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Seroprevalence of anti-SARS-CoV-2 antibodies and risk of viral exposure among healthcare workers in the South Kivu province, eastern Democratic Republic of the Congo: a cross-sectional study

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ABSTRACT

Objectives Healthcare workers (HCWs) are on the frontline of combating COVID-19, hence are at elevated risk of contracting an infection with SARS-CoV-2. The present study aims to measure the impact of SARS-CoV-2 on HCWs in central sub-Saharan Africa.

Setting A cross-sectional serological study was conducted at six urban and five rural hospitals during the first pandemic wave in the South Kivu province, Democratic Republic of the Congo (DRC).

Participants Serum specimens from 1029 HCWs employed during the first pandemic wave were collected between August and October 2020, and data on demographics and work-related factors were recorded during structured interviews.

Primary and secondary outcome measures The presence of IgG antibodies against SARS-CoV-2 was examined by ELISA. Positive specimens were further tested using a micro-neutralisation assay. Factors driving SARS-CoV-2 seropositivity were assessed by multivariable analysis.

Results Overall SARS-CoV-2 seroprevalence was high among HCWs (33.1%), and significantly higher in urban (41.5%) compared with rural (19.8%) hospitals. Having had presented with COVID-19-like symptoms before was a strong predictor of seropositivity (31.5%). Personal protective equipment (PPE, 88.1% and 11.9%) and alcohol-based hand sanitizer (71.1% and 28.9%) were more often available, and hand hygiene was more often reported after patient contact (63.0% and 37.0%) in urban compared with rural hospitals, respectively. This may suggest that higher exposure during non-work times in high incidence urban areas counteracts higher work protection levels of HCWs.

Conclusions High SARS-CoV-2 seropositivity indicates widespread transmission of the virus in this region of DRC. Given the absence of publicly reported cases during the same time period at the rural sites, serological studies are very relevant in revealing infection dynamics especially in regions with low diagnostic capacities. This, and discrepancies in the application of PPE between urban and rural sites, should be considered in future pandemic response programmes.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study highlights the importance of serological studies in revealing infection dynamics especially in regions with low diagnostic capacities.
⇒ A comprehensive set of demographic and epidemiological data of the study population permits in-depth analysis of factors affecting the exposure of healthcare workers to SARS-CoV-2.
⇒ The puzzling finding of higher seroprevalence despite the more frequent use of protective measures at urban, compared with rural hospitals, could not be fully resolved and warrants more investigations of the influence of exposure behaviour during non-work activities.

INTRODUCTION

The ongoing pandemic of COVID-19, caused by SARS-CoV-2, was first detected in Africa on 25 February 2020, and approximately 1 month later, on 10 March 2020, the first case was reported in the Democratic Republic of the Congo (DRC).[1]

The DRC had recorded 95 173 confirmed cases and 1462 deaths as of 9 January 2023 in all 26 provinces, including South Kivu

(https://data.who.int/dashboards/covid19/cases?n=c). South Kivu is among the top six high-risk provinces in DRC for SARS-CoV-2 infections, with 3855 cases reported as of 29 May 2022.[2] During the first and second pandemic waves, antigenic rapid testing was available only in urban referral centres and general hospitals of this region, and only sporadically in a few rural hospitals. At the design and implementation of this study, only two laboratories, the Institut National de la Recherche Biomédicale of South Kivu and the Panzi Hospital, were further equipped for PCR testing and covered the 34 health zones of the South Kivu province for diagnosis and epidemiological surveillance.[3] PCR testing is done to detect active SARS-CoV-2 infection among suspected cases.

