



# Risk factors for novel corona virus (COVID-19) re-infections among health care workers at tertiary care center: A case control study

Pusdekar Y <sup>a\*</sup>, Pusdekar V <sup>b</sup>, Bhagat S <sup>c</sup>, Balpande L <sup>d</sup>, Saoji A <sup>e</sup>

<sup>a\*, c, d</sup> Assistant Professor, Department of Community Medicine, NKP Salve Institute of Medical Sciences & Research Center and Lata Mangeshkar Hospital, Nagpur, India

<sup>b</sup> Assistant Professor, Department of Surgery, All India Institute of Medical Sciences, Nagpur

<sup>e</sup> Professor and Head, Department of Community Medicine, NKP Salve Institute of Medical Sciences & Research Center and Lata Mangeshkar Hospital, Nagpur, India

## Abstract

**Introduction:** Healthcare Workers (HCWs) are repeatedly exposed to SARS-CoV-2 (Severe Acute Respiratory Syndrome Corona Virus 2) or the COVID-19 virus. This study aimed to identify factors associated with SARS-CoV-2 re-infection among HCWs in a tertiary care centre.

**Methods:** We conducted a case-control study. Cases were defined as those with a second positive reverse transcription-polymerase chain reaction (RT-PCR) report after a symptom free period of at least 30 days after previous positive RT-PCR report and controls were those with a single covid -19 episode (RT-PCR positive) during Aug-2020 to Jul-2021. All HCWs (second positive report) were included as cases and matched controls (age, gender) recruited in 1:2 ratio. They were interviewed using a google form and clarifications (if any) were obtained on phone. Analyses were performed using logistic regression models.

**Results:** A total of 53 cases and 110 controls were included. Age > 50 (AOR-1.63 95%CI-1.06-5.59), Men (AOR-4.13 95% CI-1.70-10.05), Nurses (AOR-11.24 95% CI-1.05-119.63), not using N95 (AOR-2.89 95% CI-1.02-5.05), Diabetic (AOR-3.51 95%CI-2.01-8.73) and inadequate use of personal protective equipment or PPE (AOR 4.82 95% CI 1.18-19.65) were identified as risk factors. Conversely, graduate (AOR 0.06 95% CI 0.01-0.53) and postgraduate (AOR-0.05 95% CI-0.005-0.7) education, feeling scared or nervous (AOR-0.45 95% CI-0.22-0.91), not always wearing any gloves, caps and goggles/face shields (AOR 0.10 95% CI-0.02-0.41), hand hygiene (AOR-0.42 95% CI - 0.1-0.94) and consistent use of N95 masks or double masking (AOR-0.27 95% CI-0.09-0.80) even outside the workplace were protective factors.

**Conclusion:** Study highlights protection provided by high-performance filtering masks or double masking among HCWs. These modifiable risk factors should be considered while designing, implementing, and monitoring COVID-19 biosafety protocols.

**Keywords:** COVID-19, re-infection, HCW, risk factors, mask, PPE, hand hygiene

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## 1. Introduction

Novel coronavirus disease (COVID-19) or SARS-CoV-2 has affected the global economy, society, and health at large. The pandemic nature of this new virus and has resulted in a high case fatality rate of 6.81% as

of May 25<sup>th</sup> 2021 with 167,996,661 confirmed cases and 3,487,480 deaths (WHO 2021). The severity and fatality of COVID-19 is mostly related to advanced age, followed by cardiovascular disease, hypertension, chronic kidney disease, cancer, and many other co-



morbid conditions that pose a greater risk of mortality in COVID-19 infections (Zhao 2020).

