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The Impact of Covid-19 Lockdown on Missed Appointments Among HIV-infected Adults in Ekurhuleni District, South Africa, 2019 to 2021: An Interrupted Time Series Analysis

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Abstract

The coronavirus pandemic disrupted access to routine HIV healthcare services, affecting health systems flow, and PLHIV particularly those in less privileged communities. A quasi-experimental design study with interrupted time series (ITS) was conducted to determine the effects of the COVID-19 shutdown on the follow-up of HIV patients in the Ekurhuleni district. The study setting included Winnie Mandela Clinic, Tembisa HCC, Tembisa Main Clinic, and Esangweni Clinic. The study used a total sampling of eligible patients during the study period in the chosen facilities. Data was extracted from the Tier.net records for patients who were on antiretroviral therapy by 2019 and during the lockdown to December 2021. The hard lockdown in Tembisa HCC resulted in a proportion of 14.3% of missed appointments, which was comparatively higher than in other months. Interrupted time series analysis on the evaluation of missed appointments showed a statistical significance with a p-value of 0.049 <0.05 at Tembisa HCC compared to the other three clinics. The proportion of virally suppressed patients declined by 3.4% during the lockdown. In comparison to clinics, Tembisa HCC showed the most significant decrease (5.9%) in virally suppressed patients. There was a stronger correlation between acquiring an AIDS-defining disease and failing to attend clinic appointments.

Keywords: HIV/AIDS, COVID-19 pandemic, missed appointments, lockdown, ART adherence, viral load

Introduction

Globally, significant progress has been made to reduce the incidence and effect of the human immunodeficiency virus (HIV), and many people living with HIV (PLHIV) are now on lifesaving antiretroviral treatment (ART), and HIV-related mortality has been regularly decreasing over the last decade (UNAIDS,2022). The UNAIDS has established a 95-95-95 objective to be reached by 2030 to prolong the lives of PLHIV, provide treatment as prevention, and make progress toward ending new HIV infections. The goal is to diagnose 95% of all PLHIV, treat 95% of those diagnosed, and achieve viral suppression in 95% of those on

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treatment (UNAIDS,2022). South Africa's ART program for PLHIV is the largest globally (Moosa et. al,2019). Estimates of the percentage of 9PLHIV initiated and considered retained in care (RIC) on ART in South Africa vary from 66.9% to 72% (Massyn et. al,2020; UNAIDS,2020). Of those PLHIV RIC, 91% achieved a suppressed viral load in 2020, and the number of people dying from acquired immunodeficiency syndrome (AIDS) decreased from 181 497 (30.4% of all deaths) in 2002 to 85 154 (12.2% of all deaths) in 2021 as a direct result of ART availability (Statistics South Africa,2021).

The COVID-19 pandemic had a tremendous impact on many areas of our existence, including healthcare. During the COVID-19 pandemic, numerous countries enacted lockdowns and other public health measures to contain the virus. These efforts typically led to the cancellation or postponement of non-urgent medical appointments and procedures (Zhang et. al,2022). PLHIV constitute are part of the vulnerable groups that were affected. As HIV is a chronic condition requiring regular hospital visits for consultations, tests, pharmacy, and other services, it was expected that isolation and confinement measures would affect the care of PLHIV (Ballester-Arnal and Gil-Llario, 2020).

The emergence of the COVID-19 pandemic disrupted systems, livelihood patterns, and social stability in South Africa. As a control measure, lockdowns were put in place to prevent the spread of the virus. However, this worsened socio-economic stability, as well as the lives of PLHIV. Interruptions in routine healthcare services were a major consequence of the coronavirus pandemic, affecting many PLHIV, particularly those in less privileged communities (Campbell et.al, 2022). A high viral load was noted in patients who missed their appointments. More HIV infections were recorded daily as well as patients being reported as having low CD4 counts leading to hospitalization. Of great concern was the high HIV incidence rate noted after a survey was conducted during the lockdown. Moreover, missed appointments resulted in weakened immune systems and led to the spread of HIV due to area confinement (Burger et.al, 2020). In addition, unattended appointments about the Prevention of Mother-to-Child Transmission (PMTCT) have a detrimental effect on the unborn baby and can lead to the reversal of gains.

