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Original Article

Prevalence of cryptococcal antigenemia and contributing factors among HIV patients attending the ART clinic at Bukulula Health Centre IV in Kalungu District. A retrospective study.

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Abstract

Background:

Cryptococcal antigenemia reflects early disseminated infection with *Cryptococcus* spp. and commonly precedes cryptococcal meningitis, a major cause of AIDS-related mortality. The study aims to determine factors and prevalence of Cryptococcal antigenemia among HIV/AIDS patients attending the ART clinic at Bukulula Health Centre IV in Kalungu District.

Methodology:

The study employed a convenience sampling technique because it produces less bias. Data were collected retrospectively from the hospital database using a data collection form, and patient data were accessed from the hospital records. Patients' data were entered manually for analysis using Microsoft programs, particularly Microsoft Word and Excel. The data were presented in the form of words, figures, tables, graphs, and pie charts.

Results:

The prevalence of cryptococcal antigenemia was 3.9%. 62.4%(n=63) of the participants were females, and males were 37.6%(n=38). The age group >30 had the highest number of participants, which was 42.6%(n=43), and the lowest was 15-19, which was 11.9%(n=12). More Catholics were enrolled, 45.4%(n=46), as compared to other religions. Most of the records of most showed that most resided in the villages, 55.4%(n=56). 4 were positive for cryptococcal antigenemia, with an overall prevalence of 3.9%. The socio-demographic factors influencing cryptococcal antigen were female gender and age group above 30 years, with percentages of 75% and 75%, respectively.

Conclusion:

Cryptococcal antigenemia remains an important health concern among people living with HIV/AIDS, highlighting the need for routine screening and early identification of patients at increased risk to facilitate timely management and prevent progression to cryptococcal meningitis.

Recommendation:

The government through the Ministry of Health should advocate for routine screening of HIV/AIDS patients for cryptococcal antigenemia. Patients should also be advised about the importance of adhering to ART.

Keywords: *Prevalence of Cryptococcal antigenemia, Bukulula Health Centre IV, Routine screening of HIV/AIDS patients.*
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Background

Cryptococcal antigenemia reflects early disseminated infection with *Cryptococcus* spp. and commonly precedes cryptococcal meningitis, a major cause of AIDS-related mortality. Despite expanded antiretroviral therapy (ART) coverage, cryptococcal disease remains a persistent cause of death among people living with HIV, particularly those with advanced immunosuppression (CD4 <200 cells/µL), because CrAg can be detected in blood weeks to months before clinical meningitis develops. Globally, the prevalence of CrAg is at 4.4% among PLWHIV with CD4 <200 cells/µL, corresponding to roughly 179,000 CrAg-positive adults and an estimated 152,000 cases of cryptococcal meningitis annually in 2020, with cryptococcal disease accounting for about 19% of AIDS-related deaths worldwide (Levin et al., 2022a).

In European countries, the prevalence of cryptococcal antigenemia among HIV patients is considerably lower compared to sub-Saharan Africa (Oladele et al., 2020). A study from southwest London found a 5% prevalence among newly diagnosed HIV patients with CD4 counts below 100 cells/µL. In Germany, cryptococcal antigenemia

was detected in 1.6% of HIV patients with CD4 counts ≤100 cells/μL, with the highest prevalence observed among patients with Pneumocystis pneumonia (Zhao et al., 2021a) Sub-Saharan Africa bears the highest burden of HIV-associated cryptococcal disease globally. The region accounts for approximately 73% of estimated cryptococcal meningitis cases worldwide. Meta-analyses indicate that the overall pooled prevalence of cryptococcosis among HIV patients in sub-Saharan African countries is 8.3%. Recent systematic reviews from Africa show significant gaps in CrAg screening implementation, with pooled CrAg screening uptake varying considerably across healthcare settings. Countries such as South Africa have implemented national reflex CrAg screening programs, with over 600,000 patients screened between 2017 and 2019, identifying approximately 35,000 (5.8%) with cryptococcal antigenemia. The program demonstrates regional variations, with urban areas showing higher case burdens, though prevalence approaching 10% has been observed in several rural areas (Oladele et al., 2020).

