ORIGINAL ARTICLE

Active Monitoring of Persons Exposed to Patients with Confirmed COVID-19 in South of Iran

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Abstract

Background: Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) can be transmitted through direct, indirect, or close contact with infected people by contaminated respiratory droplets or saliva. This study aimed to investigate the epidemiology of coronavirus disease 2019 (COVID-19) and the secondary attack rate (SAR) in the cases' close contact.

Methods: A total of 431 confirmed COVID-19 patients were randomly selected using systematic random sampling from 15 May to 13 June 2020. The required data were extracted from the CORONALAB database of the Center for Disease Control and Prevention (CDC) at Shiraz University of Medical Sciences. Detection of COVID-19 was performed using Real-Time Polymerase Chain Reaction (RT-PCR) and nasopharyngeal swabs. SAR was also calculated for different groups.

Results: Among the index cases, 64.27% were male, 24.80% were public sector employees, and 4.87% were admitted to the intensive care unit. In addition, most of them aged 30-39 years. The SAR was 11.56% (95% CI: 9.86% to 13.25%) in the close contacts. Accordingly, the highest SAR was observed among the friends, 19.05% (95% CI: 7.17% to 30.92%), followed by the spouses of COVID-19 cases, 16.67% (95% CI: 10.81% to 22.51%). Furthermore, diabetes (6.03%) and cardiovascular disease (5.1%) were the most common comorbidities among the index cases.

Conclusion: The findings suggested that the SAR was relatively lower among the close contacts. Considering the familial and non-familial relationships between the index cases and their close contacts were the major causes of disease transmission. Therefore, it is crucial to conduct tracing for COVID-19 contacts in all cases with whom patients have had close contact.

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Introduction

In Iran, the first report of COVID-19 death was officially announced on 19 February, 2020. Genetic analysis of COVID-19 showed that the virus was similar to Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV).[1] According to the current estimates, the median incubation period for COVID-19 is three days, ranging from 0 to 24 days, with the potential transmission of the infection from asymptomatic individuals.[2, 3] Additionally, the basic reproductive number of COVID-19 (R0) has been reported to be 1.5-6.68.[4] Unlike SARS-CoV, COVID-19 transmission occurs in the prodromal period when infected persons have mild symptoms and can do their typical daily activities, which may contribute to the spread of the infection.[5, 6] This process plays a key role in disease transmission in close contact.

Evidence of the cluster infection of COVID-19 in family members and healthcare staff has confirmed person-to-person transmission[7] by droplets and fomite contact.[2, 8] Evidence has also shown that asymptomatic vectors could transmit the virus.[3] Thus, tracing contacts was reported to be important and necessary in identifying the people who might become ill. Tracking people who have had close contact with confirmed cases has been commonly used to control the disease.[9] Several preliminary studies on contact tracing have shown that the highest exposure risk of COVID-19 transmission was related to the family setting.[3, 10] The first evidence of continuous person-to-person transmission was reported in a family cluster in Shenzhen.[7]

Nonetheless, the family is the smallest unit of society, and the members can hardly be isolated. The intra-household transmission also significantly increased the number of cases in China following the national human mobility restrictions imposed in this country.[11, 12] People may also be in close contact with patients at workplaces or during traveling with acquaintances and friends. Hence, isolation of patients, screening, tracing, management optimization, and quarantining close contacts at home have often been recommended as disease control measures in COVID-19-affected countries. However, disease transmission is likely to occur in close contact before disease diagnosis or in contact with asymptomatic cases. If contact tracing is performed appropriately for close contacts, it can provide useful information about the description of the disease and its modes of transmission. Therefore, the present study investigates the epidemiology of COVID-19 cases and the Secondary Attack Rate (SAR) in their close contacts.

