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THE PREVALENCE OF *CRYPTOCOCCAL* MENINGITIS IN HIV POSITIVE PATIENTS THAT ARE ON ANTIRETROVIRAL TREATMENT. A RETROSPECTIVE QUANTITATIVE STUDY PERFORMED AT DURBAN ADDINGTON HOSPITAL IN KZN, SOUTH AFRICA.

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ABSTRACT

Introduction
HIV remains a global health challenge, with approximately 37.7 million people living with HIV in South Africa by 2020 (WHO). Among HIV-positive individuals, Cryptococcal meningitis (CM), a severe opportunistic infection, is a leading cause of morbidity and mortality. Despite the widespread use of antiretroviral therapy (ART), CM continues to be a major concern, especially in sub-Saharan Africa, where HIV prevalence is high.
Aims and Objectives: This study aimed to determine the prevalence of CM in HIV-positive patients on ART at Durban Addington Hospital between January and July 2022. The findings are intended to inform health practitioners on prevention strategies and treatment needs for this group.

Methodology
A retrospective quantitative approach was employed, analyzing medical and laboratory data from 137 HIV-positive patients. Cerebrospinal fluid (CSF) samples were tested for Cryptococcus neoformans, and the results were correlated with CD4 count and viral load data. This approach facilitated a statistical exploration of CM prevalence in HIV patients on ART.

Results
The study found that the majority of the participants were aged between 18 and 39 years. 17 patients (12.4%) tested positive for Cryptococcal antigen, indicating active CM infection. A significant portion of the cohort had low CD4 counts, putting them at higher risk for opportunistic infections. Additionally, 105 (76.6%) patients exhibited inadequate viral suppression, suggesting issues with ART adherence or treatment failure.

Conclusion
The study found a low prevalence of CM in HIV-positive patients on ART at Durban Addington Hospital. However, the high rate of advanced immunosuppression (low CD4 counts and high viral loads) highlights challenges in managing these patients and the need for improved diagnostic and monitoring practices.

Recommendations
Further longitudinal studies on adherence interventions, ART optimization, and integrated HIV care for opportunistic infections are recommended.

Keywords: *HIV, Antiretroviral, Cryptococcal meningitis, Cerebrospinal fluid*
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BACKGROUND

Cryptococcal meningitis is an infection caused by Cryptococcus fungi that can affect the brain or lungs and spread throughout the body (Parry et al., 2021). When this infection reaches the brain, it is known as Cryptococcal meningitis (CM). Cryptococcosis has particularly serious effects on immunocompromised individuals, especially

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those with HIV (Haung et al., 2020). Despite the widespread availability of antiretroviral treatment, CM remains a major cause of death among people with HIV in Sub-Saharan Africa (Link et al., 2022). It continues to pose a significant public health challenge, with mortality rates ranging from 5% to 16% (Cabellos et al., 2019).

Cryptococcal meningitis (CM) presents a multifaceted challenge beyond its medical dimensions. Factors such as the rollout of antiretroviral therapy (ART), economic challenges, hospital efficiency, and additional disease burdens contribute to the complexity of addressing CM. The widespread availability of antiretroviral medication, while significant, may not fully mitigate the consequences of CM, particularly in Sub-Saharan Africa, where it remains a leading cause of mortality among HIV-infected individuals (Link et al., 2022). Despite ART access, CM's death rate still ranges from 5% to 16%, indicating persistent challenges in management and treatment (Cabellos et al., 2019). Economic challenges exacerbate the burden of CM, as poverty and limited access to healthcare services can impede prevention, diagnosis, and treatment efforts. Additionally, healthcare infrastructure efficiency plays a crucial role, influencing factors such as diagnostic delays and treatment accessibility (Parry et al., 2021).

Moreover, CM often coexists with other health issues, including opportunistic infections and comorbidities prevalent in immunocompromised individuals. Understanding these intersecting disease burdens is vital for designing holistic healthcare interventions. Addressing CM requires a comprehensive approach that considers not only medical therapy but also the socioeconomic and healthcare system contexts. Research in this area should aim to elucidate these interconnected factors to inform effective strategies for CM prevention and management. This study aimed to investigate the prevalence of Cryptococcal meningitis (CM) in HIV-positive patients undergoing antiretroviral treatment.

