NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES
Division of the National Health Laboratory Service

Science Focus

ISSUE 23 Q2 2022/2023

The Science Focus acknowledges NICD members of staff who have published in peer-reviewed journals.
This publication is a compilation of scientific publications where an NICD staff member is either the first or last author.

EDITOR'S NOTE

MS SINENHLANHLA JIMOH

Another Set of High Standards is Set by NICD Researchers

The latest issue of Science Focus highlights the remarkable achievements of industry experts at the National Institute of Communicable Diseases for Q2 2022/2023. Statistics on peer-reviewed publications are showcased in the publication, along with key statistical information and a list of co-authored articles that recorded high-impact factor scores.

Our Centre for Respiratory Diseases and Meningitis experts are featured in the South African Medical Journal. As part of the study, Dr Sibongile Walaza and Professor Cheryl Cohen describe the rapid development of a robust data system that was essential to addressing the SA COVID-19 epidemic by leveraging epidemiology. The study makes the point that accurate and timely disease surveillance, epidemiological analyses, and the availability of data in order to make public health decisions are crucial.

A six-year review of measles frequency in South Africa from the year 2015 up until 2020 featured in the BMC Public Health, South Africa shows sporadic measles outbreaks approximately six yearly combined with inter-epidemic periods in which the country meets measles elimination targets. Dr Mukhlid Yousif and Dr Kerrigan McCarthy have co-authored a study outlining the importance of increasing vaccine coverage to avoid periodic outbreaks. This year, a nationwide vaccination campaign has been conducted to combat the current outbreak of measles.

Our researchers have contributed significantly to the field of public health and communicable diseases. Dr Tendesayi Kufa was featured in the PLoS One journal in her study Assessing HIV rapid testing practices in South African public antenatal health care facilities. Dr Selamawit Woldesenbet and Prof Adrian Puren co-authored Progress towards the UNAIDS 95-95-95 targets among pregnant women in South Africa: Results from 2017 and 2019.

A special thank you to all of the NICD researchers who continue to contribute significant public health papers to high-impact journals. Employees are invited to continue providing feedback to the Communications Unit.

We hope you enjoy reading this issue.

On behalf of the team, Sinenhlanhla Jimoh.

Senior Communications Manager

Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

Top Published Authors for Q2 2022/2023

1

PROF CHERYL COHEN

2

PROF ANNE VON GOTTBERG

3

PROF NELESH GOVENDER

4

DR JINAL BHIMAN

4

PROF PENNY MOORE

Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

DR NICOLE WOLTER

Clinical Severity of Omicron Lineage BA.2 Infection Compared With BA.1 Infection in South Africa

WOLTER N, JASSAT W, VON GOTTBERG A, **COHEN C**

The Lancet **IMPACT FACTOR: 202,731**

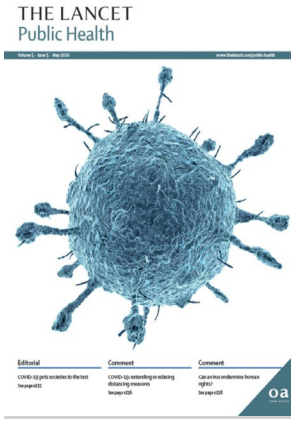
BACKGROUND

The omicron SARS-CoV-2 variant of concern (B.1.1.529) was first reported in South Africa in mid-November, 2021. Early data indicated that infection with omicron (around 99% BA.1 lineage during this period) was associated with a lower risk of hospitalisation and lower risk of severe illness, once hospitalised, compared with delta (B.1.617.2) variant infection.1 Recently, the BA.2 lineage has increased in many areas globally, including South Africa, associated with increases in case numbers in some settings. In South Africa, the BA.2 lineage was first detected on Nov 17, 2021. From week 49 of 2021 (starting Dec 5, 2021), the proportion of BA.2 lineage began to increase, making up 84% (27 of 32) of all sequenced samples by week 5 of 2022 (week ending Feb 5, 2022).2 Replacement of BA.1 by BA.2 occurred in a period when SARS-CoV-2 case numbers were declining from the fourth wave peak in South Africa and was associated with a brief increase in case numbers in children of school-going age and slowing of the rate of decline compared with previous waves. The BA.1 lineage contains a 69–70 amino acid deletion in the spike protein, which is associated with S-gene target failure (SGTF) when tested using the TaqPath COVID-19 PCR test (Thermo Fisher Scientific, Waltham, MA, USA). At the time of this study, BA.2 lacks this deletion, hence infections with BA.2 are S-gene positive on this assay.

Similar to BA.1, BA.2 is associated with substantial loss in neutralising activity in individuals infected with wild-type SARS-CoV-2 or recipients of mRNA vaccines.3 BA.2 has also been associated with increased transmissibility compared with BA.1,4 and in England was shown to have an increased growth rate compared with BA.1.5 However, data are lacking on the clinical severity of the BA.2 lineage compared with BA.1. We aimed to assess the severity of BA.2 infections compared with BA.1 in South Africa.

Click on the following link for the full study: https://doi.org/10.1016/S0140-6736(22)00981-3

PROF CHERYL COHEN

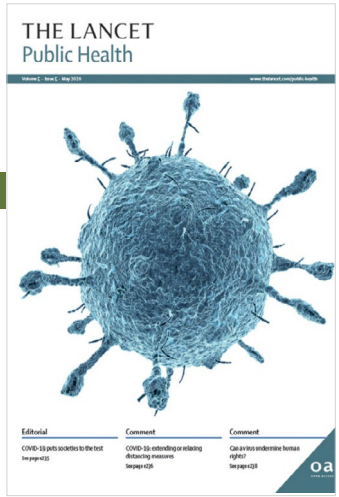


DR TENDESAYI KUFA

Dolutegravir in Late Pregnancy: Where to From Here?

TENDESAYI KUFA

The Lancet **IMPACT FACTOR: 202,731**



BACKGROUND

Strategies to eliminate the perinatal transmission of HIV include initiation of effective antiretroviral therapy (ART) as soon as possible before or during pregnancy and maintaining a suppressed viral load throughout pregnancy and postpartum. Late initiation of ART in pregnant women with HIV has been associated with increased risk of perinatal transmission and perinatal mortality in infants.

For the full study please click on the following link https://doi.org/10.1016/S2352-3018(22)00193-X

Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

DR AHMAD HAERI MAZANDERANI

Point-of-Care HIV Diagnosis for Infants: The Outcomes We Need to Achieve

KARL-GÜNTER TECHNAU, **AHMAD HAERI MAZANDERANI**

The Lancet IMPACT FACTOR: 202,731

BACKGROUND

Timely diagnosis and treatment of HIV is crucial in HIV-exposed infants to prevent the high rates of mortality seen during the first 2 years of life if HIV is untreated. However, challenges with sample transportation, testing, and result delivery to caregivers have led to long delays in treatment initiation. We aimed to compare the clinical effect of point-of-care HIV testing versus laboratory-based testing (standard of care) in HIV-exposed infants.

METHODS

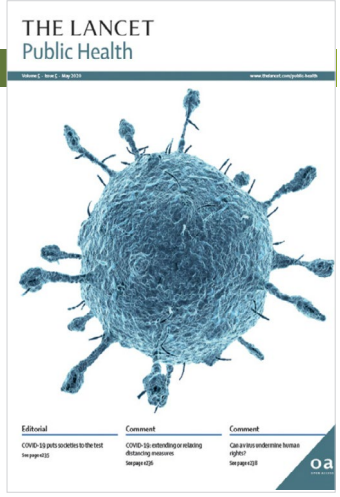
We did a systematic review and meta-analysis and searched PubMed, MEDLINE, Cochrane Central Register of Controlled Trials, Embase, Conference Proceedings Citation Index-Science, and WHO Global Index Medicus, from Jan 1, 2014, to Aug 31, 2020. Studies were included if they pertained to the use of point-of-care nucleic acid testing for infant HIV diagnosis, had a laboratory-based nucleic acid test as the comparator or standard of care against the index test (Same-day point-of-care testing), evaluated clinical outcomes when point-of-care testing was used, and included HIV-exposed infants aged younger than 2 years. Studies were excluded if they did not use a laboratory-based comparator, a nucleic acid test that had been approved by a stringent regulatory authority, or diagnostic-accuracy or performance evaluations (e.g., no clinical outcomes included). Reviews, non-research letters, commentaries, and editorials were also excluded. The risk of bias was evaluated using the ROBINS-I framework. Data were extracted from published reports. Data from all studies were analysed using frequency statistics to describe the overall populations evaluated and their results. Key outcomes were time to result delivery and antiretroviral therapy initiation, and proportion of HIV-positive infants initiated on antiretroviral therapy within 60 days after sample collection.

FINDINGS

164 studies were identified by the search and seven were included in the analysis, comprising 37 377 infants in total across 15 countries, including 25 170 (67%) who had point-of-care HIV testing and 12 207 (33%) who had standard-of-care testing. The certainty of evidence was high. Same-day point-of-care testing led to a significantly shorter time between sample collection and result delivery to caregivers compared with standard-of-care testing (median 0 days [95% CI 0–0] vs 35 days [35–37]). Time from sample collection to antiretroviral therapy initiation in infants found to be HIV-positive was significantly lower with point-of-care testing compared with standard of care (median 0 days [95% CI 0–1] vs 40 days [36–44]). When each study's result was weighted equally, 90·3% (95% CI 76·7–96·5) of HIV-positive infants diagnosed using point-of-care testing had started antiretroviral therapy within 60 days of sample collection, compared with only 51·6% (27·1–75·7) who had standard-of-care testing (odds ratio 8·74 [95% CI 6·6–11·6]; p<0·0001).