Methods

Study Design and Data Collection

A total of 431 COVID-19-positive patients were selected from the CORONALAB database of the Center for Disease Control and Prevention (CDC) at Shiraz University of Medical Sciences using systematic random sampling between 15 May and 13 June 2020. These patients were designated as the index cases. Detection of COVID-19 was performed for all index cases using throat and nasal swab samples and Real-Time Polymerase Chain Reaction (RT-PCR) targeting. Then, demographic characteristics, symptoms, treatment status, and history of the disease were recorded for the index cases. The patients were contacted during active care at home or the hospital and were asked to notify their close contacts within 14 days before the onset of the disease. Close contact was defined as beingwithin six feet of an infected person for 15 consecutive minutes from two days before the onset of the symptoms (two days before positive sample collection for asymptomatic patients).[13] Close contacts who always wore masks and kept physical distance were excluded. Also, access to casual contacts, such as contacts in public places, shopping centers, public transportation, medical centers, etc., was impossible. On the other hand, we did not have access to close contacts who had traveled to other cities.

The individuals who had close contact with confirmed COVID-19 cases were asked to refer to COVID-19 Outpatient Department (OPD) centers. If they did not refer, we contacted them frequently. We did not access about 4% of close contacts. Therein, throat and nasal swab samples were obtained from all of them, and RT-PCR was performed. Regardless of the RT-PCR test result, symptomatic individuals were isolated and treated in a COVID-19 hospital. The positive subjects were classified into three positions depending on the clinical symptoms: 1) home quarantine, 2) hospitalization in non-intensive care units, and 3) hospitalization in intensive care units. COVID-19-negative subjects were instructed to self-isolate at home and were monitored for 14 days after their last contact with the COVID-19 patient. For example, if a person were traced on the fifth day after the last unprotected contact with a patient, that person would be followed up for nine days. During the isolation period, they were monitored for clinical signs every 24 hours and were advised to notify the COVID-19 care centers if they had any symptoms while maintaining good hygiene and isolation.

Ethical Consideration

The Research Ethics Committee reviewed and approved this study of Shiraz University of Medical Sciences (IR.SUMS.REC.1399.803). In this study, from all the participants written informed consent was obtained.

Statistical Analysis

In this paper, the confirmed cases of COVID-19 and their close contacts were analyzed until 10 June 2020. Relative and absolute frequencies were calculated for the classified variables. SAR and odds ratio (OR) were also calculated for different groups. SAR and OR variations across different groups were also calculated. P values less than 0.05 were regarded as statistically significant. Statistical analyses were performed with Statistical Package for Social Science (IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp).

Results

In this study, 431 definitive cases of COVID-19 were

Table 1: Demographic and COVID-19-related characteristics of the index cases and close contacts during the COVID-19 epidemic in south of Iran, 2020

Characteristics		Index cases (n=431)		Number of close contacts who were in contact with each category of index cases (n=1367)	
Variables	**Category**	**Number***	**%**	**Number***	**%**
Gender	Male	277	64.27	737	53.91
	Female	154	35.73	630	46.09
Age group (years)	0-9	2	0.49	97	7.48
	10-19	16	3.93	133	10.26
	20-29	54	13.27	242	18.68
	30-39	102	25.06	349	26.93
	40-49	100	24.57	207	15.97
	50-59	52	12.78	156	12.04
	60-69	40	9.83	78	6.02
	≤70	41	10.07	34	2.62
Nationality	Iranian	426	98.84	1355	99.12
	Non-Iranian	5	1.16	12	0.88
Job	Heath worker	47	10.90	147	10.80
	Government staff	107	24.80	312	22.80
	Private sector worker	61	14.20	192	14.00
	Student	24	5.60	86	6.30
	Homemaker	76	17.60	219	16.00
	Others	116	26.90	411	30.10
Admission	Outpatient (OPD)	285	66.13	811	59.33
	Non-intensive care unit	125	29	490	35.84
	Intensive care unit	21	4.87	66	4.83
Sign and** symptom	Cough	137	31.79	97	7.10
	Fever	108	25.06	38	2.78
	Sore throat	64	14.85	55	4.02
	Dyspnea	84	19.49	30	2.19
	Gastrointestinal	39	9.05	12	0.88
	Rhinorrhea	19	4.41	4	0.29
	Cyanosis	4	0.93	1	0.07
	Other	8	1.86	91	6.66
Outcome	Dead	14	3.20	38	2.80
	Alive	417	96.80	1329	97.20

