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## FOREWORD

The second wave of COVID-19 in South Africa has fortunately waned, especially given that the rate of transmission of SARS-CoV-2 during the second wave was greater than in the first. This report details the preliminary results of a COVID-19 healthcare utilisation and seroprevalence survey (HUTS study) from three communities in South Africa, and shows an overall SARS-CoV-2 seroprevalence of 35.8% as of end January 2021. This suggests a substantial increase in seroprevalence during the second COVID-19 wave – most likely as a consequence of the greater transmissibility of the 501Y.V2 variant.

This information is an important contribution to improving our overall understanding of the epidemiology of COVID-19 in South Africa, and all contributors to this study are thanked for their participation and inputs.

**Prof Basil Brooke - Editor**

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# COVID-19 SEROPREVALENCE DURING THE SECOND WAVE OF THE PANDEMIC IN THREE DISTRICTS OF SOUTH AFRICA - PRELIMINARY FINDINGS

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## SUMMARY

A COVID-19 healthcare utilisation and seroprevalence survey (HUTS study) was initiated in the households of three South African communities (Pietermaritzburg in KwaZulu-Natal Province, Klerksdorp in North West Province, and Mitchell's Plain in Western Cape Province) in November – December 2020, and is ongoing. Interim results from individuals enrolled until 31 January 2021 are reported here. From 23 November 2020 through 31 January 2021, 941 individuals from 383 households were enrolled in the seroprevalence survey. Of these, 61.8% were female (582/941), and the median age of participants was 38 years (range: 6 to 91 years). The overall HIV prevalence in the study population was 25.9% (218/843), with the highest prevalence in Pietermaritzburg (32.7%, 133/407), followed by Klerksdorp (27.1%, 42/155) and Mitchell's Plain (15.3%, 43/281). These preliminary data indicate that during the second COVID-19 wave, SARS-CoV-2 seroprevalence in our study was 35.8% (332/927) overall. Seroprevalence was highest in Mitchell's Plain (45.9%, 149/325), followed by Pietermaritzburg (31.9%, 137/429), with the lowest in Klerksdorp (26.6%, 46/173). In the univariate model, individuals who had specimens collected in December 2020 (OR 4.0; 95% CI: 1.4-11.4; p=0.01) and January 2021 (OR 8.6; 95% CI: 3.1-24.4; p<0.001) were more likely to be positive for SARS-CoV-2 antibodies as compared to individuals who had specimens collected in November 2020. Age, sex and HIV status were not statistically associated with SARS-CoV-2 seroprevalence in the univariate model. These data are preliminary and based on relatively small numbers of enrolled individuals. Further reports will be released as additional data are obtained.

## BACKGROUND

In December 2019, novel coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was detected in Wuhan, China.[1] During the first few months of 2020 the virus spread rapidly throughout the world, resulting in the WHO declaring a pandemic on 11th March 2020.[2] Since then, numerous vaccines have been developed, with four being approved for use in several countries, and for emergency use in others.[3,4] Additionally, with the emergence of new variants such as the 501Y.V2 lineage in South Africa that has increased transmissibility and immune escape, rapid spread and additional waves of infections have resulted.[5-7]

As of 31 January 2021, over 102 million cases of COVID-19 were confirmed, corresponding to nearly 2.2 million deaths globally.[8] South Africa had reported nearly 1.5 million cases, and just over 44,000 deaths by that date.[9] South Africa experienced the first wave of SARS-CoV-2 infections that peaked in early July 2020, followed by a second wave that started in November 2020 and peaked in early January 2021. The timing and magnitude of the first and second waves varied between the provinces of South Africa.[10,11]

The Centre for Respiratory Diseases and Meningitis (CRDM) at the National Institute for Communicable Diseases (NICD) conducts prospective syndromic sentinel surveillance for severe respiratory illness (SRI) and influenza-like illness (ILI) at hospitals and clinics in five provinces in South Africa.[12-15] Pathogens under surveillance include influenza, respiratory syncytial virus (RSV) and *Bordetella pertussis,* with SARS-CoV-2 being included from March 2020.

These surveillance programmes are limited to include only persons who seek medical attention for their illness. There is therefore a lack of community-level data on persons who have had COVID-19 but did not seek medical attention. This may be due to mild or asymptomatic infection, lack of funds or limited access to health facilities. In order to obtain information on the true extent and distribution of infections, and how the COVID-19 pandemic has affected people's lives, community-level surveys are necessary.