Narrative and systematic studies have estimated the proportion of SARS-CoV-2 infections that remain completely free of symptoms to be 17–97.5%, leading to a severe underestimation of the virus' local circulation if asymptomatic carriers are not being tested.[4–6] SARS-CoV-2 infection induces antibody production with potentially virus neutralising capacities, which enables tracing viral exposure by serological methods.[7] In light of potentially high rates of asymptomatic infection, understanding the extent to which local populations have already been exposed to the virus may, thus, contribute to effective control strategies for the spread of SARS-CoV-2. As in other parts of the world, COVID-19 has rapidly spread in healthcare workers (HCWs) such as doctors, nurses, hospital cleaners and laboratory technicians in DRC.[8] By being on the frontline of combating COVID-19, they remain at a higher risk of contracting the infection than other members of the community. Recent studies have reported a high seroprevalence of SARS-CoV-2 cases among asymptomatic HCWs in two different hospitals in Bukavu city, South Kivu province, suggesting a high exposure and circulation of SARS-CoV-2.[3 8] However, these studies were restricted to only the urban population as with many studies on SARS-CoV-2 exposure. The impact of the virus on HCWs in rural areas remains largely unknown but would be particularly relevant to investigate, as studies from other world regions indicate that low personal protective equipment (PPE) capacities and weak health infrastructure in rural health facilities may increase the local infection risk for HCWs.[9]

At the time that this study was initiated, despite unrestricted movement of the population between rural and urban areas of South Kivu, no cases of COVID-19 had been reported in rural areas of the province, hinting at severe under-reporting and undertesting at these areas. Thus, the main objective of this study was to measure the seroprevalence of anti-SARS-CoV-2 antibodies among HCWs in different urban and rural hospitals in the South Kivu province, eastern DRC. We also assessed potential preventative and risk factors of SARS-CoV-2 exposure. The data generated here may be useful to inform future public health actions like vaccine deployment and protection measures for the hospital workforce.

METHODS

The results are reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.

Study design and participants

A cross-sectional study was carried out from August to October 2020 in 11 hospitals in the South Kivu province, eastern DRC: six urban hospitals (Panzi Hospital, Ciriri Hospital, Kadutu Hospital, BIOPHARM Health Centre, Nyantende Hospital and Kasenga Hospital) and five rural hospitals (Walungu Hospital, Katana Hospital, Kakwende Heath Centre, Kaziba Health Centre and Kavumu Health Centre). Urban areas or cities were defined as any locality of at least 100 000 inhabitants with public facilities and economic and social infrastructures, to which a decree of the prime minister of DRC has conferred the status of a city.[10] Rural areas were defined by a population density of less than 400 people per square kilometre, lack of major hubs of urban life or migration (ie, no regular market, no airport or port), and absence of the status of a city conferred by the prime minister of DRC.[10] The hospitals in these areas were conveniently selected based on their accessibility and their status of being a reference health facility in the area. In the selected hospitals, all HCWs were invited to voluntarily participate in the survey. A total of 1029 consenting HCWs were included in this study regardless of current disease symptoms (68.6% of originally 1500 HCWs who were invited).

Data and blood sample collection

Trained study staff first explained the study objectives and obtained written informed consent from participating HCWs. They were then asked to complete a risk factor questionnaire. Subsequently, 5 mL of venous blood was collected in an EDTA-coated tube. The sample tube was labelled according to the identifier on the corresponding participant questionnaire. On collection, participant blood samples were incubated at room temperature for approximately 30 min to allow clotting. All samples were brought directly to the Université Evangélique en Afrique/Panzi Hospital laboratory. Samples were then centrifuged for 10 min at 1500 rotations per minute and serum was collected into 2 mL cryotubes. The serum was stored at −20°C prior to serological analysis.

Serological analysis of antibodies against SARS-CoV-2

We employed the following testing algorithm in order to reduce the false positive rate related to the cross-reaction of anti-SARS-CoV-2 antibodies with other common coronaviruses, as described by others[11]: All serum samples were analysed to detect the presence of SARS-CoV-2 antibodies using the semiquantitative Euroimmun SARS-CoV-2 IgG antibody ELISA kit (Euroimmun AG, Lübeck, Germany) that targets viral Spike Protein 1 (S1), following manufacturer's instructions. This assay has demonstrated a high sensitivity and specificity (94.6% and 98.0%, respectively) and has been widely used throughout European

and non-European serological studies.[12] Samples with testing ratios <0.5 were considered negative and were not included in further analyses, while samples with ratios ≥0.5 were repeated in duplicate with the same assay for confirmation. Among these samples, positive and borderline samples were further confirmed by a second assay, the Wantai SARS-CoV-2 Ab ELISA, for the detection of complete antibodies against SARS-CoV-2 (Beijing Wantai Biological Pharmacy Enterprise, Beijing, China). For this assay, we used the following cut-off-values to evaluate samples: <0.9 considered negative; ≥0.9–1.1 considered borderline, and ≥1.1 confirmed as positive.