*Some variables had missing data. **Some persons had more than one symptom in the index cases and missing data in the close contacts.

recruited as index cases. These cases had close contact with 1367 people. Table 1 presents the demographic characteristics of the index cases and the number of close contacts for the subgroups of each variable. About 64.27% of the index cases were male, most aged 30-39 years (25.06%), and 24.80% were public sector employees. The most common symptom was cough (31.79%), followed by fever (25.06%). In addition, 3.20% of the index cases died due to COVID-19.

In this study, the number of close contacts for the subgroups of each variable was determined. Based on the results, the number of close contacts with male index cases was higher than females (53.91% vs. 46.09%). In addition, the largest number of close contacts was observed in the cases aged 30-39 years (26.93%), while the smallest number was detected among those aged ≤70 years (2.62%). Regarding the workplace, the largest and smallest numbers of close contacts were observed among public sector employees (22.80%) and students (6.30%), respectively. Moreover, 59.33% of the close contacts had contacts with self-isolated index cases at home. Besides, 2.80% of the close contacts had contacts with dead COVID-19 cases. Furthermore, 23% of the index cases and 15% of the close contacts had at least one comorbidity. The most common comorbidities were diabetes (6.03%) and cardiovascular disease (5.1%) among the index cases and hypertension (3.8%) and diabetes (2.53%) among the positive close contacts (Figure 1).

The SAR was calculated at 11.56% (95% CI: 9.86% to 13.25%) in the close contacts. Table 2 presents the familial and non-familial relationships of the close contacts and the COVID-19-positive close contacts with the index cases. Accordingly, the highest SAR was related to friends, 19.05% (95% CI: 7.17% to 30.92%), followed by spouses, 16.67% (95% CI: 10.81% to 22.51%).

Table 3 illustrates the average number of close contacts, the number of PCR-positive close contacts, and the related SARs. The results indicated that SAR was significantly higher in individuals aged 50-59 years than in those aged 10-19. It was also higher in non-Iranians versus Iranians ($P<0.05$).

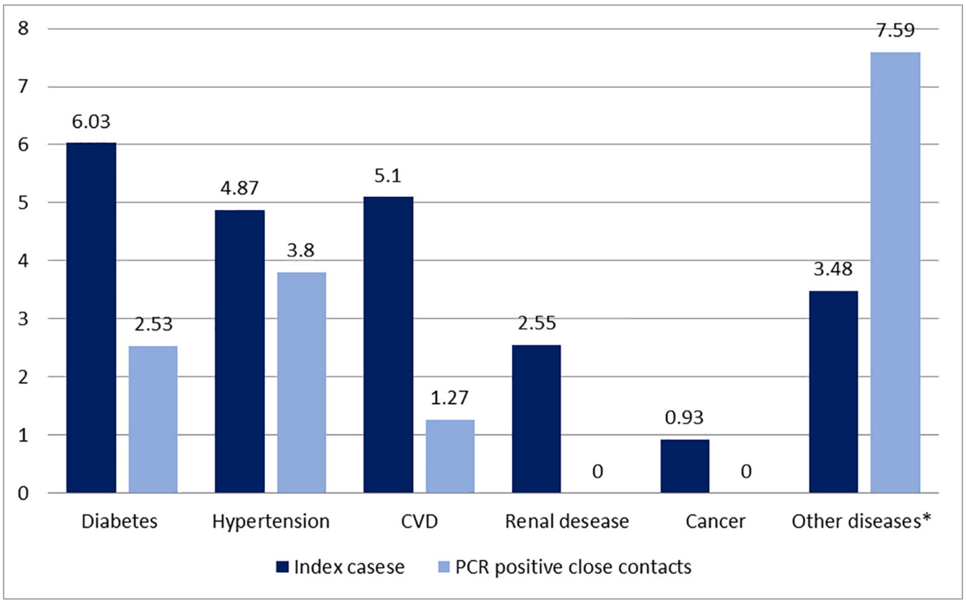

Figure 1: Frequency (%) of underlying diseases among index cases and PCR (PCR: polymerase chain reaction) positive close contacts during COVID-19 epidemic in south of Iran, 2020. *Other disease include psychiatric diseases, cerebral palsy, rheumatoid arthritis, neurodegenerative diseases, stroke, etc.

