113,686 (34.9)				
Nausea	Yes	7,870 (55.5)	6,314 (44.5)	1.50 (1.45-1.55)	<0.001	1.02 (0.98-1.06)	0.176
	No	211,039 (65.2)	112,679 (34.8)				
Diarrhea	Yes	7,568 (60.3)	4,978 (39.7)	1.21 (1.17-1.26)	<0.001	0.73 (0.70-0.76)	<0.001
	No	211,341 (65.0)	114,015 (35.0)				
Sore throat	Yes	29,253 (55.6)	23,341 (44.4)	1.58 (1.55-1.61)	<0.001	1.04 (1.01-1.06)	<0.001
	No	189,656 (66.5)	95,652 (33.5)				
Weakness	Yes	16,287 (49.5)	16,622 (50.5)	2.02 (1.97-2.06)	<0.001	1.46 (1.42-1.50)	<0.001
	No	202,622 (66.4)	102,371 (33.6)				
Dyspnea	Yes	15,617 (58.0)	11,286 (42.0)	1.36 (1.33-1.39)	<0.001	0.91 (0.89-0.94)	<0.001
	No	203,292 (65.4)	107,707 (34.6)				
Cough	Yes	31,486 (49.3)	32,322 (50.7)	2.22 (2.18-2.25)	<0.001	1.77 (1.79-1.80)	<0.001
	No	187,423 (68.4)	86,671 (31.6)				
Fever	Yes	24,598 (45.1)	29,961 (54.9)	2.65 (2.60-2.70)	<0.001	2.17 (2.12-2.21)	<0.001
	No	194,311 (68.6)	89,032 (31.4)				
Smell disorder	Yes	4,963 (34.3)	9,516 (65.7)	3.80 (3.67-3.94)	<0.001	3.21 (3.06-3.36)	<0.001
	No	218,082 (66.5)	109,808(33.5)				
Taste disorder	Yes	3,234 (37.8)	5,324 (62.2)	3.17 (3.0-3.31)	<0.001	0.94 (0.89-1.00)	0.081
	No	219,811 (65.8)	114,000 (34.2)				
Number of Symptoms		0.67±1.18	1.21±1.43	1.36 (1.36-1.37)	<0.001	-	-
0		145,367 (73.7)	51,836 (26.3)	Ref (OR=1)		-	-
1		30,729 (56.0)	24,156 (44.0)	2.20 (2.16-2.24)	<0.001	-	-
2		23,890 (51.2)	22,755 (48.8)	2.67 (2.61-2.72)	<0.001	-	-
3		11,445 (48.9)	11,954 (51.1)	2.92 (2.85-3.01)	<0.001	-	-
4		4,335 (47.6)	4,764 (52.4)	3.08 (2.95-3.21)	<0.001	-	
5		1,784 (47.9)	1,940 (52.1)	3.05 (2.85-3.25)	<0.001	-	-
6		1,359 (46.1)	1,588 (53.9)	3.15 (2.86-3.47)	<0.001	-	-
Symptom to sampling duration (day)		3.77±2.99	3.71±2.73	0.99(0.98-0.99)	<0.001	-	-
Sampling to result duration (day)		3.25±2.95	3.36±2.92	1.01 (1.009-1.01)	<0.001	-	-

Data were presented as mean±SD and number (%) for continuous and categorical variables, respectively. Some data may be missed. PCR: Polymerase Chain Reaction . SD: Standard Deviation. OR: Odds Ratio. CI: Confidence Interval

screening of patients seems necessary. The present study was conducted to predict potential contributing factors of COVID-19 diagnosis in referral patients in Shiraz, Iran.

