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Seroprevalence and seroconversion rates to SARS-CoV-2 in interns, residents, and medical doctors in a University Hospital in Bogotá, Colombia

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Abstract

Objectives: To determine the prevalence of antibodies to SARS-CoV-2 and the incidence of seroconversion in the first month of follow-up among interns, residents, and medical doctors attending patients at a University Hospital in Bogota (Colombia).

Design or methods: A cross-sectional and a prospective study were performed during June, July, and August 2020 to assess seroprevalence and seroconversion rates using CLIA IgG for SARS-CoV-2. LFA IgG and IgM and ELFA IgM were also determined to explore concordance with CLIA IgG.

Results: At baseline, 8 (2.28% 95%CI 1.16-4.43%) participants were IgG positive for SARS-CoV-2 by CLIA. At the end of the study, 21 (5.98% 95%CI 3.94-8.97%) individuals seroconverted by CLIA IgG. In all, 29 individuals had IgG by CLIA and of these 11 (3.13% 95%CI 1.76-5.52%) were asymptomatic. No associations with risk factors for infection were identified. CLIA IgG had moderate concordance (>962 samples) with LFA IgG and ELFA IgM, but minimal with LFA IgM.

Conclusions: Our report is the first in Latina America on seroprevalence and seroconversion rates in medical healthcare workers. The relatively high rate (>3%) of asymptomatic health care workers with evidence of previous SARS-CoV-2 infection underscores the need to screen this population for infection to prevent infection/disease spread.

Key Words: COVID-19; SARS-CoV-2; seroprevalence, seroconversion rate; health care workers.

Tasas de seroprevalencia y seroconversión al SARS-CoV-2 en internos, residentes y médicos en un Hospital Universitario de Bogotá, Colombia

Resumen

Objetivos: Determinar la prevalencia de anticuerpos frente al SARS-CoV-2 y la incidencia de seroconversión en el primer mes de seguimiento en internos, residentes y médicos que atienden pacientes en un Hospital Universitario de Bogotá (Colombia).

Diseño y métodos: Se realizó un estudio transversal y prospectivo durante junio, julio y agosto de 2020 para evaluar las tasas de seroprevalencia y seroconversión utilizando CLIA IgG para SARS-CoV-2. También se determinaron LFA IgG e IgM y ELFA IgM para explorar la concordancia con CLIA IgG.

Resultados: Al inicio del estudio, 8 (2,28% IC del 95% 1,16-4,43%) participantes fueron IgG positivos para SARS-CoV-2 por CLIA. Al final del estudio, 21 (5,98% IC 95% 3,94-8,97%) individuos seroconvirtieron por CLIA IgG. En total, 29 individuos tenían IgG por CLIA y de estos 11 (3,13% 95% IC 1,76-5,52%) eran asintomáticos. No se identificaron asociaciones con factores de riesgo de infección. El CLIA IgG tuvo una concordancia moderada (> 962 muestras) con LFA IgG y ELFA IgM, pero mínima con el LFA IgM.

Conclusiones: Nuestro informe es el primero en América Latina sobre tasas de seroprevalencia y seroconversión en trabajadores médicos de la salud. La tasa relativamente alta (> 3%) de trabajadores de la salud asintomáticos con evidencia de infección previa por SARS-CoV-2 resalta la necesidad de realizar pruebas de detección de infección en esta población para prevenir la propagación de la infección.

Palabras Clave: COVID-19; SARS-CoV-2; seroprevalencia, tasa de seroconversión; trabajadores de la salud.

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Introduction

During the SARS-CoV-2 pandemic healthcare workers (HCW) have been shown to have an increased risk of infection[1–6]. Studies in this population in many parts of the world have shown seroprevalences of between 2.4% and 45%, and in general above that of the general population and varing according to multiple factors[1–6]. In asymptomatic HCW, at the peak of the pandemic in England, a global seroprevalence rate of 24.4% was found[7]. Furthermore, individuals who retrospectively reported symptoms compatible with COVID-19 had a higher seroprevalence rate than those who did not report them, in this study and other studies [6,7]. Although retrospective reporting of symptoms may have evocation bias, these findings indicates that, in the context of COVID-19 a relationship can be established between retrospectively reported symptoms and seroprevalence. Seroconversion rates in HCW have been reported in fewer studies and varied between 20-44% in short term follow-up during high circulation of SARS-CoV-2[1,8].

Latin-America is one of the most affected regions of the world by the pandemic[9], with peak cases occurring between July 20 and August 16[10]. Although some studies from Latin-American countries evaluating serology in the general population[11,12] or schools have been published[13,14], to our knowledge only one study in an oncology unit in Brazil[15] has assessed seroprevalence in HCW. Our study was performed during a very active increase of SARS-CoV-2 infections in our country (Colombia) and city (Bogotá): during the five weeks of the study 248,205 new cases were identified in Colombia and 93,907 of these were in Bogotá (http://saludata.saludcapital.gov.co/osb/index.php/datos-de-salud/enfermedades-trasmisibles/covid19/ page consulted 08/19/20). Records from the Hospital Universitario San Ignacio (HUSI) show that during June-August the adult intensive care unit (28 beds in June and 32 beds in July and August) was at full (100%) occupancy with presumed or confirmed COVID-19 patients.