A saprophytic fungus is a type of fungus that derives its nutrients by breaking down dead organic matter (Benbow et al., 2019). Cryptococcus neoformans, a fungus with a widespread environmental presence, paradoxically harbors a high potential for pathogenicity, posing significant health risks to humans and animals (Rathore et al., 2022). Cryptococcus neoformans infects immunocompromised individuals and spreads to various parts of the body, especially the central nervous system, where it leads to Cryptococcal meningitis. (Ghanem et al., 2021). This fungus, which is bird-dropping is the cause of the fungal disease known as Cryptococcosis. If inhaled, the spores can proliferate and travel from the lungs to membranes lining the brain or spinal cord, where they can cause Cryptococcal meningitis. HIV patients with advanced immunosuppression are frequently susceptible to Cryptococcal meningitis, a serious opportunistic infection. The inflammation of the meninges, the membrane surrounding the brain and spinal cord, is called the meninges. (Ghia et al., 2021). While it can be detected in anyone, individuals with weakened immune systems are at higher risk.

The immune system's job is to maintain the proper ratio of tissue damage to immunity. Receptor-ligand interaction that provides either positive or negative co-stimulatory signals mediate this process (Megha et al., 2021). White blood cells, or leukocytes, play a vital role in the human immune system, circulating through blood, lymph, and tissues to defend against infections. Their main job is to support the immune system and help the body fight off illness, infections, and foreign substances that get into the bloodstream. Lymphocytes, monocytes, eosinophils, basophils, and neutrophils, the five categories of white blood cells, collaborate to provide comprehensive protection against fungal, viral, parasitic, and bacterial infections. HIV is characterized by chronic immunological activation and targets the immune system by changing immune pathways, where the immune response will be compromised (Zicari et al., 2019). Since HIV-specific CD4 T cells are the main target of HIV infection, their function in boosting immunity against HIV is compromised. This will result in immune suppression, and the individuals will be prone to opportunistic infections such as Cryptococcal neoformans (Rathore et al., 2022). In 2010, more than 20 million people worldwide contracted HIV, with most cases occurring through heterosexual transmission in Sub-Saharan Africa. (lwuji et al., 2017). Patients with Cryptococcal meningitis (CM) often exhibit symptoms like headache, neck stiffness, weight loss, and blurred vision.

Cryptococcal meningitis (CM) is a fungal infection that is becoming an increasing concern for global public health (Zhao et al., 2023). In Africa, the mortality rate for CM is approximately 10.3% (Nyazika, 2019). In countries with high HIV prevalence, such as Eswatini, Lesotho, South Africa, Mozambique, Malawi, and Uganda, CM is the main cause of meningitis. Anyone can get CM, but people with compromised immune systems are at risk (Person 2023). South Africa has a high rate of HIV transmission, with approximately 20% of new infections each quarter. This high rate may be linked to South Africa's high poverty levels and the lowest median household income compared to other

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regions. Additionally, HIV incidence is particularly high in rural areas due to lower education levels. (Allyson,2017). Research indicates that approximately 7.06 million people in South Africa are living with HIV, and individuals with low CD4 counts are particularly susceptible to Cryptococcal meningitis (CM), which has a mortality rate ranging from 30 to 50% (Ross, 2019) CD4 cells, also known as T-helper cells, facilitate the immune system's defense against pathogens by activating and coordinating various immune responses to combat viral, bacterial, and other infections. When someone has an HIV low CD4 count means that HIV has weakened the immune system, and opportunistic infections may occur (Vickers, 2017). Despite the widespread use of antiretroviral therapy, HIV remains a significant cause of illness and death across Africa (Muzazu, 2022). Antiretrovirals lower the viral load in the body, allowing the immune system an opportunity to recover. Although some HIV remains in the body, the immune system must become stronger to combat infections and HIV-related cells. (Wolday et al., 2020). Human immunodeficiency virus (HIV) infection is managed with antiretroviral therapy (ART), which involves the use of medications that target and suppress HIV. Although ART medications do not cure the virus, they prevent its spread and protect CD4 cells, which are responsible for fighting infections. An essential component of the immune system, CD4 cells combat the virus and other microbiological infections (Plein et al., 2018). ART may not cure HIV, but it successfully suppresses the virus, preventing it from causing harm and allowing the immune system to recover (Zanni et al., 2016).