For all samples testing negative using the first Euroimmun assay, this result was considered final. For samples that had undergone repeated testing by a second Euroimmun test and turned out negative, this result was considered final. For all remaining samples, results from the Wantai assay were considered final and used in statistical data analyses.

Positive samples of which sufficient material remained were aliquoted and shipped frozen to the Robert Koch Institute in Berlin, Germany, for micro-neutralisation testing (NT). The presence of neutralising antibodies was analysed by mixing sera with heparin (1.5% final concentration), then diluting 50 µL of serum 1:10 in cell culture medium (Dulbecco's Modified Eagle Medium; 10% fetal calf serum; 2 mM L-glutamine), and subsequently mixing 1:1 with SARS-CoV-2 (strain BetaCoV/Germany/BavPat1/2020, provided by Dr Roman Woelfel, Institute for Microbiology of the German armed forces; final virus concentration in serum–virus mixture: 1000 Tissue Culture Infectious $Dose_{50}$/mL). Incubation took place at room temperature for 1 hour. One hundred microlitres of diluted serum-virus mix were then added to wells of a 96-well plate containing 2×10^4 Vero E6 cells per well (#85020206, European Collection of Authenticated Cell Cultures, Porton Down, UK) and incubated for 5 days at 37°C, 5% CO_2. After this time, each well was examined by light microscopy for a visible cytopathic effect (CPE), and the number of wells without CPE (neutralised wells) was counted. The sample dilution was tested in eight replicates. A positive control with known titre was included in parallel and back-titration of the virus stock was performed. Samples with at least one neutralised well were evaluated as positive for neutralising antibodies.

The workflow is illustrated in online supplemental figure 1. Sample testing results which were considered final and used in subsequent statistical analyses are capitalised and highlighted in bold.

Demographic data and questionnaire design

We designed a questionnaire to capture sociodemographic information, potential sources and risks of exposure to SARS-CoV-2, as well as countermeasures against infection.

1. The following sociodemographic and biological variables were recorded:
   Province, age, gender, job function, occupational risks, time spent in service during the pandemic (from 1 January 2020 to the date of the survey), comorbidities (heart disease, chronic respiratory pathology, obesity, chronic kidney disease, diabetes, hypertension, immunosuppressive treatment (corticoids, chemotherapy, HIV, others), pregnancy, other immunosuppression to be specified), COVID-19-like symptoms and reported past-PCR positive test (from 19 March 2020 to the date of the survey).
2. SARS-CoV-2 occupational risks were defined based on type of profession and working site. If an HCW could not exclusively be classified into one category, she/he was assigned to the higher risk category. The risk categories were defined as follows:
   2.1. High risk: Personnel working in separate wards for the treatment of patients with COVID-19 including COVID-19 general wards and COVID-19 intensive care units (ICUs)—both strictly separated from non-COVID-19 wards—, and personnel working in front line wards such as the medical, surgical, paediatric and obstetric emergency room and the ICUs. Job functions included physicians and medical residents, nurses, other allied health professionals (eg, lab and radiology technicians, pharmacists, community agent, psychologists and social workers), and cleaning staff/catering staff/security officers.
   2.2. Moderate risk: Personnel working in wards which may also have a higher risk for SARS-CoV-2 transmission if the patient has COVID-19, including non-COVID-19 specific medical, surgical, paediatrics and gynaecology and obstetrics hospitalisation wards, the operating room department, other external consultation (including family planning and advisory centre, prenatal consultation, psychosocial consultation, HIV testing service, vaccination clinic and field officers), radiology department and the laboratory. Job functions included physicians and medical residents, nurses, midwives other allied health professionals cleaning/catering staff and security officers. In addition, laboratory and radiology personnel were included in this category.
   2.3. Low risk: Personnel having direct contact to patients outside of high and moderate risk categories. Job functions included physicians and medical residents, nurses, other allied health professionals and cleaning/catering staff and security officers, administrative staff, facility management with patient contact, technical staff and surface workers with patient contact pharmacy personnel with patients contact.
   2.4. Very low risk: Personnel having no direct contact to patients. Job functions included other administrative staff, facility management without patient contact, pharmacy personnel without patients contact and technical staff and surface workers without patient contact.
3. Other occupational exposure and infection prevention and control measure variables were also recorded including the following: Collection of nasopharyngeal

