SARS-CoV-2 seroprevalence and risk factors among oligo/asymptomatic healthcare workers(HCW): estimating the impact of community transmission.

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# Abstract

We evaluated the seroprevalence of SARS-CoV-2 and risk factors among 4,987 oligo/asymptomatic HCW. The seroprevalence was 14% and factors associated with being infected with SARS-CoV-2 were lower educational level(aOR of 1.93;95%CI1.03-3.60), using public transport to work (aOR of 1.65;95%CI 1.07-2.62), and working in cleaning or security (aOR of 10.1;95%CI 3.40-26.9).



#### Introduction

The COVID-19 pandemic has become an increasing challenge for the Brazilian healthcare system, with over 100,000 deaths reported due to SARS-CoV-2 by 11 August, 2020[1-2]. HCW providing frontline care for COVID-19 patients are a highly vulnerable group for SARS-CoV-2 infection compared to the general population[3]. Outbreaks of COVID-19 have been described among HCW in Asia, Europe, and USA[3], suggesting that transmission of SARS-CoV-2 occurs in the hospital setting, aggravated by shortages of personal protective equipment (PPE). Few studies have evaluated SARS-CoV-2 seroprevalence and risk factors in HCW[4-5].

Hospital das Clínicas (HC) is the largest hospital in Latin America – situated in the centre of the Greater Metropolitan Region of São Paulo, a densely-populated megacity, and the epicentre of COVID-19 in Brazil. The aim of this study was to evaluate the seroprevalence of SARS-CoV-2 and risk factors for oligo/asymptomatic COVID-19 among HCW at HC, and to estimate the impact of community transmission.

#### **Methods**

This was a cross-sectional study, between 14 and 28 May, 2020, evaluating the presence of anti-SARS-CoV-2 IgG/IgM antibodies (rapid chromatographic immunoassay, Wondfo-China) in HCW in the Central and the Outpatient Institutes of Hospital das Clínicas.

A voluntary questionnaire comprising 52 questions(https://www.pdf.investintech.com/preview-frames.php?id=WGMxUkVjRVMxVTZqTTBFZ25yOFhwbEY0SWZDNmlCbERtZE1xVGRSWkdlYzdkTk9xRmg4Q3ZRTDk5VVZRc3pKeTdtZW0xa09HQjA2QVQwaG96OWFWOWRHN2MyQy8xeEtvNHdHWWZjZEtCOU5ZVFIFTnNyK2Z1UzhFdFJ5Y2tVVnA=).) using the survey monkey platform was offered. This evaluated demographics, educational level, professional category, transportation to work, housing, household contacts, comorbidities, smoking status, medications, influenza vaccination status, PPE use, known prior COVID-19 infection, and respiratory symptoms. HCWs answered a question about the type of PPE that they frequently wear. This question was multiple choice and the HCW had to select which items of PPE they used.

# **Setting**

HC is a 2200-bed public teaching hospital, spread over seven buildings. The Central Institute was designated to receive COVID-19 cases and comprises an emergency department, 300 ICU and 300 ward beds, with 6000 HCW. Between 30 March and 6 July, 3,483 COVID-19 patients were

hospitalized in the Central Institute. The Outpatient Institute was considered to be COVID-19 free with 1,000 HCW. During the pandemic, HCW did not move between buildings. HC contracts third-party cleaning, security, and laundry services.

Personal protective equipment(PPE) was made available to all HCW. HCW providing direct patient care wore N95 masks and scrubs during their entire shifts. When examining or touching patients they added disposable gloves and a gown. During aerosol generating procedures, they added a gown, gloves, and a face shield. HCW used the same N95 respirator between patients. The cleaning staff wore N95 respirators during their entire shifts. As of May 4, universal surgical masks were implemented for all workers. HCW were trained to don and doff PPE in face-to-face sessions and with videos and posters.

