



Epidemiological Study of Infection and Death Due to COVID-19 in Fars Province, Iran, From February to September 2020

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What's Known

- Little and contradictory information was presented on the current epidemic, COVID-19.

What's New

- Community-wide quarantine could block the transmission of COVID-19 effectively; it enjoys no solid immunity.
- History of underlying diseases, the male sex, urban residency, and age were among the most significant causes of death due to COVID-19.

Abstract

Background: Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has entered our lives with the fear of outbreak, death, and recurrence. Our objective in this study is to evaluate the epidemiological features of Coronavirus Disease 2019 (COVID-19) infection and death in Fars province, Iran.

Methods: A cross-sectional study was conducted from February 18th to September 30th, 2020, where age, history of underlying diseases, sex, community-wide quarantine, nationality, close contact, pregnancy, medical staff job, traveling, and residency were compared between alive and deceased groups. Data were analyzed using IBM SPSS software, version 22.0, and the significance level was set at 0.05.

Results: Regarding 57958 new cases of COVID-19, the basic reproduction number (R_0) was estimated as 2.8, requiring a minimum of 65% immunization to reach herd immunity. Moreover, an $R_0=0.36$ was required to reach the endemic state in the region. The incidence, mortality, fatality, and recurrence rates of COVID-19 were estimated as 1347.9 per 100,000 dwellers, 209.5 per 1000,000 dwellers, 1.6 %, and 3.1 per 100,000 dwellers, respectively. Age, history of underlying diseases, urban residency, and the male sex were significantly higher in the deceased group (OR=1.09, 5.48, 1.24, and 1.32; All $P_s < 0.001$, < 0.001 , 0.005, and < 0.001 , respectively). In addition, the recurrence rate among positive cases was estimated as 0.23% with a median=inter-quartile range equal to 84±46.25 days. Community-wide quarantine was shown to be a protective factor for death due to COVID-19 (OR=0.58, $P=0.005$).

Conclusion: Community-wide quarantine blocks the transmission of COVID-19 effectively. COVID-19 enjoys no solid immunity. History of underlying diseases, the male sex, urban residency, and age were among the most significant causes of death due to COVID-19. Further investigations are recommended on the genetic structure of SARS-CoV-2, treatments, and vaccination.

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Introduction

At the beginning of the twentieth century, the World Health Organization (WHO) announced the epidemic of Coronavirus

disease 2019 (COVID-19) nationwide.¹ This pandemic was the third zoonotic Coronavirus outbreak in the twenty-first century, with high human-to-human transmission.² The golden tests for the diagnosis of COVID-19 were Reverse transcription-polymerase Chain Reaction (RT-PCR) and Computed Tomography (CT) scan.^{3,4} Clinical manifestations ranged from asymptomatic to mild, severe, sepsis, and death. The severe form of the disease was reported in up to 16% of hospitalized cases.³ It had a high basic reproduction number (R_0) and a high fatality rate (2.3-5%, with an average of 3%). The incubation period of COVID-19 varied from 1-14 days and could even reach up to 24 days.⁵⁻⁸ Almost 50.5% of the patients suffered from chronic diseases.⁶ Other epidemiological risk factors were old age and the male sex. National and international efforts to prevent the spread of the virus included travel restrictions, community-wide quarantines, and facility closures.⁵ Presently, prevention through isolation is the only way to curb the transmission.⁷⁻¹⁰ The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) spike binds to humans with an approximately 10- to 20-fold higher affinity than the SARS-CoV-1 spike, making it easier to spread from individual to individual. The basic reproduction number of SARS-CoV-2 varied from 1.4 to 6.49, which was higher than SARS-CoV-1 (2.5).⁹⁻¹² A previous study carried out in Qom province, Iran, showed an R_0 of 2-3.¹³ The overall mortality rate of COVID-19 was reported to be 8% globally, and the majority of deaths had occurred among the patients admitted to the Intensive Care Unit (ICU) (5-55.6%).¹⁴ A prior study on hospitalized cases in Tehran, Iran, revealed that the majority of the cases were 50-60 years old, and the fatality rate was 1.85%, out of which 8.06% were among the hospitalized patients, and 10.89% were among those suffering from underlying diseases. Overall, the male sex, old age, and underlying diseases were significantly associated with mortality.¹⁵

The present study aims to evaluate the epidemiological characteristics of infection and death due to COVID-19 in the general population of Fars province, Iran, during February and September 2020.