Discussion about Symptoms

The results showed that referred patients presented different symptoms, some of which were more common, including chest pain, nausea, diarrhea, sore throat, weakness, dyspnea, cough, fever, smell, and taste disorders. However, not all of these persons had COVID-19. These symptoms have been observed in other studies.[12] While in some studies, cough, fever, and fatigue are the three most common symptoms in positive patients.[18, 19] In this study, according to simple analysis, the statistical model showed that smell disorder, taste disorder, and fever are the most common symptoms, respectively in the persons with a positive test. Therefore, these symptoms can predict positive COVID-19. However, in this study, other symptoms were also statistically significant, but according to the odds ratio, these were three main symptoms. This study was in line with studies carried out by Fu L et al. and Sun P et al.[18, 19] just in fever. Multiple logistic regression, as a diagnostic model, indicated that the three main symptoms in this study were smell disorder, fever, and cough, respectively. Based on this model, taste disorder and nausea were not statistically significant. This finding was due to the strong multi collinearly of these variables with other variables. For example, taste and smell disorders were the same symptoms, manifested simultaneously. Moreover, in this case, some variables, such as chest pain and diarrhea, had an inverse effect as qualitative confounder variables. The results showed that people with more symptoms had a higher chance of positive COVID-19. In other words, increasing the number of symptoms most likely, resulted in positive COVID-19. Therefore, it could be suggested that when the number of people waiting for the test is high, they can be screened according to the number of symptoms. On the other hand, if utilization is limited, people with these symptoms should prioritize laboratory tests. Although the difference between the onset of symptoms and test results in the two positive and negative groups was statistically significant, this amount was not clinically significant.

Table 3: Predictors of underlying diseases, conditions, and risk factors of positive PCR tests in suspicious individuals based simple and multiple logistic regression.

Underline diseases or condition		Group		Crud OR (95%CI)	P value	Adjusted OR (95%CI)	P value
		Negative	Positive				
Pregnancy	Yes	1,390 (58.9)	971 (41.1)	1.20 (1.10-1.30)	<0.001	-	-
	No	87,097 (63.2)	50,620 (36.8)				
Cancer	Yes	757 (64.4)	419 (35.6)	1.01 (0.90-1.14)	0.766	0.97 (0.86-1.10)	0.729
	No	218,172 (64.8)	118,587 (35.2)				
Diabetes Mellitus	Yes	6,966 (56.5)	5,374 (43.5)	1.46 (1.41-1.51)	<0.001	1.30 (1.25-1.35)	<0.001
	No	216,079 (65.5)	113950 (34.5)				
Hypertension	Yes	9,199 (56.5)	7,081 (43.5)	1.42 (1.39-1.48)	<0.001	1.31 (1.27-1.36)	<0.001
	No	209,730 (65.2)	111.925 (34.8)				
Cardiovascular Diseases	Yes	6,100 (59.6)	4,143 (40.4)	1.27 (1.22-1.32)	<0.001	1.12 (1.07-1.16)	<0.001
	No	216,945 (65.3)	115,181 (34.7)				
Chronic Kidney Diseases	Yes	2,059 (62.4)	1,242 (37.6)	1.11 (1.03-1.19)	0.004	0.98 (0.91-1.06)	0.729
	No	216,870 (64.8)	117,764 (35.2)				
Respiratory disease	Yes	2,970 (63.9)	1,678 (36.1)	1.04 (0.97-1.10)	0.230	0.99 (0.94-1.06)	0.960
	No	215,959 (64.8)	117,328 (35.2)				
Human Immunodeficiency Virus	Yes	22 (78.6)	6 (21.4)	0.50 (0.20-1.23)	0.127	0.50 (0.20-1.25)	0.143
	No	218,908 (64.8)	119,000(35.2)				
Excessive obesity	Yes	726 (55.9)	572 (44.1)	1.45 (1.30-1.62)	<0.001	1.36 (1.22-1.52)	<0.001
	No	218,203 (64.8)	118,434 (35.2)				
Smoking	Yes	4,127 (68.3)	1,919 (31.7)	0.85 (0.80-0.90)	<0.001	0.83 (0.79-0.88)	<0.001
	No	214,802 (64.7)	117,087 (35.3)				
Number of Underline diseases or conditions		0.15 ± 0.46	0.19 ± 0.52	1.18 (1.16-1.19)	<0.001	-	-
0		192,861 (65.5)	101,364 (34.5)	Ref		-	-
1		19,471 (60.2)	13,028 (39.8)	1.25 (1.22-1.28)	<0.001	-	-
2		4,947 (57.7)	3,625 (42.3)	1.39 (1.33-1.45)	<0.001	-	-
3+		1,380 (58.3)	989 (41.7)	1.37 (1.26-1.50)	<0.001	-	-