The main purpose of this study was to determine the prevalence of antibodies, and the seroconversion rates to SARS-CoV-2 in a month of follow-up of interns, residents, and medical doctors of the School of Medicine of the Pontificia Universidad Javeriana attending patients at HUSI.

Methods

Study design

First, a cross-sectional study was conducted to determine the seroprevalence of SARS-CoV-2 infection in study population (interns, residents, and medical doctors that were treating patients at HUSI at the time of the study). Potential candidates were invited to participate by email. Participants who were not attending patients at HUSI in June and July and who were taking immunosuppressive drugs (chloroquine, corticosteroids, etc.) were excluded from the study (Figure 1). The remaining participants were asked to fill out a survey about risk factors and symptoms associated with COVID-19, history of previous diagnosis of COVID-19 confirmed by RT-PCR or of clinically diagnosed COVID-19 supported by the presence of anti-SARS-CoV-2 antibodies. The survey was designed in RedCap (Research Electronic Data capture[16]).

In a second step, a prospective study was conducted to determine the incidence of seroconversion at two weeks and a month after the baseline visit, among the seronegative individuals from the cross-sectional study.

As secondary objectives, we aimed to assess the relation between seropositivity either at baseline or during follow-up and risk factors and symptoms compatible with COVID-19. Finally, as an exploratory objective, we examined the concordance of CLIA IgG as a tentative gold standard with the LFA IgG and IgM and ELFA IgM and concordance of the ELFA IgM and LFA IgM.

Sampling and laboratory methods

At the HUSI's clinical laboratory, individuals updated the survey of clinical symptoms compatible with COVID-19, signed an electronic informed consent, and donated 7 ml of venous blood.

Chemiluminescent assay (CLIA): SARS-CoV-2 IgG tests (Abbott Colombia) that recognize the viral nucleoprotein were performed on an Abbott Architect i1000 analyzer, following the manufacturer's protocol. A single lot of positive and negative controls were run at the start of each batch of antibody testing. Samples with a signal-to-cutoff (S/CO) ratio greater than or equal to 1.4 were considered positive.

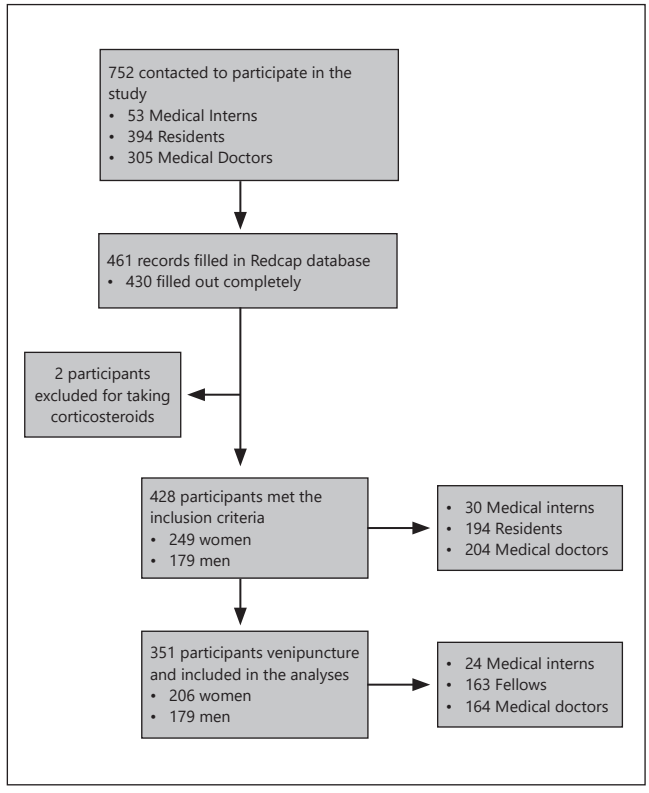

Figure 1. Study Flowchart

Lateral flow assays (LFA): SARS-CoV-2 STANDARD Q COVID-19 IgM/IgG Duo Test kits (SD Biosensor, Gyeonggi-do, Korea) that recognize the viral nucleoprotein were performed following the manufacturer's protocols. Positive results were determined by the appearance of a visible band in the designated area, simultaneously with an appropriate positive control band.

Enzyme linked fluorescence assay (ELFA): The VIDAS Anti-SARS CoV-2 IgM two-step sandwich ELFA that recognizes the viral Spike protein was performed on a VIDAS analyzer (BioMérieux, Marcy-l'Etoile, France). An index is calculated as the ratio between the relative fluorescence value measured in the sample and the relative fluorescence obtained for a calibrator (humanized recombinant anti-SARS CoV-2 IgM) and interpreted as negative (index<1) or positive (index≥1)[17].

All assays were validated with serum samples from RT-PCR+/- individuals in our laboratory. To obtain serum samples from RT-PCR+ individuals for use in the validation process subjects were bled 1-3 weeks after beginning of symptoms. RT-PCR was performed in our Clinical Laboratory on nasopharyngeal aspirates using the VIASURE Real-Time PCR Detection Kit plates (CerTest BIOTEC, Zaragoza, Spain).

