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ORIGINAL ARTICLE

Risk factors and frequency of COVID-19 among healthcare workers at a tertiary care centre in India: a case–control study

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Background: There is a paucity of data on risk factors for infection among healthcare workers (HCWs) from India. Our objective was to evaluate the risk factors and frequency of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection among HCWs.

Methods: We conducted this retrospective case–control study of 3100 HCWs between May and July 2020. HCWs positive for SARS-CoV-2 infection were the cases (n=506) and those negative for SARS-CoV-2 were the controls (n=253). Univariate analysis was followed by multivariate analysis of key demographic, clinical and infection control variables.

Results: SARS-CoV-2 infection was found in 16.32% of HCWs. Nearly 45% of infected HCWs were asymptomatic. The proportions of sanitation workers (24% vs 8%; p<0.0001) and technicians (10% vs 4%; p=0.0002) were higher and that of doctors was lower among cases as compared with controls (23% vs 43%; p<0.0001). On univariate analysis, the type of HCW, smoking, lack of training, inadequate personal protective equipment (PPE) use and taking no or fewer doses of hydroxychloroquine (HCQ) were found to be significant. On multivariate analysis, the type of HCW (risk ratio [RR] 1.67 [95% confidence interval {CI} 1.34 to 2.08], p<0.0001), inappropriate PPE use (RR 0.63 [95% CI 0.44 to 0.89], p=0.01) and taking fewer doses of HCQ (RR 0.92 [95% CI 0.86 to 0.99], p=0.03) were significant.

Conclusions: The frequency of SARS-CoV-2 infection was 16% among HCWs. Being a sanitation worker, inappropriate PPE use and lack of HCQ prophylaxis predisposed HCWs to SARS-CoV-2 infection.

Keywords: COVID-19, HCQ, **h**ealthcare worker, hydroxychloroquine, personal protective equipment, PPE, SARS-CoV-2 infection

Introduction

Human infections caused by a novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) first appeared in Wuhan, China, in December 2019.[1] Through 22 November 2020, there have been >57 million confirmed cases of coronavirus disease 2019 (COVID-19), including >1 million deaths, reported to the World Health Organization (WHO).[2] The first case in India was reported on 30 January 2020, and through 22 November 2020, a total of 8 562 641 cases had been reported in India, including 133 738 deaths.[3] Healthcare workers (HCWs) have been the backbone of the fight against this pandemic. They are also at higher risk of contracting this highly contagious virus. The proportion of HCWs infected with SARS-CoV-2 has ranged from 0.9% to 19% in various studies.[4–7] Currently the total number of SARS-CoV-2-infected HCWs worldwide is unknown, while in India it is approximately 25 000, although the true number is unknown but is steadily increasing.[8]

Optimal hand hygiene is of foremost importance in the prevention of COVID-19 among HCWs. The second aspect of protection is the quality and quantity of personal protective equipment (PPE) required in the various scenarios of patient care. Hence the Indian Ministry of Health and Family Welfare released guidelines for the rational use of PPE while caring for COVID-19 patients.[9]

In India, multiple clusters of COVID-19 infection among HCWs have been reported since the beginning of the pandemic.[8] There is a paucity of data on the risk factors for infection among HCWs

in India, with a few studies involving telephone surveys.[10] In this context, a case–control investigation was undertaken to compare the risks of and protective factors against SARS-CoV-2 infection among HCWs in India.

The primary objective was to evaluate the risk factors for COVID-19 infection among HCWs. The secondary objective was to evaluate the clinical course and outcome in HCWs with COVID-19 infection.

Methods

Design and setting

We conducted this retrospective case–control study of prospectively collected data at our tertiary care centre, medical college and hospital in North India between May and July 2020.

Participants

Cases were HCWs who tested positive for SARS-CoV-2 infection (COVID-19) (n=506) and controls were HCWs who tested negative for SARS-CoV-2 infection (COVID-19) (n=253). We excluded those who were admitted but transferred to another hospital. The Institutional Ethics Committee approved the study.

