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Investigation of the Relation Between Risk Assessment of Exposure and Nosocomial SARS-CoV-2 Transmission in Healthcare Workers: A Prospective Single-center Study

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Abstract

Objectives: Healthcare workers (HCW) are among the risk groups for COVID-19. Determining transmission routes and risk levels during healthcare is of great importance in preventing nosocomial outbreaks. In this study, it was aimed to investigate the frequency of nosocomial transmission and factors affecting the transmission in HCW.

Methods: HCWs admitted to the infectious diseases outpatient clinic due to contact with a COVID-19 patient and diagnosed with SARS-COV-2 by RT-PCR between March 20, 2020, and June 30, 2020 were included in the study.

Results: A total of 822 HCWs with 295 low, 284 intermediate, and 243 high-risk exposures were included in the study. 27.1% of the HCWs were male, and the median age was 31.9 years (20-62). 89.5% of these patients were directly in charge of patient care. Of the index cases contacted, 72.6% were HCW, and 27.4% were non-HCW patients. Most of the risky exposure (51.7%) occurred in nurses. Occurrence frequency of high-risk exposure was lower in those assigned to direct patient care when compared with occurrence frequency of moderate- or low-risk exposures (76.5%, 94.7, 95.3, respectively $p < 0.001$). In most high-risk exposures (220/253), the index cases were HCWs ($p<0.001$). Symptoms were detected in 311 of the HCWs (37.8%) during the follow-up. The median time to perform SARS-CoV-2 RT-PCR was 5.3 days (IQR) after the last risky exposure. In multivariate analysis, SARS-CoV-2 RT-PCR positivity was found to be 5.65 times higher in HCWs not directly involved in patient care compared to HCWs who are not involved in patient care (95% CI = 2.437-13.111; $p < 0.001$).

Conclusions: This study provides particularly useful information on post-exposure COVID-19 follow-up and management of working schedules and procedures of HCWs.

Keywords

COVID-19, healthcare quality improvement, infection control, risk management, nosocomial infections

Competing interests and Funding

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. The authors have no conflict of interest to declare.

Strengths and limitations of this study

- This study was planned prospectively, and negativities such as possible false recall and lack of data, which are among the weaknesses of retrospective studies, were minimized.
- The present study provides beneficial information by utilizing standardized risk classification of nosocomial transmissions in HCWs. It also provides particularly useful information on post-exposure follow-up and required working restrictions for HCWs.
- The study results revealed that adherence to infection control rules is of vital importance in terms of raising awareness about adherence to PPE usage rules and preventing transmission between personnel.
- Although most exposed HCWs (57.1%) have been screened with PCR, it is possible that positivity was not detected (underestimation) in some asymptomatic or mildly symptomatic individuals since not all exposed HCWs have been screened with SARS-CoV-2 PCR test.
- Another limitation is that compliance to proper PPE usage procedures and adherence to hand hygiene have not been investigated.

What Is Known?

In the COVID-19 pandemic, health personnel (HCW) continue to work with great devotion. Protecting health workers is very important in the fight against the epidemic. Published post-exposure follow-up guidelines for healthcare workers recommend a 14-day study restriction according to a different risk classification than our study.

What's Up

In this study, it was revealed that the 7-day study restriction was sufficient. This is very important at times when the need for healthcare workers increases. Although the rate of SARS-CoV-2 RT-PCR positivity development after high-risk exposure was higher than both intermediate and low-risk exposure groups, the difference was not statistically significant.

Introduction

While the COVID-19 pandemic continues unabated, healthcare workers (HCW) at the forefront who are in contact with and caring for COVID-19 patients are among the high-risk groups in terms of COVID-19 transmission.[1-4] Nosocomial transmission remains to cause anxiety in healthcare professionals who struggle with many factors such as excessive working hours, psychological stress, extreme fatigue, occupational burnout, and stigma. SARS-CoV-2 infection is known to be transmitted by respiratory droplets. Direct contact and aerosol-generating procedures (AGP) constitute the highest risk in terms of contamination especially in departments with confirmed or suspected COVID-19 patients.

China reported the number of infected healthcare workers as 3387, The Italian National Institute of Health as 17000, and the USA as 9200.[5-7] In a review published in December 2020, it was stated that 3.9% (152,888) of COVID-19 patients in the world were HCWs.[8] However, there are still countries that have not yet reported the number of infected healthcare personnel and studies investigating risky behavior within HCWs are very limited. In the nosocomial transmission of SARS-CoV-2, adherence of HCWs to infection prevention and control measures and appropriate use of personal protective equipment (PPE) are as significant as the virus characteristics.

Protection of HCWs is one of the most critical points in dealing with the pandemic. Therefore, determining the dynamics of nosocomial transmission within the group of healthcare workers is of great importance in preventing nosocomial outbreaks and protecting HCWs from infection.

This study aimed to investigate the incidence of nosocomial transmission and the factors affecting the transmission in healthcare professionals admitted to the Infection Control Committee (ICC) due to exposure to COVID-19 patients in our hospital.

Material and Method:

Study design

HCWs admitted due to exposure to a definite COVID-19 patient between 20 March 2020 and 30 June 2020 were included in the study. This prospective observational cohort study was approved by the local ethical committee. Written consent was not obtained from the participants since only epidemiological surveillance data was collected.

Infection control

At the beginning of the pandemic, all HCWs working in our hospital were trained by Infection Control Committee (ICC) doctors and nurses on COVID-19 transmission, prevention from the infection, appropriate PPE use, infection control measures, and hand hygiene.

During the pandemic, all necessary PPEs were provided at an adequate level. It was planned for all HCWs to work with surgical masks during the pandemic period and access appropriate PPEs when necessary. Moreover, the course of action to be followed after a risky exposure was determined, and follow-up forms were created to monitor HCWs with occupational exposure.

Determination of contact type and risk level

HCW risk assessment and follow-up were performed by ICC with active surveillance. The demographic characteristics (age, gender, and chronic disease) of the exposed-HCWs, their professions (doctor, nurse, auxiliary health personnel, other auxiliary health personnel, support personnel, and administrative staff), and whether they were directly involved in patient care were recorded. Furthermore, among with index case detection, following data related with the exposure were recorded: index case's mask usage during contact, dates of exposure, and PPE usage of the HCW during exposure.

Types of exposures listed in Table 1 were considered as risky exposure for SARS-CoV-2 transmission and HCWs that have undergone such an exposure were followed-up prospectively. Other types of exposures were categorized as "non-risky" and were excluded from follow-up.[9 10]

Table 1. Risky exposed

A. Close contact
1. Being at a distance of less than 1 meter with COVID-19 patients for 15 minutes or more in the last 5 days
2. Meeting face-to-face with a COVID-19 patient at a distance of less than 1 meter for 15 minutes or longer in the last 5 days
3. Direct contact with a COVID-19 patient (e.g., handshake) or direct contact with the person's secretions (e.g., coughing or touching used tissue) in the last 5 days
B. Intense contact
1. Performing AGP to a COVID-19 patient or assisting in this process

AGP: Aerosol-generating procedure

The World Health Organization (WHO) guideline was used to determine whether the appropriate PPE was worn.[10] The risk level was determined according to PPE usage of the exposed HCW (Table 2). Except for AGP, the use of a surgical mask was considered sufficient. AGP was defined as respiratory tract sampling, intubation, aspiration of respiratory tract secretions, non-invasive mechanical ventilation, high flow oxygen therapy, cardiopulmonary resuscitation, use of nebulizer, endoscopic procedures, bronchoscopy, video-laryngoscopy, dental practices, examinations of the mouth, throat and nose, ophthalmological examinations, and central catheter insertion.[10 11]

Table 2. Risk level determination after a risky exposure

Index case mask-wearing status	PPE using status of HCW	Risk level
No	Did not use a surgical mask or N95	High
	Used a surgical mask in case of N95 indication	Moderate
	Did not use eye protection	Low
	Did not use gloves and aprons	Low
	Used all PPE properly	No
Yes	Did not use a medical mask or N95 or Used a surgical mask in case of N95 indication	Moderate
	Did not use eye protection	Low
	Did not use gloves and aprons	Low
	Used all PPE properly	No

HCW: Healthcare worker, PPE: Personal protective equipment

Follow-up of Exposed HCWs

HCWs included in the study were followed for symptoms for 14 days after the last risky exposure. Symptoms such as fever (≥38 ^{0}C), shortness of breath, cough, sore throat, nasal congestion, or newly-onset loss of smell were considered suspicious symptoms for COVID-19 disease.[11] Nasopharyngeal swab samples were taken for SARS-CoV-2 reverse-transcriptase polymerase chain reaction (RT-PCR) to diagnose COVID-19 from cases with COVID-19 related symptoms during their follow-up. SARS-CoV-2 RT-PCR was performed on the 7th day after the risky exposure among asymptomatic exposed-HCWs with moderate or high-risk exposure (Table 3). A 7-day work restriction was applied to HCWs who had high-risk exposure after intense contact. Those with negative SARS CoV-2 RT-PCR test on the 7th day returned to work, and their 14 days follow-ups were discontinued. Negative SARS-CoV-2 RT-PCR tests of HCWs with persistent symptoms were repeated 48 hours after the initial test.

Table 3. Exposed-HCW follow-up

Risky exposure type and risk level	Management
Intense contact - high risk	1. Symptom follow-up is performed by isolating at home for 7 days. 2. If the symptom develops, the SARS-CoV-2 RT-PCR test is performed on the symptom day, if no symptoms develop, on the 7th day after the last risky exposure. 3. Those with negative test results start to work and are followed up in terms of symptoms for 14 days.
Intense contact - moderate risk	1. Works with a mask on. Active symptom follow-up is performed.

Close contact- high / moderate risk	2. If the symptom develops, the SARS-CoV-2 RT-PCR test is performed on the symptom day, if no symptoms develop, on the 7th day after the last risky exposure.
Close / intense contact - low risk	1. Works with a mask on. 2. If the symptom develops, the SARS-CoV-2 RT-PCR test is performed on the symptom day.

HCW: Healthcare worker, PPE: Personal protective equipment

Definitions

Healthcare worker was defined as all personnel working in healthcare facilities, regardless of their involvement in direct patient care. However, the personnel were grouped according to whether they were directly involved in patient care or not. Occupational groups were recorded as doctors, nurses, auxiliary health personnel, other auxiliary health personnel, support personnel, and administrative staff. The technicians working in radiology, portable x-ray, laboratory, anesthesia, and physical therapy, biologists, and physiotherapists were defined as auxiliary HCWs. Other auxiliary health personnel consisted of staff working in the cafeteria, security, waste services, hospital drivers, and secretaries. The group defined as support personnel were those who helped nurses and doctors in the patient care, cleaning the patient room, and transferring the patient between units. Apart from this, personnel who did not have direct contact with the patient and took part in administrative tasks in a separate unit were classified as administrative staff. Index case describes a case with a positive SARS-CoV-2 RT-PCR result (source of COVID-19 exposure). The index cases were also classified as patients and HCWs.

Patient and public involvement

No patient involved.

Analysis

HCW exposures identified as low-, moderate-, and high-risk were compared against demographic characteristics such as age, gender, comorbid diseases, and occupation, involvement in direct patient care, index case, exposure type (i.e. risk level), post-exposure follow-up data, and COVID-19 development. The relationship between risk level and positivity of SARS-CoV-2 RT-PCR was investigated.