Ethical considerations

Our project complied with the legal and ethical guidelines contemplated in the Declaration of Helsinki of the World Medical Association, Fortaleza, Brazil, 2013. Likewise, it adheres to the ethical considerations outlined in articles 15 and 16 of Resolution No. 008430 of 1993 of the Ministry of Health and in Law 84 of 1989. The study and the informed consent form were approved by the ethics committee of School of Medicine of the Pontificia Universidad Javeriana and HUSI.

Statistical analysis

The data was exported and analyzed in Stata 14. We conducted a descriptive analysis of the demographic characteristics of the study participants, according to the seropositivity. Continuous variables were described using median and interquartile range (percentiles 25th and 75th) and categorical variables were described using absolute and relative frequencies.

Second, we examined the relation between seropositivity either at baseline or during the follow-up and risk factors and symptoms compatible with COVID-19, we estimated the odds ratio and 95% confidence interval using logistic regression.

Third, we assessed the concordance of CLIA IgG, as a tentative gold standard, with LFA IgG and IgM and ELFA IgM, and the concordance of ELFA IgM and LFA IgM, using Cohen's kappa and the corresponding 95% confidence interval. CLIA was chosen as the gold standard due to its higher sensitivity and specificity[17–21].

Results

Study population

Seven hundred and fifty-two (752) medical trainees or medical doctors from HUSI were invited to participate by email (Figure 1). Of these, 428 answered the baseline survey, and it was possible to arrange an appointment to bleed 351 of them (Figure 1). Six individuals reported a previous diagnosis of infection with SARS-CoV-2 confirmed by RT-PCR (all but one with symptoms compatible with COVID-19) and two had been hospitalized with symptoms consistent with COVID-19 and positive SARS-CoV-2 antibodies, but their RT-PCR had not identified SARS-CoV-2 (Tables 1 and 2 and Data not shown).

Prevalence of SARS-CoV-2 antibodies in our cohort at baseline

Individuals in our cohort were bled at baseline between June 25 and the 4 of July. At baseline 8 (2.28% 95%CI 1.16-4.43%) individuals were SARS-CoV-2 IgG positive by CLIA (Table 1 and Figure 2). For comparison, we also measured IgG and IgM antibodies by LFA (Table 1) and found that six individuals of the eight indivuals were also positive for IgM and IgG by LFA. Of these six individuals, one had COVID-19 compatible symptoms and a previous diagnosis of COVID-19 by RT-PCR, two had previously been hospitalized with clinical diagnosis of COVID-19 (with negative RT-PCR but positive serology), one had a positive RT-PCR but had remained asymptomatic, and two without history of previous SARS-CoV-2 infection were also asymptomatic (Table 1). Finally, one asymptomatic and one symptomatic individual were positive for IgG by CLIA, but negative for LFA antibodies (Table 1). In addition, 18 individuals were only positive for SARS-CoV-2 LFA IgM

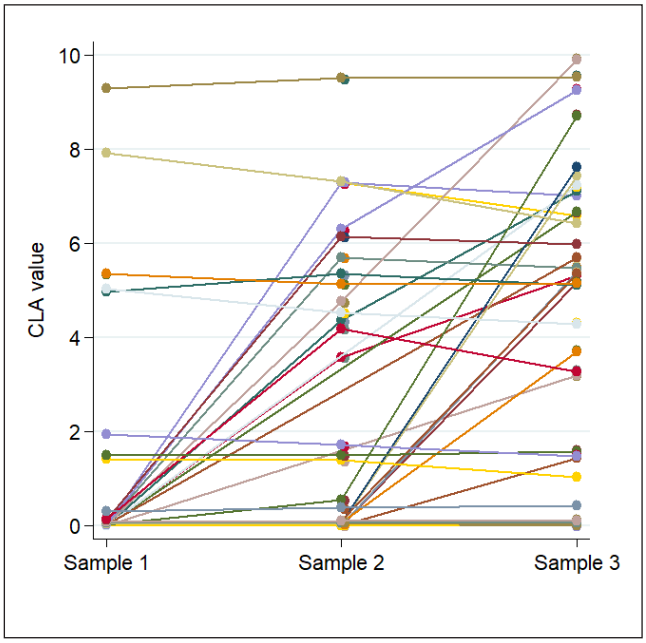

Figure 2. SARS-CoV-2 IgG CLIA values at different times of blood sampling. Sample 1 was the baseline. Sample 2 was taken 15.1 days (95%CI 14.8-15.4) days after baseline. Sample 3 was taken 28.7 days (95%CI 28.3-29.0) after baseline. CLIA; Chemiluminescence assay.

Table 1. Antibodies and symptoms of participants with at least one positive antibody results at baseline.

