Global Journal of Medicine & Public Health

Comparative evaluation of varied antibody response to SARS-CoV-2in asymptomatic High risk versus Low risk population: A cross sectional serosurvey at Sirmour District, Himachal Pradesh, India

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ABSTRACT

Covid -19 disease is a respiratory illness caused by novel Severe Acute Respiratory Syndrome Corona virus-2 (SARS CoV-2). Serological testing in Covid -19 infection can facilitate diagnostic utility for case management especially in later stages of the disease when the sensitivity of RT-PCR to diagnose COVID -19 lower. There are limited studies from low and middle-income countries like India regarding this. So, this study was designed for Comparative evaluation of the varied antibody response to SARS-CoV-2 in asymptomatic high risk versus low risk population at District level.

Method

High risk and low risk individuals were selected based on convenience sampling at the various health institutes of District at Block level. ELISA IgG blood test kits provided by the state government for serosurvey were used. CovidKavach Anti SARSCoV-2 Human Ig ELISA kit intended for detection of IgG antibodies, manufactured by Trivitron health care and validated by ICMR, NIV Pune was used.

Results

Seroprevalence of SARS COV2 was assessed among 470 health care workers and 331 participants from general population. Overall seropositivity for SARS CoV 2 was present in 61(12.9%) health care workers. No significant difference was present in various parameters like age, gender and profession between seropositive and seronegative health care workers except block wise distribution ($p<0.001$). Among general population, overall seropositivity for SARS CoV 2 was present in 30/331(9.0%). Seroprevalence in this study is seen to be higher in males than in females, both in general population and health care workers (HCW). However, no correlation was found between Diabetes, Asthma or Hypertensive patients and IgG positivity among HCW or general population. The study highlights the role of seroprevalence detection in asymptomatic or undetected infections in both groups.

GJMEDPH 2025; Vol. 14, issue 3 | OPEN ACCESS

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Conflict of Interest—none | Funding—none

INTRODUCTION

Covid -19 disease is a respiratory illness caused by notorious Severe Acute Respiratory Syndrome Corona virus-2 (SARS CoV-2). The seroprevalence surveys in Covid-19 disease are of utmost significance in understanding the epidemiology of the disease and for developing various types of strategies to contain the transmission. As per the recommendations by WHO, the population based seroprevalence studies are required for assessment of level of infection in community and hence planning recommendations for various measures of containment[1].Serological testing in Covid -19 infection can facilitate diagnostic utility for case management especially in later stages of the disease when the sensitivity of RT-PCR to diagnose COVID -19 lower[2,3,4]. Literature review shows growing number of seroprevalence surveys on representative samples from across the globe[5,6,7] but there are limited studies from low and middle-income countries like India [8,9]. Conducting cross sectional seroprevalence studies gives a valuable insight to the extent of spread of infection in the community. Based on the cases of Covid -19 disease and adjusted seroprevalence of 0.73 per cent, the estimated infections in our country were 82-130 for every RT-PCR confirmed case of COVID-19.The high infection to case ratio in India could be due to the prioritization of testing among symptomatic patients or the differences in testing rates across the States [10]. It has been seen in various sero-survey studies that around 2-8.5% of the confirmed Covid-19 patients may not have antibodies in their serum. The individuals who do not seroconvert even weeks after infection are younger than seroconverted. The seroconverted have also been found to have higher rate of comorbidities like diabetes, hypertension and obesity and higher inflammatory markers like C-Reactive Protein (CRP) [11, 12].With spread of infection through contact or aerosol exposure to the virus, it has been challenging to minimize community spread. The situation is even worsened by the spread of the virus by asymptomatic carriers, many of them unaware of being viral carriers. [13] Research experience gained during the severe acute respiratory syndrome coronavirus epidemic revealed that health care workers (HCWs) are considered to be a high-risk population for the acquisition of SARS-CoV-2. They are exposed to hazards that place them at risk of infection [14]. Studies during and around Covid active infection have shown infection rates of up to 14% in symptomatic and 7.1% in asymptomatic healthcare workers which are higher than general population studies [15,16]. However, another study depicted cumulative prevalence of 16.5% in HCW and 23.5% in the general population with a large number of asymptomatic individuals [17]. Seroprevalence assessment in an Indian study depicted that 4.1 percent of the asymptomatic general population were exposed to SARS-CoV-2 infection [18]. Few studies have reported both current and past infection among health care providers using either or both reverse transcriptase polymerase chain reaction (RT-PCR) and serological testing. [15,19] Recommendations are there for screening of all groups of HCWs exposed to COVID-19 patients. Combination of molecular and serological diagnosis helps in more reliable capture of information on SARS-CoV-2 infection dynamics in a highly exposed population. Both these approaches help in characterization of asymptomatic infections and post- infection immunity in individuals exposed to risk of Covid-19 infection [13]. There is high seroprevalence of SARS-CoV-2 antibodies in healthcare workers with and without prior symptomatic illness suggesting differential occupational risk [20]. With this background, this study has been planned and conducted.

