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Incidence and risk factors related to SARS-CoV-2 infection, reinfection, and seroconversion: Analysis of a healthcare workers cohort from a university hospital in Colombia

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ABSTRACT

Objectives: To determine the incidence and factors associated with SARS-CoV-2 infection and seroconversion among healthcare workers (HCWs) during the COVID-19 pandemic in a university hospital in Colombia.
Methods: We analyzed the CoVIDA-Fundación Santa Fe de Bogotá (FSFB) cohort, consisting of 419 HCWs from the FSFB university hospital. The cohort was followed during active surveillance (June 25, 2020, to April 30, 2021) and passive surveillance (May 01, 2021, to March 16, 2022) periods. Incidence rates for SARS-CoV-2 infection, reinfection, and seroconversion were estimated, considering pre- and post-COVID-19 vaccination. Cox proportional-hazards models were used to identify factors related to infection and seroconversion during the active surveillance period.
Results: COVID-19 incidence rate ranged between 16-52 cases per 1000 person-month. SARS-CoV-2 reinfections were rare, ranging between less than one case to 13 cases per 1000 person-month. The seroconversion rates ranged between 52-55 cases per 1000 person-month. High socioeconomic level was a protective factor for SARS-CoV-2 infection, while SARS-CoV-2 infection was the main factor associated with seroconversion.
Conclusion: This study provides insights into the incidence and risk factors of SARS-CoV-2 infection among HCWs in a Colombian university hospital. The findings may offer valuable guidance for reducing virus spread within healthcare settings.

Introduction

COVID-19 disease, caused by the SARS-CoV-2 virus, was first identified in December 2019 in Wuhan, Hubei Province, China [1]. With the virus rapidly spreading across multiple countries, the World Health Organization (WHO) declared the SARS-CoV-2 pandemic on March 11, 2020 [2].

Since the beginning of the pandemic, healthcare workers (HCWs) have been the subject of multiple studies, due to their increased exposure to the SARS-CoV-2 virus [3] and the ease of follow-up. However, the reported incidence of real-time reverse transcription polymerase chain reaction (RT-PCR)-confirmed SARS-CoV-2 infection in HCWs is not consistent in the literature, ranging from 2-43% [4]. This wide range can be attributed to contextual factors such as hospital policies regarding the use of personal protective equipment, the COVID-19 containment measures adopted by each country, and the time of the pandemic when the studies were conducted. Furthermore, the incidence of the disease is directly affected by virus-related factors, including the emergence and circulation of more contagious variants, including Delta and Omicron [5].

Individual factors, such as the immune response, play an important role in preventing COVID-19. This immune response is influenced by vaccination and previous infections, resulting in seropositive status [6]. Measurement of seropositivity can help identify healthcare workers at a higher or lower risk for SARS-CoV-2 infection and reinfection. In Colombia, there are few studies measuring SARS-CoV-2 incidence and seroprevalence in HWCs and there is only one that measures seroconversion over time in this high-risk population [7–9]. To our knowledge, there are no published studies regarding COVID-19 reinfection behavior in HCWs in the country.

Consequently, this study aims (1) to determine the incidence of SARS-COV-2 infection, reinfection, and seroconversion and (2) to iden-

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tify the factors related to SARS-COV-2 infection and seroconversion among hospital workers from a university hospital in Bogotá, Colombia in different moments of the COVID-19 pandemic.

Methods

Setting

This study was conducted in Bogotá, the capital city of Colombia. Bogotá has a population of 7.181.469 inhabitants and was the most affected city, reporting the most COVID-19 cases in the country [10,11]. As a rapid response to the pandemic, the Universidad de Los Andes led the CoVIDA project in collaboration with the District Health Department and other healthcare institutions to support the epidemiological surveillance strategies in Bogotá and surrounding municipalities [12]. This project amplified the local COVID-19 diagnostic capacity of the city by conducting 100.000 free SARS-CoV-2 RT-PCR tests in populations with increased risk of COVID-19 (essential services workers e.g., HCWs and public transportation drivers) [13]. Fundación Santa Fe de Bogotá (FSFB) was included as a study site in the CoVIDA project. This is a large university hospital that was a referral institution in the city for COVID-19 cases [14]. In addition to RT-PCR testing through the CoVIDA project, this institution decided to enhance surveillance and prevention of COVID-19 in HCWs by implementing regular clinical assessment and laboratory sampling in voluntary hospital workers. This surveillance strategy was denominated the CoVIDA-FSFB project.

Study design and participants

This is an observational longitudinal study in which we analyzed the cohort of participants of the CoVIDA-FSFB project. The inclusion criteria for the CoVIDA project were hospital workers aged 18 or older from any hospital area, regardless of their profession or educational level. Individuals with contraindications for collecting respiratory (nasopharyngeal swab) or blood samples were excluded. Hospital workers were invited to participate in the cohort via email and those interested were scheduled for an enrollment visit, where the eligibility criteria were verified and informed consent was obtained. All participants were consecutively included in the cohort between June 25 and October 30, 2020, completing 420 participants (supplementary material p 1).

