

Original Article

Prevalence of COVID-19 Infection and Identification of Risk Factors among Asymptomatic Healthcare Workers : A Serosurvey Involving Multiple Hospitals in West Bengal

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Background : The declining trend of COVID-19 infection in India has made healthcare personnel (HCP) and general public lenient about personal-protective-measures. Serosurveys to estimate the prevalence of SARS-CoV2 IgG antibodies, particularly in high-risk-zones like hospitals can give the real scenario and risk-factors can help prioritise the target population for urgent, effective vaccination.

Methods : 1470 consecutive HCP from 4 tertiary-care-hospitals in Kolkata filled a questionnaire and were tested for serum SARS-CoV2-IgG by Enzyme-linked Immunosorbent Assay (ELISA). The prevalence of SARS-CoV2-IgG among asymptomatic HCPs was studied and the work environment, clinical comorbidities, personal habits and protective measures and pharmacologic prophylaxes were compared between those with and without SARS-CoV2-IgG. Parameters of asymptomatic seroconverters were also compared to those with personal history of COVID-19-Infection. Logistic regression was done to identify independent risk-factors.

Results : Prevalence of asymptomatic seroconversion was 15.8%. Asymptomatic seroconverters (n=208) were mostly working in mixed hospitals (having both COVID-19 and non-COVID-19 wards, 57.7%), were non-doctors by profession (nurses-25.1%, others-51.4%). Among asymptomatic HCP, independent positive risk factors for SARS-CoV2 IgG-positivity were Diabetes Mellitus (DM) and multiple comorbidities ($p_{\text{both}} < 0.001$) and prophylactic use of Hydroxychloroquine and Famotidine ($p_{\text{both}} < 0.03$). However, for symptomatic COVID-19 infection, working in COVID-19 dedicated hospitals, and personal h/o COPD were positive risk-factors and Ivermectin prophylaxis a negative risk-factor ($p_{\text{all}} \leq 0.03$).

Conclusion: In our study conducted in the immediate pre-immunisation period, rate of asymptomatic seroconversion among HCPs is too low to presume herd immunity. Those working in mixed hospitals and DM, multiple comorbidities are at particularly high risk.

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Key words : COVID-19, SARS-CoV2 IgG, ELISA, Seroprevalence, Healthcare personnel.

More than a hundred million people worldwide have been infected with severe acute respiratory syndrome coronavirus 2 (SARS CoV 2) over the past fourteen months. With the vaccination campaign targeting healthcare workers and the sudden decline in the daily number of cases in the country, the

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Editor's Comment :

- Among 1470 consecutive HCP from 4 tertiary-care-hospitals in Kolkata, prevalence of asymptomatic seroconversion was 15.8%.
- Rate of asymptomatic seroconversion among HCPs in immediate pre-vaccination period is too low to presume herd immunity.
- Risk factors for asymptomatic SARS-CoV2-IgG-positivity were Diabetes Mellitus (DM), multiple comorbidities, and even prophylactic use of Hydroxychloroquine, Famotidine
- For symptomatic COVID-19 infection, working in COVID-19-dedicated hospitals, and COPD were positive risk-factors and Ivermectin prophylaxis a negative risk-factor.

possibility of a high prevalence of asymptomatic seroconversion in the community is being proposed. Healthcare personnel (HCP) are known to be at an elevated risk of contracting COVID-19. Several IgM/IgG ELISA for COVID-19 have been certified for commercial purpose or research by different agencies which can be used for easy and cost-effective tools

for the detection and surveillance of COVID-19 infection in communities and high risk areas like hospitals¹. Initial studies from China reveal a 1% COVID-19 infection rate in HCPs, with higher rates in HCP who reported no exposure to COVID-19 patients and upto 7.0% greater absolute risk among HCP than community in the United States^{2,3}. Majority of infected HCP (62.5%) were nurses³. Studies have reported higher risk of transmission in frontline healthcare workers in the United Kingdom⁴. From a recent meta-analysis of COVID-19 prevalence among health care workers, the estimated prevalence was 11%, the most frequently affected personnel were nurses (48%) and HCP working in Hospital Non-emergency Wards (43%)⁵. From different parts of India, the reported seroprevalence was around 0 to 12%, depending on the time of study, type of hospital and IgG antibody assay method used, though majority used chemiluminescence assays and many were not validated assay methods by the Indian Council of Medical Research⁶⁻⁸.