	Sample 1					Sample 2			Sample 3			
Volunteer	Date	Symptoms*	IgM LFA	IgG LFA	IgG CLIA	Date	Symptoms*	IgG CLIA	Date	Symptoms*	IgG CLIA	
1	Jul 04	NO	+	+	+	Jul 21	NO	+	Aug 05	NO	-	CLIA positive at Baseline
2	Jul 03	NO	+	+	+	Jul 17	NO	+	Aug 01	NO	+	
3	Jun 25	NO	+	+	+	Jul 09	NO	+	Jul 23	NO	+	
4	Jun 30	NO	-	-	+	Jul 16	NO	+	Jul 30	NO	+	
5	Jul 01	YES	+	+	+	Jul 15	NO	+	Jul 29	NO	+	
6	Jul 04	YES	+	+	+	Jul 18	NO	+	Aug 01	NO	+	
7	Jul 02	YES	+	+	+	Jul 16	NO	+	Jul 30	NO	+	
8	Jun 30	YES	-	-	+	Jul 14	NO	+	Jul 28	NO	+	
9	Jun 27	NO	-	+	-	Jul 11	NO	-	Jul 25	NO	-	LFA positive at Baseline
10	Jun 25	NO	+	-	-	Jul 10	NO	-	Jul 24	NO	-	
11	Jul 03	NO	+	-	-	Jul 17	NO	-	Jul 31	NO	-	
12	Jun 25	NO	+	-	-	Jul 09	NO	-	Jul 23	NO	-	
13	Jul 04	NO	+	-	-	Jul 21	NO	-	Aug 03	NO	-	
14	Jul 03	NO	+	-	-	ND	ND	ND	Jul 31	NO	-	
15	Jun 25	NO	+	-	-	Jul 10	NO	-	Jul 24	NO	-	
16	Jun 30	NO	+	-	-	Jul 14	NO	-	Jul 28	NO	-	
17	Jun 26	NO	+	-	-	Jul 10	NO	-	Jul 24	NO	-	
18	Jun 30	NO	+	-	-	Jul 14	NO	-	Jul 28	NO	-	
19	Jul 04	NO	+	-	-	Jul 21	NO	-	Aug 04	NO	-	
20	Jun 26	NO	+	-	-	Jul 10	NO	-	Jul 24	NO	-	
21	Jun 26	NO	+	-	-	Jul 10	NO	-	Jul 24	NO	-	
22	Jul 03	NO	+	-	-	Jul 17	NO	-	Jul 31	NO	-	
23	Jun 30	YES	+	-	-	Jul 15	YES	-	ND	ND	ND	
24	Jun 25	NO	+	-	-	Jul 09	NO	-	Jul 28	NO	-	
25	Jul 02	NO	+	-	-	Jul 16	NO	-	Aug 01	NO	-	
26	Jun 25	YES	+	-	-	Jul 10	NO	-	Jul 28	NO	-	
27	Jun 25	NO	+	-	-	Jul 09	NO	-	Jul 24	NO	-	
28	Jun 30	NO	-	-	-	Jul 14	YES	+	Jul 28	NO	+	Seroconversion in CLIA
29	Jun 26	NO	-	-	-	Jul 10	YES	+	Jul 25	NO	+	
30	Jun 26	NO	-	-	-	Jul 13	NO	+	Jul 24	NO	+	
31	Jun 30	NO	-	-	-	Jul 15	YES	+	Jul 30	NO	+	
32	Jun 25	NO	-	-	-	Jul 13	YES	+	Jul 23	NO	+	
33	Jul 03	NO	-	-	-	Jul 17	YES	+	Jul 31	YES	+	
34	Jul 03	NO	-	-	-	Jul 17	YES	+	Jul 31	NO	+	
35	Jun 26	NO	-	-	-	Jul 15	NO	+	Jul 24	NO	+	
36	Jul 03	NO	-	-	-	Jul 17	NO	+	Aug 03	NO	+	
37	Jun 25	NO	-	-	-	Jul 09	NO	-	Jul 27	YES	+	
38	Jul 03	NO	-	-	-	Jul 17	NO	-	Aug 10	YES	+	
39	Jun 30	NO	-	-	-	Jul 14	NO	-	Jul 30	YES	+	
40	Jul 03	NO	-	-	-	Jul 17	NO	-	Jul 31	NO	+	
41	Jun 25	NO	-	-	-	Jul 09	NO	-	Jul 28	YES	+	
42	Jul 03	NO	-	-	-	Jul 17	NO	-	Jul 31	NO	+	
43	Jul 01	NO	-	-	-	Jul 15	YES	-	Jul 31	NO	+	
44	Jun 30	NO	-	-	-	Jul 17	NO	-	Aug 08	NO	+	
45	Jun 26	NO	-	-	-	ND	ND	ND	Jul 24	NO	+	
46	Jul 01	NO	-	-	-	ND	ND	ND	Jul 29	YES	+	
47	Jul 03	NO	-	-	-	ND	ND	ND	Aug 05	YES	+	
48	Jul 02	YES	-	-	-	ND	ND	ND	Jul 31	NO	+	

* Symptoms before sample. Symptoms included cough, runny nose, fever, diarrhea, shortness of breath, sneeze, headache, odynophagia, dysgeusia, anosmia. ND; not done. CLIA; Chemiluminescence assay. LFA; Lateral Flow Assay.

and one was only positive for LFA IgG (Table 1). One of the 18 individuals that was only positive for IgM had a history of previous COVID-19 symptoms and a positive RT-PCR before joining the study (Table 1 and Supplementary Table 1). The majority of individuals (16/18) with only a positive LFA IgM result and tested for SARS-CoV-2 RT-PCR were negative for RT-PCR at a date close to the date when the antibody sample was obtained (Figure 3 and Supplementary Table 1). Somewhat unexpectedly, three of the eight individuals that declared having a positive SARS-CoV-2 RT-PCR six to twelve weeks prior to joining the study were negative for all of the antibodies measured.