As such, the NICD, in collaboration with the Perinatal HIV Research Unit (PHRU), Genesis Analytics (Genesis), and Epicentre, are conducting the Healthcare Utilisation and Seroprevalence (HUTS) study in three districts of South Africa where SRI and ILI surveillance sites exist. The HUTS study aims to explore the healthcare-seeking behaviour for and cost of respiratory illness during the pandemic, COVID-19 knowledge, attitudes and practices (KAP), and to estimate SARS-CoV-2 community seroprevalence in the selected communities. The preliminary seroprevalence findings are described in this report.

## METHODS

**Study aims, design and selection of districts**

We are conducting cross-sectional community surveys in three of the communities serviced by facilities where SRI and ILI surveillance is conducted, namely Mitchell's Plain (Western Cape Province), Pietermaritzburg (KwaZulu-Natal Province), and Klerksdorp (North West Province). Data collection started in November 2020 after the first wave of SARS-CoV-2 infections. The study aims to use complementary data from inpatient and outpatient syndromic surveillance conducted in the same target communities to document the clinical spectrum of illness, including the proportion of asymptomatic, mild, severe and fatal infections, both medically and non-medically attended. For this serosurvey study, we aimed to enrol 2,304 individuals from 768 households in each community.

**Data collection**

Households were identified using randomly selected global positioning system (GPS) coordinates to identify households located in the catchment areas of the surveillance site hospitals. All household members were approached for enrolment. If no dwelling existed within 30 metres around the GPS point, the point was considered invalid. In case a household needed to be replaced, an additional list of households was prepared, and replacement households were visited according to the order on the list (not by convenience). Field workers administered structured questionnaires electronically using Research Electronic Data Capture (REDCap, Vanderbilt University, USA) with the primary caregiver of the household, to gather information on household demographics, knowledge, attitude and practices related to COVID-19, and screening of individuals living in the household for symptoms of respiratory illness or death since the start of the COVID-19 epidemic in South Africa. The seroprevalence survey is nested in the healthcare utilisation study. For households that were randomly selected to be part of the seroprevalence survey, blood specimens were collected from each consenting individual in the household and tested for SARS-CoV-2 antibodies and HIV.

**Laboratory testing**

Blood specimens were collected from participants, centrifuged at the site laboratory and transported in cooler boxes to the NICD in Johannesburg for testing. SARS-CoV-2 ELISA was performed using the Wantai SARS-CoV-2 Ab ELISA kit (Beijing Wantai Biological Pharmacy Enterprise Co. Ltd, Beijing, China) which measures total antibodies (IgM, IgG and IgA) against the receptor binding domain (RBD) in the S1 subunit of the spike protein. The assay is estimated to have a sensitivity of 96.7% (95% CI: 83.3% - 99.4%) and a specificity of 97.5% (95% CI: 91.3% - 99.3%) (16). Overall, the assay has been found to be very specific with good sensitivity and is suitable for the identification of previous SARS-CoV-2 infection.[16-18] HIV serology was performed using the Abbott ARCHITECT® HIV Ag/Ab Combo (Abbott, Wiesbaden, Germany) assay, with confirmatory testing performed using Biorad Genscreen™ Ultra HIV Ag/Ab (Bio-rad, Redmond, United States of America). If individuals chose to receive their result, HIV testing was performed using a rapid point-of-care HIV test during the visit and after counselling was given. Patients newly diagnosed with HIV were referred to their local clinic for assessment and initiation of antiretroviral therapy.

### Data analysis

Data from laboratory results and the REDCap database were combined and analysed using Stata14.1® (StataCorp LP, College Station, United States of America). Descriptive statistics were used to describe the demographics and seroprevalence within the serosurvey sample participants, reported as numbers and percentages. Participants were stratified by sex and age groups in 10-year intervals. Data were additionally reported by research site (Pietermaritzburg, Klerksdorp and Mitchell's Plain). A univariate logistic regression was conducted to evaluate the demographic factors associated with patients' SARS-CoV-2 antibody results. Unadjusted odds ratios (OR) and 95% confidence intervals (95% CI) were calculated. P-values <0.05 were considered statistically significant. Variables included in the analyses were: site, month of data collection, 10-year age categories, sex, and HIV status.

