

ARTIGO ORIGINAL

Seroprevalence of anti-SARS-CoV-2 antibodies in health care workers in a complex South Brazilian hospital

Soroprevalência de anticorpos anti-SARS-CoV-2 em profissionais de saúde em um Complexo Hospitalar do sul brasileiro

Seroprevalencia de anticuerpos anti-SARS-CoV-2 en profesionales de la salud en un complejo hospitalario en el sur de Brasil

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ABSTRACT

Introduction: Health care workers (HCWs) are highly susceptible to SARS-CoV-2 infection because of the close contact care required by patients. **Methods:** A cross-sectional study involving HCW was conducted. Serological tests (lateral flow immunochromatographic assays) were performed from June 22 to July 17, 2020. **Results:** A total of 3,739 employees were tested, resulting in 10.2% positivity. The seroprevalence in the support group was 11.4% (71/624) and 7.3% (32/438) in the administrative group, with a higher seroprevalence among those who reported symptoms (64/469; 13.6%). **Conclusions:** Seroprevalence of anti-SARS-CoV-2 was higher in employees with related symptoms in both the support group and in professionals working in nursing wards.

Keywords: COVID-19, SARS-CoV-2, healthcare workers, seroprevalence, immunoassay.

RESUMO

Introdução: Profissionais de saúde (HCW) são altamente suscetíveis à infecção por SARS-CoV-2 devido ao contato próximo exigido pelos pacientes. **Método:** Foi realizado um estudo transversal envolvendo HCW. Os testes sorológicos (ensaios imunocromatográficos de fluxo lateral) foram realizados de 22 de junho a 17 de julho de 2020. **Resultados:** Um total de 3.739 funcionários foram testados, resultando em 10,2% de positividade. A soroprevalência no grupo de suporte foi de 11,4% (71/624) e de 7,3% (32/438) no grupo administrativo, com maior soroprevalência entre aqueles que relataram sintomas (64/469; 13,6%). **Conclusões:** A soroprevalência do anti-SARS-CoV-2 foi maior em funcionários que relataram sintomas, tanto no grupo de apoio

quanto em profissionais que trabalham em enfermarias.

Descritores: COVID-19, SARS-CoV-2, profissionais de saúde, soroprevalência, imunoensaio.

RESUMEN

Introducción: Los profesionales de la salud (HCW) son altamente susceptibles a la infección por SARS-CoV-2 debido al estrecho contacto que requieren los pacientes. **Método:** Se llevó a cabo un estudio transversal en el que participaron los HCW. Las pruebas serológicas (ensayos inmunocromatográficos de flujo lateral) se realizaron del 22 de junio al 17 de julio de 2020. **Resultados:** Se evaluó a un total de 3.739 empleados, lo que resultó en un 10,2% de positividad. La seroprevalencia en el grupo de apoyo fue del 11,4% (71/624) y del 7,3% (32/438) en el grupo administrativo, con mayor seroprevalencia entre los que informaron síntomas (64/469; 13,6%). **Conclusiones:** La seroprevalencia de anti-SARS-CoV-2 fue mayor en los empleados que reportaron síntomas, tanto en el grupo de apoyo como en los profesionales que laboran en las salas.

Descriptores: COVID-19, SARS-CoV-2, profesionales de la salud, seroprevalencia, inmunoensayo.

INTRODUCTION

In late 2019 in Wuhan, China, a new virus was identified as SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), which was found to cause COVID-19 (coronavirus disease 2019).¹ Despite attempts to contain the disease by public health institutions, the virus spread worldwide, being declared a pandemic by the World Health Organization (WHO) in March 2020. At the time this survey was conducted (June/July 2020), more than 10 million people had been infected globally, including more than two million people in Brazil alone.^{2,3}

SARS-CoV-2 can generate a wide spectrum of symptoms, ranging from asymptomatic cases to severe conditions requiring hospital support. This makes it difficult to control infections, since even without symptoms individuals can still transmit the virus.^{3,4} Among those affected, healthcare workers (HCWs) are significantly more susceptible to infection, especially those who provide direct assistance to patients. Thus, rapid diagnosis and medical assistance, as well as psychological support, is extremely important for this demographic.^{3,5}

