Original Article

Journal of Occupational Health and Epidemiology
Journal homepage: http://johe.rums.ac.ir

A Contact Tracing Prospective Cohort Retrieving Epidemiological Facts on SARS-CoV-2 Transmission Aspects: A Serological Analysis in an Iranian Community

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Citation: Vazirinejad R, Khalili P, Jafarzadeh A, Shabani Z, Jamalizadeh A, Rezaei B, Ahmadnia H, Rezayati MT, Ebrahimian M, Mehralinasab Gh, Bagherizadeh A, Bazaz S, Vazirinejad E. A Contact Tracing Prospective Cohort Retrieving Epidemiological Facts on SARS-CoV-2 Transmission Aspects: A Serological Analysis in an Iranian Community. JOHE 2021; 10(2):75-85.

Article Info

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Article history
Received: Jun 2021
Accepted: Aug 2021

10.52547/johe.10.2.75

Print ISSN: 2251-8096
Online ISSN: 2252-0902

Peer review under responsibility of Journal of Occupational Health and Epidemiology

Abstract

Background: The spread of the novel coronavirus seems mysterious enough to make us double-check the indices being used to predict its transmission. In this study, serological analysis was performed to assess some metric and epidemiological aspects of the infection and its transmissibility among people in contact with SARA-CoV-2 patients.
Material and Methods: A total of 453 contacts of 40 COVID-19 patients entered this contact tracing prospective cohort study. Accordingly, SARS-CoV-2 patients were diagnosed by the real-time polymerase chain reaction testing of nasopharyngeal samples. The infectiousness history was detected by the serological testing of IgG and IgM. Trained expert team completed two questionnaires, and blood samples were taken by experts in a laboratory. Data were analyzed using SPSS V21.0 and R software.
Results: The mean ages of the SARS-CoV-2 patients and the contacts were 53.0±18.2 and 30.8±19.3 years, respectively. The overall R_0 of the infection was 2.58. Household and non-household secondary attack rates (SAR) were 20% (95%CI; 12.7–27.3) and 11.3% (95%CI; 6.1-16.5), respectively. The transmission probability of each contact was 0.0205, and the serial interval was 6.4±4.6 (95% CI; 5.2–7.6) days. The SAR was higher among the contacts who were exposed to asymptomatic primary cases (28%, 95%CI; 10-46%) than (13.8%, 95%CI; 9.4-18.2) among those exposed to symptomatic patients.
Conclusions: It is concluded that the herd immunity of 60 to 65% is needed in human communities, based on the amount of R_0 estimated in our survey. The findings demonstrated the amount of the reduction in infection R_0, which is predicted based on both clinical and public health interventions.

Keywords: SARS-CoV-2, Serology, Transmission, Iran.

Introduction

Over one year has passed from the date when the first case of the new coronavirus (SARS-CoV-2) infection was reported in Wuhan, China. The first World Health Organization (WHO) report for COVID-19 was issued on January 21, 2020 [1]. As of that date, the disease is in the form of a pandemic, and almost all countries around the world are entangled with it. In Iran, a total of 1,558,159 COVID-19 patients and 59,341 deaths were reported due to the infection by February 19, 2021, indicating a case fatality rate of 3.8% [2]. A study reported the prevalence of antibody seropositivity in the Kerman Province at 8.2% by the end of April 2020 [3]. However, no specific prevalence or incidence has been reported in the Rafsanjan County (the area of the present study) in the Kerman Province.

In the early weeks of the infection, there were concerns about some major aspects of the disease transmission. For instance, it was predicted that asymptomatic transmission would not be a serious concern in the case of the novel coronavirus [4]. Besides, it was reported that “the extent to which asymptomatic and sub-clinical patients could pass on the virus still remained unclear” [4]. Although many epidemiological investigations have been conducted in the last several months, there are not enough findings to provide accurate evidence to policy makers to answer all related questions. Pollock and Lancaster claimed that the transmission rate among those people in contact with an asymptomatic infected person (the secondary attack rate) might be 3-25 times lower than that among people in contact with symptomatic patients. In other words, people with symptomatic infections are more contagious than people with asymptomatic infections [5]. However, people in the community would have more and closer contacts with asymptomatic patients than with symptomatic ones because of the isolation of symptomatic patients and the fear of infection transmission in the community. This means that the claim made by Pollock and Lancaster should be investigated more cautiously.

Similar to other infections, every detail about transmissibility of the novel coronavirus can play a crucial role in developing programs for controlling the spread of the infection. Household contacts and visits between people are closer than outdoor contacts and visits, with the transmission probability being clearly different. Besides, the type and duration of contacts and visits are important, which should be taken into account. Accurate contact tracing data should be collected to provide the most precise information on human-to-human transmissibility of the infectious agent. The household secondary attack rate (SAR) of SARS-CoV-2 was measured in few studies, such as in that of Jing et al [6].

Winter and Hegde stated that in the case of infectious pathogens, for the purpose of contact tracing in highly dense populations, serological analysis can be useful [7]. However, cross-reactivity of serological tests with other viral pathogens is criticized. Serological analysis along with contact tracing are effective in estimating the proportion of asymptomatic infectors in a population [7]. According to Buitrago-Garcia et al, the overall proportion of people who were infected with COVID-19 without any symptoms throughout the infection was 20% (95% CI; 17-25) [8].