This problem is further compounded by the fact that those who have recovered from COVID 19 are acquiring the infection de-novo after a disease free period. This phenomenon is being observed more frequently as we are heading into the second and the third year of the pandemic. It is considered as a major threat to the containment measures against the pandemic if those who have recovered get reinfected (Ravioli 2020). It is therefore necessary to study the characteristics of those with reinfection as compared to those who are infected only once, in order to study the risks for getting reinfection with COVID - 19. The reinfection in patients recovered from COVID-19 could create a serious challenge in tackling the COVID- 19 pandemic as they could be a source of spreading the virus in the society (Alizargar 2020). Also, the covariates for reinfection are not determined and would be useful in identifying the high risk groups for re-infections and targeting specific interventions for them to help in breaking the transmission chain further. Considering the magnitude of the pandemic and the need for urgent containment measures, it is necessary to study the factors that are associated with COVID – 19 reinfection. Very few studies have focused on the determinants of COVID-19 reinfection (Villamil 2020, Kang 2020). Therefore, a comprehensive assessment of the role of demographic characteristics and disease severity on risk of subsequent infections after a first episode of COVID 19 is needed. This has big implications for disease control policies both in terms of preventive measures and vaccination (Zhang 2020).<sup>(7)</sup> This study will provide an insight on the factors that pose a risk of getting infected by COVID – 19 after recovery and help in developing targeted interventions and precautionary measures that can prevent reinfection by COVID -19 (Hoang & Inamo 2020).

Therefore, it is necessary to assess the burden of COVID-19 reinfection among the previously recovered cases (Kassa 2020) and study the determinants for reinfection after

recovery (Kirkcaldy & Okhuese 2020) from COVID-19 in order to formulate effective prevention strategies for COVID -19 reinfections (Zhou 2020). This study aims to assess the prevalence and associated factors for COVID-19 reinfections among health care workers at a tertiary care center.

#### **Aim & Objectives:**

**Aim** – To determine the prevalence of COVID 19 reinfection after recovery from a previous episode of COVID 19 infection among health care workers

#### **Objectives –**

1. To identify the factors associated with COVID – 19 reinfections in cases as compared to controls (those who are infected only once)
2. To assess the severity of disease and hospitalization rates in COVID – 19 reinfection and compare them with controls.

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## **2 Materials and Methods**

**Study Design:** Cross sectional web-based study

**Study population:** Health care workers from two tertiary care hospitals who are affected by COVID – 19 reinfection i.e second illness episode after a 30 days disease free period as cases and age and gender matched controls (those who are affected by COVID – 19 only once so far) in the ratio of 1 case: 2 age and gender matched controls.

**Study Setting:** Tertiary care hospitals

**Study period:** One year (July 2021 to June 2022)

**Sample size:** All the health care staff at the two institutes that was tested positive on RTPCR/RAT (from January 2021 to July 2021) for the second time or later after a previous episode of COVID -19 after a minimal recovery period of 30 days or 1 month from the previous report (i.e First episode of COVID – 19) were included in the study as cases and those who were affected by the infection only once were enrolled as controls in the ratio of 1:2 respectively for cases and controls.

COVID -19 reinfection was defined as occurrence of clinical symptoms or lab tested COVID -19 after a symptom free period of at least 30 days post recovery from COVID 19 in the previous episode.

**Inclusion criteria:**



1. Health care workers who tested positive on RTPCR /RAT (Rapid Antigen Test) for the second time after a recovery period of minimum of 30 days after the initial COVID 19 infection as cases.
2. Age and gender matched health care workers who tested positive on RTPCR /RAT only once as controls.

**Exclusion criteria:** Health care workers who are not willing to participate.

### Methodology

An online survey was conducted using Google forms maintaining anonymities of the study participants. Also, telephonic conversation with the participants was done to confirm the severity of infection and other correlates. Questionnaires were circulated using social media platforms. Study was conducted after taking the approval from Institutional Ethics Committee. The questionnaire included the information on sociodemographic variables along with questions related to COVID -19 symptoms, severity of the disease, vaccination status, hospitalization rates, outcomes and precautionary measures used at the time of initial and subsequent episode of COVID 19, etc. Additional data was obtained from the investigation reports of the participants. Based on the clinical and diagnostic findings the rate of reinfection, its severity and the determinants for COVID-19 reinfection were assessed.

**Statistical analysis:** The data was exported in MS Excel and rates and proportions were calculated. Descriptive statistics were used for

