Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Letter to the editor

Cumulative seroprevalence among healthcare workers after the first wave of the COVID-19 pandemic in El Salvador, Central America

Yu Nakagama 1, 2, *1, Maria-Virginia Rodriguez-Funes 3, 1, Rhina Dominguez 4, Katherine-Sofía Candray-Medina 1, 2, 5, Naoto Uemura 6, Evariste Tshibangu-Kabamba 1, 2, Yuko Nitahara 1, 2, Natsuko Kaku 1, 2, Akira Kaneko 1, 2, Yasutoshi Kido 1, 2, 7

1) Department of Virology & Parasitology, Graduate School of Medicine, Osaka Metropolitan University, Osaka, Japan
2) Research Centre for Infectious Disease Sciences, Graduate School of Medicine, Osaka Metropolitan University, Osaka, Japan
3) National Rosales Hospital, San Salvador, El Salvador
4) El Salvador National Institute of Health, San Salvador, El Salvador
5) Centro Nacional de Investigaciones Científicas de El Salvador (CICES), San Salvador, El Salvador
6) Department of Clinical Pharmacology and Therapeutics, School of Medicine, Oita University, Oita, Japan

A total 2322 HCWs from the National Clinical Laboratory and the National Rosales Hospital were recruited, of which 973 individuals (41.9% response rate, aged 43 ± 11 years, 71.7% female) having consented to participate were eligible for analysis. The sites served as the main referral facilities for COVID-19 during May through July 2020. The same level of protection (full length gown, face shield, N95 or higher-level filter mask, and gloves) was mandated for all of the COVID-19 contacts, and training for its use was provided uniformly. During the study period of end-January through mid-February 2021, the participants completed a questionnaire through the web-based REDCap electronic data capture tool [2] and provided sera for serological evaluation. The questionnaire queried about the participants’ demographic data, anthropometric measurements, medical history, occupational role, prior COVID-19 diagnosis, and family member contracting COVID-19. The serological status was defined by the combination of two immunoassays: Roche Elecsys Anti-SARS-CoV-2 assay (Basel, Switzerland) and Abbott SARS-CoV-2 IgG II Quant (Chicago, IL, USA). The participants of ‘indeterminate’ serology with discordant results (1.7%, 17 of 973) were excluded from analyses. An χ² test was used upon comparison and the ‘non-patient—related’ occupations served as reference for risk ratio calculation. The p thresholds of Bonferroni-adjusted 0.017 defined the statistical significance. The research was approved by the Osaka City University Institutional Ethics Committee [#2020-003] and the National Research Ethics Committee of El Salvador [#CNEIS/2020/029].

The overall seropositivity rate in HCWs reached 52.6% (512 of 973). Among the seropositive individuals, 61.7% (316 of 512) had experienced documented COVID-19, of which 70.6% (223 of 316) were laboratory-confirmed by PCR (the rest were diagnosed clinically). Finally, those never having been suspected of the diagnosis nor underwent SARS-CoV-2 PCR testing, but still revealed positive for anti-SARS-CoV-2 antibodies, aggregated to the excessive 38.3% (196 of 512) of ‘unrecognized seroconversions.’ Nurses had the
highest seropositivity rate of 63.8%, followed by HCWs assigned to other patient-related work (55.9%), and medical doctors (46.7%). Auxiliary HCWs assigned to non-patient–related work, ranking bottom among occupations, still showed surprisingly high seroprevalence (44.2%). Additionally, 21.8% (97 of 444) of seronegative individuals reported of their family member contracting COVID-19.

The presented Salvadoran HCW cohort listed highest in seroprevalence (52.6%) among the pooled trend for HCWs globally (4.8% through 12.4%) [3,4], far exceeding that reported from Brazil (29.9%), another Latin American country [5]. The risk of infection per occupation generally reflected their variable degrees of proximity with COVID-19 patients; patient-related work associated with higher risk (see Table 1). Interestingly, however, respiratory care specialists who perform the highly aerosol-generating, endotracheal procedures on COVID-19 patients carried less risk in contracting the disease compared with cleaning staff entering the COVID-19 ward (45.5% vs. 71.9% in seroprevalence). Previous studies targeting HCWs have reported similar traits for cleaning personnel carrying high infection risk [6–8]. A high risk of infection among the cleaning staff has been attributed to their lower adherence to protective measures, due to less understanding about (1) the transmission mechanisms of viral respiratory infections, as well as (2) the proper use of countermeasures to mitigate them. Their circumstances outside the hospital (i.e. socioeconomic factors potentially linked to public transportation use or housing conditions prone to crowd exposure) have also been raised as contributing factors. The same logic may apply to our present cohort. Lastly, our data highlighted the possibility of the current epidemiological estimates having been under-representative of the true regional burden. Under-estimation of COVID-19 burden may be explained by the excessive number of pauci/asymptomatic, thus unrecognized, seroconversions [9]. Seroprevalence among non-patient related Salvadoran HCWs (44.2%) was highly elevated to exceed twice the community seroprevalence in United States at the time (18.4%) [10]. Together with the high frequency (21.8%) of seronegative individuals in this study reporting of household COVID-19 cases, our findings in total were indicative of substantial transmission having occurred in the communities, potentially outside the healthcare setting. Among the limitations of our study was the voluntary nature of participation. Accordingly, the response rate remained rather low, leaving room for bias if HCWs more health conscious and eager to be tested were more/less likely to be seropositive. The study targeted a single-centred cohort and thus may not have represented the general HCW population of the country. Also, the community seroprevalence in El Salvador remains to be elucidated before being conclusive on the major site of SARS-CoV-2 transmission among HCWs, whether within or outside the workplace.