Table 2: Types of relation between the close contacts as well as the RT-PCR (Real-time polymerase chain reaction) positive close contacts and the index cases during the COVID-19 pandemic in south of Iran, 2020

Type of relation	All close contacts		(RT-PCR) positive close contacts		Secondary attack rate % (SAR), (95% CI)	P value
	Number	Percent	Number	Percent		
Spouse	156	11.41	26	16.46	16.67 (10.81-22.51)	0.04
Children	306	22.38	35	22.15	11.44 (7.87-15)	
First degree	262	19.17	39	24.68	14.89 (10.57-19.19)	
Second degree	100	7.32	14	8.86	14 (7.20-20.80)	
Friend	42	3.07	8	5.06	19.05 (7.17-30.92)	
Colleague	206	15.07	10	6.33	4.85 (1.92-7.79)	
Others	295	21.58	26	16.46	8.81 (5.57-12.05)	
All	1367	100	158	100	11.56 (9.86-13.25)	-

PCR: polymerase chain reaction, CI: Confidence Interval

Discussion

The COVID-19 pandemic has spread rapidly all around the world. Several studies regarding COVID-19 have been done in Iran.[14-17] COVID-19, a respiratory disease, can be transmitted from patients to close contacts. Therefore, the disease may be easily transmitted by people who have had close contact with patients. Therefore, examining the COVID-19 cases and the SAR in their close contacts can help better understand the probability of disease transmission and control.

In the present study, the SAR was 11.56% (95% CI: 9.86% to 13.25%) in close contacts. Up to now, several studies have examined SAR in close contact. For example, a study in China reported the household SAR as 11.2%. However, this measure was computed as 12.4% in another study.[18] Additionally, it was reported as 10.5% in the United States,[19] which was almost consistent with the results of the present investigation. In another study, 3.7% of the close contacts were secondarily infected, although the household SAR was calculated as 10.3%.[20] In Iran, regional CDCs performed household isolation immediately after the disease diagnosis, significantly reducing the SAR.

The current study's findings showed that the SAR was significantly higher in people aged 50-59 years than those aged 10-19 years. It was also higher in non-Iranians than in Iranians. The highest SAR was found among individuals aged 50-59 years. According to the results, the SAR was 2.2 times higher in this age group than in the 10-19 age group (reference group). However, no significant difference was observed regarding the close contacts' SARs in other age groups, including individuals above 60. Individuals over 60 years were more likely to stay home and follow COVID-19 care instructions, including wearing masks, keeping social distance, and washing hands. However, those aged 50-59 included an economically active group who were often outdoors due to working conditions or did

Table 3: The average number of the close contacts and number of (RT-PCR) (real-time polymerase chain reaction) positive close contacts among the COVID-19 index cases and the SAR (Secondary attack rate) of COVID-19 in south of Iran, 2020