Follow-up

The cohort follow-up consisted of two periods: an active surveillance period and a passive surveillance period (supplementary material p 2). The active surveillance period comprised from June 25, 2020, to April 30, 2021, during which participants underwent periodic laboratory and clinical screening for COVID-19. This period involved a 6-month follow-up for each participant. Laboratory screening during the active surveillance period included qualitative anti-SARS-CoV-2 immunoglobulin IgG/IgM rapid tests (HighTop SARS-CoV-2 IgM/IgG Antibody Rapid Test, HIGHTOP Biotech) which were performed on the enrollment visit and days 14, 51, 81, 111, and 171 since the enrollment [15]. Additionally, SARS-CoV-2 RT-PCR (U-TOP COVID-19 detection kit. SEASUN biomaterials, Daejeon, Korea) were performed on the enrollment visit, and days 21 and 171 of follow-up [16]. Participants with a positive RT-PCR underwent further laboratory tests, including serology tests on days 7, 14, and 21, and RT-PCR tests on days 14 and 21 after the COVID-19 diagnosis. Clinical screening involved weekly phone calls to identify COVID-19-related symptoms; if participants met the definition of probable or suspected COVID-19 infection, according to the Colombian National Institute of Health (supplementary material pp 3-4), a SARS-CoV-2 RT-PCR was recommended [17].

After the active surveillance period, the cohort continued to be passively followed from May 1, 2021, until March 16, 2022. Over this passive surveillance period, as a hospital policy, participants reported COVID-19-related symptoms and any positive SARS-CoV-2 tests to the hospital's human resource department. Additionally, medical reports and laboratory results from participants who underwent medical assessment at the hospital were reviewed.

Outcomes

The primary outcome was COVID-19 infection confirmed by a positive SARS-CoV-2 RT-PCR test, regardless of symptoms. The secondary outcomes were: seroconversion, defined as a positive SARS-CoV-2 antibody in a previously seronegative participant (either IgM and/or IgG), and reinfection, defined as any positive RT-PCR test 90 days apart from the first COVID-19 episode, regardless of symptoms [18].

Data sources

The CoVIDA-FSFB project collected data from multiple sources: (1) medical records, (2) COVID-19 risk factors questionnaire adapted from WHO [19], (3) COVID-19 related symptoms questionnaire, (4) laboratory reports (RT-PCR and serological tests) and (5) human resources department COVID-19 database.

From the medical record, we extracted the following data: comorbidities, flu vaccination, previous COVID-19, and previous viral infections (dengue, chickenpox, zika, chikungunya, influenza, measles, or hepatitis) and anthropometric measures (weight and height). From the COVID-19 risk factors questionnaire, we extracted demographic characteristics (age, sex, socioeconomic status, and household location), hospital areas, job type, aerosol exposure, type of transportation used, and adherence to protection and preventive strategies (hand washing and mask use frequency and duration). In addition to collecting data on COVID-19 symptoms, the COVID-19 related symptoms questionnaire also yielded information about vaccination status, doses received, vaccine type, and vaccination dates. The laboratory reports provided information regarding SARS-CoV-2 infections/reinfection and antibody status. Finally, the human resources department COVID-19 database allowed identification of infections or reinfections of symptomatic hospital workers during the passive surveillance period. During the passive surveillance, there was no serology testing, so we only evaluated infection and reinfection outcomes for this period.

Statistical analysis

We conducted the following analysis according to the objectives of this study.

Incidence of SARS-COV-2 infection, reinfection, and seroconversion

Categorical variables were presented as frequencies and proportions and continuous variables as mean with standard deviations or median with the interquartile range according to their distribution on the Shapiro-Wilk test. We also analyzed these characteristics according to participants' contact with patients or biological samples. Proportions were compared with the $\chi 2$ test or Fisher's exact test, and continuous variables were compared with Student's *t*-test or Mann-Whitney U test to compare the characteristics of the patient contact and nonpatient-contact groups.

To estimate the incidence of infection, reinfection, and seroconversion, we used time-to-event analysis because this approach allows us to increase statistical power and handle unequal follow-up times [20].

As the vaccination program in Colombia commenced with healthcare workers (HCWs) receiving the BNT162b2 vaccine, and because vaccines can directly influence infection rates, we calculated the incidence rates of SARS-CoV-2 infection, reinfection, and seroconversion before and after vaccination during the active surveillance period. For the passive surveillance period, only 50% (170) of participants were available for the survival analysis to estimate the risk of SARS-CoV-2 infection and

reinfection. To assess the impact of contact with patients or with biological samples, we applied the log-rank test to compare the survival rates according to patient contact.