Any symptomatic HCWs were evaluated clinically, and nasopharyngeal swabs were collected for SARS-CoV-2 RT-PCR[6]. PCR-positive HCWs received 14 days of paid leave.

#### **Definitions**

HCWs were defined as any employee working within the hospital, including auxiliary services. A HCW was considered to have had oligo/asymptomatic COVID-19 if serology positive **without** previously being tested with RT-PCR.

# Data analysis

Univariable associations between possible risk factors and serostatus were tested within a logistic regression framework. A multivariable logistic regression using backward selections included professional category, socioeconomic level, number of contacts in the household, and type of transportation used. Age, sex and professional category were included *a priori*. Other variables were evaluated if p<0.05 in the univariate analysis.

Zip codes were used to geolocate HCWs' residential addresses, and assign their census tract of residence. The per capita income in each census tract was extracted from the 2010 national census (www.ibge.gov.br)[7] and we calculated the distance from home to HC.

We calculated the cumulative number of reported confirmed COVID-19 cases and severe acute respiratory syndrome (SARS) of unknown cause, in each of the 517 zones of the Greater Metropolitan

Region using information from the state epidemiologic surveillance unit<sup>15</sup>. We compared both the absolute and per capita number of cumulative cases in the residential zones of seropositive and seronegative HCW.

# **RESULTS**

Serology was performed in 5,645 HCW. Of these, 658 had previously been tested with RT-PCR and were excluded(Supplemental Figure 1). Among the remaining 4,987 HCW, 701 were positive[14.1%(95%CI 13.1-15.0%)]. Seroprevalence was similar between men and women and hospital unit. HCWs aged  $\geq$ 61 years had low seroprevalence (Supplemental **Table 1**).

2,415 of 4,987 HCW (48%) answered the questionnaire. Seroprevalence among non-responders was higher than for responders(16.6% vs 11.3%). The univariable analysis of factors associated with SARS-CoV-2 serology can be seen in **Table 2**. HCW with a higher educational level had lower seroprevalence. HCW using public transportation had higher seroprevalence than those commuting by car. The professional categories with the highest seroprevalence were cleaners and security workers. We found no association between serostatus and the use of any particular item of PPE, comorbidities, or medications (**Table 2**).

In the multivariable analysis, HCW with the lowest formal educational had an adjusted odds ratio (aOR) of 1.93 (95%CI:1.03-3.60) compared to those with a post-graduate qualification. Cleaning/security staff had an aOR of 10.1 (95%CI 3.40-26.9) compared to doctors. HCW commuting to work on public transport carried an aOR of 1.65 (1.07-2.62) compared to those commuting by car (**Table 2**).

Many symptoms were associated with a positive serology, in particular fever, loss of smell, and loss of taste (**Supplementary Table 3**). Truly asymptomatic HCW, i.e. those denying experiencing any symptoms accounted for 48% (106/221) of seropositive cases, but had a lower seropositivity than those experiencing at least one symptom (7.1% versus 13.5%).

The home address of 2,239 (93% of respondents) were geocoded. The number of HCW living in each of the 517 zones is shown according to serostatus (**Supplementary Figure 2**). Most seropositive cases lived far from the hospital. The median [IQR] distance from work among seropositive HCW was 11.5 km [4.2-18.9 km]) compared to 9.3km [3.4-17.2 km], among seronegative HCW (p:0.005) (**Supplemental Figure 2**).

Seropositive HCW tended to live in census tracts with lower average per capita income (median [IQR] R\$966/month [R\$533-R\$1,713]) compared to seronegative HCW (R\$1,060/month[R\$671-R\$2,802],p<0.001); (US\$1.00=R\$ 5.43). The income distribution among seronegative HCW was bimodal: there was a high-income peak among seronegative HCW not seen among seropositive HCW (Supplementary Figure 2).