Serological testing to assess the extent of seroconversion among HCP just prior to the vaccination campaign among healthcare workers in India could give a glimpse of the real picture in the community and also help identify high risk groups for prioritising vaccination campaign.

MATERIALS AND METHODS

The primary objective was to evaluate the prevalence of previously undiagnosed SARS-CoV-2 Infection among HCP from four tertiary-level hospitals in Kolkata, one of which was dedicated solely to the care of COVID-19 infected patients, one was a purely non-COVID-19 hospital and the other two had mixed proportion of COVID-19 positive or non-COVID-19 patients, these two will be referred to as mixed hospitals henceforth. The study was approved by the Institutional Ethics Committee of IPGMER, Kolkata vide memo no. IPGMER/IEC/2020/482. The secondary objectives were to identify the risk factors associated with COVID-19 infection and also risk factors for symptomatic COVID-19 infection among HCPs. For these, we analysed factors including age, Body Mass Index (BMI), profession (whether doctor, nurse or other HCP), area of work (whether in a COVID hospital, mixed hospital or non-COVID hospital; whether working in critical care settings), history of addiction, personal h/o comorbidities including diabetes mellitus (DM), hypertension, dyslipidemia, established atherosclerotic cardiovascular diseases (ASCVD), hypothyroidism, other autoimmune diseases, chronic kidney or liver disease, malignancies, diseases

causing immunosuppression like HIV/AIDS, history of prolonged use of steroids and/or other immunosuppressants and the use of drugs for COVID-19 prophylaxis including hydroxychloroquine, ivermectin, multivitamins, vitamin-D, famotidine, zinc and personal protective measures adopted including masks, PPE kits and sanitisers.

Participants with a history of SARS-CoV-2 infection diagnosed by rt-PCR or suggestive symptoms of COVID-19 infection were excluded from analysis for the primary and first secondary objective. However, for the other secondary objective, we compared those without personal h/o COVID-19 infection but having SARS-CoV-2-IgG with a subset of participants with personal h/o symptomatic COVID-19 infection and having SARS-CoV-2-IgG.

Participants were recruited between 1st of September 2020 to 10th of January 2021. Following informed consent, data were collected through questionnaire filled by the participants, under the supervision of study coordinators, prior to drawing blood samples for SARS-CoV2-IgG antibody estimation. Blood samples were tested for IgG antibodies against the spike proteins of SARS-CoV-2 using SARS-CoV-2 enzyme-linked immunosorbent assays (ELISAs) (# CORONA KAVACH IgG, Zydus), validated by ICMR and reported to have a sensitivity and specificity of 98.7% and 100% respectively. All ELISAs were performed at IPGME&R, Kolkata following manufacturer's instructions³. Negative and positive control samples were run every day and the threshold for a positive ELISA was determined at a value greater than the mean + 3 SD of negative controls, consistent with standard methodology⁴.

Statistical Evaluation :

Statistical analysis was performed using GraphPad Prism v.9 for Mac. Comparison was done between those with SARS-CoV2 IgG-positivity versus those without. Additionally, comparison was also done between those with SARS-CoV2-IgG positivity but without personal h/o COVID-19 infection with a subset with known h/o COVID-19 Infection. Categorical variables were analysed using Chi-square or Fisher's exact test and quantitative variables using unpaired t-test. Binary logistic regression analysis was performed to determine independent risk factors.

OBSERVATIONS

Out of total 1470 participants screened, n = 154 were having a personal h/o COVID-19 infection or suggestive symptoms. They were excluded from statistical analysis for the primary objective and n =

1316 were finally enrolled for this. Out of this, 208 (15.8%) had positive SARS-CoV2-IgG and were classified as asymptomatic seroconverters, while n=1100 did not have SARS-CoV2-IgG, and 8 participants had indeterminate response. Those with indeterminate results were excluded from further statistical analysis.

