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Impact of the COVID-19 Pandemic on HIV Care in a Paediatric and Adolescent ARV Clinic in Johannesburg: A Retrospective Cohort Study

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Impact of the COVID-19 Pandemic on HIV Care in a Paediatric and Adolescent ARV Clinic in Johannesburg: A Retrospective Cohort Study

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14 October 2024



DECLARATION

I, Masello Phasha hereby declare that this dissertation titled Impact of the COVID-19 Pandemic on HIV Care in a Paediatric and Adolescent ARV Clinic in Johannesburg: A Retrospective Cohort Study, submitted in fulfilment of the requirements for the Master of Medicine degree in Paediatrics and Child Health is my original work.

This dissertation was conducted under the supervision of Dr Gillian Sorour and Prof. Karl-Günter Technau in the Department of Paediatrics and Child Health, Rahima Moosa Mother and Child Hospital.

I have acknowledged all sources of information I have used and have conformed to the University of the Witwatersrand requirements regarding intellectual property and plagiarism.

I declare that this dissertation has not been submitted in whole or in part for any other degree or qualification at any other institution.

Signed: 

Date: 14 October 2024

DEDICATION

I dedicate this dissertation to my lovely family, to my beloved late father who always believed in me and encouraged me to reach for the stars. This dissertation is dedicated to your memory.

A special word of gratitude to my mother for her support and unconditional love.

To my very special sister Mabatho and my brother Mfundis who stood by me and were always willing to lend a helping hand, your thoughtfulness is appreciated.

To my husband Green and our dearest daughter Mokgethwa for their constant love, encouragement and for walking this journey with me.

I also dedicate this work to my friends who have demonstrated what it means to be closer than a brother and for their sweet friendship that has kept me going.

Lastly, I wish to give special thanks to my Let's go to glory church family who have supported me and covered me in prayer.

ACKNOWLEDGEMENTS

First and most important I give praise and thanks to God who has kept me and enabled me to complete this dissertation.

I wish to thank my supervisors Dr Sorour and Prof Technau for their invaluable guidance, input and endless support throughout this journey. Thank you for your time, insightful feedback and many hours of reading this manuscript to perfection. It has been a privilege to be supervised by you and I will forever be grateful for the experience.

I acknowledge and thank the Empilweni Services and Research Unit together with the Department of Paediatrics and Child Health at Rahima Moosa Mother and Child Hospital for allowing me to conduct my research and aiding when required.

I would like to acknowledge the staff at Empilweni Services and Reseach unit for their commitment to patient care and their efforts in capturing data which has been crucial for this dissertation.

Finally, I would like to thank the patients which without this work would have not been possible.

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NOMENCLATURE

AIDS	- Acquired Immunodeficiency Syndrome
ART	- Antiretroviral Therapy
ARV	- Antiretroviral
BMI	- Body Mass Index
COVID- 19	- Coronavirus disease 2019
ELISA	- Enzyme-linked immunosorbent assay
ESRU	- Empilweni Services and Research unit
HIV	- Human Immunodeficiency Virus
JHB	- Johannesburg
NWFA	- Normal Weight For Age
PCR	- Polymerase Chain Reaction
PLWHIV	- People Living with HIV
PMTCT	- Prevention of Mother to Child Transmission
RMMCH	- Rahima Moosa Mother and Child Hospital
SA	- South Africa
SARS-CoV-2	- Severe Acute Respiratory Syndrome Coronavirus 2
TB	- Tuberculosis
UWFA	- Underweight For Age
VL	- Viral load
VTP	- Vertical Transmission Prevention
WFH	- Weight For Height
WHO	- World Health Organisation

TITLE PAGE

Date: 14 October 2024
Title of article: Impact of the COVID-19 Pandemic on HIV Care in a Paediatric and Adolescent ARV Clinic in Johannesburg: A Retrospective Cohort Study
Corresponding author: Masello Phasha

Dear Editor-in-Chief

I wish to submit my original research paper entitled “Impact of the COVID-19 Pandemic on HIV Care in a Paediatric and Adolescent ARV Clinic in Johannesburg: A Retrospective Cohort Study” for consideration for publication by the Southern African Journal of HIV Medicine. I declare that this work has not been submitted for publication elsewhere.

Dr Gillian Sorour and Prof. Karl-Günter Technau have co-authored the manuscript. In this paper, we describe the impact of the COVID-19 pandemic on paediatric and adolescent HIV care at a Johannesburg HIV clinic.

The COVID-19 pandemic has had a profound impact on various sectors globally, its co-existence with the HIV/AIDS epidemic in South Africa challenged the healthcare sector and impacted healthcare service delivery, which includes HIV care services for children and adolescents.
In this paper, we highlight the impact of the COVID-19 pandemic on HIV care at a Johannesburg HIV clinic and describe the components of care which were affected by the pandemic. We report on how the pandemic negatively affected the enrolment of children and adolescents into HIV care and the vertical transmission prevention program. We also highlight the ongoing difficulties with early treatment care and monitoring in children and adolescents.

I believe it will be of interest to readers in the field of infectious diseases and HIV medicine. I look forward to the opportunity to share my research paper with the audience of the Southern African Journal of HIV Medicine.

Regards,
Dr Masello Phasha, MB Bch, DCH (SA)

Title:
Impact of the COVID-19 Pandemic on HIV Care in a Paediatric and Adolescent ARV Clinic in Johannesburg: A Retrospective Cohort Study

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Keywords: Paediatric, Adolescent, HIV care, ARV clinic, COVID-19, pandemic

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ABSTRACT

Background:
The co-existence of the HIV/AIDS epidemic and the COVID-19 pandemic in South Africa challenged the healthcare sector and negatively impacted healthcare service delivery, including through impeding access to primary healthcare services which include HIV care services for children and adolescents.

Objectives:
We describe the impact of the COVID-19 pandemic on paediatric and adolescent HIV care at an HIV clinic in Johannesburg, South Africa.

Method:
A retrospective cohort study was conducted on data from the Empilweni Services and Research Unit (ESRU) database, and a secondary data analysis was performed by comparing data of children and adolescents aged 0-18 years who had their first visit during the two study periods; March 2018- February 2019 (pre-COVID era) and March 2020- February 2021 (COVID era).

Results:
During the COVID era, a total of 113 children and adolescents were enrolled into HIV care, reflecting a 27% decline from the pre-COVID era where 154 enrolments occurred. Additionally, there was a significant decrease in the number of neonates referred via the Vertical Transmission Prevention (VTP) program, previously known as the 'Prevention of Mother-to-Child Transmission (PMTCT) program' (45 pre-COVID compared to 20 in the COVID era). However, no significant difference was observed in adherence patterns and treatment outcomes between the two study periods.

Conclusion:
The COVID-19 pandemic negatively impacted the enrolment of children and adolescents into HIV care and affected the VTP program negatively. This is evidenced by a decline in the total number of children and adolescents enrolled in

care during this period. However, there was no significant impact on the outcomes of HIV care.

What this study adds:

The findings emphasise the need to actively strengthen HIV care services, especially HIV testing and treatment monitoring in children, adolescents, and pregnant women. Moreover, it is essential to ensure that these services are not interrupted, particularly during times of crisis, such as the COVID-19 pandemic.

INTRODUCTION

South Africa is heavily affected by the HIV/AIDS (Human Immunodeficiency Virus/ Acquired Immunodeficiency Syndrome) epidemic, which remains a significant public health concern despite advancements in HIV prevention, testing and treatment.[1-3] Globally, an estimated 38.4 million people were living with HIV at the end of 2021, with 7.5 million residing in South Africa, including 270 000 children between the ages of 0-14 years.[1]

To curb the HIV epidemic, the Joint United Nations Programme on HIV/AIDS (UNAIDS) introduced a set of targets in the year 2020 termed the 95-95-95 targets.[4] The objective of these targets is to aid in the attainment of the 2030 HIV sustainable development goal 3.3, which is to end the HIV/AIDS epidemic as a public health threat by 2030 by enabling early diagnosis, timely treatment and effective management of the disease.[5] Specifically, the goal is to ensure that 95% of individuals living with HIV are aware of their HIV status, 95% of all individuals living with HIV infection are receiving antiretroviral therapy, and that 95% of all patients receiving antiretroviral therapy have attained viral suppression by 2025.[4] Pertaining to children, these targets aim to ensure that 95% of women of childbearing age have their HIV and sexual and reproductive health service needs met, that 95% of breastfeeding mothers living with HIV have attained viral suppression, and that 95% of children born to mothers living with HIV are tested for HIV by 2030.[4]

By the end of 2021, 94% of people living with HIV in South Africa knew their HIV status, of whom 79% were on treatment, and 91% of those on treatment had achieved viral suppression.[1] These figures serve as positive indicators for monitoring progress towards the commitment to achieving the UNAIDS 2025 HIV services targets and the United Nations 2030 HIV sustainable development goal.[5] However, evidence suggests that further efforts are needed as only 67% of people living with HIV in South Africa had suppressed viral loads by the end of 2021.[1] Sadly, the figures for children are significantly worse with only 83% of children living with HIV in South Africa being diagnosed, 48% starting ART and only 33% having achieved viral

suppression by the end of 2021.[6] This highlights the vulnerability of children in this context.

Globally, there are 2.73 million children between the ages of 0 and 19 years living with HIV, approximately 850 children become infected with HIV daily and 301 children die from AIDS-related illnesses each day.[1] In South Africa, HIV infection remains amongst the five leading causes of under-five mortality, alongside malnutrition, diarrhoeal diseases, lower respiratory tract infections, and low birth weight.[2] However, only 48% of children living with HIV in South Africa were reported to be on antiretroviral therapy (ART) and tragically, 2800 children died from HIV-related infections in the year 2021.[7]

The emergence of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in Wuhan, China and its rapid global spread, high morbidity and mortality led the World Health Organisation (WHO) to declare it a pandemic in March 2020, naming it the COVID-19 pandemic.