#### Discussion

Seroprevalence among oligo/asymptomatic HCW was 14%, higher than in Europe (1.6-10.7%) and Asia(0-2%)[4-5]. Seroprevalence did not vary by clinical area: HCW from the building entirely dedicated to COVID-19 had the same prevalence as in the outpatient institute, a low exposure setting. In addition, ICU and emergency department workers had the same prevalence as in other hospital wards. Factors associated with being infected with SARS-CoV-2 were: lower educational level, using public transport or walking/cycling to work, and working in cleaning or security. Furthermore, the seroprevalence of 14% is similar to a household serosurvey (12%) in São Paulo at the time of our study [8]. Taken together, this suggests that HCWs may have acquired the infection predominantly in the community. Our findings are consistent with results from the Netherlands, where whole-genome sequencing of clinical samples from HCW and patients suggested there were multiple introductions into the hospitals through community-acquired infections and local amplification[9].

We found that the distance from home to work, use of public transportation, and residing in poorer neighbourhoods were associated with infection. Brazil is a country with great social inequality, and São Paulo – a megacity with 12.252.023 inhabitants and a population density of 7.398,26 inhabitants/km² (IBGE 2019)[7]-has severe urban mobility problems and inefficient public transportation. Data from the national census show that the low-income population can spend more than two hours commuting to work[7]. Public transportation during the peak hours is usually crowded, facilitating the transmission of respiratory viruses.

The number of people at home was not associated with seropositivity, suggesting that contagion may not have primarily occurred there. The number of inhabitants per household is a cultural aspect of Brazilian society and probably does not differ much between the HCW[9]. Interestingly, working in cleaning/security carried an OR of 10.1 compared to doctors. These are outsourced third-party workers and with a lower income than other hospital workers and the lowest educational level. During this troubled period in which good information and fake news are spread equally, with mixed messages even at the government level, education may be crucial to understanding the measures necessary to avoid infection[10].

HCWs who denied respiratory symptoms during the epidemic were more likely to be negative than those with respiratory symptoms. Symptoms presented by seropositive HCW were those frequently described by patients with PCR-diagnosed COVID-19, such as fever, cough, and anosmia. Our findings suggest that among HCW, very slight symptoms may predict SARS-CoV-2 infection.

Our study has limitations. The questionnaire was not answered by all participants. We could not evaluate the usage of masks outside the workplace nor social distancing.

In conclusion, our findings point to the possibility of an important role of community SARS-CoV-2 transmission among HCW.

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# Contributorship

SFC, PB, AD, ACS, VAS and ASL contributed equally to this paper.

Conceptualization; APMP, EPES,JK, ES Formal analysis: LB, PB, RP Funding acquisition:, ESDOB, AJP. Patients samples: LGNS, AAB, MCPBF, FMS, MAJM, LQ, GFP, MCPBF, FMS, MAJM, LQ; Laboratory: MMR, CL, questionnaire data:, CMP, DMRC, ABO, MFLF, ASAP, DMRC, MCPBF, FMS, MAJM, LQ; Methodology: LB, RP, JK, MCCM, IOMS, ES Resources: MBMP, ESDOB, AJP Writing- original draft, LB, ES; SFC, ASL Writing - review & editing LB, ES; SFC, ASL

