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ORIGINAL RESEARCH

A Cohort Study of Seroprevalence of Antibodies Against SARS-CoV-2 Infection Among Healthcare Workers at a Tertiary Hospital in Saudi Arabia

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Background: The nature of the healthcare workers' jobs standing at the frontline against the coronavirus disease 2019 (COVID-19) puts them at a higher risk of unknowingly contracting the disease and potentially contributing to the spread. This study aims to assess the overall positive seroconversion prevalence of SARS-CoV-2.

Methods: This is a longitudinal cohort study of healthcare workers at Johns Hopkins Aramco Healthcare (JHAH). JHAH is a tertiary hospital located in Dhahran serving patients in several districts in the Eastern Province of Saudi Arabia. Participants were recruited between June and December 2020. Each participant had a serology blood test and completed the World Health Organization's risk factor assessment questionnaire.

Results: This study included 682 participants working in JHAH, representing 15.7% of our population. Out of the 682 participants, 15.2% had a positive SARS-CoV-2 rt-PCR before taking part in the study. However, only 87 tested positive for SARS-CoV-2 antibodies, a prevalence of 12.7% of all participants. Out of the 87 positives for SARS-CoV-2 antibodies, 17 participants never tested positive for COVID-19 rt-PCR, a prevalence of 2.9%. Moreover, not properly using alcohol-based hand rub or soap and water after the risk of body fluid exposure and wearing personal protective equipment when indicated were found to be statistically significant to having a positive SARS-CoV-2 IgG assay.

Conclusion: Positive seroconversion rate was considerably low during the first wave of COVID-19 amongst JHAH's healthcare workers and similar to other healthcare organizations in Saudi Arabia. Seropositivity correlated significantly with following infection prevention and control recommendations.

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Keywords: COVID-19, coronavirus disease-2019, HCW, healthcare workers, prevalence, SARS-CoV-2

Introduction

Since the emergence of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the entire world had been threatened.[1] As of June 2022, nearly 538 million cases of coronavirus disease 2019 (COVID-19) have been reported with more than 6.3 million deaths worldwide.[2] The pandemic has affected the healthcare systems and resources severely in

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many countries, especially with the healthcare workers (HCWs) in the highest-risk group due to the nature of their job and increased exposure while closely interacting with infected individuals.[3]

There is a level of uncertainty of epidemiological, clinical, and virological characteristics associated with a novel virus and its severity and ability to spread amongst humans. With SARS-CoV-2′s high transmission rate, the disease caused a tremendous burden on the healthcare systems and frontline HCWs.[1] As a result of the disease's nature of transmission and the HCWs high risk of infection, they may have unknowingly contracted the disease and potentially contributed to the spread.[4] Several studies have reported that the evidence of COVID-19 infection among HCWs is growing with a current rate of 2.3% in Saudi Arabia[5] and up to 17.4% globally.[4] A number of these studies also reported that 38–48% of the HCWs with positive seroconversion never experienced any symptoms.[6,7]

Questions have been risen about using reverse transcription-polymerase chain reaction (rt-PCR) solely for infection screening as there is still little to be known about the SARS-CoV-2 virus and the knowledge of asymptomatic infections among HCWs is also limited.[8] Therefore, serological testing can provide information on the proportion of individuals who have been infected with COVID-19. It is crucial to monitor the prevalence of infection in critical subgroups of the population such as HCWs and nursing home employees.[9] This is beneficial for many vital reasons, for one, it will help determine risks and levels of exposure among staff and identify high-risk departments/wards. Moreover, information about current and previous infections can be useful for healthcare resource planning as well as for avoiding unnecessary quarantines for the staff.[9]

Healthcare workers are considered our shield against COVID-19, the nature of their job has placed them in the frontline to fight this pandemic globally placing them at the highest risk to contract an infection which might lead to a heavier burden on healthcare organizations.[10] A better understanding of the pattern and prevalence of the SARS-CoV-2 infection can guide HCWs for better protection as well as assistance to policymakers to develop policies and regulations for infection prevention and control in the clinical setting.[10] Therefore, it is crucial to understand and determine the correlation between the positive seroconversion and duration of immunity as well as the possibilities of reinfection amongst HCWs.[9]