Supplementary Table 1. Date of blood sample and date and result of SARS-CoV-2 specific RT-PCR performed in the study volunteers (the same as in Table 1) with at least one antibody positive results at baseline.

Volunteer	Previous to Sample 1			Previous to Sample 2			Previous to Sample 3			
	Date Abs	Date RT-PCR	RT-PCR	Date Abs	Date R-TPCR	RT-PCR	Date Abs	Date R-TPCR	RT-PCR	
1	Jul 04	ND	ND	Jul 21	Jul 15	-	Aug 05	ND	ND	CLIA positive at Baseline
2	Jul 03	Apr 23	+	Jul 17	ND	ND	Aug 01	ND	ND	
3	Jun 25	Apr 27	-	Jul 09	Jun 28	-	Jul 23	ND	ND	
4	Jun 30	ND	ND	Jul 16	ND	ND	Jul 30	ND	ND	
5	Jul 01	Mar 27	-	Jul 15	ND	ND	Jul 29	ND	ND	
6	Jul 04	Jul 02 Jun 10 Jun 24	- + +	Jul 18	ND	ND	Aug 01	ND	ND	
7	Jul 02	Mar 22 Mar 27	- -	Jul 16	ND	ND	Jul 30	ND	ND	
8	Jun 30	ND	ND	Jul 14	ND	ND	Jul 28	ND	ND	
9	Jun 27	ND	ND	Jul 11	ND	ND	Jul 25	ND	ND	LFA positive at Baseline
10	Jun 25	ND	ND	Jul 10	Jun 27	-	Jul 24	ND	ND	
11	Jul 03	ND	ND	Jul 17	Jul 07	-	Jul 31	ND	ND	
12	Jun 25	ND	ND	Jul 09	Jun 28	-	Jul 23	ND	ND	
13	Jul 04	Jun 23	-	Jul 21	ND	ND	Aug 03	ND	ND	
14	Jul 03	ND	ND	ND	Jul 06	-	Jul 31	ND	ND	
15	Jun 25	ND	ND	Jul 10	Jun 27	-	Jul 24	ND	ND	
16	Jun 30	ND	ND	Jul 14	Jul 02	-	Jul 28	ND	ND	
17	Jun 26	ND	ND	Jul 10	Jun 27	-	Jul 24	ND	ND	
18	Jun 30	ND	ND	Jul 14	Jul 02	-	Jul 28	ND	ND	
19	Jul 04	ND	ND	Jul 21	Jul 08	-	Aug 04	ND	ND	
20	Jun 26	ND	ND	Jul 10	ND	ND	Jul 24	ND	ND	
21	Jun 26	ND	ND	Jul 10	Jun 27	-	Jul 24	ND	ND	
22	Jul 03	ND	ND	Jul 17	Jul 08	-	Jul 31	ND	ND	
23	Jun 30	ND	ND	Jul 15	Jul 02	-	ND	ND	ND	
24	Jun 25	ND	ND	Jul 09	Jun 27	-	Jul 28	ND	ND	
25	Jul 02	ND	ND	Jul 16	Jul 05	-	Aug 01	ND	ND	
26	Jun 25	ND	ND	Jul 10	Jun 29	-	Jul 28	ND	ND	
27	Jun 25	ND	ND	Jul 09	Jul 03	-	Jul 24	ND	ND	
28	Jun 30	ND	ND	Jul 14	ND	ND	Jul 28	Jul 14	+	Seroconversion in CLIA
29	Jun 26	ND	ND	Jul 10	Jun 30	-	Jul 25	ND	ND	
30	Jun 26	ND	ND	Jul 13	ND	ND	Jul 24	ND	ND	
31	Jun 30	ND	ND	Jul 15	Jul 02	+	Jul 30	ND	ND	
32	Jun 25	ND	ND	Jul 13	Jun 28 Jul 09	+ -	Jul 23	ND	ND	
33	Jul 03	ND	ND	Jul 17	Jul 3 Jul 14	+ -	Jul 31	ND	ND	
34	Jul 03	ND	ND	Jul 17	Jul 04	+	Jul 31	ND	ND	
35	Jun 26	ND	ND	Jul 15	ND	ND	Jul 24	Jul 17*	-	
36	Jul 03	ND	ND	Jul 17	ND	ND	Aug 03	ND	ND	
37	Jun 25	ND	ND	Jul 09	ND	ND	Jul 27	Jul 16	+	
38	Jul 03	ND	ND	Jul 17	ND	ND	Aug 10	Jul 20	+	
39	Jun 30	ND	ND	Jul 14	ND	ND	Jul 30	Jul 30	+	
40	Jul 03	ND	ND	Jul 17	ND	ND	Jul 31	Aug 03	+	
41	Jun 25	ND	ND	Jul 09	ND	ND	Jul 28	Jul 14	+	
42	Jul 03	ND	ND	Jul 17	ND	ND	Jul 31	Aug 03*	-	
43	Jul 01	ND	ND	Jul 15	ND	ND	Jul 31	Jul 16	+	
44	Jun 30	ND	ND	Jul 17	ND	ND	Aug 08	Jul 24	+	
45	Jun 26	ND	ND	ND	Jul 08	-	Jul 24	ND	ND	
46	Jul 01	ND	ND	ND	ND	ND	Jul 29	Jul 07	+	
47	Jul 03	ND	ND	ND	ND	ND	Aug 05	Jul 16	+	
48	Jul 02	ND	ND	ND	Jul 03*	+	ND	ND	ND	

