Original Article

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Pharmacology Section

Risk Factors for Reverse Transcriptase Polymerase Chain Reaction Positivity for SARS-CoV-2 among Healthcare Workers in a Group of Tertiary Care Hospitals in Mumbai: A Cross-sectional Study

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ABSTRACT

Introduction: Healthcare Workers (HCWs) can acquire or transmit Coronavirus Disease 2019 (COVID-19) from and to patients respectively. There is limited data on risk factors for Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) infection among HCWs.

Aim: To evaluate the risk factors for SARS-CoV-2 infection amongst HCWs of tertiary care hospitals in Mumbai, Maharashtra, India.

Materials and Methods: A questionnaire based cross-sectional study was conducted among 801 HCWs from three tertiary care hospitals. Data regarding demography, co-morbidities (hypertension, diabetes, heart disease, cancer, immunosuppressive therapy, asthma), symptoms, contact with confirmed cases of COVID-19 and protective precautions at the work place was collected. Infection diagnosed by Respiratory Tract samples- Reverse Trancriptase Polymerase Chain Reaction (RT-PCR) test was correlated with the above factors.

Results: Of the participants, 50.1% were working in designated COVID-19 area; 85.1% had no co-morbidity. A total of 62 of the 801 (7.75%) HCWs had a history of positive RT-PCR for SARS-CoV-2. Only asthma was associated with a significant higher in infection rate. Loss of taste/smell (30%), acute febrile illness (46.4%), acute respiratory illness (18.5%) were more common in persons with RT-PCR positivity ($p<0.05$). Visit to fever clinic, positive household member, and a definite history of exposure to a COVID-19 positive patient, were significantly associated with higher risk of infection. Working in designated COVID-19 hospital was not a significant risk factor (8.5% vs 5.6%). HCWs on Hydroxychloroquine (HCQ) prophylaxis had significantly lower rate of infection.

Conclusion: Rate of SARS-CoV-2 positivity among HCWs was 7.7%. Presence of symptoms, especially, loss of taste/smell, fever and respiratory symptoms are associated with high positive rates. Working in a designated COVID hospital was not a risk factor for increased rate of infection. HCQ prophylaxis is associated with reduced rate of COVID-19 among HCWs.

Keywords: Asthma, Acute respiratory distress syndrome, Coronavirus disease 2019, Infection, Severe acute respiratory syndrome coronavirus-2

INTRODUCTION

India, like the rest of world, is struggling with the COVID-19 pandemic with Mumbai, its financial capital being the worst affected city in the country [1]. Absence of HCWs from work due to illness and quarantine stresses the already overburdened medical services even more, and their replacement isn't easy due to limited numbers of trained personnel [2]. Moreover, HCWs may act as super-spreaders in the hospital set up, especially when asymptomatic and in the incubation period, transmitting the infection to vulnerable patients [3]. Two of the major government initiatives to reduce this rate of infection have been HCQ prophylaxis for HCWs at high risk, and the segregation of hospitals (public as well as private) into designated COVID-19 and non-COVID-19 facilities [4]. The former has been effective in reducing infection rates, while there is only empirical evidence of the effectiveness of the latter. The rates of SARS-CoV-2 infection among HCWs in different countries have ranged between 5-44% [3,5-7]. Currently, literature regarding risk factors for infection among HCWs in India is very limited. Such information can provide important insights for devising and implementing strategies to reduce the burden of COVID-19 cases among HCWs [8,9].

In this cross-sectional evaluation, an attempt has been made to ascertain demographic, co-morbidity and exposure characteristics with real-time RT-PCR positivity for SARS-CoV-2 infection among HCWs.

MATERIALS AND METHODS

The present study was a cross-sectional study which was conducted on HCWs including doctors, nurses and ancillary workers, working in three large public tertiary care hospitals participated in the seroprevalence study conducted during June 2020. Ancillary workers include staff cleaners, social workers, staff in mortuary, laboratory technicians, paramedical staff, security officers and porters who have direct patient contact. The study was conducted in accordance to the tenets of the Declaration of Helsinki. The study protocol was approved by the Institutional Review Board, JJ Hospital and Grant Medical College, Mumbai, Maharashtra, India (IEC/Pharm/RP/125/Jun/2020).