Despite significant advancements in access to ARV medications over the past decade, a considerable number of HIV-positive individuals worldwide still experience severe illness quickly and significantly. (Ford et al., 2016). This study seeks to investigate Cryptococcal meningitis in HIV-positive patients receiving antiretroviral treatment. These estimates will be very helpful for health practitioners. Amphotericin B is the recommended medication for induction therapy in HIV-positive patients. This antifungal drug binds to ergosterol in the fungal cell membrane, resulting in the formation of pores, ion leakage, and ultimately causing the fungal cell to die. (Ahmed et al., 2021). Findings indicate that patients should be on treatment with amphotericin B for 2 to 3 weeks, which will result in the sterilization of cerebrospinal fluid (Ngan et al., 2019), however, more studies need to be done to further confirm this. This study aims to investigate the prevalence of Cryptococcal meningitis in HIV-positive patients who are on antiretroviral treatment.

Research Aim

This research aims to investigate the prevalence of Cryptococcal meningitis in HIV patients who are on ARV treatment at Durban Addington Hospital.

Hypothesis

There is a high prevalence of Cryptococcal meningitis in HIV-positive patients who default on ARV treatment.

Research Objectives

- To investigate the prevalence of Cryptococcal meningitis in HIV patients who are currently on antiretroviral treatment based on age.
- To assess isolated Cryptococcal neoformans on CSF specimens from patients who have tested positive for HIV.
- To perform a comparative analysis between Cryptococcus neoformans positive results and CD4 count and Viral load test results.

RESEARCH METHODOLOGY

Study design

A retrospective quantitative study was performed on patients who tested positive for Human immunodeficiency virus (HIV) and subsequently got infected with Cryptococcal neoformans. The study was a cross-sectional study based on the analysis of laboratory data obtained from National Health Laboratory services for the completion of the research project. The study used a quantitative approach, which allowed the exploration of the prevalence of Cryptococcal meningitis (CM) caused by Cryptococcal neoformans in HIV patients who were on ARV treatment.

Study setting

This study was conducted at Addington Public Hospital based in Durban, KwaZulu-Natal. This hospital serves the population of central and northern Durban. It specializes in general surgery, orthopaedic surgery, otorhinolaryngology, and ophthalmic surgery.

Study population

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The target study group for this study was both males and females who had tested positive for HIV and were on ARV treatment from January to July 2022 hospitalization period.

Data sampling, sample size, and analysis

Data was gathered from each patient's medical and laboratory records, with laboratory results sourced from the National Health Laboratory Service (NHLS) track care system. The analysis concentrated on isolating Cryptococcus neoformans, the fungus responsible for CM. Upon receiving the data from the corporate data warehouse, a random sample of 137 patients was selected to ensure every member of the population had an equal chance of inclusion. Statistical techniques were employed to present the data through tables, charts, and graphs.

Data collection

The data has been requested from the Corporate Data Warehouse (CDW). The data application was uploaded to the AARMS website, data from January to July 2022, at Addington Hospital. The data request was Cryptococcus positive results from Microbiology, Viral load, and CD4 count results from Virology and Haematology for both genders in patients. Data was requested to be provided in an Excel format. Patients' personal information was removed to ensure confidentiality.
Short overview of Diagnostic procedure as per the laboratory Standard Operating Procedure for CSF specimen processing at Addington Laboratory

India ink Principle

This technique allows visualization of the encapsulated forms of Cryptococcus neoformans. The sample is combined with an equal drop of Indian ink and examined using a microscope. The capsule appears as a clear area surrounding the yeast. Typically, round or oval yeast forms are observed, occasionally showing budding with short mycelium and containing a greyish granulation.

Specimen collection

The specimen was collected through lumbar puncture.

Specimen

- CSF on plain tube

Macroscopical examination

- Clear and colourless

Microscopic examination

Cell Count on Unspun CSF

- Label the tube with the patient's episode number.
- Prepare a 1 in 10 dilution by adding 1 drop of unspun CSF to 9 drops of methylene blue reagent in the labeled tube.
- Let it sit for 10 minutes, then use a counting chamber to count lymphocyte cells under the microscope.

India Ink

- Screen the sample for encapsulated yeast.

Gram Stain on Sediments

- Expected results: yeast cells.

Procedure for Cryptococcal Antigen Test (CLAT)

- Label a tube with the patient's unique episode number.
- Add 40 µL of unspun CSF to the labelled tube.
- Add 1 drop of diluent to the tube.
- Place a test strip into the solution in the tube.
- Wait 10 minutes, then read the results.
- This CLAT test displays results as two lines: the first is the control line, and the second is the test line. A negative result shows only the control line, while the appearance of both lines indicates a positive result for Cryptococcal antigen.