Serological testing can have a crucial role in identifying convalescent cases or people with the milder disease, who might have been missed by other surveillance methods [9].

Bi et al reported some metric measures for COVID-19 transmission, including R_0 and SAR among a group of patients and their contacts [10]. In the present contact tracing prospective cohort, serological analysis was performed to obtain more accurate data to assess some metric and epidemiological measures of the infection and its transmissibility among people in contact with SARA-CoV-2 patients.

Materials and Methods

In this prospective cohort study, all COVID-19 patients whose disease was confirmed by the RT-PCR test from March 1, 2020 to April 30, 2020, (Rafsanjan County, Kerman Province, Southeastern Iran) were invited (n = 48 primary cases). Accordingly, a time period of about three months was considered for each primary case (each COVID-19 patient), and all people in contact with the patient (indoors and outdoors) in this period were identified and invited to assist us with the survey. The three-month time period started from the date of the patient's infection with COVID-19. The date for each patient was calculated based on the date of the first COVID-19 symptom minus the mean duration of the SARS-CoV-2 incubation period (14-21 days). In addition, the termination date of the three-month time period was calculated based on the recovery date of the primary case plus the duration of the convalescent period. Since there was no duration reported for the COVID-19 convalescent period, we considered a duration of three to four weeks. In other words, a three-month duration was estimated for the starting date of the disease to the end of the patient’s infectiousness period for each primary case. Besides, all people in contact with this group of COVID-19 patients

during the three-month period were invited (n = 453). The inclusion criteria of this study included confirmed RT-PCR results and patients' willingness to participate in the study. On the other hand, the exclusion criteria included unwillingness to help with the survey and being unable to give contacts' details. The Ethics Committee of Rafsanjan University of Medical Sciences approved the current study before data collection (Ethics code: IR.RUMS.REC.1399.001). In addition, all methods were followed in accordance with ethical principles and regulations introduced by the Declaration of Helsinki.

Two checklists were used to register the data collected from the COVID-19 patients and their contacts in two phases. In the first phase, demographic characteristics of the patients (n = 48), including age, gender, occupation, nationality, educational status, marital status, living place, family size, weight, height, smoking, addiction, travel history, destination, and its date were recorded. In addition, information on their medical status, including the first COVID-19 symptom and its start date, the list of all COVID-19 symptoms, the duration of COVID-19 symptoms, the COVID-19 diagnosis date, the date of admission to the hospital, the date of recovery or death, severity of the disease, the date of the contact with a COVID-19 patient, and comorbidities were recorded by protected trained experts when they were admitted to the hospital and after receiving informed written consent from the patients or their relatives. Besides, some extra questions were asked from the patients about their contacts in three time periods. These time periods included (1) the time before the first symptom of COVID-19 (at least for two weeks based on the COVID-19 incubation period), (2) the duration from the first symptom onset and admission to the hospital, and (3) the duration from the patients' admission to the data collection time.

In the second phase, the research team traced all people listed as contacts of each COVID-19 patient (n = 40, of whom eight individuals were excluded for their opposition) from the infection time until the end of their infectiousness period. At most, a three-month period was considered for this duration. Besides, all contacts who were visited by each patient during this period were invited (the mean number of the contacts for each patient was 11.32, and the overall number of the contacts was 453). The contacts were visited in their place of residence by protected trained experts. Besides, the participants were briefed on the details of the methods and objectives of the study. In addition, written informed consent was obtained from those who were willing to assist us with the study before data collection. In the case of the contacts being less than 18 years old, we received written informed consent from their parents.

Further to the demographic data that included age, gender, occupation, nationality, educational status, marital status, living place, family size, weight, height, smoking, addiction, travel history, and the type of kinship to the COVID-19 patients, some details of exposure to the COVID-19 patients were collected from the contacts. Further, the contacts were referred to the reference laboratory after recording their data in a face-to-face interview. This study was performed in accordance with the guidelines for reporting observational studies in epidemiology (STROBE). Fig. 1 shows the flowchart for recruiting the SARS-CoV-2 patients and their contacts in this study.

Trained experts recorded the data on COVID-19 patients and their contacts on two separate checklists. In the case of the contacts, some details of the diseases that the participants might suffer from, such as comorbidities, including hypertension, cardiovascular disease, respiratory diseases, diabetes, cancer, and the like were collected. Besides, they were asked about specific items, including the date of their visits of the COVID-19 patients, duration (minutes), place ("indoors at home", "indoors outside home", such as in a shop or on a bus, and "outdoors"), type ("close", such as kissing and/or hugging, "not close, not far", such as shaking hands or having food together, and "far", such as visiting at a distance over 2 meters and/or for less than 2 minutes), and the number of visits. In the last section of the contacts' checklist, some questions were asked about the symptoms of the disease, including the date of the first symptom, duration of the symptom, and date of the admission to the hospital (in case of admission).

Furthermore, all contacts were given a letter that referred them to the medical school's laboratory, and a 5cc vein blood sample was taken from the top of their forearms. The blood sample was used to measure CBC, ESR, CRP, IgG, and IgM. In addition, serological tests were performed to assess the level of specific IgG and IgM antibodies. The laboratory results were given to the participants for free. A member of the research team was asked to consult those participants whose laboratory results showed the need for further medical attention (the consultant was an infection disease specialist).