swabs, direct physical contact with patients with COVID-19, presence during aerosol-generating procedure, exposures to biological fluids or patients' belongings, sufficient and regular availability of PPE or alcohol-based hand sanitizer, use of hand hygiene after patient consultation as well as after cleaning or aseptic procedures.

Patient and public involvement

It was not appropriate or possible to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research.

Statistical analysis

Serological outcome (positive, negative) and variables collected in the questionnaire were descriptively analysed including absolute numbers and relative proportions. Differences among HCWs testing seropositive or seronegative were assessed using Pearson's test of independence or Fisher's exact test. P values ≤0.05 were considered statistically significant. A logistic regression model was run to further assess factors associated with SARS-CoV-2 serological outcome (positive, negative), including variables with a p value of ≤0.2 in the bivariate analysis, as well as biological variables likely to create confounding (age, sex) and variables linked to the occupational risk group (initial model). The then refined most parsimonious model was fitted using the stepwise (bottom-up) method (Final Model). The goodness of fit of the model—the deviations (2 Log(Likelihood))—was calculated. Potential differences in the availability and use of PPE and infection control measures between rural and urban hospitals were also examined in bivariate analyses. All analyses were performed in the XLSTAT software.

RESULTS

Among 1029 HCWs included in this study, 61.3% originated from urban hospitals and 38.7% from rural hospitals. A total of 58.9% of all HCWs were male, with a median age of 37 years (range: 18–85), and 41.1% were female, with a median age of 35 years (range: 18–70, table 1). The largest professional group was nurses (33.7%), and most participants were assigned to the moderate occupational risk group (44.8%) and had worked more than 6 months in the hospital during the pandemic. 7.5% of all participants had comorbidities. A majority (68.5%) had reported COVID-19-like symptoms previously, while 2% had had a PCR-confirmed SARS-CoV-2 infection before (including only four HCWs from rural sites, table 2).

Overall seroprevalence among HCWs in South Kivu hospitals was 33.1%. Of all 248 samples with a conclusive result from micro-NT, 197 (76.4%) contained neutralising antibodies.

The bivariate analysis indicated that seroprevalence was higher in urban areas (41.5%) as compared with rural areas (19.8%, p<0.0001, table 2). It was higher in HCWs who had developed COVID-19-like symptoms previously (42.6%) compared with those who reported no symptoms (28.8%, p<0.0001), and also in those with a previous PCR-confirmed SARS-CoV-2 infection (57.1%) compared with those without a positive test (32.6%, p=0.0182). Seropositivity of HCWs was also higher among those who reported performing nasopharyngeal swabbing of patients with suspected COVID-19 (53.5%, p=0.0038), and having direct contact with patients with COVID-19 (37.8%, p=0.0244, table 2).