Specimen Culture

Centrifuge the CSF for 10 minutes at 3000 rpm
Pour the supernatant into another labelled tube
Use the sediment to culture on 2x SAB
Incubated one set was incubated at 37°C, and the other at 24°C in a specialized biological oxygen demand incubator

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for 72 hours. Colony morphology was observed after incubation. Cryptococcus neoformans was identified through its characteristic yeast-like mucoid colonies on Sabouraud Agar (SAB) medium, subsequently confirmed by a positive urease test. For a definitive diagnosis, colonies from SAB were subcultured onto Niger seed agar, incubated at 37°C, and examined for the development of brown to black colonies, indicating melanin pigment production by C. neoformans.

Statistical analysis

Cryptococcal meningitis is highly prevalent among HIV-positive patients who do not adhere to antiretroviral (ARV) therapy. This study focused on examining the prevalence of Cryptococcal meningitis in HIV patients receiving ARV treatment at Durban Addington Hospital. A retrospective quantitative study was conducted on patients who tested positive for HIV. This quantitative approach enabled a clear exploration of Cryptococcal meningitis (CM) prevalence in HIV-positive patients on ARV therapy, effectively presenting the data through statistical measures and numerical analysis.

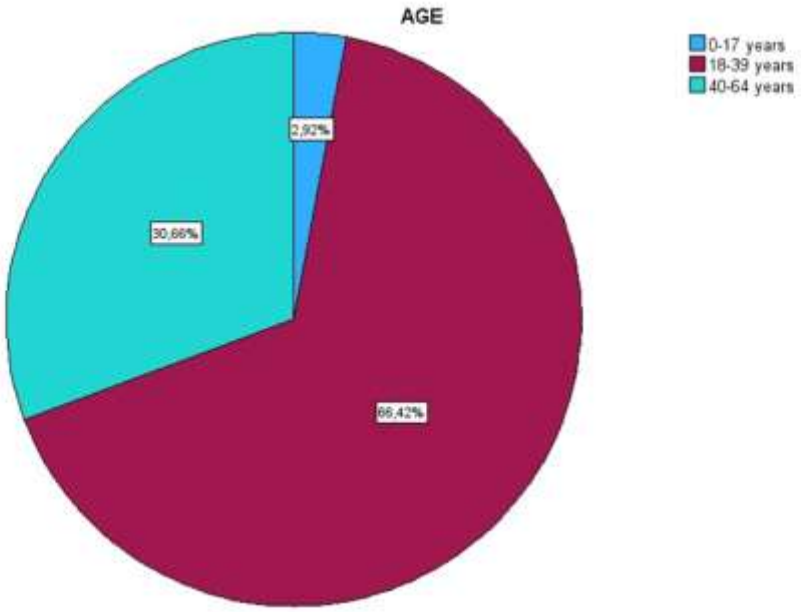
Ethical considerations

Patient information remained strictly confidential to ensure ethical compliance, with access restricted to a limited number of individuals. Only the principal investigator and study supervisor had access to this information, protected by a secure password. Patient details were kept anonymous throughout the study. Ethical approval was obtained from Mangosuthu University of Technology (MUT) on the 28th of February 2024, REF: RD5/37/2024. Permitting the study to move forward.

RESEARCH RESULTS

Descriptive Analysis

Figure 1: Age Distribution



The pie chart depicts the distribution of different age groups in a population. It is divided into three segments, each representing a distinct age range. The largest portion of the chart, shown in maroon, corresponds to individuals aged 18-39 years, indicating that this group formed the majority of the population. The second largest section, displayed in cyan, represented those aged 40-64 years. Finally, the smallest segment, coloured in blue, reflected the population aged 0-17 years, suggesting that this group constituted the smallest portion. The chart visually emphasized the

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predominance of the middle-aged group in the overall population distribution.

Table 1: Distribution of CD4 Count among 137 tested patients

Patient's CD4 Count state	Number of patients tested	Percent (%)
Urgent medical attention	137	100

These results suggest that the entire sample likely falls into a critical category for their CD4 levels, meaning all participants may have had significantly low CD4 counts, indicating advanced HIV infection or immunosuppression; hence, they need urgent medical attention.

Table 2: Distribution of viral load results among patients, indicating the levels of infections among 137 patients

Patients' Viral Load Results	Frequency in tested patients
Lower than the detectable limit	17
Acceptable levels	14
Monitoring is essential, but levels are stable	1
Urgent medical attention	105
Total	137

This distribution indicated that the majority of patients, 105 (76.6%), had high viral loads, suggesting inadequate viral suppression, which is a sign of poor HIV control. Only a small fraction had either undetectable or acceptable viral loads. On 17 (12.41%) patients, HIV Viral load was lower than the detectable limit, 14 (10.22%) patients had acceptable levels, and only 1(0.73%) patient was monitored as essential, but levels were stable.

