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Severe Acute Respiratory Syndrome Coronavirus-2 Seropositivity in South-Central Uganda, During 2019 - 2021

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Abstract

Background: Globally, key subpopulations such as healthcare workers (HCWs) have a higher risk of contracting SARS-CoV-2. In Uganda, limited access to personal protective equipment amidst lack of clarity on the extent and pattern of the community disease burden may exacerbate this situation. We assessed SARS-CoV-2 antibody seroprevalence among high-risk sub-populations in South-central Uganda, including HCWs, persons within the general population previously reporting experiencing key COVID-19 like symptoms (fever, cough, loss of taste and smell) and archived plasma specimens collected between October 2019 – 18th March 2020, prior to confirmation of COVID-19 in Uganda.

Methods: From November 2020 - January 2021, we collected venous blood from HCWs at selected health facilities in South-Central Uganda and from population-cohort participants who reported specific COVID-19 like symptoms in a prior phone-based survey conducted (between May to August 2020) during the first national lockdown. Pre-lockdown plasma collected (between October 2019 and March 18th, 2020) from individuals considered high risk for SARS-CoV-2 infection was retrieved. Specimens were tested for antibodies to SARS-CoV-2 using the CoronaChek^{TM} rapid COVID-19 IgM/IgG lateral flow test assay. IgM only positive samples were confirmed using a chemiluminescent microparticle immunoassay (CMIA) (Architect AdviseDx SARS-CoV-2 IgM) which targets the spike protein. SARS-CoV-2 exposure was defined as either confirmed IgM, both IgM and IgG or sole IgG positivity.

Results: The seroprevalence of antibodies to SARS-CoV-2 in HCWs was 21.1% [95%CI: 18.2-24.2]. Of the phone-based survey participants, 11.9% [95%CI: 8.0-16.8] had antibodies to SARS-CoV-2. Among 636 pre-lockdown plasma specimens, 1.7% [95%CI: 0.9-3.1] were reactive.

Conclusions: Findings suggest a high seroprevalence of antibodies to SARS-CoV-2 among HCWs and substantial exposure in persons presenting with specific COVID-19 like symptoms in the general population of South-central Uganda. Based on current limitations in serological test confirmation, it remains unclear whether pre-lockdown seropositivity implies prior SARS-CoV-2 exposure in Uganda.

Background

It is over a year since the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) emerged(1) as a global pandemic and as of the 2nd of August 2021, nearly two hundred million cases were reported globally with >4,000,000 fatalities(2). Transmission occurs by respiratory droplets, aerosols, and via fomites and is higher in confined or congested spaces(3). SARS-CoV-2 infection can be asymptomatic(4) with estimates ranging from 5% – 80% while symptoms are largely nonspecific and include features of flu-like illness(5). Diagnosis of asymptomatic and mild cases may be missed due to prioritization of screening/confirmatory tests for individuals with moderate to severe symptoms. However, asymptomatic and pre-symptomatic persons can be highly contagious and contribute greatly to epidemic spread(6, 7).

As of the 3rd of August 2021, more than 94,000 cases with 2,710 deaths were documented in Uganda(2). Community transmission is on the rise(8) despite earlier control measures that included a phased

nationwide lockdown between March and August 2020(9). The SARS-CoV-2 diagnostic testing landscape in Uganda prioritizes testing for symptomatic persons. It is unknown how many infected asymptomatic persons are missed due to this symptom-based testing approach and what impact this has on community transmission.

HCWs in particular are at a higher risk of contracting SARS-CoV-2(10, 11) and inadvertently transmitting it to their patients, some of whom may be immunocompromised. According to the World Health Organization (WHO), they account for 10% of the global SARS-CoV-2 burden(12). This risk may be higher in countries like Uganda, due to shortage of Personal Protective Equipment (PPE) amidst unquantified community disease burden. Notably, several HCWs in Uganda have been infected and a number have died(13).