## RESULTS AND DISCUSSION

Field work commenced in Pietermaritzburg and Klerksdorp on 23rd November 2020, and in Mitchell's Plain on 8th December 2020. By 31 January 2021, a total of 919 randomly selected households had been visited for the seroprevalence survey, of which 383 (41.7%) had primary caregivers that were at home, available, and willing to take part in the seroprevalence study. A total of 1287 individuals were screened for respiratory illness, all of whom were invited to be part of the seroprevalence study. A total of 92 (7.1%) individuals declined to be part of the study, and 254 (19.7%) individuals were not available at the time of the visit and follow-up visits are pending. Blood samples from a total of 941 (73.1%) individuals were collected for testing, comprising 437 (46.4%) from Pietermaritzburg, 173 (18.4%) from Klerksdorp and 331 (35.2%) from Mitchell's Plain.

### Demographic characteristics of participants

Of the 941 individuals enrolled in the HUTS serosurvey, a large proportion from Pietermaritzburg, Klerksdorp and Mitchell's Plain were female (62.0%, 271/437; 65.3%, 113/173; and 60.4%, 200/331, respectively) (Table 1). Across all three sites, most study participants were working-age adults with a median age of 38 years (range: 6 to 91 years).

HIV serology results were available for 843 (89.6%) individuals. The overall prevalence of HIV infection in the study population was 25.9% (218/843). The highest prevalence of HIV infection was found in Pietermaritzburg (32.7%, 133/407), followed by Klerksdorp (27.1%, 42/155) and Mitchell's Plain (15.3%, 43/281). According to the fifth South African National HIV Prevalence, Incidence, Behaviour and Communication Survey conducted in 2017, the HIV prevalence was 27.0% in KwaZulu-Natal, 22.7% in North West and 12.6% in Western Cape.[19] These interim reported HIV results from the HUTS study were therefore higher than expected.

**Table 1.** Demographic characteristics of participants stratified by site, Healthcare Utilisation and Seroprevalence (HUTS) study, South Africa, November 2020 – January 2021.