INTERPRETATION

Overall, the certainty of the evidence in this analysis was rated as high for the primary outcomes related to result delivery and treatment initiation, with no serious risk of bias, inconsistency, indirectness, or imprecision. In HIV-exposed infants, same-day point-of-care HIV testing was associated with significantly improved time to result delivery, time to antiretroviral therapy initiation, and proportion of HIV-positive infants starting antiretroviral therapy within 60 days compared with standard of care.



Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

MS RUDZANI C. MASHAU

Outcomes of Flucytosine-Containing Combination Treatment for Cryptococcal Meningitis in A South African National Access Programme: A Cross-Sectional Observational Study

MASHAU RC, MEIRING ST, QUAN VC, NEL J, GREENE GS, GARCIA A, MENEZES C, REDDY DL, VENTER M, STACEY S, MADUA M, BORETTI L, HARRISON TS, MEINTJES G, SHROUFI A, TRIVINO-DURAN L, BLACK J, **GOVENDER NP; GERMS-SA**

Lancet Infectious Diseases **IMPACT FACTOR: 71,421**

PROF NELESH GOVENDER

BACKGROUND

Although flucytosine is a key component of WHO-recommended induction treatment for HIV-associated cryptococcal meningitis, this antifungal agent is not widely available in low-income and middle-income countries due to limited production and cost. In 2018, a national flucytosine access programme was initiated in South Africa. We aimed to determine the effectiveness of flucytosine-containing induction regimens in routine care to motivate for the urgent registration of flucytosine and its inclusion in treatment guidelines.

METHODS

In this cross-sectional study, we compared outcomes of adults aged 18 years and older with incident laboratory-confirmed cryptococcal meningitis treated with or without flucytosine-containing regimens at 19 sentinel hospitals in South Africa. A case of cryptococcosis was defined as illness in an adult with: (1) positive cerebrospinal fluid (CSF) India ink microscopy; (2) a positive CSF cryptococcal antigen test; or (3) culture of *Cryptococcus neoformans* or *Cryptococcus gattii* from CSF or any other specimen. We excluded patients without a case report form, those with an unknown or negative HIV serology result, those with a recurrent episode, and those who did not receive antifungal treatment in hospital. We assessed cumulative in-hospital mortality at 14 days and 30 days and calculated the overall crude in-hospital case-fatality ratio. We used random-effects logistic regression to examine the association between treatment group and in-hospital mortality.

FINDINGS

From July 1, 2018, to March 31, 2020, 10 668 individuals were diagnosed with laboratory-confirmed cryptococcal meningitis, 7787 cases diagnosed at non-enhanced surveillance sites and 567 cases from eight enhanced surveillance sites with no access to flucytosine were excluded. Of 2314 adults with a first episode of cryptococcosis diagnosed at 19 facilities with access to flucytosine, 1996 had a case report form and of these, 1539 received induction antifungal treatment and were confirmed HIV-seropositive first-episode cases. Of 1539 patients who received antifungal therapy, 596 (38·7%) individuals received a flucytosine-containing regimen and 943 (61·3%) received another regimen. The median age was 36 years (IQR 32-43) and 906 (58·9%) participants were male and 633 (41·1%) were female. The crude in-hospital case-fatality ratio was 23·9% (95% CI 20·0-27·0; 143 of 596) in those treated with flucytosine-containing regimens and 37·2% (95% CI 34·0-40·0; 351 of 943) in those treated with other regimens. Patients admitted to non-academic hospitals (adjusted odds ratio [aOR] 1·95 [95% CI 1·53-2·48]; p<0·0001) and those who were antiretroviral treatment-experienced (aOR 1·30 [1·02-1·67]; p=0·033) were more likely to receive flucytosine. After adjusting for relevant confounders, flucytosine treatment was associated with a 53% reduction in mortality (aOR 0·47 [95% CI 0·35-0·64]; p<0·0001). Among survivors, the median length of hospital admission in the flucytosine group was 11 days (IQR 8-15) versus 17 days (13-21) in the comparison group (p=0·0010).

INTERPRETATION

In-hospital mortality among patients treated with a flucytosine-containing regimen was comparable to reduced mortality reported in patients receiving a flucytosine-containing regimen in a recent multicentre African clinical trial. Flucytosine-based treatment can be delivered in routine care in a middle-income country with a substantial survival benefit.

Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

DR WAASILA JASSAT

PROF CHERYL COHEN

Clinical Severity of COVID-19 in Patients Admitted to Hospital During the Omicron Wave in South Africa: A Retrospective Observational Study

JASSAT W, ABDOOL KARIM SS, MUDARA C, WELCH R, OZOUGWU L, GROOME MJ, GOVENDER N, VON GOTTBERG A, WOLTER N, WOLMARANS M, ROUSSEAU P; DATCOV AUTHOR GROUP, BLUMBERG L, **COHEN C**

The Lancet Glob Health **IMPACT FACTOR: 38,927**

BACKGROUND

Up to the end of January, 2022, South Africa has had four recognisable COVID-19 pandemic waves, each predominantly dominated by one variant of concern: the ancestral strain with an Asp614Gly mutation during the first wave, the beta variant (B.1.351) during the second wave, the delta variant (B.1.617.2) during the third wave, and lastly, the omicron variant (B.1.1.529) during the fourth wave. We aimed to assess the clinical disease severity of patients admitted to hospital with SARS-CoV-2 infection during the omicron wave and compare the findings with those of the preceding three pandemic waves in South Africa.

METHODS

We defined the start and end of each pandemic wave as the crossing of the threshold of weekly incidence of 30 laboratory-confirmed SARS-CoV-2 cases per 100 000 population. Hospital admission data were collected through an active national COVID-19-specific surveillance programme. We compared disease severity across waves by post-imputation random effect multivariable logistic regression models. Severe disease was defined as one or more of the following: acute respiratory distress, receipt of supplemental oxygen or mechanical ventilation, admission to intensive care, or death.

FINDINGS

We analysed 335 219 laboratory-confirmed SARS-CoV-2 hospital admissions with a known outcome, constituting 10·4% of 3 216 179 cases recorded during the four waves. During the omicron wave, 52 038 (8·3%) of 629 617 cases were admitted to hospital, compared with 71 411 (12·9%) of 553 530 in the Asp614Gly wave, 91 843 (12·6%) of 726 772 in the beta wave, and 131 083 (10·0%) of 1 306 260 in the delta wave (p<0·0001). During the omicron wave, 15 421 (33·6%) of 45 927 patients admitted to hospital had severe disease, compared with 36 837 (52·3%) of 70 424 in the Asp614Gly wave, 57 247 (63·4%) of 90 310 in the beta wave, and 81 040 (63·0%) of 128 558 in the delta wave (p<0·0001). The in-hospital case-fatality ratio during the omicron wave was 10·7%, compared with 21·5% during the Asp614Gly wave, 28·8% during the beta wave, and 26·4% during the delta wave (p<0·0001). Compared with those admitted to hospital during the omicron wave, patients admitted during the other three waves had more severe clinical presentations (adjusted odds ratio 2·07 [95% CI 2·01-2·13] in the Asp614Gly wave, 3·59 [3·49-3·70] in the beta wave, and 3·47 [3·38-3·57] in the delta wave).

INTERPRETATION

The trend of increasing cases and admissions across South Africa's first three waves shifted in the omicron wave, with a higher and quicker peak but fewer patients admitted to hospital, less clinically severe illness, and a lower case-fatality ratio compared with the preceding three waves. Omicron marked a change in the SARS-CoV-2 epidemic curve, clinical profile, and deaths in South Africa. Extrapolations to other populations should factor in differing vaccination and previous infection levels.

Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

MS RUDZANI C. MASHAU

PROF NELESH GOVENDER

Culture-Confirmed Neonatal Bloodstream Infections and Meningitis in South Africa, 2014-19: A Cross-Sectional Study

MASHAU RC, MEIRING ST, DRAMOWSKI A, MAGOBO RE, QUAN VC, PEROVIC O, VON GOTTBERG A, COHEN C, VELAPHI S, VAN SCHALKWYK E, **GOVENDER NP; BABY GERMS-SA**

The Lancet Glob Health **IMPACT FACTOR: 38,927**

BACKGROUND

Few population-level estimates of invasive neonatal infections have been reported from sub-Saharan Africa. We estimated the national incidence risk, aetiology, and pathogen antimicrobial susceptibility for culture-confirmed neonatal bloodstream infections and meningitis in South Africa.

MATERIALS AND METHODS

We conducted a cross-sectional study of neonates (<28 days of life) admitted to neonatal or paediatric wards of 256 public sector health facilities in South Africa during 2014-19. Diagnostic pathology records from Jan 1, 2014, to Dec 31, 2019, were extracted from a national pathology data warehouse. A case was defined as a neonate with at least one positive blood or cerebrospinal fluid culture during a 14-day period. Incidence risk was calculated using annual numbers of registered livebirths. Among the causative pathogens identified, we calculated the proportion of cases attributed to each of them, as well as the rates of antibiotic susceptibility of Gram-positive and Gram-negative bacteria.

FINDINGS

Among 43 438 records of positive cultures, there were 37 631 incident cases of neonatal infection with at least one pathogen isolated. The overall incidence risk of culture-confirmed infections was 6·0 per 1000 livebirths (95% CI 6·0-6·1). The incidence risk of late-onset sepsis (days 3-27 of life) was 4·9 per 1000 livebirths (4·9-5·0) and that of early-onset sepsis (days 0-2 of life) was 1·1 per 1000 livebirths (1·1-1·1); risk ratio 4·4 (95% CI 4·3-4·5). The cause of infection differed by syndrome, timing of infection onset, facility, and province, although *Klebsiella pneumoniae* (26%), *Acinetobacter baumannii* (13%), and *Staphylococcus aureus* (12%) were the dominant pathogens overall. Gram-negative bacteria had declining susceptibility to most antibiotics over the study period.