On 27 March 2020, the president in consultation with a panel of experts implemented a national lockdown in South Africa. This measure aimed to curb infection, protect those most vulnerable to severe disease and prepare and safeguard healthcare services as the pandemic was anticipated to overwhelm the healthcare system, as observed in other low and middle-income countries (LMIC) thereby causing disruptions in health care delivery.[8]

HIV testing is a crucial aspect of HIV care as it identifies people living with HIV and is the first step towards enrolment into HIV care. If testing is disrupted due to any cause, such as the reassignment of dedicated HIV community health workers to other tasks during the COVID-19 pandemic, it can contribute to the decline in the number of children and adolescents being enrolled into HIV care.[9]

The implementation of the national lockdown coupled with people's fear of contracting SARS-Cov-2 infection led to an unfortunate disruption of child health and antenatal care services, particularly during the initial months of the lockdown. As a result, there was a decline in the number of children and pregnant women accessing essential primary healthcare services.[10] HIV care services were not spared as a

study conducted in KwaZulu-Natal (KZN) reported an almost 50% decline in HIV testing and initiation of antiretroviral therapy (ART) at the onset of the pandemic in South Africa.[11]

This study aimed to assess the impact of the COVID-19 pandemic on HIV care at the Paediatric and Adolescent HIV Clinic at Rahima Moosa Mother and Child Hospital (RMMCH) by comparing components of HIV care data for new patients enrolled in care before and during the pandemic.

RESEARCH METHODS AND DESIGNS

Study design

This study is a retrospective cohort study conducted at the Rahima Moosa Mother and Child Hospital's paediatric and adolescent HIV clinic also known as Empilweni Services and Research Unit (ESRU) located in the western part of Johannesburg, South Africa. This clinic is a large paediatric and adolescent HIV clinic in South Africa and serves the greater western Johannesburg area, which has the second-highest number of children living with HIV in South Africa.[3]

The study population included patients aged 0-18 years who attended the HIV clinic as new referrals during two periods; 01 March 2018 – 28 February 2019 (pre-COVID era) and 01 March 2020 – 28 February 2021 (COVID era). Patients who were not HIV-infected and those whose parents refused consent were excluded from the study.

Data Collection

We conducted a secondary analysis on data from the ESRU database, which is hosted on the University of the Witwatersrand REDCAP platform and maintained in the clinic.[12] We obtained approval from the electronic gatekeeper to access de-identified data which we extracted and used exclusively to generate the results for this study.

Data Analysis

Descriptive statistics were used to describe the data: Frequencies and percentages for categorical data and medians, and interquartile ranges for continuous data. When examining the referral sources of the patients, we considered a patient to have been referred from the Vertical Transmission Prevention program if they were born in the hospital and had a positive HIV polymerase chain reaction (PCR) test post-delivery (also known as Birth PCR) or two post-delivery indeterminate PCRs followed by a detectable viral load. An inpatient was defined as a patient who tested positive for HIV during their hospital admission and was not receiving treatment at the time. On the other hand, an outpatient was classified as a patient referred by another clinic, not requiring hospitalisation and not receiving ART at their first visit to ESRU. A transfer-in was recorded as any patient who had already been diagnosed with HIV infection and was receiving ART at their first visit to ESRU.

An early presentation, from diagnosis to the first visit was defined as any patient who had been diagnosed with HIV infection less than eight days before their first ESRU visit while a late presentation was any patient who had been diagnosed with HIV infection eight or more days before their first visit.

Neonates were excluded from the anthropometry analysis due to variations in birthweights and different methods used to assess adequate weight gain at different time points post-delivery. Ideally, weight for height (WFH) should be used to determine children's nutritional status under five years of age while body mass index (BMI) is preferred in children older than five years of age. Unfortunately, due to incomplete height data, this could not be assessed, and weights only were used to determine whether participants were underweight for age (UWFA) or had a normal weight for age (NWFA). Patients were categorised as UWFA if their weight for age fell below the -2 standard deviations (SD) and as NWFA if their weight for age was between the -2SD and +2SD.

The World Health Organisation (WHO) clinical stages were employed to assess the patient's clinical condition at presentation and thereafter patients were classified as mild or advanced disease. Mild disease comprised of patients who were classified as

WHO stage 1 and 2, while advanced disease where patients who were classified as WHO stage 3 and 4.

Immunological staging was determined based on the WHO case definitions, which utilise CD4 count in percentages for children under 5 years of age and absolute counts for children aged five years and older. Normal CD4 counts were defined as an absolute CD4 cell count of 1000 cells per cubic millimetre and more or a CD4 percentage of 25% or more in children less than 5 years, while for children and adolescents 5 years and older an absolute CD4 cell count of 500 cells per cubic millimetre, and more was considered normal. We categorised immunosuppression into two levels: mild and advanced. For children under 1 year of age, mild immunosuppression was defined as a CD4 percentage of 25% or higher while advanced immunosuppression was classified as a CD4 percentage below 25%. In children between 1 and 5 years of age, mild immunosuppression was characterised as a CD4 percentage of 20% or higher, while advanced immunosuppression was indicated by a CD4 percentage below 20%. For all patients aged 5 years and older, mild immunosuppression was defined as an absolute CD4 count of 350 or more cells per cubic millimetre (mm3) and advanced immunosuppression when the absolute CD4 count fell below 350 cells/mm3.

Loss to follow-up was defined as the patient's failure to attend their scheduled medication refill or clinical visit beyond 90 days from their last appointment. A patient was classified as transferred out if they were successfully and formally referred to another healthcare facility for continued care. Lastly, a patient was considered virally suppressed if their viral load was lower than 50 copies per millilitre (ml) as per South African guidelines during the study periods. We also assessed viral suppression at the level of 1000 copies per ml.

Statistical analysis was performed using Statistical Analysis System (SAS – SAS institute Inc, Cary, NC, USA) and a p-value of less than 0.05 was used to indicate a statistically significant finding. When comparing the characteristics above between the groups, we used t-test for continuous data and chi-square for categorical data. Survival analysis using the log-rank test was done to compare death and loss to follow-up between the two periods.

Ethical considerations

The permissions to conduct the study were obtained from the Chief Executive Officer's (CEO) office of RMMCH, the Gauteng Health Research Committee (approval number GP_ 202208_002) and the Human Research Ethics Committee (Medical) of the University of the Witwatersrand (approval number M220848 MED 22-07-073).

This retrospective descriptive study utilised anonymised data collected as part of routine clinic procedures with consent obtained from parents for data sharing.

To ensure patient anonymity and confidentiality, no identifying information was included when extracting, analysing and reporting the study findings.

RESULTS

A total of 267 patients were identified and included in the study after screening 5027 electronic files in the clinic's database system (Figure 1). The study population consisted of 154 patients who were linked to care or referred to the clinic between 01 March 2018 to 28 February 2019 (pre-COVID era), and 113 patients who were linked to care between 01 March 2020- 28 February 2021 (COVID era).

There were 41 fewer patients linked to care during the COVID era compared to the pre-COVID era (154 in pre-COVID and 113 in COVID era) which was a 27% decline. The decline in the number of patients linked to care during the COVID-era was particularly notable at the onset of the South African national lockdown. Although there was a brief recovery in the following weeks, there were subsequent declines during the beta and delta COVID-19 waves in South Africa (Figure 2).

Demographics at presentation

Table 1 provides a summary of the key characteristics of the patients at their first visit to the ESRU HIV clinic or upon enrolment into care through the hospital's VTP program (previously known as the PMTCT program) or referral of patients admitted to the wards. As shown in Table 1, many of the patients linked to care in both the study periods were children under the age of 5 years. Specifically, 117 patients (76%) were children under the age of 5 years in the pre-COVID era while 85 patients

(75%) were children under the age of 5 years in the COVID era. There was no significant difference in the age at presentation between the two eras (Figure 3, Table 1). During both the pre-COVID era and the COVID era, the outpatient department served as the primary referral source for enrolling HIV-infected children and adolescents into HIV care. In the pre-COVID era, 78 patients (51%) were referred from the outpatient department, while in the COVID era, 61 patients (54%) were referred from the same department. However, there was a concerning decline in the number of patients linked to care through the VTP program during the COVID era. Only 20 patients (18%) were referred through the VTP program in the COVID era, compared to 45 patients (29%) in the pre-COVID era. Because of this, there was a proportional increase in the number of referrals from the inpatient departments during the COVID era and these children were acutely ill and required hospitalisation. We had a total of 32 patients (28%) referred from inpatient departments during the COVID era, in comparison to 31 patients (20%) during the pre-COVID era. In the pre-COVID era, we recorded 25 patients (16%) who were transferred in from other healthcare facilities, already diagnosed and on treatment and 129 were new patients (84%). Similarly, in the COVID era, there were 20 patients (18%) who were transferred in, and 93 patients (82%) were new patients.

The duration from the first diagnosis of HIV infection to the first visit in both study periods was commonly within 7 days of diagnosis. However, it is noteworthy that in the COVID era, there were 33 patients (29%) who presented more than 7 days after being diagnosed with HIV infection compared to 39 (25%) in the pre-COVID era. This was predominately observed among outpatients, who may have faced multiple constraints in accessing care during the COVID era.

Clinical Features

Excluding neonates, we observed that there was no significant difference in anthropometry between patients at presentation in the two study periods. Our findings revealed that many of the patients in both study periods were underweight for age (UWFA), with approximately 54% of patients in the pre-COVID era and 53% of patients in the COVID era falling into this category.