Index cases			Close contacts				
Variable		No.*	Average number	Average number of (RT-PCR) positive contacts	(SAR), (95% CI)	OR (95% CI)	P value**
Gender	Male	277	3.23±3.46	0.34±1.01	10.50 (8.49-12.51)	Reference	0.082
	Female	154	3.07±2.34	0.42±0.78	13.74(10.64-16.84)	1.34 (0.96-1.85)	
Age group (years)	0-9	2.0	2.0±0.00	0	0	Not applicable	0 .011
	10-19	16	2.68±1.08	0.24±0.58	9.30 (6.21-17.98)	Reference	
	20-29	54	4.08±5.60	0.61±1.04	15 (10.28-19.72)	1.76 (0.88-3.52)	
	30-39	102	2.63±2.32	0.23±0.52	8.95 (5.53-12.37)	0.98 (0.49-1.98)	
	40-49	100	3.27±2.63	0.42±1.07	12.84 (9.22-16.47)	1.51 (0.74-3.10)	
	50-59	52	2.88±2.46	0.58±1.52	20(13.60-26.40)	2.50 (1.23-5.09)	
	60-69	40	3.80±2.93	0.38±0.89	9.86 (5.13-14.61)	1.15 (0.45-2.95)	
	≤70	41	3.58±3.13	0.20±0.46	5.44 (1.77-9.11)	0.63 (0.13-2.96)	
Job	Health worker	47	3.13±2.32	0.36±0.73	11.56 (6.39-16.73)	Reference	0.070
	Governmental staff	107	2.91±2.50	0.32±1	10.93 (7.46-14.40)	0.94 (0.51-1.74)	
	Private sector staff	61	3.15±2.63	0.57±1.49	18.23 (12.77-23.69)	1.71 (0.91-3.18)	
	Student	24	3.58±4.25	0.62±0.97	17.44 (9.42-25.46)	1.62 (0.76-3.43	
	Homemaker	76	2.88±2.43	0.36±0.74	12.33 (7.97-16.68)	1.08 (0.56-2.05)	
	Others	116	3.54±4.10	0.26±0.61	7.30 (4.78-9.81)	0.54 (0.29-1.02)	
Nationality	Iranian	426	3.17±3.11	0.36±0.93	11.33 (9.64-13.02)	Reference	0.008
	Non-Iranian	5	2.60±2.61	1± 1.22	38.46 (12.01-64.90)	5.87 (1.75-17.77)	
Admission	Outpatient	285	2.84±2.51	0.31±0.80	10.88 (8.73-13.02)	Reference	0.588
	Non-intensive care unit	125	3.91±4.11	0.51±1.21	13.09 (10.09-16.08)	1.23 (0.76-1.98)	
	Intensive care unit	21	3.14±2.88	0.29±0.64	9.09 (2.15-16.02)	0.81 (0.34-1.93)	
Outcome	Dead	14	2.71±2.13	0.21±0.80	7.89 (-0.68-16.47)	Reference	0.474
	Alive	417	3.18±3.13	0.37±0.94	11.61 (9.88-13.33)	1.54 (0.47-5.07)	

*Some variables had missing values. **Difference in the secondary attack rate using chi-square or Fisher's exact test; PCR: polymerase chain reaction, CI: Confidence Interval, OR: odds ratio

not follow COVID-19 health instructions. Overall, older adults are more vulnerable to infection and have poor outcomes.[21] Thus, these individuals need more healthcare services. Overall, maintaining physical distance and wearing masks are essential protective measures for elderly individuals and other people in contact with them.

The present study findings demonstrated that the SAR was 5.87 times higher in non-Iranians than in Iranians. Iran is home to one-third of the world's registered refugees (over one million people).[22] Most of these refugees come from Afghanistan, without a comprehensive healthcare system to record illnesses and health events. The health needs of Afghan refugees and immigrants in Iran are very similar to those of other immigrants worldwide. Several studies have reported a high prevalence of malaria, hepatitis B, tuberculosis, cholera, and Crimean-Congo hemorrhagic fever among Afghan immigrants in Iran.[23-27] In addition, most immigrants are not covered by health insurance, and providing their healthcare needs is costly. Therefore, they rarely refer to health centers due to expensive treatments. However, Iran's Ministry of Health announced that due to the COVID-19 pandemic and the importance of creating a sustainable health status in the country, non-Iranian citizens, similar to Iranians, are provided with free COVID-19 health services. This regulation considerably increased the entrance of non-Iranians to the country for COVID-19 testing and treatment. Given the importance of COVID-19 and its rapid spread, accurate diagnosis, isolation, and quarantine of the refugees' close contacts are required. COVID-19 training interventions are also recommended to be established in this group.