INTERPRETATION

We found a high incidence risk of late-onset sepsis with provincial variations, predominance of *K pneumoniae*, and declining antibiotic susceptibility among Gram-negative bacteria. This national surveillance in an upper-middle-income country provides a baseline burden of neonatal infections against which the impact of future clinical and public health interventions can be measured.

Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

MS JACKIE KLEYNHANS

PROF CHERYL COHEN

Household Transmission of SARS-Cov-2 From Adult Index Cases Living with and without HIV in South Africa, 2020-2021: A Case-Ascertained, Prospective Observational Household Transmission Study

KLEYNHANS J, WALAZA S, MARTINSON NA, NETI M, VON GOTTBERG A, BHIMAN JN, TOI D, AMOAKO DG, BUYS A, NDLANGISA K, WOLTER N, GENADE L, MALOMA L, CHEWPARSAD J, LEBINA L, DE GOUVEIA L, KOTANE R, TEMPIA S, **COHEN C**

Clinical Infectious Diseases **IMPACT FACTOR: 20,999**

BACKGROUND

In South Africa, 19% of the adult population are living with HIV (LWH). Few data on the influence of HIV on SARS-CoV-2 household transmission are available.

METHODS

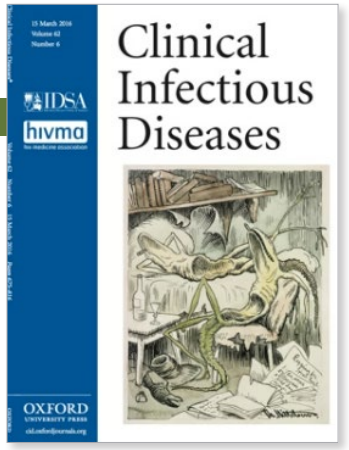
We performed a case-ascertained, prospective household transmission study of symptomatic index SARS-CoV-2 cases LWH and HIV-uninfected adults and their contacts in South Africa, October 2020 to September 2021. Households were followed up thrice weekly for 6 weeks to collect nasal swabs for SARS-CoV-2 testing. We estimated household cumulative infection risk (HCIR) and duration of SARS-CoV-2 positivity (at cycle threshold value <30 as proxy for high viral load).

RESULTS

We recruited 131 index cases and 457 household contacts. HCIR was 59% (220/373); not differing by index HIV status (60% [51/85] in cases LWH vs 58% [163/279] in HIV-uninfected cases, OR 1.0, 95%CI 0.4-2.3). HCIR increased with index case age (35-59 years: aOR 3.4 95%CI 1.5-7.8 and ≥60 years: aOR 3.1, 95%CI 1.0-10.1) compared to 18-34 years, and contacts' age, 13-17 years (aOR 7.1, 95%CI 1.5-33.9) and 18-34 years (aOR 4.4, 95%CI 1.0-18.4) compared to <5 years. Mean positivity duration at high viral load was 7 days (range 2-17), with longer positivity in cases LWH (aHR 0.4, 95%CI 0.1-0.9).

CONCLUSIONS

Index HIV status was not associated with higher HCIR, but cases LWH had longer positivity duration at high viral load. Adults aged >35 years were more likely to transmit, individuals aged 13-34 to acquire SARS-CoV-2 in the household. As HIV infection may increase transmission, health services must maintain HIV testing and antiretroviral therapy initiation.



KEYWORDS

COVID-19; HIV; SARS-CoV-2; acquisition; transmission.

Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

PROF CHERYL COHEN

Direct and Indirect Effects of The Coronavirus Disease 2019 Pandemic on Private Healthcare Utilisation in South Africa, March 2020-September 2021

PEROFSKY AC, TEMPIA S, BINGHAM J, MASLO C, TOUBKIN M, LAUBSCHER A, WALAZA S, PULLIAM JRC, VIBOUD C, **COHEN C**

Clinical Infectious Diseases **IMPACT FACTOR: 20,999**

BACKGROUND

The coronavirus disease 2019 (COVID-19) pandemic caused severe disruptions to healthcare in many areas of the world, but data remain scarce for sub-Saharan Africa.

METHODS

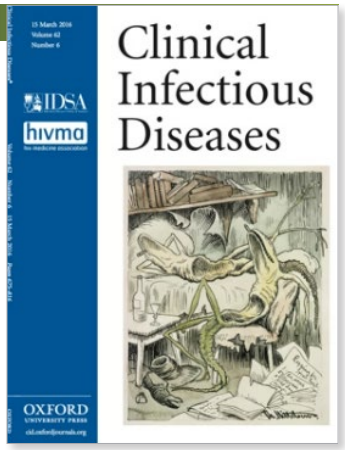
We evaluated trends in hospital admissions and outpatient emergency department (ED) and general practitioner (GP) visits to South Africa's largest private healthcare system during 2016–2021. We fit time series models to historical data and, for March 2020–September 2021, quantified changes in encounters relative to baseline.

RESULTS

The nationwide lockdown on 27 March 2020 led to sharp reductions in care-seeking behaviour that persisted for 18 months after initial declines. For example, total admissions dropped 59.6% (95% confidence interval [CI], 52.4–66.8) during home confinement and were 33.2% (95% CI, 29–37.4) below baseline in September 2021. We identified 3 waves of all-cause respiratory encounters consistent with COVID-19 activity. Intestinal infections and non–COVID-19 respiratory illnesses experienced the most pronounced declines, with some diagnoses reduced 80%, even as nonpharmaceutical interventions (NPIs) relaxed. Non-respiratory hospitalisations, including injuries and acute illnesses, were 20%–60% below baseline throughout the pandemic and exhibited strong temporal associations with NPIs and mobility. ED attendances exhibited trends similar to those for hospitalisations, while GP visits were less impacted and have returned to pre-pandemic levels.

CONCLUSION

We found substantially reduced use of health services during the pandemic for a range of conditions unrelated to COVID-19. Persistent declines in hospitalisations and ED visits indicate that high-risk patients are still delaying seeking care, which could lead to morbidity or mortality increases in the future.



Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

PROF NELESH GOVENDER

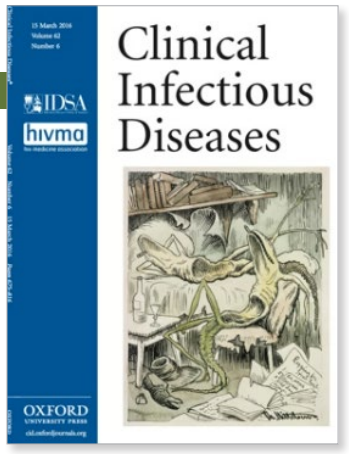
Cryptococcal Antigenemia in Advanced HIV: Pathophysiology, Epidemiology and Clinical Implications

WAKE RM, MOLLOY SF, JARVIS JN, HARRISON TS, **GOVENDER NP**

Clinical Infectious Diseases **IMPACT FACTOR: 20,999**

ABSTRACT

Cryptococcal antigen (CrAg) is detectable in blood prior to the onset of symptomatic cryptococcal meningitis, a leading cause of death among people living with advanced HIV disease globally. Highly sensitive assays can detect CrAg in blood, and screening people living with HIV with low CD4 counts, followed by pre-emptive antifungal treatment, is recommended and widely implemented as part of a global strategy to prevent cryptococcal meningitis and end cryptococcal-related deaths. Cryptococcal antigenemia encompasses a spectrum of conditions from pre-clinical asymptomatic infection (CSF CrAg-negative), through subclinical (CSF CrAg-positive without overt meningism) to clinical symptomatic cryptococcal disease, usually manifesting as cryptococcal meningitis. This review summarizes current understanding of the pathophysiology, risk-factors for and clinical implications of cryptococcal antigenemia among people living with advanced HIV disease within this spectrum. It also provides an update on global prevalence, recommended screening and treatment strategies, and future considerations for improving outcomes among patients with cryptococcal antigenemia.



KEYWORDS

HIV; acquired immunodeficiency syndrome; cryptococcal; cryptococcosis; diagnostic screening programs; meningitis.

Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

PROF CHERYL COHEN

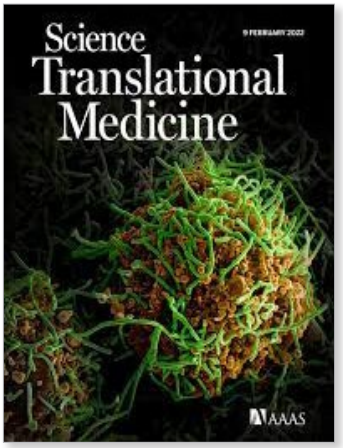
SARS-Cov-2 Transmission, Persistence of Immunity, and Estimates of Omicron's Impact in South African Population Cohorts

SUN K, TEMPIA S, KLEYNHANS J, VON GOTTBERG A, MCMORROW ML, WOLTER N, BHIMAN JN, MOYES J, DU PLESSIS M, CARRIM M, BUYS A, MARTINSON NA, KAHN K, TOLLMAN S, LEBINA L, WAFAWANAKA F, DU TOIT JD, GÓMEZ-OLIVÉ FX, MKHENCELE T, VIBOUD C, **COHEN C**

Science Translational Medicine IMPACT FACTOR: 19,343

ABSTRACT

Understanding the build-up of immunity with successive severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants and the epidemiological conditions that favour rapidly expanding epidemics will help facilitate future pandemic control. We analysed high-resolution infection and serology data from two longitudinal household cohorts in South Africa to reveal high cumulative infection rates and durable cross-protective immunity conferred by prior infection in the pre-Omicron era. Building on the history of past exposures to different SARS-CoV-2 variants and vaccination in the cohort most representative of South Africa's high urbanisation rate, we used mathematical models to explore the fitness advantage of the Omicron variant and its epidemic trajectory. Modelling suggests that the Omicron wave likely infected a large fraction (44 to 81%) of the population, leaving a complex landscape of population immunity primed and boosted with antigenically distinct variants. We project that future SARS-CoV-2 resurgences are likely under a range of scenarios of viral characteristics, population contacts, and residual cross-protection.



Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

DR CATHRINE SCHEEPERS

PROF PENNY MOORE

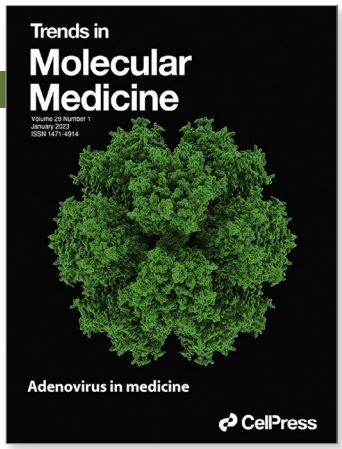
Antibody Class-Switching as A Strategy to Improve HIV-1 Neutralisation

SCHEEPERS C, RICHARDSON SI, MOYO-GWETE T, **MOORE PL**

Trends in Molecular Medicine **IMPACT FACTOR: 15,272**

ABSTRACT

Broadly neutralizing antibodies (bNAbs), when administered through passive immunisation, are protective against HIV-1 infection. Current HIV-1 vaccine strategies are aimed at guiding the immune system to make bNAbs by mimicking their development during infection. Somatic hypermutation of the variable region is known to be crucial for the development of bNAbs. More recently, however, studies have shown how class-switch recombination (CSR) resulting in the generation of different antibody isotypes may serve as an additional mechanism through which antibodies can gain neutralisation breadth and potency. In this review, we discuss the importance of different antibody isotypes for HIV-1 neutralisation breadth and potency and how this information can be leveraged to improve passive and active immunisation against HIV-1.



KEYWORDS

HIV-1 vaccine design; IgA CH1; IgG3 hinge; class-switching; isotype; neutralisation.

Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

DR NICOLE WOLTER

Pathogens Detected Using a Syndromic Molecular Diagnostic Platform in Patients Hospitalised with Severe Respiratory Illness in South Africa in 2017

MOLELEKI M, DU PLESSIS M, NDLANGISA K, REDDY C, HELLFERSCEE O, MEKGOE O, MCMORROW M, WALAZA S, COHEN C, TEMPIA S, VON GOTTBERG A, **WOLTER N**

International Journal of Infectious Diseases **IMPACT FACTOR: 12,073**

OBJECTIVES

We describe the use of a multi pathogen platform, TaqMan array card (TAC) real-time polymerase chain reaction, for the detection of pathogens in patients hospitalised with severe respiratory illness (SRI).

METHODS

Prospective hospital-based syndromic surveillance for acute and chronic SRI was carried out at two sentinel sites in South Africa between January and December 2017. We tested respiratory specimens for 21 respiratory pathogens and blood samples for nine bacteria using TAC. Pathogen detection was compared by age group and HIV status using the chi-square test.

RESULTS

During 2017, 956 patients of all ages were enrolled in the SRI surveillance, and of these, 637 (67%) patients were included in this study (637 blood, 487 naso- and oro-pharyngeal swabs, and 411 sputum specimens tested). At least one pathogen was detected in 83% (527/637) of patients. Common pathogens detected included Haemophilus influenzae (225/637; 35%), Streptococcus pneumoniae (224/637; 35%), rhinovirus (144/637; 23%), Staphylococcus aureus (129/637; 20%), Klebseilla pneumoniae (85/637; 13%), Mycobacterium tuberculosis (75/637; 12%), and respiratory syncytial virus (57/637; 9%). Multiple pathogens (≥2) were co-detected in 57% (364/637) of patients.

CONCLUSION

Although the use of a multi-pathogen platform improved pathogen yield, pathogen co-detections were common and would need clinical assessment for usefulness in individual-level treatment and management decisions.

Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

DR WAASILA JASSAT

COVID-19 Hospital Admissions and Mortality Among Healthcare Workers in South Africa, 2020-2021

TLOTLENG N, COHEN C, MADE F, KOOTBODIEN T, MASHA M, NAICKER N, BLUMBERG L, **JASSAT W**

International Journal of Infectious Diseases **IMPACT FACTOR: 12,073**

OBJECTIVES

This study describes the characteristics of admitted HCWs reported to the DATCOV surveillance system, and the factors associated with in-hospital mortality in South African HCWs.

METHODS

Data from March 5, 2020 to April 30, 2021 were obtained from DATCOV, a national hospital surveillance system monitoring COVID-19 admissions in South Africa. Characteristics of HCWs were compared with those of non-HCWs. Furthermore, a logistic regression model was used to assess factors associated with in-hospital mortality among HCWs.

RESULTS

In total, there were 169 678 confirmed COVID-19 admissions, of which 6364 (3.8%) were HCWs. More of these HCW admissions were accounted for in wave 1 (48.6%; n = 3095) than in wave 2 (32.0%; n = 2036). Admitted HCWs were less likely to be male (28.2%; n = 1791) (aOR 0.3; 95% CI 0.3-0.4), in the 50-59 age group (33.1%; n = 2103) (aOR 1.4; 95% CI 1.1-1.8), or accessing the private health sector (63.3%; n = 4030) (aOR 1.3; 95% CI 1.1-1.5). Age, comorbidities, race, wave, province, and sector were significant risk factors for COVID-19-related mortality.

CONCLUSIONS

The trends in cases showed a decline in HCW admissions in wave 2 compared with wave 1. Acquired SARS-COV-2 immunity from prior infection may have been a reason for reduced admissions and mortality of HCWs despite the more transmissible and more severe beta variant in wave 2.

KEYWORDS

SARS-CoV-2; healthcare workers; hospital admissions; hospital surveillance; in-hospital mortality.

Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

DR SUSAN MEIRING

PROF ANNE VON GOTTBERG

Case-Fatality and Sequelae Following Acute Bacterial Meningitis in South Africa, 2016 Through 2020

MEIRING S, **COHEN C, DE GOUVEIA L, PLESSIS M DU**, QUAN V, **KLEYNHANS J**, MENEZES C, REUBENSON G, DAWOOD H, NCHABELENG M, SAID M, MVELASE N, MAHABEER P, CHOMBA R, LEKALAKALA R, NANA T, CHIBABHAI V, BLACK M, **VON GOTTBERG A**

International Journal of Infectious Diseases IMPACT FACTOR: 12,073

OBJECTIVES

Providing country-specific estimates of case fatality and sequelae from bacterial meningitis (BM) is important to evaluate and monitor progress toward the World Health Organization's roadmap to "defeating meningitis by 2030".

METHODS

From 2016-2020, GERMS-SA conducted enhanced surveillance at 26 hospitals across South Africa. Episodes of laboratory-confirmed BM due to Streptococcus pneumoniae, Haemophilus influenzae, and Neisseria meningitidis were included. Risk factors for in-hospital death and sequelae at hospital discharge among survivors were analysed.

RESULTS

Of 12,717 invasive bacterial infections reported nationally, 39% (4980) were from enhanced surveillance sites, including 4159 pneumococcal, 640 H. influenzae, and 181 meningococcal infections. BM accounted for 32% (1319/4159) of pneumococcal, 21% (136/640) of H. influenzae, and 83% (151/181) of meningococcal invasive diseases. Clinical data were available for 91% (1455/1606) of BM: 26% (376/1455) were aged <5 years, 50% (726/1455) were female, and 62% (723/1171) with known HIV results, were HIV-infected. In-hospital case fatality was 37% (534/1455), and 24% (222/921) of survivors had adverse sequelae. Risk factors for death included altered mental status, HIV infection, and comorbidities. Risk factors for adverse sequelae included altered mental status and antimicrobial nonsusceptibility.

CONCLUSION

BM in South Africa has a high case fatality, and adverse sequelae frequently occur among survivors. Those with comorbidities (including HIV) are at the highest risk.

Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

DR CATHRINE SCHEEPERS

PROF PENNY MOORE

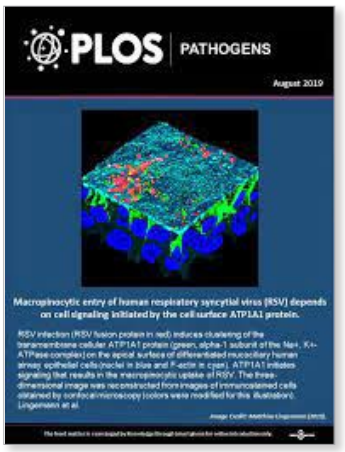
Dependence on a Variable Residue Limits the Breadth of an HIV MPER Neutralising Antibody, Despite Convergent Evolution with Broadly Neutralising Antibodies

SCHEEPERS C, KGAGUDI P, MZINDLE N, GRAY ES, MOYO-GWETE T, LAMBSON BE, OOSTHUYSEN B, MABVAKURE B, GARRETT NJ, ABDOOL KARIM SS, MORRIS L, **MOORE PL**

PLoS Pathogens **IMPACT FACTOR: 7,464**

ABSTRACT

Broadly neutralising antibodies (bNAbs) that target the membrane-proximal external region (MPER) of HIV gp41 envelope, such as 4E10, VRC42.01 and PGZL1, can neutralise >80% of viruses. These three MPER-directed monoclonal antibodies share germline antibody genes (IGHV1-69 and IGKV3-20) and form a bNAb epitope class. Furthermore, convergent evolution within these two lineages towards a 111.2GW111.3 motif in the CDRH3 is known to enhance neutralisation potency. We have previously isolated an MPER neutralizing antibody, CAP206-CH12, that uses these same germline heavy and light chain genes but lacks breadth (neutralising only 6% of heterologous viruses). Longitudinal sequencing of the CAP206-CH12 lineage over three years revealed similar convergent evolution towards 111.2GW111.3 among some lineage members. Mutagenesis of CAP206-CH12 from 111.2GL111.3 to 111.2GW111.3 and the introduction of the double GWGW motif into CAP206-CH12 modestly improved neutralisation potency (2.5-3-fold) but did not reach the levels of potency of VRC42.01, 4E10 or PGZL1. To explore the lack of potency/breadth, viral mutagenesis was performed to map the CAP206-CH12 epitope. This indicated that CAP206-CH12 is dependent on D674, a highly variable residue at the solvent-exposed elbow of MPER. In contrast, VRC42.01, PGZL1 and 4E10 were dependent on highly conserved residues (W672, F673, T676, and W680) facing the hydrophobic patch of the MPER. Therefore, while CAP206-CH12, VRC42.01, PGZL1 and 4E10 share germline genes and show some evidence of convergent evolution, their dependence on different amino acids, which impacts orientation of binding to the MPER, result in differences in breadth and potency. These data have implications for the design of HIV vaccines directed at the MPER epitope.



Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

DR MAZVITA SENGAYI-MUCHENGETI

Thirteen Cancers Associated with HIV Infection in A Black South African Cancer Patient Population (1995-2016)

SENGAYI-MUCHENGETI M, SINGH E, CHEN WC, BRADSHAW D, DE VILLIERS CB, NEWTON R, WATERBOER T, MATHEW CG, SITAS F

International Journal of Cancer **IMPACT FACTOR: 7,316**

ABSTRACT

South Africa's HIV epidemic has evolved over time in terms of numbers of people living with HIV, access to antiretroviral treatment (ART) and age. These changes have profoundly influenced local cancer patterns. The Johannesburg Cancer Study has, over a period of 22 years (1995-2016), recruited over 20 000 incident black cancer patients who consented to provide answers to a questionnaire and blood samples (serum, DNA). This has presented a unique opportunity to examine the evolving association of HIV with cancer in Africa. We used logistic regression models to explore case-control associations between specific cancers and HIV, using participants with non-infection related cancers as controls. Using data of 20 835 cancer patients with confirmed HIV status, we found the following cancers to be associated with HIV: Kaposi's sarcoma (ORadj ; 95%CI): (99.1;72.6-135.1), non-Hodgkin lymphoma (11.3;9.3-13.6), cervical cancer (2.7;2.4-3.0), Hodgkin lymphoma (3.1;2.4-4.2), cancer of the eye/conjunctiva (18.7;10.1-34.7), anogenital cancers (anus [2.1;1.4-3.2], penis [5.4;2.7-10.5], vulva [4.8;3.5-6.4], vagina [5.5;3.0-10.2]), oropharyngeal cancer (1.6;1.3-1.9), squamous cell carcinoma of the skin (3.5;2.4-4.9), melanoma (2.0;1.2-3.5) and cancer of the larynx (1.7;1.3-2.4). Kaposi's sarcoma odds ratios increased from the pre-ART (1995-2004) to the early ART (2005-2009) period but declined in the late ART (2010-2016) period. Odds ratios for cancers of the eye/conjunctiva, cervix, penis and vulva continued to increase in recent ART periods. Our study confirms the spectrum of HIV-associated cancers found in other African settings. The odds ratios of conjunctival and HPV-related cancers continue to rise in the ART era as the HIV positive population ages.

KEYWORDS

Africa; HIV associated cancers; anti-retroviral treatment.

Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

DR THANDEKA MOYO-GWETE

PROF PENNY MOORE

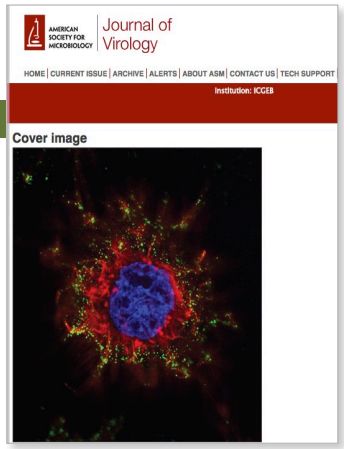
Shared N417-Dependent Epitope on the SARS-Cov-2 Omicron, Beta and Delta-Plus Variants

MOYO-GWETE T, MADZIVHANDILA M, MKHIZE NN, KGAGUDI P, AYRES F, LAMBSON BE, MANAMELA NP, RICHARDSON SI, MAKHADO Z, VAN DER MESCHT M, DE BEER Z, ROMA DE VILLIERS T, BURGERS WA, NTUSI NAB, ROSSOUW T, UECKERMANN V, BOSWELL MT, **MOORE PL**

Journal of Virology **IMPACT FACTOR: 6,549**

ABSTRACT

As severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) continues to evolve, several variants of concern (VOCs) have arisen which are defined by multiple mutations in their spike proteins. These VOCs have shown variable escape from antibody responses and have been shown to trigger qualitatively different antibody responses during infection. By studying plasma from individuals infected with either the original D614G, Beta, or Delta variants, we showed that the Beta and Delta variants elicit antibody responses that are overall more cross-reactive than those triggered by D614G. Patterns of cross-reactivity varied, and the Beta and Delta variants did not elicit cross-reactive responses to each other. However, Beta-elicited plasma was highly cross-reactive against Delta Plus (Delta+), which differs from Delta by a single K417N mutation in the receptor binding domain, suggesting that the plasma response targets the N417 residue. To probe this further, we isolated monoclonal antibodies from a Beta-infected individual with plasma responses against Beta, Delta+, and Omicron, which all possess the N417 residues. We isolated an N417-dependent antibody, 084-7D, which showed similar neutralisation breadth to the plasma. The 084-7D MAb utilised the IGHV3-23*01 germ line gene and had somatic hypermutations similar to those of previously described public antibodies which target the 417 residue. Thus, we have identified a novel antibody which targets a shared epitope found on three distinct VOCs, enabling their cross-neutralisation. Understanding antibodies targeting escape mutations, such as K417N, which repeatedly emerge through convergent evolution in SARS-CoV-2 variants, may aid in the development of next-generation antibody therapeutics and vaccines. IMPORTANCE The evolution of SARS-CoV-2 has resulted in variants of concern (VOCs) with distinct spike mutations conferring various immune escape profiles. These variable mutations also influence the cross-reactivity of the antibody response mounted by individuals infected with each of these variants. This study sought to understand the antibody responses elicited by different SARS-CoV-2 variants and to define shared epitopes. We show that Beta and Delta infections resulted in antibody responses that were more cross-reactive than the original D614G variant, but they had differing patterns of cross-reactivity. We further isolated an antibody from Beta infection which targeted the N417 site, enabling cross-neutralisation of Beta, Delta+, and Omicron, all of which possess this residue. The discovery of antibodies which target escape mutations common to multiple variants highlights conserved epitopes to target in future vaccines and therapeutics.



KEYWORDS

SARS-CoV-2; antibody cross-reactivity; antibody isolation; variant.

Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

DR MICHELLE LOWE

PROF OLGA PEROVIC

Molecular Characterisation of Acinetobacter baumannii Isolates from Bloodstream Infections in a Tertiary-Level Hospital in South Africa

LOWE M, SINGH-MOODLEY A, ISMAIL H, THOMAS T, CHIBABHAI V, NANA T, LOWMAN W, ISMAIL A, CHAN WY, **PEROVIC O**

Front in Microbiol **IMPACT FACTOR: 6,064**

ABSTRACT

Acinetobacter baumannii is an opportunistic pathogen and causes various infections in patients. This study aimed to describe the clinical, epidemiological and molecular characteristics of *A. baumannii* isolated from BCs in patients at a tertiary-level hospital in South Africa. Ninety-six isolates from bloodstream infections were collected. Clinical characteristics of patients were recorded from patient files. Organism identification and AST was performed using automated systems. PCR screening for the mcr-1 to mcr-5 genes was done. To infer genetic relatedness, a dendrogram was constructed using MALDI-TOF MS. All colistin-resistant isolates (n = 9) were selected for WGS. The patients were divided into three groups, infants (<1 year; n = 54), paediatrics (1-18 years; n = 6) and adults (≥19 years; n = 36) with a median age of 13 days, 1 and 41 years respectively. Of the 96 *A. baumannii* bacteraemia cases, 96.9% (93/96) were healthcare-associated. The crude mortality rate at 30 days was 52.2% (48/92). The majority of the isolates were multidrug-resistant (MDR). All isolates were PCR-negative for the mcr-1 to mcr-5 genes. The majority of the isolates belonged to cluster 1 (62/96) according to the MALDI-TOF MS dendrogram. Colistin resistance was confirmed in nine *A. baumannii* isolates (9.4%). The colistin-resistant isolates belonged to sequence type (ST) 1 (5/6) and ST2 (1/6). The majority of ST1 isolates showed low SNP diversity (≤4 SNPs). All the colistin-resistant isolates were resistant to carbapenems, exhibited an XDR phenotype and harboured the bla OXA-23 gene. The bla NDM gene was only detected in ST1 colistin-resistant isolates (n = 5). The lpsB gene was detected in all colistin-resistant isolates as well as various efflux pump genes belonging to the RND, the MFS and the SMR families. The lipooligosaccharide OCL1 was detected in all colistin-resistant ST1 and ST2 isolates and the capsular polysaccharide KL3 and KL17 were detected in ST2 and ST1 respectively. This study demonstrated a 9.4% prevalence of colistin-resistant ST1 and ST2 *A. baumannii* in BC isolates. The detection of the lpsB gene indicates a potential threat and requires close prospective monitoring.

KEYWORDS

Acinetobacter baumannii is an opportunistic pathogen and causes various infections in patients.

Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

DR KERRIGAN MCCARTHY

The Show is Not Over - Wild-Type Polio in Malawi is a Wake-Up Call and An Opportunity for Elimination Efforts

MCCARTHY K, HOWARD W, YOUSIF M, MOONSAMY S, SUCHARD M

International Journal of Infectious Diseases **IMPACT FACTOR: 5,838**

ABSTRACT

Despite recent challenges, polio eradication is tantalisingly close. Gary Humphreys reports. (c) 2022 The authors; licensee World Health Organization.