Furthermore, although not significant it is important to note that there were more patients in the COVID era (41%) who presented with advanced HIV disease and co-infections necessitating hospital admission and in-hospital treatment when compared to 36% of patients in the pre-COVID era. This is consistent with the observed general population's health seeking behaviour during the pandemic where majority of people who sought healthcare, specifically hospital care where individuals with severe symptoms and life threatening conditions.[13, 14]

Outcomes

Table 2 provides a summary of the outcomes of the patients one year after their first visit. In the pre-COVID era, there were a total of 9 deaths, including one non-HIV-related early neonatal death. In the COVID era, there were 10 deaths, including two neonatal deaths that were also not HIV-related. The median age at death in the pre-COVID era was 3 months (with a mean of 21 months), and the median number of days from the first visit to death was 14 days (with a mean of 20 days). In comparison, in the COVID era, the median age at death was 8 months (with a mean of 11 months) and the median number of days from first visit to death was 18 days (with a mean of 83 days). There was no difference in poor outcome (combining loss to follow-up and death) between the groups. In both the pre-COVID and COVID era there was a 23% chance of death or loss to follow-up by 12 months (log-rank test p=0.93).

Regarding loss to follow-up, seven percent of patients in the pre-COVID era were lost to follow-up at the end of their first year in care, compared to 11% of patients in the COVID era which was not significantly different. In the pre-COVID era 27 (18%) patients missed their appointments by 30 days or more, including up to 90 days, compared to 9 (8%) patients in the COVID era.

In the pre-COVID era, 50 patients (34%) achieved viral suppression (VL <1000 copies/ml) at six months post-initiation of ART, while in the COVID era, 31 patients (29%) achieved viral suppression during the same period. One year post the first visit, it was concerning to note that only 41% of the pre-COVID era patients who were retained in care achieved viral suppression (viral load of less than 1000

cells/ml). Among these patients, only a half of them had a viral load of less than 50 copies/ml which is a stricter definition of viral suppression. Similarly, in the COVID era, 43% of the patients in care achieved viral suppression (VL < 1000 copies/ml) at one year post the first visit, and almost half of them had a viral load less than 50 copies/ml.

DISCUSSION

The findings of this study provide valuable insights into the impact of the COVID-19 pandemic on HIV care at the RMMCH HIV Clinic (ESRU), which is one of the larger Johannesburg clinics dedicated to providing HIV services to children and adolescents in Gauteng and has over 1600 children in active care. The clinic receives most of its patients from drainage clinics and the hospital's outpatient department. Patients are also referred via the hospital's VTP program and via in-patient referrals. Any disruption to this referral pathway negatively impacts the enrolment of patients into HIV care at this clinic.

The goals of HIV care are to; identify people living with HIV, initiate them on treatment, maintain viral suppression and sustain them on treatment. Maintaining viral suppression in people living with HIV decreases their risk of opportunistic infections, morbidity and mortality with an overall improvement in their quality of life.[15]

We observed a significant decline in the enrolment of children and adolescents into HIV care during the COVID-19 pandemic, but further research is needed to discern the pandemic's specific impact. Keeping children in care was an ongoing concern that was already noted before the pandemic. Although there was no statistical difference, approximately 11% of patients were lost to follow up during the COVID era. This is a significant number. Missed visits were less during the pandemic than before. A possible reason for this could be that there was less movement of patients between provinces due to lockdowns or a form of improved health-seeking behaviour amongst people living with HIV during the COVID pandemic period.

South Africa has recorded a significant decline in the number of new HIV infections among children since 2005. Between 2016 and 2021 (a five-year period), the annual percentage decline of new HIV infections in children ranged from 5% to 18.3% at the end of 2021. However, at the end of 2022 we recorded for the first time in 17 years a 5.2% increase in number of new infections amongst children.[16]

We reported a 27% decline in the number of children and adolescents enrolled in care during the first year of the COVID-19 pandemic compared to the year before the pandemic. Additionally, there was a decline in the number of neonates accessing care through the hospital's VTP program (p=0.025). The decline was primarily observed during the first four months of the pandemic and at the peak of subsequent waves, with children under the age of five years being the most affected. A decline in enrolment could also be due to fewer infants and children becoming HIV-infected due to better VTP programs, however, a 27% decline is greater than the expected decline from fewer new HIV infections due to improved vertical transmission prevention programs.

These findings have the potential to impede the progress already made in South Africa towards meeting the United Nation's sustainable development goal 3.2, which aims to end preventable deaths of newborns and children under the age of five by the year 2030.[7] Our finding highlights that the vertical transmission prevention programme is vulnerable and needs to be strengthened such that future critical events similar to COVID have a lesser impact.

A national decline in HIV testing was reported during the first year of the pandemic, with Gauteng being one of the provinces most affected. Similar studies conducted in other Low and Middle-income Countries (LMIC) have also demonstrated a decrease in the number of primary healthcare attendances and utilisation of HIV care and ART services.[3, 11, 17, 18] These findings underscore the need to intensify HIV testing and prevention efforts in children and adolescents during all healthcare consultations and as part of community outreach programs. These measures will help bridge the gap created by the early stages of the pandemic and most importantly, work towards achieving the United Nation's Sustainable Development Goal of ending preventable deaths and eliminating AIDS as a public threat by the year 2030.[1]

The decline in the number of neonates enrolled in care through the VTP program can be attributed to the global and national decrease in attendance for antenatal care services during the pandemic.[19, 20] A study conducted in South Africa reported a reduction in antenatal care attendance during the initial four months of the pandemic. Interestingly, the study also noted an increase in deliveries in public health facilities during the same period.[14] These findings raise concerns regarding the effectiveness of HIV testing in our healthcare facilities during periods of significant strain, such as the pandemic when there is a surge in the number of people accessing healthcare services. This disruption of antenatal HIV testing and the increased number of neonates diagnosed with HIV infection in the outpatient setting suggests that pregnant women living with HIV before the pandemic had a higher rate of vertical transmission during the pandemic which possibly alludes to poorer maternity services during the COVID-19 pandemic.

We may have missed diagnosing mothers living with HIV and their exposed children during the COVID era, emphasising the importance of HIV awareness and testing for all children and mothers presenting for child health care services. This is particularly crucial for children born during the first year of the COVID-19 pandemic. By promoting awareness and considering every mother and child healthcare visit as an opportunity to offer HIV testing, we can uphold our commitment to meeting the WHO 95-95-95 testing and treatment targets.

Paediatric HIV care is largely dependent on caregivers, whom we rely on to assist with administering medication and adherence to treatment plans. However, despite improvements in accessibility and medication formulations, high rates of loss to follow-up and poor adherence are still being reported among children and adolescents living with HIV.[20] Children under the age of five years are particularly at risk of loss to follow-up.[20] Our findings indicate that loss to follow-up is most pronounced during the first six months of enrolment into care in both study periods. This highlights the urgency for our HIV health care centres and providers to prioritise the improvement of current HIV care strategies. Additionally, there is a need for the development of strategies that focus on early ART care including support for children and adolescents who are newly enrolled in HIV care.

Studies investigating the high rate of loss to follow-up and non-suppression in HIV-infected children have reported a range of factors contributing to loss to follow-up across different groups. These studies also highlight that a significant proportion of children enrolling into HIV care fail to achieve viral suppression and are subsequently lost to follow-up shortly after initiating ART which was also reported to be true during the pandemic.[20, 21] Among younger children, there is an increased risk of loss to follow-up during the first six months following the initiation of ART. The most important factors contributing to this trend are often related to caregivers.[20] In contrast, the adolescent group presents with different factors including; lack of support, stigma, school absenteeism, unpleasant clinic visits and the impact of living with HIV on their mental health.[22]

South African guidelines applicable during the two study periods stipulated viral load testing at six months, twelve months, and every twelve months if the viral load was below 50 copies/ml. Consequently, every child living with HIV should have at least one viral load test a year. However, viral load testing in children remains inadequate in South Africa.[20]
A study conducted in KwaZulu-Natal found that the COVID-19 pandemic did not impact the frequency of viral load testing or viral load suppression rates. However, they observed a decreasing trend in viral load testing even before the pandemic. This further reinforces the need for the development of strategies to address early ART care and support for children and adolescents.[23]

Our study revealed that there was no significant difference in treatment outcomes during the two study periods. The percentage of patients lost to follow-up was similar, as were the rates of viral suppression. Furthermore, no notable difference in mortality rates was observed. It is crucial to recognize that the true effects of the pandemic on HIV care in children and adolescents may be understated during this immediate period. These effects are expected to emerge over the next five years. Consequently, it is of utmost importance to enhance the delivery of HIV healthcare services to adequately address the anticipated surge in demand that may arise in the coming years.[24]

The COVID-19 pandemic has had a profound impact on the healthcare sector as well as various other sectors globally. It has provided us with valuable lessons, highlighting the importance of preparedness and the need to establish and maintain robust systems that guarantee healthcare access and service delivery while safeguarding the vulnerable population during periods of heightened healthcare demand.[25]

Limitations

This study is based on one centre and uses data from one year prior to the pandemic which may not be a true reflection of other years prior to the COVID-19 pandemic. Due to the routine nature of the clinic, there is missing data making some conclusions more difficult to make.

CONCLUSION

The COVID-19 pandemic has had a detrimental impact on the enrolment of children and adolescents into HIV healthcare services, primarily due to restricted access to healthcare and disruptions in HIV care delivery. This challenge can be attributed in part to insufficient human resources dedicated to HIV care, the healthcare system's inability to handle sudden surges in demand, and the social implications created by the pandemic, including income loss, food insecurity, and fear of contracting the virus. The pandemic has also shed light on existing challenges in HIV care, presenting an opportunity for our nation to strengthen HIV services and strive towards ending AIDS as a public health threat.