Due to the limited testing capacity, there are likely to be many undetected community infections fueling the epidemic. It is also unknown if SARS-CoV-2 importation or exposure in Uganda might have occurred earlier than the first (official) case reported on the 21st of March 2020. We aimed at determining the prevalence of antibodies to SARS-CoV-2 among selected high-risk sub-populations in South-central Uganda, including HCWs, persons who previously reported specific Coronavirus disease 2019 (COVID-19) like symptoms (fever, cough, loss of taste and smell) in the preceding 30 days, between May and August 2020. Additionally, we aimed at exploring the possibility of prior SARS-CoV-2 importation/exposure in South-Central Uganda before confirmation of the first (official) case on the 21st of March 2020.

Methods

Study design and setting

This study was cross-sectional and was conducted at the Rakai Health Sciences Program (RHSP) with participants recruited from within and outside the Rakai Community Cohort Study (RCCS) in four districts of South-central Uganda (Masaka, Kyotera, Rakai and Lyantonde). The RCCS is an open, population-based cohort in 40 communities in these districts with surveys conducted ~ every 18 months among ~ 23,000 adults, resident in fishing, agrarian, or peri-urban/trading community settings(14).

Study population and sample size

A total of 980 participants including 753 HCWs and 227 individuals from the RCCS phone-based survey were recruited into the study. Participants from the cohort had previously reported experiencing COVID-19 like symptoms (fever, cough, loss of taste and/or loss of smell) in the preceding 30 days during an earlier phone-based survey conducted between May and August 2020. HCWs were identified from health facilities in the region, prioritizing high volume facilities located near the Uganda-Tanzania border or along the Kampala-Mutukula highway serving mobile persons who may be at higher risk of SARS-CoV-2 acquisition. At the selected health facilities, all available, willing HCWs were recruited into the study.

Additionally, we retrieved 636 archived plasma specimens collected between October 2019 and March 18th, 2020, before the first national lockdown took effect. Selected samples of persons living in RCCS communities close to the Tanzanian border and along the Kampala-Mutukula highway were considered to have a high risk for SARS-CoV-2 infection due to their high mobility and interaction with cross-border populations. They included traders/vendors, commercial sex work clients, fisher folks, bike (boda-boda) riders, truck drivers, mechanics, shopkeepers, and bar owners/workers.

Sample / Data collection

Participants in the phone-based survey conducted during the first lockdown and reported having previously experienced at least one of the above COVID-like symptoms were contacted for participation in this study. Additionally, study field teams approached HCWs at selected health facilities for participation. Consenting participants provided 4mls of venous blood specimens while a short questionnaire was administered to HCWs to collect data on participant demographics, cadre, prior SARS-CoV-2 exposure, and PPE access/use. Plasma was frozen (-80°C) until laboratory analysis.

Laboratory analysis

Frozen plasma was thawed and tested for antibodies to SARS-CoV-2 using the CoronaChek^{TM} rapid COVID-19 IgM/IgG lateral flow test assay as per manufacturer's instructions. This assay was previously validated with Ugandan samples, including 1077 pre-pandemic samples from the RCCS(15). Low specificities of SARS-CoV-2 antibody assays have been reported, particularly from malaria endemic regions(16, 17). Therefore, any sample that was solely IgM positive by CoronaChek^{TM} was retested by the Abbott ARCHITECT AdviseDx SARS-CoV-2 IgM chemiluminescent microparticle immunoassay (CMIA) (Abbott, Chicago, IL).

Data analysis

SARS-CoV-2 exposure was defined as either IgM confirmed by the ARCHITECT CMIA assay, both IgM and IgG or IgG sole positivity. Point prevalence and 95% confidence intervals were determined for each sub-group using the exact Clopper-Pearson method of calculating confidence intervals for binomial proportions.

Results

Healthcare workers' SARS-CoV-2 antibody test results: Most of the participants were female (64.54%) and were 25-34 years of age (31.6%). In the initial screening using the CoronaChek^{TM}, 30.8% (232/753) of HCWs had detectable SARS-CoV-2 antibodies irrespective of isotype class. Of these, 119 tested positive for IgM only, 102 for both IgM and IgG and 11 for IgG only. Of the initially 119 IgM only reactive samples, 46 were confirmed positive when re-tested using the ARCHITECT assay. The overall seroprevalence of SARS-CoV-2 antibodies among HCWs was 21.1% [95%CI: 18.2-24.2] (159/753). Majority (24/26) of the

sampled health facilities had at least one healthcare worker who had antibodies to SARS-CoV-2. Seropositivity was highest among nurses and lowest among medical officers (Table 1).