Methods

Study Design and Population

This cross-sectional study was conducted on new COVID-19 cases from February 18th to September 30th, 2020, to evaluate the epidemiological features of COVID-19 in the population of Fars province, Iran. The COVID-19

cases were RT-PCR-confirmed cases recorded daily in all diagnostic laboratories in 36 cities of Fars province. All data were reported to Shiraz University of Medical Sciences (SUMS) either on www.coronalab.sums.ac.ir or by manual registration. The majority of the records were reported from Jahrom, Fasa, Gerash, and Lar Universities of Medical Sciences.

Eligibility Criteria

Inclusion criteria: all PCR-positive cases for which the COVID-19 information form was filled entered the study. Exclusion criteria: patients with incomplete COVID-19 information forms were excluded from the study.

Variable Definitions

Age was defined quantitatively, and other variables were defined as the history of underlying diseases (yes=any underlying disease/no), close contact (yes=history of exposure to an infected individual during the past two weeks/no), pregnancy (yes/no), traveling (yes=having traveled during the past two weeks/no), community-wide quarantine (yes=before April 20th, 2020, when there were strict stay-at-home policies and travel bans/no=after), medical staff job (no/yes=), sex (male/female), nationality (Iranian, immigrant), and residency (urban/rural). Recurrence cases were infected more than once.

Epidemiological Parameters

Basic reproduction number, R_0 , was defined as the expected number of secondary cases produced by a single infection in a completely susceptible population, and was estimated as:

$$R_0 = 1 + \frac{\text{life expectancy in the study population}}{\text{average of age at the time of infection}}$$

Where:

Life expectancy in the study population refers to the number of years a person can expect to live and is estimated as the average age that members of a particular population will be when they die. The average age at the time of infection is the average age at which infection had occurred in the study population.¹²

Herd immunity is defined as a form of protection from an infectious disease that occurs, when a sufficient percentage of a population have become immune to that infection, whether through vaccination (inactive immunity) or previous infections (active immunity) and is estimated as:

$$p_c = 1 - \frac{1}{R_0}$$

Where:

p_c is the critical proportion of the population required to be immune to reach the endemic state in the region, and R_0 is the basic reproduction number.¹² The incidence, mortality, and recurrence rates were, respectively, the number of COVID-19 incidences, death, and recurrence cases divided by the mid-year population of Fars province in 2020. The fatality rate and recurrence rate among positive cases equaled the number of death and recurrence cases divided by positive cases (%), respectively. Odds Ratio (OR) is a measure of association between an exposure and an outcome, representing the odds by which the outcome would occur in the presence of that exposure than the odds of the outcome occurring in the absence of that exposure.¹⁶

Statistical Analysis

Median±Inter Quartile Range (IQR) and frequency (relative frequency) were used to describe the quantitative and qualitative variables, respectively. The data were analyzed using the independent-samples *t* test, median, ANOVA, Kruskal-Wallis, Chi square, Mann-Whitney U, Curve estimation, SOBEL test (method of testing the significance of a mediation effect), univariate logistic regression, multiple logistic regression, and the Receiving Operating Characteristic (ROC) curve accompanied by Uden index (sensitivity+specificity-1, which is used to choose for the optimal cut-off point in ROC). To adjust for confounding, all variables with $P < 0.2$ in the univariate analysis were entered into the multiple logistic regression with removal and entry levels of 0.1 and 0.05, respectively. Data were analyzed using IBM SPSS software, version 22.0, and the significance level was set at 0.05. A power analysis was carried out at the end of the study to examine the ability of the study to detect a difference that really exists (<https://www.stat.ubc.ca/~rollin/stats/ssize/caco.html>).