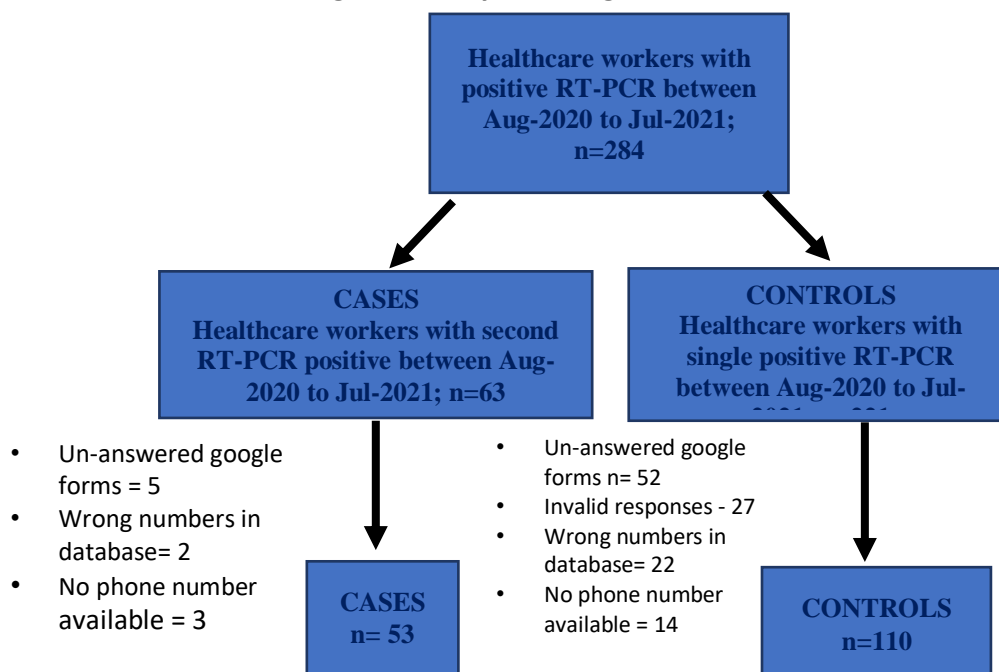
summarizing the data using means and standard deviations, and inferential statistics, were utilized to draw conclusions from data and to account for random variation. The data was organized using contingency tables and estimates for the odds ratio were calculated for identifying independent risk factors for COVID - 19 reinfection in the cases as compared to the controls. The data was analysed using the epi-info software version 7.2.2.

### 3 Results and Discussions

The study invited 284 participants who experiences a positive RT-PCR during the study period between Aug 2020 to July 2021. Among these, there were 63 (22.18%) participants who had a positive RT-PCR for a second time after an interval of > 30 days of the first positive RT-PCR report. Thus, the prevalence of COVID-19 reinfection was 22.18%. There were in all 53 participants from the cases who completed the google forms giving an overall response rate of 82.16% among cases. The controls were the healthcare workers who tested positive for RT-PCR only once. There were 221 HCWs who had a single positive RT-PCR during the study period and they were invited to participate in the study. Of them, 110 participants were included in the study after excluding the invalid responses and non-response including that due to non-availability of contact details or wrong contact details being provided. The study flow diagram is given in figure 1.



**Figure 1: Study Flow diagram**



**Table 1: Association between sociodemographic, clinical, lifestyle, and psychological characteristics with SARS-CoV-2 re-infection among HCWs**

Characteristics	Second positive RT-PCR (CASES) n=53	Single positive RT-PCR (CONTROLS) n=110	Unadjusted OR (95% CI)	p value*
<b>Mean Age (years)</b>	51.7	43.2	1.98 (0.95–3.02)	<b>0.040*</b>
<b>Gender</b>				
Female	26 (49.0)	68 (61.8)	Ref	
Male	27 (51.0)	42 (38.2)	2.66 (1.40–5.04)	<b>&lt;0.01*</b>
<b>Education</b>				
Secondary	15 (28.4)	19 (17.4)	Ref	
Higher Secondary	24 (45.3)	27 (24.5)	1.12 (0.9-1.42)	0.63
Graduate	8 (15.0)	48 (43.6)	0.54 (0.14-0.73)	0.325
Post Graduate	6 (11.3)	16 (14.5)	0.47 (0.21-0.91)	0.064
<b>SES - Lower</b>	19 (35.8)	23 (21.0)	Ref	0.83
Lower middle	28 (52.8)	49 (44.5)	0.93 (0.53-1.0)	0.0932
Upper Middle	4 (7.6)	28 (25.5)	1.82 (1.14-3.51)	0.0711
Upper	2 (3.8)	10 (9.0)	1.33 (0.92-1.62)	
<b>Marital status</b>		83 (75.5)	Ref	0.533
Married	46 (86.8)	19 (17.3)	2.82 (1.9-6.92)	0.0765
Separated/Divorced	7 (13.2)	8 (7.2)	1.10 (1.0-4.39)	
Widowed	0 (0)			
<b>BMI</b>				
< 30 (N and Uwt)	37 (69.9)	71 (64.5)	Ref	0.548
> 30 (Ow & Obesity)	16 (30.1)	39 (35.5)	0.54 (0.43-0.68)	



