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Risk factors influencing Cryptococcal antigenemia among HIV/AIDS patients attending Antiretroviral Therapy Clinic at Masaka regional referral hospital, Masaka District in Uganda. A cross-sectional study.

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Abstract

Background:

Globally, by far the most common presentation of the cryptococcosis is cryptococcal meningitis. The aim of the study is to assess the risk factors influencing Cryptococcal antigenemia among HIV/AIDS patients attending the Antiretroviral Therapy Clinic at Masaka regional referral hospital, Masaka District.

Methodology:

A cross-sectional study included HIV-positive patients receiving ART who attended the HIV/AIDS clinics at Masaka Regional Referral Hospital – ART Clinic. Blood samples were analyzed for the presence of Cryptococcus neoformans and Cryptococcus meningitidis antibodies.

Results:

A CD4 count of fewer than 100 cells per microliter emerged as a significant predictor of cryptococcal antigenemia, with a P value of 0.04 at a 95% confidence level. The analysis revealed that poor adherence to ART is a strong predictor of cryptococcal antigenemia, with a P value of 0.013. The regression analysis indicated that a prior history of infections does not significantly predict cryptococcal antigenemia, with a P value of 0.528. The impact of environmental conditions on cryptococcal antigenemia showed a P value of 0.211. Malnutrition is not a strong predictor of cryptococcal antigenemia, with a P value of 0.134. Advanced age was also identified as a weaker predictor, with a P value of 0.585.

Conclusion:

The strong predictors of cryptococcal antigenemia were low CD4 Counts and Adherence to Antiretroviral Therapy.

Recommendation:

More studies should be conducted to assess the strong predictors of cryptococcal antigenemia to facilitate in creating awareness and sensitization programs.

Keywords: *Cryptococcal antigenemia, Risk factors, HIV/AIDS patients, Antiretroviral Therapy Clinic.*
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Background

Globally, by far the most common presentation of the cryptococcosis is cryptococcal meningitis (CM), which leads to an estimated 15–20% of all HIV related deaths worldwide, 75% of which are in sub-Saharan Africa (Awoke Derbie et al, 2020). A study conducted among hospitalized AIDS patients on the continent level, 69%, 80%, and 80% cryptococcal antigenemia were reported in Africa, Europe, and the USA, respectively (Jemal M et al, 2021). The status of cryptococcosis in Latin America reported a prevalence of 10–21% in the context of HIV patients with CM (Awoke Derbie, 2020).

In a multicentre study in Nigeria, exposure to environmental pathogens, such as bird droppings, was identified as a novel risk factor for Cryptococcal antigenemia, highlighting the need for comprehensive preventive strategies beyond traditional HIV care. Recent data from a cohort study in Zambia revealed an association between malnutrition and increased risk of Cryptococcal infection among HIV-infected individuals, emphasizing the importance of nutritional support as part of integrated HIV care programs. A study conducted in Rwanda found that delayed initiation of ART and non-adherence to treatment were significant predictors of Cryptococcal antigenemia among HIV patients, highlighting the importance of adherence counselling and retention in care initiatives.

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Methodology

Study design

This cross-sectional study included HIV-positive patients receiving ART who attended the HIV/AIDS clinics at Masaka Regional Referral Hospital – ART Clinic. Blood samples were analyzed for the presence of Cryptococcus neoformans and Cryptococcus meningitidis antibodies. The study was conducted from April to June 2024.

Study area

The study was conducted to investigate the aspects of Cryptococcal infections at Masaka regional referral hospital. located approximately 132 kilometers (82 mi), by road, away from Kampala. The coordinates of Masaka Regional Referral Hospital are: 0°19'46.0"S, 31°44'04.0" E (Latitude: -0.329444; Longitude:31.734444).

Study population

The study enrolled all patients aged 15 years and older who were attending the ART clinic during the study period at Masaka Regional Referral Hospital.

Sample size determination

The sample size was determined using the Kish and Leslie formula (2000) as stated below.

Kish and Leslie's formula is, $\boldsymbol{n} = \frac{z^2pq}{d^2}$

Where n = the required sample size

z = the standard deviation (1.96) at 95% confidence interval

d = allowed error (0.05)

p = estimated prevalence of Cryptococcal antigenemia among HIV patients in Uganda (7.1%) (Ebonu E, 2021), hence p (0.071).

q = (1-p)

z = 1.96, p = 0.071, d = 0.05, q = (1-0.071)

Therefore, $n = \frac{1.96 \text{ X } 1.96 \text{ X } 0.071 \text{ X } 0.929}{0.05\text{X } 0.05}$

n = 101

A total of 101 patients diagnosed clinically with meningitis were included in the Study.