We used the following definitions for the purpose of the study:[11–13]

- COVID-19 patient: individuals with laboratory-confirmed SARS-CoV2 infection (by reverse transcription polymerase chain reaction [RT-PCR].
- Mild disease: patients with uncomplicated upper respiratory tract infection who may have mild symptoms such as fever, cough, sore throat, nasal congestion, malaise or headache without evidence of breathlessness or hypoxia (normal saturation).
- Moderate disease: pneumonia with no signs of severe disease with the presence of clinical features of dyspnoea and/or hypoxia, fever, cough, including a blood oxygen saturation level (SpO_2) <94% (range 90–94%) on room air and a respiratory rate ≥24/min.
- Severe disease: clinical signs of pneumonia plus one of the following: respiratory rate >30 breaths/min, severe respiratory distress or SpO_2 <90% on room air.
- Acute respiratory distress syndrome (ARDS): mild ARDS: partial pressure of oxygen (PaO_2)/fraction of inspired oxygen (FiO_2) >200–≤300 mmHg (with positive end expiratory pressure [PEEP] or continuous positive airway pressure [CPAP] ≥5 cm of H_2O); moderate ARDS: PaO_2/FiO_2 >100–≤200 mmHg with PEEP ≥5 cm of H_2O); severe ARDS: PaO_2/FiO_2 ≤100 mmHg with PEEP ≥5 cm of H_2O). When PaO_2 is not available, SpO_2/FiO_2 ≤315 mmHg suggests ARDS (including in non-ventilated patients).
- Sepsis: acute life-threatening organ dysfunction caused by a dysregulated host response to suspected or proven infection. Signs of organ dysfunction include altered mental status, difficult or fast breathing, low oxygen saturation, reduced urine output, fast heart rate, weak pulse, cold extremities, low blood pressure, skin mottling or laboratory evidence of coagulopathy, thrombocytopenia, acidosis, high lactate or hyperbilirubinaemia.
- Septic shock: persisting hypotension despite volume resuscitation, requiring vasopressors to maintain mean arterial pressure (MAP) ≥65 mmHg and serum lactate level >2 mmol/L.
- High-risk exposure:
  - HCW or other person providing care to a COVID-19 case or lab worker handling respiratory specimens from COVID-19 cases without recommended PPE or with possible breach of PPE.
  - Performed aerosol-generating procedures without appropriate PPE.
  - HCWs without mask, face shield or goggles having face-to-face contact with COVID-19 cases within 1 m for >15 min or having accidental exposure to body fluids.
- Low-risk exposure: contacts who do not meet the above criteria of high-risk exposure.

Methods

HCWs tested for SARS-CoV-2 infection at the hospital were eligible for inclusion. We screened the pre-structured data extraction form of all HCWs to identify subjects fulfilling the inclusion criteria. We retrieved information including demographic features such as age, gender, duration of illness, signs and symptoms at admission, laboratory parameters, treatment received and outcome and the risk factors for infection among HCWs, including the area of duty and category of HCW (doctors, nurses, technicians, sanitation workers, security personnel and others). We also recorded information on underlying comorbidities and lifestyle habits such as smoking and alcohol consumption. We also determined if they received training in PPE and hand hygiene, what kind of procedure they had performed during the exposure, the use of appropriate PPE during exposure, the risk of exposure (high or low), whether they received hydroxychloroquine (HCQ), and if they did, how many doses they had received. All of these variables were collected in a pre-structured data extraction form.

Statistical analysis

Data were entered into Excel 2013 (Microsoft, Redmond, WA, USA) and analysed using Stata 11 (StataCorp, College Station, TX, USA). Missing values of clinical and laboratory variables were assumed to be normal for the purpose of statistical analysis. Continuous variables are presented as mean (standard deviation [SD]) or median (interquartile range [IQR]) as appropriate. Categorical variables are presented as absolute numbers (%). Continuous variables were compared using either the independent Student's t-test or Wilcoxon rank sum test (based on the distribution of the data). Categorical data were compared using the χ^2 test or Fischer's exact test as appropriate. For assessing the factors associated with SARS-CoV-2 infection, univariate analysis followed by multivariate analysis of clinically important variables such as age in years, HCW type, comorbidities, smoker, alcohol, PPE training, PPE use, procedure performed during exposure and HCQ doses was performed.