Factors related to SARS-COV-2 infection and seroconversion

We estimated the factors associated with SARS-CoV-2 infection and seroconversion during the active surveillance using two independent regression models: (1) Cox Proportional-Hazards model for infection and (2) Cox Proportional-Hazards model for seroconversion. For both outcomes, we first estimated bivariate regressions and identified possible interactions between variables. Afterward, we estimated the full multivariate regression model and used a stepwise hierarchical approach to estimate the most parsimonious model (using 0.1 cut-off to include variables and 0.2 cut-off to exclude variables). Finally, we tested the assumptions and performance of the models for each outcome. Proportional-hazards assumption was tested by the Schoenfeld test, we assessed the overall model fit using Cox-Snell residuals, evaluated martingale's and deviance's outliers, and applied Harrell's C statistic to measure the concordance of each model (supplementary material pp 5-10).

We estimated that the sample size of the cohort would provide 78.35% power for a two-sample comparison (patient-contact and nonpatient-contact HCWs) survival analysis. All statistical analyses were conducted using Stata 17 (StataCorp LLC, Texas, USA). Two-sided *P*-values were used, and statistical significance was set at $P < 0.05$.

Results

Participants baseline characteristics

The median age of participants was 39.63 (interquartile range 14) years, 75.90% were female, 29.59% had comorbidities, 31.5% reported past SARS-CoV-2 infection and 84.25% (353) had direct patient contact. Compared with patient-contact HCWs, nonpatient-contact HCWs reported less mask use duration (*P*-value <0.001), hand washing frequency (*P*-value <0.05), hand washing duration (*P*-value <0.001), and exposure to aerosol procedures (*P*-value <0.001) (Table 1).

Incidence of SARS-COV-2 infection, reinfection, and seroconversion

Active surveillance period

The overall incidence of SARS-COV-2 infection before COVID-19 vaccination in HCWs was 28 cases per 1000 person per month and the rate after receiving at least one dose of the COVID-19 vaccine was 16 per 1000 person per month (Table 2). The risk of SARS-COV-2 infection in nonpatient-contact HCWs was lower compared to patient-contact HCWs, but this difference was not statistically different (before vaccination incidence rate [IR] 0.028 vs 0.025, *P*-value 0.706. After vaccination IR 0.028 vs 0.025 *P*-value 0.679). Overall, SARS-CoV-2 reinfection during this period was low (IR <0.001) with only one case in the patient-contact group and no cases in the nonpatient-contact group. The seroconversion rate before COVID-19 vaccination was not significantly higher between patient-contact and nonpatient-contact groups (IR 0.056 vs 0.052, *P*-value 0.920). Conversely, the seroconversion rate after COVID-19 vaccination in patient-contact HCWs was higher compared to nonpatient-contact participants. However, it is important to note that this difference lacks statistical significance (seven seroconversion cases in patient-contact HCWs vs zero cases in nonpatient-contact participants, *P*-value = 0.519).

Passive surveillance period

All participants included in the passive surveillance period analysis were vaccinated against COVID-19. Overall, SARS-COV-2 infection incidence was 52 cases per 1000 person per month, and there was no difference between patient contact and nonpatient-contact groups (IR 0.053 vs 0.052, respectively, *P*-value 0.798). COVID-19 reinfections had a low incidence rate (IR 0.013), and reinfection cases were only present in the patient-contact group (*P*-value 0.466) (Table 2).

Factors related to SARS-CoV-2 infection and seroconversion

The final Cox regression model for SARS-CoV-2 infection during the active surveillance period (Table 3) showed that high socioeconomic level, previous viral infections (dengue, chickenpox, zika, chikungunya, influenza, measles or hepatitis), working in more than one hospital area, high hand hygiene adherence during work shift are protective factors for COVID-19 in HCWs. Conversely, aerosol exposure, low hand hygiene adherence, and a higher number of cohabitants are risk factors for COVID-19. Nonetheless, high socioeconomic level (hazard ratio 0.470, 95% IC [0.231 - 0.958]) was the only variable with statistical significance.

Finally, the Cox regression model for SARS-CoV-2 seroconversion during the active surveillance period (Table 4) showed that those who presented COVID-19 (hazard ratio 3.606, 95% IC [2.326 -5.592]) had more risk of seroconversion. Also, aerosol exposure and reception of the COVID-19 vaccine were associated with seroconversion, but these associations were not statistically significant.

Discussion

In our study, we determined the incidence of SARS-CoV-2 infection, reinfection, and seroconversion. The rate of COVID-19 infection ranged between 16-52 cases per 1000 person-month. SARS-CoV-2 reinfections were rare, ranging between less than one case to 13 cases per 1000 person-month. The seroconversion rates ranged between 52-55 cases per 1000 person-month. We also identified factors related to infection and seroconversion. High socioeconomic level was a protective factor for SARS-CoV-2 infection, while SARS-CoV-2 infection during the follow-up was the main factor associated with seroconversion.