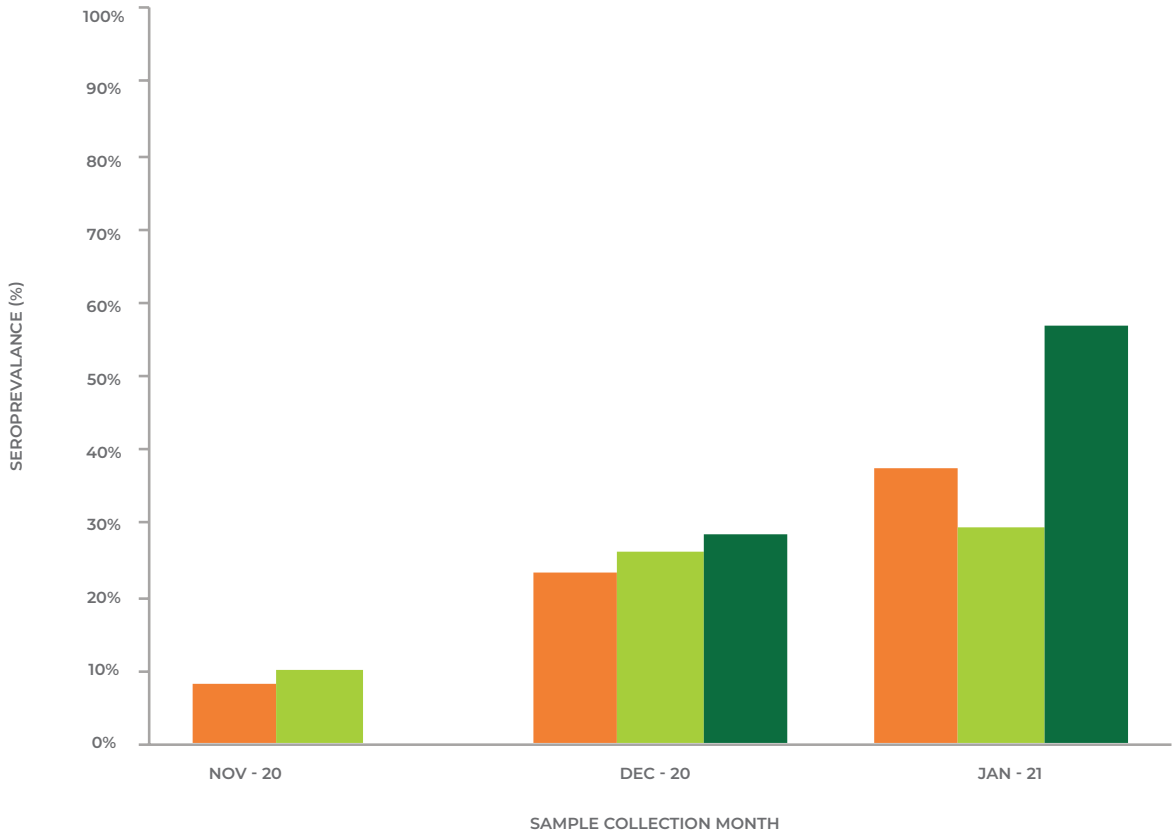
| | Pietermaritzburg n/N (%) | Klerksdorp n/N (%) | Mitchell's Plain n/N (%) | Total n/N (%) |
|---|---|---|---|---|
| Overall | 437/941 (46.4) | 173/941 (18.4) | 331/941 (35.2) | 941/941 (100) |
| Sex | | | | |
| Male | 166/437 (38.0) | 60/173 (34.7) | 131/331 (39.6) | 357/941 (37.9) |
| Female | 271/437 (62.0) | 113/173 (65.3) | 200/331 (60.4) | 582/941 (61.8%) |
| Age group (years) | | | | |
| 0-9 | 21/437 (4.8) | 3/173 (1.7) | 8/331 (2.4) | 32/941 (3.4) |
| 10-19 | 85/437 (19.5) | 25/173 (14.5) | 46/331 (13.9) | 156/941 (16.6) |
| 20-29 | 81/437 (18.5) | 20/173 (11.6) | 57/331 (17.2) | 158/941 (16.8) |
| 30-39 | 64/437 (14.7) | 22/173 (12.7) | 74/331 (22.4) | 160/941 (17.0) |
| 40-49 | 74/437 (16.9) | 29/173 (16.8) | 61/331 (18.4) | 164/941 (17.4) |
| 50-59 | 48/437 (11.0) | 29/173 (16.8) | 45/331 (13.6) | 122/941 (13.0) |
| 60-69 | 36/437 (8.2) | 28/173 (16.2) | 27/331 (8.2) | 91/941 (9.7) |
| 70-79 | 23/437 (5.3) | 12/173 (6.9) | 12/331 (3.6) | 47/941 (5.0) |
| >79 | 5/437 (1.1) | 5/173 (2.9) | 1/331 (0.3) | 11/941 (1.2) |
| HIV status | | | | |
| HIV infected | 133/407 (32.7) | 42/155 (27.1) | 43/281 (15.3) | 218/843 (25.9) |
| HIV uninfected | 274/407 (67.3) | 113/155 (72.9) | 238/281 (84.7) | 625/843 (74.1) |

## SARS-COV-2 SEROPREVALENCE BY DEMOGRAPHIC CHARACTERISTICS AND SITE

Of the 941 individuals enrolled in the study, 927 had available SARS-CoV-2 antibody results. The average seroprevalence across all three sites from November 2020 through January 2021 was 35.8% (332/927). SARS-CoV-2 seroprevalence was highest among individuals from Mitchell's Plain (45.9%, 149/325), individuals enrolled into the study in January 2021 (44.3%, 239/540), individuals in the 30-39 year age group (45.2%, 71/157), females (37.7%, 216/573) and HIV-infected individuals (36.6%, 79/216) (Table 2).

SARS-CoV-2 seroprevalence increased at all three sites over the three-month period (Figure 1). In January 2021, the highest SARS-CoV-2 seroprevalence was observed in Mitchell's Plain (56.1%; 115/205), followed by Pietermaritzburg (37.8%; 111/294) and Klerksdorp (31.7%; 13/41). However, the number of specimens collected in Klerksdorp was relatively small compared to other sites.