This study aims to assess the immune status of HCWs at Johns Hopkins Aramco Healthcare (JHAH). We aim to assess the overall positive seroconversion prevalence of SARS-CoV-2 as well as the prevalence of asymptomatic infections. Moreover, we aim to assess the risk factors of seroconversion amongst HCWs using the World Health Organization's (WHO) protocol for assessment of potential risk factors for 2019-novel coronavirus (2019-nCoV) infection among healthcare workers in a healthcare setting as one of their Early Investigation protocols.[11]

Materials and Methods

Study Design

This is a longitudinal cohort study of healthcare workers at Johns Hopkins Aramco Healthcare (JHAH). JHAH is a tertiary hospital located in Dhahran serving patients in several districts in the Eastern Province of Saudi Arabia. JHAH's patients are Saudi Aramco employees and their dependents which entails a population of 300,000 people. The study took place from June 2020 until the end of April 2021.

The study complies with the Declaration of Helsinki and received JHAH's Institutional Board approval (IRB # 20-09) on the 13th of May 2020.

Study Population and Sample

Initially, the participants were randomly selected from JHAH's employees' database and invited to participate in the study via email. However, due to the slow recruitment, an open invitation was sent to all staff members through staff announcements in their emails. Recruitment was completed by December 2020, and follow-up appointments were carried out until April 2021. Participants were asked to visit the research team in 2 months period for a follow-up test. Participants with positive SARS-CoV-2 IgG assay were asked to return to the research team for a third follow-up visit. As of December 2020, JHAH had 3939 staff members and 383 housekeepers working in all departments. This study included 682 participants working in different departments at JHAH from front-liners dealing with COVID-19 patients on daily basis to administrators who had minimal contact with any patient.

Data Collection

Blood samples were collected from participants by a phlebotomist at the local hospital laboratory. The SARS-CoV-2 IgG assay results were then sent to the research team as positive or negative and their index which then entered into the study database.

The WHO Questionnaires extracted from their protocol for assessment of potential risk factors for 2019-novel coronavirus (2019-nCoV) were administered to all participants upon consenting to the study and before their blood collection appointments. All completed questionnaires were entered into the study database by two nurses and validated by the study's principal investigator.

ARCHITECT SARS-CoV-2 IgG Assay

ARCHITECT SARS-CoV-2 IgG Assay was used throughout the whole study. The assay is an automated, two-step immunoassay for the qualitative detection of IgG antibodies to SARS-CoV-2 in human serum using chemiluminescent microparticle immunoassay (CMIA) technology.

The index reference range interpretation for this qualitative IgG test is positive if the index was 1.4 or above and negative if the index was below 1.4.

Validation of SARS-CoV-2 IgG Testing

The validation study of the SARS-CoV-2 IgG test was carried out on Architect i2000SR System. Precision study with in-run and total is not applicable as this is a qualitative method. Positive and negative controls for SARS-CoV-2 IgG Assay were run daily for fifteen days, and it has been indicated acceptable result. A total of 23 patient serum specimens were tested on the Architect i2000SR System, and at the same time on the Architect i2000SR in King Fahad Specialist Hospital for the SARS-CoV-2 IgG test, and results were compared for parallel testing. The comparison study showed that the results of the SARS-CoV-2 IgG on the DH-Architect i2000SR System and KFSH-Architect i2000SR System were compared and correlated. The comparison study indicates 100% specificity and sensitivity. The validation study concluded that the SARS-CoV-2 IgG test performed on Architect i2000SR System is acceptable for patient testing.

Summary and Explanation of the Test

The assay is designed to detect IgG antibodies to the nucleocapsid protein of SARS-CoV-2 in serum from patients with signs and symptoms of infection who are suspected of coronavirus disease (COVID-19) or in serum of subjects that may have been infected by SARS-CoV-2. The SARS-CoV-2 IgG assay can be used as an indication of a possible recent infection. However, negative results do not rule out previous infections, especially for those who have been in contact with positive cases.

The incubation period of COVID-19 ranges between 1 and 14 days. The host immune system reacts to the infection by SARS-CoV-2 by producing specific antibodies. These antibodies have been reported to appear in serum or plasma of infected individuals after the detection of viral ribonucleic acid (RNA) in swabs and a few days to 2 weeks after the onset of symptoms. Specific IgG antibodies to SARS-CoV-2 are detectable during the symptomatic phase of the disease after RNA is no longer detectable.

The sensitivity of combining RNA with antibody results has been reported as above 99%. The persistence of IgG antibodies allows the identification of people who have been infected in the past, recovered from the illness, and possibly become immune.