The baseline characteristics of participants are given

in Table 1. Majority were HCP other than doctors/nurses (40.5%) and majority worked in non-COVID-19-dedicated hospitals (41.3%). Among comorbidities; systemic hypertension was the commonest (10.9%) followed by DM (8.4%) and hypothyroidism (4.8%). A total of 46.1% of participants were using some form of pharmacologic agents for prophylaxis, multivitamins (31.7%) being the most commonly used agent followed by hydroxychloroquine (31.3%), while 9.7% used Ivermectin.

Among the 208 asymptomatic seroconverters, majority were HCP other than doctors/nurses (20.2%), majority worked in mixed hospitals (57.7%). Compared to those who didn't have SARS-CoV2-IgG antibodies, a significantly higher number of asymptomatic seroconverters were HCP other than doctors/nurses (51.4% *versus* 38.5%, $p = 0.0001$), worked in mixed hospitals (57.7% *versus* 36%, $p < 0.0001$), had higher prevalence of DM (16.8% *versus* 6.3%, $p < 0.0001$), had autoimmune diseases other than Hashimoto's thyroiditis (4.3% *versus* 1.3%, $p = 0.002$), presence of ≥ 2 comorbidities (11.5% *versus* 6.5%, $p = 0.011$) and history of prolonged intake of steroids/other immunosuppressants (7.7% *versus* 2.6%, $p = 0.0002$) (Table 2). A total of 25 patients in our cohort had autoimmune disorders other than Hashimoto's thyroiditis, including Rheumatoid arthritis (n=8), Psoriasis (n=3), Vitiligo (n=3), Systemic Lupus Erythematosus (n=3), Graves' disease (n=3), Myasthenia Gravis (n=2), Immune thrombocytopenic purpura (n=1), Inflammatory bowel disease (n=1) and T1DM (n=1).

There was a slightly higher prevalence of use of some form of pharmacologic prophylaxis in those having SARS-CoV2-IgG than those without (46.4% *versus* 44.7%, $p = 0.56$). Use of hydroxychloroquine and Famotidine were significantly more common in those having SARS-CoV2-IgG (37.5% *versus* 30.1%,

Table 1 — Demographic and clinical characteristics of study participants

Parameter	Total no of participants without personal h/o COVID-19 infection (N= 1316)
Mean age in years (SD)	38.6 (11.8)
Mean BMI in kg/m ² (SD)	25.1(4.1)
Gender (M = Male, F = Female)	M : 647 F : 669
Designation (D=Doctor, N=Nurse, O=Other healthcare worker)	D : 315 (23.9%) N : 468 (35.6%) O : 533 (40.5%)
Working in COVID dedicated hospital (CDH) or non COVID dedicated hospital (NCDH) or Mixed hospital (having both COVID dedicated and non-COVID wards)	CDH : 254 (19.3%) NCDH : 543 (41.3 %) Mixed hospital : 519 (39.4%)
Working in critical care settings (ICU/CCU/ITU/ dialysis units/RTU)	337 (25.6%)
Performing intubation, tracheostomy, bone drilling surgeries and other aerosol generating procedures	236 (17.9%)
Presence of comorbidities :	
Diabetes Mellitus	110 (8.4%)
Hypertension	143 (10.9%)
Dyslipidemia	72 (5.5%)
Atherosclerotic cardiovascular disease	23 (1.7%)
COPD/Bronchial asthma	50 (3.8%)
Chronic kidney disease/Chronic liver disease	9 (6.8%)
HIV or other immunosuppression disorders	7(0.5%)
Known malignancy	3 (2.3%)
Hypothyroidism	63 (4.8%)
Autoimmune diseases (excluding Hashimoto's thyroiditis)	25 (19%)
≥ 2 comorbidities	97 (7.4%)
Drug history :	
Receiving steroids / other immunosuppressants	45 (3.4%)
Receiving monoclonal antibodies	0
Addiction :	
Smoking	170 (12.9%)
Alcohol	119 (9%)
Other addiction	25 (1.9%)
Agents used for COVID-19 prophylaxis :	
Hydroxychloroquine	412 (31.3)
Ivermectin	128 (9.7%)
Multivitamin	417 (31.7%)
Vitamin D	249 (18.9%)
Famotidine/ Other H2 antihistaminics	60 (4.6%)
Zinc	316 (24%)

p=0.03 and 9.1% versus 3.4%, p = 0.0002). Ivermectin use was slightly higher in the group not having SARS-CoV2 IgG antibodies (8.6% versus 9.8%, p = 0.6).