Statistical analysis

All statistical analyses were performed using SPSS for Windows 18 (SPSS Inc, Chicago, IL, USA). Kolmogorov-Smirnov test was used to assess the normality assumption. The continuous variables that did not have normal distribution were expressed as median (minimum-maximum) values. Categorical variables were summarized as counts (percentages). For non-normally distributed continuous variables, differences between groups were tested using the Kruskal Wallis test. Pearson chi-square/Fisher Exact Test determined the relationship

between categorical variables. Univariate logistic regression analysis was used to analyze the factors leading to SARS- CoV-2 PCR positivity. The variables that were considered in the analyses for SARS- CoV-2 PCR positivity were age, sex, profession, involvement in direct patient care, index case, index case mask usage, HCWs PPE usage, and risk level. A two-sided p-value ≤ 0.05 was considered as statistically significant. Multivariable logistic regression model was used to predict potential risk factors of SARS- CoV-2 PCR positivity. The variables which had a significance level of p≤0.20 from the univariate analysis were identified as candidate variables for the multivariable model.

Results

During the study period, a total of 1268 HCWs were admitted with suspicion of risky exposure. After the initial evaluation, exposures that have not met the criteria for risky exposure for COVID-19 were excluded from the follow-up. A total of 822 HCW contacts were classified as risky and were followed up prospectively. 295 of these exposures were low-risk, 284 were intermediate-risk, and 243 were high-risk. The median age was 31.9 years (20-62), and 27.1% of exposed HCWs were male. Risky exposure was detected most frequently in nurses (51.7%). Of the exposed HCWs, 89.5% were directly involved in patient care. The index cases were HCWs in 72.6% of risky exposures and COVID-19 patients in 27.4%. With respect to contact types, 95.5% were identified as close contact and 4.5% as intense contact. Demographic and clinical characteristics of exposed HCWs are shown in Table 4.

Table 4. Demographic and clinical characteristics of HCWs admitting after exposure

	HCW n=822 (%)
Median age (years) min-max	31.9 (20-62)
Gender (Male)	223 (27.1)
Profession	
Nurse	425 (51.7)
Doctor	180 (21.8)
Supportive personnel	91 (11)
Other auxiliary health personnel	66 (8.1)
Auxiliary health personnel	33 (4.1)
Administrative staff	27 (3.2)
Taking part in direct patient care	736 (89.5)
Underlying disease	111 (13.5)
Exposed-index case	
HCW	597 (72.6)
Patient	225 (27.4)
Risky exposed	
Close contact	785 (95.5)
Intense contact	37 (4.5)

Risk level	
Low risk	295 (35.9)
Moderate risk	284 (34.5)
High risk	243 (29.6)

All data are given as a number (percentage) unless specifically stated.
HCW: Healthcare workers
Underlying diseases (patients number): chronic respiratory disease (26), chronic cardiovascular disease (23), thyroid disease (17), chronic rheumatological disease (13), allergic diseases (9), diabetes mellitus (6), chronic neurological disease (5), other (12)

The comparison of the groups by their risk levels is summarized in Table 5. There was a statistically significant difference between age, comorbid diseases, occupation, direct involvement in patient care, index case, and risky exposure type (*p <0.001, p= 0.011, p<0.001, p<0.001, p<0.001, p<0.001*, respectively). As a result of the dual comparison of the groups, the median age was determined to be higher in HCWs with high-risk exposure than in the low-risk and moderate-risk group, comorbiditiy rate was detected to be higher than in low-risk level (*p <0.001, p= 0.011*, respectively). As a result of the dual comparison of the groups, the median age was determined to be higher in HCWs with high-risk exposure than in the low-risk and moderate-risk group (*p<0.001*). Comorbiditiy rate was detected to be higher in HCWs with high-risk exposure than in the low-risk group (*p = 0.011*). High-risk exposure was lowest in nurses (21.9%) and highest in other assistant healthcare personnel (77.3%) (*p<0.001*). High-risk exposure was lower in those directly involved in patient care (76.5%, *p<0.001*). In the vast majority of high-risk exposures (220/253), the index case was an HCW.

Table 5. Comparison of exposed-HCWs by the risk level

	Low risk n=295	**Moderate risk n=284**	**High risk n=243**	***P* value**
Age (years), median (min-max)	29[b] (20-62)	28[b] (20-56)	31[a] (21-62)	**<0.001**
Gender (Male)	80 (35.9)	73 (32.7)	70 (31.4)	0.72
Underlying disease*	31[a] (10.5)	34[a,b] (12)	46[b] (18.9)	**0.011**
Profession				**<0.001**
Nurse	171[a] (40.2)	161[a] (37.9)	93[b] (21.9)	
Doctor	76[a] (42.2)	61[a] (33.9)	43[a] (23.9)	
Supportive personnel	20 [a] (22)	38 [b] (41.8)	33 [b] (36.3)	
Other auxiliary health personnel	5[a] (7.6)	10[a] (15.2)	51[b] (77.3)	
Auxiliary health personnel	14 [a] (42.2)	7 [a] (21.2)	12 [a] (36.4)	
Administrative staff	9[a] (33.3)	7[a] (25.9)	11[a] (40.7)	
Taking part in direct patient care				**<0.001**
Yes	281[a] (38.2)	269[a] (36.5)	186[b] (25.3)	
No	14 (16.3%)	15 (17.4%)	57 (66.3%)	
Exposed-index case				**<0.001**
Patient	56[a] (19)	146[b] (51.4)	23[c] (9.5)	

HCW	239[a] (81)	138[b] (48.6)	220[c] (90.5)	
Risky exposed				**<0.001**
Intense contact	1 [a] (0.3)	29 [b] (10.2)	7[c] (2.9)	
Close contact	294[a] (99.7)	255[b] (89.8)	236 [c] (97.1)	

All data are given as a number (percentage) unless specifically stated.
HCW: Healthcare workers
[a], [b], [c]: There is a difference between the groups indicated by different indices.

Post-exposure follow-up features by risk levels are shown in Table 6. Symptoms developed during follow-up in a total of 311 (37.8%) HCWs. The most common symptoms were sore throat (24.2%) and cough (14.5%). A higher rate of complaints occurred in the moderate and high-risk group than in the low risk exposed group (*p= 0.001*). During the study, SARS-CoV-2 PCR positivity was detected in 28 exposed HCWs. The rate of SARS-CoV-2 RT-PCR positivity development after high-risk exposure was higher than both moderate- and low-risk exposure groups (7.1%, 3.3, 4.5, respectively) but the difference was not found to be statistically significant (*p = 0.205*).

Table 6. Post-contact follow-up results by the risk level

	Low risk n=295(%)	Moderate risk n=284 (%)	High risk n=243 (%)	*P* value
Presence of symptom	87[a] (29.5)	120[b] (42.3)	104[b] (42.8)	**0.001**
Throat ache	51[a] (17.3)	79[b] (27.8)	69[b] (28.4)	**0.002**
Cough	33 (11.2)	41 (14.4)	45 (18.5)	0.055
Diarrhea	8[a] (2.7)	8[a] (2.8)	18[b] (7.4)	**0.009**
Fever	5[a] (1.7)	8[a] (2.8)	19[b] (7.8)	**0.001**
Shortness of breath	11 (3.7)	8 (2.8)	10 (4.1)	0.704
Inability to taste/smell	1 (0.3)	1 (0.4)	2 (0.8)	0.089
Duration to test after last risky exposure, days, median (min-max	5 (1-12)	6 (1-18)	5 (1-14)	0.065
SARS-CoV-2 RT-PCR positivity	8 (4.5)	7 (3.3)	13 (7.1)	0.205
In asymptomatic HCW (n=511)	4 (1.9)	1 (0.6)	5 (3.5)	0.191
Number of tests in asymptomatic HCW	107	110	84	
In symptomatic HCW (n=311)	4 (4.5)	6 (5.0)	8 (7.6)	0.056
Number of tests in symptomatic HCW	69	102	98	

All data are given as a number (percentage) unless specifically stated.
HCW: Healthcare workers, RT-PCR: reverse transcriptase-polymerase chain reaction
[a], [b], [c]: There is a difference between the groups indicated by different indices.

When exposed HCWs with and without SARS-CoV-2 RT-PCR positivity were compared; age, gender, index case type, index case mask usage, HCW's PPE usage, and contact type were not found as independent risk factors for the development of PCR positivity. The only significant factor for the development of SARS-CoV-2 RT-PCR positivity was found to be direct involvement in patient care. Risk of

developing COVID-19 was observed to be 5.65 times higher in those who were not directly involved in patient care (OR = 5.65, 95% CI = 2.437-13.11; *p<0.001*).

Discussion

Protection HCWs who are under high-risk due to COVID-19 is vital in fighting the pandemic. In the face of a new disease, the anxiety and fear of HCWs have decreased with the elimination of uncertainty, the increase in knowledge about the means of transmission and prevention measures, and the acceleration of vaccination studies. However, during this period, many HCWs were infected with SARS-CoV-2 and a considerable number of them died. Knowledge on COVID-19 infection rates in HCWs and epidemiological dynamics of the infection is still insufficient. The knowledge, skills, and adaptation of healthcare professionals regarding infection control measures and PPE use vary widely among HCWs. The concerns that COVID-19 vaccines do not eliminate the infection development, the infections developing with mutant strains, and the decrease in vaccine protection against these mutant strains remind once again the importance of dealing with the characteristics of the infection development in HCWs in more detail. In this study, which was carried out in HCWs applied to ICC due to risky exposure with COVID-19 patients, we aimed to obtain more detailed epidemiological data in terms of behaviors carrying risk for HCWs, to evaluate the exposure risks in detail, and nosocomial SARS-CoV-2 transmission.

Considering that the increase in knowledge and experience with age and that comorbid chronic diseases are risk factors for the poor prognosis of COVID-19, HCWs of older ages and with chronic diseases are expected to be more prudent on measures to prevent infection transmission and appropriate PPE use. However, in our study, the ages of those who have undergone high-risk exposures were higher than the HCWs with low- and moderate-risk exposure (*p <0.001*) and had a higher rate of comorbid chronic diseases (*p = 0.011*). Similarly, in the study of Maltezou et al., chronic diseases were more common in high-risk exposures when compared to low-risk exposures (2.5% - 1.5%, *p=0.001*).[12]

A vast majority of HCWs admitted to ICC with a risky exposure were directly involved in patient care, most of them were nurses and doctors. This can be explained by the fact that nurses are more involved in patient care than other occupational groups and the number of nurses working in the health institution is higher than other personnel. However, in terms of risk levels, it was observed that rate of high-risk exposures was less in doctors (23.9%) and nurses (21.9%). In the study of Maltezou et al., unlike our results, it was reported that high-risk exposure was more common in nurses and doctors (43.4% vs. 36.1, *p <0.001*). Similar to our study, it was found that high-risk exposure was higher among administrative staff in the same study.[12] In our country, after the first case was reported in March 2020,

it has become obligatory for all hospital personnel to work with a mask. Adherence to this measure reduces many exposures to moderate and low-risk categories. However, the occurrence of high-risk exposure among administrative staff, auxiliary HCWs, and other auxiliary HCWs suggests that they suffer from the misconception that they are under less risk in terms of infection development due to not directly taking part in patient care and that often do not adhere to use of masks. A possible reason for this is lower awareness of the fact that infections can be transmitted from colleagues. It seems that the appropriate use of PPE is lower in these groups and proper training and information sharing should be made individually and more emphatically. Although it can be thought that high percentage of moderate and high-risk exposure in the support personnel is due to their tasks directly involving patient care, the fact that the index cases are mostly HCWs rather than the patients does not support this idea.