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|                                    | Seronegative                          | Seropositive      |   |                    |
|------------------------------------|---------------------------------------|-------------------|---|--------------------|
|                                    | N=2,122                               | N=221             | OR (95%CI)                              | aOR (95%CI)        |
|                                    | n (%)                                 | n (%)             |   |                    |
|                                    | Univaria                              | able associations |   |                    |
| Educational level                  |                                       |                   |   |                    |
| ost-graduate education             | 861 (92.8)                            | 67 (7.2)          | 1.0                                     | 1.0                |
| ligher education                   | 995 (90.7)                            | 102 (9.3)         | 1.32 (0.96 – 1.82)                      | 1.36 (0.88 – 2.11) |
| ligh school or less                | 234 (83.3)                            | 47 (16.7)         | 2.58 (1.72 – 3.84)                      | 1.93 (1.03 – 3.60) |
| Type of transportation to hospital |                                       |                   |   |                    |
| Car (own/taxi)                     | 684 (94.6)                            | 39 (5.4)          | 1.0                                     | 1.0                |
| On foot/bicycle                    | 254 (91.7)                            | 23 (8.3)          | 1.59 (0.92 – 2.69)                      | 1.65 (1.07 – 2.62) |
| rublic transport                   | 1,151 (88.3)                          | 153 (11.7)        | 2.33 (1.64 – 3.40)                      | 2.05 (1.04 – 4.03) |
| Motorcycle                         | 25 (83.3)                             | 5 (16.7)          | 3.51 (1.14 – 8.98)                      | 2.31 (0.60 – 7.11) |
| ype of housing                     |                                       |                   |   |                    |
| partment                           | 1,169 (91.8)                          | 104 (8.2)         | 1.0                                     |                    |
| louse                              | 946 (89.2)                            | 115 (10.8)        | 1.37 (1.03 – 1.81)                      |                    |
| umber of contacts in the household |                                       |                   |   |                    |
|                                    | 310 (93.7)                            | 21 (6.3)          | 1.0                                     | 1.0                |
|                                    | 649 (91.9)                            | 57 (8.1)          | 1.30 (0.78 – 2.22)                      | 1.13 (0.65 – 2.03) |
|                                    | 509 (89.8)                            | 58 (10.2)         | 1.68 (1.02 – 2.88)                      | 1.52 (0.86 – 2.76) |
| +                                  | 634 (88.4)                            | 83 (11.6)         | 1.93 (1.20 – 3.25)                      | 1.50 (0.86 – 2.70) |
| umber of bathrooms at the esidence |                                       |                   |   |                    |
|                                    | 958 (89.8%)                           | 109 (10.2%)       | 1.0                                     |                    |
|                                    | 652 (90.2%)                           | 71 (9.8%)         | 0.96 (0.70 – 1.31)                      |                    |
|                                    | 284 (92.2%)                           | 24 (7.8%)         | 0.74 (0.46 – 1.16)                      |                    |
| +                                  | 196 (93.3%)                           | 14 (6.7%)         | 0.60 (0.26 – 1.18)                      |                    |
| haring of face towels at home      | · · · · · · · · · · · · · · · · · · · | · · · · · ·       | , · · · · · · · · · · · · · · · · · · · |                    |
| 'es                                | 991 (91.3)                            | 95 (8.7)          | 1.0                                     |                    |
| Jo                                 | 1081 (90.2)                           | 118 (9.8)         | 0.88 (0.66 – 1.17)                      |                    |
| 10                                 |                                       |                   |   |                    |
| rofessional category               |                                       |                   |   |                    |
|                                    | 614 (94.2)                            | 38 (5.8)          | 1.0                                     | 1.0                |