Methodology

Primary Objective:-

Comparative evaluation of the varied antibody response to SARS-CoV-2 in asymptomatic high risk versus low risk population at Sirmour District level, Himachal Pradesh.

Secondary Objectives:-

i. Comparative estimation of age and sex specific seroprevalence.
ii. Determination of socio-demographic risk factors and other risk factors like comorbidities for SARS-CoV-2 infection.
iii. Determination of immunity (IgG) status conferred by natural infection of SARS-

CoV-2 in individuals, previously RTPCR positive.

Study design and setting: Cross Sectional Study at Sirmour District level, Himachal Pradesh, which includes both rural and urban population

Study period: October 2020- December 2020

Inclusion criteria:

i. High Risk Groups (Health care workers)
ii. Low risk groups: OPD attendees with non-ILI (Influenza like illness) and pregnant ladies

Exclusion criteria:

i. Those who did not give consent
ii. Age less than18 years
iii. Symptoms of COVID-19 on the day of survey
iv. Those health care workers at home due to any symptomatic illnesses or any other reason.

Sample size: Sample size calculated based on formula N=t2*PQ/d2, where t is 95% confidence interval (1.96), P is the prevalence of seroprevalence in asymptomatic health care workers as 24.4% [20], d is degree of accuracy as 5%. Sample size is calculated as 320. So, a sample of 320 health care workers was required to be enrolled with equal representation of the general population.

List of health care workers from all the study sites was prepared as an initial step. Systematic random sampling method was considered to meet the sample size. Health care workers were categorised as Doctors (Clinical, Pre-Clinical and Para-Clinical),Paramedical staff (Nurses, Pharmacists, Laboratory Technicians and attendants, Health workers and health educators),Administrative supportive staff(Clerical, Data entry operators) and other supportive staff (Drivers, Peons, SafaiKaramcharis).Low risk individuals were selected based on Convenience sampling at the various Block level health institutes of the District. OPD attendees with non- ILI (Influenza like illness) and pregnant ladies were taken as low risk individuals.

Data collection, and testing

Separate Questionnaires were used for High and low risk participants. For each participant detailed proforma was administered to collect socio-demographic data (age, gender, locality, Profession), comorbidities (Diabetes, Hypertension, Heart disease, Chronic kidney disease, COPD, immunocompromised status, history of cancers etc), past history of Covid 19 infection, time since onset of illness to testing and history of contact with Covid-19 patient. ELISA IgG blood test kits provided by the state government for serosurvey were used. CovidKavach Anti SARSCoV-2 Human Ig ELISA kit intended for detection of IgG antibodies, manufactured by Trivitron health care and validated by ICMR, NIV Pune was used. 3ml of blood was collected by trained laboratory technician from each participant via venepuncture. Further, the tube with the blood sample was left at room temperature for clot formation (Approx. 30Mins). Clotted whole blood was kept in the refrigerator and sent to the laboratory on the same day. Documentation of the test result was done at the laboratory.