In the present study, a primary confirmed case was a symptomatic or an asymptomatic case with the positive detection of SARS-CoV-2 nucleic acid by the Real-time Polymerase Chain Reaction (RT-PCR). To this end, specimens taken from

respiratory excretions, or viral genes highly homologous to SARS-CoV-2 were used by the sequencing method. In the contact tracing phase, an individual with the serology test results of IgG and IgM ≥ 1, with or without clinical symptoms, was defined as the secondary case. The serum levels of anti-SARS-CoV-2 IgM/IgG were detected using commercial as well as Iran Food and Drug Administration-approved ELISA kits (Pishtaz-tab, Tehran, Iran). According to the manufacturer's guidelines, the sensitivity and specificity of the ELISA kits were 79.4 and 99.4% for IgM a well as 94.1 and 98.3% for IgG, respectively.

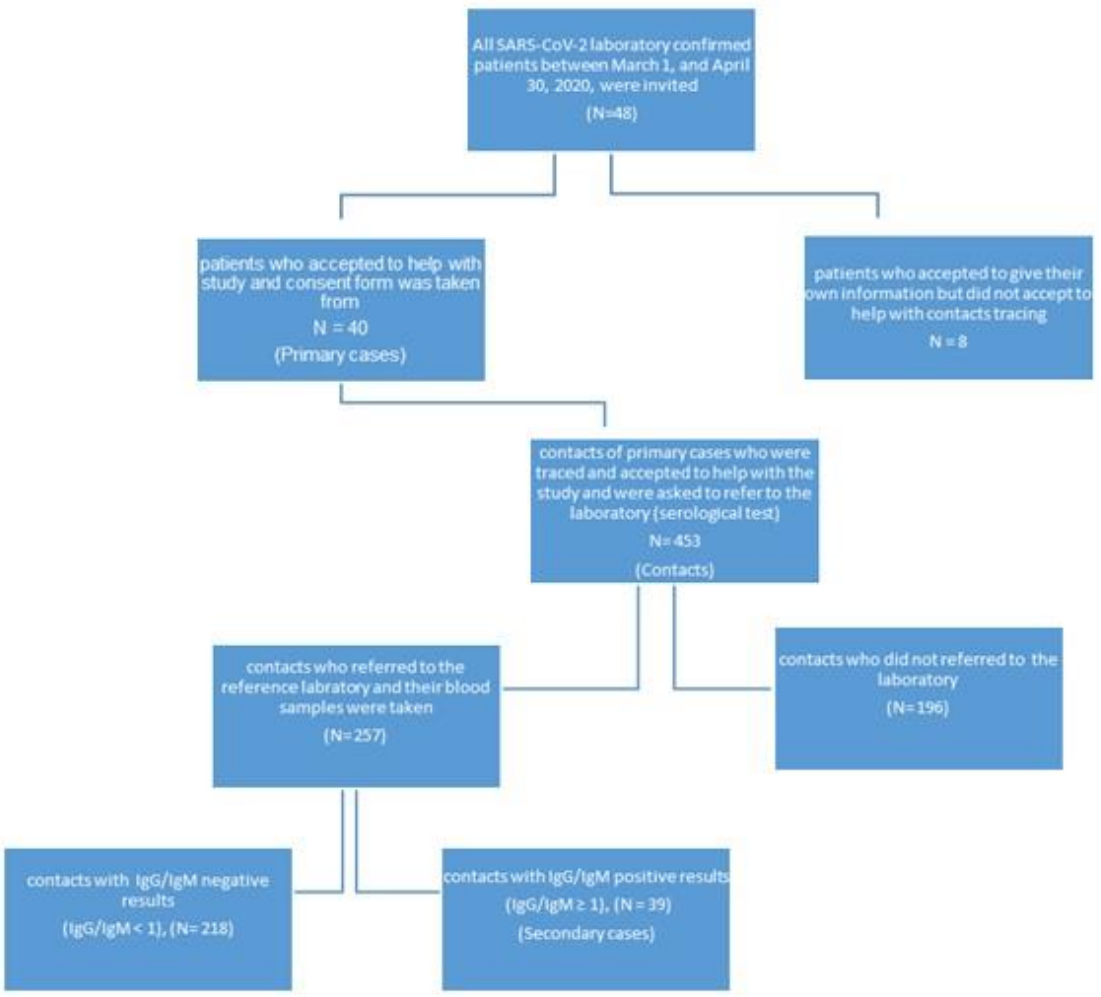

Fig. 1. The flowchart for recruiting the SARS-CoV-2 patients and their contacts in the present cohort

Standard methods, based on the type and scale of the measured variables, were followed using SPSS V21.0. Besides, charts, tables, and descriptive statistical indices, such as the mean and median, were used to present the data. Furthermore, parametric tests (a t-test, the one-way ANOVA, correlation, and regression) as well as non-parametric tests (Chi-square, Fisher's exact, Mann-Whitney U, and Kruskal Wallis tests) were used to compare different groups based on the distribution and deviation features of the data. In addition, the odds ratio (OR) and its 95% confidence interval (95% CI) were used to measure the risk of infection transmission based on different factors.