<b>Co-morbidities</b>	41 (77.4)	33 (30.0)	3.63 (2.27-9.42)	0.025*
Yes	12 (22.6)	77 (70.0)	Ref	
No				
<b>Feeling scared/nervous</b>	14 (26.4)	67 (61.0)	0.32 (0.13-0.71)	<0.01*
Yes	39 (73.6)	43 (39.0)	Ref	
No				

\*p<0.05 is statistically significant

Table 1 demonstrates the socio-demographic characteristics of the study participants. The mean age of the cases (51.7 years) was significantly higher than the controls (43.2 years); (p=0.040). The age range for the cases was 22-58 years and that for the controls was 24-52 years. COVID-19 reinfections were significantly higher among males as compared to females (p<0.01). Other factors that were

found to be significantly associated with COVID-19 reinfections among HCWs were the presence of any co-morbid conditions (p=0.025) and the fear of acquiring infection (p<0.01). However, there was no association of factors like educational or marital status and BMI with the occurrence of COVID-19 reinfections.

**Table 2: Association between occupational, exposure and social behavior factors & SARS-CoV-2 infection among HCWs**

Characteristics	Second positive RT-PCR (CASES) n=53	Single positive RT-PCR (CONTROLS) n=110	Unadjusted OR (95% CI)	P value
<b>Occupation</b>				
Nurse	12 (22.6)	6 (5.5)	5.32 (3.95-16.46)	<0.0001*
Resident Doctors	27 (51.0)	63 (57.3)	2.18 (1.75-3.91)	0.942
Doctors	7 (13.2)	27 (24.5)	0.35 (0.12-1.48)	0.693
Other HCWs	7 (13.2)	14 (12.7)	Ref	
<b>Place of Work</b>				
Covid wards	36 (67.9)	72 (65.5)	1.70 (1.32-2.42)	0.867
Non Covid areas	17 (32.1)	38 (34.5)	Ref	
<b>Face to face contact with cases</b>				
Yes	42 (79.2)	24 (21.8)	2.76 (1.15-6.49)	<0.01*
No	11 (20.8)	86 (78.2)	Ref	
<b>Visiting crowded places</b>				
Yes	39 (73.6)	29 (26.4)	4.75 (2.58-16.49)	0.042*
No	14 (26.4)	81 (73.6)	Ref	
<b>Use of High Perf. Masks (N 95)</b>				
Always	7 (13.2)	81 (73.6)	Ref	<0.001*
Sometimes	37 (69.8)	15 (13.6)	2.68 (1.62-8.63)	<0.001*
Fabric mask at home/outside	9 (17.0)	14 (12.8)	3.84 (1.04-16.41)	<0.001*
<b>Use of Gloves</b>				
Always	33 (62.3)	79 (71.8)	Ref	0.0729
Sometimes	20 (37.7)	31 (28.2)	0.58 (0.33-1.01)	



<b>Use of Surgical cap</b>				
Always	29 (54.7)	76 (69.0)	Ref	
Sometimes	24 (45.3)	34 (31.0)	0.43 (0.25–0.74)	<b>0.064</b>
<b>Use of PPE</b>				
Always	12 (22.6)	66 (60.0)	Ref	
Sometimes	41 (77.4)	44 (40.0)	3.58 (1.14-19.52)	<b>&lt;0.01*</b>
<b>Hand hygiene</b>				
Always	17 (32.2)	48 (43.6)	Ref	
Sometimes	36 (67.8)	62 (56.4)	2.48 (1.42 – 8.31)	<b>&lt;0.01*</b>
<b>Training support for PPE use</b>				
Yes	43 (81.1)	97 (88.1)	Ref	
No	10 (18.9)	13 (11.9)	0.73 (0.35-3.56)	<b>0.0928</b>

Table 2 shows the Association of occupational, exposure related and socio-behavioral factors with SARS-CoV-2 reinfections among HCWs. It was observed that HCWs of the nursing cadre, direct face to face exposures, visiting crowded places as well as inconsistent use of face masks, PPE and practicing infrequent hand sanitization were significantly associated with the risk of COVID-19 reinfections.