Table 1
Factors associated with SARS-CoV-2 seropositivity among Healthcare workers

Sociodemographic characteristics		n (%) seropositive N=159	Univariate Odds Ratio (95% CI)
Sex	Male	61 (38.4)	0.9 (0.6-1.2)
	Female	98 (61.6)	Ref
Age category	15-24	33 (20.8)	0.7 (0.4- 1.1)
	25-34	57 (35.8)	Ref.
	35-44	39 (24.5)	0.8 (0.5-1.3)
	45-54	21 (13.2)	1.1 (0.6-1.9)
	55+	9 (5.7)	0.7 (0.3-1.5)
Cadre	Medical Officer	3 (1.9)	1.3 (0.4-5.1)
	Clinical Officer	8 (5.0)	1.8 (0.7-4.3)
	Nurse (all levels)	57 (35.8)	Ref
	Lab tech (all levels)	16 (10.1)	1.4 (0.8-2.7)
	Other staff	75 (47.2)	1.0 (0.7-1.5)

A total of 128 HCWs reported having undergone prior SARS-CoV-2 RT-PCR testing with 16 reporting a positive result. Of the 16 individuals, 8 had detectable antibodies to SARS-CoV-2. Out of the 128, a total of 108 HCWs reported previous negative RT-PCR results and 27% of these, subsequently tested antibody positive. Only face masks were reported to have been used by all HCWs who reported prior contact with a confirmed COVID-19 case. Despite reporting consistent use of face masks, 40% (63/156) of the HCWs reporting previous contact with a confirmed COVID-19 case had antibodies to SARS-CoV-2.

Cohort participants' SARS-CoV-2 antibody test results: Females comprised 69.1% and most participants were aged 35-44 years. Upon initial screening using the CoronaChek^{TM}, 16.3% of the participants (37/227) tested positive on IgM only, 2.2% (5/227) tested positive on IgG only whereas 6.6% (15/227) were positive on both IgM and IgG. Following retesting of the initially IgM only reactive samples using the ARCHITECT assay, 7/37 were confirmed positive. The overall seroprevalence of antibodies to SARS-CoV-2 in this population was 11.9% [95%CI: 8.0-16.8] (27/227). There was nearly no difference in seropositivity among HIV positive and negative participants (Table 2).

Table 2
Factors associated with SARS-COV-2 seropositivity among phone-based survey participants

Sociodemographic characteristics		n (%) seropositive N=27	Univariate Odds Ratio (95% CI)
HIV status	Negative	14 (51.9)	Ref
	Positive	13 (48.1)	1.0 (0.5-2.3)
Sex	Male	9 (33.3)	0.9 (0.4-2.1)
	Female	18 (66.7)	Ref
Age category	15-24	0 (0.0)	
	25-34	7 (25.9)	0.9 (0.4. 2.4)
	35-44	14 (51.9)	Ref
	45-54	6 (22.2)	1.5 (0.5–4.2)
Occupation	Agriculture for home use/barter	10 (37.0)	Ref
	Agriculture for selling	1 (3.7)	0.1 (0.0-1.1)
	Fishing	3 (11.1)	1.2 (0.3-4.8)
	Shopkeeper	3 (11.1)	1.5 (0.4-6.7)
	Trading/vending	5 (18.5)	0.6 (0.2-2.0)
	Bar worker or owner	2 (7.4)	2.3 (0.4-14.3)
	Waitress/Waiter/restaurant owner	1 (3.7)	0.9 (1.0-8.8)
	Construction	1 (3.7)	4.6 (0.3-79.9)
	Boda Boda	1 (3.7)	1.5 (0.1-16.3)

Pre-lockdown SARS-CoV-2 antibody test results: Upon initial screening using the CoronaChek^{TM}, 7% (47/363) of specimens had detectable antibodies to SARS-CoV-2 irrespective of isotype class. The majority (44) were IgM sole reactive, 2 were positive on IgG only whereas 1 reacted for both IgM and IgG. Out of the 44 IgM sole positive samples, 8 were confirmed following re-testing using the ARCHITECT assay. The overall seroprevalence of antibodies to SARS-CoV-2 in this sample category was 1.7% [95%CI: 0.9-3.1] (11/636).