Upon multiple regression analysis, working in mixed hospitals, being a HCP other than doctor/nurse, presence of Diabetes Mellitus, presence of ≥ 2 comorbidities and the use of Hydroxychloroquine and Famotidine for pharmacologic prophylaxis were found as significant independent predictors for the development of SARS-CoV2-IgG among HCP (Table 4).

Personal protective behavior including the use of Personal Protective Equipment (PPE) gears, sanitisers or hand washing were similar in both groups. 95% of the participants used N95 masks, 3% used triple layered masks and 1% used cloth masks while at hospital. Masks were worn all the time at hospital in 80% of the participants, and doffed off at home (68%), in the car (22%) or disposed in the hospital (10%). Reuse of N95 masks was quite common (56%) mostly at an interval of 4-5 days. PPE kits were used by most during duty hours in COVID dedicated wards/hospitals. Head shields were used by 66%, surgical caps in 70%, gloves in 50% of the participants. 90% used alcohol based hand sanitisers while hand washing with soap and water was practised by around 56%, mostly before meals.

Out of the 154 participants with a personal h/o rt-PCR proven COVID-19 infection, n=35(22.73%) participants couldn't mount a IgG antibody response while n = 110 (71.42%) were positive for SARS-CoV2-IgG. Remaining nine had an indeterminate response. The median time from symptoms of COVID-19 infection to IgG antibody testing were not different in the two groups with and without SARS-CoV2-IgG (7.3 versus 8.8

weeks, p=0.12). Neither were there any differences in median age, severity of infection or the number of symptoms between the two groups.

We also compared the group with SARS-CoV2-IgG seropositivity but without personal h/o COVID-19 infection (n=208) with a group having personal history of COVID-19 infection and positive SARS-CoV2-IgG antibodies (n=110) in order to identify risk factors or

Table 2 — Comparison of parameters between asymptomatic healthcare workers with SARS-CoV-2 IgG antibodies versus those who did not have SARS-CoV2 IgG antibodies

Parameter	SARS CoV-2 IgG + N = 208	SARS CoV-2 IgG -ve N = 1100	p value
Mean age in years (SD)	38.5(0.82)	38.6 (0.36)	0.88
Mean BMI in kg/m ² (SD)	25.4 (0.6)	25.1(0.16)	0.96
Designation	D : 28 (13.5%) N : 73 (35.1%) O : 107 (51.4%)	D : 283 (25.7%) N : 393 (35.7%) O : 424 (38.5%)	0.0001
Type of hospital :			
CDH :	26 (12.5%)	225 (20.5%)	<0.0001
NCDH :	62 (29.8%)	479 (43.5%)	
MIXED :	120 (57.7%)	396 (36%)	
Working in critical care units/emergencies	46 (22.1%)	285 (25.9%)	0.26
Performing intubation, tracheostomy, other aerosol generating procedures	34 (16.3 %)	197 (17.9%)	0.66
Presence of comorbidities :			
Diabetes Mellitus	35 (16.8%)	69 (6.3%)	<0.0001
Hypertension	21 (10.1%)	119 (10.8%)	0.77
Dyslipidemia	8 (3.8%)	61 (5.5%)	0.31
Atherosclerotic cardiovascular disease	4 (1.9%)	19 (1.7%)	0.78
COPD/Bronchial asthma	7 (3.4%)	41 (3.7%)	1
CKD/CLD	3 (1.4%)	6 (5.5%)	0.16
HIV or other immunosuppression disorders	2 (1%)	5 (0.5%)	0.35
Known malignancy	1 (0.5%)	2 (0.2%)	0.41
Hypothyroidism	10 (4.8%)	52 (4.7%)	0.96
Autoimmune diseases (excluding Hashimoto's thyroiditis)	9 (4.3%)	14(1.3%)	0.002
>2 comorbidities	24 (11.5 %)	72 (6.5%)	0.011
On steroids/immunosuppressants	16 (7.7%)	29(2.6%)	0.0002
Addiction :			
Smoking	21 (10.1%)	148(13.5%)	0.185
Alcohol	16 (7.7%)	102 (9.3%)	0.729
Other addiction	5 (2.4%)	20 (1.8%)	0.579
Agents used for prophylaxis :			
Hydroxychloroquine	78 (37.5%)	331 (30.1%)	0.03
Ivermectin	18 (8.6%)	108 (9.8%)	0.6
Multivitamin	76 (36.5%)	339 (30.8%)	0.10
Vitamin D	36 (17.3%)	211(19.2%)	0.63
Famotidine/ Other H2 antihistaminics	19 (9.1%)	38 (3.4%)	0.0002
Zinc	59 (28.3%)	257(23.4%)	0.122
Any	93 (44.7%)	514 (46.4%)	0.557