Table 3: Distribution of Antiretroviral Treatment-Experienced and Treatment-Naïve

	Tested Patients	Percentage (%)	Results
ART- Experienced	137	100	True
ART-Naïve	137	100	False

All 137 patients (100%) had prior experience with antiretroviral therapy, as none were antiretroviral-naïve, meaning no patients were not taking treatment, hence the results displayed falsely.

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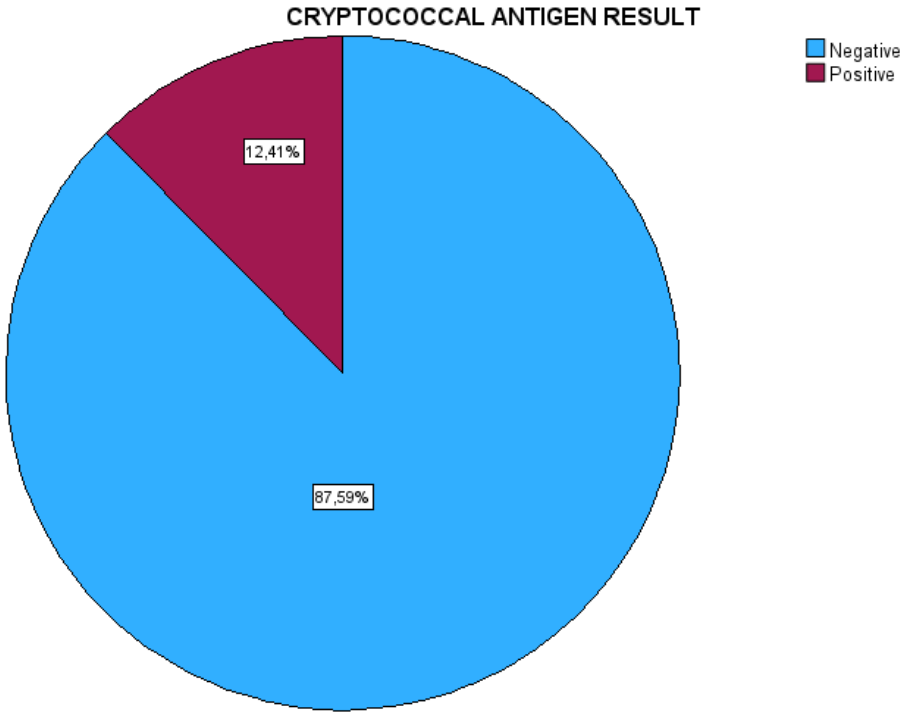
Figure 2: Distribution of *Cryptococcal* Antigen Test Results



Cryptococcal antigen testing is a diagnostic measure used to detect *Cryptococcal* meningitis, a common opportunistic infection in HIV-positive patients. These results suggested that approximately 12% of the patients had an active *Cryptococcal* infection, while 87.59% indicated patients who were *Cryptococcal* antigen test negative, indicating no *Cryptococcal* meningitis infection.

Inferential Analysis

Table 4: Inferential Analysis

			CRYPTOCOCCAL ANTIGEN RESULT	VIRAL LOAD	CD4_COUNT
Spearman's rho	CRYPTOCOCCAL ANTIGEN RESULT	Correlation Coefficient	1,000	-,001	.
		Sig. (1-tailed)	.	,496	.
		N	137	137	137
	VIRAL LOAD	Correlation Coefficient	-,001	1,000	.
		Sig. (1-tailed)	,496	.	.
		N	137	137	137
	CD4_COUNT	Correlation Coefficient	.	.	.
		Sig. (1-tailed)	.	.	.
		N	137	137	137

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Cryptococcal Antigen Result and Viral Load

Correlation Coefficient: -0.001, suggesting that there was virtually no correlation between the Cryptococcal Antigen Result and Viral Load.
P-value: 0.496, indicating that this result was not statistically significant.

Viral Load and CD4 Count

No correlation data was provided between these two variables.

CD4 Count and Cryptococcal Antigen Result

No correlation data was reported.