The World Health Organization estimated that a 6-month interruption of ART may have resulted in more than 500,000 extra deaths from AIDS-related illnesses in 2021 and an increase in mother-to-child transmission (WHO,2022). From the beginning of the lockdown, about 1,090 TB patients and 10950 PLHIV, respectively, across the South African provinces did not collect their scheduled medication (Gauteng Province Department of Health,2020). Unattended appointments pose challenges for all healthcare facilities and notably affect the operation of clinics or hospitals due to patients needing to be traced and recovered into hospitals or clinics (Abebe et.al,2020). Follow-up on PLHIV is important because HIV/AIDS cannot be cured. Patients need ART on a continuous treatment basis. PLHIV on ART receives personalized care per visit.

In April 2020, a rapid survey in Zimbabwe revealed that 19% of HIV patients were unable to refill their antiretroviral drugs or received only a partial refill (COVID-19 DSD,2020). Similarly,

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the Finmark Trust conducted a telephone-based survey in Kenya and Nigeria in April 2020, revealing that 14% of patients could not collect necessary medications (Finmark Trust,2020). In Australia (Ejima et. al,2021), where HIV care is rarely interrupted, HIV tests and Pre-Exposure Prophylaxis (PrEP) use declined. This could be attributed to lower risk behaviours or a reluctance to risk COVID-19 infection when visiting a hospital or clinic.

Defaulting presents a significant difficulty in achieving and maintaining the benefits of RIC on ART. There are two types of defaulting: those who discontinue ART and return within 89 days (early missing) and those who miss a dose while on ART (late missing). Appointments are scheduled for 2-3 weeks or 2 weeks to 89 days. Those who do not return for 90 days or more are considered lost to follow-up (LTF) (National Department of Health,2019). Loss of follow-up diminishes the immunological advantages of ART, increasing the likelihood of treatment failure, opportunistic infections, viral load increase, CD4 cell decline, drug resistance, and mortality.

Delays in care and ART commencement, as well as disruptions in services, can lead to treatment resistance and poor outcomes among PLHIV, increasing the risk of HIV transmission in the population (Katbi et. al,2021). The study aimed to assess the impact of the lockdown on follow-up appointments of HIV patients in Ekurhuleni district.

Methodology

Study design

A quasi-experimental design study with interrupted time series (ITS) was conducted to determine the impact of lockdown due to COVID-19 on the follow-up of HIV patients. This study used secondary data routinely collected and captured in the Tier.net register. Data of patients from local clinics was collected from the data extraction form. Data collection lasted for a month

Study settings and population

The study setting included four HIV clinics in Ekurhuleni district, namely Winnie Mandela Clinic, Tembisa HCC, Tembisa Main Clinic, and Esangweni Clinic. These clinics were of relevance to the study since they are close to one another and have a reasonably large number of HIV patients. The study population was all PLHIV on the ART programme at these clinics. Data was extracted from the Tier.net records for patients who started ART before the lockdown from September 2019 to September 2020 and during the lockdown from October 2020 to October 2021. The same patients were used before and during the lockdown.

Study sampling

The study used a total sampling of the eligible patients during the study period in the chosen facilities. Secondary data from Tier.net was analyzed thus there was no selection of participants. Total sampling was used for this study because ART has different characteristics and subgroups that cannot be quantified into strata such as men who have sex with men which might as well be

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associated with missing appointments. To avoid selection bias by omitting such sub-populations total sampling was used.

Inclusion criteria

The study focused on all patients who were on ART treatment before the lockdown from September 2019 to September 2020 and during the lockdown from October 2020 to October 2021. This enabled tracking changes in viral load during the lockdown. Individuals aged 18 years and above were included in the study. Only patients registered at the clinics were part of the study.