The R statistical software was used to estimate basic reproductive numbers (R_0) based on the details obtained from contact tracing data and to fit predictive models. To measure R_0, we needed the number of the daily contacts (C) among the COVID-19 patients, the probability of infection transmission for each contact (visit) (P), and the infectiousness duration (D). The infectiousness duration consisted of the incubation period, the duration of symptom presentation, and the convalescent duration. We considered the maximum mean duration of 7 days for the incubation period of SARS-CoV-2 based on previous publications that reported a mean of 5.5 and a maximum of 14 days [11, 12]. In the present study, the mean duration of symptom presentation among the patients (n = 48) was calculated (Mean = 6.4, Sd = 6.6, Min = 1, Max = 30). However, our search did not lead to finding any measures reported for the convalescent duration of COVID-19 as of August 15, 2020; thus, we assumed at

most 7 days for this stage of the infection and considered an overall infectiousness duration of 21 days for the novel coronavirus. Long et al reported the median duration for viral shedding in asymptomatic COVID-19 patients to have been 19 days (Interquartile range (IQR), 15–26 d) [13]. Furthermore, Wu et al reported a median disease duration of 22 days (IQR, 18-26) for SARS-CoV-2 patients [14].

In the present study, the participants' contacts were divided based on their social relationship (living status) as household and non-household contacts. Accordingly, we calculated the transmission probability for every household contact (people living with the primary case in one house) and every non-household contact (people not living with the primary case in the same house).

Accordingly, our model calculated the basic reproductive number based on the aforementioned characteristics of the contacts, with a 95% confidence interval reported. Besides, the results included household and non-household secondary attack rates (SARs) of the infection (SARS-CoV-2). Regarding the objectives of the study, some characteristics of the SARS-CoV-2 infection were calculated, which included the proportion of COVID-19 asymptomatic secondary cases, the infection's serial interval, and the local average number of the contacts or visits of each primary case.

Results

Table 1 shows some characteristics of the participants in the two groups of SARS-CoV-2 patients (primary cases, n = 48) and their contacts (n = 453) in the two household and non-household groups. Accordingly, a total of 48 laboratory confirmed SARS-CoV-2 infections were identified in the only university hospital of Rafsanjan (local population = 320,000), from March to April 2020, among whom 9 cases (18.8%) were asymptomatic. The mean ages of the patients and the contacts were 53.0 ± 18.2 (median = 50.5, Min = 25, Max = 95) and 30.77 ± 19.3 years (median = 31, Min = 1, Max = 91), respectively.

Table 1. Some characteristics of the participants in the two groups of COVID-19 patients (primary cases) and their contacts in the two household and non-household groups

Characteristics		Primary cases		Contacts*					
				Household		Non-household		Total	
		N	%	N	%	N	%	N	%
Age	< 50	21	43.8	159	82.4	196	83.8	355	83.1
	50 - 59	9	18.8	17	8.8	18	7.7	35	8.2
	≥ 60	18	37.5	17	8.8	20	8.5	37	8.7
Gender	Male	21	43.8	107	51.9	121	49.0	228	50.3
	Female	27	56.3	99	48.1	126	51.0	225	49.7
Job	No job	6	12.5	62	32.1	76	32.9	138	32.5
	Housekeeper	17	35.4	45	23.3	47	20.3	92	21.7
	Working	25	52.1	86	44.6	108	46.8	194	45.8
Educational status	≤ Primary	14	29.2	44	25.7	49	22.8	93	24.1
	Intermediate	6	12.5	24	14.0	32	14.9	56	14.5
	≥ High school	28	58.3	103	60.2	134	63.3	237	61.4
Infection	Asymptomatic	9	18.8	156	75.7	197	79.8	353	77.9
	Symptomatic	39	81.3	50	24.3	50	20.2	100	22.1
Family size	< 4	15	31.3	54	27.7	65	21.7	119	27.4
	≥ 4	33	68.7	141	72.3	175	78.3	316	72.6

All of the contacts of the 40 primary cases who visited the patients in the three-month period (from the date when the SARS-CoV-2 patients became infected to the end of their infectiousness period) were traced. The contact tracing task identified 453 contacts, which included the two groups of 206 household and 247 non-household contacts.

Among primary cases (n = 48), the first and most common symptoms were coughs (10, 21%) as well as fever and chills (10, 21%). Besides, the first symptom of SARS-CoV-2 in a primary case was eye irritation (1, 2%). However, nine (18.8%) primary cases of SARS-CoV-2 were asymptomatic (Table 2).

