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ORIGINAL ARTICLE

A cross sectional study found differential risks for COVID-19 seropositivity amongst health care professionals in Chile

Marcela Zuñiga[a], Anne J Lagomarcino[d], Sergio Muñoz[e], Alfredo Peña Alonso[f], María Andrea Rodriguez[g,h], Miguel L O'Ryan[b,c,*]

[a] Health Care Networks Under Secretariat, Ministry of Health, Monjitas 565, Santiago, Chile
[b] Microbiology and Mycology Program, Institute of Biomedical Sciences, Faculty of Medicine, Universidad de Chile, Avenida Independencia 1027, Independencia, Santiago, Chile
[c] Millennium Institute on Immunology and Immunotherapy, Faculty of Medicine, Universidad de Chile, Avenida Independencia 1027, Independencia, Santiago, Chile
[d] Office of Innovation, Faculty of Medicine, Universidad de Chile, Avenida Independencia 1027, Independencia, Santiago, Chile
[e] Department of Public Health, CIGES, Faculty of Medicine, Universidad de La Frontera, Claro Solar 115, Temuco, Chile
[f] Management Control and Quality Department, Primary Care Division, Health Care Networks Under Secretariat, Ministry of Health, Monjitas 565, Santiago, Chile
[g] Computer Science Department, Universidad de Concepción, Edmundo Larenas 219, Concepción, Chile
[h] Millennium Institute of Foundational Research on Data, Campus San Joaquín, Pontificia Universidad Católica de Chile, Vicuña Mackenna 4860, Macul, Chile

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Abstract

Objective: Health care workers (HCWs) are at increased risk for SARS-CoV-2 infection, however not all face the same risk. We aimed to determine IgG/IgM prevalence and risk factors associated with seropositivity in Chilean HCWs.

Study Design and Setting: This was a nationwide, cross-sectional study including a questionnaire and COVID-19 lateral flow IgG/IgM antibody testing. All HCWs in the Chilean public health care system were invited to participate following the country's first wave.

Results: IgG/IgM positivity in 85,529 HCWs was 7.2%, ranging from 1.6% to 12.4% between regions. Additionally, 9.7% HCWs reported a positive PCR of which 47% were seropositive. Overall, 10,863 (12.7%) HCWs were PCR and/or IgG/IgM positive. Factors independently associated with increased odds ratios (ORs) for seropositivity were: working in a hospital, night shifts, contact with Covid-19, using public transport, male gender, age>45, BMI ≥30, and reporting ≥2 symptoms. Stress and/or mental health disorder and smoking were associated with decreased ORs. These factors remained significant when including PCR positive cases in the model.

Conclusions: HCWs in the hospital were at highest risk for COVID-19, and several independent risk factors for seropositivity and/or PCR positivity were identified.

Keywords: Health care workers; COVID-19; Antibody prevalence; Vaccine priority; SARS-CoV-2; Antibody testing

HCWs, Health care workers.

Conflict of interest: The authors do not declare any conflict of interest.

* Corresponding author: Tel. +569 61401237
E-mail address: Moryan@uchile.cl (M.L. O'Ryan).

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What's new

- HCWs working in the hospital as compared to primary care were at increased risk for COVID-19, especially if working night shifts.
- Increasing age was independently associated with seropositivity as was use of public transport.
- HCWs with BMI ≥30 were at increased risk for COVID-19.
- Identification of individuals within different settings, such as HCWs, at higher risk for infection is relevant for vaccination priorities, especially in countries with vaccine shortage
- Risk factors differed albeit mildly depending on the overall seropositivity of the Region of Chile.

1. Introduction

In 2013, the Global World Health Force Alliance estimated that worldwide there were nearly 43.5 million health care workers (HCWs), accounting for a total of 6.2 workers per 1,000 people [1]. In Chile, the most recent estimates indicate a total health care workforce of 635,285 individuals for a population of ∼19.5 million, or 32.6 workers per 1,000 people [2]. HCWs have been at increased risk for SARS-CoV-2 infection both worldwide and in Chile [3–8]. This increased risk, which in some reports has been accompanied by an increased overall risk of hospitalization [5,9], has led to the general recommendation to include HCWs as a priority group for early vaccination [10].

In Chile, as of September 27, 2020, there were three times as many PCR tests performed in HCWs as compared to the general population, with a total of 289,307 tests performed [5]. Adjusted incidence rates were 53.4 of 1,000; 1.9 times greater than that of the general population. Nurses had the highest positivity rates, followed by physicians and nurse assistants. Large seroprevalence based studies in HCWs have been scarce [11–15].

Previously identified risk factors for Covid-19 include workplace (i.e., patient-facing [9,16], exposure to Covid-19 patients [11]), lack of PPE or reuse of PPE [7], being a nurse and/or nurse assistant [12] (rather than a physician). There are differing results on the infection risk to HCWs working in the ICU, inpatient and ER settings; with some studies saying inpatient staff [7] are at higher risk, while others saying ER workers are at higher risk [17]. These differences may be due to confounding of other risk factors, such as job type and PPE availability and/or changes in transmission prevention plans over the course of the pandemic, as most published data focuses on the early phases (March to May 2020). Thus, it is important to parse which variables are putting HCWs at increased risk by looking at a broad range of HCWs in various settings.

We aimed to determine antibody prevalence in the Chilean HCW community by performing a simultaneous, nationwide survey along with antibody testing during the COVID-19 spring plateau (September to October), three to four months following the peak of the country's first wave, which occurred in the southern hemisphere's winter (Supplementary Figure 1). A secondary objective was to assess risk factors independently associated with seropositivity.