**Table 3: Multiple regression model of factors associated with SARS-CoV-2 re-infection in HCWs**

Characteristics	Second positive RT-PCR (CASES) n=53	Single positive RT-PCR (CONTROLS) n=110	Adjusted OR (95% CI)	P value
<b>Mean Age (years)</b>	51.7	43.2	11.24 (1.05–119.63)	<b>&lt;0.001*</b>
<b>Gender</b>				
Female	26 (49.0)	68 (61.8)	Ref	
Male	27 (51.0)	42 (38.2)	4.13 (1.70–10.05)	<b>&lt;0.01*</b>
<b>Occupation</b>				
Nurse	12 (22.6)	6 (5.5)	5.24 (1.05–11.37)	<b>&lt;0.001*</b>
Resident Doctors	27 (51.0)	63 (57.3)	3.43 (2.12-5.32)	0.734
Doctors	7 (13.2)	27 (24.5)	Ref	
Other HCWs	7 (13.2)	14 (12.7)	1.54 (1.12-9.54)	0.0832
<b>Co-morbidities</b>				
Yes	41 (77.4)	33 (30.0)	3.51 (2.01-8.73)	<b>&lt;0.01*</b>
No	12 (22.6)	77 (70.0)	Ref	
<b>Use of PPE</b>				
Always	12 (22.6)	66 (60.0)	4.82 (1.18–19.65)	<b>&lt;0.01*</b>
Sometimes	41 (77.4)	44 (40.0)	Ref	
<b>Education</b>				
Secondary	15 (28.4)	19 (17.4)	Ref	
Higher Secondary	24 (45.3)	27 (24.5)	1.23 (0.93-6.62)	0.091
Graduate	8 (15.0)	48 (43.6)	0.06 (0.01–0.53)	<b>&lt;0.01*</b>
Post Graduate	6 (11.3)	16 (14.5)	0.05 (0.005–0.7)	<b>0.03**</b>
<b>Feeling scared or nervous</b>				
Yes	14 (26.4)	67 (61.0)	0.45 (0.22–0.91)	<b>0.031*</b>
No	39 (73.6)	43 (39.0)	Ref	



<b>Use of Gloves/face shields/cap/goggles (PPE)</b>				
Always	12 (22.6)	66 (60.0)	0.10 (0.02–0.41)	<b>&lt;0.01*</b>
Sometimes	41 (77.4)	44 (40.0)	Ref	
<b>Consistent use of N95 or double masking</b>				
Always	9 (17.0)	69 (82.7)	0.27 (0.09–0.80)	<b>&lt;0.001*</b>
Sometimes	44 (83.0)	41 (37.3)	Ref	
<b>Hand Hygiene</b>				
Always	17 (32.2)	48 (43.6)	0.42 (0.1-0.94)	<b>&lt;0.001*</b>
Sometimes	36 (67.8)	62 (56.4)	Ref	

This case control study was conducted at a tertiary care centre to assess the prevalence and risk factors associated with COVID 19 reinfections among health care workers. The study successfully identified the modifiable and non-modifiable factors that were associated with a repeat positive RT-PCR among the HCWs i.e the cases. The comparison of the risk factors among those who were infected only once versus those who had a repeat infection were studied. To the best of our knowledge, this is the first study assessing the reinfection risk of COVID-19 among health workers in India.

#### Risk Factors

It was observed that age >50 years (AOR-1.63 95%CI-1.06-5.59; <0.001), and male gender (AOR-4.13 95% CI-1.70–10.05; p<0.01), independently posed a risk of acquiring COVID-19 reinfection among the HCWs. Advanced age by itself is recognized as the greatest risk factor for COVID-19 mortality, independent of underlying co-morbidities (Williamson 2020). This is attributed to the aging immune system that undergoes immune-senescence, leading to major alterations in the T-cell diversity and chronic activation of the innate immune system that leads to inability to clear the attacking microbes particularly viruses. These characteristics of ageing on the immune system prevent the clearance of infective agents from the body and thereby they are affected frequently by repeated infections as also in the case of SARS-CoV-2 virus or COVID 19 (Santesmasses 2020).