Specimen

No special patient preparation was required. The serum is the recommended sample type for this assay, and it was separated from whole blood as soon as possible to avoid hemolysis to use non-hemolyzed samples. The volume of blood withdrawn from each participant was 10 mL for the test.

Serum samples were stored at a certain temperature as recommended by the manufacturer: 15 to 30 degree Celsius (°C) for two days, 2 to 8 °C for 7 days, or freeze the sample at below −20°C if testing was delayed for over 7 days. Therefore, frozen samples were completely thawed and mixed well (by low-speed vortex or by inverting 10 times) and

recentrifuged before testing. For Lipemic specimens, only clarified specimens excluding the lipemic material were used. Moreover, to ensure consistency in results, specimens were recentrifuged before testing as needed to omit fibrin, red blood cells, and/or other particulate matter. If any of these materials were observed, the specimen was mixed by low-speed vortex or by inverting 10 times before recentrifuge. Any heat-inactivated specimens, pooled specimens, grossly hemolyzed specimens, specimens with obvious microbial contamination, and specimens with fungal growth were rejected.

Equipment and Materials

The ARCHITECT i2000SR system was used for the serology test. The following materials and reagents were used to perform the test: reaction vessels, sample cups, septum, replacement caps, disposable waste containers, ARCHITECT SARS-CoV-2 IgG reagent kit, calibrator kit, and control kit. In addition to the pre-trigger solution, trigger solution, and wash buffer.

Procedure

Before loading the ARCHITECT SARS-CoV-2 IgG Reagent Kit on the system for the first time, the microparticle bottle required mixing to resuspend microparticles that may have settled during shipment, which was accomplished by inverting the microparticle bottle 30 times, visually inspect the bottle to ensure microparticles are resuspended, then the cap was removed and discarded. After that, while wearing clean gloves, the septum from the bag was carefully removed and snapped onto the top of the bottle. The IgG reagent kits were then loaded on the ARCHITECT I System, and calibration of the load was ordered as necessary and then the test was ordered. The ARCHITECT SARS-CoV-2 IgG Calibrator and Control were mixed by gentle inversion before use. The bottles were held vertically, and 4 drops of the calibrator or control were dispensed into the sample cup to obtain the recommended volume requirement for the system. Then, the samples were loaded into the system and processed.

To prevent potential interactions, daily maintenance before and following the batching of SARS-CoV-2 IgG samples was performed. Finally, for quality control, the ARCHITECT SARS-CoV-2 IgG Negative and Positive controls were run on each day of use before testing patients.

Statistical Analysis

The distribution of quantitative values of variables for the subjects has been examined with descriptive statistics (such as Mean, and Standard deviation). The distribution of all-qualitative (ie close-ended) values of variables for both demographic and research variables of the study samples has been examined with frequency tables. The association tables have been calculated by using the chi-square test with cross-tabulation. A P-value <0.05 is considered for statistical significance. Binary logistic regression has been used to predict the odds of the cases based on the independent variables which were the reported symptoms concerning the dependent variables such as the previous infection of COVID-19 and positive seroconversion. The statistical analysis has been done using SPSS (Statistical Package for Social Sciences) Package with version 25.

Results

A total of 682 HCWs consented to participate in the study. The overall participation rate was 15.7% among all the hospital staff. Out of the 682 participants, 52.8% were females, 39% were Saudi nationals, 88.2% were non-smokers, and 56.8% of the participants were clinicians (physicians and nurses), following that 26.3% are from supporting services departments (such as patient safety and quality improvement, maintenance, population health, and housekeeping), and finally 16.9% were from the applied medicine departments (such as rehabilitation, laboratory, and pharmacy). The mean age of the participants was 44.5 (±10), and the mean years of professional experience was 16 (±10) years (Table 1).

One hundred and twelve (15.2%) participants had a positive SARS-CoV-2 rt-PCR before taking part in the study. However, only 87 tested positive for SARS-CoV-2 antibodies, a prevalence of 12.7% of all participants. Out of the 87 positives for SARS-CoV-2 antibodies, 17 participants never tested positive for COVID-19 rt-PCR, a prevalence of 2.9% of all participants who never tested positive for COVID-19 rt-PCR (Table 1).