Discussion

These findings suggest a relatively high SARS-CoV-2 seroprevalence among HCWs at almost all the selected health facilities (24/26) in South-central Uganda and substantial seroprevalence in persons previously reporting specific COVID-19 like symptoms within the general population. There was also

potentially a spike in transmission a few weeks prior to this evaluation with predominance of IgM only antibodies in most of the participants.

There are challenges interpreting SARS-CoV-2 rapid serology in regions with high malaria endemicity as infection with *Plasmodium* species was shown to induce cross-reactive antibodies to carbohydrate epitopes on the SARS-CoV-2 spike protein(17, 18). It is thus unclear whether seropositivity in pre-lockdown plasma specimens implies prior SARS-CoV-2 or other related coronavirus exposure or malaria in Uganda.

HCWs are minimally protected by face masks and only a few had accesses to other PPE (face shields, gowns, aprons etc.) and this, coupled with likelihood of improper face mask use or lack of N95-level protection, could explain the positive COVD-19 antibody results observed even among participants reporting face mask use. Several undetected cases among HCWs in this region is a potential driver of nosocomial spread. A moderate concordance between reported RT-PCR COVID-19 positives and antibody test outcome may reflect waning antibody levels as reported in several publications (19, 20).

Conclusions

Findings suggest a high seroprevalence of antibodies to SARS-CoV-2 among HCWs and substantial exposure in persons presenting with specific COVID-19 like symptoms in the general population of South-central Uganda. Based on current limitations in serological test confirmation, it remains unclear whether pre-lockdown seropositivity implies prior SARS-CoV-2 exposure in Uganda.

Abbreviations

SARS-CoV-2 Severe Acute Respiratory Syndrome Coronavirus 2

HCWs Healthcare workers

COVID-19 Coronavirus disease 2019

CMIA chemiluminescent microparticle immunoassay

WHO World Health Organization

PPE Personal Protective Equipment

UNCST Uganda National Council for Science and Technology

RCCS Rakai Community Cohort Study

RHSP Rakai Health Sciences Program

Declarations

Ethics approval and consent to participate: All methods of this study were carried out in accordance with the Uganda National Council for Science and Technology (UNCST) guidelines, the body that regulates research in Uganda. It was approved by the Uganda Virus Research Institute's Research Ethics Committee (Ref. GC/127/20/08/785), registered, and cleared by the UNCST (registration number HS878ES). Written informed consent was obtained from participants before blood specimens and other data were collected. Also, only archived pre-lockdown plasma specimens from Rakai Community Cohort Study (RCCS) participants that had provided prior written informed consent for use of their blood specimens in future studies were retrieved to assess prior SARS-CoV-2 exposure in Uganda. All participants were aged 18 years and above. No informed consent from 'Legally authorized representatives/parents' of minors below 16 years of age was thus required.

Consent for publication: Not applicable

Availability of data and materials: All data generated or analyzed during this study are included in this published article.

Competing interests: The authors declare that they have no competing interests.

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Authors' contributions: Protocol development: RMG, DS, ENK, CS, TCQ, KMG, LWC, SJR, MJW, RHG; **Study implementation:** CS, RMG, DS, RS, JBW, AN, EM, MCN, SJ, JBO, AM, MA, MS, GC; **Manuscript development:** CS, DS, RMG, ENK, JK, GK, GN, TCQ, KMG, LWC, SJR, TL, MJW, RHG, OL

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References

1. Lescure F-X, Bouadma L, Nguyen D, Parisey M, Wicky P-H, Behillil S, et al. Clinical and virological data of the first cases of COVID-19 in Europe: a case series. The Lancet Infectious Diseases. 2020.
2. Johns Hopkins University, cartographer JHU Corona Virus Resource Center. Baltimore, MD 21218, United States2020.
3. Meyerowitz EA, Richterman A, Gandhi RT, Sax PE. Transmission of SARS-CoV-2: a review of viral, host, and environmental factors. Annals of internal medicine. 2020.
4. Yanes-Lane M, Winters N, Fregonese F, Bastos M, Perlman-Arrow S, Campbell JR, et al. Proportion of asymptomatic infection among COVID-19 positive persons and their transmission potential: A

systematic review and meta-analysis. PloS one. 2020;15(11):e0241536.