The current study results revealed no significant relationship between occupation and the SAR. The SAR was higher in the private sector employees, students, and homemakers than in the medical personnel, but the difference was not statistically significant (P=0.07). Although healthcare personnel was in contact with patients, they used standard protective equipment regularly, which reduced their SAR. However, hospital and non-hospital staff were considered one group in this study, while the SAR may differ when healthcare professionals are separated from healthcare staff. The screening results on healthcare workers showed that 3% of the asymptomatic patients tested positive, and 40% experienced COVID-19 symptoms more than seven days before the test.[28] In another study, the SAR was lower in healthcare settings compared to family settings.[20]

In the present study, depending on the severity of the disease, the index cases were treated as outpatients and were isolated at home or hospitalized in intensive or non-intensive care units. The results showed that the severity of COVID-19 was not associated with the SAR. Accordingly, the SAR was higher among the patients admitted to non-intensive care units than those admitted to intensive care units and those isolated at home, but the difference was not statistically significant. Generally, the patients admitted to intensive and non-intensive care units do not have close contact with anyone except the medical staff who can transmit the disease. However, some studies have shown that hospitalized index cases with severe critical symptoms reported greater infectiousness.[29-31] In addition, it was proven that the SAR was positively associated with disease severity in index cases, so the patients with more severe clinical symptoms were more likely to infect their close contacts than those with lower severity index cases.[20]

The current study findings indicated no statistically significant difference between males and females concerning the SAR (p=0.082). Similar results were also obtained in another research.[18] However, a literature review has demonstrated that being a female index case was associated with infectiousness.[29, 31]

The present study results showed that the highest SAR was found in friends, followed by spouses, first-degree relatives, and second-degree relatives of the COVID-19 patients. The high SAR in friends could be attributed to people's contact with their friends in gatherings or parties and restaurants, entertainment centers, and crowded places without wearing masks and keeping physical distance. Also, asymptomatic patients may not wear a mask in meeting friends. Therefore, among the friends, SAR was higher than in other groups. Another study indicated that the highest risk of infection was related to the spouses, followed by other family members, close relatives, and other relatives.[30]

In the current research, about a quarter of the index cases and one-sixth of the close contacts had at least one comorbidity. Diabetes was the most common comorbidity among index cases and close contacts, followed by cardiovascular disease in the index cases and hypertension in the positive close contacts. A previous study emphasized that diabetes should be considered a risk factor for rapid progression and poor disease prognosis.[32] The systematic review results also showed that diabetes and hypertension were associated with the severity of COVID-19.[33] The mean age of index cases was higher than close contacts (44.86±17.79 vs.35.07±16.97). At older ages, underlying diseases are more prevalent. Some non-communicable diseases, such as diabetes, hypertension, CVD, renal disease, and cancer, had more prevalence among the index cases.

One of the present research strengths was that it was the first study on the close contacts of COVID-19 patients in Iran. However, one of the study limitations was that only the close contacts who were in contact with confirmed symptomatic cases of the disease were investigated. Therefore, future studies are recommended to evaluate the SAR among close contacts with symptomatic and asymptomatic positive cases.

Conclusion

The study findings showed that the SAR was 11.56%. Among the familial and non-familial close contacts, contacts with friends and spouses were the major causes of disease transmission. Moreover, the SAR was significantly associated with nationality, age, and economic activity. Given the relatively high transmission speed of COVID-19, masks and maintaining physical distance are suggested to avoid disease transmission. Training interventions should also be established to increase awareness of the isolation of individuals with COVID-19 signs and symptoms from their family members and friends.

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Author' Contribution

All authors contributed to the study's conception and design. AMA and FR participated in the design of the study. MMG and MN performed data collection and wrote the manuscript. HG and JH participated in the design of the study. MK and ZKH revised the manuscript. MGG and FR helped with statistical analysis and prepared the illustrations. Finally, KJ, FR, and ZM edited the manuscript. All authors read and approved the final manuscript. They would also like to thank Ms. A. Keivanshekouh at the Research Improvement Center of Shiraz University of Medical Sciences for improving the use of English in the manuscript.

Conflict of interest*:* None declared.

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