Exclusion criteria

All newly diagnosed patients on ART from the beginning of the lockdown in March 2020 were excluded. Those who already had a high viral load greater than 50 copies/ml were also excluded before the study began. This was done to eliminate any discrepancies as some patients would already have a high viral load due to antiretroviral failure

Data collection

Researcher district health department granted permission to collect data. The researcher entered data extracted from Tier.net into the Microsoft Excel 2016 data form. A monthly cohort report was analyzed to check the frequency of patients' visits. The files of the patients who missed their appointments were reviewed to confirm their viral load results.

Data collection instruments

Data extraction forms were utilized to acquire the information. The Ekurhuleni District Health Department sent a permission letter to view clinic data. Patients who skipped their appointments were reviewed using data from the ART registry (TIER.net). Data was obtained using an electronic extraction form. Tier.net's data variables included date of birth, sex, clinic, date of diagnosis, ART start date, viral load, and CD4 counts. The hard copies of the forms were preserved at the University of Pretoria to protect the privacy of the patient's data. To ensure secrecy and anonymity, file numbers were employed to identify patients.

Data analysis

Proportions were used to estimate the prevalence of HIV patients who missed their appointments. An interrupted time series analysis was used to determine the impact of the COVID-19 lockdown on the number of missed appointments and to compare the proportion with non-viral suppression before and during the lockdown for each health facility. Results were presented in tables and figures. All analyses were done using Stata version 18 software and a *p-value* < 0.05 was used to determine statistical significance.

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Ethical Considerations

Approval from the Gauteng Department of Health Ethics Committee and the University of Pretoria Health Sciences Research Ethics Committee was obtained. A non-disclosure agreement was signed by the researcher for confidentiality and privacy. The research was designed not to intentionally hurt or harm anyone by protecting their identity. Justice was made possible by avoiding bias when sampling from a larger population and not exposing participants to a research that could disadvantage them in one way or another. The research will increase awareness and knowledge of the effects of missed appointments on patients' health and encourage self-drive on adherence to medication and review dates. The waiver of patient informed consent was sought as secondary data was used in the project.

Results

1. To determine the proportion of HIV patients who missed their appointments before and during lockdown

Table 1: Proportion of HIV patients who missed their appointments before and during lockdown

	Booked and missed ART appointment			
	Before Covid-19 lockdown‡		**During Covid-19 lockdown†**	
	Booked	**Missed**	**Booked**	**Missed**
Health Facility	**N**	**N (%)**	**N (%)**	**N (%)**
Winnie	2486	361(14.5)	3015	372 (12.3)
Esangweni	1752	410 (23.4)	2547	358 (14.1)
Tembisa HHC	904	164 (18.1)	1431	204 (14.3)
Tembisa Main Clinic	1278	233 (18.2)	1730	243 (14.0)
All clinics	6420	1168 (18.2)	8723	1177 (13.5)

‡Before the lockdown (up to February 2020); †During the lockdown (March 2020 to December 2021

2. To evaluate the effectiveness of the COVID-19 lockdown on the number of missed appointments among HIV patients using Interrupted time series analysis

In this study, we aimed to understand the dynamics of missed ART clinic appointments by clients monthly, particularly in the context of the Covid-19 lockdown. The relationship between the time and the proportion of missed appointments is represented through this model:

$$Y_t = \beta_0 + \beta_1 T_t + \beta_2 X_{1t} + \beta_3 X_{1t} T_{1t} + \epsilon_t$$

where Y_t signified the outcome variable, that was, the proportion of clients who missed their scheduled appointments per month. The model started with an intercept, $\beta_0$representing the baseline proportion of missed appointments before considering any temporal changes or the impact of the lockdown. The coefficient β_1 captured the trend or slope of missed appointments