The ethical considerations were approved by

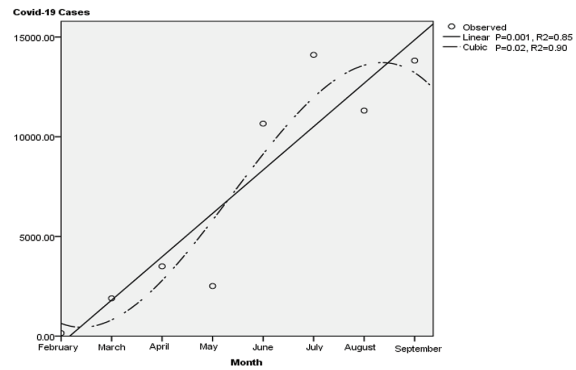


Figure 1: The figure shows the trend of 57958 new COVID-19 cases during the period of February 18th to September 30th, 2020, in Fars province, Iran.

the Ethics Committee of the Ministry of Health, Treatment, and Medical Education of Shiraz University of Medical Sciences, Shiraz, Iran (IR.SUMS.REC.1399.574).

Results

A total of 57958 new COVID-19 cases in the region followed a cubic trend rather than a linear trend ($R^2=0.9$ v.s $R^2=0.85$). The linear and cubic trends of these 57958 new COVID-19 cases during the period of February 18th to September 30th, 2020, are presented in figure 1.

Regarding the 57958 new COVID-19 cases, R_0 was estimated as 2.8 in February, resulting in minimum immunization coverage of 65% (active or passive) to reach herd immunity. $R_0=0.36$ was required to reach the endemic state in the region. Moreover, incidence, mortality, recurrence, and fatality rates were 1347.9 (57958/4299676) per 100,000 dwellers, 209.5 (901/4299676) per 1000,000 dwellers, 3.1 (134/4299676) per 100,000 dwellers, and 1.6% (901/57824), respectively. The trends of the incidence, mortality, and fatality rates of the 57958 new COVID-19 cases during the period of February 18th to September 30th, 2020, are presented in figure 2.

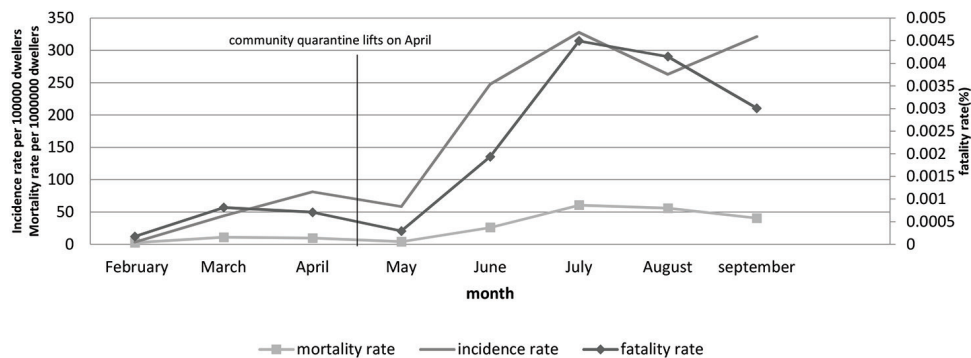


Figure 2: The figure shows the trends of the incidence, mortality, and fatality rates of the 57958 new COVID-19 cases during the period of February 18th to September 30th, 2020, in Fars province, Iran.

The incidence, mortality, and fatality rates had increasing trends from February to September 2020, with the lowest and highest peaks belonging to February and July, respectively, (The lowest and the highest incidence rates were 0.26% (150/57958) and 24.34% (14106/57958), out of the total cases in February and July, respectively; the lowest and the highest mortality rates were 1.11% (10/901) and 28.86% (260/901) out of the total deaths in February and July, respectively; and the lowest and the highest fatality rates were 0.017% (10/57824) and 0.45% (260/57824) out of the total cases in February and July, respectively). The incidence, mortality, and fatality rates of COVID-19 increased almost two weeks after the community-wide quarantine was lifted on April 20th, 2020. The characteristics of the 56923 alive and the 901 deceased cases are compared in table 1.