2. Methods

2.1. Study design and sampling

This was a nationwide, cross-sectional, voluntary study open to all HCWs in the Chilean public health care system, which comprises 42.6% of the total health care workforce in the country. Workers, including clinical, administrative and support staff, were identified using national registries as of June 30, 2020 (sources: Division of Human Resources Ministry of Health for Hospital Workers, Secondary Health Care; Division of Primary Care for Workers within the Municipal Primary Health Care System). The only exclusion criteria were the presence of symptoms compatible with COVID-19 at the time of consultation, in which case the subject was referred for RT-PCR testing for SARS-Cov-2. After informed consent, participants responded to a questionnaire followed by blood sample collection for SARS-Cov-2 IgG and IgM antibody detection using a lateral flow device.

2.2. Procedures

The study was designed by Health Ministry personnel in conjunction with an academic advisory board; the study was approved by the Ethical Committee of the Servicio de Salud Araucanía Sur (N° CEC-201, August 10, 2021). All HCWs, regardless of whether they were working in person, from the country's 29 health care services were invited to participate through various channels (see supplement for description of local health care system). Study sites were set up in hospitals and primary care centers. Each health care facility assembled a local team in charge of the informed consent process, blood sample collection, application and interpretation of rapid tests, face-to-face application of the questionnaire (in 5% of cases face-to-face interviews were not possible and the survey was filled out on paper by the respondent alone), the transfer of data to a central server, and referral to RT-PCR when needed (See supplement for further details). Training was performed by study investigators in conjunction with technical advisors from each regional health care service. PPE was provided for all study personnel by the Health Care Services.

Venipuncture and fingerstick were both allowed based on local experience. The kit for IgM/IgG Antibodies to Coronavirus (SARSCoV-2) (Lateral Flow; Zhukai Livzon

Table 1. Overall characteristics of study population as compared to total public health care worker population.

Characteristic, *n* (%)	Study population $n = 85{,}529$	Total HCW population $n = 262{,}243$
Gender[a]		
Female	62,033 (72.5)	18, 504 (68.8)
Male	23,369 (27.3)	81,737 (31.2)
Age		
18-24	5,746 (6.7)	8,021 (3.1)
25-34	36,522 (42.7)	98,342 (37.5)
35-44	21,419 (25.0)	71,770 (27.4)
45-54	13,691 (16.0)	45,475 (17.3)
55-64	7,627 (8.9)	33,325 (13.0)
>64	524 (0.6)	5,310 (2.0)
Workplace		
Outpatient Primary Health Care	37,996 (44.4)	116,812 (44.5)
Hospital	47,533 (55.6)	14, 431 (55.5)
Profession		
Technical nurse assistant	24,930 (29.1)	74,380 (28.4)
Administrative personnel	14,634 (17.1)	25,695 (9.8)
Registered nurse	10,427 (12.2)	28,759 (11.0)
Janitorial and other support staff	8,606 (10.1)	34,024 (13.0)
Medical doctors	6,935 (8.1)	33,803 (12.9)
Nurse assistant	5,305 (6.2)	30,553 (11.6)
Physical therapist	3,417 (4.0)	8,590 (3.3)
Midwife	2,780 (3.3)	7,766 (3.0)
Transportation services[b]	2,105 (2.5)	-
Dentist	2,080 (2.4)	6,815 (2.6)
Medical technician	1,667 (1.9)	4,926 (1.9)
Nutritionist	1,544 (1.8)	4,219 (1.6)
Pharmacist	733 (0.9)	1,989 (0.8)
Speech therapist	366 (0.4)	724 (0.3)

[a] In the study population 127 individuals and in the total HCW population 2 individuals did not declare or declared a non-male or -female gender.

[b] In the national registry, “transportation services” were included in “other support staff”

Diagnostic Inc. China) was used for all tests, following the manufacturer’s instructions (details in supplement).

2.3. Data collection and analysis

Variables included in the questionnaire (Supplementary Material) were related to demographics, profession, place of work, shifts worked, place of residence, mode of transportation, household size, COVID-19 contact history and degree of exposure, potentially risky behaviors, the presence of COVID-19 symptoms since the start of the pandemic, access to PPE, previous RT-PCR testing for COVID-19, and test results (spontaneous declaration, not certified by study personnel).

Statistical analyses were performed using Stata 16.1. Summary measures were used to describe continuous variables; counts and percentages were used for categorical variables. Chi-square test was used to compare categorical variables. 95% confidence intervals were computed for seroprevalence by demographic and workplace characteristics, exposure to COVID-19, symptoms, and pre-existing health conditions. Incidence rate ratios for positive results were computed for all associated factors. We used logistic models to evaluate risk factors for seropositivity, see Supplement for details. Variables included in the logistic models included: sector (hospital vs. primary care), workplace (emergency services, non-emergency patient care, and non-patient facing-services), working night shifts, profession, contact with a Covid-19 case at work or outside of work, Covid-19 symptoms, use of PPE, gender, age, use of public transport, and comorbidities including tobacco use.

3. Results

From September 11 to October 24, the entire workforce of the public health care system, a total of 262,243 HCWs, were deemed eligible for participation. One of the 29 health care services declined to participate due to logistical issues (Araucanía Sur with over 13,000 HCWs). A total of 88,926 (33.9%) HCWs consented to participate (see supplement for reasons for non-participation). Of the 88,926 participants, 2,095 were excluded, due to incomplete data, invalid or repeated national ID numbers, or an inconsistent date of birth. Of the remaining 86,831 participants, 1,302 (1.5%) presented symptoms at the time of the study and were recommended for PCR testing, leaving a total of 85,529 HCWs with valid serology results for analysis.