The gold standard for COVID-19 diagnosis consists of reverse transcriptase polymerase chain reaction (RT-PCR) analysis of the nasopharynx and oropharynx combined swab, which must be collected during the acute phase of the disease. However, the sensitivity of RT-PCR testing may be affected by the infection period. The initial and late phases of infection may not have the sufficient viral load required for detection, which can result in false-negative results. In such cases, serological tests, such as immunochromatographic tests (lateral flow chromatographic assays) or enzyme-linked assays (ELISA), are important for confirmation of infection. These testing methods detect the presence of specific SARS-CoV-2 antibodies in the patient's serum.^{6,7}

Though immunochromatographic tests offer rapid results and easy execution, they are limited by their variable sensitivities which depend on the timepoint of infection. The presence of IgM or IgA antibodies indicates current acute infection, whereas IgG antibodies indicate previous contact with the virus. Thus, serological tests play a fundamental role in identifying previous infections by SARS-CoV-2, which could help assess the seroprevalence of the disease in specific population subgroups.^{4,6-9} Based on this assertion, our study aimed to estimate the seroprevalence of SARS-CoV-2 antibodies in different HCW groups and to verify the IgM and IgG antibody profiles of these groups within a highly complex South Brazilian hospital.

METHODS

A cross-sectional study involving HCWs was carried out at Hospital de Clínicas/Universidade Federal do Paraná (CHC/UFPR), a tertiary academic hospital with 500 beds. In total, 3,739 professionals were included and divided into three different groups: administration, care, and support. The administrative group included secretaries, and others such as managers. The care group included health professionals from assistance areas, such as the COVID and non-COVID nurseries and laboratories, as well as diagnostic imaging staff and medical or multiprofessional residents. The support group was composed of individuals from outsourced services such as cleaning, nutrition, maintenance, and transportation. Data collected included age, sex, and the presence of symptoms in the months before blood collection. This study was approved by the Ethical Committee Board of CHC-UFPR (CAAE: 31687620.0.0000.0096).

Volunteers' venous blood was collected (~8mL) in a tube with a serum clot activator (Vacuette®) from June 22 to July 17 2020. Samples were centrifuged for 5 min at 3,500 rpm and the serum was used to perform the point-of-care test (POCT). Lateral flow immunochromatographic assay kits from two different brands approved by the National Health Surveillance Agency (ANVISA) were used: either MedTeste Coronavirus (COVID-19) IgG/IgM (1696/3739; 45.4%) or COVID-19 IgG/IgM ECO Test (2043/3739; 54.6%), both of which were performed according to the manufacturers' instructions. Before carrying out this study, the diagnostic performance of both kits was evaluated.¹⁰

For employees who agreed to sample collection and tested positive for IgM, nasopharyngeal swabs were collected to perform RT-PCR. The Mini Spin Virus DNA/RNA Biopur Extraction Kit (Möbius Life Science, Brazil) was used for RNA isolation, and amplification was performed using the One Step RT-PCR Master Mix Kit (Instituto de Biologia Molecular do Paraná, Brazil), on an Applied Biosystems™ instrument, 7500 Real Time PCR System (Thermo Fisher Scientific Inc., USA), all according to the relevant manufacturer's instructions.

Excel™ was used for data analysis and production of all figures. Results were then presented as median (interquartile range), number (n), and percentage, where appropriate. Categorical variables were compared between the groups studied, using Fisher's exact test. The results were considered significant at the 5% alpha level. The adjusted seroprevalence was assessed, considering the specificity and sensitivity of the

tests. The results were as follows: 78.38% and 92.86% for the ECO test and 100.00% and 97.14% for MedTeste.¹⁰

RESULTS

Overall, 3,739 HCWs participated in the study (Figure 1-A). Of these, 2,609 (69.7%) were women, and the median age was 43 years (IQR, 36–53 years). In total, 438 (11.7%), 2,677 (71.6%), and 624 (16.7%) professionals were tested in the administrative, care, and support groups, respectively (Figure 1-A). A total of 3,307 volunteers answered questions regarding their symptoms.

