European Journal of Public Health, Vol. 32, No. 5, 813–817

https://doi.org/10.1093/eurpub/ckac121 Advance Access published on 7 September 2022

SARS-CoV-2 transmission by asymptomatic healthcare workers positive to screening swab: an Italian study

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Background: SARS-CoV-2 spreads primarily through respiratory droplets of symptomatic individuals. With respect to asymptomatic individuals, there are conflicting results in the literature and a lack of studies specifically examining transmission in healthcare settings. **Methods:** The aim of this retrospective study, conducted in a northeastern Italian region, was to estimate the contagiousness of asymptomatic healthcare workers (HCWs) who tested positive for SARS-CoV-2. Asymptomatic HCWs who tested positive for SARS-CoV-2 by real-time reverse transcription polymerase chain reaction (rRT-PCR) at a regular screening nasopharyngeal or oropharyngeal swab between 1 February 2020 and 15 September 2020 were considered index cases. Contacts who were at high risk of infection and had follow-up swabs were included. Contacts were considered infected if they had a positive follow-up swab and/or symptoms associated with COVID-19 confirmed by a positive test within 14 days of exposure. Information was taken from records previously collected to identify contacts. Infectivity was estimated using the attack rate (AR) with a 95% confidence interval (95% CI). **Results:** Thirty-eight asymptomatic HCWs who were positive at the screening swab and 778 contacts were identified. Contacts included 63.8% of colleagues, 25.6% of patients, 7.7% of family members and 3.0% of other contacts. Seven contacts tested positive for SARS-CoV-2 (AR: 0.91%, 95% CI: 0.89–0.93). Five of them were family members (AR: 8.3%), one was a colleague (0.2%) and one was a contact of other type (4.2%). **Conclusions:** Viral spread by asymptomatic HCWs was less than in other settings. Identification of risk factors for transmission and reliable indicators of infectivity would be important to prioritize preventive measures.

Introduction

SARS-CoV-2 is a respiratory virus spread primarily from respiratory droplets from infected persons.[1] The main source of virus transmission is close contact with symptomatic persons. With regard to infected individuals who remain asymptomatic, the existing literature on this topic is relatively sparse and shows conflicting results. Indeed, some studies report a percentage of secondary cases caused by asymptomatic individuals ranging from 2.1% to 24%[2–4] and the percentage of infected contacts from asymptomatic individuals varies from 0% to 100%.[5–9] While an Italian contact tracing study[10] found that new infections were equally likely to be attributed to asymptomatic individuals as they were to symptomatic persons, a Chinese study[11] reported that the relative risk of becoming infected after contact with an asymptomatic person compared with a symptomatic person was 0.67 [95% confidence interval (95% CI): 0.29–1.42]. Similarly, a Brunei study[12] showed that in the home setting, asymptomatic cases had lower attack rates (ARs) (4.4%) than symptomatic cases (14.4%).

Because of this uncertainty about the role of asymptomatic infections in the spread of SARS-CoV-2, Italian healthcare facilities have implemented a screening procedure for their asymptomatic healthcare workers (HCWs). It consists of nasopharyngeal (NF) or oropharyngeal (OF) swabs (which are then analysed by real-time reverse transcription polymerase chain reaction, rRT-PCR) performed at regular intervals.[13,14] In the event that an HCW, even if asymptomatic, tests positive for SARS-CoV-2, follow-up is performed on his or her contacts (patients, colleagues, family members, acquaintances, etc.) who are considered to be at particular risk of infection because of the specific exposure situation (timing of exposure, use of personal protective equipment—PPE—during exposure, etc.). Follow-up monitoring consists of serial swabs or clinical surveillance within 14 days (estimated maximum incubation period of SARS-CoV-2[15]) after the last exposure to the index case.

To our knowledge, there are no studies in the literature that specifically address the study of asymptomatic transmission of SARS-CoV-2 in healthcare settings, which are characterized by strict behavioural and PPE protocols to prevent the spread of the virus. In this context, the present study aims to estimate the infectivity of asymptomatic HCWs who tested positive at the SARS-CoV-2 screening swab.