over time, until the lockdown's initiation, $T_t$indicating the elapsed time since the study's commencement. The introduction of the Covid-19 lockdown policy was hypothesized to induce a sudden change in the proportion of missed appointments, which is modelled through β_2 and an indicator variableX_{1t}, the latter distinguishing between the pre-lockdown (0) and post-lockdown (1) periods. Furthermore, β_3 is designed to assess the interaction between the time and the lockdown period, capturing any difference in trends between the pre-and post-lockdown periods. This interaction term$X_{1t}T_{1t}$, allowed us to examine whether the slope of missed appointments was altered following the lockdown, providing insights into its temporal effects on patient attendance behaviour. Through this model, we seeked to dissect the nuanced impact of the Covid-19 lockdown on the pattern of missed ART clinic appointments, distinguishing between immediate changes and longer-term trends.

Table 2: A summary of the ITSA on the proportion of clients who missed their booked ART clinic appointments per month at Winnie clinic

Indicator	Coefficient (95% CI)	p-value
Pre-Covid-19 lockdown (Jan 19 – Mar 20) trend,	-0.0042 (-0.0086, 0.0001)	0.057
1st Implementation month (Apr 20) sudden change in level	0.049 (-0.0240, 0.1221)	0.181
Slope change (pre- vs during - Covid-19 lockdown),	0.0007 (-0.0053, 0.0066)	0.822

Table 3: A summary of the ITSA on the proportion of clients who missed their booked ART clinic appointments per month at Esangweni clinic

Indicator	Coefficient (95% CI)	p-value
Pre-Covid-19 lockdown (Jan 19 – Mar 20) trend,	-0.0008 (-0.0128, 0.0112)	0.891
1st Implementation month (Apr 20) sudden change in level	0.0331 (-0.1217, 0.1878)	0.666
Slope change (pre- vs during- Covid-19 lockdown),	-0.0106 (-0.0247, 0.0034)	0.134

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Table 4: A summary of the ITSA on the proportion of clients who missed their booked ART clinic appointments per month at Tembisa HHC

Indicator	Coefficient (95% CI)	p-value
Pre-Covid-19 lockdown (Jan 19 – Mar 20) trend,	-0.0079 (-0.0175, 0.0016)	0.100
1st Implementation month (Apr 20) sudden change in level	-0.0065 (-0.0793, 0.0663)	0.857
Slope change (pre- vs during - Covid-19 lockdown),	0.0099 (0.00003, 0.0199)	0.049

Table 5: A summary of the ITSA on the proportion of clients who missed their booked ART clinic appointments per month at Tembisa Main clinic

Indicator	Coefficient (95% CI)	p-value
Pre-Covid-19 lockdown (Jan 19 – Mar 20) trend,	-0.0013 (-0.0104, 0.0078)	0.777
1st Implementation month (Apr 20) sudden change in level	-0.0654 (-0.1419, 0.0111)	0.091
Slope change (pre- vs during- Covid-19 lockdown),	0.0055 (-0.0053, 0.0162)	0.309

3. To compare the proportion of HIV patients with viral load suppression before and during the lockdown

Table 6: Proportion of HIV patients with suppressed viral load before and during Covid-19 lockdown

	Viral load test			
	Before Covid-19 lockdown‡		**During Covid-19 lockdown†**	
	Viral load test done	**Viral load suppressed**	**Viral load test done**	**Viral load suppressed**
Health Facility	**N**	**N (%)**	**N (%)**	**N (%)**
Winnie	1888	1179(62.8)	2012	1228 (61.4)
Esangweni	1818	1112 (61.4)	1306	769 (59.1)
Tembisa HHC	1114	676 (60.8)	1080	590 (54.9)
Tembisa Main Clinic	1123	702 (62.7)	932	540 (58.4)
All clinics	5943	3669 (61.9)	5330	3127 (58.5)

‡Before the lockdown (up to February 2020); †During the lockdown (March 2020 to December 2021