The multivariable analysis including hospital site (urban/rural), professional risk group, professional activities with potential exposure to SARS-CoV-2, COVID-19-like symptoms and SARS-CoV-2 infection revealed that

Table 1 SARS-CoV-2 seropositivity according to hospital sites and among female and male HCWs in South Kivu, DRC

	Overall	Female	Male
Total	1029	423/1029 (41.1%)	606/1029 (58.9%)
Rural zone	79/398 (19.8%)	26/151 (17.2%)	53/247 (21.5%)
Kakwende Health Centre	1/35 (2.9%)	0/17 (0.0%)	1/18 (5.6%)
Kavumu Health Centre	30/95 (31.6%)	12/34 (35.3%)	18/61 (29.5%)
Katana Hospital	18/72 (25.0%)	5/25 (20.0%)	13/47 (27.7%)
Kaziba Health Centre	12/89 (13.5%)	0/21 (0.0%)	12/68 (17.6%)
Walungu Hospital	18/107 (16.8%)	9/54 (16.7%)	9/53 (17.0%)
Urban zone	262/631 (41.5%)	120/272 (44.1%)	142/359 (39.6%)
BIOPHARM Health Centre	7/19 (36.8%)	5/10 (50.0%)	2/9 (22.2%)
Kasenga Hospital	21/58 (36.2%)	8/15 (53.3%)	13/43 (30.2%)
Nyantende Hospital	33/76 (43.4%)	14/35 (40.0%)	19/41 (46.3%)
Panzi Hospital	173/423 (40.9%)	81/188 (43.1%)	92/235 (39.1%)
Ciriri Hospital	19/39 (48.7%)	7/18 (38.9%)	12/21 (57.1%)
Kadutu Hospital	9/16 (56.3%)	5/6 (83.3%)	4/10 (40.0%)

DRC, Democratic Republic of the Congo; HCW, healthcare worker.

Table 2 Demographic characteristics and SARS-CoV-2 exposures of HCWs in urban and rural hospitals in South Kivu, DRC

	Seronegative	Seropositive	P value*
Total	688/1029 (66.9%)	341/1029 (33.1%)	
Zone			
Rural	319/398 (80.2%)	79/398 (19.8%)	**<0.0001**
Urban	369/631 (58.5%)	262/631 (41.5%)	
Age (years)			
18–25	91/124 (73.4%)	33/124 (26.6%)	0.4683
26–35	226/346 (65.3%)	120/346 (34.7%)	
36–45	158/240 (65.8%)	82/240 (34.2%)	
46–55	112/174 (64.4%)	62/174 (35.6%)	
56–65	78/109 (71.6%)	31/109 (28.4%)	
>65	23/36 (63.9%)	13/36 (36.1%)	
Gender			
Male	411/606 (67.8%)	195/606 (32.2%)	0.4332
Female	277/423 (65.5%)	146/423 (34.5%)	
Function			
Administrative	46/63 (73%)	17/63 (27%)	0.3303
Medical resident	41/68 (60.3%)	27/68 (39.7%)	
Nurse	235/347 (67.7%)	112/347 (32.3%)	
Technical and manual staff	183/268 (68.3%)	85/268 (31.7%)	
Physician	69/116 (59.5%)	47/116 (40.5%)	
Other allied health professional	114/167 (68.3%)	53/167 (31.7%)	
Professional risk group			
High	187/294 (63.6%)	107/294 (36.4%)	0.0659
Moderate	305/461 (66.2%)	156/461 (33.8%)	
Low	99/129 (76.7%)	30/129 (23.3%)	
Very low	97/145 (66.9%)	48/145 (33.1%)	
Time spent in service (months)			
≤2	54/74 (73.0%)	20/74 (27.0%)	0.5088
3–5	68/103 (66.0%)	35/103 (34.0%)	
≥6	566/852 (66.4%)	286/852 (33.6%)	
Comorbidities			
No	639/949 (67.3%)	310/949 (32.7%)	0.2669
Yes	49/80 (61.3%)	31/80 (38.8%)	
COVID-19-like symptoms			
No	502/705 (71.2%)	203/705 (28.8%)	**< 0.0001**
Yes	186/324 (57.4%)	138/324 (42.6%)	
Reported past COVID-19 positive PCR			
No	679/1008 (67.4%)	329/1008 (32.6%)	**0.0182**
Yes	9/21 (42.9%)	12/21 (57.1%)	
Nasopharyngeal swabbing of patients			
No	668/986 (67.7%)	318/986 (32.3%)	**0.0038**
Yes	20/43 (46.5%)	23/43 (53.5%)	
Contact with patients with COVID-19			
No	476/688 (69.2%)	212/688 (30.8%)	**0.0244**
Yes	212/341 (62.2%)	129/341 (37.8%)	