Incidence of SARS-COV-2 infection, reinfection, and seroconversion

The incidence of SARS-CoV-2 infection before vaccination, during the active surveillance period, in the cohort was within the range of COVID-19 incidence reported in other studies conducted before vaccination (cumulative incidence from 15-35%) [9,21–23]. Our cumulative incidence was 13.63%, which is similar to the 13.60% incidence in HCWs reported in Italy and close to the 15% incidence reported in Mexico in 2020 [23]. Conversely, our cumulative incidence was low compared to the 24.00% rate of infection in HCWs in Iran and to the 35.7% incidence reported in a similar university hospital located in Bogotá [24]. Though the incidences during the period of active and passive surveillance are not comparable, this lower incidence in the CoVIDA-FSFB cohort may be due to the important role of an early diagnosis in preventing transmission between coworkers [25]. Additionally, during the active surveillance period, we identified a lower risk of infection after COVID-19 vaccination (cumulative incidence 1.92%), which is related to the high effectiveness of the vaccine during the first months to prevent infection [26].

In passive surveillance, the cumulative incidence of infection was 41.1%, which is higher compared to the incidence reported in other countries after BNT162B2 vaccination [22,27]. We highlight that during this passive surveillance period, our analysis focused exclusively on participants who exhibited COVID-19 symptoms and sought medical services. As symptomatic individuals are more likely to be infected the observed incidence rate is higher. In that respect, the incidence between both periods is not comparable as the definition of individuals at risk differs in both cases.

In the active surveillance period, only one SARS-CoV-2 reinfection occurred (cumulative incidence 0.24%). This low incidence is expected as infection (natural immunity) provides immunity which is associated with a lower risk of SARS-CoV-2 reinfection [28]. This is consistent with the reinfection incidence reported in other studies on HCWs which ranges between 1-5% [29–31].

In the passive surveillance period, we found a higher SARS-CoV-2 reinfection rate (CI 11.76). During this period, the Omicron vari-

Table 1
Baseline characteristics of the COVIDA-FSFB cohort according to patient contact exposure.

		Patient contact		
	Total (%) n = 419	Yes (%) n = 353	No (%) n = 66	*P*-value
Gender				
Male	101 (24.10)	78 (22.10)	23 (34.85)	0.026[a]
Female	318 (75.90)	275 (77.90)	43 (65.15)	
Age				
Median (interquartile range)	39.63 (14)	39.67 (12)	39.42 (18)	0.936[b]
Socioeconomical level				
Low	225 (53.70)	192 (54.39)	33 (50.00)	0.512[c]
High	194 (46.30)	161 (45.61)	33 (50.00)	
Place of residency				
Bogota	378 (90.24)	314 (88.95)	64 (96.97)	0.044[a]
Outside Bogota	41 (9.76)	39 (11.05)	2 (3.03)	
Comorbidities				
No	295 (70.41)	261 (73.94)	34 (51.52)	<0.001[a]
Yes	124 (29.59)	92 (26.06)	32 (48.48)	
Hypertension	35	26 (74.29)	9 (25.71)	0.988[a]
hypothyroidism	45	10 (22.22)	35 (77.7)	0.188[a]
Diabetes	6	5 (83.33)	1 (16.67)	0.600[a]
Asthma	14	12 (85.71)	2 (14.29)	0.296[a]
Immunosuppression	9	7 (77.78)	2 (22.22)	0.799[a]
Former or current smoker				
No	290 (69.21)	250 (70.82)	40 (60.61)	0.145[a]
Yes	129 (30.30.79)	103 (29.18)	26 (39.39)	
Body mass index				
Underweight	6 (1.43)	4 (1.13)	2 (3.03)	0.600[a]
Normal weight	214 (51.07)	179 (50.71)	35 (53.03)	
overweight	151 (36.04)	128 (35.98)	23 (34.85)	
Obesity	48 (11.46)	42 (11.90)	6 (9.09)	
Previous COVID-19				
No	382 (91.16)	326 (92.35)	62 (93.94)	0.651[a]
Yes	31 (07.39)	27 (7.65)	4 (6.06)	
Other previous viral infections[d]				
No	287 (68.50)	238 (67.42)	49 (74.24)	0.274[a]
Yes	132 (31.50)	115 (32.58)	17 (25.76)	
Mask use duration during shift				
Less than half of the time	1 (0.24)	0 (0)	1 (1.54)	**<0.001**[a]
More than half of the time	5 (1.19)	0 (0)	5 (7.58)	
Always	410 (98.6)	350 (99.15)	60 (90.91)	
Hand washing frequency during shift				
1 to 3 times	11 (2.64)	10 (2.85)	1 (1.54)	**<0.001**[c]
4 to 6 times	90 (21.63)	59 (16.81)	31 (47.69)	
7 to 9 times	37 (8.89)	25 (7.12)	12 (18.46)	
10 or more times	278 (66.83)	257 (73.22)	21 (32.31)	
Hand washing duration during shift				
0-20 sec	128 (30.77)	98 (28.00)	30 (45.45)	**0.005**[c]
20-30 sec	149 (35.82)	128 (36.57)	21 (31.82)	
> 30 sec	139 (33.41)	124 (35.43)	15 (22.73)	
Exposure to aerosol-generating procedures				
No	194 (48.26)	129 (38.28)	65 (100.00)	**<0.001**[a]
Yes	208 (38.46)	208 (61.72)	0 (0.00)	
Household members				
1	46 (10.98)	40 (11.33)	6 (9.09)	0.5826[c]
2	103 (24.5)	91 (25.78)	12 (18.18)	
3	114 (27.21)	89 (25.21)	25 (37.88)	
4 or more	156 (37.23)	133 (37.68)	23(34.85)	
Transport type				
Public transport	211 (52.49)	101 (29.97)	12 (18.46)	0.132[a]
Private transport	113 (28.11)	170 (50.45)	41 (63.08)	
Both	78 (19.40)	66 (19.58)	12 (18.46)	
Commute time				
< 15 minutes	71 (17.66)	61 (18.10)	10 (15.38)	0.534[c]
15 to 30 minutes	131 (32.59)	107 (31.75)	24 (36.92)	
30 to 60 minutes	107 (26.62)	86 (25.52)	21 (32.31)	
> 60 minutes	93 (23.13)	83 (24.63)	10 (15.38)	