Shown are results (RT-PCR) and dates (Date RT-PCR) in which SARS-CoV-PCR was performed prior to each one of the three blood study samples (Date Abs). ND; not done. RT-PCR were not part of the study protocol but were performed in our Clinical Laboratory from nasopharyngeal aspirates using the VIASURE Real-Time PCR Detection Kit plates (CerTest BIOTEC, Zaragoza, Spain).* RT-PCR reported by participants to have been performed outside of our Clinical Laboratory.

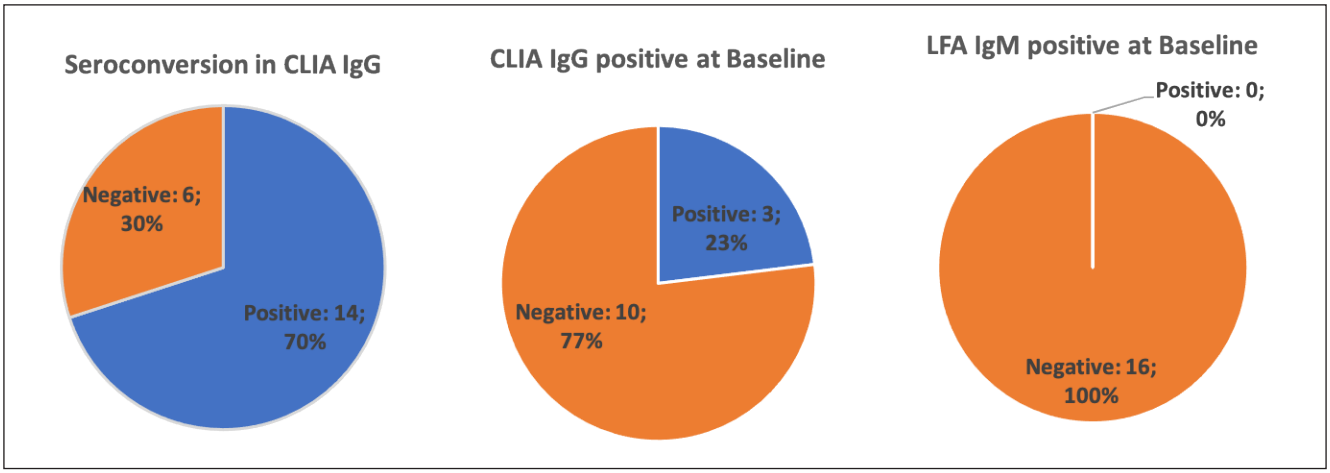

Figure 3. Frequency of individuals positive for SARS-CoV-2 specific RT-PCR performed in the study volunteers with at least one antibody positive results at baseline for whom RT-PCR was performed (individuals depicted in Table 1 and Supplementary Table 1). Dates at which RT-PCR was performed in these indivuals are presented in Supplementary Table 1. Please note that RT-PCR was not performed on some individuals.

Incidence of seroconversion to SARS-CoV-2 antibodies

A second and third blood samples was taken approximately two weeks (15.1 days 95%CI 14.8-15.4) and one month (28.7 days 95%CI 28.3-29.0) after baseline for each individual, from the 9th-21st of June and from June 23 to August 10, respectively.

Three hundred and thirty-five (335) of the original 351 (95.4%) individuals presented for the second bleeding. All eight initially positive individuals by CLIA IgG remained positive (Table 1). Of the remaining 327 individuals, nine seroconverted in SARS-CoV-2 CLIA IgG (2.75% 95%CI 1.45-5.14%, Table 1 and Figure 2). Three of these nine individuals were asymptomatic and the other six, symptomatic. None of the previously IgM positive individuals by LFA or the individual that only was IgG positive by LFA seroconverted by CLIA IgG (Table 1) in the second bleed.