One of the striking findings of the study is the index cases. In 72.6% of contacts, the index cases were HCWs. Similar to our results, previous studies have shown that HCWs had mostly risky exposure with their colleagues and most of their exposures developed during eating and drinking activities.[12 13] The fact that lowest rates of high-risk exposure were observed in contacts with patients and among HCWs directly involved in patient care indicate that HCW's are better in adhering to PPE use in contact with COVID-19 patients. However, they do not pay enough attention to PPE use and infection control measures in their contacts with colleagues.

The SARS-CoV-2 RT-PCR status became positive in median 5 days after risky exposure, consistent with the disease incubation period. In the study of Maltezou et al., the infection had developed at the end of the first week after risky exposure, and the authors stated that a 7-day work restriction is sufficient.[12] The WHO and the Centers for Disease Control and Prevention (CDC) recommend a 14-day work restriction regardless of the risk level.[1 9] In our study, in line with COVID-19 guidelines of the Ministry of Health, only seven days of work restriction was applied after intense high-risk exposure.[11] In our study, a work restriction was applied to only seven HCWs with high-risk and intense exposure. Other personnel continued to work with masks, and a super-spreader was not detected. In times where the need for HCWs has increased, it is crucial for countries to form policies regarding the protection of HCWs based on their internal dynamics.

Although at least one symptom developed in 37.8% of the risky occupational exposures during the study, SARS-CoV-2 PCR positivity was detected in much less of the cases. In the study by Maltezou et al., at least one symptom was detected in 22.2% of 3398 HCWs exposed to SARS-CoV-2. Symptom development was lower in HCWs with low-risk exposure than in the other two groups with moderate and high risk. Unsurprisingly, the positivity of SARS-CoV-2 after high-risk exposure was higher, but there was no statistically significant

difference between the groups. In the study of Maltezou et al., it was indicated that the development of COVID-19 after high-risk exposure was six times higher than moderate and low-risk exposures (5% in high risk, and 1% in moderate and low risk, $p < 0.001$).[12] Infection development is expected to be higher in high-risk exposure. The lack of difference between the groups in terms of infection development suggests the transmission may occur through direct exposure due to not paying enough attention to hand hygiene despite the use of appropriate equipment.

Among the factors evaluated for development of SARS-CoV-2 positivity, only providing direct care to COVID-19 patients was statistically significant, and contrary to expectations, infection development was found 5.65 times higher in HCWs who did not directly provide care for COVID-19 patients. This finding suggests that the staff caring for a COVID-19 patient adhere more strictly to PPE and other infection control measures, while the staff who do not provide direct care do not comply with the measures adequately with a false sense of safety. In the study of Hunter et al., symptomatic HCWs were divided into three groups: HCWs involved in direct patient care (group 1), HCWs not directly involved in patient care that work in high-risk areas such as laboratories (group 2), and non-clinical workers (group 3). SARS-CoV-2 positivity was detected at a rate of 15% (128 of 834) in group 1, 16% (14 of 86) in group 2, and 18% (20 of 109) in group 3. Furthermore, taking part in direct patient care was not found to be risky for SARS-CoV-2 RT-PCR positivity (group 1 *vs.* group 2: odds ratio 1·08, 95% CI 0·59–1·97; group 1 *vs.* group 3: 1·24, 0·74–2·09; $p = 0.71$).[14] The researchers have drawn attention to community transmission since the study was conducted before the restrictions in society. In studies conducted in Spain and England, no difference was found between the administrative staff and the personnel working in direct patient care in terms of infection development, and it was stated that in-house or community transmission was more effective in HCW infections.[14 15] In a study from France, the infection rate was significantly higher in HCWs who did not directly provide care for COVID-19 patients (odds ratio 2.3, $p = 0.005$).[16] Similarly, in a study conducted in Germany, the fact that only 3% of 86 HCWs with a positive SARS-CoV-2 RT-PCR test had contact with COVID-19 patients was accepted as a supporting finding for community transmission.[17] On the contrary, in a study conducted in Wuhan, 72 exposed HCWs were examined, and it was found that HCWs working in areas with COVID-19 patients were 2.13 times more under risk.[18] However, in this study, the number of personnel exposed to SARS-CoV-2 is very low. Besides, since it is the emerging point of the pandemic, the dynamics of HCWs adherence to the infection control measures in contact with patients and each other may differ compared to other studies.

In addition to use of PPE, the adherence of HCWs with other infection control measures such as hand hygiene and unknown/possible community transmission may have contributed to the difference between the groups. Studies related with HCW risk factors indicate that practicing suboptimal hand hygiene before and after patient exposure, long working hours, inappropriate PPE use and PPE insufficiency, inadequate training on infection control measures, and the unit where an HCW is employed were found to be risk factors for COVID-19 transmission in HCWs. Previous studies report failure to evaluate the effect of remembering bias and other environmental factors as limitations.[13 19-28] This study was planned prospectively, and negativities such as possible false recall and lack of data, which are among the weaknesses of retrospective studies, were minimized. Also, more categorized information has been obtained by using a standardized risk classification in the follow-up and management of exposed HCWs. However, there are several limitations: Although most exposed HCWs (57.1%) have been screened with PCR, it is possible that positivity was not detected (underestimation) in some asymptomatic or mildly symptomatic individuals since not all exposed HCWs have been screened with SARS-CoV-2 PCR test. Moreover, although exposed-HCWs were followed up prospectively, the risk groups in the study were determined based on HCW's own statements. Another limitation is that compliance to proper PPE usage procedures and adherence to hand hygiene have not been investigated.

Conclusions

In the present study, many HCWs were actively followed according to a prospective, post-exposure standardized risk classification. HCWs have a high risk of being infected while providing care for COVID-19 patients. However, prevention of the infections that will develop during the contact of HCWs with other hospital employees seems to be a priority. Increasing infection rates among healthcare workers may lead to health system collapse and worsening of the pandemic. The present study provides beneficial information by utilizing standardized risk classification of nosocomial transmissions in HCWs. It also provides particularly useful information on post-exposure follow-up and required working restrictions for HCWs. The study results revealed that adherence to infection control rules is of vital importance in terms of raising awareness about adherence to PPE usage rules and preventing transmission between personnel. In such a period where the need for HCWs has increased, it will contribute to reorganizing regulatory actions by revealing situations carrying risk of infection.

Data availability statement

Data are available upon reasonable request. All data relevant to the study are included in the article or uploaded as supplementary information. Should further details or materials be required, please contact the corresponding author.

Ethics statement

This prospective observational cohort study was approved by the Turkish Ministry of Health and Ankara City Hospital Ethical Committee.

Contributorship Statement

Conception and design of study: Ayse Kaya Kalem, Rahmet Güner

acquisition of data: Ayse Kaya Kalem, Imran Hasanoglu, Fatma Eser, Muge Ayhan, Belgin Erdogan

analysis and/or interpretation of data: Ayse Kaya Kalem, Bircan Kayaaslan, İmran Hasanoğlu

Drafting the manuscript: Ayse Kaya Kalem, Bircan Kayaaslan

All authors discussed the results and contributed to the final manuscript.

Competing Interest

There are no competing interests for any author.

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Data sharing

No additional data available.

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STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*5*
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	3
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5-6
		(*b*) Describe any methods used to examine subgroups and interactions	5-6
		(*c*) Explain how missing data were addressed	5-6
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	5-6
		(*e*) Describe any sensitivity analyses	5-6
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	6-7
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6-7

		(*b*) Report category boundaries when continuous variables were categorized	6
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	7
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	7-9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10
Generalisability	21	Discuss the generalisability (external validity) of the study results	10
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Investigation of the Relation Between Risk Assessment of Exposure and Nosocomial SARS-CoV-2 Transmission in Healthcare Workers: A Prospective Single-center Study

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Investigation of the Relation Between Risk Assessment of Exposure and Nosocomial SARS-CoV-2 Transmission in Healthcare Workers: A Prospective Single-center Study

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Abstract

Objectives: Healthcare workers (HCW) are among the risk groups for COVID-19. Determining transmission routes and risk levels during healthcare is of great importance in preventing nosocomial outbreaks. This study aimed to investigate the frequency of nosocomial transmission and factors affecting the transmission in HCW.

Methods: HCWs admitted to the infectious diseases outpatient clinic due to contact with a COVID-19 patient and diagnosed with SARS-COV-2 by RT-PCR between March 20, 2020, and June 30, 2020, were included in the study.

Results: A total of 822 HCWs with 295 low, 284 intermediate and 243 high-risk exposures were included in the study. 27.1% of the HCWs were male, and the median age was 31.9 years (20-62). 89.5% of these patients were directly in charge of patient care. Of the index cases contacted, 72.6% were HCW, and 27.4% were non-HCW patients. Most of the risky exposure (51.7%) occurred in nurses. The occurrence frequency of high-risk exposure was lower in those assigned to direct patient care when compared with the occurrence frequency of moderate- or low-risk exposures (76.5%, 94.7, 95.3, respectively $p < 0.001$). In most high-risk exposures (220/253), the index cases were HCWs ($p<0.001$). Symptoms were detected in 311 of the HCWs (37.8%) during the follow-up. The median time to perform SARS-CoV-2 RT-PCR was 5.3 days (IQR) after the last risky exposure. In multivariate analysis, SARS-CoV-2 RT-PCR positivity was 5.65 times higher in HCWs not directly involved in patient care than HCWs who are not involved in patient care (95% CI = 2.437-13.111; $p < 0.001$).

Conclusions: This study provides particularly useful information on post-exposure COVID-19 follow-up and management of working schedules and procedures of HCWs.

Keywords

COVID-19, healthcare quality improvement, infection control, risk management, nosocomial infections

Competing interests and Funding

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. The authors have no conflict of interest to declare.

Strengths and limitations of this study

The advantages of the study;

- ✓ This study was planned prospectively, and it had a large sample size. Negativities such as possible false recall and lack of data, which are among the weaknesses of retrospective studies, were minimized.
- ✓ This study explores the hospital-acquired transmissions in healthcare workers by using standardized risks classification.
- ✓ The present study provides particularly useful information on post-exposure follow-up and required working restrictions for HCWs.

Limitations of the study;

- ✓ Compliance with other infection control measures such as hand hygiene was not investigated in our study.
- ✓ Although most exposed HCWs (57.1%) have been screened with PCR, it is possible that positivity was not detected (underestimation) in some asymptomatic or mildly symptomatic individuals since not all exposed HCWs have been screened with the SARS-CoV-2 PCR test.

Introduction

While the COVID-19 pandemic continues unabated, healthcare workers (HCW) at the forefront who are in contact with and caring for COVID-19 patients are among the high-risk groups in terms of COVID-19 transmission.[1-4] Nosocomial transmission remains to cause anxiety in healthcare professionals who struggle with many factors such as excessive working hours, psychological stress, extreme fatigue, occupational burnout, and stigma. SARS-CoV-2 infection is known to be transmitted by respiratory droplets. Direct contact and aerosol-generating procedures (AGP) constitute the highest risk in terms of contamination, especially in departments with confirmed or suspected COVID-19 patients.

China reported the number of infected healthcare workers as 3387, The Italian National Institute of Health as 17000, and the USA as 9200.[5-7] A review published in December 2020 stated that 3.9% (152,888) of COVID-19 patients in the world were HCWs.[8] However, there are still countries that have not yet reported the number of infected healthcare personnel, and studies investigating risky behavior within HCWs are very limited. In the nosocomial transmission of SARS-CoV-2, adherence of HCWs to infection prevention and control measures and appropriate use of personal protective equipment (PPE) are as significant as the virus characteristics.