5. Arons MM, Hatfield KM, Reddy SC, Kimball A, James A, Jacobs JR, et al. Presymptomatic SARS-CoV-2 infections and transmission in a skilled nursing facility. New England journal of medicine. 2020.
6. Nikolai LA, Meyer CG, Kremsner PG, Velavan TP. Asymptomatic SARS Coronavirus 2 infection: Invisible yet invincible. International Journal of Infectious Diseases. 2020.
7. Furukawa NW, Brooks JT, Sobel J. Evidence supporting transmission of severe acute respiratory syndrome coronavirus 2 while presymptomatic or asymptomatic. Emerging infectious diseases. 2020;26(7).
8. B. Oketch., P. Ebong., R. Muhereza., A. Ssenkabirwa., M.F. Jjingo., P. Kalokwera., et al. Health facilities run out of space as Covid-19 cases rise. Daily Monitor. 2020.
9. P. Ahimbisibwe. Museveni orders two-week lockdown as COVID-19 cases rise. Daily Monitor. 2020.
10. Ran L, Chen X, Wang Y, Wu W, Zhang L, Tan X. Risk factors of healthcare workers with corona virus disease 2019: a retrospective cohort study in a designated hospital of Wuhan in China. Clinical Infectious Diseases. 2020.
11. Wang X, Jiang X, Huang Q, Wang H, Gurarie D, Ndeffo-Mbah M, et al. Risk factors of SARS-CoV-2 infection in healthcare workers: a retrospective study of a nosocomial outbreak. Sleep Medicine: X. 2020;2:100028.
12. Papoutsi E, Giannakoulis VG, Ntella V, Pappa S, Katsaounou P. Global burden of COVID-19 pandemic on healthcare workers. Eur Respiratory Soc; 2020.
13. Twinamukye P. Uganda loses 58 doctors, nurses within one year. Daily Monitor 2021.
14. Chang LW, Mbabali I, Kong X, Hutton H, Amico KR, Kennedy CE, et al. Impact of a community health worker HIV treatment and prevention intervention in an HIV hotspot fishing community in Rakai, Uganda (mLAKE): study protocol for a randomized controlled trial. Trials. 2017;18(1):1-12.
15. Baker OR, Grabowski MK, Galiwango RM, Nalumansi A, Serwanga J, Clarke W, et al. Differential Performance of CoronaCHEK SARS-CoV-2 Lateral Flow Antibody Assay by Geographic Origin of Samples. Journal of Clinical Microbiology. 2021:JCM. 00837-21.
16. Woodford J, Sagara I, Kwan J, Zeguime A, Zaidi I, Attaher O, et al. SARS-CoV-2 seroassay optimization and performance in a population with high background reactivity in Mali. 2021.
17. Lapidus S, Liu F, Casanovas-Massana A, Dai Y, Huck JD, Lucas C, et al. Plasmodium infection induces cross-reactive antibodies to carbohydrate epitopes on the SARS-CoV-2 Spike protein. medRxiv. 2021.
18. Grifoni A, Weiskopf D, Ramirez SI, Mateus J, Dan JM, Moderbacher CR, et al. Targets of T cell responses to SARS-CoV-2 coronavirus in humans with COVID-19 disease and unexposed individuals. Cell. 2020;181(7):1489-501. e15.
19. Choe PG, Kang CK, Suh HJ, Jung J, Song K-H, Bang JH, et al. Waning Antibody Responses in Asymptomatic and Symptomatic SARS-CoV-2 Infection. Emerg Infect Dis. 2020;27.

20. Perreault J, Tremblay T, Fournier M-J, Drouin M, Beaudoin-Bussières G, Prévost J, et al. Waning of SARS-CoV-2 RBD antibodies in longitudinal convalescent plasma samples within 4 months after symptom onset. Blood, The Journal of the American Society of Hematology. 2020;136(22):2588-91.