The higher risk of acquiring COVID 19 infections among males in general is particularly due to several factors like their

behavioural predisposition for more outdoor tasks, higher prevalence of smoking and alcoholism as also other comorbidities among them as compared to their female counterparts (Bwire 2020). There is also higher differential morbidity and mortality among males due to COVID that is attributed by these factors (Jordan 2020). Other plausible factors that may be responsible for selective male affliction might include higher density of angiotensin-converting enzyme-2 (ACE 2) receptors in males that also act as the receptors for coronavirus, sex-based immunological differences that are driven by sex hormones and X chromosome (de la Vega & Wu 2020).

Lastly, behavioral factors like a more responsible attitude toward the Covid-19 pandemic restrictions among women may have additionally protected them from acquiring the infection. On the other hand, irresponsible attitude among men may reversibly affect their utilization personal protective and preventive measures such as frequent handwashing, wearing of face mask, and following the stay-at-home orders, that may have contributed to a higher prevalence of COVID-19 reinfections among males (Klein 2020 & Ghazeeri 2011).

Overall, among the modifiable risk factors were nursing staff, presence of comorbid conditions like DM and inconsistent use of high filtering or N 95 masks. In our study, it was observed that the nursing staff was at a greater risk of acquiring COVID-19 reinfections (AOR-11.24 95% CI-1.05–119.63; p<0.001). Similar findings were observed in a study conducted in the UK, that stated higher risk of COVID 19 among the frontline HCWs



who were in direct contact with COVID\_19 cases and failed to use adequate PPE (AOR - 5.91 (95% CI: 4.53 to 7.71) as against those who used adequate PPE and were not in close contact with suspected or documented COVID-19 patients (Nguyen 2020). Other studies have also reported higher incidence among the frontline workers that also correlates with the inconsistencies in the use of personal protective gear (Black & WHO 2020).

This is attributed to the fact that the frontline workers like the nurses and the paramedical staff are in close contact with the cases. Moreover, they come into direct contact with severely moribund and critical cases while taking care of them which exposes them to higher dose of infection leading to greater risk of acquiring infection.

Another risk factor that was identified for COVID 19 reinfections was the presence of comorbidities like diabetes (AOR-3.51 95%CI-2.01-8.73,  $p < 0.01$ ) and were identified as risk factors. Diabetes mellitus increased the risk of covid-19 re-infections by two folds. It has already been established that presence of comorbidities increases the risk of covid-19. Not only is the rate of infection higher in patients with comorbidities, also likely to have severe symptoms and also suffer from complications covid-19 (Jordan & Baron 2020).

Diabetes increases the risk of COVID 19 reinfections due to blood glucose dysregulation which is closely linked to immune failure and thereby leading to increased susceptibility to repeated infections (Cariou 2020). Additionally, COVID 19 in patients with diabetes increases the risk of diabetic ketoacidosis and hyperglycemic hyperosmolar syndrome. Whereas Diabetes secondary to COVID 19 infections has also been reported (Kim, Li & Reddy 2020). Interestingly, new-onset diabetes has also been reported in patients hospitalized with COVID-19 (Heaney 2020).

Inadequate use of high-performance filtering masks or N95 masks (AOR-2.89 95% CI-1.02–5.05  $p < 0.01$ ) and personal protective equipment (AOR 4.82 95% CI 1.18–19.65)

were significant risk factors associated with COVID 19 reinfections. Though the PPE use in our study was higher as compared to other studies from Nigeria, Gondar, Ethiopia and China in which HCWs who always complied with appropriate use of PPEs ranged from 4.3 to 18.1% (Aguwa 2016, Haile 2017 & Tan 2020).

#### Protective Factors

Conversely, graduate (AOR 0.06 95% CI 0.01–0.53) and postgraduate (AOR-0.05 95% CI-0.005–0.7) education, feeling scared or nervous (AOR-0.45 95% CI-0.22–0.91), not always wearing any gloves, caps and goggles/face shields (AOR 0.10 95% CI-0.02–0.41), maintaining hand hygiene (AOR-0.42 95% CI - 0.1-0.94) and consistent use of N95 masks or double masking (AOR-0.27 95% CI-0.09–0.80) even outside the workplace were found to be protective against COVID 19 reinfections.