[a] pearson chi[2]
[b] mann-Whitney U test
[c] kruskal–Wallis.
[d] dengue, chickenpox, zika, chikungunya, influenza, measles or hepatitis

Table 2
Incidence rate of SARS-CoV-2 infection, reinfection, and seroconversion.

	Total				Patient contact				Nonpatient contact				*P*-value[a]
	Person-month follow-up	N	Cases	Incidence rate (95% CI)	Person-month follow-up	N	Cases	Incidence rate (95% CI)	Person-month follow-up	N	Cases	Incidence rate (95% CI)	
Active surveillance period													
Infection before COVID-19 vaccine	1957.566	396	54	0.028 (0.021-0.036)	1,636.867	337	46	0.028 (0.021-0.038)	320.7	59	8	0.025 (0.012-0.050)	0.736
Infection after COVID-19 vaccine	187.767	156	3	0.016 (0.005-0.050)	179.3	142	3	0.017 (0.005-0.052)	8.467	14	0	-	0.679
Reinfection before COVID-19 vaccine	3013.167	409	1	<0.01 (0.00004-0.002)	2526.866	345	1	0.0004 (0.00006-0.003)	486.300	64	0	-	0.665
Seroconversion before COVID-19 vaccine	1975.070	416	102	0.055 (0.046-0.067)	1516,.400	350	85	0.056 (0.045-0.069)	325.033	66	17	0.052 (0.033-0.084)	0.920
Seroconversion after COVID-19 vaccine	134.230	128	7	0.052 (0.025-0.109)	128.467	118	7	0.054 (0.026-0.114)	5.767	10	0	-	0.519
Passive surveillance period[b]													
Infection	1295.333	165	68	0.052 (0.041-0.067)	1102.267	135	58	0.0526 (0.041-0.068)	193.067	30	10	0.0518 (0.028-0.096)	0.798
Reinfection	637.067	68	8	0.013 (0.006-0.025)	549.233	58	8	0.015 (0.007-0.029)	87.833	10	0	-	0.466

CI, confidence interval.
[a] log-rank test
[b] only participants who received COVID-19 vaccine were analyzed in the passive surveillance period analysis

Table 3
Multivariate regression analysis for infection during the active surveillance period using Cox Proportional-Hazards model.