The protection of HCWs is one of the most critical points in dealing with the pandemic. Therefore, determining the dynamics of nosocomial transmission within the group of healthcare workers is of great importance in preventing nosocomial outbreaks and protecting HCWs from infection.

This study aimed to investigate the incidence of nosocomial transmission and the factors affecting the transmission in healthcare professionals admitted to the Infection Control Committee (ICC) due to exposure to COVID-19 patients in our hospital.

Material and Method:

Study design

HCWs admitted due to exposure to a definite COVID-19 patient between 20 March 2020 and 30 June 2020 were included in the study. This prospective observational cohort study was approved by the Turkish Ministry of Health and Ankara City Hospital Ethical Committee (E1-20-559).Written consent was not obtained from the participants since only epidemiological surveillance data was collected.

Infection control

At the beginning of the pandemic, all HCWs working in our hospital were trained by Infection Control Committee (ICC) doctors and nurses on COVID-19 transmission, prevention from the infection, appropriate PPE use, infection control measures, and hand hygiene.

During the pandemic, all necessary PPEs were provided at an adequate level. It was planned for all HCWs to work with surgical masks during the pandemic period and access appropriate PPEs when necessary. Moreover, the course of action to be followed after a risky exposure was determined, and follow-up forms were created to monitor HCWs with occupational exposure.

Determination of contact type and risk level

HCW risk assessment and follow-up were performed by ICC with active surveillance. The demographic characteristics (age, gender, and chronic disease) of the exposed-HCWs, their professions (doctor, nurse, auxiliary health personnel, other auxiliary health personnel, support personnel, and administrative staff), and whether they were directly involved in patient care were recorded. Furthermore, along with index case detection, the following data related to the exposure were recorded: index case's mask usage during contact, dates of exposure, and PPE usage of the HCW during exposure.

Types of exposures listed in Table 1 were considered risky for SARS-CoV-2 transmission, and HCWs that had undergone such exposure were followed up prospectively. Other types of exposures were categorized as "non-risky" and were excluded from follow-up.[9 10]

Table 1. Risky exposed

A. Close contact
1. Being at a distance of less than 1 meter with COVID-19 patients for 15 minutes or more in the last 5 days
2. Meeting face-to-face with a COVID-19 patient at a distance of less than 1 meter for 15 minutes or longer in the last 5 days
3. Direct contact with a COVID-19 patient (e.g., handshake) or direct contact with the person's secretions (e.g., coughing or touching used tissue) in the last 5 days
B. Intense contact
1. Performing AGP to a COVID-19 patient or assisting in this process

AGP: Aerosol-generating procedure

The World Health Organization (WHO) guideline was used to determine whether the appropriate PPE was worn.[10] The risk level was determined according to PPE usage of the exposed HCW (Table 2). Except for AGP, the use of a surgical mask was considered sufficient. AGP was defined as respiratory tract sampling, intubation, aspiration of respiratory tract secretions, non-invasive mechanical ventilation, high flow oxygen therapy, cardiopulmonary resuscitation, use of nebulizer, endoscopic procedures, bronchoscopy, video-laryngoscopy, dental practices, examinations of the mouth, throat, and nose, ophthalmological examinations, and central catheter insertion.[10 11]

Table 2. Risk level determination after a risky exposure

Index case mask-wearing status	PPE using status of HCW	Risk level
No	Did not use a surgical mask or N95	High
	Used a surgical mask in case of N95 indication	Moderate
	Did not use eye protection	Low
	Did not use gloves and aprons	Low
	Used all PPE properly	No
Yes	Did not use a medical mask or N95 or Used a surgical mask in case of N95 indication	Moderate
	Did not use eye protection	Low
	Did not use gloves and aprons	Low
	Used all PPE properly	No

HCW: Healthcare worker, PPE: Personal protective equipment

Follow-up of Exposed HCWs

HCWs included in the study were followed for symptoms for 14 days after the last risky exposure. Symptoms such as fever (≥38 ^{0}C), shortness of breath, cough, sore throat, nasal congestion, or newly-onset loss of smell were considered suspicious symptoms for COVID-19 disease.[11] Nasopharyngeal swab samples were taken for SARS-CoV-2 reverse-transcriptase polymerase chain reaction (RT-PCR) to diagnose COVID-19 from cases with COVID-19 related symptoms during their follow-up. SARS-CoV-2 RT-PCR was performed on the 7th day after the risky exposure among asymptomatic exposed-HCWs with moderate or high-risk exposure (Table 3). A 7-day work restriction was applied to HCWs who had high-risk exposure after intense contact. Those with negative SARS CoV-2 RT-PCR test on the 7th day returned to work, and their 14 days follow-ups were discontinued. Negative SARS-CoV-2 RT-PCR tests of HCWs with persistent symptoms were repeated 48 hours after the initial test.

Table 3. Exposed-HCW follow-up

Risky exposure type and risk level	Management
Intense contact - high risk	1. Symptom follow-up is performed by isolating at home for 7 days. 2. If the symptom develops, the SARS-CoV-2 RT-PCR test is performed on the symptom day, if no symptoms develop, on the 7th day after the last risky exposure. 3. Those with negative test results start to work and are followed up in terms of symptoms for 14 days.
Intense contact - moderate risk **Close contact- high / moderate risk**	1. Works with a mask on. Active symptom follow-up is performed. 2. If the symptom develops, the SARS-CoV-2 RT-PCR test is performed on the symptom day, if no symptoms develop, on the 7th day after the last risky exposure.

Close / intense contact - low risk	1. Works with a mask on. 2. If the symptom develops, the SARS-CoV-2 RT-PCR test is performed on the symptom day.

HCW: Healthcare worker, PPE: Personal protective equipment

Definitions

A healthcare worker was defined as all personnel working in healthcare facilities, regardless of their involvement in direct patient care. However, the personnel were grouped according to whether they were directly involved in patient care or not. Occupational groups were recorded as doctors, nurses, auxiliary health personnel, other auxiliary health personnel, support personnel, and administrative staff. The technicians working in radiology, portable x-ray, laboratory, anesthesia, and physical therapy, biologists, and physiotherapists were defined as auxiliary HCWs. Other auxiliary health personnel consisted of staff working in the cafeteria, security, waste services, hospital drivers, and secretaries. The group defined as support personnel were those who helped nurses and doctors in the patient care, cleaning the patient room, and transferring the patient between units. Apart from this, personnel who did not have direct contact with the patient and took part in administrative tasks in a separate unit were classified as administrative staff. Index case describes a case with a positive SARS-CoV-2 RT-PCR result (source of COVID-19 exposure). The index cases were also classified as patients and HCWs.

Patient and public involvement

No patients were involved.

Analysis

HCW exposures identified as low-, moderate-, and high-risk were compared against demographic characteristics such as age, gender, comorbid diseases, occupation, involvement in direct patient care, the index case, exposure type (i.e., risk level), post-exposure follow-up data, and COVID-19 development. The relationship between risk level and positivity of SARS-CoV-2 RT-PCR was investigated.

Statistical analysis

All statistical analyses were performed using SPSS for Windows 18 (SPSS Inc, Chicago, IL, USA). Kolmogorov-Smirnov test was used to assess the normality assumption. The continuous variables that did not have normal distribution were expressed as median (minimum-maximum) values. Categorical variables were summarized as counts (percentages). For non-normally-distributed continuous variables, differences between groups were tested using the Kruskal Wallis test. Pearson chi-square/Fisher Exact Test determined the relationship between categorical variables. Univariate logistic regression analysis was used to analyze the factors leading to SARS- CoV-2 PCR positivity. The variables considered in the analyses for SARS- CoV-2 PCR positivity were age, sex, profession, involvement in direct

patient care, the index case, index case mask usage, HCWs PPE usage, and risk level. A two-sided p-value ≤ 0.05 was considered statistically significant. A multivariable logistic regression model was used to predict potential risk factors of SARS- CoV-2 PCR positivity. The variables with a significance level of p≤0.20 from the univariate analysis were identified as candidate variables for the multivariable model.

Results

During the study period, a total of 1268 HCWs were admitted with suspicion of risky exposure. After the initial evaluation, exposures that had not met the criteria for risky exposure for COVID-19 were excluded from the follow-up. A total of 822 HCW contacts were classified as risky and were followed up prospectively. Two hundred ninety-five of these exposures were low-risk, 284 were intermediate-risk, and 243 were high-risk. The median age was 31.9 years (20-62), and 27.1% of exposed HCWs were male. Risky exposure was detected most frequently in nurses (51.7%). Of the exposed HCWs, 89.5% were directly involved in patient care. The index cases were HCWs in 72.6% of risky exposures and COVID-19 patients in 27.4%. Concerning contact types, 95.5% were identified as close contact and 4.5% as intense contact. Demographic and clinical characteristics of exposed HCWs are shown in Table 4.

Table 4. Demographic and clinical characteristics of HCWs admitting after exposure

	HCW n=822 (%)
Median age (years) min-max	31.9 (20-62)
Gender (Male)	223 (27.1)
Profession	
Nurse	425 (51.7)
Doctor	180 (21.8)
Supportive personnel	91 (11)
Other auxiliary health personnel	66 (8.1)
Auxiliary health personnel	33 (4.1)
Administrative staff	27 (3.2)
Taking part in direct patient care	736 (89.5)
Underlying disease	111 (13.5)
Exposed-index case	
HCW	597 (72.6)
Patient	225 (27.4)
Risky exposed	
Close contact	785 (95.5)
Intense contact	37 (4.5)
Risk level	
Low risk	295 (35.9)
Moderate risk	284 (34.5)
High risk	243 (29.6)

All data are given as a number (percentage) unless specifically stated.
HCW: Healthcare workers
Underlying diseases (patients number): chronic respiratory disease (26), chronic cardiovascular disease (23), thyroid disease (17), chronic rheumatological disease (13), allergic diseases (9), diabetes mellitus (6), chronic neurological disease (5), other (12)

The comparison of the groups by their risk levels is summarized in Table 5. There was a statistically significant difference between age, comorbid diseases, occupation, direct involvement in patient care, the index case, and risky exposure type (*p <0.001, p= 0.011, p<0.001, p<0.001, p<0.001, p<0.001*, respectively). As a result of the dual comparison of the groups, the median age was higher in HCWs with high-risk exposure than in the low-risk and moderate-risk group, and the comorbidity rate was higher than in low-risk level (*p <0.001, p= 0.011*, respectively). As a result of the dual comparison of the groups, the median age was determined to be higher in HCWs with high-risk exposure than in the low-risk and moderate-risk group (*p<0.001*). The comorbidity rate was higher in HCWs with high-risk exposure than in the low-risk group (*p = 0.011*). High-risk exposure was lowest in nurses (21.9%) and highest in other assistant healthcare personnel (77.3%) (*p<0.001*). High-risk exposure was lower in those directly involved in patient care (76.5%, *p<0.001*). In the vast majority of high-risk exposures (220/253), the index case was an HCW.