Table 1. Baseline characteristics and univariate analysis of risk factors between the cases and controls

Variables	Cases (n=506)	Controls (n=253)	RR (95% CI), p-value
Age (years), mean (SD)	32 (9)	30 (7)	0.17
Gender (male), n (%)	333 (66)	154 (61)	1.08 (0.96 to 1.21), 0.18
Area of duty, n (%)			
COVID	217 (43)	96 (38)	1.13 (0.94 to 1.36), 0.19
Non-COVID	289 (57)	157 (62)	
HCW category, n (%)			
Doctor	118 (23)	110 (43)	0.54 (0.43 to 0.66), <0.0001
Nurse	166 (33)	102 (40)	0.81 (0.67 to 0.99), 0.02
Technician	51 (10)	11 (4)	2.32 (1.23 to 4.37), 0.0002
Sanitation worker	123 (24)	19 (8)	3.24 (2.05 to 5.12), <0.0001
Security	44 (9)	11 (4)	2 (1.05 to 3.80), 0.01
Other	4 (1)	0 (0)	0.09
Comorbidities, n (%)	53 (11)	16 (6)	1.16 (0.97 to 2.83), 0.061
DM	7 (1)	3 (1)	–
HTN	23 (5)	11 (4.3)	–
DM and HTN	12 (2)	0 (0)	–
Hypothyroidism	01 (0.2)	2 (0.8)	–
CAD	01 (0.2)	0 (0)	–
DM, HTN and hypothyroidism	02 (0.4)	0 (0)	–
DM and hypothyroidism	03 (0.6)	0 (0)	–
HTN and hypothyroidism	01 (0.2)	0 (0)	–
HTN and CAD	03 (0.6)	0 (0)	–
Lifestyle, n (%)			
Smoker	81 (16)	20 (8)	2.02 (1.27 to 3.23), 0.002
Alcoholic	155 (31)	66 (26)	1.17 (0.92 to 1.5), 0.19
PPE training, n (%)	327 (65)	217 (86)	0.75 (0.69 to 0.82), <0.0001
Hand hygiene training, n (%)	496 (98)	253 (100)	0.98 (0.97 to 0.99), 0.02
Procedure performed during exposure, n (%)	80 (16)	47 (19)	0.85 (0.61 to 1.18), 0.33
Appropriate PPE during exposure, n (%)	171 (34)	131 (52)	0.65 (0.55 to 0.77), <0.0001
Risk of exposure, n (%)			
High	311 (61)	43 (17)	3.61 (2.73 to 4.79), <0.0001
HCQ prophylaxis, n (%)	155 (31)	105 (42)	0.74 (0.61 to 0.90), 0.003
HCQ doses taken, median (IQR)	0 (0–3)	0 (0–4)	0.0009
Symptomatic, n (%)	285 (56)	–	–

DM: diabetes mellitus; HTN: hypertension; CAD: coronary artery disease.

Results

Baseline characteristics

A total of 3100 HCWs were screened during the study period and 506 were enrolled as cases and 253 were enrolled as controls. The positivity for SARS-CoV-2 infection was found to be 16.32%. The baseline characteristics of the enrolled subjects are described in Table 1. The mean age was 32 y (SD 9) and 30 y (SD 7) for cases and controls, respectively, and >60% of both cases and controls were males.

Comparison of risk factors between cases and controls

A total of 43% (n=217) of cases and 38% (n=96) of controls worked in COVID-19 areas. The proportion of sanitation workers (24% vs 8%; p<0.0001) and technicians (10% vs 4%; p=0.0002) was higher in the cases compared with controls, while the proportion of doctors was lower among cases compared with controls (23% vs 43%; p<0.0001).

Comorbidities were present in 11% (n=53) of cases and 6% (n=16) of controls. More cases were smokers as compared with controls (16% vs 8%; p=0.002). Fewer cases had received training in the use of PPE as compared with controls (65% vs 86%; RR 0.75 [95% CI 0.69 to 0.82]; p<0.0001). A total of 98% of cases and 100% of controls had received training in hand hygiene (95% CI 0.97 to 0.99; p=0.02). Only 34% of cases were using appropriate PPE during contact with patients as compared with 52% of controls (0.65 [95% CI 0.55 to 0.77]; p<0.0001). The risk of exposure was high in 61% of the cases as compared with 17% of the controls (3.61 [95% CI 2.73 to 4.79]; p<0.0001).

Table 2. Clinical course and treatment received in admitted cases

Variables	Cases (n=506)	Controls (n=253)	p-Value
Hospital admission, n (%)	210 (42)	–	–
Severity of disease, n (%)			
Mild	491 (97)	–	–
Moderate	15 (3)	–	–
Severe	0 (0)	–	–
Duration of hospital stay (days), median (IQR)	0 (0–14)	–	–
Oxygen requirement, n (%)	11 (2)	–	–
Ventilator requirement, n (%)	0 (0)	–	–
Outcome as discharge, n (%)	506 (100)	–	–

Table 3. Multivariate analysis of factors associated with COVID-19 infection among HCWs