Table 1 Clinical and Non-Clinical Characteristics of the Study Participants

	Frequency	Percentage	Mean (SD)
Age			44.5(10.2)
Gender			
Male	360	47.2	
Female	322	52.8	
Nationality			
Saudi	248	39	
Non-Saudi	388	61	
Smoker			
Yes	87	11.8	
No	648	88.2	
Occupation			
Physician	181	28	
Nurse	186	28.8	
Applied medicines	109	16.9	
Supporting services	170	26.3	
Years of Experience			16(10.3)
Diagnosed with COVID-19 before serology testing			
Yes	112	15.2	
No	623	84.8	
SARS-COV-2 ANTIBODY			
Positive	87	12.7	
Negative	595	87.3	
Underlying medical conditions			
Obesity	115	15.6	
Cancer	12	1.6	
Diabetes	54	7.3	
HIV/other immune deficiency	5	0.7	
Heart disease	21	2.9	
Asthma	43	5.9	
Chronic lung disease	7	1.0	
Chronic liver disease	3	0.4	
Chronic hematological disorder	9	1.2	
Chronic kidney disease	4	0.5	
Chronic neurological impairment/ disease	5	0.7	
Organ or bone marrow recipient	3	0.4	
Pregnancy	6	0.8	

Of the initial participants, 665 completed the WHO's assessment questionnaire of potential risk factors for COVID-19 infection among healthcare workers in a healthcare setting. The most prevalent comorbidity was obesity (15.6%), then diabetes mellitus (7.3%), asthma (5.9%), heart diseases (2.9%), and cancer (1.6%) (Table 1).

Two factors were found statistically significant in the infection prevention and control measures to having a positive SARS-CoV-2 IgG assay. The first factor was using alcohol-based hand rub or soap and water after the risk of body fluid exposure with (P = 0.02, CI: 95%), and the second factor was wearing personal protective equipment (PPE) when indicated with (P = 0.03, CI: 95%) (Table 2). In addition, exposure to the community such as delivery personnel and/or family visits was not a statistically significant difference between positive and negative SARS-CoV-2 IgG assay (P > 0.05, CI: 95%), however, exposure to co-workers had a statistical significance to testing positive for COVID-19 rt-PCR with (P = 0.01, CI: 95%).

The 87 participants with positive SARS-CoV-2 IgG assay have experienced symptoms that were statistically significant compared to HCWs with negative serology. The most reported symptoms before taking part in the study were fever 38 (43.6%), chills 32 (36.7%), muscle aches 47 (54%), fatigue 47 (54%), joint ache 33 (37.9%), loss of appetite 33 (37.9%), headache 44 (50.5%), general malaise 34 (39%), diarrhea 25 (28.7%), shortness of breath 22 (25.2%), cough 38 (43.6%), runny nose 26 (29.8%), and sore throat 32 (36.7%) (Table 3). Moreover, obesity was the highest comorbidity reported, it was also significantly linked to all symptoms related to COVID-19 (P < 0.05, CI: 95%), while another comorbidity like diabetes was statistically insignificant to the exhibited symptoms (Table 4).

In the regression analysis, fever was the only common symptom with statistical significance to be reported by both participants who had tested positive for COVID-19 rt-PCR and SARS-CoV-2 IgG assay. Moreover, it was also found that it is 33% likely that participants with positive COVID-19 rt-PCR would suffer from cough, 24% are likely to report headaches, 22% are likely to feel fatigued, and it is also most likely that 5 out of 10 would suffer from conjunctivitis

Table 2 Cross Tabulation Between Positive SARS-CoV-2 IgG Assay and Infection Prevention and Control Measures

Infection Prevention and Control (IPC) Measures		COVID-19 Serology		Chi Square	P-value
		Positive	Negative		
Did you attend any IPC training within JHAH?	Yes	73 (15.2)	407 (84.8)	0.07	0.79
	No	27 (16.1)	141 (83.9)		
How much cumulative IPC training (standard precautions, additional precautions) have you had at JHAH?	Less than 2 hours	32 (14.7)	185 (85.3)	1.17	0.68
	More than 2 hours	65 (14.3)	399 (85.7)		
Do you follow the recommended hand hygiene practice?	Always as recommended	92 (15.9)	486 (84.1)	1.95	0.58
	Most of the time	14 (19.4)	58 (80.6)		
	Occasionally	0	3 (100)		
	N/A	0	4 (100)		
Do you use alcohol-based hand rub or soap and water before and after touching a patient?	Always as recommended	83 (17.1)	401 (82.9)	4.12	0.39
	Most of the time	8 (19.5)	33 (80.5)		
	Occasionally	1 (33.3)	2 (66.7)		
	Rarely	0	1 (100)		
	N/A	14 (10.9)	114 (89.1)		

(*Continued*)

Table 2 (Continued).