Table 5. Comparison of exposed-HCWs by the risk level

	Low risk n=295	**Moderate risk n=284**	**High risk n=243**	***P*-value**
Age (years), median (min-max)	29[b] (20-62)	28[b] (20-56)	31[a] (21-62)	**<0.001**
Gender (Male)	80 (35.9)	73 (32.7)	70 (31.4)	0.72
Underlying disease*	31[a] (10.5)	34[a,b] (12)	46[b] (18.9)	**0.011**
Profession				**<0.001**
Nurse	171[a] (40.2)	161[a] (37.9)	93[b] (21.9)	
Doctor	76[a] (42.2)	61[a] (33.9)	43[a] (23.9)	
Supportive personnel	20 [a] (22)	38 [b] (41.8)	33 [b] (36.3)	
Other auxiliary health personnel	5[a] (7.6)	10[a] (15.2)	51[b] (77.3)	
Auxiliary health personnel	14 [a] (42.2)	7 [a] (21.2)	12 [a] (36.4)	
Administrative staff	9[a] (33.3)	7[a] (25.9)	11[a] (40.7)	
Taking part in direct patient care				**<0.001**
Yes	281[a] (38.2)	269[a] (36.5)	186[b] (25.3)	
No	14 (16.3%)	15 (17.4%)	57 (66.3%)	
Exposed-index case				**<0.001**
Patient	56[a] (19)	146[b] (51.4)	23[c] (9.5)	
HCW	239[a] (81)	138[b] (48.6)	220[c] (90.5)	
Risky exposed				**<0.001**
Intense contact	1 [a] (0.3)	29 [b] (10.2)	7[c] (2.9)	
Close contact	294[a] (99.7)	255[b] (89.8)	236 [c] (97.1)	

All data are given as a number (percentage) unless specifically stated.

HCW: Healthcare workers
[a], [b], [c]: There is a difference between the groups indicated by different indices.

Post-exposure follow-up features by risk levels are shown in Table 6. Symptoms developed during follow-up in a total of 311 (37.8%) HCWs. The most common symptoms were sore throat (24.2%) and cough (14.5%). A higher rate of complaints occurred in the moderate and high-risk group than in the low-risk exposed group (*p= 0.001*). During the study, SARS-CoV-2 PCR positivity was detected in 28 exposed HCWs. The rate of SARS-CoV-2 RT-PCR positivity development after high-risk exposure was higher than both moderate- and low-risk exposure groups (7.1%, 3.3, 4.5, respectively), but the difference was not found to be statistically significant (*p = 0.205*).

Table 6. Post-contact follow-up results by the risk level

	Low risk n=295(%)	Moderate risk n=284 (%)	High risk n=243 (%)	*P*-value
Presence of symptom	87[a] (29.5)	120[b] (42.3)	104[b] (42.8)	**0.001**
Throat ache	51[a] (17.3)	79[b] (27.8)	69[b] (28.4)	**0.002**
Cough	33 (11.2)	41 (14.4)	45 (18.5)	0.055
Diarrhea	8[a] (2.7)	8[a] (2.8)	18[b] (7.4)	**0.009**
Fever	5[a] (1.7)	8[a] (2.8)	19[b] (7.8)	**0.001**
Shortness of breath	11 (3.7)	8 (2.8)	10 (4.1)	0.704
Inability to taste/smell	1 (0.3)	1 (0.4)	2 (0.8)	0.089
Duration to test after last risky exposure, days, median (min-max	5 (1-12)	6 (1-18)	5 (1-14)	0.065
SARS-CoV-2 RT-PCR positivity	8 (4.5)	7 (3.3)	13 (7.1)	0.205
In asymptomatic HCW (n=511)	4 (1.9)	1 (0.6)	5 (3.5)	0.191
Number of tests in asymptomatic HCW	107	110	84	
In symptomatic HCW (n=311)	4 (4.5)	6 (5.0)	8 (7.6)	0.056
Number of tests in symptomatic HCW	69	102	98	

All data are given as a number (percentage) unless specifically stated.
HCW: Healthcare workers, RT-PCR: reverse transcriptase-polymerase chain reaction
[a], [b], [c]: There is a difference between the groups indicated by different indices.

When exposed HCWs with and without SARS-CoV-2 RT-PCR positivity were compared; age, gender, index case type, index case mask usage, HCW's PPE usage, and contact type were not found as independent risk factors for the development of PCR positivity. The risk of developing COVID-19 was observed to be 5.65 times higher in those who were not directly involved in patient care (OR = 5.65, 95% CI = 2.437-13.11; *p<0.001*).

Discussion

Protection HCWs who are at high risk due to COVID-19 is vital in fighting the pandemic. In the face of a new disease, the anxiety and fear of HCWs have decreased with the elimination of uncertainty, the increase in knowledge about the means of transmission and prevention measures, and the acceleration of vaccination studies. However, during this period, many HCWs were infected with SARS-CoV-2, and a considerable number of them died. Knowledge on COVID-19 infection rates in HCWs and epidemiological dynamics of the infection is still insufficient. The knowledge, skills, and adaptation of healthcare professionals regarding infection control measures and PPE use vary widely among HCWs. The concerns that COVID-19 vaccines do not eliminate the infection development, the infections developing with mutant strains, and the decrease in vaccine protection against these mutant strains remind once again the importance of dealing with the characteristics of the infection development in HCWs in more detail. In this study, which was carried out in HCWs applied to ICC due to risky exposure with COVID-19 patients, we aimed to obtain more detailed epidemiological data regarding behaviors carrying risk for HCWs, to evaluate the exposure risks in detail and nosocomial SARS-CoV-2 transmission.

Considering that the increase in knowledge and experience with age and comorbid chronic diseases are risk factors for the poor prognosis of COVID-19, HCWs of older ages and with chronic diseases are expected to be more prudent on measures to prevent infection transmission and appropriate PPE use. However, in our study, the ages of those who have undergone high-risk exposures were higher than the HCWs with low- and moderate-risk exposure ($p < 0.001$) and had a higher rate of comorbid chronic diseases ($p = 0.011$). Similarly, in the study of Maltezou et al., chronic diseases were more common in high-risk exposures when compared to low-risk exposures (2.5% - 1.5%, $p=0.001$).[12]

A vast majority of HCWs admitted to ICC with a risky exposure were directly involved in patient care, and most of them were nurses and doctors. This situation can be explained by the fact that nurses are more involved in patient care than other occupational groups and the number of nurses working in the health institution is higher than other personnel. However, in terms of risk levels, it was observed that the rate of high-risk exposures was less in doctors (23.9%) and nurses (21.9%). In the study of Maltezou et al., unlike our results, it was reported that high-risk exposure was more common in nurses and doctors (43.4% vs. 36.1, $p < 0.001$). Similar to our study, it was found that high-risk exposure was higher among administrative staff in the same study.[12] In our country, after the first case was reported in March 2020, it has become obligatory for all hospital personnel to work with a mask. Adherence to this measure reduces many exposures to moderate and low-risk categories. However, the occurrence of high-risk exposure among administrative staff, auxiliary HCWs, and other auxiliary HCWs suggests that they suffer from the misconception that they are under less risk in terms of infection

development due to not directly taking part in patient care and that often do not adhere to use of masks. A possible reason for this is lower awareness of the fact that infections can be transmitted from colleagues. It seems that the appropriate use of PPE is lower in these groups, and proper training and information sharing should be made individually and more emphatically. Although it can be thought that a high percentage of moderate and high-risk exposure in the support personnel is due to their tasks directly involving patient care, the fact that the index cases are mostly HCWs rather than the patients does not support this idea.

One of the striking findings of the study is the index cases. In 72.6% of contacts, the index cases were HCWs. Similar to our results, previous studies have shown that HCWs had mostly risky exposure with their colleagues, and most of their exposures developed during eating and drinking activities.[12 13] The fact that lowest rates of high-risk exposure were observed in contacts with patients and among HCWs directly involved in patient care indicate that HCW's are better in adhering to PPE use in contact with COVID-19 patients. However, they do not pay enough attention to PPE use and infection control measures in their contacts with colleagues.

The SARS-CoV-2 RT-PCR status became positive in the median 5 days after risky exposure, consistent with the disease incubation period. In the study of Maltezou et al., the infection had developed at the end of the first week after risky exposure, and the authors stated that a 7-day work restriction is sufficient.[12] The WHO and the Centers for Disease Control and Prevention (CDC) recommend a 14-day work restriction regardless of the risk level.[1 9] In our study, in line with COVID-19 guidelines of the Ministry of Health, only seven days of work restriction was applied after intense high-risk exposure [11], and only seven HCWs with high-risk and intense exposure underwent a work restriction. Other personnel continued to work with masks, and a super-spreader was not detected. When the need for HCWs has increased, countries must form policies regarding the protection of HCWs based on their internal dynamics.

Although at least one symptom developed in 37.8% of the risky occupational exposures during the study, SARS-CoV-2 PCR positivity was detected in much less of the cases. In the study by Maltezou et al., at least one symptom was detected in 22.2% of 3398 HCWs exposed to SARS-CoV-2. Symptom development was lower in HCWs with low-risk exposure than in the other two groups with moderate and high risk. Unsurprisingly, the positivity of SARS-CoV-2 after high-risk exposure was higher, but there was no statistically significant difference between the groups. The study of Maltezou et al. indicated that the development of COVID-19 after high-risk exposure was six times higher than moderate and low-risk exposures (5% in high risk, and 1% in moderate and low risk, $p < 0.001$).[12] Infection development is expected to be higher in high-risk exposure. The lack of difference between the groups in terms of infection development

suggests the transmission may occur through direct exposure due to not paying enough attention to hand hygiene despite the use of appropriate equipment.

Among the factors evaluated for the development of SARS-CoV-2 positivity, only providing direct care to COVID-19 patients was statistically significant, and contrary to expectations, infection development was found 5.65 times higher in HCWs who did not directly provide care for COVID-19 patients. This finding suggests that the staff caring for a COVID-19 patient adhere more strictly to PPE and other infection control measures, while the staff who do not provide direct care do not comply with the measures adequately with a false sense of safety. In addition, 28 HCWs with positive SARS-CoV-2 RT-PCR tests were included in the comparison. The low number of participants should be considered when interpreting our results. In the study of Hunter et al., symptomatic HCWs were divided into three groups: HCWs involved in direct patient care (group 1), HCWs not directly involved in patient care that work in high-risk areas such as laboratories (group 2), and non-clinical workers (group 3). SARS-CoV-2 positivity was detected at a rate of 15% (128 of 834) in group 1, 16% (14 of 86) in group 2, and 18% (20 of 109) in group 3. Furthermore, taking part in direct patient care was not found to be risky for SARS-CoV-2 RT-PCR positivity (group 1 *vs.* group 2: odds ratio 1·08, 95% CI 0·59–1·97; group 1 *vs.* group 3: 1·24, 0·74–2·09; *p =0.71*).[14] The researchers have drawn attention to community transmission since the study was conducted before the restrictions in society. In studies from Spain and England, no difference was found between the administrative staff and the personnel working in direct patient care in terms of infection development, and it was stated that in-house or community transmission was more effective in HCW infections.[14 15] In a study from France, the infection rate was significantly higher in HCWs who did not directly provide care for COVID-19 patients (odds ratio 2.3, *p =0.005*).[16] Similarly, in a study conducted in Germany, the fact that only 3% of 86 HCWs with a positive SARS-CoV-2 RT-PCR test had contact with COVID-19 patients was accepted as a supporting finding for community transmission.[17] On the contrary, in a study conducted in Wuhan, 72 exposed HCWs were examined, and it was found that HCWs working in areas with COVID-19 patients were 2.13 times more under risk.[18] However, in this study, the number of personnel exposed to SARS-CoV-2 is very low. Besides, since it is the emerging point of the pandemic, the dynamics of HCWs' adherence to the infection control measures in contact with patients and each other may differ compared to other studies.