All three hospitals belong to the same management group ensuring standardisation of COVID protection protocols across the hospitals. One hospital is a designated non-COVID hospital admitting only COVID-19 negative patients while the other two hospitals are designated COVID-19 hospitals admitting only COVID positive patients. During the pandemic HCWs have been working across the hospitals to cover for colleagues who have taken ill or required quarantine due to exposure to a COVID-19 patient either at work or at home.

Sample size was not formally calculated, all the HCWs in the above three hospitals were contacted and those willing to participate and gave

informed consent were included in the study. A total of 801 HCWs were enrolled in this seroprevalence study for antibodies against COVID-19. In the present study the sub cohort of RT-PCR positive HCWs and the risk factors associated with the infection were examined.

All participants were self-administered a pre-designed, validated questionnaire. The english questionnaire was validated by forward-back translations into Hindi and Marathi, the lingua franca of most of the ancillary staff.

The questionnaire had questions designed to elicit demographic details, information related to co-morbidities, history of COVID-19 related symptoms, contact with confirmed COVID-19 patients, risk factors for COVID infection at home, protective precautions taken at the work place, visit to a fever clinic during last one month, prior diagnosis of COVID-19, and if positive, date of test performed.

STATISTICAL ANALYSIS

Frequency and percentages were calculated for categorical variables. Median and range was reported for continuous variables. The overall and risk group specific RT-PCR positivity rates were reported with 95% confidence intervals using Open Epi (Open Source Epidemiologic Statistics for Public Health). Additionally, positive RT-PCR rates were reported according to demographics, co-morbidities, work related risk/exposures and prevention practices. Difference in proportion was examined by Chi-square tests with Yates' correction, if required. According to needs, Fishers-exact test was also used. The p-value of <0.05 using two-tailed test was considered as statistically significant.

RESULTS

Total of 801 HCWs included 201 doctors (25.1%), 308 nurses (38.5%), and 292 ancillary staff (36.4%). Four hundred one (50.1%) study participants were working in a dedicated COVID-19 hospital, whereas 400 (49.9%) were working in a non-COVID-19 hospital. Of these, 386 (48.2%) were males, with only 8 (1%) subjects being over the age of 60 years. A total of 682 (85.1%) study participants did not have any co-morbidity requiring treatment [Table/Fig-1].

Parameter	n (%)
Profile of healthcare workers n (%)	
Doctors	201 (25.1%)
Nurses	308 (28.5%)
Support staff	292 (36.4%)
Gender n (%)	
Male	386 (48.2%)
Female	415 (51.8%)
Age group n (%)	
20-40 years	413 (51.6%)
41-60 years	380 (47.4%)
>61 years	8 (1%)
Co-morbidities n (%)	
Atleast one co-morbidity	103 (12.9%)
Two or more co-morbidities	16 (2%)
Diabetes	38 (4.7%)
Asthma	35 (4.4%)
Previous diagnosis of cancer	5 (0.6%)
Receiving immunosuppressive treatment	11 (1.4%)
Cardiac disease	48 (6%)

[Table/Fig-1]: Baseline demographics of the study participants.

A total of 62 (7.7%) study participants had tested positive with RT-PCR test for COVID in the past [Table/Fig-2]. Of these, the highest rate of infection was found in doctors, followed by nurses and ancillary staff. The rate of infection was significantly higher in non-COVID-19 hospitals as compared to COVID-19 (p=0.032).