The prevalence rate of seropositivity (unadjusted) for CHC-UFPR employees was 383/3,739 (10.2%), with 32/438 (7.3%) in the administrative group, 280/2,677 (10.4%) in the care group, and 71/624 (11.4%) in the support group (Figure 1-B). The global adjusted seroprevalence was 10.8%. A higher prevalence of antibodies was observed among men (136/1,130; 12.0%) compared to women (247/2,609; 9.5%); however, this difference was not statistically significant ($p=0.667$). In total,

469/3,306 (14.2%) of the volunteers reported symptoms in previous months, and antibody positive results were higher in those who reported symptoms (64/469; 13.6%) than in those who did not (281/2,837; 9.9%; $p=0.018$; Table 1). Of the HCWs who presented positive IgM serum results, 40/97 (41.2%) were tested by RT-PCR for SARS-CoV-2, and only 1 (1/40; 2.5%) returned a positive result.

DISCUSSION

The challenge of POCs lies in the sensitivity variability between serological assays, especially when individuals present no symptoms, which is particularly relevant in areas with low seroprevalence. Another factor is the possibility of cross-reactivity or false-positive results that can be generated when using these testing methods.⁶ In these cases, the ideal situation would be to perform a molecular assay by RT-qPCR, confirming infection by the virus. In this study, 383 of 3,739 (10.2%) employees had antibodies detected in their serum.

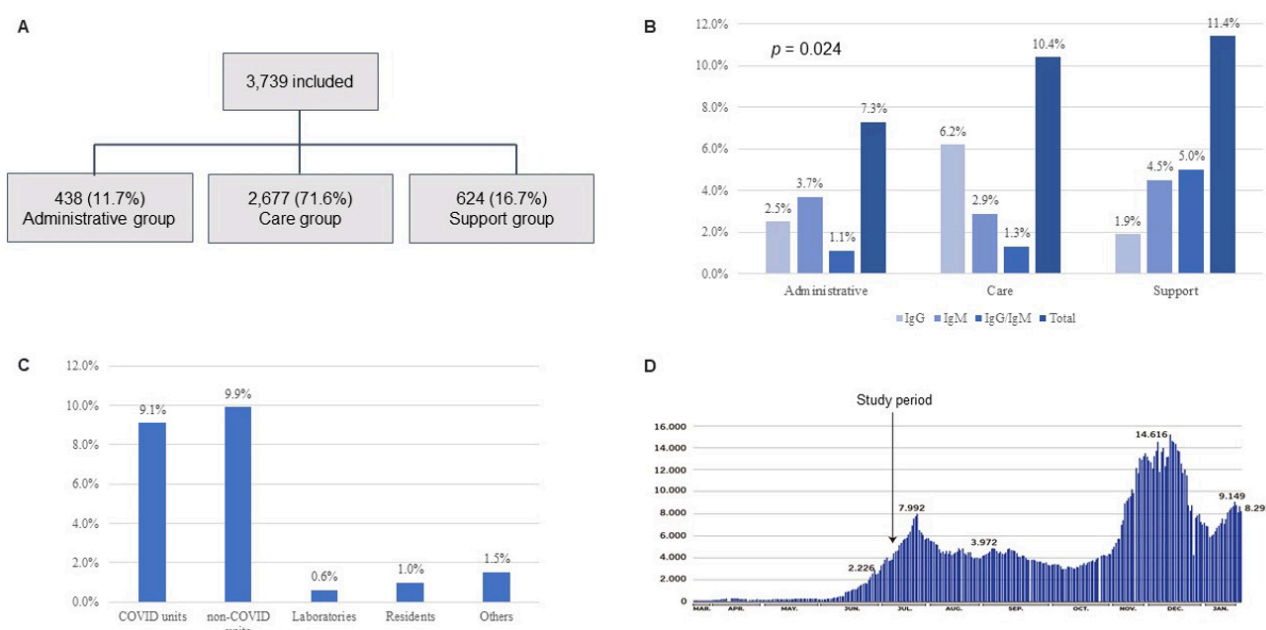


Figure 1. (A) Flow chart of participants. (B) Seroprevalence and antibody profile by group. (C) Seroprevalence in the care group: COVID and non-COVID nurseries; Laboratories: clinical and pathology laboratories; Residents were considered a separate group as they circulate in all sectors; Others: academics and diagnostic imaging. (D) Number of weekly COVID-19 cases in Curitiba - Brazil (Source: Modified from SMS/CE/ COVID-19 monitoring).

Table 1. Comparison between symptomatic and asymptomatic by group.