In addition to the use of PPE, the adherence of HCWs to other infection control measures such as hand hygiene and unknown/possible community transmission may have contributed to the difference between the groups. Studies related to HCW risk factors indicate that practicing suboptimal hand hygiene before and after patient exposure, long working hours, inappropriate PPE use and PPE insufficiency,

inadequate training on infection control measures, and the unit where an HCW is employed were found to be risk factors for COVID-19 transmission in HCWs. Previous studies report failure to evaluate the effect of remembering bias and other environmental factors as limitations.[13 19-28] This study was planned prospectively, and negativities such as possible false recall and lack of data, which are among the weaknesses of retrospective studies, were minimized. Also, more categorized information has been obtained by using a standardized risk classification in the follow-up and management of exposed HCWs. However, there are several limitations: Although most exposed HCWs (57.1%) have been screened with PCR, it is possible that positivity was not detected (underestimation) in some asymptomatic or mildly symptomatic individuals since not all exposed HCWs have been screened with SARS-CoV-2 PCR test. Moreover, although exposed-HCWs were followed up prospectively, the risk groups in the study were determined based on HCW's own statements. Another limitation is that compliance to proper PPE usage procedures and adherence to hand hygiene have not been investigated.

Conclusions

In the present study, many HCWs were actively followed according to a prospective, post-exposure standardized risk classification. HCWs have a high risk of being infected while providing care for COVID-19 patients. However, prevention of the infections that will develop during the contact of HCWs with other hospital employees seems to be a priority. Increasing infection rates among healthcare workers may lead to health system collapse and worsening of the pandemic. The present study provides beneficial information by utilizing standardized risk classification of nosocomial transmissions in HCWs. It also provides particularly useful information on post-exposure follow-up and required working restrictions for HCWs. The study results revealed that adherence to infection control rules is of vital importance in terms of raising awareness about adherence to PPE usage rules and preventing transmission between personnel. In such a period where the need for HCWs has increased, it will contribute to reorganizing regulatory actions by revealing situations carrying the risk of infection.

Data availability statement

Data are available upon reasonable request. All data relevant to the study are included in the article or uploaded as supplementary information. Should further details or materials be required, please contact the corresponding author.

Ethics statement

This prospective observational cohort study was approved by the Turkish Ministry of Health and Ankara City Hospital Ethical Committee (E1-20-559).

Contributorship Statement

Conception and design of study: Ayse Kaya Kalem, Rahmet Güner

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All authors discussed the results and contributed to the final manuscript.

Competing Interest

There are no competing interests for any author.

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Data sharing

No additional data is available.

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STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*5*
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	3
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5-6
		(*b*) Describe any methods used to examine subgroups and interactions	5-6
		(*c*) Explain how missing data were addressed	5-6
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	5-6
		(*e*) Describe any sensitivity analyses	5-6
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	6-7
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6-7

		(*b*) Report category boundaries when continuous variables were categorized	6
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	7
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	7-9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10
Generalisability	21	Discuss the generalisability (external validity) of the study results	10
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Investigation of the Relation Between Risk Assessment of Exposure and Nosocomial SARS-CoV-2 Transmission in Healthcare Workers: A Prospective Single-center Study

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Investigation of the Relation Between Risk Assessment of Exposure and Nosocomial SARS-CoV-2 Transmission in Healthcare Workers: A Prospective Single-center Study

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Abstract

Objectives: Healthcare workers (HCW) are among the risk groups for COVID-19. Determining transmission routes and risk levels during healthcare is of great importance in preventing nosocomial outbreaks. This study aimed to investigate the frequency of nosocomial transmission and factors affecting the transmission in HCW.

Methods: HCWs admitted to the infectious diseases outpatient clinic due to contact with a COVID-19 patient and diagnosed with SARS-COV-2 by RT-PCR between March 20, 2020, and June 30, 2020, were included in the study.

Results: A total of 822 HCWs with 295 low, 284 intermediate and 243 high-risk exposures were included in the study. 27.1% of the HCWs were male, and the median age was 31.9 years (20-62). 89.5% of these patients were directly in charge of patient care. Of the index cases contacted, 72.6% were HCW, and 27.4% were non-HCW patients. Most of the risky exposure (51.7%) occurred in nurses. The occurrence frequency of high-risk exposure was lower in those assigned to direct patient care when compared with the occurrence frequency of moderate- or low-risk exposures (76.5%, 94.7, 95.3, respectively $p < 0.001$). In most high-risk exposures (220/253), the index cases were HCWs ($p<0.001$). Symptoms were detected in 311 of the HCWs (37.8%) during the follow-up. The median time to perform SARS-CoV-2 RT-PCR was 5.3 days (IQR) after the last risky exposure. In multivariate analysis, SARS-CoV-2 RT-PCR positivity was 5.65 times higher in HCWs not directly involved in patient care than HCWs who are not involved in patient care (95% CI = 2.437-13.111; $p < 0.001$).

Conclusions: This study provides particularly useful information on post-exposure COVID-19 follow-up and management of working schedules and procedures of HCWs.

Strengths and limitations of this study

The advantages of the study;

- ✓ This study was planned prospectively.
- ✓ This study had a large sample size.
- ✓ This study explores the hospital-acquired transmissions in healthcare workers by using standardized risks classification.

Limitations of the study;

- ✓ Compliance with other infection control measures such as hand hygiene was not investigated in our study.

- ✓ It is possible that positivity was not detected in some asymptomatic or mildly symptomatic individuals since not all exposed HCWs have been screened with the SARS-CoV-2 PCR test.

Keywords

COVID-19, healthcare quality improvement, infection control, risk management, nosocomial infections

Competing interests and Funding

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. The authors have no conflict of interest to declare.

Introduction

While the COVID-19 pandemic continues unabated, healthcare workers (HCW) at the forefront who are in contact with and caring for COVID-19 patients are among the high-risk groups in terms of COVID-19 transmission.[1-4] Nosocomial transmission remains to cause anxiety in healthcare professionals who struggle with many factors such as excessive working hours, psychological stress, extreme fatigue, occupational burnout, and stigma. SARS-CoV-2 infection is known to be transmitted by respiratory droplets. Direct contact and aerosol-generating procedures (AGP) constitute the highest risk in terms of contamination, especially in departments with confirmed or suspected COVID-19 patients.

China reported the number of infected healthcare workers as 3387, The Italian National Institute of Health as 17000, and the USA as 9200.[5-7] A review published in December 2020 stated that 3.9% (152,888) of COVID-19 patients in the world were HCWs.[8] However, there are still countries that have not yet reported the number of infected healthcare personnel, and studies investigating risky behavior within HCWs are very limited. In the nosocomial transmission of SARS-CoV-2, adherence of HCWs to infection prevention and control measures and appropriate use of personal protective equipment (PPE) are as significant as the virus characteristics.

The protection of HCWs is one of the most critical points in dealing with the pandemic. Therefore, determining the dynamics of nosocomial transmission within the group of healthcare workers is of great importance in preventing nosocomial outbreaks and protecting HCWs from infection.

This study aimed to investigate the incidence of nosocomial transmission and the factors affecting the transmission in healthcare professionals admitted to the Infection Control Committee (ICC) due to exposure to COVID-19 patients in our hospital.

Material and Method:

Study design

HCWs admitted due to exposure to a definite COVID-19 patient between 20 March 2020 and 30 June 2020 were included in the study. This prospective observational cohort study was approved by the Turkish Ministry of Health and Ankara City Hospital Ethical Committee (E1-20-559).Written consent was not obtained from the participants since only epidemiological surveillance data was collected.

Infection control

At the beginning of the pandemic, all HCWs working in our hospital were trained by Infection Control Committee (ICC) doctors and nurses on COVID-19 transmission, prevention from the infection, appropriate PPE use, infection control measures, and hand hygiene. During the pandemic, all necessary PPEs were provided at an adequate level. It was planned for all HCWs to work with surgical masks during the pandemic period and access appropriate PPEs when necessary. Moreover, the course of action to be followed after a risky exposure was determined, and follow-up forms were created to monitor HCWs with occupational exposure.

Determination of contact type and risk level

HCW risk assessment and follow-up were performed by ICC with active surveillance. The demographic characteristics (age, gender, and chronic disease) of the exposed-HCWs, their professions (doctor, nurse, auxiliary health personnel, other auxiliary health personnel, support personnel, and administrative staff), and whether they were directly involved in patient care were recorded. Furthermore, along with index case detection, the following data related to the exposure were recorded: index case's mask usage during contact, dates of exposure, and PPE usage of the HCW during exposure.

Types of exposures listed in Table 1 were considered risky for SARS-CoV-2 transmission, and HCWs that had undergone such exposure were followed up prospectively. Other types of exposures were categorized as "non-risky" and were excluded from follow-up.[9 10]

Table 1. Risky exposed

A. Close contact
1. Being at a distance of less than 1 meter with COVID-19 patients for 15 minutes or more in the last 5 days
2. Meeting face-to-face with a COVID-19 patient at a distance of less than 1 meter for 15 minutes or longer in the last 5 days
3. Direct contact with a COVID-19 patient (e.g., handshake) or direct contact with the person's secretions (e.g., coughing or touching used tissue) in the last 5 days
B. Intense contact
1. Performing AGP to a COVID-19 patient or assisting in this process

AGP: Aerosol-generating procedure

The World Health Organization (WHO) guideline was used to determine whether the appropriate PPE was worn.[10] The risk level was determined according to PPE usage of the exposed HCW (Table 2). Except for AGP, the use of a surgical mask was considered sufficient. AGP was defined as respiratory tract sampling, intubation, aspiration of respiratory tract secretions, non-invasive mechanical ventilation, high flow oxygen therapy, cardiopulmonary resuscitation, use of nebulizer, endoscopic procedures, bronchoscopy, video-laryngoscopy, dental practices, examinations of the mouth, throat, and nose, ophthalmological examinations, and central catheter insertion.[10 11]

Table 2. Risk level determination after a risky exposure

Index case mask-wearing status	PPE using status of HCW	Risk level
No	Did not use a surgical mask or N95	High
	Used a surgical mask in case of N95 indication	Moderate
	Did not use eye protection	Low
	Did not use gloves and aprons	Low
	Used all PPE properly	No
Yes	Did not use a medical mask or N95 or Used a surgical mask in case of N95 indication	Moderate
	Did not use eye protection	Low
	Did not use gloves and aprons	Low
	Used all PPE properly	No

HCW: Healthcare worker, PPE: Personal protective equipment

Follow-up of Exposed HCWs

HCWs included in the study were followed for symptoms for 14 days after the last risky exposure. Symptoms such as fever (≥38 ^{0}C), shortness of breath, cough, sore throat, nasal congestion, or newly-onset loss of smell were considered suspicious symptoms for COVID-19 disease.[11] Nasopharyngeal swab samples were taken for SARS-CoV-2 reverse-transcriptase polymerase chain reaction (RT-PCR) to diagnose COVID-19 from cases with COVID-19 related symptoms during their follow-up. SARS-CoV-2 RT-PCR was performed on the 7th day after the risky exposure among asymptomatic exposed-HCWs with moderate or high-risk exposure (Table 3). A 7-day work restriction was applied to HCWs who had high-risk exposure after intense contact. Those with negative SARS CoV-2 RT-PCR test on the 7th day returned to work, and their 14 days follow-ups were discontinued. Negative SARS-CoV-2 RT-PCR tests of HCWs with persistent symptoms were repeated 48 hours after the initial test.