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Discussion

The study evaluated the effects of COVID-19 lockdown measures on the follow-up of HIV patients in Ekurhuleni. There was relatively a large number of missed appointments during the hard lockdown compared to other months with Tembisa HCC (Table 1) having the greatest proportion 14.3%. A higher chance of contracting an AIDS-defining illness is linked, on its own, to missing clinic appointments (Ridgeway et. al,2018). Moreover, COVID-19 has impacted the amount and caliber of HIV treatment that medical facilities can offer, which has resulted in a breakdown in HIV testing and care continuation. Increased clinical, psychological, and structural barriers to receiving HIV treatment services, such as higher transportation costs and lockdown restrictions, as well as the perception of increased COVID-19 exposure from health facilities, could be the cause of the high rate of missed appointments among PLHIV during this period, as reported by Nalubega *et al*. (2021) and Linnemayr *et al.* (2021).

A study in Zimbabwe found that women on ART had difficulty accessing medication during the COVID-19 lockdown due to transportation difficulties, COVID-19 restrictions, police abuse, short medication supply, clinical check-up disruptions, involuntary ART non-adherence, and a lack of personal protective equipment (PPE) (Nyashanu et. al,2021).

With major emotional and financial effects that result in lower ART adherence, the COVID-19 epidemic has disproportionately affected the poorest people and communities (Bogart et. al,2021). In the first month of lockdown, nearly half of respondents to a nationally representative survey said they ran out of money for food, with those residing in informal settlements experiencing the most financial hardship (Schotte and Zizzamia,2021). In a study conducted by Seyed et al (2023), the pandemic had a significant impact on healthcare delivery, particularly in-person visits and clinical follow-up services. However, telemedicine helped ameliorate the situation significantly.

The results from the evaluation of the effectiveness of the COVID-19 lockdown on the number of missed appointments among HIV patients using Interrupted time series analysis (Table 4) show that there was a statistical significance with a *p-value* of $0.049 < 0.05$. This was noted at Tembisa HCC when analyzing slope change between pre-and during lockdown. This is an indicator that missed appointments had an impact on the patients in this clinic. In addition to clinical factors, provider attitudes, and structural problems (such as lengthy wait times for medical attention at clinics), Bisnauth *et al*. (2021) highlighted that social-interpersonal factors, fear, and unstable income are some of the reasons why people disengage from healthcare.

Individuals with a comprehensive awareness of their HIV status are more likely than those with incomplete information to adhere to treatment regimens. According to some research, disengagement from care can be caused by a variety of individual variables, including prevalent mental health conditions like depression and unfavourable attitudes toward healthcare (Bisnauth *et al*. 2021).

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The pandemic has had a significant impact on all aspects of life for PLHIV caused by COVID-19. The virus's confinement and containment procedures marked a turning point for both individuals and society. The evolution of healthcare has led to increased reliance on phone consultations and delayed treatment for various health issues. The pandemic has had a considerable impact on healthcare users, among others. Chronically ill people, particularly those with HIV, have been disproportionately affected by pandemic measures due to their inability to get healthcare (Chenneville et. al,2020).

In general, Key Populations (KPs) were unable to access facilities due to movement restrictions, e.g., they did not have authorization letters that were needed to allow movements during the lockdown period, fear of contracting COVID-19, threats to confidentiality and privacy due to the possibility of unintentionally disclosing their HIV status to the police, and service unavailability due to preoccupation with the implementation of initiatives to conduct COVID-19 screening (Moyo et. al,2022; Macharia et. al,2021).

The number of patients who were virally suppressed (Table 6) decreased significantly during the lockdown with a 3.4% drop. Tembisa HCC had the greatest decline of 5.9% compared to the other clinics. It was expected of this as the number of missed appointments also increased during the same period. While viral load is not a reliable predictor of patient adherence, it can serve as an early screening tool (Nyashanu et. al,2021). According to Ridgway (2020), PLHIV may have evolved to preserve their health during the epidemic. However, further research is needed to understand the reasons for this shift in treatment adherence and the involvement of adverse drug reactions (ADRs). Poor treatment experiences may lead to reduced drug adherence rates due to reluctance or distrust among patients. Although contemporary ART has low rates of adverse effects, patients should be educated about the likelihood of transient or typical side effects that can be treated by changing medications. Missed appointments by HIV patients are associated with delayed viral load suppression, increased HIV burden, an increase in HIV-related opportunistic illnesses, and death (Pence et.al,2019). If a patient's viral loads are unsuppressed, the chance of mutations is high, possibly leading to drug resistance (Meintjes et .al,2017).