Three hundred and thirty-nine (339) of the original 351 (96.5%) individuals presented for the third bleeding. Seven of eight initially IgG positive individuals by CLIA remained positive (Table 1), with one individual scoring marginally below the cutoff level of the assay (Figure 2). All nine individuals that seroconverted in IgG CLIA in the second bleed remained positive and 12 new individuals (3.93% 95%CI 2.31-6.61%) seroconverted. Four of the twelve individuals that seroconverted in the last sample were asymptomatic (Table 1). None of the previously IgM positive individuals by LFA or the individual that only was IgG positive by LFA seroconverted by CLIA (Table 1) in the third bleed. Altogether, we identified 21 individuals (5.98% 95%CI 3.94-8.97%) that *de novo* seroconverted to SARS-CoV-2 IgG by CLIA amongst our initial cohort of 351 individuals (Table 1 and Figure 2). Thus, adding the 21 individuals that seroconverted with the eight that had IgG by CLIA at baseline, 29 individuals (8.26 95%CI 5.81-11.61%) had SARS-CoV-2 IgG by CLIA and of these 11 (3.13% 95%CI 1.76-5.52%) were asymptomatic (Table 1).

Associations of seroprevalence and seroconversion with risk factors and symptoms compatible with COVID-19

Demographic, infection risk factors, and prevalence of symptoms compatible with COVID-19 for this population are presented in Table 2 for individuals with or without a positive SARS-CoV-2 CLIA test in the study. No risk factors were associated with seroprevalence or seroconversion to SARS-CoV-2.

Concordance of the antibody assays

To further evaluate concordance of the LFA and CLIA assays and to extend this analysis to ELFA IgM, thawed samples from the first bleed were tested by ELFA and thawed samples from bleeds 2 and 3 were tested by ELFA IgM and LFA IgG and IgM. Concordance of CLIA IgG with LFA IgG and ELFA IgG was moderate and with LFA IgM, minimal (Table 3)[22]. The ELFA IgM and LFA IgM also had minimal concordance (Table 4).

Discussion

We have performed one of the first SARS-CoV-2 seroprevalence/seroconversion rate studies in Latin-America and found that at baseline 2.28% of HCW were IgG positive by CLIA (Table 1). At the end of the study, 5.98% of individuals had seroconverted by CLIA IgG and, in all, 29 individuals (8.26%) had SARS-CoV-2 IgG by CLIA, of which 11 (3.13%) were asymptomatic (Table 1). No associations between seroprevalence/seroconversion in CLIA and risk factors for infection were identified (Table 2). Concordance of CLIA IgG with LFA IgG and ELFA IgG was moderate and with LFA IgM, minimal (Table 3). The ELFA IgM and LFA IgM also had minimal concordance (Table 4).

The levels of seroprevalence for CLIA IgG (2.28%) at the beginning of the study and of seroconversion to this antibody (5.98%) are comparable to those reported in other studies of HCW and, overall, higher than those observed in the general population[1–6]. In a comparable study in England that followed

Table 2. Comparison of demographics and risk factors of CLIA IgG negative and positive patients

Characteristic	Negative (n = 322)	Positive (n = 29)	OR (95% CI)
Demographics			
Age, years; Median (IQR)	31.5 (27.5 - 38.6)	29.4 (26.9 - 37)	0.98 (0.94 - 1.03)
Sex; n (%)			
Women	192 (59.6)	14 (48.3)	Reference
Men	130 (40.4)	15 (51.7)	1.58 (0.74 - 3.39)
Mode of transport; n (%)			
Public transport	7 (2.2)	1 (3.4)	Reference
Car/moto	256 (79.5)	21 (72.4)	0.57 (0.07 - 4.89)
Walking/Bycicle	59 (18.3)	7 (24.1)	0.83 (0.09 - 7.78)
Service; n (%)			
Emergencies	66 (20.5)	8 (27.6)	Reference
ICU	11 (3.4)	1 (3.4)	0.75 (0.09 - 6.6)
Outpatient consultation	60 (18.6)	5 (17.2)	0.69 (0.21 - 2.22)
Other services	185 (57.5)	15 (51.7)	0.67 (0.27 - 1.65)
Occupation; n (%)			
Healthcare worker in training	167 (51.9)	20 (69)	Reference
Healthcare worker	155 (48.1)	9 (31)	0.48 (0.21 - 1.1)
Risk Factors			
Obesity; n (%)			
No	306 (95)	27 (93.1)	Reference
Yes	16 (5)	2 (6.9)	1.42 (0.31 - 6.49)
Smoking behavior; n (%)			
No	301 (93.5)	26 (89.7)	Reference
Yes	21 (6.5)	3 (10.3)	1.65 (0.46 - 5.91)
Diabetes diagnosis; n (%)			
No	319 (99.1)	28 (96.6)	Reference
Yes	3 (0.9)	1 (3.4)	3.8 (0.38 - 37.72)
Hypertension diagnosis; n (%)			
No	306 (95)	26 (89.7)	Reference
Yes	16 (5)	3 (10.3)	2.21 (0.6 - 8.07)
Symptoms before recruitment; n (%)			
No	255 (79.2)	24 (82.8)	Reference
Yes	67 (20.8)	5 (17.2)	0.79 (0.29 - 2.16)
COVID-19 exposure			
Close contact with COVID-19 patients; n (%)			
No	76 (23.6)	7 (24.1)	Reference
Yes	180 (55.9)	17 (58.6)	1.03 (0.41 - 2.57)
Not known	66 (20.5)	5 (17.2)	0.82 (0.25 - 2.71)
Contact with body fluids; n (%)			
No	194 (60.2)	13 (44.8)	Reference
Yes	107 (33.2)	13 (44.8)	1.81 (0.81 - 4.05)
Not known	21 (6.5)	3 (10.3)	2.13 (0.56 - 8.09)
Use of Personal Protection Elements; n (%)			
No	1 (0.3)	0 (0)	-
Yes, complete per protocol	294 (91.3)	27 (93.1)	Reference
Yes, incomplete	27 (8.4)	2 (6.9)	0.81 (0.18 – 3.58)