Table 2. Frequency distribution of COVID-19 patients (primary cases) based on the type and mean duration of the first SARS-CoV-2 infection symptom

First symptom	N	%	Mean Duration (days) ± SD	Min	Max
Fever, chills	10	20.8	4.9 ± 3.3	1	12
Coughs	10	20.8	8.2 ± 8.6	1	28
Body pain	6	12.5	5.2 ± 3.9	1	12
Fatigue, weakness	6	12.5	8.5 ± 11.0	1	30
Sore throat	5	10.4	7.0 ± 6.2	2	14
Headache	1	2.1	4.0 ± NA	4	4
Eye irritation	1	2.1	1.0 ± NA	1	1
No symptom	9	18.8	-	-	-
Total	48	100	6.4 ± 6.6	1	30

The number of primary cases visits; Our results showed that some of the contacts were permanently living with a primary case. We considered only one permanent visit per day for such contacts. The visits were recorded based on the three stages of (1) the incubation period equaling 7 days, (2) the illness period being 6.4 ≈ 7 days, and (3) the convalescent period equaling 7 days. Accordingly, the overall number of the visits during the incubation period was 1,348. Since the data on 63 contacts were not recorded in full, we divided the overall number of the visits by 34.5 instead of 40 primary cases (63/453 * 40 ≈ 5.5, with 63 contacts belonging to 5.5 primary cases). The mean number of the visits was 39.1, which amounted to 5.6 (39.1/7 = 5.6 ≈ 6) daily visits for each primary case during the incubation period. Similarly, the number of the daily visits in the illness and convalescent periods was estimated, using the same method, which amounted to 5.6 (≈ 6) and 5.4 (≈ 6) visits per day, respectively.

SARS-CoV-2 household and non-household secondary attack rates (SARs);

Table 3 shows the household and non-household SARs among the contacts with the 95% confidence interval. Out of 257 contacts with serological results, 39 showed IgG antibody titer ≥ 1, indicating an overall attack rate of 15.2% (95%CI; 10.9 - 19.7). Besides, our results demonstrated that the SAR increased with an increase in the contacts' age (Table 4). In addition, the household and non-household SARs of the SARS-CoV-2 infection were 20% (95%CI; 12.7 - 27.3) and 11.3% (95%CI; 6.1 - 16.5), respectively. The infection transmission risk in the household contacts was 1.41 (OR = 1.41, 95%CI; 0.96-2.1) times higher than that in the non-household contacts.

Table 3. Secondary attack rates among the contacts in the two household and non-household groups as well as the 95% confidence interval

Characteristics		Primary cases		Number of all infected/exposed cases (Secondary attack rate*, 95% CI)					
				Household		Non-household		Total**	
		N	%	n/N	CI	n/N	CI	n/N	CI
Age	**< 50**	18	45	13/82	15.9, 8-24	10/110	9.1, 4-14	23/192	12, 7-17
	50 - 59	7	17.5	3/11	27.3, 1-54	3/11	27.3, 1-54	6/22	27.3, 9-46
	≥ 60	15	37.5	6/10	60, 30-90	2/14	14.3, 4-33	8/24	33.3, 14-52
	Total	40	100	29/103	21.3, 13-29	15/135	11.1, 9-16	37/238	15.5, 11-20
Gender	**Male**	19	47.5	11/62	17.7, 8-27	6/66	9.1, 2-16	17/128	13.3, 7-19
	Female	21	52.5	12/53	22.6, 11-34	10/76	13.2, 6-21	22/129	17.1, 11-24
	Total	40	100	23/115	20, 13-27	16/142	11.3, 8-14	39/257	15.1, 11-19
Job	**No job**	6	15	12/56	21.4, 11-32	8/62	12.9, 5-21	20/118	16.9, 1-24
	Housekeeper	11	27.5	5/30	16.7, 3-30	4/34	11.8, 1-23	9/64	14.1, 6-23
	Working	23	57.5	3/18	16.7, 1-34	4/36	11.1, 1-21	7/54	13, 4-22
	Total	40	100	20/104	19.2, 12-26	16/132	12.1, 9-15	36/236	15.2, 11-20
Educational status	**≤ Primary**	13	32.5	6/12	50, 22-78	2/20	10, 3-23	8/32	25, 10-40
	Intermediate	4	10	10/52	19.2, 8-30	5/52	9.6, 2-18	15/104	14.4, 8-21
	≥ High school	23	57.5	3/18	18.8, 1-37	3/21	14.3, 1-29	6/36	16.2, 4-28
	Total	40	100	19/82	23.2, 14-32	10/93	10.7, 5-17	29/172	16.9, 11-22
Months	**March**	14	35.0	10/38	26.3, 12-40	6/70	8.6, 2-15	16/108	14.8, 8-21
	April	26	65.0	13/69	18.8, 10-28	10/69	14.5, 6-23	23/138	16.7, 10-23
	Total	40	100	23/107	21.5, 14-29	16/139	11.5, 6-17	39/246	15.8, 11-20
Infection	**Asymptomatic**	8	20	12/85	14.1, 7-54	6/106	5.7, 1-10	18/191	9.4, 5-14
	Symptomatic	32	80	11/30	36.7, 19-54	10/36	27.8, 13-42	21/66	31.8, 21-43
	Total	40	100	23/115	20, 13-27	16/142	11.2, 6-16	39/257	15.2, 11-20
Family size	**< 4**	12	30	11/28	39.3, 21-57	5/35	14.3, 3-26	16/63	25.4, 15-36
	≥ 4	28	70	10/76	13.2, 6-21	11/103	10.7, 5-17	21/179	11.7, 7-16
	Total	40	100	21/104	20.2, 12-28	16/138	11.6, 6-17	37/242	15.2, 11-20

Data are shown in the form of n/N (%) or secondary attack rates (95% CI), and a household was defined on the basis of close relatives (people living with the patients in the same house).*- Calculated as the number of secondary cases divided by the sum of secondary cases and non-cases **- Data on some of the contacts were missing.