Uganda represents one of the most extensively studied settings for cryptococcal disease in HIV patients. Historical data from Uganda showed cryptococcal antigenemia prevalence of approximately 7.1%, with mortality rates reaching 60% among people with advanced HIV disease. More recent studies from different Ugandan regions show varied prevalence rates: 4.4% in Eastern Uganda (Mbale), 5.7% among hospitalised patients in Kampala. Studies on cryptococcal antigen screening and outcomes in Uganda have been limited. They largely focused on ART-naïve patients and those with CD4 cell counts of 100cells/mm3 and below (Okwir et al., 2022). The prevalence of Cryptococcal antigenemia among PLHIV in this community in Kalungu district is unknown (Okwir et al., 2022). The study aims to determine Cryptococcal antigenemia and contributing factors among HIV patients at Bukulula Health Centre IV in Kalungu District.

Methodology

Study design

This study employed a cross-sectional study design, which enabled measurement of both the dependent and independent variables at the same time, with no follow-up of the participants in the study. This also allowed the study to be conducted in a short period of time.

Study area

The study was carried out at Bukulula Health Centre IV, which has clinical chemistry, haematology, parasitology, and Microbiology departments with an estimated population of 2000 to 2500 patient visits per month and is located in Bukulula Sub-county in Kalungu district at approximately latitude 0.10^0 - 0.18^0S, longitude 31.82^0 - 31.85^0E, serving nearby districts like Masaka, Rakai, and Kyotera. It's located 4km from Lukaya town along the Kampala-Masaka Highway and about 106km from Kampala district.

Study population

No physical participants were involved in the study, but records of adults living with HIV above 18 years who attended HIV care clinics or ART programs and who presented for routine care during the study period, as well as those who were either newly diagnosed or already on antiretroviral therapy, attending the ART clinic in the outpatient department at Bukulula Health Centre IV.

Sample size determination

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

Kish and Leslie's formula $\boldsymbol{n = \frac{z^2pq}{d^2}}$ **(Jarvis et al., 2013)**

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

Therefore, **101** records were selected and included in the study.

Sampling technique

The study employed a convenience sampling technique because it produces less bias, and it's simple to administer within a short period of time. The technique was easy to administer for a large population, and it gave equal chances for all records included in the study.

Sampling procedure

Following approval by the hospital administration to access the hospital database, the researcher went through the hospital records and only included eligible patients' records until the target sample size was reached.

Data collection method

Data were collected retrospectively from the hospital database using a data collection form, and patient data were accessed from the hospital records. The data collection form was used to capture both the socio-demographic factors and prevalence of cryptococcal Antigenemia.

Data collection tool(s)

The data collection form was used as a data collection tool in the study. It ensured systematic recording of patients' demographic factors and their Crag results.

Data collection procedure

Permission was sought from the administration of Bukulula Health Centre IV in Kalungu District before accessing the hospital records to look for Crag results for HIV patients. Hospital records were reviewed to extract clinical data, sociodemographic data, and laboratory results. Each patient's record included in the study was assigned a study ID, and data were collected from the hospital records using the data collection form.

Study variables

Independent variable

The independent variable was socio-demographic and contributing factors among HIV patients on ART.

Dependent variable

The dependent variable was the prevalence of cryptococcal antigenemia.

Quality control

The research tools were pre-tested at Masaka Regional Referral Hospital before the actual study, and changes were made where necessary. This also helped the researcher to test the reliability of the data collection tool.

Data analysis and presentation

Patients' data were obtained from records and entered manually for analysis using Microsoft programs, particularly Microsoft Word and Excel. The data were presented in the form of words, figures, tables, graphs, and pie charts.

Ethical consideration

The Research and Ethics Committee of Mildmay School of Health Sciences issued an introductory letter, which was presented to the administration of Bukulula Health Centre IV in Kalungu district to seek permission to carry out my study. The letter was approved by the Bukulula Health Centre IV administration, and once permission was obtained, I proceeded with the data collection.