Symptoms	YES					NO				
	A- Administrative	B- Care	C- Support	D- Total	p value (A, B, C)	E- Administrative	F- Care	G- Support	H- Total	p value (E, F, G)
Overall	68/469	296/469	105/469	469		322/2837	2013/2837	502/2837	2837	
Sex										
Female	45/344	231/344	68/344	344	0.011	207/1977	1453/1977	317/1977	1977	<0.0001
Male	23/125	65/125	37/125	125		115/860	560/860	185/860	860	
Positive**										
IgG*	4/30	24/30	2/30	30	0.096	5/143	128/143	10/143	143	<0.0001
IgM*	2/15	8/15	5/15	15		13/94	58/94	23/94	94	
IgG/IgM*	2/19	10/19	7/19	19		3/44	19/44	22/44	44	
Negative**	60/405	254/405	91/405	405		301/2556	1808/2556	447/2556	2556	

p value: Sex B vs C = 0.009; E vs F = 0.005; F vs G = 0.0001; *D vs H = 0.024; *B vs F = 0.023; *E vs F = 0.0023; *F vs G < 0.0001; **D vs H = 0.018; **B vs F = 0.036. Other comparisons were omitted because $p > 0.05$.

This result is on par with the situation of the pandemic in Curitiba, Brazil at the time of testing, when the number of cases was rising (Figure 1- D). A study in the United Kingdom showed the rate of seroprevalence was 18.0% among health professionals,¹¹ while in New York City, USA, the individuals of the same professional activity presented 35.4% of positivity.¹² In Spain, a seroepidemiological study of national scope showed that the health sector was the occupational group with the highest seroprevalence at 10.2%¹³ positivity. In addition, a large Spanish reference hospital reported seroprevalence of 9.3%,¹⁴ which is a similar rate to that reported in the present investigation. However, seroprevalence is highly dependent on the local epidemiological profile and moment in time, making comparisons of subgroups difficult.

Although most individuals tested were women, as the majority of health workers are female, we observed no difference in seroprevalence based on sex.

With regards to occupation, support groups were the most seroprevalent, with a positive result frequency of 11.4%. In this group, most workers are part of outsourced hospital services such as cleaning, maintenance, and transportation. Based on this, we can postulate that contamination likely occurs outside the hospital environment.

In the care group, despite greater exposure, only 10.4% of individuals showed positive results. Furthermore, in the administrative group, only 7.3% were reactive, likely due to the lower direct contact with potentially infected people.¹⁴

As for the symptoms reported by employees, the chance of being seropositive was greater for participants who reported having previously had any symptoms compatible with COVID-19.¹⁴

Only a portion of the employees who tested positive for IgM underwent RT-PCR, and of these, only 2.5% were positive. These results show that the testing window is one of the most important factors to consider, as it influences the sensitivity of the test and has the potential to generate false-negative results. Another point to consider is the fact that POCTs have relatively common cross-reactivity, which can result false-positive antibody reactions.⁶

This study examines the seroprevalence of antibodies against SARS-CoV-2 among a representative sample of CHC-UFPR employees. As expected, the group with the highest seroprevalence had direct contact with patients. Surprisingly, workers in non-COVID units had higher seroprevalence than those in COVID units (Figure 1-C), confirming the high transmissibility of the virus from asymptomatic individuals. This highlights the fact that POCTs are very useful for detecting real seroprevalence in a community at high risk of contracting SARS-CoV-2, especially in cases of mild or moderate infection.

This study has some limitations, the first being due to the fact that two different POCTs were used. During the diagnostic performance of the tests,¹⁰ we observed that the sensitivity and specificity values of both kits were different, which may have interfered with the results. However, the separation of the results between the kits was not possible, as some groups would be without any participant. Secondly, due to the kinetics of antibody production falling over time, the number of people previously exposed to the virus may be underestimated.¹⁶ Finally, multiple repetition of testing procedures would help to better understand the epidemiological dynamics. However, studies on antibody seroprevalence have been scarce in our region, and knowing the impact of this infection among the selected groups allows for guidance of preventive measure implementation, helping to offer protection to HCW as well as the patients they assist.

CONCLUSION

In conclusion, our study demonstrated that the seroprevalence of anti-SARS-CoV-2 antibodies in CHC-UFPR employees was higher in those with related symptoms as well as in members of the support group. Among care professionals, who reported related symptoms, generally those who worked in ward nursery presented greater seroprevalence than the support group.

CONFLICT OF INTEREST STATEMENT

All authors declare that they have no conflict or competing interests.

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