Table 4. Secondary attack rates among the contacts based on serological analysis results (IgG titer) and age

Age groups	IgG titer				Total	
	Negative (< 1)		Positive (≥ 1)			
	N	%	N	%	N	%
< 10	9	100	0	0.0	9	100
10-19	32	88.9	4	11.1	36	100
20-39	93	86.9	14	13.1	107	100
40-59	51	82.3	11	17.7	62	100
≥ 60	16	66.7	8	33.3	24	100
Total	201	84.5	37	15.5	238	100

The chi-square test showed significant differences in IgG positive proportions between different age groups ($\chi 2 = 8.2$, df = 3, $p < 0.05$)

The proportion of asymptomatic COVID 19 infections: Among the traced contacts with serological results (n = 257), 191 contacts showed no symptoms, among whom 18 secondary cases were infected, accounting for about 9.5% of the infected asymptomatic contacts. On the other hand, this group of secondary cases (n = 18) consisted of 46% of all infected secondary cases.

Out of 257 participants with serological analysis results, 25 were exposed to asymptomatic primary cases, of whom 7 (28%, 95%CI; 10 - 46) were IgG positive. Besides, among 232 participants exposed to symptomatic primary cases, there were 32 (13.8%, 95%CI; 9.4 - 18.2) IgG positive participants. In addition, the transmission risk of SARS-CoV-2 in the contacts exposed to asymptomatic patients was significantly higher than that in the contacts exposed to symptomatic primary cases (OR = 2.3, CI: 1.01 - 4.11).

How long antibodies against SARS-CoV-2 infection may last? Serological levels of IgG were measured in 257 contacts who gave the blood sample, and the dates of the contacts' exposure to primary cases were recorded. Accordingly, the mean duration between the last exposure and the date of the serological assessment of the contacts in the two IgG positive (n = 39) and IgG negative (n = 218) (40.5 ± 15.9 and 36.9 ± 15.2, respectively) groups was not significantly different. However, there was no significant correlation between the titer of IgG and the time passed from the exposure date among the contacts. This indicated that antibodies against the SARS-CoV-2 infection might remain proportionally for a long time.

SARS-CoV-2 serial interval: The time between the date of the first symptom in the primary cases (SARS-CoV-2 patients) and the date of the first symptom in the secondary cases was measured as well. Accordingly, the mean SARS-CoV-2 serial interval was 6.4 ± 4.6 (95% CI; 5.21 - 7.6) days with a median of 5 days (Min = 1, Max = 17 days).

Comorbidity effect on SARS-CoV-2 transmission: According to the results, there was no higher risk of the SARS-CoV-2 infection in the contacts who reported comorbidities than in those who did not. The proportions of the people with IgG ≥ 1 among the participants with and without comorbidities (13.7% and 15.5%, respectively) were not statistically different. However, among the traced contacts with serology results (n = 257), 19 suffered from hypertension and probably had positive results of IgG (31.6%, n = 6) compared to the participants who did not report this health issue (13.9%, 33 out of 238) (OR = 2.9, 95% CI; 1.02 - 8.7).

Novel coronavirus transmission probability per each contact: To measure the probability of infection transmission per each contact (Pt), the number of the visits of each primary case among the participants with serological analysis was recorded. The number of the visits was recorded based on the three stages of the SARS-CoV-2 patients' infectiousness, including (1) the incubation period (Ninc) = 645 (in 7 days), (2) the illness period (Nill) = 644 (in 6.4 ≈ 7 days), and (3) the convalescent period (Ncon) = 613 (in 7 days). Besides, the number of the infected secondary cases (Nsec) was 39.

$Pt = Nsec / Ninc + Nill + Ncon$
$Pt = 39/645+644+613 = 0.0205$

The overall probability of SARS-CoV-2 transmission per each contact or visit was about 0.0205. Besides, the probability of SARS-CoV-2 transmission per household and non-household contact was 0.0161 and 0.0337, respectively.

The basic reproductive number of SARS-CoV-2 infection (R_0): Given the aforementioned indices computed in the present survey, it was possible to fit suitable models to predict SARS-CoV-2 infection spread in human populations. To this end, we used R statistical software to produce the models.

$R_0 = P*C*D$

Where, P (= 0.0205), C (= 6), and D (= 21) stand for the probability of transmission per contact, the number of the contacts per unit time (day), and the

duration of SARS-CoV-2 infectiousness, respectively. Based on our findings, the value of R_0 was 2.58.

As Fig. 2 shows, the regression model illustrates the extent of the value of R_0, depends on the number of daily household and non-household contacts and visits among the contacts. This model predicts the size of the change in the R_0 value when the number of daily contacts or visits to the infected cases decreases in the household and non-household contacts.