Increases in SARS-CoV-2 seroprevalence from November 2020 until January 2021 (Figure 1) reflects the increasing number of infected individuals as a result of the second COVID-19 wave.




| | Nov - 20 | Dec - 20 | Jan - 21 |
|---|---|---|---|
| Pietermaritzburg | 3/37 (8.1%) | 23/98 (23.5 %) | 111/294 (37.8%) |
| Klerksdorp | 1/10 (10.0%) | 32/122 (26.2%) | 13/41 (31.7%) |
| Mitchell's Plain | 0 | 34/120 (28.3%) | 115/205 (56.1%) |

**Figure 1.** SARS-CoV-2 seroprevalence by month and site, Healthcare Utilisation and Seroprevalence (HUTS) study, South Africa, November 2020-January 2021.

On univariate analysis, individuals from Mitchell's Plain were more likely to be positive for SARS-CoV-2 antibodies as compared to those from Klerksdorp (OR 2.4; 95% CI: 1.6-3.5; p<0.001). Individuals who had specimens collected in December 2020 (OR 4.0; 95% CI: 1.4-11.4, p=0.01) and January 2021 (OR 8.6; 95% CI: 3.1-24.4; p<0.001) were more likely to be positive for SARS-CoV-2 antibodies as compared to individuals who had specimens collected in November 2020, likely reflecting epidemic progression over time and increasing numbers of infections during the second wave. Age, sex and HIV status were not associated with SARS-CoV-2 seroprevalence.

**Table 2.** SARS-CoV-2 seroprevalence by demographic characteristics, month and site, Healthcare Utilisation and Seroprevalence (HUTS) study, South Africa, November 2020 – January 2021.

| | SARS-CoV-2 antibody positive n/N (%) | Univariate analysis | |
|---|---|---|---|
| | | Unadjusted OR (95% CI) | P-value |
| Overall | 332/927 (35.8%) | - | - |
| Site | | | |
| Pietermaritzburg | 137/429 (31.9%) | 1.3 (0.91-1.99) | 0.14 |
| Klerksdorp | 46/173 (26.6%) | 1 | Reference |
| Mitchell's Plain | 149/325 (45.9%) | 2.4 (1.59-3.54) | <0.001 |
| Month of specimen collection | | | |
| November 2020 | 4/47 (8.5%) | 1 | Reference |
| December 2020 | 89/340 (26.2%) | 4.0 (1.4-11.4) | 0.01 |
| January 2021 | 239/540 (44.3%) | 8.6 (3.1-24.4) | <0.001 |
| Age group (years) | | | |
| 0-9 | 9/32 (28.1%) | 1 | Reference |
| 10-19 | 60/152 (39.5%) | 1.7 (0.73-3.91) | 0.22 |
| 20-29 | 56/156 (35.9%) | 1.5 (0.64-3.42) | 0.36 |
| 30-39 | 71/157 (45.2%) | 2.1 (0.93-4.92) | 0.07 |
| 40-49 | 59/163 (36.2%) | 1.5 (0.64-3.39) | 0.36 |
| 50-59 | 41/120 (34.2%) | 1.4 (0.58-3.20) | 0.48 |
| 60-69 | 21/90 (23.3%) | 0.8 (0.31-1.94) | 0.59 |
| 70-79 | 12/90 (23.3%) | 1.0 (0.36-2.66) | 0.96 |
| >79 | 3/11 (27.3%) | 1.0 (0.21-4.45) | 0.96 |
| Sex | | | |
| Male | 116/354 (32.8%) | 1 | Reference |
| Female | 216/573 (37.7%) | 1.2 (0.96-1.67) | 0.10 |
| HIV status | | | |
| HIV infected | 79/216 (36.6%) | 0.9 (0.67-1.34) | 0.76 |
| HIV uninfected | 220/623 (35.3%) | 1 | Reference |

## CONCLUSIONS

The preliminary results from the HUTS study suggest that SARS-CoV-2 seroprevalence increased over the study period, and by January 2021 estimates of SARS-CoV-2 seroprevalence were ≥30% at all three sites, although differences were detected between sites. Although these are interim results and included numbers are substantially smaller than our target sample size, these data suggest that there has been a substantial increase in seroprevalence during the second COVID-19 wave. In addition, the preliminary results show no statistically significant differences in SARS-CoV-2 seroprevalence by age, sex and HIV status.

## LIMITATIONS

The results of this study are not nationally representative and a clustering effect has not been accounted for in this interim analysis. Given that not all individuals produce antibodies, there is limited understanding of the duration of antibodies following infection, and we have not performed an adjustment for assay sensitivity, the seroprevalences at each site may be underestimated. The HUTS study is ongoing and the required sample size has not yet been reached.

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