Variable	Bivariate		Full[a]		Final[b]	
	Hazard ratio	95% confidence interval	Hazard ratio	95% confidence interval	Hazard ratio	95% confidence interval
Sex Men Women						
	Ref.	Ref.	Ref.	Ref.	.	.
	1.244	0.655-2.360	1.117	0.495-2.524		
Socioeconomic level Low High	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
	0.373	0.203-0.685	0.384	0.130-1.138	0.470	0.231-0.958
Body mass index	Ref.	Ref.	Ref.	Ref.	.	.
Normal weight	1.235	0.727-2.099	1.282	0.681-2.411		
Overweight or obesity						
Comorbidities No Yes	Ref.	Ref.	Ref.	Ref.	.	.
	0.796	0.554-2.497	1.056	0.453-2.458		
Smoker or former smoker No	Ref.	Ref.	Ref.	Ref.	.	.
Yes	0.911	0.514-1.616	0.985	0.431-2.251		
Previous viral infections No	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Yes	0.647	0.332-1.260	0.364	0.116-1.141	0.572	0.249-1.313
Work in more than one	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
hospital area No Yes	0.457	0.182-1.146	0.384	0.113-1.307	0.355	0.107-1.178
Aerosol exposure No Yes	Ref. 1.174	Ref.	Ref.	Ref.	Ref.	Ref.
		0.671-2.055	1.854	0.890-3.861	1.691	0.851-3.357
Commute risk[c]	Ref.	Ref.	Ref.	Ref.	.	.
Low risk	1.606	0.855-3.015	1.830	0.859-3.900		
Medium risk	1.588	0.778-3.241	0.904	0.382-2.139		
High risk						
Hand Hygiene adherence	Ref.	Ref.	Ref.	Ref	Ref.	Ref.
during work shift[d]	1.087	0.475-2.486	0.943	0.339-2.620	0.955	0.349-2.611
Very high High Medium	1.172	0.599-2.294	2.285	0.961-5.433	2.128	0.917-4.942
Low	0.667	0.292-1.525	2.028	0.681-6.043	1.934	0.658-5.686
Number of cohabitants	1.186	0.995-1.413	1.171	0.950-1.443	1.173	0.958-1.435
COVID-19 vaccine doses	Ref.	Ref.	Ref.	Ref.	.	.
received None1 dose 2 doses	0.338	0.046-2.502	0.448	0.057-3.528		
	1.471	0.778-2.782	1.656	0.746-3.675		
Previous viral infection[e]	Ref.	Ref.	Ref.	Ref.	.	.
#socioeconomic level No#low	0.397	0.201-0.786	.	.		
no#high yes#low Yes#high	0.730	0.336-1.589	.	.		
	0.239	0.073-0.783	1.801	0.323-10.023		
Smoker or former Smoker#	Ref.	Ref.	Ref.	Ref.	.	.
socioeconomic level no#low	0.370	0.175-0.781	.	.		
no#high yes#low yes#high	0.958	0.488-1.878	.	.		
	0.367	0.142-0.947	.	.		
			1.508	0.335-6.784		
Comorbidities #socieconomic	Ref.	Ref.	Ref.	Ref.	.	.
level No#low no#high	0.4460.984	0.223-0.894	.	.		
yes#low Yes#high	0.231	0.501-1.931	.	.		
		0.070-0.758	0.795	0.161-3.935		

[a] Full model: n=338, log-likelihood Cox Proportional-Hazards= -211.91, LR chi2: 28.75, p value : 0.070

[b] Final model: n=338, log-likelihood Cox Proportional-Hazards= -215.52, LR chi2: 21.53 , p value : 0.006

[c] Commute risk: low risk is private transport type with any commute time, medium risk is 15-60 min commute time in public transport and high risk is more than one hour commute time in public transport.

[d] Hand Hygiene adherence during work shift: very high adherence is more than 10 times hand washing frequency (HWF) and more than 30 seconds hand washing duration (HWD); high adherence is seven to nine times HWF and more than 30 seconds HWD or more than 10 times HWF and 20-30 sec HWD; medium adherence is four to nine HWF and less than 30 seconds HWD; low adherence is one to three HWF and less than 20 seconds HWD.

[e] dengue, chickenpox, zika, chikungunya, influenza, measles or hepatitis.

ant was circulating in Colombia, which may have increased the reinfection rate. The Omicron variant has more than 30 mutations in the Spike protein, which allows it to evade neutralizing antibodies and reduce vaccine effectiveness against SARS-CoV-2 infections [32,33] These results are consistent with the reported by Chemaitelly et al. [34], who found that Omicron variant led to a large increase in the incidence of reinfections in participants with natural and vaccine-induced immunity.

To contextualize our findings, we compared our seroconversion rates with those reported in other studies conducted in Colombia. Seroconversion was measured only in the active surveillance period (June 25, 2020, to April 30, 2021), with a cumulative incidence of SARS-CoV-2 seroconversion of 24.5% before the vaccine and 5.4% after vaccination.

A multicenter study conducted in 4042 HCWs in 10 cities in Colombia in the second semester of 2020 shows an overall seroprevalence of 32%, with a 35% seroprevalence in Bogotá [7]. This seroprevalence exceeds the 23.2% SARS-CoV-2 seroprevalence of our cohort at the beginning of this study (June to October 2020), whose results are published elsewhere [8].

A longitudinal study conducted in a similar university hospital reported a 23.4% initial seroprevalence and a 12.3% seroconversion rate [9]. While our initial seroprevalence is similar to their finding, the seroconversion rate before vaccination was higher in our cohort. We attribute this difference to several factors contributing to seroconversion, such as asymptomatic COVID-19 cases, serology tests diagnostic accuracy, and seropositive cases due to crossed-reaction with other viruses, such as dengue and other coronaviridae viruses [35,36].