Methods

Setting

This retrospective study was conducted in Friuli-Venezia Giulia, a northeastern Italian region, and covers a health district with ~800 000 inhabitants.

At the time of the study, none of the subjects had been vaccinated against COVID-19, because vaccination against COVID-19 was introduced later in Italy (December 2020).

Cases

Asymptomatic HCWs in hospitals, prevention departments and health districts who tested positive for SARS-CoV-2 by rRT-PCR at regular screening NF or OF swab specimens from 1 February 2020 to 15 September 2020, were considered index cases.

To be included in the study, HCWs had to be asymptomatic, i.e. not have had symptoms associated with COVID-19

- in the 14 days before the swab test was performed;
- in the 14 days following the execution of the swab test; and
- at the time the swab test was performed.

Contacts

Contacts considered to be at high risk of infection were included in the study. They were defined as:

- 'close contacts' (any person living in the same household as a confirmed patient or anyone who had been in an enclosed space within 1 m of a confirmed patient >15 min)[16];

  and/or

- contacts at particular risk of infection because of the context in which they were exposed to the index case.[17]

Contacts were considered eligible for the study if they underwent post-exposure surveillance through serial swabs.

Contacts were considered infected if:

- they had a positive follow-up swab;

  and/or

- they had symptoms or signs associated with COVID-19 within 14 days of exposure that were confirmed by a subsequent positive test.

Data collection

For each index case, we retrospectively obtained information on his/her contacts from electronic medical records previously collected by prevention departments, hospital medical directorates and occupational health services for the purpose of contact tracing. Specifically, the following data were collected: date of last contact before diagnosis of the index case, use of PPE (i.e. surgical masks or FFP2/FFP3 filtering face masks) during contact (present, absent, doubtful), type of contact (patients, colleagues, family members, contacts of other types), date of follow-up swabs, result of follow-up swabs (positive, negative) and presence of symptoms associated with COVID-19 in the 14 days after exposure (present, absent, unknown).

Statistical analysis

Descriptive analyses (absolute number, percentage, mean) of the data were performed.

Contagiousness of HCWs was estimated using AR, which was calculated globally and for each setting by dividing the number of positive contacts by the total number of contacts considered to be at high risk of contagion, as a percentage (with 95% CI).

All analyses were performed using Excel (Microsoft).

The study was approved by the Friuli-Venezia Giulia Regional Ethics Committee with resolution No. CEUR-2020-OS-197.

Results

During the study period, 38 asymptomatic HCWs (30 women and 8 men) who were positive at screening NF or OF swabs were identified. A total of 798 contacts were considered to be at high risk for infection and were therefore traced. Of these, 20 contacts were followed up exclusively clinically and not by NF or OF swabs, so we did not include them in our study. For each case, the number of traced contacts ranged from 0 to 136 (mean: 21.0). Among the contacts, 45 were neonates, who were classified as both 'close contacts' and 'particularly vulnerable to infection' because this type of patient is especially susceptible.

Of the 778 contacts recorded, 63.8% were colleagues (496), 25.6% were patients (198), 7.7% were family members (60) and 3.0% were contacts of other types (24).

Of the contacts, 306 (39.3%) had definite contact with the case when wearing a PPE, whereas 83 (10.7%) had not. Doubtful use of PPE was reported in 62 contacts (8.0%), whereas in the majority of them (327; 42.0%) the use of PPE was not reported or not recorded on the exposure assessment forms.

Table 1 shows the frequency of PPE use for each type of contact. It is notable that the frequency of definite PPE use ranges from 0.0% among family members and other contacts to 68.7% among patients.

As a result of the positivity of the cases, each contact underwent a variable number of swabs, ranging from 1 to 6 (mean 2.2), as shown in table 2, giving a total of 1714 surveillance swabs.