During the lockdown, few patients were virally suppressed at Winnie and Esangweni clinics respectively. This was unexpected as these two clinics had increased appointment attendance during this period. This could be due to people not adhering to their medication or area confinement that may lead them to be reinfected. COVID-19 legislation led to financial constraints for HIV treatment providers, causing them to charge lower fees and work fewer hours (Chenneville et. al,2020). Food insecurity prevented some KPs from accessing and adhering to ART therapy (Ridway et.al, 2020; Macharia et. al,2021). COVID-19 had a significant impact on HIV treatment services initially, but evidence-based interventions improved access, linkage, utilisation, and retention later on. KPs may face barriers to accessing evidence-based interventions due to social stigma, discrimination, violence, and criminalization, making them more vulnerable (Bukenya et. al,2019).

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Restrictions disproportionately affect vulnerable subpopulations that rely on social, economic, and medical support. These disruptions can worsen challenges such as food insecurity, gender-based violence, medical condition management, and drug use. Individuals living with or at risk of HIV infection are vulnerable to these consequences, despite good management. The restrictions may have limited the access to clinics and services necessary for HIV prevention and treatment. Without access, individuals may lack diagnostic testing, viral load testing, ART, PrEP, safe injection materials, condoms, and other services needed to manage pathogens in vulnerable areas. COVID-19 limits have led to decreased access to HIV treatment and prevention services in many countries. This has been linked to worsened HIV outcomes, including viral load rebound and progression to AIDS (Musuka and Dzinamarira,2021).

Strengths and limitations of the study

The use of a quasi-experimental research design to assess the impact of the COVID-19 lockdown on the follow-up appointments of HIV-infected adults in Ekurhuleni district. The objectives of the study were met during data collection. Social aspects of the impact of lockdown on HIV patients were not covered in the study as the focus was on numerical data. Possibility of bias as some clinics use manual registers and they may not be updated daily. The data could not be grouped according to gender as some factors were not disaggregated according to it. This could reveal additional insights into missed appointments.

Conclusion

The COVID-19 lockdown did have an impact on the appointments of PLHIV in two of the Ekurhuleni clinics. The number of missed appointments increased in Tembisa HCC and Tembisa Main clinic during the lockdown period. Though Winnie Clinic and Esangweni Clinic had fewer missed appointments during the lockdown period, the number of virally suppressed patients was also less in those clinics. Tembisa HCC and Tembisa Main clinic had fewer patients who were virally suppressed. It can be concluded that other factors such as non-adherence, reinfection, and area confinement could have contributed to fewer people being virally suppressed especially in clinics where clinical attendance was good.

Recommendations

The district should have programmes in place that will cater for chronic patients to have access to their medication in cases of emergency such as a pandemic. Telemedicine should be highly encouraged to do the tracing of those patients who miss their appointments. More patients should be decanted to different collection facilities to collect medication so that they would not be overcrowded in the clinics. In the event of future lockdowns, patients can be assigned staggered times to visit clinics in smaller groups, reducing their chance of getting other infections. Artificial Intelligence can also be used to predict pandemics in future.

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SN conceived the study design, selected indicators for analysis, and acquired the data. SN and MLM analysed/interpreted the data. SN wrote the article. MLM provided critical revision and final approval. The authors did not have funding to conduct the study The data supporting the results are available from the authors upon reasonable request. The views and opinions expressed in this article are those of the authors and are the product of professional research. It does not necessarily reflect the official policy or position of any affiliated institution, funder, agency, or that of the publisher. The authors are responsible for this article's results, findings, and content.

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