Table 5: Results of patients with positive C*ryptococcal* antigen test

Patients	Cryptococcal Antigen Test	HIV Viral Load	CD4 count
1	Positive	>200 copies/ml	< 300 cells/ul
2	Positive	>200 copies/ml	< 300 cells/ul
3	Positive	Lower than the detectable limit	< 300 cells/ul
4	Positive	>200 copies/ml	< 300 cells/ul
5	Positive	>200 copies/ml	< 300 cells/ul
6	Positive	>200 copies/ml	< 300 cells/ul
7	Positive	>200 copies/ml	< 300 cells/ul
8	Positive	20-75 copies/ml	< 300 cells/ul
9	Positive	>200 copies/ml	< 300 cells/ul
10	Positive	>200 copies/ml	< 300 cells/ul
11	Positive	>200 copies/ml	< 300 cells/ul
12	Positive	>200 copies/ml	< 300 cells/ul
13	Positive	>200 copies/ml	< 300 cells/ul
14	Positive	Lower than the detectable limit	< 300 cells/ul
15	Positive	20-75 copies/ml	< 300 cells/ul
16	Positive	>200 copies/ml	< 300 cells/ul
17	Positive	>200 copies/ml	< 300 cells/ul

DISCUSSION

Age Distribution

The analysis of the age distribution within the study cohort highlights that the majority of participants were aged 18-39 years, representing a substantial portion of the population. This age group often corresponds to the working-age demographic, which is disproportionately affected by HIV, particularly in sub-Saharan Africa (Risher et al., 2021). The age distribution in this study is consistent with previous findings, where younger adults are predominantly impacted by HIV, given their higher levels of sexual activity and economic mobility, which often expose them to greater risk (Camlin and Charlebois, 2019). On the other hand, individuals aged 0-17 years comprised the smallest proportion, suggesting that either fewer children were included in the study, or they are less frequently tested, potentially due to underreporting or less frequent exposure compared to adults. Cite your results that are significant about age.

Distribution of CD4 Count and Viral Load

Regarding the CD4 count distribution, the data indicated that all 137(100%) patients required urgent medical attention, with severely low CD4 counts, suggesting advanced immunosuppression. This finding aligns with

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research by Nakanjako et al. (2009), which noted that in resource-limited settings, many patients are diagnosed late in the course of HIV infection, contributing to lower CD4 counts and higher mortality rates. Additionally, the high viral loads observed in the majority of the participants further underscore the issue of poor HIV control in this population. Notably, 105 (76.6%) of participants had viral loads that required urgent medical attention. This is reflective of similar studies, such as those by Dubrocq and Rakhmanina (2018), which found that insufficient adherence to antiretroviral therapy (ART) and treatment interruptions lead to increased viral replication and immune system decline.

Distribution of Antiretroviral Treatment-Naïve and Treatment-Experienced

Moreover, the fact that none of the participants were antiretroviral-naïve, as all were classified as treatment-experienced, suggests that the high viral loads were likely due to treatment failure rather than lack of access to ART. This resonates with findings from Foka and Mufhandu (2023), who identified treatment fatigue, drug resistance, and inadequate follow-up as key drivers of poor treatment outcomes in HIV-positive patients on ART. Despite the availability of ART, the failure to achieve viral suppression in a large portion of the cohort suggests a need for more robust monitoring and intervention strategies.

Distribution of *Cryptococcal* Antigen Test Results

Additionally, the study revealed that 17 (12.4%) of patients tested positive for Cryptococcal Antigen, indicating an active cryptococcal infection. Cryptococcal meningitis remains a significant cause of morbidity and mortality among HIV-positive individuals with low CD4 counts, especially in regions with limited healthcare resources (Rajasingham et al., 2017). The correlation analysis further demonstrated no significant relationship between cryptococcal antigen results and viral load (p=0.496), suggesting that while both viral suppression and management of opportunistic infections are critical, they may progress independently in this population.

However, the hypothesis suggests that patients who default to ARV treatment may be at higher risk for such infections due to compromised immune function. In this study, the data analysis revealed a P value of (P=0.496) while the accepted value is (P=0.05). This resulted in the null hypothesis being rejected because the patient's viral load does not necessarily correlate with the *Cryptococcal* meningitis.

GENERALISABILITY OF THE RESULTS

Cryptococcal meningitis is a serious infection primarily caused by Cryptococcus neoformans. While the fungi often enter the body through the lungs after inhalation of spores, the infection can disseminate and, in the case of cryptococcal meningitis, invade the brain and spinal cord. This inflammation of the meninges, the membranes surrounding the brain and spinal cord, can lead to a range of neurological symptoms. Although initially affecting the lungs, the systemic spread of Cryptococcus can impact various organs and systems, making it a potentially life-threatening condition, particularly in individuals with weakened immune systems. *Cryptococcus neoformans* is known to be prevalent in patients with HIV infections, causing a mortality rate of five to 16 percent. This study aimed to highlight the prevalence of *Cryptococcus neoformans* in HIV-positive patients who are on antiretroviral (ARV) treatment. The findings of the study showed that the prevalence of *Cryptococcus neoformans* in HIV patients was 12%. This was a remarkable finding because these patients were diagnosed with Cryptococcal meningitis due to HIV infection, which weakens their immune system.