Baseline characteristics of the study population and comparisons to the total population of Chilean public sector HCWs are displayed in Table 1 and Supplementary Tables 1 and 2. Importantly, the study population was representative of the total HCW force in terms of basic characteristics with a slight overrepresentation of women, younger workers and administrative personnel, and a mild underrepresentation of workers >55 years old, doctors and nurse assistants. Participation varied regionally as described in Supplementary Table 1. The study population was predominantly female (68.4%) with a mean age of 37 (SD 10.5 years) and 38 years (SD 11.3 years) for women and men respectively; the majority of participants were between 25 and 44 years of age (68.1%). Most HCWs lived in households with three or less individuals (64.5%). Hospital workers composed just over half of the sample (55.6%). The most common professions in the sample were technical nurse assistants (29.1%) and administrative personnel (17.1%). Registered nurses and medical doctors represented 20.3% of the study population. Additional characteristics of the study population are provided in the supplement.

Overall, 6,139 of 85,529 (7.2%) subjects were seropositive for IgG and/or IgM, of which 2,279 (2.7%) were positive for IgG alone, 1,413 (1.7%) were positive for IgM alone, and 2,447 (2.9%) were positive for both IgG and IgM. Importantly, there were no differences in seropositivity by sample type: 3,829 of 53,253 (7.2%) for venipuncture and 2,312 of 32,276 (7.2%) for fingerstick samples (Supplementary Table 3). Throughout the country, seropositivity varied widely, ranging from 1.6-12.4%; furthermore, positivity was directly, albeit weakly, correlated with rates of accumulated Covid-19 cases in the region (Spearman's rho 0.2147; $P = 0.43$; Fig. 1). In univariate analysis (Table 2), slightly more men were seropositive than women, and seropositivity increased with age. Hospital HCWs had 2 times the infection risk compared to those working in primary care facilities; working night shifts was also associated with increased risk. Contact with an individual either confirmed or potentially suffering from Covid-19 in the workplace or at home was associated with an increased risk of seropositivity; the univariate risk of seropositivity based on a known Covid-19 contact, either at work or outside of work, were nearly identical (OR 2.4; Table 2). The presence of two or more Covid-19 related symptoms was also associated with an increased risk of

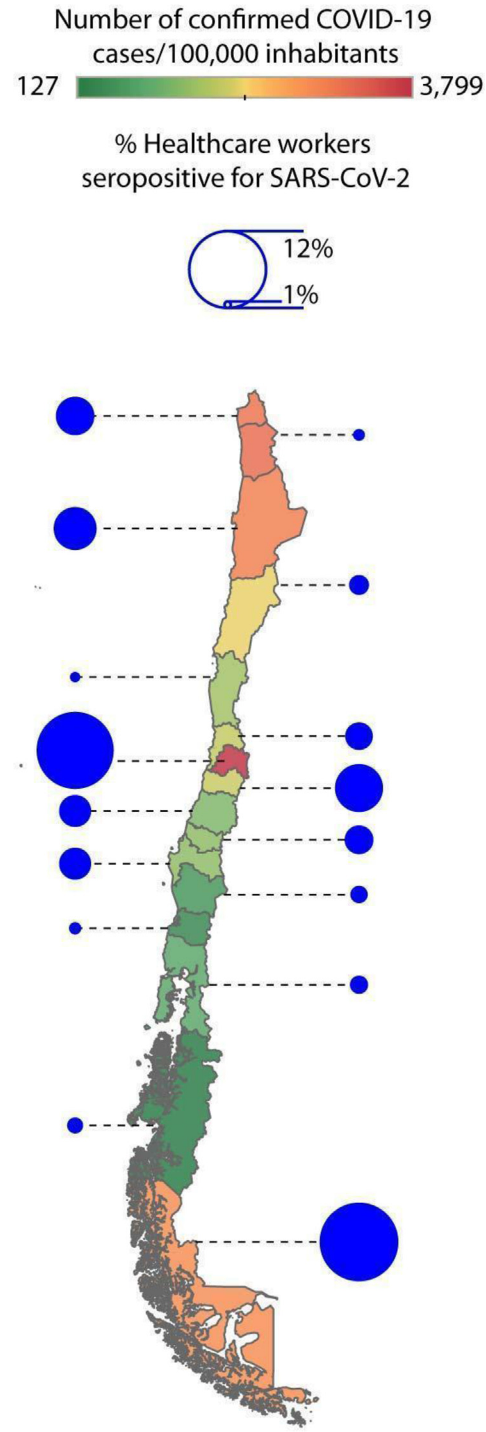

Fig. 1. Regional distribution of accumulated PCR positive cases reported for the entire population in each region up to September 7, 2020 (color gradient from lowest[green] to highest[red]) and SARS-Cov-2 seropositivity in health care workers (magnitude represented by the size of the blue circles).

Table 2. Study variables associated with increased IgG and/or IgM SARS-COV-2 seropositivity.