Continued

Table 2 Continued

	Seronegative	Seropositive	P value*
Presence during aerosol generating procedure			
No	669/999 (67.0%)	330/999 (33.0%)	0.677
Yes	19/30 (63.3%)	11/30 (36.7%)	
Biological fluid exposure			
No	664/989 (67.1%)	325/989 (32.9%)	0.3471
Yes	24/40 (60.0%)	16/40 (40.0%)	
Had contact with patients' belongings			
No	657/981 (67.0%)	324/981 (33.0%)	0.7313
Yes	31/48 (64.6%)	17/48 (35.4%)	

*P values <0.05 are highlighted in bold.
DRC, Democratic Republic of the Congo; HCW, healthcare worker.

working at urban hospitals and having had COVID-19-like symptoms were significant positive predictors of SARS-CoV-2 seropositivity of HCWs (table 3).

A detailed analysis of reported symptoms typical for COVID-19 in the past 8 months prior to the study revealed that loss of taste or smell (68.9%, p=0.001), asthenia (57.6%, p=0.0058), myalgia (51.9%, p=0.0195) and cough (49.6%, p=0.0493) were significantly associated with seropositivity (table 4).

PPE materials during the pandemic were reported as reliably available in only 50.5% of all considered hospitals, including 88.1% in urban hospitals compared with 11.9% in rural hospitals (p<0.0001, table 5). Urban hospitals also had more access to alcohol-based hand sanitizers compared with rural hospitals (71.1% and 28.9%, respectively, p<0.0001). The vast majority of HCWs reported using hand hygiene at 'all times' or 'often' after patient contact (94.4%) and after cleaning contaminated materials (93.1%). Hand hygiene was significantly more often applied at urban (63.0% after consultation, 63.5% after cleaning) than at rural sites (37.0% after consultation, 36.5% after cleaning, p<0.0001, table 5).

DISCUSSION

In the present study, we assessed the seroprevalence of SARS-CoV-2 and associated potential risk factors in 11 urban and rural hospitals in South Kivu, DRC, where differences in demography and infection prevention and control measures may influence SARS-CoV-2 exposure. We found that over one-third of 1029 HCWs were SARS-CoV-2 seropositive, indicating an overall high exposure to the virus during the first pandemic wave in 2020. 76.4% of 269 positive HCWs' sera contained neutralising antibodies, which is high compared with other studies,[11] which may indicate high levels of immune protection. Along with COVID-19 vaccination efforts, the high number of HCWs with (neutralising) antibodies in the first wave may thus also suggest the potential for greater protection against COVID-19 in subsequent pandemic waves in DRC.[11] It should be noted that there are differences in the setups of assays used for the detection of neutralising antibodies among studies and therefore the results cannot easily be compared. The highly sensitive micro-neutralisation assay used in our study detects titres as low as 1:15, which likely results in an overall larger number of positive samples.[13]

Previous research conducted in the same region of Bukavu, based on a smaller sample of HCWs at two urban hospitals, revealed somewhat higher overall seroprevalence estimates (41.2%,[8] 40.5%[14]). The sampling period during the first pandemic wave in that study was, slightly earlier (May–August 2020) than in our study (August–October 2020). Anti-spike IgG antibody levels were shown to decrease significantly at 5–6 months compared with 0–3 months after infection in an Austrian population (by 44%[15]), and had a half-life of, for instance, 36 days in patients in the USA during the first pandemic wave.[16] This antibody decay potentially contributes to the observed lower seropositivity in the same region in our study. Comparisons of seroprevalences even during the limited time of pandemic wave one should thus be made with caution and consider the waning of antibodies over time.