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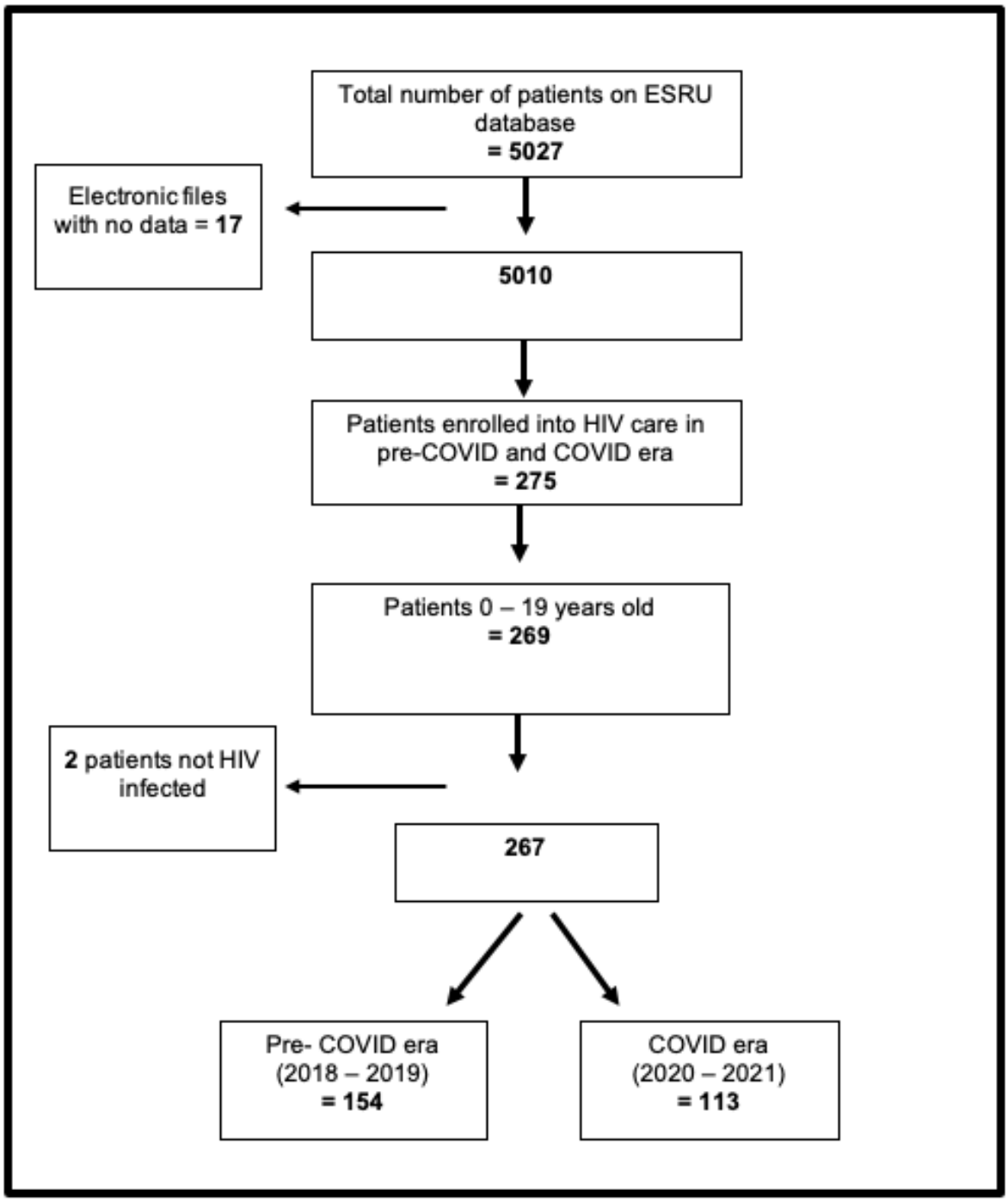
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524



525
526 ***Figure 1:*** Selection Process of The Study Population- From Initial Screening to Final
527 Cohort

528 *Values represent absolute number of patients*
529 ESRU= Empilweni Services and Research Unit.
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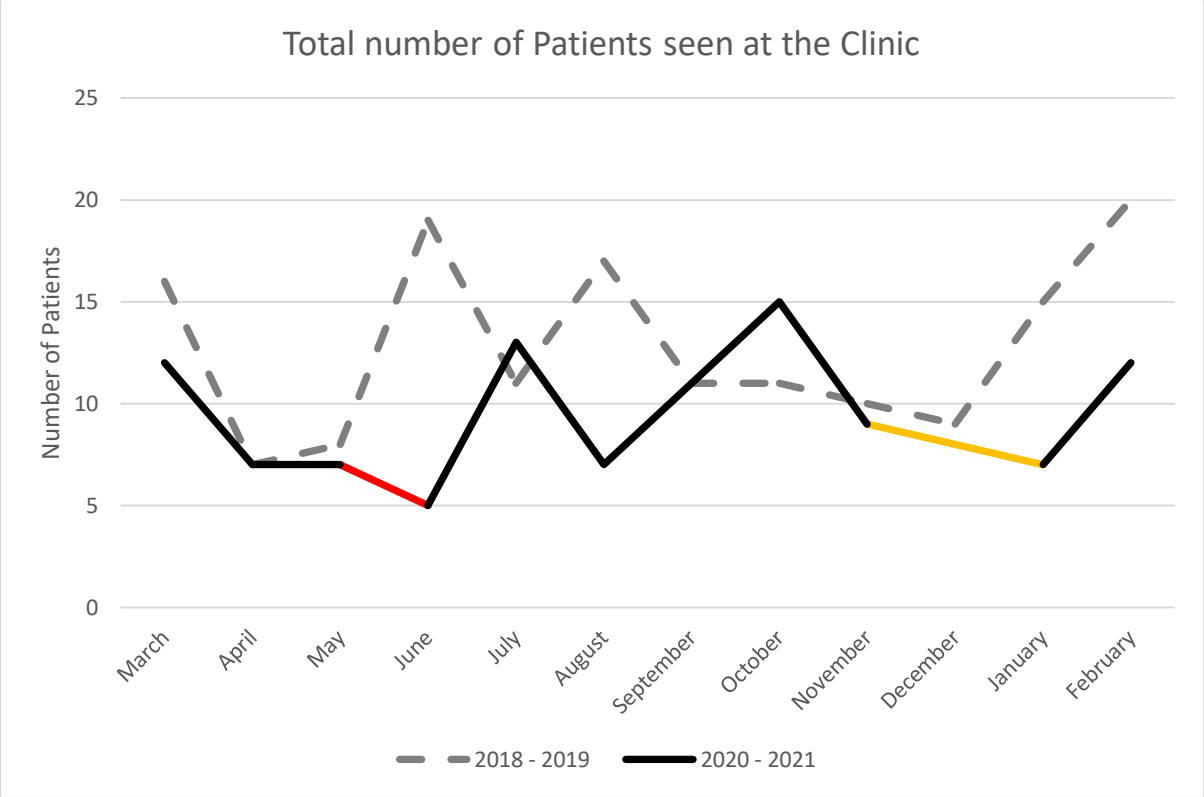


Figure 2: Total number of patients who presented to the HIV clinic during the two study periods; 2018- 2019 (pre-COVID era) and 2020- 2021 (COVID era)

Number of patients represented as absolute numbers.
Red interval corresponds to first COVID-19 wave in South Africa (D614G variant)
Yellow interval corresponds to second COVID-19 wave in South Africa (Beta variant)

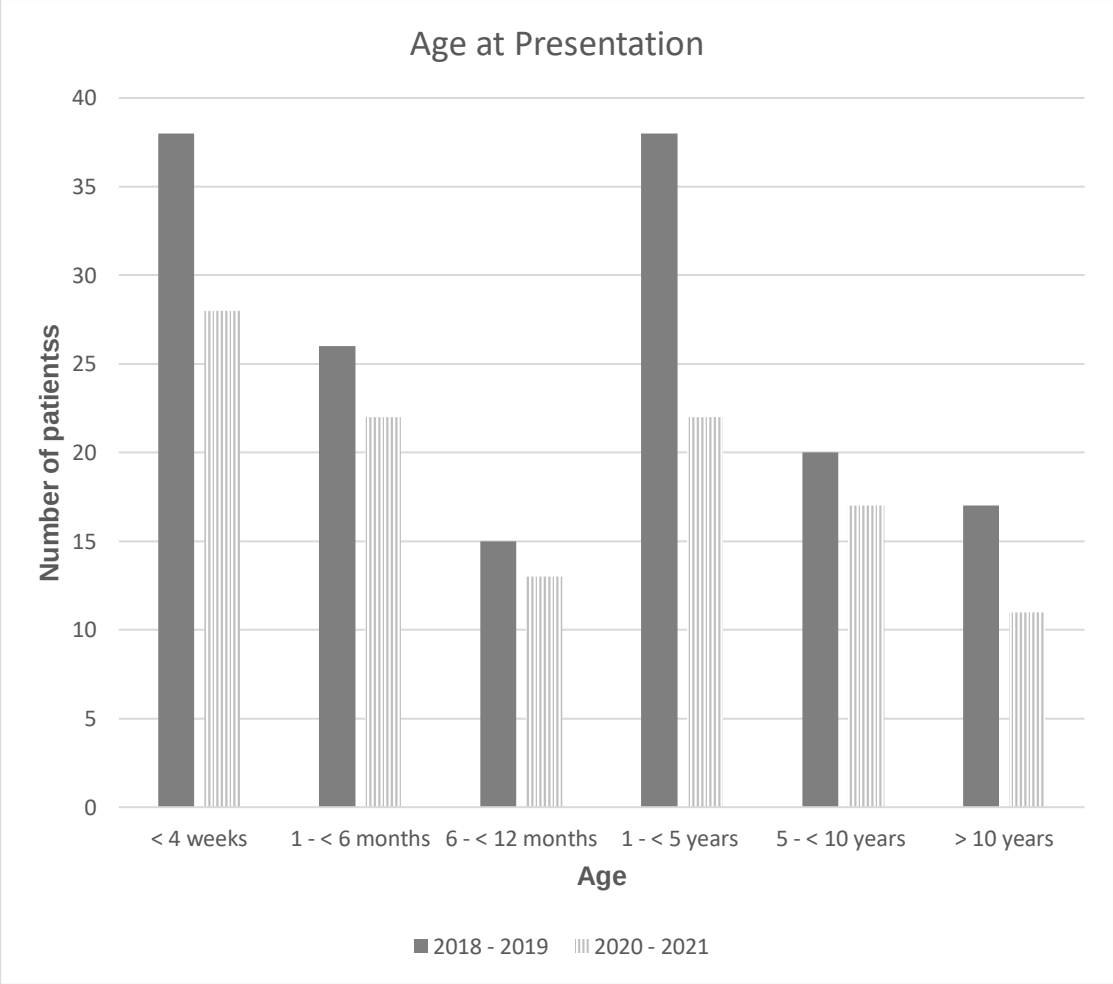


Figure 3: Age of the patients at presentation to the HIV clinic in age groups during the two time periods; 2018-2019 (pre-COVID era) and 2020- 2021 (COVID era)

Number of patients represented in absolute numbers.