| Cleaning/security                    | 24 (54.5)   | 20 (45.5) | 13.5 (6.81 – 26.6)  | 10.1 (3.40 – 26.9) |
|--------------------------------------|-------------|-----------|---------------------|--------------------|
| Lab/radiology technician             | 64 (97.0)   | 2 (3.0)   | 0.51 (0.08 – 1.70)  | 0.66 (0.10 – 2.57) |
| Nurse                                | 328 (88.6)  | 42 (11.4) | 2.07 (1.31 – 3.28)  | 2.37 (1.22 – 4.70) |
| Nursing assistant                    | 495 (89.5)  | 58 (10.5) | 1.89 (1.24 – 2.92)  | 1.59 (0.81 – 3.19) |
| Other                                | 243 (93.5)  | 17 (6.5)  | 1.13 (0.61 – 2.01)  | 1.01 (0.46 – 2.18) |
| Pharmacist/nutritionist/psychologist | 103 (92.0)  | 9 (8.0)   | 1.41 (0.63 – 2.88)  | 1.78 (0.69 – 4.23) |
| Physiotherapist                      | 142 (89.3)  | 17 (10.7) | 1.93 (1.04 – 3.47)  | 2.18 (0.96 – 4.80) |
| Use of tobacco use                   |             |           |                     |                    |
| Never                                | 1692 (90.6) | 175 (9.4) | 1.0                 |                    |
| Past                                 | 227 (90.4)  | 24 (9.6)  | 1.10 (0.64 – 1.79)  | <b>Q</b>           |
| Current                              | 158 (89.8)  | 18 (10.2) | 1.02 (0.64 – 1.57)  |                    |
| Influenza vaccination                | 1912 (91.0) | 188 (9.0) | 0.69 (0.46 – 1.08)  |                    |
| Comorbidities                        |             |           |                     |                    |
| Heart disease                        | 17 (94.4)   | 1 (5.6)   | 0.56 (0.03 – 2.76)  |                    |
| Hypertension                         | 178 (91.3)  | 17 (8.7)  | 0.91 (0.52 – 1.49)  |                    |
| Diabetes                             | 56 (94.9)   | 3 (5.1)   | 0.51 (0.12 – 1.39)  |                    |
| Asthma                               | 77 (93.9)   | 5 (6.1)   | 0.62 (0.214 – 1.39) |                    |
| COPD                                 | 19 (90.5)   | 2 (9.5)   | 1.01 (0.16 – 3.51)  |                    |
| Obesity                              | 142 (90.7)  | 13 (9.3)  | 0.87 (0.46 – 1.51)  |                    |
| Medications                          |             |           |                     |                    |
| ACE inhibitors                       | 18 (90.0)   | 2 (10.0)  | 1.07 (0.17 – 3.73)  |                    |
| Angiotensin receptor blockers        | 10 (100)    | 0 (0.0)   | NA                  |                    |
| Oral hypoglycaemic agents            | 38(92.7)    | 3(7.3)    | 0.76 (0.18 – 2.11)  |                    |
| Insulin                              | 6 (85.7)    | 1 (14.3)  | 1.6 (0.08 – 9.44)   |                    |
| Nasal steroids                       | 103 (90.5)  | 9 (9.5)   | 0.832 (0.39 – 1.58) |                    |
| Inhaled steroids                     | 28 (100)    | 0 (0.0)   | NA                  |                    |
| Oral steroid                         | 14 (82.4)   | 3 (17.6)  | 2.07 (0.48 – 6.41)  |                    |
| IM steroid                           | 5 (100)     | 0 (0.0)   | NA                  |                    |
| Immunosuppression                    | 3 (100)     | 0 (0.0)   | NA                  |                    |
| Personal protective equipment        |             |           |                     |                    |
| Surgical mask                        | 1205 (91.6) | 111 (8.4) | 0.77 (0.58 – 1.01)  |                    |
| Filter mask (N95, N99, R95, PFF2)    | 1636 (90.4) | 173 (9.6) | 1.07 (0.77 – 1.51)  |                    |
| Other type of mask                   | 146 (88.5)  | 19 (11.5) | 1.27 (0.75 – 2.05)  |                    |

| Gloves         | 1668 (90.6) | 173 (9.4) | 0.98 (0.71 – 1.39) |
|----------------|-------------|-----------|--------------------|
| Facial shield  | 1236 (90.2) | 134 (9.8) | 1.10 (0.83 – 1.47) |
| Eye protection | 1434 (90.4) | 153 (9.6) | 1.08 (0.80 – 1.46) |
| Gown           | 1412 (90.2) | 153 (9.8) | 1.13 (0.84 – 1.53) |
| Cap            | 1396 (90.5) | 146 (9.5) | 1.01 (0.76 – 1.36) |

Table 2- Univariate and multivariate analysis of factors pottentially associated with SARS-CoV-2 serostauts among HCW.