DR CONSTANTINOS KURT WIBMER

MS POPPY MASHILO

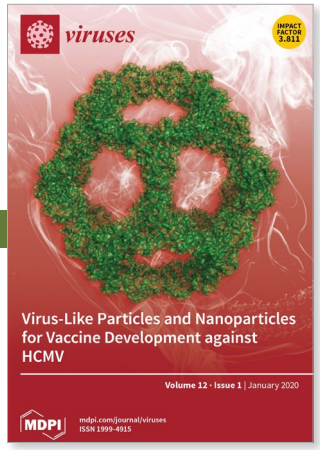
Exploiting V-Gene Bias for Rapid, High-Throughput Monoclonal Antibody Isolation from Horses

CONSTANTINOS KURT WIBMER AND **POPPY MASHILO**

Viruses **IMPACT FACTOR: 5,818**

ABSTRACT

Horses and humans share a close relationship that includes both species' viromes. Many emerging infectious diseases can be transmitted between horses and humans and can exhibit mortality rates as high as 90% in both populations. Antibody biologics represents an emerging field of rapidly discoverable and potent antiviral therapeutics. These biologics can be used to provide passive immunity, as well as blueprints for the rational design of novel active vaccine antigens. Here, we exploit the limited diversity of immunoglobulin variable genes used by horses to develop a rapid, high-throughput monoclonal antibody discovery pipeline. The antibodies isolated from two horses in this study were developed with near exclusivity from a few highly related germline genes within a single IgHV and IgλV gene family and could be recovered for cloning with just three primer pairs. This variable gene pairing was compatible with both horse and human immunoglobulin G isotypes, confirming the suitability of an equine antibody discovery pipeline for developing novel therapeutics to meet the One Health approach to infectious diseases.



KEYWORDS:

Antibody discovery; antigen-specific B-cell sorting; equine humoral immune system; immunoglobulin repertoire; immunotherapeutics and biologics.

Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

MS RUTENDO MAPENGO

PROF NELESH GOVENDER

Endemic Mycoses in South Africa, 2010-2020: A Decade-Long Description of Laboratory-Diagnosed Cases and Prospects for the Future

MAPENGO RE, MAPHANGA TG, GRAYSON W, **GOVENDER NP**

PLoS Negl Trop Dis **IMPACT FACTOR: 4,781**

BACKGROUND

Emergomycosis, histoplasmosis, sporotrichosis and blastomycosis are endemic to southern Africa; the first two are AIDS-related mycoses. We described laboratory-diagnosed cases of endemic and imported mycoses in South Africa over a decade and discuss available diagnostic tools, reasons for the current under-estimation of cases and future strategies to improve case ascertainment.

MATERIALS AND METHODS

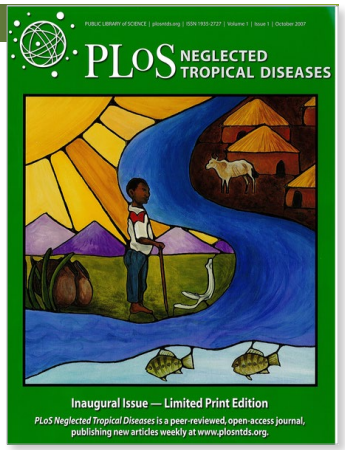
We analysed electronic pathology laboratory data from all public laboratories and one large private laboratory in South Africa from 2010–2020. Diagnostic specimens processed at the national mycology reference laboratory were also included. We classified cases as proven, probable and possible based on the method of identification.

METHODS

We identified 682 cases, of which 307 were proven, 279 were probable and 96 were possible. Of 307 culture-confirmed cases, 168 were identified by phenotypic methods plus sequencing, 128 by phenotypic methods alone and 11 by direct PCR. Of 279 probable cases, 176 had yeasts observed on histology, 100 had a positive *Histoplasma* antigen test and 3 a positive pan-dimorphic PCR test. All 96 possible cases had compatible clinical syndrome with inflammatory infiltrates on skin tissue histology. A majority of cases had an unspecified endemic mycosis (207/682, 30.4%), followed by sporotrichosis (170/682, 24.9%), emergomycosis (154/682, 22.6%), histoplasmosis (133/682, 19.5%), blastomycosis (14/682, 2.1%) and talaromycosis (4/682, 0.6%).

CONCLUSIONS

This study reports a relatively low number of cases over a decade considering an estimated large population at risk, suggesting that a substantial fraction of cases may remain undiagnosed. There is a need to increase awareness among healthcare workers and to develop rapid point-of-care diagnostic tools and make these widely accessible.



Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

DR MUKHLID YOUSIF

Measles Incidence in South Africa: A Six-Year Review, 2015-2020

YOUSIF M, HONG H, MALFELD S, SMIT S, MAKHATHINI L, MOTSAMAI T, TSELANA D, MANAMELA M, KAMUPIRA M, MASETI E, RANCHOD H, OTWOMBE K, MCCARTHY K, SUCHARD M

BMC Public Health IMPACT FACTOR: 4,138

ABSTRACT

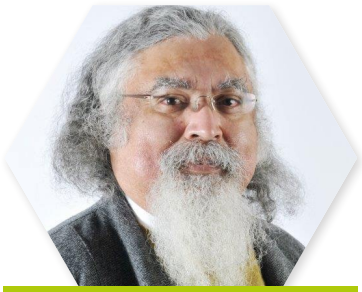
In 2012 the World Health Organization (WHO) aimed to eliminate measles in five regions by 2020. This retrospective descriptive study reviewed measles surveillance data in South Africa for the period 2015-2020 to document the epidemiology of measles and the progress made towards meeting the 2020 measles elimination goal. A total of 22,578 specimens were tested over the period 2015-2020 yielding 401 (1.8%) confirmed measles cases, 321 (1.4%) compatible and 21,856 (96.8%) discarded cases. The most affected age group was 0–4-year-olds. At the provincial level, South Africa achieved adequate surveillance, defined as more than two cases of febrile rash notified annually per 100 000 population, except for KwaZulu-Natal and Limpopo in 2020, probably due to COVID-19 lockdown restrictions. Of confirmed cases, only 26% were vaccinated, 3% were too young to receive vaccines, 5% were not vaccinated, and 65% had unknown vaccination status. Measles vaccine effectiveness amongst 1–4-year-olds was 80%. Using the standard case definition, South Africa achieved the measles elimination target of less than one case per one million nationally in years 2015, 2016 and 2020. The years 2017 to 2019 had incidence rates exceeding one per million nationally. Using a narrow case definition, that excluded positive rubella cases, improved the indicators with only the year 2017 having an incidence rate of more than one per million. South Africa displays intermittent measles outbreaks approximately six-yearly interspersed by inter-epidemic periods in which the country meets measles elimination targets. Intense effort is needed to increase the vaccine coverage to avoid periodic outbreaks. Enhanced molecular testing of each case will be required as measles incidence declines regionally.

KEYWORDS

Elimination; Febrile; Incidence rate; Rash; Vaccination; Vaccine.

Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

DR SELAMAWIT WOLDESENBET



PROF ADRIAN PUREN

Progress Towards the UNAIDS 95-95-95 Targets Among Pregnant Women in South Africa: Results from the 2017 and 2019 National Antenatal HIV Sentinel Surveys

SELAMAWIT WOLDESENBET, MIREILLE CHEYIP, CARL LOMBARD, SAMUEL MANDA, KASSAHUN AYALEW, TENDESAYI KUFA, **ADRIAN PUREN**

PLoS One **IMPACT FACTOR: 3,752**

OBJECTIVES

The UNAIDS 95-95-95 global targets for epidemic control aim to ensure by 2030 that 95% of HIV-positive people know their HIV status, 95% of people diagnosed with HIV receive sustained antiretroviral therapy (ART), and 95% of people on ART have viral suppression. While data on the first and second 95 targets are routinely reported nationally, data on the third 95 target are not available for pregnant women in South Africa. The lack of data on the third 95 target limits the inclusion of low viral suppression as one of the contributing factors in MTCT root cause analyses. This study assessed progress towards the 95-95-95 targets among pregnant women between the ages of 15–49 years attending public health facilities in South Africa.

METHODS

Data were obtained from two consecutive national cross-sectional antenatal HIV sentinel surveys conducted between 1 October and 15 November in both 2017 and 2019. In each survey, data on age, knowledge of HIV status, ART initiation, and geographical location (province) were extracted from medical records. A blood specimen was collected from each woman and tested for HIV. Viral load tests were performed on HIV-positive specimens. Descriptive and multiple logistic regression analyses were performed to examine association between province and viral suppression (defined as viral load <50 copies/mL) using the combined dataset (i.e., both 2017 and 2019 data combined). All analyses considered the survey design.

RESULTS

Of 10 065 and 11 321 HIV-positive women included in the 2017 and 2019 surveys, respectively, 96.0% (95% confidence interval (CI): 95.6–96.4%) and 97.6% (95% CI: 97.3–97.8%) knew their HIV-positive status; 86.6% (95% CI: 85.9–87.3%) and 96.0% (95% CI: 95.6–96.4%) of those who knew their HIV status were receiving ART; while 64.2% (95% CI: 63.2–65.2%) and 66.0% (95% CI: 65.1–66.8%) of those receiving ART were virally suppressed. Achievement of the third 95 target significantly varied by province ranging from 33.9–72.6% in 2017 and 43.4–77.3% in 2019. Knowledge of HIV-positive status, ART initiation, and viral suppression increased in both 15–24 and 25–49-year age groups between 2017 and 2019. In a multivariable analysis adjusting for survey year, gravidity, and education, the odds of viral suppression significantly varied by province (except KwaZulu-Natal and Western Cape, other provinces were less likely to attain viral suppression compared to Gauteng), age (adjusted odds ratio (AOR) for 15–24 years vs 25–49 years: 0.7, 95% CI: 0.6–0.8), and timing of ART initiation (AOR for ART initiation during pregnancy vs before pregnancy: 0.4, 95% CI: 0.5–0.6).