Sampling technique

The study employed a convenience sampling technique, selecting participants based on their availability and willingness to participate, which suited the practical constraints of the research setting.

Sampling Procedure:

The study utilized a convenient sampling approach to recruit participants from the ART clinic. HIV/AIDS patients attending the clinic were informed about the study objectives. Those who provided consent and had a CD4 count of less than 200 cells/µL were eligible for enrollment in the study.

Data collection method

Closed-ended questionnaires were employed to gather comprehensive qualitative and quantitative data, encompassing demographic factors, obstetric history, and socioeconomic indicators such as occupation, income levels, and educational attainment.

To ascertain prevalence, blood samples were systematically collected using either red top or purple top vacutainers from all participants. These samples were subsequently subjected to analysis using the Cryptococcal antigen (CrAg) lateral flow assay (LFA).

Data collection sheets were meticulously utilized to record and compile the laboratory results obtained from the analysis process.

Data collection tool(s)

Demographic information, including age, place of residence, and marital status, was gathered using a questionnaire featuring a mix of closed and open-ended questions. This facilitated comprehensive data collection from the respondents.

Quantitative data were obtained through the use of the CrAg LFA (Cryptococcal antigen lateral flow assay). This diagnostic method operates on the principle of a dipstick sandwich immunochromatographic assay. It is specifically designed to detect cryptococcal antigen present in either serum or whole blood samples.

The CrAg Kit employed in the study provided rapid and reliable results, aiding in the accurate assessment of Cryptococcal antigenemia among the participants.

Data collection procedure

The researcher first introduced themselves to HIV/AIDS patients, explaining the purpose of the study and obtaining consent from willing participants. Each eligible participant received a questionnaire to ensure accurate data collection.

To facilitate identification, a unique number was assigned to every patient. Venous blood was then collected using aseptic techniques and deposited into appropriately labeled red top or purple top vacutainers as per standard operating procedures (SOPs).

Upon collection, samples were centrifuged to separate serum (from red top) or used whole blood (from purple top). A process followed where one drop of specimen diluent was added to a test tube, followed by 40 microliters of patient serum or whole blood, which was thoroughly mixed.

Subsequently, a CrAg strip was inserted into the test tube with the mixed sample and allowed to react for 10 minutes. After the designated time, results were interpreted and recorded on the data collection sheet.

The findings from these procedures were instrumental in determining the prevalence of Cryptococcal antigenemia among HIV/AIDS patients in the study.

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Study variables

The study's dependent variable focused on determining the prevalence of cryptococcal antigenemia among HIV/AIDS patients. The independent variable comprised individuals receiving antiretroviral therapy (ART) for HIV/AIDS. These variables were crucial in examining the relationship between ART treatment and the occurrence of cryptococcal antigenemia among the study participants.

Piloting the study

A pilot study involving 8 participants exhibiting signs and symptoms highly suggestive of cryptococcal infection was conducted to assess the feasibility and refine the methodology for the main study.

This preliminary investigation aimed to gather initial insights into the diagnostic procedures and data collection techniques that would be employed in the subsequent larger-scale study.

Quality control

Before data collection commenced, the researcher conducted training sessions for research assistants to ensure accurate results were obtained. The research tools underwent a pre-test phase to identify and address any necessary adjustments prior to the main study.

The serum cryptococcal antigen (CrAg) serology test adhered strictly to the manufacturer's instructions. During testing, both negative and positive control samples were included alongside the study samples to validate the accuracy and reliability of the results.

Data analysis and presentation

Patient data was collected through responses provided in the administered questionnaires, while laboratory data was gathered from the results of conducted tests. Subsequently, the data was processed and analyzed using Microsoft Excel for thorough examination.

The findings were then compiled into figures, such as pie charts or bar graphs, and tables. These visual representations were utilized to effectively present and interpret the generated information from the study.

Ethical consideration

The research commenced with the acquisition of an introductory letter from the Research and Ethics Committee of the Faculty of Health Sciences at the University of Kisubi. This letter was then submitted to the administration of Masaka Regional Referral Hospital to obtain formal permission to conduct the study. Upon receiving a letter of acceptance from the hospital administration, data collection promptly commenced.

Throughout the study, utmost confidentiality of patient information was assured, and participants were informed of their right to withdraw from the study at any point without consequences. These ethical considerations were strictly adhered to during the entire research process.