Table 3. Exposed-HCW follow-up

Risky exposure type and risk level	Management
Intense contact - high risk	1. Symptom follow-up is performed by isolating at home for 7 days. 2. If the symptom develops, the SARS-CoV-2 RT-PCR test is performed on the symptom day, if no symptoms develop, on the 7th day after the last risky exposure. 3. Those with negative test results start to work and are followed up in terms of symptoms for 14 days.
Intense contact - moderate risk **Close contact- high / moderate risk**	1. Works with a mask on. Active symptom follow-up is performed. 2. If the symptom develops, the SARS-CoV-2 RT-PCR test is performed on the symptom day, if no

	symptoms develop, on the 7th day after the last risky exposure.
Close / intense contact - low risk	1. Works with a mask on. 2. If the symptom develops, the SARS-CoV-2 RT-PCR test is performed on the symptom day.

HCW: Healthcare worker, PPE: Personal protective equipment

Definitions

A healthcare worker was defined as all personnel working in healthcare facilities, regardless of their involvement in direct patient care. However, the personnel were grouped according to whether they were directly involved in patient care or not. Occupational groups were recorded as doctors, nurses, auxiliary health personnel, other auxiliary health personnel, support personnel, and administrative staff. The technicians working in radiology, portable x-ray, laboratory, anesthesia, and physical therapy, biologists, and physiotherapists were defined as auxiliary HCWs. Other auxiliary health personnel consisted of staff working in the cafeteria, security, waste services, hospital drivers, and secretaries. The group defined as support personnel were those who helped nurses and doctors in the patient care, cleaning the patient room, and transferring the patient between units. Apart from this, personnel who did not have direct contact with the patient and took part in administrative tasks in a separate unit were classified as administrative staff. Index case describes a case with a positive SARS-CoV-2 RT-PCR result (source of COVID-19 exposure). The index cases were also classified as patients and HCWs.

Patient and public involvement

No patients were involved.

Analysis

HCW exposures identified as low-, moderate-, and high-risk were compared against demographic characteristics such as age, gender, comorbid diseases, occupation, involvement in direct patient care, the index case, exposure type (i.e., risk level). In our study, the SARS-CoV-2 RT-PCR test was not planned to be performed on low-risk asymptomatic HCWs. However, it was determined from the electronic database that some HCWs had SARS-CoV-2 RT-PCR test, and this information was also recorded. Afterward, follow-up and COVID-19 development characteristics were compared according to risk groups. The correlation between the positivity of SARS-CoV-2 RT-PCR and the risk level was compared between the tested health personnel and had negative and positive results. In addition, factors affecting SARS-CoV-2 RT-PCR positivity were investigated.

Statistical analysis

All statistical analyses were performed using SPSS for Windows 18 (SPSS Inc, Chicago, IL, USA). Kolmogorov-Smirnov test was used to assess the normality assumption. The continuous variables that did not have normal distribution were expressed as median (minimum-maximum) values. Categorical variables were summarized as counts (percentages). For non-normally-distributed continuous variables, differences between groups were tested using the Kruskal Wallis test. Pearson chi-square/Fisher Exact Test determined the relationship between categorical variables. Univariate logistic regression analysis was used to analyze the factors leading to SARS- CoV-2 PCR positivity. The variables considered in the analyses for SARS- CoV-2 PCR positivity were age, sex, profession, involvement in direct patient care, the index case, index case mask usage, HCWs PPE usage, and risk level. A two-sided p-value ≤ 0.05 was considered statistically significant. A multivariable logistic regression model was used to predict potential risk factors of SARS- CoV-2 PCR positivity. The variables with a significance level of $p \leq 0.20$ from the univariate analysis were identified as candidate variables for the multivariable model.

Results

During the study period, a total of 1268 HCWs were admitted with suspicion of risky exposure. After the initial evaluation, exposures that had not met the criteria for risky exposure for COVID-19 were excluded from the follow-up. A total of 822 HCW contacts were classified as risky and were followed up prospectively. Two hundred ninety-five of these exposures were low-risk, 284 were intermediate-risk, and 243 were high-risk. The median age was 31.9 years (20-62), and 27.1% of exposed HCWs were male. Risky exposure was detected most frequently in nurses (51.7%). Of the exposed HCWs, 89.5% were directly involved in patient care. The index cases were HCWs in 72.6% of risky exposures and COVID-19 patients in 27.4%. Concerning contact types, 95.5% were identified as close contact and 4.5% as intense contact. Demographic and clinical characteristics of exposed HCWs are shown in Table 4.

Table 4. Demographic and clinical characteristics of HCWs admitting after exposure

	HCW n=822 (%)
Median age (years) min-max	31.9 (20-62)
Gender (Male)	223 (27.1)
Profession	
Nurse	425 (51.7)
Doctor	180 (21.8)
Supportive personnel	91 (11)
Other auxiliary health personnel	66 (8.1)
Auxiliary health personnel	33 (4.1)
Administrative staff	27 (3.2)

Taking part in direct patient care	736 (89.5)
Underlying disease	111 (13.5)
Exposed-index case	
HCW	597 (72.6)
Patient	225 (27.4)
Risky exposed	
Close contact	785 (95.5)
Intense contact	37 (4.5)
Risk level	
Low risk	295 (35.9)
Moderate risk	284 (34.5)
High risk	243 (29.6)

All data are given as a number (percentage) unless specifically stated.
HCW: Healthcare workers
Underlying diseases (patients number): chronic respiratory disease (26), chronic cardiovascular disease (23), thyroid disease (17), chronic rheumatological disease (13), allergic diseases (9), diabetes mellitus (6), chronic neurological disease (5), other (12)

The comparison of the groups by their risk levels is summarized in Table 5. There was a statistically significant difference between age, comorbid diseases, occupation, direct involvement in patient care, the index case, and risky exposure type (*p <0.001, p= 0.011, p<0.001, p<0.001, p<0.001, p<0.001*, respectively). As a result of the dual comparison of the groups, the median age was higher in HCWs with high-risk exposure than in the low-risk and moderate-risk group, and the comorbidity rate was higher than in low-risk level (*p <0.001, p= 0.011*, respectively). As a result of the dual comparison of the groups, the median age was determined to be higher in HCWs with high-risk exposure than in the low-risk and moderate-risk group (*p<0.001*). The comorbidity rate was higher in HCWs with high-risk exposure than in the low-risk group (*p = 0.011*). High-risk exposure was lowest in nurses (21.9%) and highest in other assistant healthcare personnel (77.3%) (*p<0.001*). High-risk exposure was lower in those directly involved in patient care (76.5%, *p<0.001*). In the vast majority of high-risk exposures (220/253), the index case was an HCW.

Table 5. Comparison of exposed-HCWs by the risk level

	Low risk n=295	**Moderate risk n=284**	**High risk n=243**	***P*-value**
Age (years), median (min-max)	29[b] (20-62)	28[b] (20-56)	31[a] (21-62)	**<0.001**
Gender (Male)	80 (35.9)	73 (32.7)	70 (31.4)	0.72
Underlying disease*	31[a] (10.5)	34[a,b] (12)	46[b] (18.9)	**0.011**
Profession				**<0.001**
Nurse	171[a] (40.2)	161[a] (37.9)	93[b] (21.9)	
Doctor	76[a] (42.2)	61[a] (33.9)	43[a] (23.9)	
Supportive personnel	20 [a] (22)	38 [b] (41.8)	33 [b] (36.3)	
Other auxiliary health personnel	5[a] (7.6)	10[a] (15.2)	51[b] (77.3)	
Auxiliary health personnel	14 [a] (42.2)	7 [a] (21.2)	12 [a] (36.4)	

Administrative staff	9[a] (33.3)	7[a] (25.9)	11[a] (40.7)	
Taking part in direct patient care				**<0.001**
Yes	281[a] (38.2)	269[a] (36.5)	186[b] (25.3)	
No	14 (16.3%)	15 (17.4%)	57 (66.3%)	
Exposed-index case				**<0.001**
Patient	56[a] (19)	146[b] (51.4)	23[c] (9.5)	
HCW	239[a] (81)	138[b] (48.6)	220[c] (90.5)	
Risky exposed				**<0.001**
Intense contact	1 [a] (0.3)	29 [b] (10.2)	7[c] (2.9)	
Close contact	294[a] (99.7)	255[b] (89.8)	236 [c] (97.1)	

All data are given as a number (percentage) unless specifically stated.
HCW: Healthcare workers
[a], [b], [c]: There is a difference between the groups indicated by different indices.

Post-exposure follow-up features by risk levels are shown in Table 6. Symptoms developed during follow-up in a total of 311 (37.8%) HCWs. The most common symptoms were sore throat (24.2%) and cough (14.5%). A higher rate of complaints occurred in the moderate and high-risk group than in the low-risk exposed group (*p= 0.001*). During the study, the SARS-CoV-2 RT-PCR test was performed on 59.7% (176/295) of low-risk HCWs, 74.6% (212/284) of medium-risk HCWs, and 74.9% of high-risk HCWs (182/243). SARS-CoV-2 PCR positivity was detected in 28 exposed HCWs. The rate of SARS-CoV-2 RT-PCR positivity development after high-risk exposure was higher than both moderate- and low-risk exposure groups (7.1%, 3.3%, 4.5%, respectively), but the difference was not found to be statistically significant (*p = 0.205*). SARS-CoV-2 RT-PCR was tested in 58.9% (301) of 511 asymptomatic HCWs and 86.4% (269) of 311 symptomatic HCWs. SARS-CoV-2 RT-PCR positivity rates were 3.3% (10/301) and 6.7% (18/269) between asymptomatic and symptomatic HCW, respectively. No statistically significant difference was determined between SARS-CoV-2 RT-PCR positivity and risk levels in asymptomatic and symptomatic HCWs (Table 6).

Table 6. Post-contact follow-up results by the risk level

	Low risk n=295 (%)	Moderate risk n=284 (%)	High risk n=243 (%)	*P*-value
Presence of any symptom	87[a] (29.5)	120[b] (42.3)	104[b] (42.8)	**0.001**
Throat ache	51[a] (17.3)	79[b] (27.8)	69[b] (28.4)	**0.002**
Cough	33 (11.2)	41 (14.4)	45 (18.5)	0.055
Diarrhea	8[a] (2.7)	8[a] (2.8)	18[b] (7.4)	**0.009**
Fever	5[a] (1.7)	8[a] (2.8)	19[b] (7.8)	**0.001**
Shortness of breath	11 (3.7)	8 (2.8)	10 (4.1)	0.704

Inability to taste/smell	1 (0.3)	1 (0.4)	2 (0.8)	0.089
Duration to test after last risky exposure, days, median (min-max	5 (1-12)	6 (1-18)	5 (1-14)	0.065
SARS-CoV-2 RT-PCR positivity	8 (4.5)	7 (3.3)	13 (7.1)	0.205
In asymptomatic HCW	4 (3.7)	1 (0.9)	5 (6)	0.191
Number of tests in asymptomatic HCW	107	110	84	
In symptomatic HCW	4 (5.8)	6 (5.9)	8 (8.2)	0.056
Number of tests in symptomatic HCW	69	102	98	

All data are given as a number (percentage) unless specifically stated.
HCW: Healthcare workers, RT-PCR: reverse transcriptase-polymerase chain reaction
[a], [b], [c]: There is a difference between the groups indicated by different indices.