DISCUSSION

Although in 2019 the first and second 95 targets were achieved among pregnant women, meeting the third 95 target remains a challenge. This study highlighted the importance of promoting early ART initiation and the need to target young women in efforts to improve progress towards the third 95 target. Additionally, the provincial variation in viral suppression could be further investigated in future studies to identify and address the root causes underlying these differences.

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Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

PROF OLGA PEROVIC

DR HUSNA ISMAIL

Acinetobacter baumannii Complex, National Laboratory-Based Surveillance in South Africa, 2017 to 2019

PEROVIC O, DUSE A, CHIBABHAI V, BLACK M, SAID M, PRENTICE E, WADULA J, MAHABEER Y, HAN KSS, MOGOKOTLENG R, STRASHEIM W, LOWE M, JALLOW S, **ISMAIL H; FOR GERMS-SA**

PLoS One **IMPACT FACTOR: 3,752**

OBJECTIVE

We aimed to provide an analysis of *A. baumannii* complex (ABC) isolated from blood cultures in South Africa.

MATERIALS AND METHODS

ABC surveillance was conducted from 1 April 2017 to 30 September 2019 at 19 hospital sites from blood cultures of any age and sex. Organism identification was performed using the MALDI-TOF MS and antimicrobial susceptibility testing (AST), MicroScan Walkaway System. We confirmed colistin resistance with Sensititre, FRCOL panel, and selected for whole-genome sequencing.

RESULTS

During the study period, we identified 4822 cases of ABC, of which 2152 cases were from 19 enhanced surveillance sites were reported during the enhanced surveillance period (1 August 2018 to 30 September 2019). Males accounted for 54% (2611/4822). Of the cases with known age, 41% (1968/4822) were infants (< 1-year-old). Seventy-eight percent (1688/2152) of cases had a known hospital outcome, of which 36% (602/1688) died. HIV status was known for 69% (1168/1688) of cases, and 14% (238/1688) were positive. Eighty-two percent (1389/1688) received antimicrobial treatment in admission. Three percent (35/1389) of cases received single colistin. Four percent (75/2033) were resistant to colistin. At least 75% of the isolates (1530/2033) can be classified as extensively drug-resistant (XDR), with resistance to most antibiotics except for colistin. The majority, 83% (20/24), of the colistin-resistant isolates were of the sequence type (ST) 1. Resistance genes, both plasmid- and chromosomal- mediated were not observed. Although all isolates had, nine efflux pump genes related to antimicrobial resistance.

CONCLUSIONS

Our surveillance data contributed to a better understanding of the natural course of *A. baumannii* disease, the patient characteristics among infants, and the level of resistance. At least two-thirds of the isolates were extensively drug-resistant, and four percent of isolates were resistant to colistin.

Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

PROF NELESH GOVENDER

REVIEW: Emergomycosis

REDDY DENASHA L, NEL JEREMY, **GOVENDER NELESH P**

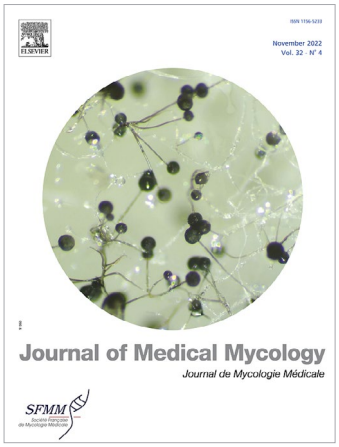
Journal of Medical Mycology **IMPACT FACTOR: 3,747**

ABSTRACT

Purpose of Review In this review, we provide an overview of emergomycosis from a clinical perspective and discuss the taxonomy and classification of the pathogens, epidemiology, pathophysiology of infection and mechanisms of pathogenesis, immunology, clinical manifestations, laboratory culture and diagnosis, molecular characterisation, therapy and prognosis.

Recent Findings While Emergomyces pasteurianus is the most geographically-widespread species, Emergomyces africanus is endemic to Southern Africa and causes disseminated disease with cutaneous involvement primarily among patients with advanced human immunodeficiency virus (HIV) disease.

Summary Emergomycosis, a disseminated clinical disease resulting from infection with dimorphic fungi in the genus Emergomyces, occurs primarily among immunocompromised patients. Further knowledge is needed on the pathophysiology, diagnosis and management of emergomycosis.



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MS WILHELMINA STRASHEIM

PROF OLGA PEROVIC

Method to Assess Farm-Level Vaccine and Antibiotic Usage Utilising Financial Documentation: A Pilot Study in a Commercial Pig Farm in South Africa from 2016 to 2018

STRASHEIM W, ETTER EMC, LOWE M, **PEROVIC O**

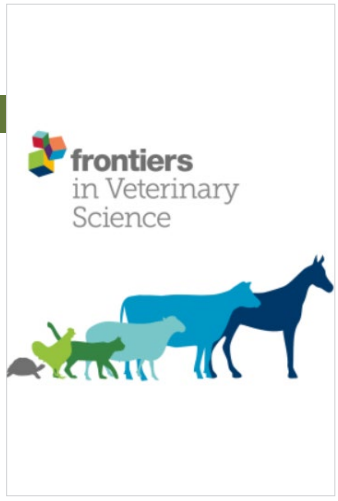
Frontiers in Veterinary Science **IMPACT FACTOR: 3,471**

ABSTRACT

The purpose of the study was to develop a blueprint using financial documentation to describe and quantify vaccine and antibiotic usage (ABU). This method was piloted in a commercial pig farm in South Africa, with the ultimate hope to serve as a tool in a future species-specific vaccine and ABU surveillance system. Data collection was based on templates from the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) network and the World Organisation for Animal Health (WOAH). Invoices from 2016 to 2018 were used as the main data source. In addition, monthly statement of accounts was used to check for missing invoices. An inventory check was done to ensure that the correct antibiotic concentrations were used in subsequent calculations. Livestock counts and slaughter statistics were also collected to be used as denominator data. Cost calculations for the procurement of antibiotics and vaccines were also done. The study showed that veterinary medicinal products were purchased only from a single veterinary practice. A total of 291 invoices were issued over 3 years, of which 2.75% (8/291) were missing and could therefore not be used in quantification. Tetracyclines (453.65 ± 25.49 kg and 135.16 ± 3.31 mg/kg), followed by quinoxalines (258.33 ± 8.04 kg and 77.07 ± 3.93 mg/kg) were used in the highest amounts, both in terms of weight (kg) and adjusted for animal biomass (mg/kg). Vaccines used on the farm targeted seven different diseases, namely enzootic pneumonia, erysipelas, ileitis, infectious infertility, leptospirosis, neonatal pig diarrhoea and porcine circovirus disease. An average of 103 546 vaccine dosages was purchased for ZAR1 302,727 ($ 84,620) per year, whereas the average cost for the procurement of antibiotics was ZAR 907,372 ($ 69,561) per year. The study showed that invoices and monthly statement of accounts, in combination with an inventory check and on-farm production statistics, are useful data sources to quantify vaccine and ABU in the absence of veterinary prescriptions. In addition, vaccinating pigs were more expensive than administering antibiotics.

KEYWORDS

South Africa; antibiotic (antimicrobial) growth promoters; antibiotic usage; method; pig farm; pigs; pork production; vaccine usage.



Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

PROF NELESH GOVENDER

Evaluation of the Effectiveness of a South African Laboratory Cryptococcal Antigen Screening Programme Using a Retrospective Cohort and a Cluster-Randomised Trial Design

DESANTO DJJ, BANGDIWALA AS, VAN SCHALKWYK E, SKIPPER CP, GREENE G, PAXTON J, HULLSIEK KH, MASHAU R, RAJASINGHAM R, BOULWARE DR, **GOVENDER NP**

BMJ Open **IMPACT FACTOR: 3,007**

ABSTRACT

Introduction Cryptococcal meningitis is a common fungal opportunistic infection and a leading cause of death among people with advanced HIV disease in sub-Saharan Africa. The WHO recommends cryptococcal antigen (CrAg) screening followed by pre-emptive therapy to prevent cryptococcal meningitis and death in this population. In 2016, South Africa was the first country to implement reflexive laboratory CrAg screening nationally. The Cryptococcal Antigen Screen-and-Treat National Evaluation Team (CAST-NET) aims to evaluate the effectiveness of this national screening programme to optimise health outcomes.

Methods and analysis the CAST-NET study consists of two integrated parts: a retrospective cohort study and a cluster-randomised trial (CRT). The retrospective cohort study will determine 6-month cryptococcal meningitis-free survival among CrAg-positive patients. Secondary outcomes include the proportion of CrAg-positive results noted for action in the CrAg-positive patient chart, the proportion of CrAg-positive patients offered and accept/decline a lumbar puncture, the proportion of CrAg-positive patients prescribed antifungal therapy and the proportion of CrAg-positive patients who have antiretroviral therapy initiated or reinitiated at an appropriate time according to South African national guidelines. Cohort data will be analysed by the type of facility (ie, hospital vs primary health clinic) at which the patient was diagnosed with antigenaemia. The CRT will determine if the appointment and mentoring of a healthcare worker, or 'crypto champion', at intervention facilities is associated with a higher proportion of CrAg-positive persons initiating pre-emptive fluconazole therapy. Secondary outcomes will include 6-month cryptococcal meningitis-free survival and the proportion prescribed fluconazole maintenance treatment.

Ethics and dissemination Ethics approvals were received from the University of the Witwatersrand Human Research Ethics Committee (Medical), the University of KwaZulu-Natal Biomedical Research Ethics Committee and the University of Pretoria Faculty of Health Sciences Research Ethics Committee. Study results will be disseminated to the South African Department of Health and participating facilities through peer-reviewed publications and reports.