Parameter	RT-PCR Negative	RT-PCR positive	% positive	95% CI	p-value (Chi-square/ Fisher's Test)
COVID-19 result (n=801)	739	62	7.74	6.07-9.81	
Profile					0.39
Doctors (n=201)	182	19	9.45	6.06-14.36	
Nurses n (n=308)	283	25	8.12	5.51-11.75	
Support staff (n=292)	274	18	6.16	3.87-9.58	
Hospital					0.032*
COVID hospital (n=401)	366	35	8.72	6.95-12.76	
Non-COVID-hospital (n=400)	346	54	13.5	4.02-8.08	
Gender					0.97
Male (n=386)	356	30	7.77	5.46-10.91	
Female (n=415)	383	32	7.71	5.48-10.71	
Age group					0.17
20-40 years (n=413)	380	33	7.99	5.71-11.04	
41-60 years (n=380)	353	27	7.11	4.89-10.17	
>61 years (n=8)	6	2	25.00	6.3-59.91	
Immunocompromised (Cancer/Immunosuppressants)					0.98
No (n=105)	97	8	7.62	3.7-14.52	
Yes (n=14)	13	1	7.14	0-33.54	
Asthma					0.048*
Yes (n=35)	32	3	5.71	62-19.57	
No (n=766)	760	6	0.78		
Cardiac problem					0.83
Yes (n=48)	44	4	8.33	2.76-20.08	
No (n=753)	695	58	7.70		
Diabetes					0.92
Yes (n=38)	35	3	7.89		
No (n=763)	704	59	7.73		

[Table/Fig-2]: RT-PCR positivity rate as per demographic details and co-morbidities. *p-value significant

There was significant difference in rate of RT-PCR positivity in those with asthma (95% CI 62-19.57; p=0.048) as compared to those without asthma. For other risk factors i.e., immunocompromised status because of cancer/immunosuppressant drugs, cardiovascular morbidity/diabetes there was no significant difference in RT-PCR positivity rate [Table/Fig-2].

There was significant difference in RT-PCR positivity rates in symptomatic patients versus asymptomatic people (p<0.001). Symptoms like loss of taste/smell, acute febrile illness, acute respiratory illness, non-specific illness were associated with higher rates of RT-PCR positive rates than those without these symptoms (p<0.005, highly significant statistically). Other less common symptoms such as acute gastric/enteric illness/redness of eyes and skin rash were not associated with significant rates of RT-PCR positivity (p>0.05) [Table/Fig-3].

RT-PCR positivity rate was significantly higher in those who visited fever clinic, having positive household member and directly exposed to COVID-19 patient (p<0.05 for all; [Table/Fig-4]). There was no difference in the rate of RT-PCR positivity in HCWs having neighbours positive for COVID-19, using shared toilet, living in hotspot/containment zone or working in the tertiary care hospitals (p>0.05) [Table/Fig-4].

Use of protective measures like mask use outside home (irrespective of type of mask), use of PPE at work, social distancing outside home and persons in room were not associated with significant difference in positive rates for RT-PCR for COVID-19. Hydroxychloroquine (HCQ) use was associated with significantly lesser rates of RT-PCR positivity than those who did not use it (p<0.05) [Table/Fig-5].

Parameter	RT-PCR negative	RT-PCR positive	% positive	95% CI	p-value (Chi-square/ Fisher's-test)
Symptomatic					
Yes (n=167)	33	134	80.24	73.51-85.61	0.001*
No (n=634)	605	29	4.57	3.18-6.51	
Loss of taste/smell					
Yes (n=10)	7	3	30.00	10.33-60.77	0.03377*
No (n=791)	736	55	6.95		
Acute febrile illness					
Yes (n=28)	15	13	46.43	29.53-64.19	0.001*
No (n=773)	724	49	6.34	4.81-8.29	
Acute respiratory illness					
Yes (n=97)	79	18	18.56	4.67-8.3	0.001*
No (n=704)	660	44	6.25	11.98-27.52	
Non-specific illness					
Yes (n=90)	76	14	15.56	9.37-24.56	0.008*
No (n=711)	663	48	6.75	5.11-8.55	
Acute gastric/enteric illness					
Yes (n=8)	7	1	12.50	0.11-49.21	0.5986
No (n=793)	732	61	7.69	6.02-9.76	
Redness of eyes					
Yes (n=12)	11	1	8.33	0	0.8587
No (n=789)	728	61	7.73	6.05-8.54	
Skin rash					
Yes (n=9)	9	0	0	0	0.4825
No (n=792)	730	62	7.83	6.14-9.92	