Still, overall seroprevalence among HCWs employed during the first pandemic wave in 2020 varied widely on the African continent, from 1.2% in Cairo, Egypt (sampling in June 2020[17]), to 45.1% in Ibadan, Nigeria (exact study period in 2020 unknown[18]; reviewed by Müller *et al*,[19] with sampling periods of the included studies between April and December 2020). In Europe, rates of seropositive HCWs included similar to much lower estimates such as in the UK (31%, sampling period May–June 2020[20]), Italy (17.11%, sampling period May–June 2020[21]), Belgium (6% in April 2020[22]) and Germany (1.8% in July 2020[23]). The findings from the present study fall within the upper part of this range.

Rates of infection with SARS-CoV-2 early in the pandemic and subsequent seroprevalences were shown to

Table 3 Logistic regression analysis of variables potentially affecting SARS-CoV-2 serological outcomes (positive, negative) among HCWs working in urban and rural hospitals in South Kivu, DRC

	Initial model		Final model	
	P value*	OR (95% CI)	P value*	OR (95% CI)
Zone				
Rural		Reference		
Urban	**<0.0001**	2.6 (1.9 to 3.6)	**<0.0001**	2.6 (1.9 to 3.5)
Professional risk group				
High		Reference		
Moderate	0.6371	0.9(0.7 to 1.3)		
Low	0.2706	0.8(0.5 to 1.2)		
Very low	**0.0230**†	0.6 (0.3 to 0.9)		
Gender				
Female		Reference		
Male	0.3846	0.9 (0.7 to 1.2)		
Age	0.1961	1 (1 to 1)		
Nasopharyngeal swabbing of patients				
No		Reference		
Yes	0.0808	1.8 (0.9 to 3.4)		
Contact with patients with COVID-19				
No		Reference		
Yes	0.2132	0.8 (0.6 to 1.1)		
Comorbidities				
No		Reference		
Yes	0.9282	1 (0.6 to 1.7)		
COVID-19-like symptoms				
No		Reference		
Yes	**0.0196**†	1.4 (1.1 to 1.9)	**0.0073**	1.5 (1.1 to 2)
Reported past COVID-19 positive PCR				
No		Reference		
Yes	0.13	2 (0.8 to 5.2)		

Variables with a p value of ≤0.2 in the bivariate analysis, possible confounders (age and sex) and variables linked to the occupational risk group were selected for the logistic regression analysis (initial model). The final model is obtained using stepwise (bottom-up) variable selection.
*P values <0.05 are highlighted in bold.
†–2 Log(Likelihood).
DRC, Democratic Republic of the Congo; HCW, healthcare worker.

be affected, for instance, by the extent of and compliance with local lockdown measures.[24] In addition, most of the published HCW investigations represent urban hospital settings, and the causative link of seropositivity to urban versus rural settings has been much less often analysed. Our study revealed a twofold higher seroprevalence of SARS-CoV-2 in urban as compared with rural hospital sites. In another study conducted on the African continent in Zambia, no difference in seroprevalence among HCWs was detected in hospitals compared with smaller rural health centres, but no information on the size of the city or town was provided.[25] Studies from across the globe show, however, regional differences (reviewed by Galanis *et al*[9]).

Although working in urban hospitals was significantly associated with SARS-CoV-2 seropositivity in South Kivu, a seroprevalence of 19.8% among also rural HCWs is striking, given that no cases from the same rural areas had yet been officially reported in DRC. In fact, virtually no HCWs from rural sites included in our study reported having been tested positive by PCR before at their respective hospitals. Also, at the urban sites very few HCWs had had a PCR-confirmed SARS-CoV-2 infection before (ie, 95% of seropositive HCWs were not tested positive

Table 4 COVID-19-like symptoms according to SARS-CoV-2 seropositivity among HCWs employed at urban and rural hospitals in South Kivu, DRC