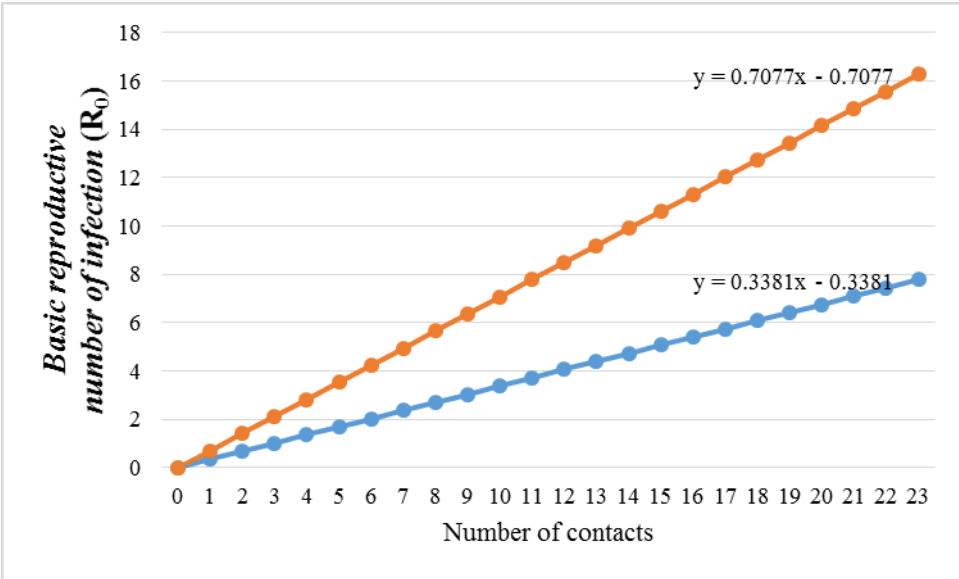

Fig 2. The regression model showing the correlation between R0 values and the number of daily contacts among the household (red line) and non-household (blue line) contacts

Besides, our data demonstrated the size of the reduction in the R_0 value based on the decrease in the duration of the symptoms (the illness period) among the infected cases (Fig. 3).

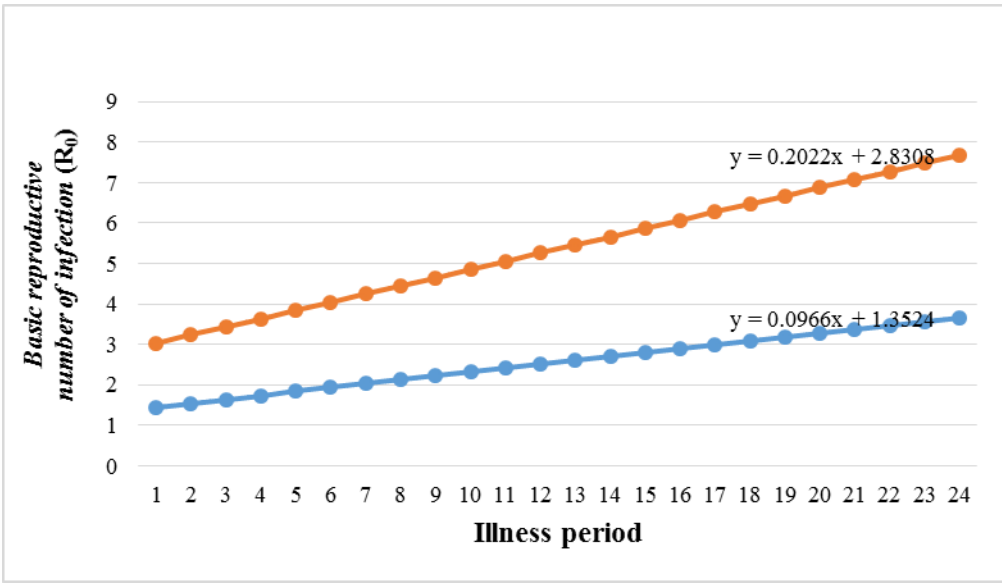

Fig. 3. The regression model showing the correlation between R_0 values and the duration of symptoms (the illness period) among the infected cases (days) among the household (red line) and non-household (blue line) contacts

Discussion

The most common symptoms at the onset of the illness were similar to those reported by many other publications [15-17]. Interestingly, the first symptom of the infection in one of our patients was eye irritation, yet nine (18.8%) SARS-CoV-2 patients (out of 48) were asymptomatic.

The close follow-up of the primary cases and their contacts in this survey helped us calculate almost accurate values for both the number of the contacts as well as the number of the contacts or visits per primary case. The accuracy of these values was effective in predicting the infection spread in the community as well as the extent of the herd immunity (using the $P > 1\text{-}1/ R_0$ formula) we needed to control the pandemic of the SARS-CoV-2 infection.

According to research, serological analysis is useful in estimating the proportion of

asymptomatically infected individuals [7]. Besides, serology is a useful tool for describing the SAR and understanding dynamics of outbreaks, including risk factors. Secondary cases in the present study were detected based on the serum level of the specific IgG antibody of 1 or higher. Suhandynata reported the high positive prediction value of IgG and IgM serologic results in detecting real SARS-CoV-2 secondary cases [18].

The attack rate of the SARS-CoV-2 infection in the present study was 15.3%. Accordingly, the household and non-household secondary attack rates were 20 and 11.3%, respectively. This finding is close to the results reported by Jing et al [3]. Wanga et al reported a secondary transmission rate of 30% among household contacts of SARS-CoV-2 patients [19]. A systematic review by Shah et al presented a list of COVID-19 secondary attack rates in different regions of related surveys with a very wide range (a minimum of 6% in South Africa and a maximum of 49.56% in East Asia and the Pacific) [20]. Our results, being the first report of this type in the Middle East, was based on serological analysis, yet most of the attack rates reported by Shah et al were estimated based on different methods. Moscola et al reported that 13.7% (95% CI, 13.4% - 14.0%) of the US healthcare personnel were seropositive [21]. However, it could not be reliable to compare this finding with our results because the contacts in the present study were definitely in contact with the infected primary cases.