Variables, n/Total (%)	Seropositive/Total $n = 6{,}139/85{,}529$	Incidence Rate Ratio (95% CI)	P value
Gender[a]			
Female	4,348/62,033 (7.0)	ref	
Male	1,784/23,369 (7.6)	1.09 (1.03 - 1.15)	0.01
Age			
18-24	439/5,746 (7.6)	1.22 (1.10 - 1.36)	< 0.001
25-34	2,547/36,522 (7.0)	1.12 (1.04 - 1.19)	< 0.001
35-44	1,338/21,419 (6.2)	ref	
45-54	1,104/13,691 (8.1)	1.29 (1.19 - 1.40)	< 0.001
55-64	663/7,627 (8.7)	1.39 (1.27 - 1.53)	< 0.001
>64	48/524 (9.2)	1.47 (1.10 - 1.96)	< 0.001
Workplace			
Outpatient Primary Health Care	1,692/37,996 (4.4)	ref	
Hospital	4,447/47,533 (9.4)	2.10 (1.99 - 2.22)	< 0.001
Day and Night Shifts			
8-12 hour day shift	2,892/56,771 (5.1)	ref	
8-12 hour weekdays with one 12 hour night shift	704/8,455 (8.3)	1.63 (1.50 - 1.77)	< 0.001
12 hour day shift-12 hour night-2 days off	1,674/13,574 (12.3)	2.42 (2.28 - 2.57))	< 0.001
24 hour shift-3 days off[b]	869/6,729 (12.9)	2.53 (2.35 - 2.73)	< 0.001
Covid-19 exposure or contact history			
Confirmed Covid-19 positive contact[c]			
Yes	4,186/35,577 (12.5)	3.31 (3.14 - 3.49)	< 0.001
No	1,953/51,952 (3.8)	ref	
Possible contact with Covid-19 positive patient			
Yes	3,382/34,496 (9.8)	1.81 (1.72 - 1.91)	< 0.001
No	2,757/51,033 (5.4)	ref	
Possible contact with a Covid-19 positive coworker			
Yes	3,002/33,753 (8.9)	1.47 (1.40 - 1.54)	< 0.001
No	3,137/51,776 (6.1)	ref	
Possible contact with a Covid-19 positive family member			
Yes	1,129/12,614 (9.0)	1.30 (1.22 - 1.39)	< 0.001
No	5,010/72,915 (6.9)	ref	
Subject to quarantine due to confirmed close contact			
Yes	2,850/16,001 (17.8)	2.37 (2.22 - 2.53)	< 0.001
No	1,336/17,576 (7.6)	ref	
Covid-19 contact at work			
Yes	5,477/67,019 (8.2)	2.40 (2.21-2.61)	<0.001
No	662/18,510 (3.6)	ref	
Covid-19 contact outside of work			
Yes	354/4,357 (8.3)	1.18 (1.06-1.32)	0.003
No	5,785/81,272 (7.1)	ref	

(continued on next page)

Table 2 (*continued*)

Variables, n/Total (%)	Seropositive/Total $n = 6,139/85,529$	Incidence Rate Ratio (95% CI)	*P* value
Principal mode of transport			
Public transport	2,016/20,446 (9.9)	1.56 (1.48 - 164)	< 0.001
All other	4,123/65,083 (6.3)	ref	
Previous Covid-19 Symptoms			
None	1,491/40,166 (3.7)	ref	
One	608/15,849 (3.8)	1.03 (0.94 - 1.14)	0.49
Two or more	4,040/29,514 (13.7)	3.69 (3.47 - 3.91)	< 0.001
Comorbidities			
Stress or mental health disorder			
Yes	551/7,721 (7.1)	0.99 (0.91 - 1.08)	0.89
No	5,588/77,808 (7.2)	ref	
Diabetes			
Yes	250/2,518 (9.9)	1.40 (1.23 - 1.59)	< 0.001
No	5,889/83,011 (7.1)	ref	
Hypertension			
Yes	642/7,195 (8.9)	1.27 (1.17 - 1.38)	< 0.001
No	5,497/78,334 (7.0)	ref	
Asthma			
Yes	307/3,966 (7.7)	0.97 (0.73 - 1.30)	0.85
No	5,832/81,563 (7.2)	ref	
Cancer			
Yes	46/659 (7.0)	1.08 (0.96-1.21)	0.18
No	6,093/84,870	ref	
Tobacco Use			
Yes	1,090/16,862 (6.5)	0.87 (0.81-0.93)	<0.001
No	5,049/68,667 (7.4)	ref	
BMI≧30			
Yes	1,895/22,092 (8.6)	1.31 (1.24-1.38)	<0.001
No	4,240/63,381 (6.7)	ref	
Hygiene and personal protective equipment			
Use of recommended hand hygiene procedures			
Never	11/182 (6.0)	0.84 (0.46 - 1.51)	0.551
Occasionally	40/657 (6.1)	0.84 (0.62 - 1.15)	0.277
Frequently	180/2,166 (8.3)	1.15 (0.99 - 1.33)	0.067
Always	5,612/77,571 (7.2)	ref	
Administrative/Not applicable	296/4,953 (6.0)	0.83 (0.73 - 0.93)	0.001
Use of protective gloves			
Never	72/1,498 (4.8)	0.60 (0.47-0.76)	<0.001
Occasionally	105/2,141 (4.9)	0.61 (0.50-0.75)	<0.001
Frequently	185/2,182 (8.5)	1.10 (0.95-1.28)	0.218
Always	5,081/65,478 (7.8)	ref	
Administrative/Not applicable	696/14,230 (4.9)	0.61 (0.56-0.66)	<0.001
Use of protective robes			

(continued on next page)

Table 2 (*continued*)