BMJ Open

Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

DR MICHELLE LOWE

PROF OLGA PEROVIC

Carbapenem-resistant Enterobacterales in patients with bacteraemia at tertiary academic hospitals in South Africa, 2019-2020: An update

LOWE M, SHUPING L, **PEROVIC O**

South African Medical Journal **IMPACT FACTOR: 0,556**

BACKGROUND

The emergence of carbapenem-resistant Enterobacterales (CRE) has become a serious and significant public health threat worldwide, owing to the limited antimicrobial therapy options, and the elevated mortality rates associated with these infections.

OBJECTIVES

To present an update on the epidemiology of CRE bloodstream infections among hospitalised patients reported under the Group for Enteric, Respiratory and Meningeal Diseases Surveillance in South Africa (GERMS-SA) between January 2019 and December 2020.

METHODS

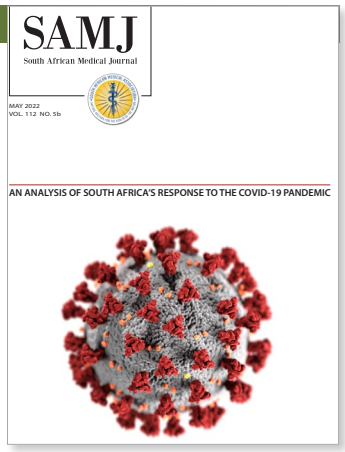
Patients of all ages with CRE bacteraemia were included and isolates, when available, were sent to the reference laboratory for confirmatory testing and molecular characterisation. Multivariable logistic regression analysis was performed to assess factors associated with in-hospital mortality.

RESULTS

We included 2 144 patients with CRE bacteraemia with a median age of 33 (interquartile range 1 - 51) years, of whom 1 145 (54.2%) were male. Klebsiella pneumoniae accounted for 79.8% of infections (n=863/1 082), of which 89.5% (n=611/683) were healthcare associated (HA). The most common carbapenemase genes were carbapenem-hydrolysing oxacillinase-48 (blaOXA-48-like) (76.8%; n=761/991), New Delhi metallo-β-lactamase (blaNDM) (21.1%; n=209/991) and Verona integron-encoded metallo-β-lactamase (blaVIM) (1.3%; n=13/991). None of the screened isolates with a colistin minimum inhibitory concentration >2 µg/mL harboured the mobilised colistin resistance (mcr)-1 to mcr-5 genes. The crude in-hospital mortality rate was 36.6% (n=377/1 029). Patients aged ≥60 years (v. 1.6 - 9 years) (adjusted odds ratio (aOR) 4.53; 95% confidence interval (CI) 2.21 - 9.28), those with comorbidities (diabetes, malignancy, renal and/or cardiovascular failure) (aOR 1.72; 95% CI 1.17 - 2.52), those with altered mental state (aOR 5.36; 95% CI 3.21 - 8.92) and those with previous antimicrobial use (aOR 1.88; 95% CI 1.27 - 2.77) had increased odds of in-hospital mortality.

CONCLUSION

The epidemiology of CRE bloodstream infections remained similar compared with the previous surveillance report. Most infections were HA and caused by OXA-48-like carbapenemase-producing K. pneumoniae with no plasmid-mediated colistin resistance. Standard infection control measures should be strengthened.



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DR WAASILA JASSAT

Undiagnosed Comorbidities among Individuals Hospitalised with COVID-19 in South Africa Public Hospitals

JASSAT W, MUDARA C, VIKA C, DRYDEN M, MASHA M, ARENDSE T, GROOME MJ, MOULTRIE H, ISMAIL F, MVUSI L, SINGH S, SAYED B, PARKER A, BLACK J, POTGIETER S, COHEN C, BLUMBERG L

South African Medical Journal **IMPACT FACTOR: 0,556**

BACKGROUND

Previous studies have reported comorbid disease, including hypertension, diabetes mellitus, chronic cardiac and renal disease, malignancy, HIV, tuberculosis (TB) and obesity, to be associated with COVID-19 mortality. National demographic surveys have reported a high proportion of undiagnosed and untreated comorbid disease in South Africa (SA). Objectives. To determine the number of individuals with previously undiagnosed HIV, TB and non-communicable diseases (NCDs) among patients hospitalised with COVID-19, and the level of medical control of these chronic diseases.

METHODS

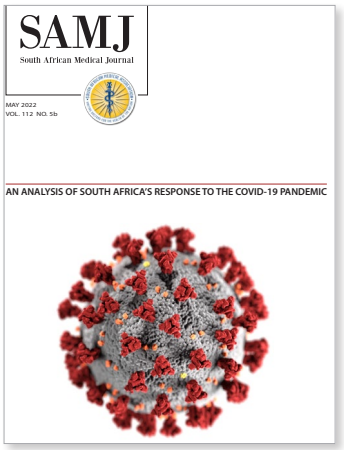
We conducted a sentinel surveillance study to collect enhanced data on HIV, TB and NCDs among individuals with COVID-19 admitted to 16 secondary-level public hospitals in six of the nine provinces of SA. Trained surveillance officers approached all patients who met the surveillance case definition for inclusion in the study, and consenting patients were enrolled. The data collection instrument included questions on past medical history to determine the self-reported presence of comorbidities. The results of clinical and laboratory testing introduced as part of routine clinical care for hospitalised COVID-19 patients were collected for the study, to objectively determine the presence of hypertension, diabetes, HIV and TB and the levels of control of diabetes and HIV.

RESULTS

On self-reported history, the most prevalent comorbidities were hypertension (n=1 658; 51.5%), diabetes (n=855; 26.6%) and HIV (n=603; 18.7%). The prevalence of self-reported active TB was 3.1%, and that of previous TB 5.5%. There were 1 254 patients admitted with COVID-19 (39.0%) who met the body mass index criteria for obesity. On clinical and laboratory testing, 87 patients were newly diagnosed with HIV, 29 with TB, 215 with diabetes and 40 with hypertension during their COVID-19 admission. There were 151/521 patients living with HIV (29.0%) with a viral load >1 000 copies/mL and 309/570 (54.2%) with a CD4 count <200 cells/µL. Among 901 patients classified as having diabetes, 777 (86.2%) had a glycated haemoglobin (HbA1c) level ≥6.5%.

CONCLUSION

The study revealed a high prevalence of comorbid conditions among individuals with COVID-19 admitted to public hospitals in SA. In addition, a significant number of patients had previously undiagnosed hypertension, diabetes, HIV and active TB, and many and poorly controlled chronic disease, as evidenced by high HbA1c levels in patients with diabetes, and high viral loads and low CD4 levels in patients with HIV. The findings highlight the importance of strengthening health systems and care cascades for chronic disease management, which include prevention, screening for and effectively treating comorbidities, and ensuring secure and innovative supplies of medicines in primary healthcare during the COVID-19 pandemic.



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DR NAAZNEEN MOOLLA

DR JACQUELINE WEYER

First Report of An Imported Case of Haemorrhagic Fever with Renal Syndrome in South Africa

N MOOLLA, D. ADLER, L BLUMBERG, A GLASS, A GROBBELAAR, C LE ROUX, J PAWESKA, **J WEYER**

SAMJ in Practice **IMPACT FACTOR: 0,556**

ABSTRACT

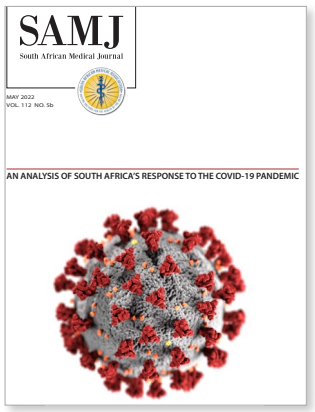
Haemorrhagic fever with renal syndrome (HFRS) is caused by hantavirus infection. Hantaviruses are not endemic to South Africa, and we report the first detection of an imported case of HFRS in the country. The case involved a traveller from Croatia who presented to a Johannesburg hospital with an acute febrile illness with renal dysfunction. The patient reported visiting rurally located horse stables in Croatia before falling ill, and that a worker in the stables with similar illness was diagnosed with HFRS. Given the exposure history and clinical findings of the case, a clinical diagnosis of HFRS was made and confirmed by laboratory testing.

DR SIBONGILE WALAZA

Leveraging Epidemiology as a Decision Support Tool During the COVID-19 Epidemic in South Africa

SILAL SP, GROOME MJ, GOVENDER N, PULLIAM JRC, RAMADAN OP, PUREN A, JASSAT W, LEONARD E, MOULTRIE H, MEYER-RATH KG, RAMKRISHNA W, LANGA T, FURUMELE T, MOONASAR D, COHEN C, **WALAZA S**

South African Medical Journal **IMPACT FACTOR: 0,556**



ABSTRACT

By May 2021, South Africa (SA) had experienced two 'waves' of COVID-19 infections, with an initial peak of infections reached in July 2020, followed by a larger peak of infections in January 2021. Public health decisions rely on accurate and timely disease surveillance and epidemiological analyses, and accessibility of data at all levels of government is critical to inform stakeholders to respond effectively.

In this paper, we describe the adaptation, development and operation of epidemiological surveillance and modelling systems in SA in response to the COVID-19 epidemic, including data systems for monitoring laboratory-confirmed COVID-19 cases, hospitalisations, mortality and recoveries at a national and provincial level, and how these systems were used to inform modelling projections and public health decisions. Detailed descriptions on the characteristics and completeness of individual datasets are not provided in this paper.

Rapid development of robust data systems was necessary to support the response to the SA COVID-19 epidemic. These systems produced data streams that were used in decision-making at all levels of government. While much progress was made in producing epidemiological data, challenges remain to be overcome to address gaps to better prepare for future waves of COVID-19 and other health emergencies.

Disclaimer: Impact factor scores contained in this publication were compiled in August 2022.

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