[Table/Fig-3]: RT-PCR positivity rate based on symptoms.
*p-value significant

Parameter	RT-PCR Negative	RT-PCR positive	% positive	95% CI	p-value (Chi-square/ Fisher's test)
Visited fever clinic					
Yes (n=132)	109	23	17.42	11.84-24.85	0.001*
No (n=669)	630	39	5.83	4.27-7.88	
Household member positive					
Yes (n=74)	57	17	22.97	14.78-33.83	0.001*
No (n=727)	682	45	6.19		
Neighbourhood positive					
Yes (n=397)	364	33	8.31	5.95-11.47	0.55
No (n=404)	375	29	7.18	5.01-10.15	
Quarantined					
Yes (n=176)	135	41	23.30	17.64-30.1	0.001*
No (n=625)	604	21	3.36	2.18-5.11	
Shared toilet					
Yes (n=314)	292	22	7.01	4.62-10.43	0.53
No (n=487)	447	40	8.21	6.06-11.01	
Living in hotspot/containment zone					
Yes (n=531)	485	46	8.66	6.53-10.76	0.17
No (n=270)	254	16	5.93	3.61-6.56	
Directly exposed to COVID-19 patient					
Yes (n=343)	304	39	11.37	8.4-15.19 9.46-7.44	0.003*
Maybe (n=283)	266	17	6.01		
No (n=175)	169	6	3.43		
Worked in COVID hospital					
Yes (n=603)	542	61	8.46	6.47-10.97	0.185
No (n=198)	187	11	5.56	3.02-9.77	

[Table/Fig-4]: RT-PCR positivity rate based on exposure.
*p-value significant

Parameter	RT-PCR Negative	RT-PCR positive	% positive	95% CI	p-value (Chi-square/ Fisher's-test)
Mask use outside home					
>75% (n=577)	532	45	7.80	5.86-10.29	0.74
50-75% (n=163)	152	11	6.75	3.68-11.8	
<50% (n=61)	55	6	9.84	4.24-20.19	
Mask type					
N95 (n=559)	515	44	7.87	5.89-10.42	0.52
Surgical (n=189)	173	16	8.47	5.19-13.39	
Cloth (n=53)	51	2	3.77	0.3-13.48	
PPE use frequency at work					
Always (n=130)	117	13	10	5.81-16.48	0.35
On direct contact (n=449)	413	36	8.02	5.82-10.92	
Never (n=222)	209	13	5.86	3.36-9.84	
Six feet distancing outside home					
>75% times (n=292)	269	23	7.88	5.25-11.59	0.93
50-75% times (n=312)	287	25	8.01	5.44-11.6	
<50% times (n=197)	183	14	7.11	4.19-11.66	
Persons in room					
<5 (n=639)	587	52	8.14	6.24-10.53	0.41
>5 (n=162)	152	10	6.17	3.25-11.12	
Hydroxychloroquine use					
Yes (n=488)	300	13	4.15	2.37-7.04	0.003*
No (n=313)	439	49	10.04	7.66-13.05	

[Table/Fig-5]: RT-PCR positivity rate based on protective measures.
*p-value significant

DISCUSSION

In this cross-sectional study, authors had compared positive rates of COVID-19 based on the RT-PCR test among HCWs in COVID-19 designated hospitals and non-COVID-19 hospitals Mumbai, Maharashtra, India. Overall rate of infection diagnosed with RT-PCR was 7.74%. In a study from the United Kingdom, the rate of positivity among 1533 symptomatic HCWs was 18% [3]. Another study from London reported 44% out of 200 HCWs to have SARS-CoV-2 infection as identified by either serology or RT-PCR [5] whereas a study from Belgium reported that overall infection rate of 12.6% [6]. In another study from Netherland, 5% HCWs out of 1796 were positive for SARS-CoV-2 [7].

The percentage of infection among HCWs in COVID hospitals in present study was significantly less than those with non-COVID hospitals (8.72% vs 13.5%; p=0.032). These observations from present study, provides an important message that HCWs in non-COVID-19 designated hospitals also need to take adequate precautions and cannot afford to be complacent towards the infection.