Variables, n/Total (%)	Seropositive/Total $n = 6,139/85,529$	Incidence Rate Ratio (95% CI)	*P* value
Never	126/2,611 (4.8)	0.59 (0.49-0.71)	<0.001
Occasionally	218/3,238 (6.7)	0.84 (0.73-0.97)	0.016
Frequently	337/3,729 (9.0)	1.16 (1.03-1.30)	0.013
Always	4,479/56,676 (7.9)	ref	
Administrative/Not applicable	979/19,275 (5.1)	0.62 (0.58-0.67)	<0.001
Use of facemasks			
Never	12/215 (5.6)	0.78 (0.44 - 1.36)	0.378
Occasionally	54/597 (9.0)	1.26 (0.96 -1.64)	0.095
Frequently	138/1,331 (10.4)	1.43 (1.22 - 1.70)	< 0.001
Always	5,639/78,311 (7.2)	ref	
Administrative/Not applicable	296/5,075 (5.8)	0.81 (0.72 - 0.91)	< 0.001
Use of facial shields			
Never	155/2,759 (5.6)	0.74 (0.63-0.87)	<0.001
Occasionally	275/3,683 (7.5)	1.00 (0.88-1.13)	0.963
Frequently	401/4,469 (9.0)	1.23 (1.10-1.26)	<0.001
Always	4,662/62,608 (7.5)	ref	
Administrative/Not applicable	646/12,010 (5.4)	0.71 (0.65-0.77)	<0.001

[a] 127 subjects did not mention their gender
[b] Includes other possibilities, such as one week in this regimen followed by one week off.
[c] Not confirmed by study personnel

seropositivity. Loss of smell and/or taste was associated with the highest risk, followed by fever and difficulty breathing anytime from March onwards (Supplementary Table 4). HCWs with diabetes and/or hypertension were at slightly greater risk of infection. Tobacco use was associated with a lower risk of seropositivity and a BMI $\geq$ 30 with a higher risk of seropositivity (Table 2).

Nurses, physical therapists and technical nurse assistants had the highest rate of seropositivity within the hospital setting, followed by medical doctors and nurse assistants, while dentists had the lowest seropositivity rates (Fig. 2). In the primary care setting, these differences were not observed (Fig. 2). Working in the emergency room (hospital) or urgent care (primary care) was associated with higher seropositivity; in the hospital, working in medical units or critical care was also associated with higher seropositivity.

Results of the logistic models are shown in Table 3; Models were divided by overall regional seropositivity: low (<4%), medium (4-8%), and high (>10%). Factors that implied a greater risk of seropositivity under all three scenarios included: working night shifts, a Covid-19 contact at work, a Covid-19 contact outside of work (higher OR than work contact), two or more self-reported Covid-19 symptoms, and a BMI $\geq$30. Factors that were only associated with a greater risk of seropositivity in regions with medium or high seropositivity included: working in a hospital setting, working in non-emergency patient care, being a registered nurse, male gender, increasing age for those over 45 years old, and the use of public transport. Stress or mental health disorders and smoking were associated with a lower risk of infection in regions with medium and high seroprevalence. In regions with low and medium seroprevalence, being a doctor or nurse assistant increased the risk of seropositivity. In regions with high seroprevalence, diabetes and not using facial shields were risk factors, while not using protective robes, being a midwife, nutritionist or dentist were protective. Finally, in regions with medium seroprevalence, nurses, technical nurse assistants, nurse assistants, physical therapists, doctors and janitorial and other support staff were at increased risk of infection as compared to administrative personnel.

Of those HCWs that declared a positive SARS-CoV-2 PCR test during the pandemic (n = 8,330), 43.3% (n = 3,606) were seropositive in this study (Supplementary Table 5). Seropositivity increased when PCR tests were performed closer to the time of antibody testing and among individuals who reported more COVID-19 associated symptoms; however even selecting for these criteria, agreement between self-reported positive PCR results and seroprevalence did not surpass 54% (Supplementary Table 5). In a post-hoc analysis combining seropositivity and/or self-reported positive PCR results (n = 10,863; 12.7%), likely a closer estimation of the true number of infected individuals, 3,606 (33.2%) were positive by both PCR and antibody test, 4,724 (43.5%) were only PCR positive, and 2,533 (23.3%) were only antibody positive. Logistic regressions for the combined population including antibody seropositivity and/or PCR positivity are shown in Supplementary Table 6; importantly results were consistent with models for seropositivity alone. Differences are described in the supplement.