Variables	Cases	Controls	Adjusted RR (95% CI), p-value
Baseline			
Age (years), mean (SD)	32 (9)	30 (7)	1.01 (0.98 to 1.03), 0.64
HCW type, n (%)			
Doctor	118 (23)	110 (43)	
Nurse	166 (33)	102 (40)	
Technician	51 (10)	11 (4)	1.67 (1.34 to 2.08), <0.0001
Sanitation worker	123 (24)	19 (8)	
Security	44 (9)	11 (4)	
Other	4 (1)	0 (0)	
Comorbidity (yes), n (%)	53 (11)	16 (6)	1.19 (0.52 to 2.72), 0.69
Smoker, n (%)	81 (16)	20 (8)	1.09 (0.58 to 2.07), 0.77
Alcohol, n (%)	155 (31)	66 (26)	1.30 (0.86 to 1.95), 0.20
PPE training, n (%)	327 (65)	217 (86)	1.10 (0.60 to 2.04), 0.74
PPE use, n (%)	171 (34)	131 (52)	0.63 (0.44 to 0.89), 0.01
Procedure performed during exposure, n (%)	80 (16)	47 (19)	1.95 (1.25 to 3.04), 0.003
HCQ doses taken, median (IQR)	0 (0–3)	0 (0–4)	0.92 (0.86 to 0.99), 0.034

Fewer cases took HCQ prophylaxis compared with controls (31% vs 42%; 0.74 [95% CI 0.61 to 0.90]; p=0.003; number needed to treat=9). The difference in the number of doses of HCQ taken by the cases and controls was statistically significant (p=0.0009). There was no difference between the groups with regard to the presence of comorbidity, consumption of alcohol or performing a procedure during exposure (Table 1).

Treatment and clinical course

A total of 44% (n=221) of cases were asymptomatic and 42% (n=210) required hospitalisation. The majority (97%) had only mild disease and 15 cases (3%) had moderate disease, with 11 of these cases requiring oxygen. The median duration of hospital stay was 0 d (IQR 0–14). All were discharged (Table 2).

Multivariate analysis of factors associated with COVID-19 infection among HCWs

On multivariate analysis of factors associated with COVID-19 infection, there was a significant association between the type of HCW and COVID-19 infection (adjusted odds ratio [aOR] 1.67 [95% CI 1.34 to 2.08]; p<0.0001), use of PPE (aOR 0.63 [95% CI 0.44 to 0.89]; p=0.01), performing a procedure during exposure (aOR 1.95 [95% CI 1.25 to 3.04]; p=0.003) and the number of doses of HCQ (aOR 0.92 [95% CI 0.86 to 0.99); p=0.034) **(**Table 3).

Discussion

HCWs are at continued risk of exposure to SARS-CoV-2, with significant numbers being reported infected as well as those succumbing to the infection. Our observations reinforce the vulnerability of HCWs in acquiring the infection in the process of patient

care. We found that 16% of the HCWs screened were infected with the virus and 44% of these were asymptomatic and had undergone screening because of high-risk exposure. Our findings are similar to those reported in a recent systematic review and meta-analysis where, among RT-PCR-positive HCWs, 40% (95% CI 17 to 65) were asymptomatic.[14]

We also observed the following risk factors predisposed HCWs to infection. We observed that nurses and sanitation workers have the highest frequency of positive tests (33% and 24%, respectively) as compared with doctors in our cohort (RR 0.54 for doctors and 3.24 for sanitation workers). Our observations are in contrast to those of an Italian cohort of 1573 HCWs in which physicians had the highest frequency of positive tests (61/582 [10.5%]), whereas clerical workers and technicians had the lowest frequency (5/137 [3.6%]).[15] The probable reasons why this group had a higher incidence may be related to longer exposure to patients, differences in following infection control measures, differences in training and exposure to higher viral loads (e.g. sanitation workers are exposed to linens, secretions and aerosols in greater amounts than physicians or nurses). However, various other studies have found no consistent difference in the risk between physicians and other HCW categories.