Results and Analysis:

Records of study were entered in the google forms and spread sheet was extracted followed by analysis using SPSS [Statistical Package for Social Sciences] version 25. Analysis included percentage, range, mean, standard deviation and unpaired T test.

Table 1: Demographic profile of Health care workers

	Seropositive n (%)	Seronegative n (%)	Seroprevalence (%)	P value
N (470)	61(12.9)	409(87.0)	12.9	
Sex				
Male (203)	28(45.9)	175(42.7)	13.7	
Female (267)	33(54.0)	234(57.2)	12.3	0.647
Age				
Years (Range)	39(21-69)	39(23-64)		0.845

Age group				
21-30 (114)	13(21.3)	101(24.6)	11.4	
31-40 (158)	21(34.4)	137(33.4)	13.2	0.304
41-50 (119)	19(31.1)	100(24.4)	15.9	
51-60 (73)	6(9.8)	67(16.3)	8.2	
>60 (6)	2(3.2)	4(0.9)	33.3	
Profession				
Doctors (109)	10(16.3)	99(24.2)	9.17	
Paramedical staff (233)	33(54.0)	200(48.8)	14.1	
Administrative supporting staff (76)	14(22.9)	62(15.1)	18.4	0.193
Other supporting staff (52)	4(6.5)	48(11.7)	7.6	
Block				
I (296)	21(34.4)	275(67.2)	7.6	
II (60)	20(32.7)	40(9.7)	33.3	
III (22)	13(21.3)	9(2.2)	59.0	<0.001
IV (28)	5(8.1)	23(5.6)	17.8	
V (13)	1(1.6)	12(2.9)	7.6	
VI (51)	1(1.6)	50(12.2)	1.9	

Table 2: Demographic profile of General population

	Seropositive n (%)	Seronegative n (%)	Seroprevalence (%)	P value
N (331)	30(9.1)	301(90.9)	9.0	
Category				
Out Patient Department (n=241)	25(83.3)	216(65.2)	10.3	0.149
Obstetrics Out Patient Departments(n=90)	5(16.7)	85(25.6)	5.5	
Sex				
Male (74)	9 (30)	65(21.5)	12.1	
Female (257)	21(70)	236(78.4)	8.1	0.292
Age				
Years (Range)	39.53(11-76)	36.57(11-80)		0.117
Age group				
11-20 (156)	11(36.6)	145(48.1)	7.05	
21-30 (50)	7(23.3)	43(14.2)	14.0	
31-40 (47)	5(16.6)	42(13.9)	10.6	0.383
41-50 (28)	2(6.6)	26(8.6)	7.1	
51-60 (27)	3(10.0)	24(7.9)	11.1	
>60 (23)	2(6.6)	21(6.9)	8.6	

Block				
I (185)	16(53.3)	169(56.1)	8.64	
II (18)	5(16.6)	13(4.3)	27.7	
III (55)	2(6.6)	53(17.6)	3.6	0.083
IV (10)	1(3.3)	9(2.9)	10	
V(29)	3(10.0)	26(8.6)	10.3	
VI (34)	3(10.0)	31(10.2)	8.8	

Table 3: Comparative comorbidity profile between Health care workers and general Population

Comorbidities						
Health care workers				General population		
Comorbidity	Seropositive	Seronegative	P value	Seropositive	Seronegative	P value
Asthma	1(1.6)	1(0.24)		0(0)	0(0)	0.531
Hypertension	0(0)	6(1.46)	0.061	2(6.6)	12(3.9)	
Diabetes	0(0)	2(0.48)		3(10.0)	16(5.3)	
Hypertension and Diabetes	0(0)	2(0.48)		0(0)	0(0)	

Table 4: RTPCR/Antigen test positivity within last 6 months among seropositive health care workers and general population

Category	RTPCR/Antigen test positive for last 6 months	P value
Health care workers (n=61)	17 (27.8%)	<0.001
General population (n=30)	1(3.33%)	