Infection Prevention and Control (IPC) Measures		COVID-19 Serology		Chi Square	P-value
		Positive	Negative		
Do you use alcohol-based hand rub or soap and water before cleaning/aseptic procedures?	Always as recommended	74 (16.4)	157 (86.3)	2.74	0.43
	Most of the time	6 (21.4)	408 (87)		
	Occasionally	1 (50)	1 (50)		
	N/A	23 (14.2)	139 (85.8)		
Do you use alcohol-based hand rub or soap and water after (risk of) body fluid exposure?	Always as recommended	81 (16.5)	410 (83.5)	12.28	0.02*
	Most of the time	6 (37.5)	10 (62.5)		
	Occasionally	1 (100)	0		
	Rarely	0	2 (100)		
	N/A	17 (12.5)	119 (87.5)		
Do you use alcohol-based hand rub or soap and water after touching a patient's surroundings?	Always as recommended	85 (71.3)	407 (82.7)	9.13	0.06
	Most of the time	11 (20)	39 (78)		
	Occasionally	0	2 (100)		
	Rarely	1 (50)	1 (50)		
	N/A	8 (7.8)	95 (92.2)		
Do you follow IPC standard precautions when in contact with any patient?	Always as recommended	91 (16.3)	466 (83.7)	1.22	0.94
	Most of the time	6 (16.7)	30 (83.3)		
	Occasionally	1 (33.3)	2 (66.7)		
	Rarely	1 (20)	4 (80)		
	N/A	2 (10.5)	17 (89.5)		
	I do not know what IPC standard are	3 (18.8)	13 (81.3)		
Do you wear Personal protective Equipment (PPE) when indicated?	Always as recommended	90 (16.2)	465 (83.8)	11.02	0.03*
	Most of the time	7 (12.7)	51 (87.9)		
	Occasionally	3 (50)	3 (50)		
	Rarely	3 (37.5)	5 (62.5)		
	N/A	0	13 (100)		

Note: *Shows statistical significance with p value < 0.05.

(Table 5). However, no significance other than fever was found in the regression between positive SARS-CoV-2 IgG assay and symptom presentation.

In this study, standardized techniques and analytical methods have been adopted. The inclusion of symptoms in the regression analysis has been taken with the appropriate frequency to find the relationship between COVID-19 Positive

Table 3 Cross Tabulation Between Positive SARS-CoV-2 IgG Assay and Symptoms

Symptoms		SARS-COV-2 Antibody		Chi Square	P-value
		Positive	Negative		
Fever	Yes	38 (49.4)	39 (50.6)	100.73	0.000
	No	49 (8.3)	539 (91.7)		
Sore Throat	Yes	32 (25.8)	92 (74.2)	21.70	0.000
	No	55 (10.2)	486 (89.8)		
Cough	Yes	38 (36.2)	67 (63.8)	58.55	0.000
	No	49 (8.8)	511 (91.3)		
Runny Nose	Yes	26 (27.4)	69 (72.6)	19.89	0.000
	No	61 (10.7)	509 (89.3)		
Shortness of Breath	Yes	22 (32.4)	46 (67.6)	24.74	0.000
	No	65 (10.9)	532 (89.1)		
Chills	Yes	32 (45.7)	38 (54.3)	73.26	0.000
	No	55 (9.2)	540 (90.8)		
Vomiting	Yes	9 (37.5)	15 (62.5)	13.06	0.000
	No	78 (12.2)	563 (87.8)		
Nausea	Yes	21 (42)	29 (58)	39.76	0.000
	No	66 (10.7)	549 (89.3)		
Diarrhea	Yes	25 (32.5)	52 (67.5)	28.78	0.000
	No	62 (10.5)	526 (89.5)		
Headache	Yes	44 (34.9)	82 (65.1)	65.20	0.000
	No	43 (8.0)	496 (92.0)		
Rash	Yes	5 (26.3)	14 (73.7)	3.01	0.08
	No	82 (12.7)	564 (87.3)		
Conjunctivitis	Yes	4 (17.4)	19 (82.6)	0.39	0.53
	No	83 (12.9)	559 (87.1)		
Muscle Aches	Yes	47 (45.2)	57 (54.8)	111.78	0.000
	No	40 (7.1)	521 (92.9)		
Joint Aches	Yes	33 (47.1)	37 (52.9)	79.82	0.000
	No	54 (9.1)	541 (90.9)		

and Negative. COVID-19 variable has been taken as a dependent variable and all the symptoms have been considered as independent variables. Therefore, no confounding factors in this study to control as per our knowledge and other confounding factors cannot be completely ruled out.