554 ***Table 1:*** First visit demographics and clinical characteristics of patients at
555 presentation

		2018 - 2019	2020 - 2021	P Value
Total number of Patients		154	113	
Referral Site	VTP program	45 (29%)	20 (18%)	0.059
	Inpatients	31 (20%)	32 (28%)	
	Outpatients	78 (51%)	61 (54%)	
Age at Diagnosis	≤ 4 weeks	45 (29%)	34 (30%)	0.66
	1- < 6 months	31 (20%)	27 (24%)	
	6- < 12 months	13 (8%)	9 (8%)	
	1- < 5 years	35 (23%)	18 (16%)	
	5- < 10 years	19 (12%)	16 (14%)	
	> 10 years	11 (8%)	9 (8%)	
Duration from diagnosis to 1st visit	Transfer In	25 (16%)	20 (18%)	0.75
	Early	90 (59%)	60 (53%)	0.54
	Late	39 (25%)	33 (29%)	
Age at Presentation	≤ 4 weeks	38 (25%)	28 (25%)	0.91
	1- < 6 months	26 (16%)	22 (19%)	
	6- < 12 months	15 (10%)	13 (12%)	
	1- < 5 years	38 (25%)	22 (19%)	
	5- < 10 years	20 (13%)	17 (15%)	
	> 10 years	17 (11%)	11 (10%)	
Anthropometry	Neonates	*38 (25%)	*28 (25%)	1.0
	UWFA	63 (54%)	45 (53%)	
	NWFA	53 (46%)	40 (47%)	
WHO Clinical staging of HIV/AIDS	Neonates	*38 (25%)	*28 (25%)	0.98
	Mild disease	48 (48%)	34 (46%)	0.74
	Advanced disease	51 (52%)	40 (54%)	
Immunological Stage	Mild immunosuppression	70 (46%)	52 (46%)	1.0
	Advanced immunosuppression	59 (38%)	44 (39%)	
	Not staged	25 (16%)	17 (15%)	

556 Numbers in absolute numbers
557 VTP = Vertical Transmission Prevention program
558 Transfer in = participant already initiated on antiretroviral therapy at presentation
559 Early duration from diagnosis to 1st visit = diagnosed less than 8 days ago at presentation
560 Late duration from diagnosis to 1st visit = diagnosed 8 or more days ago at presentation
561 UWFA= Underweight for age, weight for age less than -2 SD for age and sex
562 NWFA= Normal weight for age, weight for age between -2 and +2 SD for age and sex
563 WHO = World Health Organisation
564 * Neonates which have been excluded from the rest of the population's calculations for the value

Table 2: Treatment Outcomes of patients enroled in care during the two study periods; 2018-2019 (pre-COVID) and 2020- 2021 (COVID) at one year post enrolment into care

			2018 - 2019	2020 - 2021	P Value
Total number of Patients			154	113	
Outcome at one year post enrolment into care	Lost to follow-up		11 (7%)	12 (11%)	0.53
	Death		9 (6%)	10 (9%)	
	Transferred out		32 (21%)	23 (20%)	
	In care		102 (66%)	68 (60%)	
Loss to Follow-Up	0 – 3 months		5 (46%)	6 (50%)	0.73
	3 – <6 months		2 (18%)	3 (25%)	
	≥6 – 12 months		4 (36%)	3 (25%)	
Missed appointments in the first year of ART	30 Days		50 (32%)	24 (21%)	0.043
	90 Days		27 (18%)	9 (8%)	0.024
Viral Load	6 Months	<50 copies/ml	21 (14%)	14 (13%)	0.74
		<1000 copies/ml	29 (20%)	17 (16%)	
	12 Months	< 50 copies/ml	21 (21%)	15 (22%)	0.74
		<1000 copies/ml	20 (20%)	14 (21%)	

Table 3: Neonatal diagnosis demographics and treatment outcomes

			2018 - 2019	2020 - 2021	P Value
Total number of Patients			38	28	
Referral Site	VTP program		36 (94%)	17 (61%)	0.0025
	Inpatients		1 (3%)	3 (11%)	
	Outpatients		1 (3%)	8 (28%)	
Place of Birth	RMMCH		36 (94%)	19 (68%)	0.0038
	Gauteng Clinic		2 (6%)	9 (32%)	
Maternal diagnosis	Before Pregnancy		6 (16%)	11 (39%)	0.065
	During Pregnancy		25 (66%)	10 (36%)	
	At Delivery / After pregnancy		7 (18%)	7 (25%)	
Duration from diagnosis to 1st visit	Early		35 (92%)	23 (82%)	0.22
	Late		3 (8%)	5 (18%)	
	Transfer In		0 (0%)	0 (0%)	NA
Age at Presentation	≤ 7 days		30 (79%)	20 (71%)	0.64
	8 – 14 days		4 (11%)	3 (11%)	
	15 – 21 days		2 (5%)	4 (14%)	
	22 – 28 days		2 (5%)	1 (4%)	
Birthweight	≥4000g		0 (0%)	0 (0%)	NA
	2500 - <4000g		24 (63%)	19 (68%)	0.54
	1500 - <2500g		13 (34%)	7 (25%)	
	<1500g		1 (3%)	2 (7%)	
Weight at 1st visit in relation to birthweight	Appropriate		37 (97%)	27 (96%)	1.0
	Inappropriate		1 (3%)	1 (4%)	
Outcome at 1 year post ART initiation	In care		25 (66%)	15 (54%)	0.56
	Transferred out		5 (13%)	3 (10%)	
	Loss to follow-up		5 (13%)	5 (18%)	
	Death		3 (8%)	5 (18%)	
Viral load of patients in care	6 months	<50 copies/ml	2 (8%)	3 (20%)	0.22
		<1000 copies/ml	9 (36%)	2 (13%)	
		Not done	14 (56%)	10 (67%)	
	12 months	<50 copies/ml	2 (8%)	3 (20%)	0.51
		<1000 copies/ml	5 (20%)	2 (13%)	
		Not done	18 (72%)	10 (67%)	
Loss to Follow-up	0 - <3 months		2 (40%)	2 (40%)	1.0
	3 – <6 months		2 (40%)	2 (40%)	
	≥6 – 12 months		1 (20%)	1 (20%)	

VTP = Vertical Transmission Prevention program
RMMCH = Rahima Moosa Mother and Child Hospital
Early duration from diagnosis to 1st visit = diagnosed less than 8 days ago at presentation
Late duration from diagnosis to 1st visit = diagnosed 8 or more days ago at presentation
Appropriate weight = ≥10g/kg/day weight gain if neonate >10 days, Inappropriate weight = weight less than birthweight or <10g/kg/day weight gain if neonate >10 days
ART= Antiretroviral Therapy

ETHICS CLEARANCE CERTIFICATE

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

R49 Dr M Phasha

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M220848

NAME: (Principal Investigator)	Dr M Phasha
DEPARTMENT:	School of Clinical Medicine Department of Paediatrics and Child Health Medical School University
PROJECT TITLE:	*Impact of the COVID- 19 pandemic on HIV care in a paediatric and adolescent ARV Clinic in Johannesburg: A retrospective cohort study*
DATE CONSIDERED:	2022/08/26
DECISION:	Approved unconditionally
CONDITIONS:	
NOTE:	If contact information regarding student study participants is required, please contact the Registrar's office - <Nicoleen.Potgieter@wits.ac.za>
SUPERVISOR:	Dr G Sorour and Professor K-G Technau
APPROVED BY:	Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	2022/11/21

This Clearance Certificate is valid for 5 years from the date of approval. An extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office secretariat on the 3rd floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated from the research protocol as approved, I/we undertake to submit details to the Committee. **I agree to submit a yearly progress report**. When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in **August** and therefore reports and re-certification will be due in the month of **August** each year. Unreported changes to the study may invalidate the clearance given by the HREC (Medical).