SD = Standard Deviation, D = Doctors, N = Nurses , O = Other healthcare staff, CDH = COVID dedicated hospital, NCDH = Non COVID dedicated hospital, C = COVID wards/OPDs, NC = Non COVID wards/OPDs, COPD = Chronic Obstructive Pulmonary Disease, CKD = Chronic Kidney Disease, CLD = Chronic Liver Disease

protective factors that might contribute to manifestations or severity of COVID-19 infections. Compared to asymptomatic seroconverters, those with symptomatic COVID-19 infections and SARS-CoV2-IgG were older in age (43.5 versus 38.5 years, p= 0.004), majority were doctors (34.5% versus 13.5%, p =0.019) , working in COVID-19 dedicated hospitals (24.6 % versus 12.5% , p<0.0001), worked in critical care settings/emergencies (34.5% versus 22.1%, p =0.017) and/or performing aerosol generating procedures (27.3% versus 16.3%, p=0.027). Participants with symptomatic COVID-19 infections and SARS-CoV2-IgG were also more likely to have ≥2 co-morbidities (20% versus 11.5%, p=0.041), established atherosclerotic cardiovascular disease (ASCVD) (8.2% versus 1.9%, p=0.014) and COPD (10% versus 3.4%, p=0.021) (Table 3). There were no significant differences in the use of pharmacologic prophylaxis with most agents in the groups except ivermectin use which was higher in the group of asymptomatic seroconverters (8.7% versus 1.8%, p=0.017). Upon binary logistic regression, working in a mixed hospital, having COPD as a co-morbidity were found to be independent risk factors for development of symptomatic COVID-19 infection whereas ivermectin prophylaxis was found to be a significant negative predictor for the same (Table 4) .

DISCUSSION

In our study involving multiple hospitals in Eastern India, the prevalence of IgG

seroconversion among HCP without a known history of COVID-19 infection was 15.8%. This was slightly higher than a study from Mumbai in whom the reported

Table 3 — Comparison of parameters between asymptomatic and symptomatic healthcareworkers with SARS-CoV2 IgG antibodies