CONCLUSION

In conclusion, the study's findings underscore the critical need for enhanced HIV management strategies, particularly for treatment-experienced individuals with advanced disease. The challenges of maintaining viral suppression, managing opportunistic infections, and addressing drug resistance remain prevalent, echoing the findings of other regional studies (Koay et al., 2021). More comprehensive strategies, including intensified ART adherence counseling, routine viral load monitoring, and prompt treatment of opportunistic infections, are essential for improving outcomes in this cohort.

Conclusion and recommendations

KEY FINDINGS

Age Distribution

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The majority were younger adults (18–39 years), reflecting the higher HIV prevalence in this working-age group in sub-Saharan Africa.

CD4 Count and Viral Load

All participants had low CD4 counts, and 76.6% had high viral loads, indicating inadequate viral suppression despite ART experience, likely due to issues like treatment fatigue or drug resistance.

ART History

All patients had prior ART exposure, yet many showed unsuppressed viral loads, highlighting the need for improved ART monitoring, adherence support, and drug resistance testing.

Cryptococcal Antigen Positivity

With 12.4% testing CrAg positive, the study underscores the need for proactive screening and management of opportunistic infections in severely immunosuppressed patients.

CrAg and Viral Load Correlation

No significant link was found between CrAg positivity and viral load, suggesting independent progression of viral replication and opportunistic infections.

IMPLICATIONS

Enhanced ART Adherence

Improved counseling and support systems are needed to address barriers to consistent ART use.

Routine Monitoring

Regular viral load and CD4 monitoring, plus drug resistance testing, are critical to identify and manage treatment failure early.

Opportunistic Infection Management

Routine screening and early treatment of infections like cryptococcal meningitis are essential for reducing HIV-related mortality.

CONCLUSION

This study provides important insights into the epidemiology of CM in a high-burden setting. It highlights the need for routine screening for opportunistic infections among immunosuppressed HIV patients, particularly for CM. Enhanced ART adherence programs, improved diagnostic tools, and early detection strategies are recommended to help reduce CM-related mortality in this vulnerable population.

The findings underscore that, while viral load and CM presence were not significantly correlated, both require independent and rigorous management to reduce morbidity and mortality. This suggests that even with viral load suppression, patients may still be at risk for CM if their immune systems remain severely compromised. Therefore, comprehensive strategies involving routine monitoring, patient adherence counseling, prompt identification of opportunistic infections, and addressing potential drug resistance are essential to enhance health outcomes in this population.

Addressing these multifaceted challenges demands a more proactive approach to HIV care, particularly for treatment-experienced patients with advanced disease stages. Efforts to reinforce ART adherence, ensure frequent viral load testing, and facilitate immediate treatment for opportunistic infections can significantly improve survival rates and quality of life for HIV patients in resource-limited settings like Durban Addington Hospital.

LIMITATIONS

Sample Size

While 137 patients were included in the study, the sample size might not be large enough to draw broad conclusions, particularly regarding rare outcomes like Cryptococcal meningitis. A larger sample could enhance the generalizability of the findings.

Single-Centre Study

The research was conducted at a single hospital, Durban Addington Hospital. This limits the generalizability of the results to other hospitals or regions with different healthcare resources or patient demographics.

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Lack of Long-Term Follow-Up

The study covers a short period (January to July 2022), which may not capture the long-term effects of ART on CM or identify changes in the prevalence of CM over time.

RECOMMENDATIONS

Longitudinal Studies to assess the effects of adherence interventions and treatment modifications on long-term outcomes. Research into advanced therapies for overcoming resistance and treatment fatigue on ART optimization. Further study on the interaction between viral suppression and infection management to improve integrated HIV care regarding opportunistic infections.