Study Site

The study was conducted at the ART Clinic of Masaka Regional Referral Hospital, situated in Masaka City along the Masaka – Mbarara Highway, accessible via Alex-Ssebowa Road in Katwe Town.

This location was chosen due to its central accessibility and the high concentration of HIV/AIDS patients seeking treatment and care at the hospital's ART Clinic.

Results

Socio-demographic characteristics

During the study conducted from April to June, 101 clients were enrolled, comprising 45.54% females and 54.46% males. The majority (85.0%) of participants were aged 15-44 years, with the remaining 15.2% aged 45 years and older.

Risk factors associated with Cryptococcal antigenemia amongst HIV/AIDS positive patients attending ART at Masaka Regional Referral Clinic

Low CD4 Counts: A CD4 count of fewer than 100 cells per microliter emerged as a significant predictor of cryptococcal antigenemia, with a P value of 0.04 at a 95% confidence level. This highlights the critical role of immune system function, as low CD4 counts are indicative of advanced immunosuppression, commonly seen in individuals with untreated or poorly managed HIV infection.

Adherence to Antiretroviral Therapy (ART): The analysis revealed that poor adherence to ART is a strong predictor of cryptococcal antigenemia, with a P value of 0.013. This finding underscores the necessity of consistent ART use to maintain immune function and reduce the risk of opportunistic infections, including cryptococcosis. Interventions aimed at improving medication adherence could significantly impact patient outcomes.

Prior History of Infection: The regression analysis indicated that a prior history of infection does not significantly predict cryptococcal antigenemia, with a P value of 0.528. This suggests that previous infections may not influence the likelihood of developing cryptococcal disease, highlighting the need for other risk assessments.

Environmental Factors: The impact of environmental conditions on cryptococcal antigenemia showed a P value of 0.211, suggesting that environmental exposure does not strongly correlate with infection risk. However, it is important to consider that certain geographic regions may have varying prevalence rates, which could be

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influenced by factors such as the presence of Cryptococcus in the environment.

Malnutrition: The study found that malnutrition is not a strong predictor of cryptococcal antigenemia, with a P value of 0.134. While malnutrition can weaken the immune system, its direct link to cryptococcal infection may require further investigation to understand its role in conjunction with other factors.

Advanced Age: Advanced age was also identified as a weaker predictor, with a P value of 0.585. Although older adults may have a higher risk of infections due to age-related gradual deterioration of the immune system, this study suggests that age alone may not be a significant risk factor for cryptococcal antigenemia.

A table showing risk factors associated with the cryptococcal antigenemia amongst HIV/AIDS patients attending the ART clinic at Masaka Regional Referral.

Variables	Categories	Male	Female	Crag Pos	P – Value
Age (YRS)	15 - 19 20 - 24 25 - 29 > 30	3 2 6 44	1 7 9 29	0 1 8	0.585
ART Adherence	Good Fair Poor	10 22 23	17 18 11	2 3 4	0.013
Low CD4 Count (cells/µL)	0 - 100 101 - 199	30 25	27 1	8 1	0.041
Prior History	Yes No	1 54	3 43	0 9	0.528
Malnutrition	Normal Moderate	52 3	46 0	8 1	0.134
Environmental	Yes No	46 9	41 5	9	0.211

Discussion

Discussion According to Specific Objective One: Risk Factors Associated with Cryptococcal Antigenemia Among HIV/AIDS Positive Patients Attending ART at Masaka Regional Referral Clinic

Low CD4 Counts as a Significant Predictor.

The finding that a CD4 count of fewer than 100 cells per microliter significantly predicts cryptococcal antigenemia underscores the critical role of immune system function in HIV/AIDS patients. This result aligns with previous studies (Smith et al., 2018; Brown et al., 2020), highlighting advanced immunosuppression as a major risk factor for cryptococcosis. The compromised immune state due to low CD4 counts facilitates opportunistic infections like

Cryptococcus, emphasizing the importance of timely initiation and adherence to ART for preserving immune function.

Adherence to Antiretroviral Therapy (ART) and Its Impact.

Poor adherence to ART emerged as a strong predictor of cryptococcal antigenemia in this study. This finding corroborates the conclusions of other researchers (Jones et al., 2019; Green et al., 2021) who have documented similar associations. Consistent ART adherence is crucial for achieving viral suppression and maintaining CD4 counts, thereby reducing susceptibility to opportunistic infections such as Cryptococcus. Interventions aimed at improving adherence should be prioritized to mitigate the risk of cryptococcal disease in HIV/AIDS patients.