The age, history of underlying diseases, the male sex, non-medical staff job, and urban residency were higher in the deceased group than the alive group according to the univariate analysis. However, no significant difference was observed regarding close contact, pregnancy, travelling, and nationality. Community-wide quarantine was shown to be a protective factor against death due to COVID-19.

The age, history of underlying diseases, the male sex, and urban residency were higher in the

deceased group than the alive group according to the multiple analysis. However, no significant difference was observed regarding close contact, pregnancy, travelling, nationality, and non-medical staff job. Community quarantine was shown to be a protective factor against death due to COVID-19.

A total of 44.3 % (25603/ 57824) reported a history of underlying diseases. Age, Iranian nationality, and urban residency were significantly higher in the patients with a history of underlying diseases ($P < 0.001$ for all). However, close contact, pregnancy, medical staff job, and traveling were lower ($P < 0.001$ for all), and there was no difference regarding sex ($P = 0.09$). The path diagram of the 57824 COVID-19 positive cases adjusted for sex, age, history of underlying diseases, medical staff job, and residency is illustrated in figure 3.

Age, sex, residency, and history of underlying diseases directly affected death from COVID-19, with the largest effect size being related to the history of underlying diseases ($OR = 5.27$, $P < 0.001$). The history of underlying diseases mediated the effect of age on death due to COVID-19 (SOBEL test statistic=4.85, $se = 0.001$, $P < 0.001$). The medical staff job was omitted from the multiple logistic regression model ($P = 0.25$).

An accurate age at death due to COVID-19 was estimated to be 57.5 years. ROC analysis results are shown in table 2.

Table 1: Comparison of the features of the 57824 COVID-19 positive cases in Fars province, Iran during February 18th and September 30th 2020

Variable		Status			Univariate analysis*		Multiple analysis**	
		Total, n (%) 57824 (100%)	Alive, n (%) 56923 (98.4%)	Dead, n (%) 901 (1.6%)	OR _{crude} (95% CI)	P value	OR _{Adjusted} (95% CI)	P value
Age (year)	Median± IQR	38±22	38±21	69±22	1.09 (1.09-2)	<0.001	1.09 (1.08-1.1)	<0.001
History of underlying diseases	Yes	25603 (44.3%)	24874 (43.7%)	729 (80.9%)	5.46 (4.62-6.45)	<0.001	5.48 (4.56-6.58)	<0.001
	No	32221 (55.7%)	32049 (56.3%)	172 (19.1%)				
Sex	Male	30278 (56.2%)	29755 (56.2%)	523 (61.5%)	1.25 (1.08-1.43)	0.002	1.32 (1.13-1.54)	<0.001
	Female	23553 (43.8%)	23225 (43.8%)	328 (38.5%)				
Community quarantine	Yes	1564 (2.7%)	1514 (2.7%)	50 (5.5%)	0.46 (0.35-0.62)	<0.001	0.58 (0.38-0.88)	0.005
	No	56260 (97.3%)	55409 (97.3%)	851 (94.5%)				
Nationality	Iranian	50148 (86.7%)	49359 (86.7%)	789 (87.6%)	1.08 (0.88-1.32)	0.45	1.03 (0.87-1.25)	0.37
	Immigrant	7676 (13.3%)	7564 (13.3%)	112 (12.4%)				
Close contact	Yes	1697 (2.9%)	1664 (2.9%)	33 (3.7%)	1.26 (0.88-1.79)	0.07	1.27 (0.79-2.02)	0.32
	No	56127 (97.1%)	55259 (97.1%)	868 (96.3%)				
Pregnancy	Yes	31 (0.1%)	30 (0.1%)	1 (0.1%)	0.47 (0.06-3.48)	0.19	0.23 (0.03-2.09)	0.19
	No	5793 (99.9%)	56893 (99.9%)	900 (99.9%)				
Medical Staff job	No	56342 (97.4%)	55454 (97.4%)	888 (98.6%)	1.81 (1.04-3.14)	0.03	1.29 (0.72-2.34)	0.39
	Yes	1482 (2.6%)	1469 (2.6%)	13 (1.4%)				
Travelling	Yes	337 (0.6%)	333 (0.6%)	4 (0.4%)	1.32 (0.49-3.54)	0.58	0.87 (0.29-2.61)	0.81
	No	57487 (99.4%)	56590 (99.4%)	897 (99.6%)				
Residency	Urban	31031 (54%)	30594 (54.1%)	448 (50.6%)	1.21 (1.06-1.38)	0.005	1.24 (1.06-1.43)	0.005
	Rural	26439 (46%)	25991 (45.9%)	437 (49.4%)				