Table 4 Cross Tabulation Between Symptoms and Comorbidities

Symptoms		Obesity				Diabetes			
		Yes	No	Chi Square	P-value	Yes	No	Chi Square	P-value
Fever	Yes	23 (29.5)	55 (70.5)	12.67	0.000	10 (12.8)	68 (87.2)	3.84	0.05
	No	92 (14.0)	565 (86.0)			44 (6.7)	613 (93.3)		
Sore Throat	Yes	26 (20.6)	100 (79.4)	2.87	0.09	12 (9.5)	114 (90.5)	1.06	0.30
	No	89 (14.6)	520 (85.4)			42 (6.9)	567 (93.1)		
Cough	Yes	24 (22.9)	81 (77.1)	4.83	0.03	8 (7.6)	97 (92.4)	0.01	0.91
	No	91 (14.4)	539 (85.6)			46 (7.3)	584 (92.7)		
Runny Nose	Yes	24 (25)	72 (75)	7.32	0.01	7 (7.3)	89 (92.7)	0.000	0.98
	No	91 (14.2)	548 (85.8)			47 (7.4)	592 (92.6)		
Shortness of Breath	Yes	19 (27.9)	49 (72.1)	8.58	0.00	9 (13.2)	59 (86.8)	3.82	0.05
	No	96 (14.4)	571 (85.6)			45 (6.7)	622 (93.3)		
Chills	Yes	19 (26.8)	52 (73.2)	7.36	0.007	9 (12.7)	62 (87.3)	3.28	0.07
	No	96 (14.5)	568 (85.5)			45 (6.8)	619 (93.2)		
Vomiting	Yes	8 (32)	17 (68)	5.24	0.02	4 (16)	21 (84)	2.85	0.09
	No	107 (15.1)	603 (84.9)			50 (7)	650 (93)		
Nausea	Yes	13 (25.5)	38 (74.5)	4.02	0.04	5 (9.8)	46 (90.2)	0.49	0.49
	No	102 (14.9)	582 (85.1)			49 (7.2)	635 (92.8)		
Diarrhea	Yes	22 (28.2)	56 (71.8)	10.43	0.001*	5 (6.4)	73 (93.6)	0.11	0.74
	No	93 (14.2)	564 (85.8)			49 (7.5)	608 (92.5)		
Head Ache	Yes	33 (25.8)	95 (74.2)	12.06	0.001*	12 (9.4)	116 (90.6)	0.94	0.33
	No	82 (13.5)	525 (86.5)			42 (6.9)	565 (93.1)		
Rash	Yes	7 (36.8)	12 (63.2)	6.64	0.01*	3 (15.8)	16 (84.2)	2.04	0.15
	No	108 (15.1)	608 (84.9)			51 (7.1)	665 (92.9)		
Conjunctivitis	Yes	8 (34.8)	15 (65.2)	6.59	0.01*	4 (17.4)	19 (82.6)	3.52	0.06
	No	107 (15)	605 (85)			50 (7)	662 (93)		
Muscle Aches	Yes	25 (24)	79 (76)	6.46	0.011*	10 (9.6)	94 (90.4)	0.92	0.34
	No	90 (14.3)	541 (85.7)			44 (7)	587 (93)		
Joint Ache	Yes	18 (25.7)	52 (85.4)	5.94	0.02	7 (10)	63 (90)	0.80	0.37
	No	97 (14.6)	568 (85.4)			47 (7.1)	618 (92.9)		
Loss of Appetite	Yes	18 (25)	54 (75)	5.29	0.02	9 (12.5)	63 (87.5)	3.11	0.08
	No	97 (14.6)	566 (85.4)			45 (6.8)	618 (93.2)		
Nose Bleed	Yes	6 (40)	9 (60)	6.88	0.01*	3 (20)	12 (80)	3.60	0.06
	No	109 (15.1)	611 (84.9)			51 (7.1)	669 (92.9)		

(*Continued*)

Table 4 (Continued).