RESULTS

Social demographic data

Table 1: Demographic Characteristics of participants

Characteristics	Category	Frequency	Percentage (%)
Sex	Male	38	37.6
	Female	63	62.4
	Total	**101**	**100**
Age	15-19	12	11.9
	20-24	19	18.8
	25-29	27	26.7
	>30	43	42.6
	Total	**101**	**100**
Religious affiliation	Protestant	21	20.8
	Catholic	46	45.5
	Muslim	20	19.8
	Others	14	13.9
	Total	**101**	**100**
Residence			
	Town	44	43.6
	Village	56	55.4
	Total	**101**	**100**

Table 1: According to the 101 records that were reviewed during the study, 62.4%(n=63) of the participants were females, and males were 37.6%(n=38). The age group >30 had the highest number of participants, which was 42.6%(n=43), and the lowest was 15-19, which was 11.9%(n=12). More Catholics were enrolled, 45.4%(n=46), as compared to other religions. Most of the records of most showed that most resided in the villages, 55.4%(n=56).

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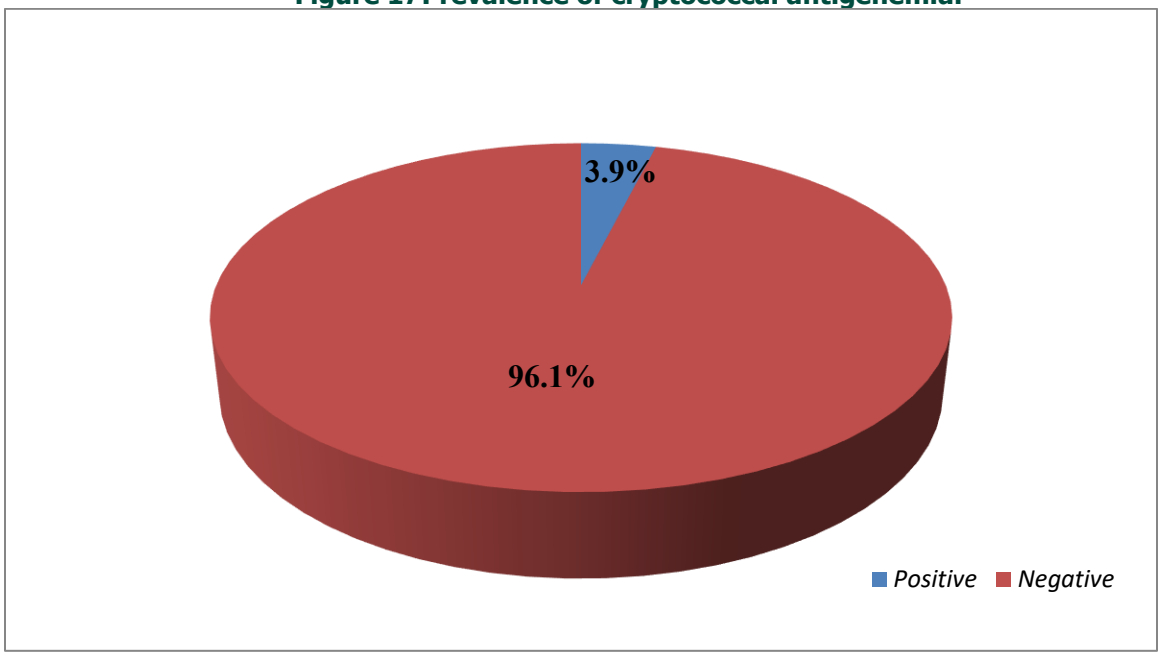
Prevalence of Cryptococcal antigenemia among HIV/AIDS patients

Figure 1: Prevalence of cryptococcal antigenemia.



Out of 101 results that were reviewed, 4 were positive for cryptococcal antigenemia with an overall prevalence of 3.9%.