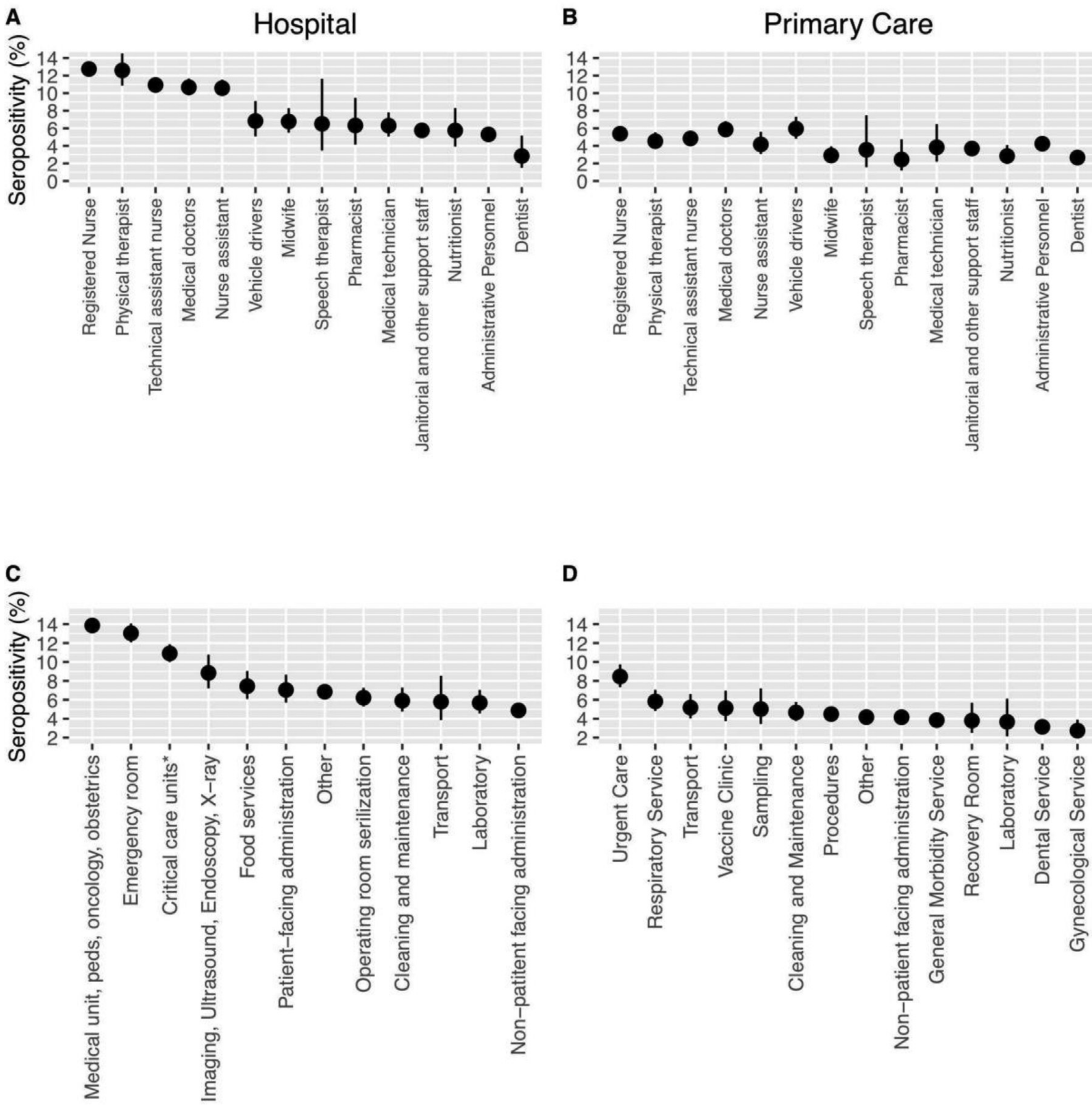

Fig. 2. Seropositivity (IgG and/or IgM) by profession and workplace. (A) Profession within the hospital; (B) Profession within primary care; (C) Workplace within the hospital; (D) Workplace within primary care. The bars represent 95% confidence intervals. * both adult and pediatric.

4. Discussion

In this large SARS-CoV-2 seroprevalence study including over one-third of the Chilean public sector health care workforce, overall seropositivity was 7.2% two to three months after the country's winter 2020 peak. These results occurred in a community of HCWs in which over half self-declared exposure to someone with Covid-19 and prior PCR testing, with reported PCR positivity close to 10%. Seroprevalence rates varied regionally; regions with higher overall accumulated Covid-19 cases tended to have higher seropositivity rates, as observed in population studies in the United States, Brazil and Spain [14,18,19]. These results are in line, and add, to the few population based seroprevalence studies focusing on HCWs [11,12,14,15]. In Michigan, seroprevalence rates were similar, at 6.9% vs. 7.2% in our study; this study found greater risk among nurses, those working in the emergency room and those working closer to the urban center of Detroit [11]. Rates were also similar in Belgium, 6.4% among tertiary care workers [20]; and rates in Brussels while higher than our overall findings were similar to those of Santiago 12.6% vs. 12% [21]. In Denmark and the USA, seroprevalence was much lower, at ∼4% [13,14]. In a Swedish hospital seroprevalence rates were much higher, 19.1%, possibly due to differences in protection protocols (lack of RT-PCR testing and subsequent isolation of infected HCWs, and no RT-PCR testing of all in-hospital patients, regardless of typical COVID-19 symptoms) [15]. A number of factors were associated with higher seropositivity in univariate analysis, however here we will focus on the multivariate models separated by regional seropositivity.

Prior data on seropositivity in Chile is limited. In a study conducted on the general population from March to July 2021, 5 to 9 months following our data collection, 3,726 of 59,987 (6.2%) reported a previous PCR positive result and seropositivity by anti-SARS-COV-2 finger prick testing (only IgG) reached 18% among non-vaccinated individuals [22]. A study focusing on frontline HCWs from a tertiary-care hospital in Santiago, conducted from April to July of 2021, found a much higher seroprevalence of 24% ($n = 446$) [23] compared to 12% of HCWs in Santiago in our study. This may be due to the inclusion of only frontline workers, and/or the use of a more sensitive antibody detection method (importantly we report that the test used in our study detected nearly 50% of known PCR positive cases).

Workplace related factors that were associated with seropositivity in regions with medium and high seropositivity included working in a hospital as opposed to primary care settings, working night shifts, contact with a Covid-19 case at work, and working in non-emergency services (including surgical wards). This is consistent with a previous study that also found that working in surgery wards was associated with antibody positivity [24]. Whereas, a recent study from the United States concluded that job roles and workplace factors were not associated with seropositivity when considering community Covid-19 contact and cumulative incidence rates [14]. However, in our study, when controlling for these factors nurses and to a lesser extent medical doctors and physical therapists were at increased risk. A study in Italy, also found that nurses were at increased risk of infection [25]. Conversely, seropositivity was low among dentists; however, this may be an artifact due to the fact that dental activities were paused and these HCWs were resigned to administrative tasks from March-December 2020. Medical personnel with potentially diminished patient contact, such as nutritionists and midwives, also had lower rates of seropositivity. Use of PPE was generally not protective when controlling for all other factors. Use of face masks was almost universal in this population, which may play a role in this lack of association.