Table 4
Multivariate regression analysis for seroconversion during the active surveillance period using Cox proportional-hazards model.

Variable	Bivariate		Full[a]		Final[b]	
	Hazard ratio	95% confidence interval	Hazard ratio	95% confidence interval	Hazard ratio	95% confidence interval
Sex Men Women					.	.
	Ref.	Ref.	Ref.	Ref.		
	0.949	0.614 - 1.466	1.092	0.454 - 1.391		
Socioeconomic level Low High					.	.
	Ref.	Ref.	Ref.	Ref.		
	0.668	0.453 - 0.986	0.795	0.391 - 1.155		
Overweight or obesity No Yes					.	.
	Ref.	Ref.	Ref.	Ref.		
	0.689	0.348 - 1.364	1.227	0.804 - 1.874		
Comorbidities No Yes					.	.
	Ref.	Ref.	Ref.	Ref.		
	1.002	0.665 - 1.510	1.227	0.801 -2.057		
COVID-19 during active surveillance period No Yes	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
	4.073	2.754 - 6.023	3.590	2.255 - 5.716	3.606	2.326 - 5.592
Vaccination against COVID-19 No Yes	Ref.	Ref.	Ref. 1.321	Ref.	Ref.	Ref.
	1.432	0.960 - 2.134		0.802 - 2.175	1.209	0.780 - 1.874
Other previous viral infections[c]					.	.
No Yes	Ref.	Ref.	Ref.	Ref.		
	0.842	0.541 - 1.310	0.749	0.365-1.539		
Aerosol exposure No Yes						
	Ref. 1.432	Ref.	Ref. 1.428	Ref.	Ref.	Ref.
		0.960 - 2.134		0.899 - 2.267	1.408	0.929 - 2.134
Commute risk[d]	Ref.	Ref.	Ref.	Ref.	.	.
Low risk	1.125	0.709 - 1.786	0.848	0.492 - 1.462		
Medium risk	1.182	0.719 - 1.943	0.911	0.508 - 1.634		
High risk						
Number of cohabitants	1.053	0.928-1.194	0.990	0.561 - 1.747	.	.
Hand Hygiene adherence during work shift[e]	Ref.	Ref.	Ref.	Ref.	.	.
Very high High Medium	0.796	0.424 - 1.495	0.830	0.490 - 2.072		
Low	0.938	0.557 - 1.524	1.005	0.583 - 1.732		
	0.812	0.483 - 1.366	0.882	0.463 - 1.488		
Flu vaccine received in the last year No Yes					.	.
	Ref.	Ref.	Ref.	Ref.		
	1.154	0.702 - 1.896	0.990	0.561 - 1.747		
Other previous viral infections#Socioeconomic level					.	.
	Ref.	Ref.	Ref.	Ref.		
No#Low No#High Yes#Low	0.635	0.403 - 0.999	.	.		
Yes#High	0.783	0.439 - 1.396	.	.		
	0.616	0.327 - 1.159	1.404	0.527 - 3.735		

[a] Full model: n=374, Log likelihood Cox Proportional-Hazards: log-likelihood = -497.51 LR chi2: 36.04 p value: 0.003
[b] Final model: n=374 Log likelihood Cox Proportional-Hazards: -499.89 LR chi2: 31.28 p value: < 0.001
[c] Dengue, chickenpox, zika, chikungunya, influenza, measles or hepatitis.
[d] Commute risk: low risk is private transport type with any commute time, the medium risk is 15-60min commute time in public transport and high risk is more than one hour commute time in public transport.
[e] Hand hygiene adherence during a shift: very high adherence is more than 10 times hand washing frequency and more than 30 seconds hand washing duration; high adherence is seven to nine times hand washing frequency and more than 30 seconds or more than 10 times hand washing frequency and 20-30sec hand washing duration; medium adherence is four to nine hand washing frequency and less than 30 seconds hand washing frequency duration; low adherence is one to three hand washing frequency and less than 20 seconds duration

Factors related to SARS-CoV-2 infection and seroconversion

In low and middle-income countries age, exposure to COVID-19 cases, unvaccinated status, adherence to personal protection elements, nonfrontline-HCWs, affiliation to the health system, and socioeconomic status are factors associated with SARS-CoV-2 infection in HCWs [12,37,38]. Our study found that high socioeconomic status is related to a lower risk of COVID-19 compared to low socioeconomic status. This is consistent with the literature in different countries indicating that low socioeconomic status is associated with a higher risk of SARS-CoV2 infections [39,40]. We highlight that socioeconomic status is related to several Social Determinants of Health such as education level, household income, and access to healthcare services that vary in each country's context. In Colombia, there is already evidence that healthcare access is an important determinant, as people with public health insurance have a higher risk of COVID-19 compared to those having private, contributive, or special health affiliations [12].