When exposed HCWs with and without SARS-CoV-2 RT-PCR positivity were compared; age, gender, index case type, index case mask usage, HCW's PPE usage, and contact type were not found as independent risk factors for the development of PCR positivity. The risk of developing COVID-19 was observed to be 5.65 times higher in those who were not directly involved in patient care (OR = 5.65, 95% CI = 2.437-13.11; $p<0.001$).

Discussion

Protection HCWs who are at high risk due to COVID-19 is vital in fighting the pandemic. In the face of a new disease, the anxiety and fear of HCWs have decreased with the elimination of uncertainty, the increase in knowledge about the means of transmission and prevention measures, and the acceleration of vaccination studies. However, during this period, many HCWs were infected with SARS-CoV-2, and a considerable number of them died. Knowledge on COVID-19 infection rates in HCWs and epidemiological dynamics of the infection is still insufficient. The knowledge, skills, and adaptation of healthcare professionals regarding infection control measures and PPE use vary widely among HCWs. The concerns that COVID-19 vaccines do not eliminate the infection development, the infections developing with mutant strains, and the decrease in vaccine protection against these mutant strains remind once again the importance of dealing with the characteristics of the infection development in HCWs in more detail. In this study, which was carried out in HCWs applied to ICC due to risky exposure with COVID-19 patients, we aimed to obtain more detailed epidemiological data regarding behaviors carrying risk for HCWs, to evaluate the exposure risks in detail and nosocomial SARS-CoV-2 transmission.

Considering that the increase in knowledge and experience with age and comorbid chronic diseases are risk factors for the poor prognosis of COVID-19, HCWs of older ages and with chronic diseases are expected to be more prudent on measures to prevent infection transmission and appropriate PPE use. However, in our study, the ages of those who have undergone high-risk exposures were higher than the HCWs with low- and moderate-risk exposure ($p <0.001$) and had a higher rate of comorbid chronic diseases ($p = 0.011$).

Similarly, in the study of Maltezou et al., chronic diseases were more common in high-risk exposures when compared to low-risk exposures (2.5% - 1.5%, *p=0.001*).[12]

A vast majority of HCWs admitted to ICC with a risky exposure were directly involved in patient care, and most of them were nurses and doctors. This situation can be explained by the fact that nurses are more involved in patient care than other occupational groups and the number of nurses working in the health institution is higher than other personnel. However, in terms of risk levels, it was observed that the rate of high-risk exposures was less in doctors (23.9%) and nurses (21.9%). In the study of Maltezou et al., unlike our results, it was reported that high-risk exposure was more common in nurses and doctors (43.4% vs. 36.1, *p <0.001*). Similar to our study, it was found that high-risk exposure was higher among administrative staff in the same study.[12] In our country, after the first case was reported in March 2020, it has become obligatory for all hospital personnel to work with a mask. Adherence to this measure reduces many exposures to moderate and low-risk categories. However, the occurrence of high-risk exposure among administrative staff, auxiliary HCWs, and other auxiliary HCWs suggests that they suffer from the misconception that they are under less risk in terms of infection development due to not directly taking part in patient care and that often do not adhere to use of masks. A possible reason for this is lower awareness of the fact that infections can be transmitted from colleagues. It seems that the appropriate use of PPE is lower in these groups, and proper training and information sharing should be made individually and more emphatically. Although it can be thought that a high percentage of moderate and high-risk exposure in the support personnel is due to their tasks directly involving patient care, the fact that the index cases are mostly HCWs rather than the patients does not support this idea.

One of the striking findings of the study is the index cases. In 72.6% of contacts, the index cases were HCWs. Similar to our results, previous studies have shown that HCWs had mostly risky exposure with their colleagues, and most of their exposures developed during eating and drinking activities.[12 13] The fact that lowest rates of high-risk exposure were observed in contacts with patients and among HCWs directly involved in patient care indicate that HCW's are better in adhering to PPE use in contact with COVID-19 patients. However, they do not pay enough attention to PPE use and infection control measures in their contacts with colleagues.

The SARS-CoV-2 RT-PCR status became positive in the median 5 days after risky exposure, consistent with the disease incubation period. In the study of Maltezou et al., the infection had developed at the end of the first week after risky exposure, and the authors stated that a 7-day work restriction is sufficient.[12] The WHO and the Centers for Disease Control and Prevention (CDC) recommend a 14-day work restriction regardless of the risk level.[1 9] In our study, in line with COVID-19 guidelines of the Ministry of Health, only

seven days of work restriction was applied after intense high-risk exposure [11], and only seven HCWs with high-risk and intense exposure underwent a work restriction. Other personnel continued to work with masks, and a super-spreader was not detected. When the need for HCWs has increased, countries must form policies regarding the protection of HCWs based on their internal dynamics.

Although at least one symptom developed in 37.8% of the risky occupational exposures during the study, SARS-CoV-2 PCR positivity was detected in much less of the cases. In the study by Maltezou et al., at least one symptom was detected in 22.2% of 3398 HCWs exposed to SARS-CoV-2. Symptom development was lower in HCWs with low-risk exposure than in the other two groups with moderate and high risk. Unsurprisingly, the positivity of SARS-CoV-2 after high-risk exposure was higher, but there was no statistically significant difference between the groups. The study of Maltezou et al. indicated that the development of COVID-19 after high-risk exposure was six times higher than moderate and low-risk exposures (5% in high risk, and 1% in moderate and low risk, $p < 0.001$).[12] Infection development is expected to be higher in high-risk exposure. The lack of difference between the groups in terms of infection development suggests the transmission may occur through direct exposure due to not paying enough attention to hand hygiene despite the use of appropriate equipment. Moreover, the fact that all HCWs participating in the study were not tested may have affected these rates.

Among the factors evaluated for the development of SARS-CoV-2 positivity, only providing direct care to COVID-19 patients was statistically significant, and contrary to expectations, infection development was found 5.65 times higher in HCWs who did not directly provide care for COVID-19 patients. This finding suggests that the staff caring for a COVID-19 patient adhere more strictly to PPE and other infection control measures, while the staff who do not provide direct care do not comply with the measures adequately with a false sense of safety. In addition, 28 HCWs with positive SARS-CoV-2 RT-PCR tests were included in the comparison. The low number of participants should be considered when interpreting our results. In the study of Hunter et al., symptomatic HCWs were divided into three groups: HCWs involved in direct patient care (group 1), HCWs not directly involved in patient care that work in high-risk areas such as laboratories (group 2), and non-clinical workers (group 3). SARS-CoV-2 positivity was detected at a rate of 15% (128 of 834) in group 1, 16% (14 of 86) in group 2, and 18% (20 of 109) in group 3. Furthermore, taking part in direct patient care was not found to be risky for SARS-CoV-2 RT-PCR positivity (group 1 *vs.* group 2: odds ratio 1·08, 95% CI 0·59–1·97; group 1 *vs.* group 3: 1·24, 0·74–2·09; $p = 0.71$).[14] The researchers have drawn attention to community transmission since the study was conducted before the restrictions in society. In studies from Spain and England, no difference was found between the administrative staff and the personnel working in direct

patient care in terms of infection development, and it was stated that in-house or community transmission was more effective in HCW infections.[14 15] In a study from France, the infection rate was significantly higher in HCWs who did not directly provide care for COVID-19 patients (odds ratio 2.3, *p =0.005*).[16] Similarly, in a study conducted in Germany, the fact that only 3% of 86 HCWs with a positive SARS-CoV-2 RT-PCR test had contact with COVID-19 patients was accepted as a supporting finding for community transmission.[17] On the contrary, in a study conducted in Wuhan, 72 exposed HCWs were examined, and it was found that HCWs working in areas with COVID-19 patients were 2.13 times more under risk.[18] However, in this study, the number of personnel exposed to SARS-CoV-2 is very low. Besides, since it is the emerging point of the pandemic, the dynamics of HCWs' adherence to the infection control measures in contact with patients and each other may differ compared to other studies.

In addition to the use of PPE, the adherence of HCWs to other infection control measures such as hand hygiene and unknown/possible community transmission may have contributed to the difference between the groups. Studies related to HCW risk factors indicate that practicing suboptimal hand hygiene before and after patient exposure, long working hours, inappropriate PPE use and PPE insufficiency, inadequate training on infection control measures, and the unit where an HCW is employed were found to be risk factors for COVID-19 transmission in HCWs. Previous studies report failure to evaluate the effect of remembering bias and other environmental factors as limitations.[13 19-28] This study was planned prospectively, and negativities such as possible false recall and lack of data, which are among the weaknesses of retrospective studies, were minimized. Also, more categorized information has been obtained by using a standardized risk classification in the follow-up and management of exposed HCWs. However, there are several limitations: Although most exposed HCWs have been screened with PCR, it is possible that positivity was not detected (underestimation) in some asymptomatic or mildly symptomatic individuals since not all exposed HCWs have been screened with SARS-CoV-2 PCR test. Weekly screening of all health personnel is also included in the recommendations. It would be more beneficial to perform these to increase our study's strength. However, it does not seem possible in terms of both cost and laboratory capacity for our hospital, where 15,000 SP works and shouldering the pandemic burden of the region. Screenings were performed according to risk level and symptom presence within the scope of national guideline recommendations. Moreover, although exposed-HCWs were followed up prospectively, the risk groups in the study were determined based on HCW's own statements. Another limitation is that compliance to proper PPE usage procedures and adherence to hand hygiene have not been investigated.

Conclusions

In the present study, many HCWs were actively followed according to a prospective, post-exposure standardized risk classification. HCWs have a high risk of being infected while providing care for COVID-19 patients. However, prevention of the infections that will develop during the contact of HCWs with other hospital employees seems to be a priority. Increasing infection rates among healthcare workers may lead to health system collapse and worsening of the pandemic. The present study provides beneficial information by utilizing standardized risk classification of nosocomial transmissions in HCWs. It also provides particularly useful information on post-exposure follow-up and required working restrictions for HCWs. The study results revealed that adherence to infection control rules is of vital importance in terms of raising awareness about adherence to PPE usage rules and preventing transmission between personnel. In such a period where the need for HCWs has increased, it will contribute to reorganizing regulatory actions by revealing situations carrying the risk of infection.

Data availability statement

Data are available upon reasonable request. All data relevant to the study are included in the article or uploaded as supplementary information. Should further details or materials be required, please contact the corresponding author.

Ethics statement

This prospective observational cohort study was approved by the Turkish Ministry of Health and Ankara City Hospital Ethical Committee (E1-20-559).

Contributorship Statement

Conception and design of study: Ayse Kaya Kalem, Rahmet Güner

acquisition of data: Ayse Kaya Kalem, Imran Hasanoglu, Fatma Eser, Muge Ayhan, Belgin Erdogan

analysis and/or interpretation of data: Ayse Kaya Kalem, Bircan Kayaaslan, İmran Hasanoğlu

Drafting the manuscript: Ayse Kaya Kalem, Bircan Kayaaslan

All authors discussed the results and contributed to the final manuscript.

Competing Interest

There are no competing interests for any author.

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Data sharing

The identified data associated with this study is stored by Ankara City Hospital İnfectious Diseases and Clinical Microbiology department. And all data relevant to the study are included in the article.

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STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*5*
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	3
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5-6
		(*b*) Describe any methods used to examine subgroups and interactions	5-6
		(*c*) Explain how missing data were addressed	5-6
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	5-6
		(*e*) Describe any sensitivity analyses	5-6
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	6-7
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6-7

		(*b*) Report category boundaries when continuous variables were categorized	6
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	7
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	7-9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10
Generalisability	21	Discuss the generalisability (external validity) of the study results	10
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.