Contagions

Six contacts tested positive, while one contact had a negative result on a follow-up swab, but had a positive sputum test. This was performed in the hospital on the same day as the swab test, after symptoms suggestive of COVID-19 had occurred. Thus, there were seven contacts who tested positive for SARS-CoV-2, which, when accounting for all high-risk contacts monitored by OF or NF swabs, corresponds to an overall AR of 0.91% (95% CI: 0.89–0.93). The timing of positive tests in cases and contacts is showed in table 3. Among contacts, the first positive test occurred between 1 and 11 days (mean: 6.4) after case positivity. Five contacts had a positive result on the first swab, and two had a positive result on the second test, which was performed a few days later.

On average, there were 0.18 positive contacts associated with each index case. Five of these were family members (5 of 60; AR: 8.3%, 95% CI: 2.7–19.4), one was a colleague (1 of 496; 0.2%, 0.01–1.1) and one was a contact of another type (a friend; 1 of 24; 4.2%, 0.1–23.4). In the family members, exposure to the index case definitely occurred without PPE, whereas in the colleague and in the friend, the use of PPE at the time of infection is unknown. No infection occurred in the secure presence of PPE.

Three of the cases infected one contact each, while two cases infected two contacts each.

Table 1 Use of PPE during contacts' exposure to the index case

	Contacts	
	Absolute number	Percentage (%)
Use of PPE during exposure (total)		
Not declared/not reported	327	42.0
Present	306	39.3
Absent	83	10.7
Doubtful	62	8.0
Use of PPE during exposure (by contact type)		
Colleagues		
Not declared/not reported	261	52.6
Present	170	34.3
Absent	17	3.4
Doubtful	48	9.7
Patients		
Not declared/not reported	62	31.3
Present	136	68.7
Absent	0	0.0
Doubtful	0	0.0
Family members		
Not declared/not reported	0	0.0
Present	0	0.0
Absent	60	100
Doubtful	0	0.0
Contacts of other types		
Not declared/not reported	4	16.7
Present	0	0.0
Absent	6	25.0
Doubtful	14	58.3

Table 2 Number of surveillance swabs performed on contacts

	Contacts	
	Absolute number	Percentage (%)
Number of surveillance swabs[a]		
1	234	30.1
2	258	33.2
3	215	27.6
4	38	4.9
5	31	4.0
6	2	0.3
Total	*778*	*100*

a: Twenty high-risk contacts underwent exclusively clinical follow-up (number of surveillance swabs = 0), therefore they were not included in our study.

Table 3 The timing of positive tests in cases and contacts

	Date of positive test (days intercurring between case's and contacts' positive tests)		
	Index case	Contacts	
Index case 1	23 March 2020	03 April 2020 (11)	–
Index case 2	16 March 2020	27 March 2020 (11)	–
Index case 3	12 March 2020	13 March 2020 (1)	19 March 2020 (7)
Index case 4	28 April 2020	09 May 2020 (11)	–
Index case 5	18 August 2020	20 August 2020 (2)	20 August 2020 (2)

No information is available on the symptoms of the positive contacts, except for the contact in whom the swab was negative but the examination of the sputum was positive and who had SARS-CoV-2-related pneumonia.

Discussion

The infectiousness of 38 asymptomatic HCWs who tested positive at a SARS-CoV-2 screening swab was estimated from contact tracing records of their 778 contacts.

Our data showed that the highest ARs occurred outside the healthcare setting, whereas they were extremely low or zero among colleagues and patients.

Relatively high ARs among family members (8.3%) and other non-healthcare contacts (4.2%) reflect close relationships with high levels of interaction and closeness, where physical distancing and other types of control measures are less practical.

These ARs are slightly higher than in a Bruneian study[12] that used contract tracing data and estimated that asymptomatic cases had an AR of 4.4% in the home setting.

Based on our findings, encounters between individuals characterized by some degree of physical distance, proper use of PPE and short time spans (as is generally the case in healthcare settings) appear to play a minor role in transmission of SARS-CoV-2. This enhances the effectiveness of educational initiatives organized by healthcare facilities aimed at teaching the appropriate use of tools useful to reduce the risk of infection, such as hand hygiene and the correct wearing of PPE (surgical face masks in ordinary contexts and filtering face masks and special protective clothing in high-risk contexts).