Symptoms		Obesity				Diabetes			
		Yes	No	Chi Square	P-value	Yes	No	Chi Square	P-value
Fatigue	Yes	27 (24.1)	85 (75.9)	7.17	0.01*	12 (10.7)	100 (89.3)	2.20	0.14
	No	88 (14.1)	535 (85.9)			42 (6.7)	581 (93.3)		
General Malaise	Yes	23 (27.4)	61 (72.6)	9.90	0.002*	10 (11.9)	74 (88.1)	2.89	0.09
	No	92 (14.1)	559 (85.9)			4 (6.8)	607(3.2)		

Note: *Shows statistical significance with p value < 0.05.

Table 5 Association of Variables with Odds Ratio and Respective Significance with Confidence Intervals

Symptoms	B	S.E.	Wald	df	P-value	Odds Ratio	95% C.I. for Odds	
							Lower	Upper
Fever (≥37.8 °C) or history of fever	−0.800	0.407	3.868	1	**0.049***	0.449	0.202	0.997
Sore throat	0.704	0.441	2.555	1	0.110	2.022	0.853	4.796
Cough	−1.115	0.426	6.866	1	0.009*	0.328	0.142	0.755
Runny Nose	0.677	0.435	2.423	1	0.120	1.969	0.839	4.620
Shortness of Breath	0.483	0.442	1.196	1	0.274	1.621	0.682	3.855
Chills	0.049	0.486	0.010	1	0.920	1.050	0.405	2.721
Vomiting	−1.269	0.795	2.548	1	0.110	0.281	0.059	1.335
Nausea	0.859	0.589	2.128	1	0.145	2.360	0.745	7.479
Diarrhea	−0.781	0.414	3.558	1	0.059	0.458	0.204	1.031
Headache	−1.418	0.367	14.940	1	0.000*	0.242	0.118	0.497
Rash	−0.246	0.698	0.124	1	0.724	0.782	0.199	3.072
Conjunctivitis	1.644	0.751	4.795	1	0.029*	5.177	1.188	22.549
Muscle aches	−0.446	0.496	0.811	1	0.368	0.640	0.242	1.690
Joint ache	−0.404	0.529	0.584	1	0.445	0.668	0.237	1.882
Loss of appetite	−0.568	0.481	1.398	1	0.237	0.567	0.221	1.453
Nose bleed	1.272	0.846	2.261	1	0.133	3.569	0.680	18.733
Fatigue	−1.500	0.447	11.263	1	0.001*	0.223	0.093	0.536
General malaise	0.092	0.479	0.037	1	0.848	1.096	0.429	2.803

Note: *Shows statistical significance with p value < 0.05.

Bivariate analysis has been utilized since there are two outcomes under as Positive and Negative. For the chi square, analysis in Table 4 has been done to find the association between obesity and diabetes with symptoms. Multivariate analysis was not considered since there are only two outcomes for obesity and diabetes as yes or no and thus the bivariate regression analysis was applied.

In Table 5, we included all variables for the regression analysis. None of the variables have been excluded from the analysis.

Discussion

In this study, we evaluated the seroprevalence of anti-SARS-CoV-2 antibodies among hospital staff with an overall prevalence of 2.9%.[5] In a previous study from Saudi Arabia, seroprevalence among HCWs was 2.36% with a statistical difference between hospitals that had COVID-19 cases with a prevalence of 2.9% vs 0.8% for hospitals that did not have COVID-19 cases.[5] Since JHAH admitted COVID-19 patients and had actively participated in the management of COVID-19 cases,[12–14] thus the prevalence in our study is consistent with that of the nationwide prevalence among HCWs. However, more targeted HCWs who worked in the operating room and intensive care units showed a seroprevalence of 12.2% in a study from KSA.[15] A third study conducted from June to August 2020 in KSA showed a higher rate of seropositivity of 32.2% in referral hospitals and quarantine sites.[16] In a study from Spain, seroprevalence among HCWs was 16.6%[17] and a longitudinal study in the United States showed a prevalence of 2.8% at baseline and 4.8% in a follow-up after six months.[18] During the first wave in Italy, 2.8% of HCWs tested seropositive.[19] Information about the community prevalence of anti-SARS-CoV-2 antibodies may be used as a gauge of community immunity before the introduction of vaccines.[20] Such a study was done in KSA among blood donors and the seroprevalence was 1.4%[21] which is similar to those reported among HCWs in most of the KSA studies. Another study that included over 6000 HCWs in Spain conducted in 17 hospitals across four regions in the country had a seroprevalence of 4.32% amongst the participants.[22]