Other factors including the number of cohabitants, previous viral infection due to other viruses, aerosol exposure, low adherence to hand hygiene, and working in more than one hospital area were related to a higher risk of infection, though these associations were not statistically significant. A higher number of people living in the same house may relate to an increased risk due to the contact patterns between infected and exposed individuals. Similarly, viral infections due to other pathogens may produce an immune heterologous effect, meaning that the immunity developed from previous viral infections also affects the host response to unrelated pathogens, such as SARS-CoV-2 [41]. The proximity and duration of exposure play crucial roles in de-

termining transmission. In the case of aerosol particles, they can travel longer distances and remain suspended in the air for extended periods [42]. Consequently, this increases the risk of infection following exposure.

In our study, the only variable statistically significantly related to seroconversion was being diagnosed with COVID-19. This association was expected, as this is the course of the adaptative immunity response against the infection [43]. In the literature, there are more factors related to seroconversion, such as obesity, blood type, COVID-19 vaccination, history of viral infections, and some comorbidities such as immunodeficiencies [44]. We included all the above variables in our full model except for the blood type, nonetheless, these were not statistically significant probably due to a low sample size analyzed in the regression.

This study has some strengths; we analyzed the COVID-19 dynamics during a long-term period of the COVID-19 pandemic (17 months). We considered multiple factors associated with COVID-19 infection and seroconversion. We accounted for COVID-19 vaccination to analyze our data, providing knowledge on how the infection rate changed before and after vaccination. During the CoVIDA-FSFB project researchers were trained in completing questionnaires to increase internal consistency and reliability of the data obtained. Finally, we adjusted for multiple confounders and accounted for effect modifiers.

Among the limitations of the study, we analyzed a cohort that included consecutive volunteer HCWs and there was no sample size calculation. CoVIDA-FSFB project was designed to implement an epidemiological surveillance strategy in hospital workers to aid institutional decisionmaking regarding COVID-19 dynamics and transmission. Therefore, there is no external validity to extrapolate our results to different contexts. As the follow-up consisted of two different surveillance strategies, the results in each period are not comparable as they are in two different contexts.

We highlight that we did not evaluate vaccine effectiveness as this is out of the scope of our study and our sample size has insufficient power to evaluate the real-life effectiveness of the BNT162b2 vaccine. We also clarify that the seroconversion rate after COVID-19 vaccination in our study should not be interpreted as the immunogenicity produced by vaccines, as we utilized qualitative serological kits that were not specific to detect antibodies against the Spike protein (the target protein in SARS-CoV-2 virus of Pfizer-BioNTech BNT162b2 vaccine).

As the COVID-19 pandemic transitions into a post-pandemic phase, further research is warranted to understand the long-term impact of immune responses following vaccination and natural infection. This ongoing exploration will provide a comprehensive understanding of COVID-19 dynamics and inform future public health measures.

Conclusion

Our study provides important insights into the incidence of SARS-CoV-2 infection, reinfection, and seroconversion among HCWs during a long period of the pandemic. We have identified factors related to COVID-19 infection and seroconversion, shedding light on the ongoing risks of infection faced by HCWs even after vaccination.

The role of epidemiological surveillance in the context of emergent diseases is crucial, and our study demonstrates its value in understanding COVID-19 dynamics among HCWs. In addition, our results highlight the importance of individual characteristics- such as socioeconomic status, previous viral infections, and household size- and protective measures influencing the risk of infection in hospital environments.

It is important to acknowledge the limitations of our study, including its focus on a specific cohort of volunteer HCWs and the absence of a sample size calculation which limits the power and validity of our results. However, providing our experience implementing surveillance strategies in our hospital may offer valuable guidance for mitigating the transmission of viruses and addressing the challenges posed by emerging diseases in healthcare settings. We encourage future interventions to account for socioeconomic disparities and effectively safeguard vulnerable HCW populations.

Declarations of competing interest

The authors have no competing interests to declare.

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Ethical approval

The study protocol was approved in June 2020 by both ethics committees, Fundación Santa Fe de Bogotá and Los Andes University (Approval No. 1181). All participants provided written, informed consent before enrolling in the study adheres to the international regulations stated in the Declaration of Helsinki of 1975, Nuremberg's Code and Belmont inform.

Authors' contributions

María A. Nieto Rojas: Conceptualization, investigation, methodology, data curation, formal analysis, visualization, writing - original draft, writing - review and editing. **Nohemí Caballero Prada:** Investigation, methodology, data curation, formal analysis, writing - review and editing. **Camila Remolina Bermeo:** conceptualization, methodology, data curation, investigation, writing - review and editing. **Sergio Moreno Lopez:** formal analysis, methodology, writing - review and editing. **Daniela Vega Hoyos:** conceptualization, methodology, data curation, writing – review. **Juliana Quintero:** conceptualization, methodology, funding acquisition, resources, investigation, study administration, supervision, writing – review, and editing.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijregi.2023.09.003.

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