Large healthcare-associated outbreaks not only endanger the assurance of quality care in the midst of a pandemic but also may impact the extent and kinetics of spread within the whole society. Alongside occupational exposures, protective measures are ought to target exposures outside the working environment with potential of subsequent introduction into the healthcare setting.

**Author’s contributions**

YNa and MVRF conceptualized the study and performed the formal analyses. RD and YK provided supervision. YNa, MVRF, RD, and KSCM led the investigation. KSCM curated the data and ETK, YNi, and NK validated the outputs of the study. YNa visualised the data and wrote the original draft of the manuscript. MVRF, RD, ETK, NU, AK, and YK reviewed and edited the manuscript. YNa, NU, AK, and YK took parts in funding acquisition.

**Transparency declaration**

Yu Nakagama and Yasutoshi Kido report ownership of equity of Quantum Molecular Diagnostics, an Osaka City University spinout providing innovative diagnostics for infectious diseases. Yu Nakagama and Yasutoshi Kido also receive financial support outside the work from Abbott Japan, LLC.

**Funding**

This work was supported by Japan Agency for Medical Research and Development [grant numbers JP20jk01010021 and JP20h01220001]; the Osaka City University Strategic Research Grant 2021 for Young Researchers [grant number OCU-SRG2021_YR09]; Japan Society for the Promotion of Science KAKENHI [grant number 21K09078]; and the Osaka City University Special Reserves Fund for COVID-19.

**Acknowledgements**

The authors thank all healthcare workers who participated in the study as well as the co-investigators that facilitated data collection and material transfer.

**References**

[1] Burki T. COVID-19 in Latin America. Lancet Infect Dis 2020;20:547–8.
[2] Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap) – a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009;42:377–81.
[3] Hossain A, Nasrullah SM, Tasnim Z, Hasan MK, Hasan MM. Seroprevalence of SARS-CoV-2 IgG antibodies among health care workers prior to vaccine administration in Europe, the USA and East Asia: a systematic review and meta-analysis. EClinicalMedicine 2021;33:100770.

---

**Table 1**

| Occupational category | Seropositive % (n = 512) | Seronegative % (n = 444) | Risk p² ratio |
|-----------------------|--------------------------|--------------------------|--------------|
| Nurse                 | 63.8 (120)               | 34.5 (144)               | 1.44 <0.0001¹ |
| Medical doctor        | 46.7 (56)                | 52.3 (105)               | 0.69         |
| Other patient-related | 55.9 (38)                | 40.9 (128)               | 0.0027       |
| Respiratory care      | 45.3 (5)                 | 45.5                     |              |
| Radiology personnel   | 52.2 (9)                 | 39.1                     |              |
| Cleaning staff        | 71.9 (9)                 | 28.1                     |              |
| Other                 | 44.4 (15)                | 55.6                     |              |
| Non-patient related   | 44.2 (230)               | 54.1 (–)                 | –            |
| Blood bank personnel  | 21.4 (11)                | 78.6                     |              |
| Laboratory professional| 28.0 (65)               | 69.9                     |              |
| Administrative officer| 51.3 (90)                | 47.1                     |              |
| Nutritionist          | 60.0 (3)                 | 30.0                     |              |
| Pharmacist            | 68.0 (8)                 | 32.0                     |              |
| Other                 | 41.3 (53)                | 57.6                     |              |

¹: χ² test.
²: Statistically significant.
³: Reference group.
[4] Kayi I, Madran B, Keske Ş, Karanfil O, Arribas JR, Pshenichnaya N. The sero-prevalence of SARS-CoV-2 antibodies among health care workers before the era of vaccination: a systematic review and meta-analysis. Clin Microbiol Infect 2021;27:1242–9.

[5] Correia RF, da Costa ACC, Moore DCBC, Junior SCG, de Oliveira MPC, Zuma MCC, et al. SARS-CoV-2 seroprevalence and social inequalities in different subgroups of healthcare workers in Rio de Janeiro, Brazil. Lancet Reg Health Am 2022;7:100170.

[6] Costa SF, Giavina-Bianchi P, Buss L, Peres CHM, Rafael MM, Santos LGND, et al. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) seroprevalence and risk factors among oligo/asymptomatic healthcare workers: estimating the impact of community transmission. Clin Infect Dis 2021;73: e12148.

[7] Oliveira MS, Lobo RD, Detta FP, Vieira-Junior JM, Castro TL, Zambelli DB, et al. SARS-CoV-2 seroprevalence and risk factors among health care workers: estimating the risk of COVID-19 dedicated units. Am J Infect Control 2021;49:1197–9.

[8] Eyre DW, Lumley SF, O’Donnell D, Campbell M, Sims E, Lawson E, et al. Differential occupational risks to healthcare workers from SARS-CoV-2 observed during a prospective observational study. Elife 2020;9:e60675.

[9] Nakagama Y, Komase Y, Candray K, Nakagama S, Sano F, Tsuchida T, et al. Serological testing reveals the hidden COVID-19 burden among health care workers experiencing a SARS-CoV-2 nosocomial outbreak. Microbiol Spectr 2021;9:e0108221.

[10] Jones JM, Stone M, Sulaeman H, Fink RV, Dave H, Levy ME, et al. Estimated US infection- and vaccine-induced SARS-CoV-2 seroprevalence based on blood donations. JAMA 2021;326:1400–9.