*Logistic regression was used; **Multiple logistic regression was used

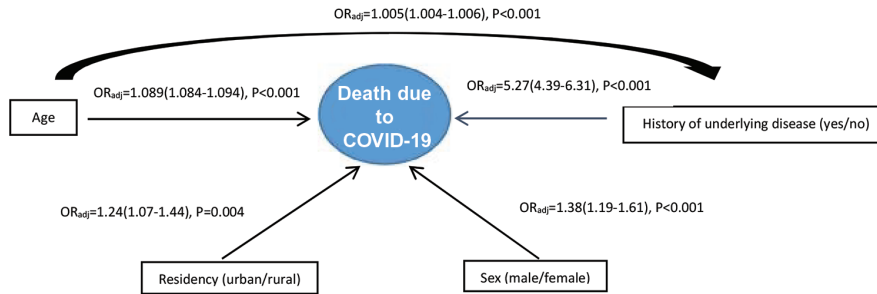


Figure 3: Path diagram illustrates the 57824 COVID-19 positive cases during the period of February 18th to September 30th, 2020, in Fars province, Iran.

Table 2: Receiving Operating Characteristic results of age at death from COVID-19 in 57824 COVID-19 positive cases in Fars province, Iran during February 18th and September 30th 2020

Area under ROC	Std. Error	P value	95% CI	Cut-off point	Uden Index	Sensitivity	Specificity
0.87	0.007	<0.001	0.85-00.88	57.5	0.609	81%	80%

ROC: Receiving operating characteristic; Uden index: Sensitivity+specificity-1

The rate of death due to COVID-19 was significantly higher in individuals with an age of ≥ 57.5 years than those with an age of < 57.5 years (OR=17.56, 95% CI: 15.05-20.48, $P < 0.001$). The recurrence rate of COVID-19 was estimated as 0.23% (134/57958) among the positive cases, with a median \pm IQR equal to 84 \pm 46.25 days.

The sample size was large enough to distinguish between true differences and chance, resulting in an estimated power equal to 100%.

Discussion

R_0 was estimated as 2.8, requiring at least 65% immunization to reach herd immunity, and an $R_{0=}$ 0.36 was required to reach the endemic state in the region. The incidence, mortality, fatality, and recurrence rates of COVID-19 were estimated as 1347.9 per 100,000 dwellers, 209.5 per 1000,000 dwellers, 1.6%, and 3.1 per 100,000 dwellers, respectively. Increasing trends were seen in the incidence rate, mortality rate, and fatality rate during the period of the study. The slopes got especially higher after the quarantine was lifted on April 20th, 2020. The observed increasing trend of fatality rate could be potentially due to the community-wide quarantine lift, non-compliance with health protocols, reopening of recreational, sports, and educational facilities and schools, indoor gatherings causing the warming of the air, the genetic drift of the virus toward a more severe state in terms of the nature and the tentacles of the virus, occupancy of all available hospital beds, and the inability of the health system to treat patients in time.