Signature of Principal Investigator _____ Date _____

RESEARCH PROTOCOL

Title:

Impact of the COVID-19 Pandemic on HIV Care in a Paediatric and Adolescent ARV Clinic in Johannesburg:
A Retrospective Cohort Study

Student: Dr Masello Phasha
Student Number: 358603
Degree: Master of Medicine in Paediatrics and Child Health

Supervisors:

Dr Gillian Sorour, Paediatric Infectious Diseases, Rahima Moosa Mother and Child Hospital

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NOMENCLATURE

AIDS	- Acquired Immunodeficiency Syndrome
ART	- Antiretroviral Therapy
ARV	- Antiretroviral
COVID- 19	- Coronavirus disease 2019
ELISA	- Enzyme- linked immunosorbent assay
ESRU	- Empilweni Services and Research unit
HIV	- Human Immunodeficiency Virus
JHB	- Johannesburg
PCR	- Polymerase Chain Reaction
PLWHIV	- People Living with HIV
PMTCT	- Prevention of Mother to Child Transmission
RMMCH	- Rahima Moosa Mother and Child Hospital
SA	- South Africa
SARS-CoV-2	- Severe Acute Respiratory Syndrome Coronavirus 2
TB	- Tuberculosis
VL	- Viral load
WHO	- World Health Organisation

INTRODUCTION

South Africa reported the first case of Human Immunodeficiency Virus (HIV) infection in 1982 when it was initially thought to be limited to homosexuals and recipients of blood transfusions [26].

The epidemic became of particular concern to the paediatric population in the 1990s when HIV was first detected in pregnant women and there was subsequent spread to the paediatric population mainly through vertical transmission from mother to child during the antenatal, perinatal and post-natal period mainly through breastfeeding [26].

South Africa has the biggest HIV epidemic in the world with 7.8 million (>12%) of its 59 million population documented to be living with HIV at the end of 2020. Globally there are now approximately two million children living with HIV and it is reported that 310 000 of these children (age 1- 14 years) are living in South Africa and that less than half of them are on antiretroviral therapy (ART) [27].

There have been significant advances in the prevention of new HIV infections in children mainly through the prevention of mother to child transmission of HIV program (PMTCT), with 97% of HIV infected pregnant women receiving ART for PMTCT in 2020 and over 52000 new HIV infections averted due to PMTCT [27].
HIV related illnesses however are still among the leading causes of infant morbidity and mortality in our country [2].

In March 2020, South Africa recorded its first case of the novel Coronavirus in Natal. The government soon after instituted a national lockdown on 27 March 2020. The aim of the lockdown was to curb transmission of the virus now called SARS-CoV-2

and thereby protect those most vulnerable to severe disease – the elderly and immunocompromised- and to protect healthcare services from being overwhelmed. The lockdown was unfortunately accompanied by unforeseen negative consequences for the provision of other health care services and for the well-being of children who were thankfully largely spared severe disease due to SARS-CoV-2 infection [9].

At the beginning of the COVID-19 pandemic national lockdown there was a shift of focus and resources from most health care services to the prevention, containment, and management of SARS-CoV-2 infections. This resulted amongst other things in pregnant and breastfeeding women and at-risk children missing routine HIV testing and initiation onto antiretroviral therapy when indicated [28].
The disruption of child health and antenatal care services by the COVID-19 pandemic especially during the lockdown months meant that fewer children had access to basic primary health care services with possible reversal of milestones in the advancements of HIV care in South Africa [28].

Epidemics in the past such as Ebola, Smallpox, Polio, HIV and Swine flu have resulted in high levels of anxiety in parents and patients due to concerns of becoming infected with subsequent severe disease or even death. They indirectly affect children's development and health due to parents socially isolating their children and not attending routine clinic visits with resultant negative consequences to schooling and to mental and physical health [29]. It is possible that the COVID-19 pandemic has had a similar effect especially because of the high morbidity and mortality rates reported globally.

For children living with HIV the initial concern that people living with HIV may be at an increased risk of suffering severe disease from COVID-19 infection, with resultant restriction of movement and other lockdown measures has put their health at risk [30]. Their wellbeing has been compromised either directly by them limiting access to healthcare services or indirectly by the effects of the pandemic on food security and the inequalities of poverty [31].

Retention in care has been reported to be a major issue in the management of HIV infection in children even before the COVID-19 pandemic despite treatment being widely available and accessible [16]. It is presumed that the co-existence of the HIV epidemic with the COVID-19 pandemic has resulted in a significant compromise in HIV care of children and that the effects maybe noted for as long as the next 5 years [31] .

The ongoing provision of HIV care services is important in ensuring the health of all HIV infected individuals while working towards achieving the global 90:90:90 HIV targets which are that 90% of people living with HIV know their status, 90% of them are receiving ART and that 90% of those on ART are virally suppressed, to keep the HIV epidemic controlled [32].

In a country such as South Africa which has such a high burden of children living with HIV, the continued care and uptake of new patients should remain a priority alongside the management of the pandemic.

It is therefore important to assess if the COVID-19 pandemic has had an impact on HIV care in our paediatric population. The aim of this study is to highlight the

consequences of the COVID-19 pandemic and help guide future management strategies and policies.

LITERATURE REVIEW

HIV services during the COVID-19 pandemic

The COVID- 19 pandemic has impacted global health care service delivery and the redistribution of health care resources in response to the pandemic in an attempt to curb the spread of the SARS-Cov-2 infections has negatively affected health care including through impeding the access to primary public health programs, including HIV care services [33].

There was an almost 50% decline of access to HIV services reported in KwaZulu-Natal during the pandemic with the largest decline reported at the beginning of the national lockdown which largely affected HIV testing and initiation of ART at local clinics [11].

Approximately 28000 South African HIV community health workers were diverted from their HIV outreach programs to be part of the COVID-19 symptoms screening teams. This left a notable gap in the HIV care services in the communities during the initial period of the COVID-19 pandemic in South Africa [9].

In an article that analysed differentiated service delivery for HIV treatment during the COVID-19 pandemic, authors found that the pandemic has mostly affected newly diagnosed patients including their access to HIV prevention services, testing, and initiation onto ART [32].

However, little data is available on the effect of the Covid-19 pandemic on HIV care services in children.

Child healthcare during the Covid-19 pandemic

The ongoing health care of children is important as we work towards achieving the Sustainable Development Goals which include decreasing under 5 mortality and achieving good health for all. The effects of the Covid-19 pandemic on child healthcare have been observed throughout communities in sub-Saharan Africa. The greatest impact is thought to have been felt by children from poorer communities [31].

The institution of the national lockdown in South Africa and the closure of schools as part of the measures to manage the pandemic posed an increased risk of morbidity and mortality from infectious diseases in children. Child health care programs were affected, including school programs that are aimed at prevention, screening, and management of vaccine preventable infectious diseases amongst children [31]. During this lockdown period, children who are dependent on meals provided at schools were exposed to hunger, malnutrition, poor growth, and development [29].

Alongside the disruption of school services and food programs during the national lockdown, there was a noticeable decline of children's access to immunisations mainly because of missed appointments during isolation, relocation to homes outside of usual place of residence and by avoiding health facilities because of fear of contracting COVID-19 infection [31].

Children's immunisation visits provide important health care promotion opportunities as during these visits in addition to actual administration of immunisations for vaccine preventable diseases, children's growth is monitored and they are screened for diseases including HIV testing and initiation of antiretroviral therapy where necessary and appropriate.

The observed disruption of children's healthcare programs during the pandemic is concerning and it can be presumed that we will notice a decline in the number of newly diagnosed children accessing HIV care services during the pandemic period when compared to the period prior to the pandemic. We can also expect to notice a surge in morbidity and mortality from HIV related infections especially in newly diagnosed HIV infected children who may have missed their clinic visits during the COVID-19 pandemic's national lockdown in South Africa.

Covid-19 and HIV co-infection

The co-existence of the HIV epidemic and the COVID- 19 pandemic has challenged the health care sector and revealed gaps in health care provision. HIV infection was thought to be a risk factor for severe disease from SARS-Cov-2 infection at the beginning of the pandemic largely because HIV causes immunosuppression [34]. A study in the Western Cape showed that there was an increased mortality from COVID-19 infection for adults living with HIV [35].

Studies have been conducted to assess the interaction between COVID- 19 and HIV but there is still insufficient data to establish the interaction and this gap highlights the need for further research and the need to strengthen current HIV care services [36].

The goals of HIV care is to; identify people living with HIV, initiate them on treatment, maintain viral suppression and to sustain them on treatment, we therefore need to establish ways of maintaining these goals while dealing with the pandemic [15].

The youth living with HIV are reported to be facing multiple challenges during the COVID- 19 pandemic, which include loss of income and mental health difficulties which has affected their adherence to treatment [37].

A study which looked at HIV and Covid disease found that in people living with HIV, COVID- 19 infections rate were low and caused a mild disease course in people on ART, virally suppressed and with CD4 count of more than 200cells/microlitre [30].

A review found that there is currently no evidence to suggest that HIV infection puts one at an increased risk for Covid-19 infection (6).

There is great anxiety experienced by people living with HIV in regards to their presumed increased risk of severe COVID-19 disease, it is for this reason that we will most probably find that there was a decline in follow up of old patients during the pandemic.

AIMS AND OBJECTIVES

AIMS

To assess the impact of the COVID-19 pandemic on HIV care in the Paediatric and Adolescent ARV Clinic at Rahima Moosa Mother and Child Hospital (RMMCH) by comparing components of HIV care data of new patients retained in care before and during the pandemic.

OBJECTIVES

1. To compare the characteristics of new patients referred to the Paediatric and Adolescent ARV clinic at Rahima Moosa Hospital in the year before (March 2018 – March 2019) and the first year of the COVID-19 pandemic (March 2020 – March 2021) in terms of:
    a) Absolute numbers of new patients seen
    b) Duration from diagnosis and referral to initiation of ART and the reasons for delay where applicable
    c) Age at presentation
    d) Clinical features, anthropometry (WHZ BMI), WHO stage and immunological stage at presentation

2. To assess the first twelve months of care for patients initiated on ART in the same two periods above in terms of adherence to treatment plans and appointments, loss to follow up, level of viral suppression and mortality.

The working hypothesis of the study is that the COVID-19 pandemic has had a negative impact on HIV care in children and as a result we will most probably find

that we had a decline in numbers of patients newly diagnosed with HIV and referred to the HIV clinic during the first year of the COVID-19 pandemic.