Our results highlight the potential for silent transmission chains, which has several consequences. First, it supports public health measures such as social distancing and the use of face masks indoors. It also underscores the importance of contact tracing and proposed large-scale testing to identify asymptomatic individuals to break otherwise undetectable chains of infection. Indeed, asymptomatic individuals are unaware that they are infected and are therefore less likely to adhere to practices designed to prevent transmission from infected individuals. In this context, in our setting, regular screening of HCWs is tailored to the level of risk (generally every 30 days for HCWs in low-risk departments and every 7–15 days if they work in high-risk departments).[13,14]

The transmission potential of asymptomatic individuals is probably lower than that of individuals with clinical symptoms. A review[18] indicates that asymptomatic individuals have a level of infectivity that is approximately 0.40–0.70 times that of symptomatic individuals. One reason for this lower infectious potential could be a possible lower excretion of the virus. While a study from Cambridge[19] found a significantly lower viral load in asymptomatic HCWs than in HCWs tested because of the presence of symptoms, most studies have not demonstrated a significant difference between asymptomatic and symptomatic individuals.[10,20–23] However, these studies are generally based on small samples, and viral excretion data from two studies with raw data[10,20] show that viral loads were numerically lower in asymptomatic patients. These observations suggest that statistically significant differences might have been detected with a larger number of observations.[18] In this context, some authors[23,24] suggested the use of the cycle threshold (Ct) of rRT-PCR as a proxy value for viral load in biological samples, useful to reflect the infectiousness of the subject. In our opinion, the Ct value may also depend in part on the adequacy of the sample itself, possibly leading to biased conclusions regarding contagiousness. In addition, there is no Ct value defined in the literature that is associated with the ability to transmit infection *in vivo*.[25]

Further research in this area to find a reliable indicator of contagiousness appears to be extremely important as a screening program for asymptomatic HCWs is implemented and follow-up in the form of serial swabs and/or clinical surveillance is established for SARS-CoV-2 infected individuals and their contacts who are considered to be at particular risk of infection. This has a number of consequences. First, the introduction of regular and systematic screening programs for HCWs inevitably leads to an enormous consumption of resources that are diverted away from other areas of the healthcare system. In

addition, the identification of a positive individual (even if asymptomatic) leads to the need to follow-up both the individual and his or her contacts, which in turn ties up resources, and to impose the designated isolation or quarantine measures on them, with the attendant discomfort. In the case of a positive HCW, isolation measures lead to staff shortages and thus difficulties in delivering health services. In the experience of the prevention and control team responsible for contact tracing, this sometimes leads to reluctance or even refusal to provide information on the part of contacts who fear the social and economic consequences of being identified as a person at high risk of infection.

To potentially grade the risk of transmission in asymptomatic infected individuals and thus to optimally grade the preventive measures to be taken by them, it would be desirable to identify risk factors in the host (e.g. immune system status, comorbidities, use of certain medications, etc.) and environmental risk factors (e.g. presence of artificial ventilation, airspace available per person, etc.) that are highly implicated in viral transmission.

The lack of solid knowledge about the role of individual and environmental characteristics in SARS-CoV-2 transmission is reflected in the recommendations of the Italian Superior Institute of Health (Istituto Superiore di Sanità, ISS) guidelines,[26] which leave room for interpretation. While they provide criteria for categorizing contacts as close (high risk) or not close (low-risk exposure), they also state that it is possible to consider some individuals at high risk based on individual risk assessments, regardless of the duration and context in which contact occurred.

Most of the few studies available on the contagiousness of SARS-CoV-2 in positive asymptomatic individuals[5–9] are case reports on small contact groups (ranging from family clusters to a group of 455 contacts) generated in China, and none of them addresses the specific issue of HCW contagiousness. The present study, on the other hand, involves 38 cases and 778 contacts and is, to our knowledge, the first to focus on the contagiousness of the special category of HCWs, who adhere to specific rules of conduct in their workplace and strictly use PPE. The family members among the contact persons in the present sample represent a kind of control group.