Seroprevalence of SARS COV2 was assessed among 470 health care workers and 331 participants from general population. Among health care workers 203(43.1%) were males and 267(62.1%) were females. Average age of the participants was 39(21-69) years. Majority 158(33.6%) health care workers were in the age group of 31-40 years.Profession-wise segregation of health care workers comprised of 109 (23.1%) doctors,233(49.5%) paramedical staff,76(16.1%) administrative supportive staff and 52(11.6%) other supportive staff. No significant difference was present in various parameters like age, gender and profession between seropositive and seronegative health care workers except block wise distribution (p<0.001). Seroprevalence for SARS CoV2 was present among 28/203(13.7%) males and 33/267(12.3%)females. Overall seropositivity for SARS CoV 2 was present in 61(12.9%) health care workers. RTPCR or Antigen test positivity for last 6 months was present among 17/61 (27.8%) health care workers. Participants from general population included 241(72.8%) patients from general outpatient department and 90(27.1%) patients from obstetrics outpatient department. Gender distribution included 74(22.3%)males and 257(77.6%) females. Average age of the participants was 37.5(11-80)years. Majority 156(47.1%) general population were in the age group of 11-20 years. No significant difference was present in various parameters like age, gender and block wise distribution between seropositive and seronegative participants from general population. Seroprevalence for SARS CoV2 was present among 9/74(12.1%) males and 21/257(8%) females among

general population and, overall seropositivity for SARS CoV 2 was present in 30/331(9.0%). RTPCR or Antigen test positivity for last 6 months was present in only one patient (3.33%).. There was no significant difference in comparative comorbidity profile between health care workers and general population.

DISCUSSION

As per National wide sero survey, conducted by ICMR in 2020(16), nation wise seroprevalence was 0.73%. The same year, seroprevalance in Delhi [17] was reported to be 22.86%, which is much higher as compared to seroprevalence seen in this study. This study reported seroprevalence of 9% in general population and 12.9% in HCW. As seroprevalance in Sirmour District area is still low, means majority of population in this area is still prone for infection.

Seroprevalence in this study is seen to be higher in males than in females, both in general population and HCW, which is in accordance to others studies [18,19,20] across the globe, though it was seen to be statistically insignificant. Both sex and age had no stastically significant difference. Another stastically significant finding in the study was block wise distribution of seroprevalence. It ranged from 59% in block III, 1.9% at block VI, seen to be least in case of HCW. Whereas in general population, seroprevalence was seen to be highest in (27.7%) block II, and lowest in block III (3.6%).

No correlation was found between Diabetes, Asthma or Hypertensive patients and IgG positivity among HCW or general population. This correlation stands in concordance with a study conducted by Li Guo in China in 2020 (3), but differs from South Korean study (21), which claims diabetes as risk factor for IgG seropositivity. In our study, we found 27.8%, of HCW as RT PCR positive for COVID-19withIgG antibodies and the percentage in general population was 3.33% and in other studies, it was found to be 36.67%(18) and 53% in a Delhi serosurvey [21]. There was very low level of seroconversion even in antigen positive SARS COV 2 6 months previous to the study. This indicates that previous infection with SARS- Cov2 does not provide long term immunity as determined by IgG seropositivity. So, there is a chance of reinfection even after recovery.

CONCLUSION

The study assessed the seroprevalence of SARS-CoV-2 among healthcare workers and the general population. Seropositivity was observed in 12.9% of healthcare workers and 9.0% of the general population, with no significant differences based on age, gender, or profession in either group. However, a significant block-wise difference was noted among healthcare workers. Past RT-PCR/antigen positivity was higher in healthcare workers (27.8%) compared to the general population (3.3%). The study highlights the role of asymptomatic or undetected infections in both groups.

Ethical considerations: All the data was stored securely under responsibility, with a focus on ensuring the participant's confidentiality. A database with password-restricted access was used. State Health Department was engaged to ensure smooth operationalization of the survey. Participant information sheet was provided in Hindi and English. Consent was implied within the purview of Covid-19 pandemic. Test results were conveyed to the participants well in time. Approval for the protocol was obtained from the Institutional Ethics Committee Dr YSPGMC, Nahan.

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