200 front line HCW for two weeks, they found that 20% of them seroconverted during the study, but 25% were already seropositive at the beginning of the study [1]. Most likely, the higher prevalence in the English study compared with our study are due to the fact that the latter study was performed with front line workers that are at higher risk than the individuals in our study (a mixed population of medical doctors).

One of the main findings of our study, is the relatively high numbers (3.18%) of asymptomatic individuals positive for IgG by CLIA (Table 1). This number is very close to the number of asymptomatic HCW detected by screening with PCR in nasofaringeal swabs (3%) [23] or saliva (2,6%) [24] in England. Although it is incompletely clear how much pre-symptomatic and asymptomatic individuals contribute to virus spread, focusing only on stopping symptomatic individuals is insufficient to control the spread of the virus [25,26]. None-invasive rapid screening strategies for SARS-CoV-2 infection are needed to evaluate symptomatic and asymptomatic HCW.

The lack of association between demographic and risk factors and SARS-CoV-2 seroprevalence/seroconversion in CLIA (Table 2) may be explained because some of the risk factors evaluated (sex, obesity, diabetes, hypertension, and smoking) can be risk factors for disease and not infection. Moreover, most of the participants used PPE and followed biosafety recommendations (Table 2).

Our results seem comparable to previous studies in which the CLIA test that we used showed a sensitivity and specificity close to 100% when compared with PCR +/- samples [18–20], while the LFA [21] and the ELFA [17] appear to be less sensitive and specific. The LFA IgG seems to have missed 20 samples positive by CLIA IgG (Table 3), and all but one of the 11 samples positive by LFA IgG but negative by CLIA IgG were only positive for this antibody, suggesting they may be false positives. The minimal concordance of the LFA IgM with other assays can probably be explained because of a high level of false positives: at baseline most (18, 5.13% 95%CI 3.27-7.96) of the individuals that had any positive antibody were positive for LFA IgM only (Table 1). However, none of these individuals had a positive PCR at or close to the time when the sample was taken (Figure 3 and Supplementary Figure 1). With few exceptions, they did not present with COVID-19 compatible symptoms (Table 1) and none of them seroconverted to IgG by CLIA on follow-up. These results are consistent with the hypothesis that most, if not all, of these results are false-positive results. This hypothesis is in agreement with the validation performed by the Colombian National Institute of Health that reports that the IgM LFA assay may have 4% false positives defined using serums from prepandemic individuals (https://www.ins.gov.co/Pruebas_Rapidas/4.%20Informe%20de%20validaci%C3%B3n%20PR%20SD%20Biosensor.pdf page consulted August 25). Posible crossreactivity with seasonal coronavirus (not addresed in this study) may partially explain this result.

Our study may have a sampling bias. Independent data from our hospital indicate that up to the 15th of June 13 medical doctors and 7 residents from approximately 800 individuals had been diagnosed with COVID-19 (with PCR or clinical

Table 3. Concordance between CLIA IgG and LFA IgG, LFA IgM, and ELFA IgM

	Cohen´s Kappa		CLIA IgG	
			+	-
LFA IgG	0.6646 95% CI (0.5541-0.7751)	+	33	11
		-	20	956
LFA IgM	0.3663 95% CI (0.2387-0.4939)	+	19	24
		-	34	943
ELFA IgM*	0.6207 95% CI (0.5034-0.7380)	+	30	13
		-	21	941

* Fifteen samples were read as invalid by ELFA and three individuals did not authorize for their sample to be used after the initial test.

Table 4. Concordance between ELFA IgM and LFA IgM

	Cohen´s Kappa		ELFA IgM	
			+	-
LFA IgM	0.2468 95% CI (0.1191-0.3745)	+	12	31
		-	31	931

* Fifteen samples were read as invalid by ELFA and three individuals did not authorize for their sample to be used after the initial test.

symptoms/serology). By the 15th of August, these numbers had increased to 44 medical doctors and 55 residents diagnosed with COVID-19. These numbers are higher than what we found in our population an suggest that our values of seroprevalence and seroconversion may be underestimated. A probable explanation for this is that volunteers with COVID-19 were isolated at the time of sampling and were unable to participate in the study or that having been previously tested were uninterested in participating.

Ethical disclosure

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Conflicts of interest: The authors have no conflicts of interest to declare.

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Protection of human and animal subjects: This study was approved by the Ethics Committee of the School of Medicine of Pontificia Universidad Javeriana Bogotá, Colombia and was done in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki). An informed consent form, approved by the Ethics Committee of HUSI and the Pontificia Universidad Javeriana School of Medicine, was signed by all volunteers.

Confidentiality of data: No names of participants is presented nor data that can reveal their identity.

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