We found that HCWs working in non-COVID-19 areas had higher rates of infection as compared with those working in designated COVID-19 areas (57% vs 43%). Our findings are similar to the results of a survey conducted in China of HCWs with respiratory symptoms. Individuals working in a high-risk department with interventional medical or surgical procedures that generate respiratory aerosols, such as in the pulmonary medicine department, infectious diseases department, intensive care unit or surgical department, had an increased risk of contracting the infection.[16]

Use of appropriate PPE has been shown to decrease the risk of infection among HCWs. In the survey described above,[14] the RRs of incomplete hand-washing, suboptimal hand hygiene before and after contact with patients and improper PPE use were 2.64 (95% CI 1.04 to 6.71; $p<0.05$), 3.10 (95% CI 1.43 to 6.73; $p<0.01$), 2.43 (95% CI 1.34 to 4.39; $p<0.01$) and 2.82 (95% CI 1.11 to 7.18; $p<0.05$), respectively.[16] Our findings are similar to this study and we observed reduced risk of infection with the use of appropriate PPE and hand hygiene (RR 0.65 and 0.98, respectively). In another survey of 105 HCWs who had tested positive, the common causes identified were throat swab collection, physical examination and improper use of PPE.[17] Appropriate use of PPE has been shown to reduce the rate of infections. In a systematic review it was inferred that the use of face masks could result in a significant reduction in risk of infection (n=2647; aOR 0.15 [95% CI 0.07 to 0.34], difference −14.3% [95% CI −15.9 to −10.7]). The association was stronger with N95 or similar respirators compared with disposable surgical masks or similar masks (e.g. reusable 12- to 16-layer cotton masks). Eye protection was also associated with less infection (n=3713; aOR 0.22 [95% CI 0.12 to 0.39], difference −10.6% [95% CI −12.5 to −7.7]).[18] Liu et al.[19] observed that none of the 420 doctors and nurses relocated to frontline work from January to April 2020 at Wuhan hospitals contracted COVID-19. These studies and the present study highlight the role that PPE has played in protecting HCWs during this pandemic.

In a prospective study conducted in Paris to assess the source of infection, 1344 HCWs were tested who had respiratory symptoms, of which 373 (28%) were positive. The major reasons were contact without PPE with an index case, taking off masks during breaks in the presence of colleagues, using public transportation and not wearing a mask outside homes. It was also apparent that implementation of control measures such as universal masking and PPE and physical distancing between workers led to a reduction of infection among HCWs, even in COVID-19 areas.[20]

Along with implementation of infection control measures, efforts are also being made towards identification of possible drugs that can be used for treatment as well as prophylaxis for this disease. One of the extensively researched drugs from the onset of this pandemic has been HCQ. The role of HCQ has been debated and continues to be studied in various trials. We found a lower risk of SARS-CoV-2 infection among HCWs who received pre-exposure HCQ (RR 0.74 [95% CI 0.61 to 0.90]; p=0.003). Similar findings were reported in an Indian cohort, where consumption of four or more maintenance doses of HCQ was associated with a significant reduction in the odds of being infected (aOR 0.44 [95% CI 0.22 to 0.88]).[9] This is in contrast to a randomized clinical trial conducted in an American cohort that did not find a reduction in SARS-CoV-2 transmission with prophylactic administration of HCQ. However, given the small sample size in the study, the possibility of an undetected modest potential prophylactic effect of HCQ could not be excluded.[21]

Our findings are in concurrence with existing data that suggest almost one-fifth of the confirmed cases of COVID-19 are HCWs. Our study reinforces existing literature on the factors associated with SARS-CoV-2 infections among HCWs when compared with non-infected HCWs. The study also highlights the importance of hand hygiene training, PPE training and the use of appropriate PPE during procedures in minimizing the risk of SARS-CoV-2 infection.

The strengths of this study include the prospective nature of data collection, even though analysed retrospectively. We also collected information from HCWs irrespective of their symptoms, which provided us with an opportunity to assess risk factors with minimal recall bias. We also evaluated the factors associated with the risk of COVID-19 infection among HCWs and added important information to the existing literature.

There are several limitations as well. We did not have details of the procedures during exposure. We could not collect data on the consistency of HCQ dosing. Our findings are also limited by the single-centre nature of the study.

In conclusion, HCWs face a significant risk from COVID-19. The use of appropriate PPE, hand hygiene, PPE training, low-risk exposure and HCQ prophylaxis are associated with a reduced risk of infection. A significant proportion of infected HCWs remain asymptomatic. The importance of hand hygiene, appropriate use of PPE and probably HCQ prophylaxis need to be highlighted among HCWs in order to reduce the frequency of COVID-19 disease and deaths among HCWs.

Authors' contributions: ND, RCM, JS, DKG and NG conceived the study. ND, RCM, DKG and NG collected the data. ND, RCM and JS verified the data. ND and JS performed the statistical analyses. ND and JS cleaned data. ND, RCM, JS, DKG and NG drafted the manuscript and approved the final draft.

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Data availability: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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