While workplace COVID-19 contact was associated with seropositivity, contact at home had a stronger association with seropositive. This is similar to a Belgian study that found COVID-19 work contact was not associated with seropositivity while household contacts were [20].

Demographic variables and self-reported behavioral characteristics associated with higher transmission risks included male gender and increasing age, similar to previous studies [26]; however, this pattern was only true in those HCWs over 45 year of age. Importantly, to our knowledge this is only the second study reporting an increased risk of infection among HCWs using public transport [27,28]. Comorbidities, with the exception of BMI$\geq$30, did not seem to infer a greater risk of infection, possibly due to the option for those HCWs to be reassigned to remote work duties. Smoking and stress or mental health disorder were inversely correlated with seropositivity; however, the latter should be interpreted with caution, as it is likely related to other non-recorded factors associated with smoking that may be the cause of this apparent protection, for example socializing outside. Importantly, smoking has been clearly associated with more severe disease [29]. We can speculate several reasons as to why stress and mental health disorders were protective, such as temporary leave from clinical activities, but this would have to be confirmed.

Individuals declaring two or more symptoms of Covid-19 any time after the epidemic onset in Chile had significantly higher positivity rates (reported PCR and serology results). This was also expected. Nevertheless, the fact that seropositivity was 43% among individuals with a self-reported positive PCR for SARS-COV-2 indicates that seropositivity rates are underrepresenting true infection rates. The combination of declared PCR positivity and seropositivity increased the number of likely infected HCWs to 12.4%. This figure is probably closer to the true infection rate after the first wave in the Chilean HCW population. It is reassuring that the multivariable model in the post-hoc analysis including both seropositive and self-reported PCR positive cases sustains the risk factors identified in the original models. Combining PCR and serology results of asymptomatic HCWs in an English hospital, Eyre *et al.* [12] reported a positivity rate of 11.2%, slightly lower than our estimate. Covid-19 contact both at work and outside of work were significant risks for infection, however the OR for non-work contacts was slightly higher, indicating this was a greater source of infection. Just as reported by Shah *et al*. [9], the risk of infection to HCWs outside the hospital or the direct patient-care environment is similar to that of the general population.

Several limitations can be identified in this large seroprevalence study. First and foremost is the relatively low test sensitivity, as discussed above. Conversely, false positive tests, mostly due to over interpretation of visual bands, are also possible, especially when only IgM is detected [29]. Strict compliance with test reading at 15 minutes was enforced in order to decrease the reading of non-specific bands, which may occur after this period. Two sampling methods, venipuncture and fingerstick, were used as requested by the territorial medical services, which could have potentially impacted results. It was reassuring that results were similar irrespective of sampling method. This study relies on a questionnaire, with variables not confirmed by medical record review, and thus relies on recall bias and question interpretation. Some questions may not have been sufficiently clear or may have been perceived as intimidating, especially those related to appropriate behaviors for Covid-19 prevention, and thus responses may have been inaccurate. Although the study ensured confidentiality for participants, some may have felt reluctant to take part in this study. Due to the logistics of large studies, $\sim$5% of interviews were not conducted face-to-face and thus there may have been a slight bias in responses to questions on risky behavior based on questionnaire format. Furthermore,

Table 3. Logistic regression model. Outcome variable SAR-CoV-2 antibody positivity in Chilean health care workers in 2020, separated by regions with low, medium and high overall seropositivity