METHODS

STUDY DESIGN

The study will be a retrospective cohort study that aims to describe the changes in patterns of HIV care at the Rahima Moosa paediatric HIV clinic during the COVID-19 pandemic when compared to time before the pandemic.

The study will draw its data from a prospectively collected database which is maintained in the clinic.

STUDY SITE

The study will take place at the Rahima Moosa Mother and Child Hospital's Paediatric HIV Clinic, also known as Empilweni Services and Research unit (ESRU) which is one of the larger paediatric HIV clinics in South Africa that currently is serving the majority of the Westrand, parts of Soweto and some of the north of Johannesburg.

The clinic receives referrals from the paediatric and neonatal wards at RMMCH, the hospital's outpatient's department and from the local clinics in its drainage areas.

The clinic ran uninterrupted during the COVID- 19 pandemic without any staff or drug shortages.

The clinic provides multidisciplinary team management of patients. The team includes the following professionals: doctors, nurses, social worker, dietician and

rehabilitative services from physiotherapy and occupational therapy where necessary. The clinic manages neonates, children and adolescents living with HIV. The adolescent clinic sees adolescents up until the age of 18 years and beyond if needed, but for the purpose of this study only data of patients aged 0 – 18 years will be included.

Adolescent patients seen at the clinic have been diagnosed at a younger age and are almost all exclusively infected though vertical transmission.

The daily management services at the clinic include assessment of newly diagnosed HIV infected patients alongside with their caregivers, initiation of HIV treatment, regular follow up of patients on ART, including those on second and third line treatment. The clinic also monitors for and manages patients with complications that may arise.

STUDY POPULATION

The patients aged 0-18 years attending the ART clinic at Rahima Moosa hospital as new referrals.

INCLUSIONS

1. Patients aged 0-18 years referred to and seen at the HIV clinic during the period 01 March 2018 – 01 March 2019 and 01 March 2020 – 01 March 2021.

EXCLUSIONS

1. Patients whose parents refused data sharing consent.

DATA COLLECTION

Data is collected from the patient's hospital records at every consultation and entered onto the ESRU database which is hosted on the University of the Witwatersrand REDCAP platform [12].

An application will be made to the electronic gatekeeper to grant us access during the study period to collect the necessary data for the study which will be received in a de-identified format and exclusively used for the purposes of conducting the research study.

The data requested from the existing ESRU database for the identified patients who meet the study's inclusion criteria will be collected using a data collection sheet for each patient, see appendix 1 and appendix 2.

DATA ANALYSIS

Characteristics of new patients

The aim is to compare the characteristics of new patients referred to the clinic between the periods; March 2018 – February 2019 and March 2020 – February 2021 as follows:

Absolute number of new patients

We will quantify the actual number of how many new patients were seen from the clinic's database.

Duration from diagnosis to initiation of ART

We will measure the period from diagnosis to initiation of ART in days and classify depending on days from referral to presentation to the clinic or consultation in the ward if it was an inpatient referral. Patients will be categorized into two groups: early initiation (equals to or less than seven days) and late initiation (more than seven days).

Age at presentation and demographic features

We will note the age at presentation and categorize it in three groups: under one year (< 12 months), one to five years (12- 60 months) and above five years (> 60 months). Other demographic features will include gender and nature of caregiver (biological parent/ caregiver who is not the biological parents).

Clinical features at presentation

We will use weight for height standard deviations and mid upper arm circumference to classify each patient under 5 years of age and we will use BMI for patients above 5 years of age to assess their nutritional status.

Assessment of HIV care

The aim is to assess the response to HIV care for patients initiated on ART in the same two periods as follow:

Adherence to appointments and loss to follow up

We will assess the visit schedule for each patient and check if they have honoured appointments at the time they were scheduled to come, and if they missed the appointment we will determine how long after the scheduled date they presented.

Patients will be classified as:

1) Death (timing will be described)
2) Loss to follow-up (no visits after a certain date in the absence of transfer out)

   Loss to follow-up will be categorized as

   a) No linkage (no contact after the first interaction)
   b) Early (first follow-up visit done but lost to follow-up before six months of care)
   c) Late (after six months of care)

3) No loss to follow up

   a. Full attendance to visits
   b. Poor visit attendance (a gap of > 30 days late for a scheduled appointment at least once)

Level of viral suppression

We will use the identified patient's viral load (VL) results from the database to assess:

1) VL at ART initiation where available
2) Compliance with VL testing schedule
3) Six and twelve month VL suppression rates (percentage with VL <1000 copies/ml and <50 copies/ml)
4) Time to first VL <1000 copies/ml and <50 copies/ml

Descriptive statistics will be used to describe the data: Frequencies and percentages for categorical data and medians, and interquartile ranges for continuous data.

When comparing the characteristics above between the groups, we will use t-test for continuous data and chi-square for categorical data. Kaplan Meier analysis will be done to compare death and loss to follow-up between the two periods.

ETHICS

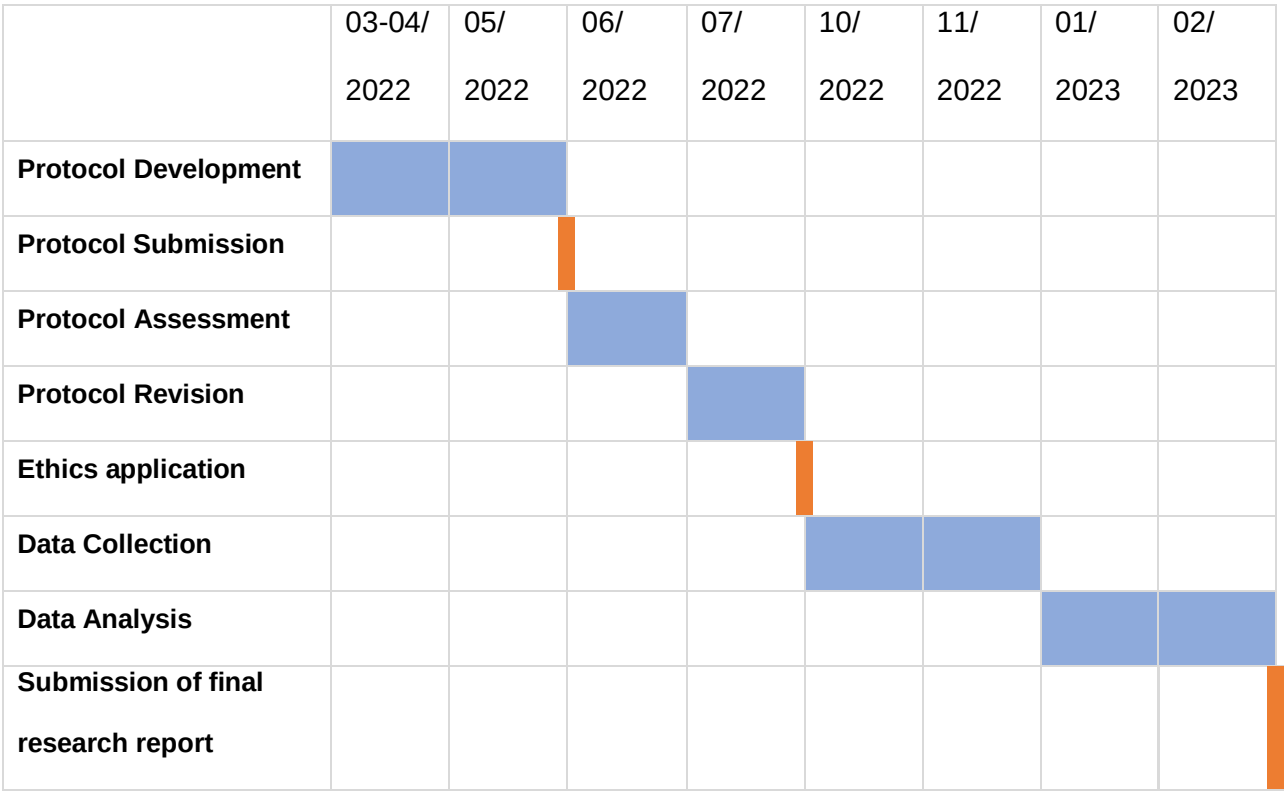
Permissions to conduct the research study at RMMCH will be requested from the hospital's CEO office and an application to conduct the study will be made to The Faculty Graduate Studies Committee and the Human Research Ethics committee of the University of the Witwatersrand.

As this is a retrospective descriptive study, prospective patient consent to use the data will not be ascertained but the clinic has since 2008 implemented a routine data sharing consent for all patients attending the clinic.

The anonymity and confidentiality of the patients will be preserved by not revealing names or any form of identity when collecting data, analysis and reporting the study findings.

STUDY TIMELINE

Gant Chart



BUDGET

All costs incurred during this study will be self-funded and are estimated at R3000 and divided as follows:

Stationary	R500
Printing of research proposal and related documents	R500
Printing of final research paper	R1 000
Travel expenses	R1000
Total	R3000

Furthermore, The Faculty of Health Sciences at the University of the Witwatersrand will be approached to assist with publication costs for any journal articles that may emanate from this research.