Particularly, a greater protective effect was observed with the use of high-performance masks, or double masking at as well as outside the workplace. Conversely, infrequent use of caps, goggles, face shields/goggles and gloves were found to be protective (Verbeek 2020). This may be due to the fact that these equipment's are used repetitively and there might be poor disinfection of these, leading to a false sense of security (Fischer, Chou & Thomas 2020). Among the psychological factors that protected the participants was the fear of acquiring infection as it may enforce protective behaviors. Higher education levels were protective as also observed in other similar studies. This shows that educated participants display higher levels of awareness for COVID preventive practices. Another protective factor was maintenance of Hand Hygiene. Other similar studies have also shown that Hand hygiene is one of the essential practices for preventing infection, especially SARS-CoV-2. A systematic review conducted at several countries indicated that hand hygiene was practiced by 40.0% of the health care workers (Erasmus 2010). Thus, appropriate and consistent use of PPE and hand hygiene were considered to be the cornerstone for preventing COVID 19 infections in some of the studies conducted in





other regions (Deressa 2021, Kaleb 2021 & Zenbaba 2020).

#### 4 Conclusion

Therefore, to conclude, the study highlights the non-modifiable risk factors for COVID 19 reinfections among the HCWs that were age, male gender and the non-modifiable risk factors that included presence of comorbidities, particularly DM, belonging to the nursing cadre of profession, inconsistent use of high-performance filtering masks and PPE measures. At the same time, protection against COVID 19 reinfection was offered by consistent use of high-performance filtering masks, PPE, maintaining hand hygiene consistently and fear of acquiring infection. Additionally, factors such as gender, level of education and occupational characteristics, that were associated with the risk of infection need to be taken into consideration for planning public health measures at the health care facilities for preventing the spread of COVID 19 reinfections.

The present study therefore highlights the importance of protection provided by high-performance filtering masks or double masking among HCWs, maintaining hand hygiene and prioritizing the training on precautionary measures along with specific protective measures for the most vulnerable health care staff.

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### Biography of Authors

	<p>Dr. Yamini Pusdekar was a post-graduate student from Government Medical College Nagpur and is recently working as Assistant Professor in Community Medicine at NKP Salve Institute of Medical Sciences and Research Centre, Nagpur. She is the member of the institutional Research unit and Board of Research Studies. Her research interests are Early childhood development, affordable Medical technology, Impact evaluation and Health Economics.  <i>Email:</i> <a href="mailto:dryaminipusdekar@gmail.com">dryaminipusdekar@gmail.com</a></p>
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	<p>Dr. Vinod Pusdekar is presently working as Assitant Professor in the Department of Surgery at All India Institute of Medical Sciences, Nagpur and was previous working at MGIMS, Sewagram. He has authored a book on Surgery entitled, "Systematic Approach to Describe Instruments &amp; Operative procedures in Surgery Orthopedics and Anesthesia". He is an academican and researcher with interests in Surgical oncology and Transplant surgery.  <i>Email: <a href="mailto:drvinodpusdekar20@gmail.com">drvinodpusdekar20@gmail.com</a></i></p>
	<p>Dr. Sayli Bhagat post-graduated from MIMER Medical College, Talegaon (D), Pune and is currently working as Assistant Professor in Community Medicine at NKP Salve Institute of Medical Sciences and Research Centre, Nagpur. Her research interests are infectious diseases, health administration and implementation research.  <i>Email: <a href="mailto:sayali.bhagat2012@gmail.com">sayali.bhagat2012@gmail.com</a></i></p>
	<p>Dr. Leena Balpande post-graduated from Peoples College of Medical Sciences &amp; Research Centre, Bhopal, and is currently working as Assistant Professor in Community Medicine at NKP Salve Institute of Medical Sciences and Research Centre, Nagpur. Her research interests are health administration, adolescent health and Health administration.  <i>Email: <a href="mailto:drleena29@gmail.com">drleena29@gmail.com</a></i></p>
	<p>Dr. Ajeet Saoji is the Professor and Head of the Department of Community Medicine at NKP Salve Institute of Medical Sciences and Research Centre, Nagpur. He has a teaching experience of more than 25 years and several international and national publications in reputed medical journals. He is the senior mentor for Research Methodology and the presides over the board of research studies. His research interests include Non communicable diseases, health economics, International Public Health and Infectious disease epidemiology.  <i>Email: <a href="mailto:ajeetsaoji@gmail.com">ajeetsaoji@gmail.com</a></i></p>