Parameter	Participants with h/o COVID -19 infection and SARS CoV-2 IgG + (n = 110)	Participants without h/o COVID -19 infection SARS CoV2 Ig G + N = 208	p value
Mean age in years (SD)	43.5 (1.5)	38.5 (0.82)	0.004
Mean BMI in kg/m ² (SD)	24.7 (0.6)	25.4 (0.6)	0.46
Type of hospital			0.019
CDH:	18(24.6%)	26 (12.5%)	
MIXED:	58(52.7%)	120 (57.7%)	
NON CDH:	25(22.7%)	62(29.8%)	
Working in critical care settings / emergencies	38 (34.5%)	46 (22.1%)	0.017
Performing intubation, tracheostomy, other aerosol generating procedures	30 (27.3%)	34 (16.3%)	0.027
Designation :			0.0001
D :	38 (34.5%)	28 (13.5%)	
N :	42 (38.2%)	73 (35.1 %)	
O :	30 (27.3%)	107 (51.4%)	
Presence of comorbidities :			
Diabetes Mellitus	17 (15.5%)	35 (16.8%)	0.874
Hypertension	11 (9.4%)	21 (10.1%)	0.978
Dyslipidemia	7 (6.4%)	8(3.8%)	0.405
Atherosclerotic cardiovascular disease	9(8.2%)	4(1.9%)	0.014
COPD/Bronchial asthma	11(10%)	7(3.4%)	0.021
CKD/CLD	5(4.5%)	3 (1.4%)	1
HIV or other immunosuppression disorders	0	2	
Known malignancy	0	1	
Hypothyroidism	3 (2.7%)	10 (4.8%)	0.554
Autoimmune diseases (excluding Hashimoto's thyroiditis)	5(4.5%)	9(4.3%)	1
≥2 comorbidities	22 (20%)	24 (11.5 %)	0.041
On Glucocorticoids/ other immunosuppressants	6(5.5%)	16(7.7%)	0.454
Smoking	14 (12.7%)	21 (10.1%)	0.476
Alcohol	8 (7.3%)	16 (7.7%)	0.5
Other addiction	0	5 (2.4%)	
Prophylaxis used :			
Hydroxychloroquine	46 (41.1%)	78 (37.5%)	0.532
Ivermectin	2 (1.8%)	18 (8.7%)	0.017
Multivitamin	55 (46.3%)	76 (36.5%)	0.080
Vitamin D	28 (25.5%)	36 (17.3%)	0.085
Famotidine/ Other H2 antihistaminics	12 (10.9%)	19 (9.1%)	0.692
Zinc	38 (34.5%)	59 (28.3%)	0.254

SD = Standard Deviation, D = Doctors, N = Nurses , O = Other healthcare staff, CDH = COVID dedicated hospital, NCDH = Non COVID dedicated hospital, C = COVID wards/OPDs, NC = Non COVID wards/OPDs, COPD = Chronic Obstructive Pulmonary Disease, CKD = Chronic Kidney Disease, CLD = Chronic Liver Disease

Table 4 — Independent predictors for asymptomatic seroconversion and of symptomatic COVID-19 infection on multivariate logistic regression

Parameter	p value	OR (CI)
Independent risk factors for having contracted COVID-19 infection among asymptomatic healthcare workers		
Working in a mixed hospital	0.008	2.45 (1.61 -3.74)
Designation :		
Nurse	<0.001	3.03 (1.76 – 5.21)
Other healthcare staff		3.69 (2.07 – 6.59)
Diabetes Mellitus	<0.001	2.38 (1.46 – 3.89)
Presence of ≥ 2 comorbidities	<0.001	4.35 (2.37 – 8.01)
Prophylactic use of Hydroxychloroquine	<0.001	1.97 (1.36 – 2.83)
Prophylactic use of Famotidine	0.03	2.02 (1.07 – 3.82)
Independent risk factors for symptomatic COVID-19 infection		
Working in a COVID hospital	0.03	2.32 (1.09 – 4.92)
COPD	0.075	4.15 (1.32 – 13.02)
Prophylactic use of Ivermectin	0.006	0.11 (0.01 – 0.52)

prevalence was 11.1%, at a time when the city was one of the worst affected in the nation⁹.

We found a higher risk of COVID-19 infection in HCP working in mixed hospitals rather than COVID-19-dedicated hospitals. However, those working in COVID-19-dedicated hospitals had a higher likelihood of developing symptomatic COVID-19 infection. HCP other than doctors/nurses were at a higher likelihood of having contracted asymptomatic COVID-19 infection; whereas doctors had higher chances of developing symptomatic COVID-19 infection. Our findings were similar to the study from Mumbai where seroprevalence was significantly higher in ancillary workers (18.5%) and also higher in non-COVID-19 Hospitals⁹. Published data on community seroprevalence of COVID-19 in India is around 6.6%¹⁰. The overall modest prevalence of infection among the HCPs, especially non-doctors and nurses and rather lower prevalence in COVID-19 dedicated hospitals may indicate community source of infection and also hint at the need for universal vaccination of all HCP as well as community dwellers.