Our finding about the proportion of the contacts who might turn into asymptomatic secondary cases plays a vital role in fitting models for predicting the future spread of the SARS-CoV-2 infection in the community. Besides, our findings showed that about 10% (9.5%) of all contacts with no symptoms became infected and generated antibodies against the SARS-CoV-2 infection without any symptoms (18/191). In the present study, 46% of all secondary cases were asymptomatic. This finding shows that 46% of the infected secondary cases had no symptoms and could spread the novel coronavirus into the community without laboratory detection. This is a suitable explanation for the new pandemic waves in many countries. If we considered the attack rate at 15.3, in addition to this finding, it might be a proper explanation for the spread status of the novel coronavirus in the human communities. Asymptomatic cases spread the SARS-CoV-2 infection in communities without detection. Shah et al concluded that asymptomatic cases have a lower risk of spreading the infection than symptomatic ones [20], being inconsistent with our results. The present study showed that the secondary attack rate in the contacts exposed to asymptomatic primary cases (28%) was significantly higher (OR=2.3, CI: 1.01 - 4.11) than that in the contacts exposed to symptomatic cases (13.8%). The report presented by Long et al supports our results [13]. Therefore, health policymakers should pay more attention to asymptomatic novel coronavirus infections in terms of controlling the pandemic. Furthermore, the titer of serum antibodies against SARS-CoV-2 was not significantly different between asymptomatic and symptomatic cases, in the present survey.

No data have been reported so far to specify the definite duration of immunity after recovery from the infection. In the present study, there was no significant correlation between the titer of IgG and the exposure time passed among the contacts. Thus, one could conclude that naturally acquired active immunity against the SARS-CoV-2 infection might protect recovered cases for a considerable duration. However, further investigations should be conducted on this issue.

In this study, the serial interval of SARS-CoV-2 was 6.4 (median = 5) days. Nishiura et al reported the mean and the median serial interval for SARS-CoV-2 at 4.7 ± 2.9 and 4 days, respectively [22]. Similar to the results of Nishiura et al, the median serial interval in the present survey was shorter than the mean incubation period (7.32 ± 6.7 days), indicating that transmission often took place before the onset of the symptoms, i.e. during the incubation period.

Based on the results of this study, the contacts suffering from hypertension were at a significantly higher risk of the SARS-CoV-2 infection (OR = 2.9, 95% CI; 1.02 - 8.7). Although many studies have confirmed the higher risk of mortalities caused by the SARS-CoV-2 infection among patients with the comorbidities of hypertension, diabetes, cardiovascular disease, etc. [23-24], no survey has reported the increased risk of becoming infected with the novel coronavirus due to comorbidities. Accordingly, the present study suggests that more investigation should be conducted to clarify this issue.

The accuracy of the probability of SARS-CoV-2 infection transmission estimated in our survey plays a vital role in fitting the model for predicting the novel coronavirus spread in the community. In this study, we estimated the value of R_0 for the SARS-CoV-2 infection at 2.58. Given this value, from 60 to 65% of the population should be immune (as the herd immunity) to control the pandemic ($P > 1\text{-}1/ R_0$). Although characteristics of human communities have strong effects on R_0 and varied values of R_0 have been reported by different authors, our estimation is very close to the results

of Wu et al who reported an estimation of 2.68 (95% CrI 2.47 - 2.86) for R_0 of the SARS-CoV-2 infection in China [25].

The direct association of the value of R_0 with the two factors of the number of daily contacts and the duration of the illness helps health policymakers estimate the effectiveness of their measures for controlling the spread of the SARS-CoV-2 infection.

Although our findings clarified some specific characteristics of the SARS-CoV-2 infection, some limitations yet exist. Firstly, there is no idea about the probability of detecting secondary cases, which might be the serological result of false positive serology results, or missing cases with false negative serology results. This could lead to overestimation or underestimation of the indices; secondly, as long as there was no clear report on the duration of the convalescent period, we considered a mean of 7 days based on our experiences and consultations we received from others for this stage of the infection; thirdly, we assumed in the present study that our contacts were only in contact with the COVID-19 patients in their own cluster, whereas there might be other sources of the infection that they contacted.

Conclusion

As a conclusion, the herd immunity between 60 and 65% is needed in human communities based on the value of R_0 obtained in the present study. The findings of this study demonstrated the amount of the reduction that could be predicted in the infection R_0 based on both clinical (a reduction in the illness period of SARS-CoV-2 patients) and public health (a reduction in the number of contacts or visits of SARS-CoV-2 patients) interventions.

Acknowledgement

We would like to appreciate the Iranian Minister of Health and Medical Education, Rafsanjan University of Medical Sciences, and the Social Determinants of Health Research Center of the university for having supported this survey financially. Besides, we thank all participants in the two groups of the SARA-CoV-2 patients and their contacts who assisted us with this survey.

Conflict of interest: None declared.

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