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Appendix 1

Data Collection Sheet

Patient Code:

Gender:

Male	Female

Age at Presentation:

< 5years	≥ 5 years

Caregiver:

Biological parent	Non biological parent

Date of Diagnosis:

Date of ART initiation:

Age at ART initiation:

	Consultation 1:	Consultation 2:	Consultation 3:	Consultation 4:
Date				
Age				
Duration on ART				
Type of ARVs				
CD4 (Date)				
Viral Load (Date)				
Weight				
Height				
MUAC				
Nutritional Status (WFH/BMI)				
WHO Staging				
Missed Appointment				
Next Follow up date				

Appendix 2

Flow Chart

Name:_____						Hosp No:_____
Date						
Age						
Weight (kg)						
Height (cm)						
BMI ≥5years						
MUAC (cm) <5years						
Head Circ <2 years						
BP						
Urine Dipstix						
Co-Trimoxazole						
MVTs						
INH						
TB Meds:						
HAART:						
Other:						
Bloods: CD4 count						
CD4 %						
POC Viral Load						
Viral Load						
WBC						
Hb						
MCV						
PLTs						
RDW						
Neutrophils (Abs)						
Creatinine						
TB investigations						
Cholesterol / Trigs						
Other						
Lab stickers (Barcodes)						
TCB						

Appendix 3

Data Sharing Consent

Consent for Data Use Version 5.1 (2018/04/07). Protocol M170778 (amendment approved 2018/07/03 adjusted 2020/07/16)- Please direct any queries to Dr Karl Technau or Sr Lesley Rose at 011 470 9421. This document must be explained to the patient/family member/guardian and child/adolescent and a copy of the signed document is to be given to the patient/family.

CONSENT FORM: USE OF CLINICAL INFORMATION

Dear Guardian, Parent and Patient,

You/your child are currently attending Rahima Moosa Mother and Child Hospital for treatment of problems you/your child are/is currently experiencing. The Hospital not only renders treatment but is also actively involved in conducting research aimed at improving the quality of care we deliver. From time to time such research involves the use of patient records from which information is extracted. The use of such information is subject to:

1) Approval from the Committee for Research on Human Subjects (University of the Witwatersrand)
2) Anonymity i.e. the identity of the patient from whose file information is extracted is never revealed to anyone but the researcher unless specific consent is obtained to do so.

We are part of an international collaboration called IeDEA that aims to improve our knowledge about HIV/AIDS by sharing information with other sites and doing scientific analysis. We share our routine clinic information (e.g. weight and height measurements, blood test results and treatment details which are all routinely collected) with IeDEA regularly but do not include your name or any identifying details.

Part of the IeDEA work involves specific "LINKAGE" projects where we use identifying details (e.g. names or ID numbers) to match with other databases (e.g. the home affairs data or the cancer register) with the purpose of understanding patient movement between institutions and services. In the process data is transferred with high level security and only by professionals approved by the Ethics committee so that no information is accidentally released. If data is matched with other databases, only the match is reported, not the person who is matched. We will then only use the information to help services improve. Only in rare cases where we see that the match may help us to help you/your child (e.g. we see that a parent of one of the children in our clinic has died) will we act or try help.

As other projects using routinely collected data arise we would like to obtain your consent to use information from your file/your child's file for the purpose of research, subject to the aforementioned conditions. If research arises that needs more detailed information we will approach you for further specific consent first. If you choose not to give consent, this will not compromise your treatment/your child's treatment in any way. If at any time you choose to withdraw consent you are free to do so and will not be prejudiced in any way. For any concerns about the approval processes followed at the University of the Witwatersrand please contact the Human Research Ethics Committee: Ms Zanele Ndlovu (Administrative Officer) 011 717 2700, zanele.ndlovu@wits.ac.za or Mr Rhulani Mkansi (Administrative Officer) 011 717 2656, Rhulani.mkansi@wits.ac.za .

PATIENT NAME:…….

A.

I.....hereby give consent for my/my child's records to be used as per the abovementioned conditions for the purposes of research:

GUARDIAN NAME and RELATION:.....

SIGNATURE:…….. DATE:.....

CHILD/ADOLESCENT:..... WITNESS:.....

B.

I.....do not give consent for my/my child's records to be used:

GUARDIAN NAME and RELATION:……..

SIGNATURE:..... DATE:.....

CHILD/ADOLESCENT:..... WITNESS:.....

SUBMISSION GUIDELINES TO THE SOUTHERN AFRICAN JOURNAL OF HIV MEDICINE

An original article provides an overview of innovative research in a particular field within or related to the focus and scope of the journal, presented according to a clear and well-structured format.

Submission status	Open
Word limit	3500-5000 words (excluding the abstract, tables, figures, graphs, and references)
Abstract	maximum: 250 words requires structural headings: Background, Objectives, Method, Results, Conclusion and What this study adds
Main text	requires structural headings, refer to the full structure 'Ethical considerations' is a sub-section in the manuscript and must include: • Name of the ethical review committee • Study approval number • Manner of consent (written, oral) for human participants • Description of measures taken to maintain the confidentiality of data • If the study was not human or animal research or the study was determined to be non-human subjects research or exempt, the authors must provide a statement with those details in this section.
References	60 or less, adhere to the **Vancouver referencing style**
Tables, figures and graphs	7 or less, adhere to the Illustrations requirements found in the AOSIS House style guide
Formatting requirements	apply the guidelines located on the **Formatting requirements page** and the **AOSIS house style guide**
Compulsory supplementary file(s)	he **Authorship, disclosure statements, copyright, and license agreement form**, **Ethical Clearance/Waiver Documentation** and any other relevant form applicable to your submission

Ethical clearance/waiver documentation	evidence of ethical clearance for the study, such as the study approval letter or certificate from the Institutional Review Board (IRB), a waiver from the IRB et cetera

Title: The article's full title should contain a maximum of 95 characters (including spaces).

Abstract: The abstract, written in English, should be no longer than 250 words and must be written in the past tense.
The abstract should give a succinct account of the objectives, methods, results and significance of the matter. The structured abstract for an Original Research article should consist of six paragraphs labelled Background, Objectives, Method, Results, Conclusion and What this study adds.

- *Background: Why do we care about the problem?* State the context and purpose of the study. (What practical, scientific or theoretical gap is your research filling?)
- *Objectives: What problem are you trying to solve*? What is the scope of your work (e.g. is it a generalised approach or for a specific situation)? Be careful not to use too much jargon.
- *Method: How did you go about solving or making progress on the problem*? State how the study was performed and which statistical tests were used. (What did you actually do to get the results?) Clearly express the basic design of the study; name or briefly describe the basic methodology used without going into excessive detail. Be sure to indicate the key techniques used.
- *Results: What is the answer*? Present the main findings (that is, as a result of completing the procedure or study, state what you have learnt, invented or created). Identify trends, relative changes or differences on answers to questions.
- *Conclusion: What are the implications of your answer*? Briefly summarise any potential implications. (What are the larger implications of your findings, especially for the problem or gap identified in your motivation?)
- *What this study adds:* What key insights into the research results and its future function are revealed? How do these insights link to the focus and scope of the journal? It should be a concise statement of the primary contribution of the manuscript; and how it fits within the scope of the journal.

Do not cite references and do not use abbreviations excessively in the abstract.

Introduction: The introduction must contain your argument for the social and scientific value of the study, as well as the aim and objectives:

- Social value: The first part of the introduction should make a clear and logical argument for the importance or relevance of the study. Your argument should be supported by the use of evidence from the literature.
- Scientific value: The second part of the introduction should make a clear and logical argument for the originality of the study. This should include a summary of what is already known about the research question or specific topic and should clarify the knowledge gap that this study will address. Your argument should be supported by the use of evidence from the literature.
- Conceptual framework: In some research articles it will also be important to describe the underlying theoretical basis for the research and how these theories are linked together in a conceptual framework. The theoretical evidence used to construct the conceptual framework should be referenced from the literature.
- Aim and objectives: The introduction should conclude with a clear summary of the aim and objectives of this study.

Research methods and design: This must address the following:

- Study design: An outline of the type of study design.

- Setting: A description of the setting for the study; for example, the type of community from which the participants came or the nature of the health system and services in which the study is conducted.

- Study population and sampling strategy: Describe the study population and any inclusion or exclusion criteria. Describe the intended sample size and your sample size calculation or justification. Describe the sampling strategy used. Describe in practical terms how this was implemented.

- Intervention (if appropriate): If there were intervention and comparison groups, describe the intervention in detail and what happened to the comparison groups.

- Data collection: Define the data collection tools that were used and their validity. Describe in practical terms how data were collected and any key issues involved, e.g. language barriers.

- Data analysis: Describe how data were captured, checked and cleaned. Describe the analysis process, for example, the statistical tests used or steps followed in qualitative data analysis.

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Results: Present the results of your study in a logical sequence that addresses the aim and objectives of your study. Use tables and figures as required to present your findings. Use quotations as required to establish your interpretation of qualitative data. All units should conform to the **SI convention** and be abbreviated accordingly. Metric units and their international symbols are used throughout, as is the decimal point (not the decimal comma).

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- Discussion of key findings: Explain how the key findings relate to previous research or to existing knowledge, practice or policy.

- Strengths and limitations: Describe the strengths and limitations of your methods and what the reader should take into account when interpreting your results.

- Implications or recommendations: State the implications of your study or recommendations for future research (questions that remain unanswered), policy or practice. Make sure that the recommendations flow directly from your findings.

Conclusion: Provide a brief conclusion that summarises the results and their meaning or significance in relation to each objective of the study.

Acknowledgements: Those who contributed to the work but do not meet our authorship criteria should be listed in the Acknowledgments with a description of the contribution. Authors are responsible for ensuring that anyone named in the Acknowledgments agrees to be named. Refer to the acknowledgement structure guide on our *Formatting Requirements* page.

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- Funding: Provide information on funding if relevant

- Data availability: All research articles are encouraged to have a data availability statement.

- Disclaimer: A statement that the views expressed in the submitted article are his or her own and not an official position of the institution or funder.

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Acknowledgements structure

Acknowledgements

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Example 8	A.B., B.C. and C.D. designed the study. A.B., D.E. and E.F. performed the xyz experiments. F.G. and G.H. performed XYZ simulations. I.H. and M.C. expressed and purified all proteins. A.B., H.J.., B.C. and C.D. analysed the data. A.B., B.C. and C.D. wrote the paper with input from all authors.
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