We didn't find an increased risk of contracting COVID-19 infection in those working in critical care settings. However, those working in COVID wards/OPDS, in critical care settings and/or performing aerosol generating procedures were at higher risk of developing symptomatic COVID-19 infection rather than being asymptomatic seroconverters. This is likely due

to exposure to higher viral load and reinforce the need for strict implementation of infection control measures in all areas of the hospital, and particularly in all critical care units of the hospital and wherever aerosol generating procedures or surgeries are being performed.

Results from different prior trials and meta-analyses have revealed that DM, hypertension, ASCVD, COPD, dyslipidemia could be independent predictors for severity and mortality in COVID-19 infection¹¹⁻¹³. In the current study, on multiple logistic regression analysis, Diabetes mellitus and the presence of multiple comorbidities were found to be independent risk factors for asymptomatic COVID-19 infection whereas the presence of COPD and multiple comorbidities were independent risk factors for symptomatic COVID-19 infection.

The presence of autoimmune diseases was significantly higher in those with COVID-19 seroconversion, although it was not an independent risk factor. Around one third of these participants were receiving steroids or immunosuppressants for their underlying autoimmune diseases. While the prevalence of middle aged female nurses could have a bearing on these results, these diseases could also lead to altered immune response to COVID-19 infection. Few studies have reported autoimmune systemic conditions to be an independent risk factor predicting hospitalisation in COVID-19 patients¹⁴. The role of steroids or other immunosuppressants in enhancing the risk or severity of COVID-19 is unclear. There is a suggestion that low dose prednisolone and tacrolimus might have some beneficial effects on COVID-19 infection whereas with other agents, there is no definite evidence to suggest an enhanced risk¹⁴. However, we don't have data on the multitude of chronic immunosuppressant therapy being used.

Though there are some evidence favoring ivermectin, hydroxychloroquine, famotidine and Vitamin D in preventing or controlling the severity of COVID-19 infection, there is very low certainty of evidence¹⁵⁻²⁰. In our study, use of Hydroxychloroquine and Famotidine were higher in those having contracted COVID-19 infection. Ivermectin use was an independent negative predictor of symptomatic COVID-19 infection.

Our study also revealed that out of those with a personal h/o COVID-19 infection, around one-fourths didn't develop detectable IgG antibodies, even though testing was conducted within a median time of 8.1

weeks from the time to first symptom. We could not identify any risk factors that could predict seronegativity despite having had symptomatic COVID-19 infection in our cohort. This again re-emphasises the need to vaccinate all, irrespective of a prior history of COVID-19 infection.

This study had few limitations. Questionnaires were not anonymous and therefore subject to volition of the participants. The ELISA kit used was not quantitative. Our results could be biased due to greater representation of middle aged nurses and "other" healthcare personnel.