In our study, 112 (15.2%) participants had a positive SARS-CoV-2 rt-PCR before taking part in the study. The occurrence of SARS-CoV-2 infection among HCWs was found among 4.5% of 4462 patients in one hospital in KSA and 90.6% were community-acquired infection, and 61.3% of HCW infection in Oman was also community-acquired.[23] Another study described a hospital outbreak and thus 88% of infections in HCWs were hospital-acquired.[24] However, we did not study the source of infection among those HCWs. It is important to note that the current pandemic of COVID-19 had occurred mainly among the communities with limited healthcare-associated outbreaks. This is an important distinction of the occurrence of multiple outbreaks in healthcare settings in the previous coronavirus, mainly the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) in the Kingdom of Saudi Arabia.[25]

We evaluated the occurrence of symptoms among the 87 participants with a positive SARS-CoV-2 IgG assay. These individuals experienced symptoms that were statistically significant compared to HCWs with negative serology. The most-reported symptoms were fever 38 (43.6%), chills 32 (36.7%), muscle aches 47 (54%), fatigue 47 (54%), joint ache 33 (37.9%), loss of appetite 33 (37.9%), headache 44 (50.5%), general malaise 34 (39%), diarrhea 25 (28.7%), shortness of breath 22 (25.2%), cough 38 (43.6%), runny nose 26 (29.8%), and sore throat 32 (36.7%). These symptoms are not specific to COVID-19 patients. However, the occurrence of such symptoms had been reported among patients with COVID-19 as well. One study from KSA showed that the most common symptoms were cough (53.6%), fever (36.2%), fatigue (26.4%), dyspnea (21.9%), and sore throat (21.9%)[26] and similar symptomatology in other studies.[24,27–29]

Elucidating factors associated with positive SARS-CoV-2 serology revealed two associated factors with positivity in bivariate analysis. These are always using alcohol-based hand rub or soap and water after (risk of) body fluid exposure and always wearing PPE when indicated. The data showed that those staff who were positive were less likely to wear PPE and to perform hand hygiene. The practice of hand hygiene is of paramount activity to reduce infection.[30] Multiple interventions were used to promote hand hygiene even before[30–32] the current pandemic. During the pandemic, isolation of suspected patients, the use of facemasks, and intensified hand hygiene were important for the prevention of nosocomial transmission of COVID-19.[33] One study showed that multiple services were contaminated and had positive SARS-CoV-2 RNA.[34] Another study from KSA showed high knowledge and practice scores concerning hand hygiene and the use of masks.[35] In a case–control study, frequent handwashing, social distancing, and avoidance of close contact were independently associated with a lower risk for SARS-CoV-2 infection.[36]

One of the main limitations we exhibited in this study was the inability to categorize our participants into groups according to their level of exposure whether it was high or low to the virus/COVID-19 patients, as this information was not comprehensively provided by the participants. In addition, due to the slow accrual, the study protocol was amended from randomized selection to open invitation, which eventually resulted in achieving the targeted sample size (more than 10% of JHAH staff) at the expense of risk of selection bias. Finally, this study was conducted prospectively, and participants depended fully on their memory and personal interpretation of their symptoms and association with the infection.

Conclusion

This study was carried out during the first wave of COVID-19 and before the availability of vaccination. Our findings showed that positive seroconversion rate was considerably low amongst JHAH's healthcare workers and similar to other national and international healthcare organizations. Although the results of the study can be interpreted as a success in following the recommendations of the Intervention Prevention and Control Division, seropositivity correlated significantly with two factors of infection prevention which were appropriately alcohol-based hand rub or soap and water after the risk of body fluid exposure and wearing personal protective equipment when indicated.

Institutional Review Board

The study received Johns Hopkins Aramco Healthcare's Institutional Review Board's approval (IRB # 20-09) on the 13th of May 2020.

Data Sharing Statement

Datasets including demographic data, serology testing results, and questionnaire responses can be provided upon request. Please contact the corresponding author for the encrypted dataset and it can be shared with the reviewers accordingly.

Informed Consent

Each participant was assigned a study ID, and a written informed consent was obtained as well as a hardcopy of the WHO's risk factor assessment questionnaire.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

All authors report no conflicts of interest in this work.

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