Furthermore, old age, history of underlying diseases, urban residency, and the male sex

were higher in the deceased group even after adjustment for other factors. Additionally, the history of underlying diseases was the strongest, in terms of association, and mediated the effect of age on death. An accurate cut-off point for age at death due to COVID-19 was estimated as 57.5 years. The recurrence rate was estimated as 0.23% among the positive cases. Although community-wide quarantine could effectively block the transmission of COVID-19 infection, it was shown that there was no life-long immunity against COVID-19.

The mortality rate of SARS-CoV-2 was estimated as 2.9% globally, and close to 2.095% in Iran.¹⁷ In addition, the SARS-CoV-2 fatality rate was calculated as 6.25, which is higher than the value reported in the current study. Fatality rates of 2.8% and 1.7% for men and women were reported confirming the current findings.¹⁸

The R_0 of SARS-CoV-2 ranged from 1.4 to 6.49 universally,^{9, 10, 15} equal to three in Wuhan, China,¹⁹ and between two and three in Qom province, Iran,¹³ covering the current R_0 .

The SARS-CoV-2 infection occurred more frequently among the male patients, which is in line with the results of the present study. However, no significant association was observed between COVID-19 infection and death among the children aged ≤ 4 years old and those between five and 15 years old.²⁰ The results of a study on COVID-19 in Fars province, Iran, showed a median \pm IQR of age equaling 46.50 \pm 26 years, which was higher than the value obtained in the current study. In addition, a larger number of men (54.4%) got the infection, which is similar to the value currently reported. However, close contact and the number of medical staff jobs were higher.¹⁴

A previous study in Shiraz, Iran, demonstrated

that 62.8% of the cases were male, which was higher than the percentage of men in the alive group (56.2%), but close to that in the deceased group (61.5%).¹⁵ Another study performed in Tehran, Iran, showed that 10.89% of the patients had underlying diseases. In that study, the male sex, old age, and underlying diseases were reported as the risk factors for death due to COVID-19, which were consistent with the findings of the current study.¹⁵

In a meta-analysis conducted on 484,919 men and 605,229 women positive for COVID-19 in 23 European countries, the mortality rate was significantly higher in men than in women, which was in line with the findings of this research.²¹ In another study, the male sex, underlying disease, and age of over 65 years were the risk factors for mortality among patients with COVID-19. These results were in line with the results of the present study.²² Some studies demonstrated no hazard for neonates, consistent with the present study results.²³⁻²⁶ In addition, 55% of the mothers suffered from the underlying diseases.²⁷ Some case reports have reported the recurrence of COVID-19. However, the recurrences had happened on a larger scale.²⁸⁻³² Strict community-wide quarantine could curb the COVID-19 outbreak in Italy,³³ a strategy through which the policymakers were able to manage the crisis.^{34, 35} Other aspects, such as nutritional considerations, were not evaluated in their research.^{36, 37}

A drawback of the current work is that the reporting system of infectious diseases in Iran is a passive system; and consequently, the estimated parameters are prone to underestimation. In addition, due to being overwhelmed by new COVID-19 cases from the manifestation onward, the diagnostic samplings were slowed down, and test responses were obtained on retard, resulting in much lower estimations. However, as the turning points of the work, maximum health care capacities were used, and outpatient treatment centers and the CORONALAB online system (coronalab.sums.ac.ir) were set up to provide access to a COVID-19 registry system in a timely fashion, which led to the study being carried out with minimum biases.

Conclusion

There was no solid immunity for COVID-19. The history of underlying diseases, the male sex, urban residency, and age were among the most significant causes of death due to COVID-19. In addition, further investigations are recommended on the genetic structure of SARS-CoV-2, clinical treatments, and vaccination.

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Authors' Contribution

A.S, M.Z, A.M, A.H, M.E: Study concept and design, Acquisition, and interpretation of data, Drafting and critical revision of the manuscript; All authors have read and approved the final manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of Interest: None declared.

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