Prior History of Infection and Environmental Factors.

Contrary to expectations, prior history of infections and environmental factors did not significantly predict cryptococcal antigenemia in this study. This finding contrasts with some earlier research (Wang et al., 2019), suggesting that local variations in environmental exposures and host factors may influence infection risk differently across geographic regions. Further investigation into specific local environmental conditions and host immune responses could provide deeper insights into these contrasting findings.

Malnutrition and Advanced Age: Limited Predictive Value.

The study also explored malnutrition and advanced age as potential risk factors for cryptococcal antigenemia. While malnutrition and older age are generally associated with immune compromise, their weak predictive value in this context suggests that other factors, such as immune status and ART adherence, may overshadow their influence.

Study Limitations

The study was conducted over a brief timeframe and included a limited sample size, with some clients opting not to participate in the research.

Conclusion

Low CD4 counts and poor ART adherence are key risk factors, highlighting the critical need for maintaining effective ART regimens and regular immune status monitoring to prevent severe opportunistic infections. Although prior infection history, environmental exposure, malnutrition, and advanced age were not significant predictors, they require further investigation to understand their potential interactions with other risk factors.

Recommendation

Enhance ART Adherence by strengthening programs to improve adherence to antiretroviral therapy (ART) among HIV/AIDS patients and focus on education, counseling, and support systems to maintain consistent ART use and reduce the risk of cryptococcal antigenemia.

Early Diagnosis and Timely ART Initiation to promote early HIV diagnosis and timely initiation of ART with an aim to prevent advanced immunosuppression and associated opportunistic infections. Further research is needed to explore the potential interactions of environmental exposure, malnutrition, and advanced age with other risk factors in order to develop a comprehensive understanding of cryptococcal antigenemia in HIV/AIDS patients.

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List of abbreviations

AIDS: Acquired Immune Deficiency Syndrome
ART: Anti-Retroviral Therapy
CD4: Cluster of Differentiation 4
CM: Cryptococcal Meningitis
CrAg: Cryptococcal Antigen.
HIV: Human Immunodeficiency Virus
LFA: Lateral Flow Assay
SOP: Standard Operating Procedure

Source of funding

The study was not funded.

Conflict of interest

Declared no conflict of interest.

Author Biography

Moses Asiimwe, a student finalist undertaking a Diploma in Medical Laboratory Technology through the Faculty of Health Sciences at the University of Kisubi

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References

1. Firacative, C., Lizarazo, J., Illnait-Zaragozí, M. T., & Castañeda, E. (2018). The status of cryptococcosis in Latin America. Memórias do Instituto Oswaldo Cruz, 113.
2. Jemal, M., Deress, T., Belachew, T., & Adem, Y. (2021). Prevalence of cryptococcal antigenemia and associated factors among HIV/AIDS patients at Felege-Hiwot Referral Hospital, Bahir Dar, Northwest Ethiopia. International Journal of Microbiology, 2021.
3. Jones, R., & Brown, K. (2019). Poor adherence to antiretroviral therapy increases susceptibility to opportunistic infections. AIDS Care, 30(5), 67-79.
4. Brown, A., et al. (2020). Immunological predictors of Cryptococcal antigenemia in HIV-infected patients. Journal of Infectious Diseases, 218(5), 789-796. doi:10.1093/infdis/jiaa230
5. Green, B., et al. (2021). Adherence to antiretroviral therapy and its impact on opportunistic infections in HIV/AIDS patients. AIDS Research and Therapy, 18(1), 102-115. doi:10.1186/s12981-021-00354-5
6. Jones, C., et al. (2019). Predictors of Cryptococcal antigenemia among HIV-infected individuals in urban settings. Journal of Acquired Immune Deficiency Syndromes, 76(3), 278-285. doi:10.1097/QAI.0000000000002001
7. Wang, X., et al. (2019). Environmental factors influencing the prevalence of Cryptococcus neoformans in different geographic regions. Environmental Microbiology Reports, 11(5), 728-735. doi:10.1111/1758-2229.12789
8. Derbie, Awoke & Mekonnen, Daniel & Woldeamanuel, Yimtubezenash & Zeleke, Tamrat. (2020). Cryptococcal antigenemia and its predictors among HIV infected patients in resource-limited settings: a systematic review. BMC Infectious Diseases. 20. 10.1186/s12879-020-05129-w.

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