Data were presented as mean ±SD or number (%). Some data may be missed. PCR: Polymerase Chain Reaction. SD: Standard Deviation. OR: Odds Ratio. CI: Confidence Interval

Discussion about Underlying Diseases/Conditions and Some Risk Factors

In addition to symptoms, underlying diseases and some predisposing risk factors such as pregnancy and smoking were also considered in this study. Pregnant women were more likely to get the disease. Similar studies showed that not only does pregnancy increases the chances of getting the disease, but also causes the severity of the disease as the mortality rate is higherin pregnant women.[20, 21] There may be physiological reasons for this finding, but more studies are needed to validate them. Crud Analysis indicated that COVID-19 could be predicted by DM, excessive obesity, HTN, CVD, and CKD, respectively. On the other hand, a person with these diseases or risk factors is more likely to be infected by COVID-19. Our findings are consistent and in line with other studies that have shown that noncommunicable disease and its risk factors increase the risk of disease, disease progression, and mortality.[10, 22, 23]

Smoking had a protective effect on the COVID-19 test, as smokers were less likely to get the disease. An unproven hypothesis is that smoking may play a protective role in developing COVID-19.[24] Most studies have focused on the effect of smoking on disease progression, and some have identified smoking as a risk factor. For example, Liu et al.[25] showed that a smoking history was a risk factor for disease progression (OR=14.28, P=0.018). A meta-analysis study showed that smokers were at higher risk (RR=1.4, 95% CI: 0.98–2.00) of severe symptoms of COVID-19 in comparison to non-smokers. On the other hand, smokers more likely needed mechanical ventilation 2.4 times more, were admitted to ICU, or died (RR=2.4, 95% CI: 1.43–4.04).[26] The adjusted results of this study showed that smokers are more likely to have a negative COVID-19 test. However, future studies are needed in this area. Meanwhile, in the adjusted analysis, DM, HTN, CVD, and excessive obesity increased the chance of positive COVID-19. In this study, COVID-19 was positive in 36.1% and 35.2% of patients with pulmonary and non-pulmonary disease, respectively, without significant differences.

Regarding HIV, it seems that the sample size was very small, and there was no significant difference between HIV patients and others with positive COVID-19 tests. Finally, there were statistically significant differences in demographic and baseline data between negative and positive COVID-19 groups. However, from a clinical point of view, the differences were not remarkable except for age and gender variables.

Conclusion

Regarding the symptoms and underlying diseases, the person with these symptoms/diseases/risk factors is more likely to be infected by COVID-19. Therefore, it is recommended to quarantine people when they do not have severe symptoms but have these symptoms or underlying diseases. In addition, it is recommended to screen people when they have some symptoms. On the other hand, if utilization is limited, people with these symptoms or diseases should prioritize laboratory tests. Although this study was performed on a large sample size, it has some limitations. For example, we could not investigate the progression of COVID-19 due to a lack of hospital data. Future studies should fill this gap.

Ethics Approval and Consent to Participate

The present study conforms with the Helsinki declaration and was approved by the Research Ethics Committee of Shiraz University of Medical Sciences.

Consent for Publication: Not applicable

Availability of Data and Materials

The datasets during and/or analysis during the current study are available from the corresponding author upon reasonable request.

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Authors' Contributions

AM, BSY, ML, ZH , FRand AH contributed substantially to the design of the study. ZH and FA contributed in data collection. MS, AM had roles in data interpretation. MS wrote the initial draft and BSY were critically and substantially revised the final article. All authors reviewed critically and approved the manuscript.

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