	Seronegative	Seropositive	
	186/324 (57.4%)	138/324 (42.6%)	P value*
Fever/chill	68/122 (55.7%)	54/122 (44.3%)	0.6367
Cough	61/121 (50.4%)	60/121 (49.6%)	**0.0493**
Loss of taste or smell	14/45 (31.1%)	31/45 (68.9%)	**0.0001**
Asthenia	28/66 (42.4%)	38/66 (57.6%)	**0.0058**
Body aches	50/104 (48.1%)	54/104 (51.9%)	**0.0195**
Rhinorrhea	82/144 (56.9%)	62/144 (43.1%)	0.8802
Sore throat	7/16 (43.8%)	9/16 (56.3%)	0.2572
Diarrhoea	20/38 (52.6%)	18/38 (47.4%)	0.5263
Shortness of breath	8/13 (61.5%)	5/13 (38.5%)	0.7585
Other symptoms	94/167 (56.3%)	73/167 (43.7%)	0.6741

*P values <0.05 are highlighted in bold.
DRC, Democratic Republic of the Congo; HCW, healthcare worker.

by PCR before, despite the presence of typical symptoms). This highlights the dramatic undertesting and under-reporting of SARS-CoV-2 cases in this region of DRC. Especially rural areas seem often to be neglected in containing the pandemic, as seen also in other Africa countries,[3], highlighting the importance of serological investigations. The finding that having had symptoms of COVID-19 before was associated with SARS-CoV-2 seropositivity among HCWs also underscores that testing of symptomatic HCWs is an important strategy to identify cases of COVID-19 and reduce further transmission. Like others, we showed that a significant proportion of seropositive HCWs remained asymptomatic,[4 26] demonstrating that routine testing strategies of exposed hospital staff could have been an important strategy to mitigate the risk of COVID-19 transmission at healthcare facilities.

The inaccessibility of some rural areas due to poor transport infrastructure and insecurity in this particular region of DRC might explain the lower level of hygiene interventions and availability of PPE found in this study, and HCWs are at a potentially high risk of getting infected by patients with COVID-19. Also, the overall population incidence of SARS-CoV-2 at the densely populated urban sites is most likely higher than at rural sites given cross-border influx and high population movement. These are factors we could not control for in our analysis. Thus, higher reported infection prevention and control measures applied in urban hospitals—though shown to

Table 5 Infection prevention and control materials and measures reported in urban and rural hospitals in South Kivu, DRC

	Rural	Urban	P value*
PPE always available when treating patients with COVID-19			
Yes	62/520 (11.9%)	458/520 (88.1%)	**<0.0001**
No	336/509 (66.0%)	173/509 (34.0%)	
Alcohol based hand sanitizer available			
Yes	215/744 (28.9%)	529/744 (71.1%)	
Sometimes	169/264 (64.0%)	95/264 (36.0%)	**<0.0001**
No	14/21 (66.7%)	7/21 (33.3%)	
Hand hygiene after consultation			
Often/always	359/971 (37.0%)	612/971 (63.0%)	**<0.0001**
Rarely/never	39/58 (67.2%)	19/58 (32.8%)	
Hand hygiene after cleaning or aseptic procedures			
Often/always	350/958 (36.5%)	608/958 (63.5%)	**<0.0001**
Rarely/never	48/71 (67.6%)	23/71 (32.4%)	

*P values <0.05 are highlighted in bold.
DRC, Democratic Republic of the Congo; PPE, personnel protective equipment.

be highly effective in preventing transmission (reviewed by Schoberer *et al*[27])—do not translate into lower HCW seroprevalence at urban as compared with rural hospitals, and exposure of HCWs remains high in urban hospitals as reported by others (eg, in India[28] and the USA[29]).

CONCLUSIONS

We show that inhabitants of urban as well as rural communities in South Kivu, DRC, were highly exposed to SARS-CoV-2 during the first pandemic wave the country was facing. Given the absence of publicly reported cases during this period at the rural sites, serological studies are highly relevant in revealing infection dynamics especially in regions with low diagnostic capacities. This, and discrepancies in the application of protective measures between urban and rural sites, should be considered in future pandemic response programmes.

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