A limitation of this study is that it is a retrospective study based on review of data previously collected for public health purposes and not specifically for research purposes. This means that most of the data on PPE use during contact person exposure to the index case are missing and cannot be recovered. Also, the exposure forms used for contact tracing did not include information on the exact type of PPE that may have been used and the exact duration and frequency of each contact, but only indicate whether the contact lasted more or <15 min. Because of this crude distinction, we were unable to correlate the different types of PPE used and total contact time with infection risk.

Other weaknesses of the present study are the relatively short time frame, the modest size of the sample studied, and the limitation to a single Italian region, which makes its generalizability to other contexts difficult.

Furthermore, the fact that a contact reacted positively to the diagnostic swab does not provide certainty that the infection was due to the HCW identified as the index case. This is because the virus could have been transmitted by another unknown infector. One way to establish a definite link between infector and infected person is to sequence the genome from the positive swabs. Unfortunately, at the time of our study, genome sequencing was performed in Italy only in special cases, mainly in experimental settings and not for the purpose of contact tracing. Be that as it may, when the contacts became positive, they were subjected to a standard telephone interview (as with any other positive subject) to clarify the possible chain of transmission. If the positive contacts had been in contact with two or more known COVID cases, this would be reported on the contact tracing form, but none of our positive contacts did this. As a result, the contagiousness of asymptomatic HCWs could be overestimated. Conversely, determining contagiousness based on swab positivity could lead to falsely negative results, in turn leading to an underestimation of virus transmission. Indeed, the percentage of negative samples was estimated to range from 3% to 71% among infected individuals.[27] In this respect, the ISS recommends collecting biological samples from the respiratory tract at subsequent times and in different sites if a patient is strongly suspicious for SARS-CoV-2 infection but has a negative result from the first swab.[26] This situation occurred to one of the contacts in our sample.

Lastly, the definition of infected cases and contacts we adopted exposes us to the risk of false diagnoses based on false positive swab results. For this purpose, World Health Organization[28] stated that a positive (particularly if weakly positive) swab analysed by means of rRT-PCR needs careful interpretation. To confirm the result, a new specimen should be taken and tested, and clinical, laboratory, and epidemiological information should be accurately considered, especially in the case of asymptomatic clinical presentation and low prevalence of the disease (which is related to a low positive predictive value of the test).

In conclusion, in our findings, viral spread by asymptomatic HCWs in healthcare settings resulted lower than in other settings, but imposed the adoption of preventive and control measures for cases and contacts. Determining the risk factors for SARS-CoV-2 transmission that occurs from asymptomatic HCWs would be important to prioritize infection preventive practices, also given that the role of COVID-19 vaccination in preventing virus transmission is still uncertain.[29,30] In this regard, studies aimed at identifying reliable indicators of infectivity appear desirable.

Funding

This study did not receive any financial support.

Conflicts of interest: None declared.

Key points

- There are conflicting findings in the literature regarding the contagiousness of asymptomatic individuals infected with SARS-CoV-2, as well as a lack of studies specifically addressing viral spread in the healthcare settings.
- Using the attack rate (AR), this retrospective study calculated the contagiousness of asymptomatic healthcare workers (HCWs) who tested positive at regular SARS-CoV-2 screening swabs.
- Among 778 high-risk contacts, seven tested positive for SARS-CoV-2 (AR: 0.91%): five where family members (AR: 8.3%), one was a colleague (0.2%) and one was a contact of another type (4.2%). None of the patients tested positive.
- Viral spread by asymptomatic HCWs was much lower in healthcare settings than in other settings.
- Given the uncertainty surrounding the role of COVID-19 vaccination in preventing viral transmission, identifying risk factors for transmission and reliable indicators of infectivity would be critical in prioritizing preventive practices.

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