SOURCE OF FUNDING

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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ACRONYMS AND ABBREVIATIONS

AARMS: Academic Affairs and Research Management System
ART Antiretroviral Therapy
CDW Corporate Data Warehouse
CM Cryptococcal Meningitis
CLAT Cryptococcal Latex Agglutination Test
CSF Cerebrospinal Fluid
HIV: Human Immunodeficiency Virus
MUT Mangosuthu University of Technology
SAB Sabouraud dextrose agar
SA South Africa
WHO World Health Organization

AUTHOR CONTRIBUTIONS

Ms N Zondi Principal Investigator
Study Design and Conceptualization: As the principal investigator, Ms. Zondi was responsible for developing the study's objectives, research questions, and overall design. She formulated the study hypothesis and guided the methodological approach for data collection and analysis.
Data Collection and Analysis: Ms Zondi oversaw the collection of medical and laboratory data from the patients, ensuring that relevant data were accurately extracted from medical records. She also played a central role in analyzing the data and interpreting the findings.
Drafting the Manuscript: Ms Zondi contributed to writing the research paper, particularly the Introduction, Methodology, Results, and Conclusion sections, ensuring that the study's aims and findings were effectively communicated.
Ethics and Compliance: Ms Zondi ensured that the study adhered to ethical standards and complied with regulations regarding patient confidentiality and informed consent.
Research Oversight: She provided leadership in the overall conduct of the study, managing the logistics and coordinating between different departments to ensure smooth execution.

Mr S Shangase, Research Supervisor
Guidance and Mentorship: Mr Shangase provided oversight and mentorship throughout the study process. He advised Ms Zondi on refining the research design and methodology, ensuring that the study was robust and scientifically sound.
Data Interpretation and Statistical Analysis: He assisted in the analysis of the data, offering expert advice on statistical methods and ensuring the validity of the results.
Review and Editing of the Manuscript: Mr Shangase reviewed drafts of the manuscript, providing feedback on clarity, coherence, and scientific accuracy. He contributed to the refinement of the Discussion and Recommendations sections, ensuring that the conclusions were well-supported by the data.

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Quality Control and Assurance: He ensured that the study followed best research practices and was conducted with the highest scientific rigor. Mr Shangase also helped ensure that the results were interpreted correctly and that any limitations were communicated.

Ethical Oversight: As the research supervisor, he was involved in the ethical approval process and monitored the study's compliance with ethical guidelines, ensuring that all research activities met institutional and regulatory standards.

AUTHOR BIOGRAPHY

Ms . Nobuhle Zondi is a new graduate and public health researcher with expertise in infectious diseases, particularly HIV and its complications. She holds a Bachelor of Health Science in Medical Laboratory Science degree in the biomedical laboratory science field; she is also registered with HPCSA as an MLS in Clinical pathology and has a strong focus on HIV-associated opportunistic infections, including Cryptococcal meningitis. As the principal investigator of this study, she was responsible for its design, data collection, and analysis, aiming to improve patient outcomes through evidence-based research.

Mr Simangaliso Shangase
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Designation: Lecturer at Mangosuthu University of Technology
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DEFINITION OF TERMS

Antiretroviral Drugs

Medications are used to treat HIV infection. These drugs work by inhibiting various stages of the HIV life cycle, thereby reducing viral load and preventing the progression of the disease.

Cryptococcus neoformans

A species of fungus that can cause severe infections, particularly in immunocompromised individuals. It is the primary causative agent of Cryptococcal Meningitis.

Cryptococcal Meningitis (CM)

An opportunistic fungal infection of the central nervous system caused by Cryptococcus neoformans. It is a leading cause of morbidity and mortality among HIV-positive patients with advanced immunosuppression.

Drug Resistance

The reduction in effectiveness of a medication in curing a disease or condition. In the context of HIV, it refers to the virus's ability to mutate and evade the effects of antiretroviral drugs.

Immunocompromised

Having an impaired or weakened immune system makes an individual more susceptible to infections and diseases.

Immunosuppression

The reduction of the activation or efficacy of the immune system. This can be a result of diseases like HIV/AIDS, certain medications, or other medical conditions.

Opportunistic Infections

Infections that occur more frequently and are more severe in individuals with weakened immune systems, such as those with HIV/AIDS. Examples include Cryptococcal Meningitis, tuberculosis, and Pneumocystis pneumonia.

Serological Screening

Diagnostic testing is performed on blood samples to detect the presence of specific antigens or antibodies, such as the Cryptococcal Antigen (CrAg) test used to identify Cryptococcus neoformans infection.

Viral Load

The amount of HIV present in a blood sample. Monitoring viral load helps assess the effectiveness of antiretroviral therapy and the progression of the disease.

Viral Suppression

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The reduction of the HIV viral load to undetectable levels in the blood through effective antiretroviral therapy. Achieving viral suppression helps maintain immune function and prevents disease progression.

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