The rate of infection was numerically higher among doctors than nurses and support staff however this did not reach the statistical significance. Authors did not segregate the number of doctors with infection based on their profile of work i.e., involved in endotracheal intubation, intensive care or regular outpatient examination. This sub-group analysis might provide more insights into the high risk work among doctors. A case control study from India has reported higher risk of infection in doctors performing endotracheal intubation [4].

Symptoms are important for screening and predicting risk of COVID-19 among HCWs. Studies have reported loss of smell or taste, fever, and myalgia as the strongest predictors for positive results for COVID-19 [10,11]. This has been corroborated in present study also presence of symptoms was associated with significantly higher rates of RT-PCR positive rates as compared to those without symptoms. Authors observed significantly higher rates of positive RT-PCR among those with loss of taste/smell, fever and respiratory symptoms than without

these symptoms. It should be remembered that some HCWs may not have symptoms, but still they are infected with SARS-CoV-2 [11].

Based on the analysis of those having co-morbidities with asthma were associated with higher risk of infection due to SARS-CoV-2. Cancer or use of immunosuppressant medicines was not associated with increased risk of COVID-19 among HCWs. Similarly, diabetes and cardiac problems were also not associated with increased risk of infection with SARS-CoV-2. It is known that patients with COVID-19 having hypertension or diabetes mellitus are at higher risk of more severe disease course and progression of the disease [12]. A study from China reported that laboratory confirmed cases of COVID-19 with co-morbidity have poorer outcomes as compared to those without co-morbidities. Similarly, in the same study, higher number of co-morbidities correlated with poorer outcomes [13].

A case-control study among HCWs in India reported significantly lower risk among those having taken four or more maintenance doses of HCQ. Use of PPE was also associated with a reduced risk of infection due to SARS-CoV-2 [4]. In this study, also it was found that the risk of infection was lower in those consuming HCQ. In present study, mask use outside home, PPE use frequency at work, six feet distancing outside home and number of persons in a room were not associated with significant difference in the increased risk of RT-PCR positive rates.

Interestingly, highest infection rates were seen with surgical masks (8.47%) followed by N95 masks (7.87%), and the lowest infection rates with cloth masks (3.77%). While this was not found to be statistically significant because of the small sample size, this is a very interesting finding. A possible explanation could be the fact that those working in close contact with COVID-19 patients invariably wear N95 masks as a part of disease protocol, while those working in supporting functions often wear cloth masks. The finding of the highest infection rates with surgical masks may be attributed to the hierarchy of distribution of PPE, consistent with reports of PPE shortage across the globe: where N95 masks are prioritised for doctors and nurses, with the latter, along with ancillary staff often having to make-do with surgical masks. A correlation with the role of hospital hierarchy in PPE distribution in each mask category was not possible due to the small sample size. These findings are contradictory to available evidence about the superiority of N95 masks in limiting the spread of COVID-19, and authors reiterate the importance of protective measures at work, in home and outside work to limit the spread of virus.

A small study (n=4) suggests that although RT-PCR is a useful test for diagnosis of COVID-19, some recovered patients may still be carriers of the virus [14].

Limitation(s)

This study had several limitations. While the participation was multicentric, it was limited geographically to Mumbai, and there is no representative of the prevalence rates across other healthcare facilities. Also, since the study cohort was largely voluntary, it may not be considered representative of the entire facility. Additionally, the veracity of questionnaire-based information is always susceptible to recall bias. Also, asymptomatic COVID-19 infections are not accounted for, which may constitute a significant percentage of COVID-19 infections, since RT-PCR is mandated only for those with symptoms. Considering these limitations, observations of present study should be extrapolated with caution to general population.

CONCLUSION(S)

Infection rate with SARS-CoV-2 among HCWs in three public hospitals in Mumbai was found to be 7.7%. Presence of symptoms, especially, loss of taste/smell, fever and respiratory symptoms are associated with high positive rates. HCQ prophylaxis was associated with reduced rate of COVID-19 infection among HCWs.

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