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REFERENCES

- 1 Available from : <https://www.icmr.gov.in/ckitevaluation.html>
- 2 Lai X, Wang M, Qin C, Tan L, Ran L, Chen D, *et al* — Coronavirus disease 2019 (COVID-2019) infection among health care workers and implications for prevention measures in a tertiary hospital in Wuhan, China. *JAMA network open* 2020; **3(5)**: e209666-.
- 3 Barrett ES, Horton DB, Roy J, Gennaro ML, Brooks A, Tischfield J, *et al* — Prevalence of SARS-CoV-2 infection in previously undiagnosed health care workers at the onset of the US COVID-19 epidemic. *MedRxiv*. 2020 Jan 1.
- 4 Nguyen LH, Drew DA, Joshi AD, Guo CG, Ma W, Mehta RS, *et al* — Risk of COVID-19 among frontline healthcare workers. *MedRxiv*. 2020 Jan 1.
- 5 Gómez-Ochoa SA, Franco OH, Rojas LZ, Raguindin PF, Roa-Díaz ZM, Wyssmann BM, *et al* — COVID-19 in health-care workers: a living systematic review and meta-analysis of prevalence, risk factors, clinical characteristics, and outcomes. *American Journal of Epidemiology* 2021; **190(1)**: 161-75.
- 6 Kumar A, Sathyapalan D, Ramachandran A, Subhash K, Biswas L, Beena KV — SARS-CoV-2 antibodies in healthcare workers in a large university hospital, Kerala, India. *Clinical Microbiology and Infection* 2020 Sep 16.
- 7 Hawaldar R, Sodani S, Sodani V, Sodani RK — Seroprevalence of COVID-19 infection among healthcare professionals in Central India using SARS-CoV-2 antibody test. *The Journal of Community Health Management* 2020; **7(4)**: 146-51.
- 8 Kumar N, Bhartiya S, Desai S, Mutha A, Beldar A, Singh T — Seroprevalence of Antibodies Against SARS-CoV-2 Among Health Care Workers in Mumbai, India. *Asia Pacific Journal of Public Health* 2020; **1(1)**: 1010539520977307.
- 9 Kumar N, Bhartiya S, Desai S, Mutha A, Beldar A, Singh T — Seroprevalence of Antibodies Against SARS-CoV-2 Among Health Care Workers in Mumbai, India. *Asia Pacific Journal of Public Health* 2020; **1(1)**: 1010539520977307.
- 10 Murhekar MV, Bhatnagar T, Selvaraju S, Saravanakumar V, Thangaraj JW, Shah N, *et al* — SARS-CoV-2 antibody seroprevalence in India, August–September, 2020: findings from the second nationwide household serosurvey. *The Lancet Global Health* 2021; **27(1)**.
- 11 Meng M, Zhao Q, Kumar R, Bai C, Deng Y, Wan B — Impact of cardiovascular and metabolic diseases on the severity of COVID-19: a systematic review and meta-analysis. *Aging (Albany NY)* 2020; **12(22)**: 23409.
- 12 Grasselli G, Greco M, Zanella A, Albano G, Antonelli M, Bellani G, *et al* — Risk factors associated with mortality among patients with COVID-19 in intensive care units in Lombardy, Italy. *JAMA Internal Medicine* 2020; **180(10)**: 1345-55.
- 13 Fang X, Li S, Yu H, Wang P, Zhang Y, Chen Z, *et al* — Epidemiological, comorbidity factors with severity and prognosis of COVID-19: a systematic review and meta-analysis. *Aging (Albany NY)* 2020; **12(13)**: 12493.
- 14 Nuñez DD, Leon L, Mucientes A, Rodriguez-Rodriguez L, Urgelles JF, García AM, *et al* — Risk factors for hospital admissions related to COVID-19 in patients with autoimmune inflammatory rheumatic diseases. *Annals of the Rheumatic Diseases* 2020; **79(11)**: 1393-9.
- 15 Hernandez AV, Roman YM, Pasupuleti V, Barboza JJ, White CM — Hydroxychloroquine or chloroquine for treatment or prophylaxis of COVID-19: a living systematic review. *Annals of Internal Medicine* 2020; **173(4)**: 287-96.
- 16 Behera P, Patro BK, Singh AK, Chandanshive PD, Ravikumara SR, Pradhan SK, *et al* — Role of ivermectin in the prevention of COVID-19 infection among healthcare workers in India: A matched case-control study. *medRxiv*. 2020 Jan 1.
- 17 Grant WB, Baggerly CA, Lahore H — Reply: "Vitamin D Supplementation in Influenza and COVID-19 Infections. Comment on: Evidence That Vitamin D Supplementation Could Reduce Risk of Influenza and COVID-19 Infections and Deaths *Nutrients* 2020, 12 (4), 988". *Nutrients* 2020; **12(6)**: 1620.
- 18 Jayawardena R, Sooriyaarachchi P, Chourdakis M, Jeewandara C, Ranasinghe P — Enhancing immunity in viral infections, with special emphasis on COVID-19: A review. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*. 2020; **14(4)**: 367-82.
- 19 Pal A, Squitti R, Picozza M, Pawar A, Rongioletti M, Dutta AK, *et al* — Zinc and COVID-19: basis of current clinical trials. *Biological Trace Element Research* 2020; Oct 22:1-1.
- 20 Malone RW, Tisdall P, Fremont-Smith P, Liu Y, Huang XP, White KM, *et al* — COVID-19: Famotidine, histamine, mast cells, and mechanisms.