Variables, Odds ratio (95% Confidence interval)	Regions with seropositivity rates in health care workers of		
	<4% *n* = 17,104 Pseudo R^2=0.0678	4-8% *n* = 36,895 Pseudo R^2=0.1243	>10% *n* = 30,227 Pseudo R^2=0.1029
Sector (reference: Primary Care)			
Hospital	1.14 (0.89-1.44)	2.06 (1.82-2.32)	1.56 (1.42-1.71)
Workplace (reference: Non-patient facing services)			
Emergency services	0.89 (0.64-1.25)	1.11 (0.95-1.30)	1.39 (1.23-1.56)
Non-emergency patient care	1.20 (0.95-1.53)	1.43 (1.27-1.62)	1.30 (1.19-1.43)
Shifts worked (reference: does not work the night shift)			
Night shifts	1.81 (1.41-2.34)	1.641 (1.45-1.86)	1.50 (1.359-1.661)
Profession (reference: Administrative personnel; professions in order from highest to lowest seroprevalence)			
Registered nurse	1.32 (0.81-2.15)	2.01 (1.61-2.51)	1.30 (1.11-1.52)
Physical therapist	1.46 (0.76-2.81)	1.89 (1.41-2.54)	1.11 (0.90-1.39)
Technical nurse assistant	1.32 (0.86-2.02)	1.54 (1.26-1.89)	1.13 (0.99-1.30)
Medical doctors	1.74 (1.03-2.95)	2.24 (1.75-2.87)	1.08 (0.91-1.28)
Nurse assistant	1.93 (1.20-3.12)	1.64 (1.28-2.10)	1.08 (0.90-1.29)
Transportation services	0.94 (0.45-1.97)	1.26 (0.88-1.81)	1.28 (0.95-1.74)
Midwife	0.93 (0.44-1.98)	0.80 (0.53-1.21)	0.63 (0.48-0.81)
Speech therapist	1.36 (0.18-10.45)	1.94 (0.95-3.95)	0.55 (0.26-1.15)
Pharmacist	1.19 (0.28-5.04)	1.24 (0.62-2.49)	0.84 (0.52-1.36)
Medical technician	0.77 (0.31-1.88)	1.18 (0.75-1.85)	0.88 (0.66-1.18)
Janitorial and other support staff	1.12 (0.68-1.85)	1.37 (1.07-1.74)	0.85 (0.71-1.01)
Nutritionist	2.03 (0.91-4.53)	1.28 (0.80-2.06)	0.61 (0.40-0.94)
Dentist	0.77 (0.29-2.05)	1.04 (0.64-1.69)	0.47 (0.31-0.70)
Covid-19 contact at work (reference: No)			
Yes	1.54 (1.17-2.04)	2.19 (1.78-2.68)	2.13 (1.77-2.57)
Covid-19 contact outside of work (reference: No)			
Yes	3.78 (2.58-5.55)	2.76 (2.09-3.65)	2.774 (2.186-3.52)
Covid-19 Symptoms (reference: no symptoms)			
1 symptom	1.14 (0.84-1.54)	1.05 (0.88-1.24)	1.02 (0.89-1.161)
2 or more symptoms	3.18 (2.55-3.97)	4.12 (3.69-4.60)	3.41 (3.12-3.72)
Personal protection (reference: always use)			
Hand Hygiene: No	1.11 (0.68-1.78)	1.07 (0.84-1.36)	1.04 (0.87-1.23)
Gloves: No	0.93 (0.63-1.38)	1.05 (0.86-1.28)	0.88 (0.76-1.01)
Protective robes: No	0.84 (0.60-1.18)	1.08 (0.92-1.27)	0.87 (0.77-0.97)
Face masks: No	0.91 (0.55-1.52)	0.91 (0.71-1.18)	1.14 (0.96-1.36)
Facial shield: No	1.10 (0.81-1.49)	0.86 (0.74-1.01)	1.14 (1.02-1.26)
Gender (reference: Female)			
Male	1.07 (0.84-1.35)	1.16 (1.04-1.30)	1.34 (1.23-1.46)
Age (reference: 18-25 years old)			
25-35 years old	0.79 (0.54-1.17)	1.165 (0.962-1.411)	1.07 (0.92-1.24)
35-44 years old	0.82 (0.54-1.24)	1.195 (0.974-1.467)	1.16 (0.99-1.36)
45-54 years old	0.94 (0.60-1.45)	1.75 (1.412-2.169)	1.55 (1.31-1.83)
55-64 years old	1.47 (0.92-2.37)	1.844 (1.437-2.366)	1.73 (1.44-2.08)
>65 years old	0.42 (0.06-3.11)	2.677 (1.455-4.928)	2.28 (1.50-3.48)

(*continued on next page*)

Table 3 (*continued*)

Variables, Odds ratio (95% Confidence interval)	Regions with seropositivity rates in health care workers of <4% $n = 17{,}104$ Pseudo R^2=0.0678	4-8% $n = 36{,}895$ Pseudo R^2=0.1243	>10% $n = 30{,}227$ Pseudo R^2=0.1029
Transport (reference: does not take public transport)			
Public Transport	0.96 (0.74-1.25)	1.32 (1.18-1.478)	1.12 (1.04-1.21)
Comorbidities (reference: does not have listed comorbidity)			
Diabetes	1.11 (0.67-1.86)	1.24 (0.97-1.58)	1.27 (1.04-1.55)
Hypertension	1.23 (0.85-1.76)	1.07 (0.90-1.27)	0.97 (0.85-1.10)
COPD	0.89 (0.12-6.72)	1.63 (0.75-3.53)	1.17 (0.63-2.19)
Asthma	0.61 (0.35-1.08)	0.85 (0.69-1.06)	0.97 (0.83-1.15)
Cancer	0.92 (0.29-2.96)	0.80 (0.45-1.42)	0.82 (0.55-1.23)
Stress or mental health disorder	0.79 (0.55-1.15)	0.66 (0.55-0.78)	0.75 (0.67-0.85)
Tobacco consumption	0.85 (0.66-1.10)	0.66 (0.58-0.75)	0.62 (0.57-0.68)
BMI≧30	1.34 (1.08-1.66)	1.29 (1.16-1.43)	1.32 (1.21-1.43)
Constant	0.007 (0.004-0.012)	0.003 (0.002-0.004)	0.015 (0.011-0.019)

Blue: OR significantly higher compared to the reference
Green: OR significantly lower compared to the reference

possible participation by HCWs who were telecommuting or on leave may have slightly lowered our prevalence estimates. Finally, this is one of the largest seroprevalence studies to date; nevertheless, just under half of the total eligible population participated. Participation was likely influenced by several factors related to the pandemic, particularly difficulty in attending in-person testing sites. We made an effort to compare the participating population to descriptive data available for the general HCW population (Table 1), showing that differences were relatively minor and likely did not introduce significant bias into our conclusions.

In the imminent onset of new waves in the upcoming months in the southern hemisphere, our findings together with others should assist countries with similar health care conditions, especially those that have been slower in their vaccination campaigns, in the prioritization of individuals and groups for vaccination and in enforcement of PPE measures. Our results indicate that HCWs in the hospital setting, participating in activities likely to increase exposure risk (such as night shifts, increased age, and using public transport) should be prioritized for vaccination.

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Data Availability Statement

Study databases have been made available on Github: https://github.com/MinCiencia/Datos-COVID19/tree/master/output/producto84.

Author Contributions

Study conception and design (MZ, MLO, MAR, AJL, SM), questionnaire construction (MZ, MLO, MAR, AJL), study implementation and field supervision (MZ), support for study implementation with regional health care authorities (MZ, MLO, MAR), data collection and management (AP), data analysis (SM, AP, MAR, AJL), manuscript conception (MLO), manuscript writing (MLO, AJL, MAR, SM).

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jclinepi.2021.12.026.

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