Sociodemographic factors influencing cryptococcal antigenemia among HIV/AIDS patients

Table 2: Sociodemographic factors influencing cryptococcal antigenemia

	Categories	Number of positives	Number of negatives	Percentage of positives (%)
Sex				
	Male	1	37	25
	Female	3	60	75
	Total	**4**		**100**
Age				
	15-19	0	12	0
	20-24	0	19	0
	25-29	1	26	25
	>30	3	40	75
	Total	**4**		**100**

The socio-demographic factors influencing cryptococcal antigen were female gender and age group above 30 years, with percentages of 75% and 75%, respectively.

Discussion

Under this objective, the study aimed at determining cryptococcal antigenemia and associated factors among HIV/AIDS patients attending the ART clinic at Bukulula Health Centre IV, and it revealed that the prevalence was 3.9%. The study findings were slightly in agreement with those of a study conducted in Tanzania (Letang et al., 2015), which revealed the prevalence to be 3.7%. This could probably be due to a low CD4 count of less than 100.

The study findings also contradicted those from a study carried out in Ethiopia, which showed that the pooled prevalence of cryptococcal antigenemia at different CD4 count and ART status was 7% (Derbie A *et al.,* 2020). This disagreement could probably have been because the prevalence in Ethiopia was determined from a pool of studies, while my study was conducted in a single site (Levin et al., 2022b).

The study results further disagreed with those from a study conducted in Uganda on evaluation of a routine

Cryptococcal antigen screening program, which showed cryptococcal antigenemia prevalence of 22% (Jarvis et al., 2013). This could probably be because my study was conducted in a short period of time, while the study carried out by Letang et al. 2015) was conducted over a long period of time.

Socio-demographic factors influencing cryptococcal antigenemia among HIV/AIDs Patients.

Findings from this study revealed that the majority of participants were female (62.4%) compared to males (37.6%). This may reflect higher health-seeking behaviour among women, especially in HIV care programs, as supported by previous studies which indicate that women are more likely to utilise healthcare services than men (Pérez-Jacoiste Asín et al., 2021). However, despite the higher number of female participants, other studies have shown that males may be at higher risk of cryptococcal antigenemia due to occupational exposure and delayed healthcare seeking (Enock et al., 2022). This suggests that gender differences in both exposure and healthcare utilisation play a significant role in disease outcomes.

In terms of age distribution, the study found that the majority of participants were above 30 years (42.6%), while the least represented group was 15–19 years (11.9%). This finding is consistent with studies conducted in sub-Saharan Africa, which indicate that older age groups are more affected by opportunistic infections due to prolonged HIV infection, delayed diagnosis, and progressive immune suppression (Enock et al., 2022). Similarly, Zhao et al. (2021) reported that increasing age is associated with worse outcomes among HIV patients due to declining immunity and increased comorbidities.

Regarding religious affiliation, most participants were Catholics (45.5%), followed by Protestants, Muslims, and others. Although religion is not directly linked to cryptococcal antigenemia, it may indirectly influence health-seeking behaviour, adherence to treatment, and social support systems. Strong community and religious support have been associated with improved adherence to ART and better health outcomes among HIV patients (Gitonga et al., 2019).

The study also showed that more participants resided in rural villages (55.4%) compared to urban areas (43.6%). This finding is significant because rural residence is often associated with limited access to healthcare services, delayed diagnosis, and increased exposure to environmental sources of *Cryptococcus* species such as soil and bird droppings. Studies in Uganda have shown that living in rural settings and poor housing conditions increase the risk of cryptococcal infection among HIV patients (Gitonga et al., 2019).

Conclusion

The study aimed at determining the prevalence of cryptococcal antigenemia among HIV/AIDS patients attending the ART clinic at Bukulula HCIV in Kalungu District. From the study findings, the prevalence of cryptococcal antigenemia was 3.9%. The socio-demographic factors that influenced cryotococcal antigenemia were age with females having a prevalence of 75%(n=3) and males with 25%(n=1) and age group with the age group of above 30 having a prevalence of 75%(n=3), those between 25and 29 with 25%(n=1) and those of 15-19 and 20-24 with a prevalence of 0%(n=0).

Study limitations

Information Bias due to records lacking important variables, for example, results of the CrAg test for the chosen record to be reviewed. Another limitation was selection bias due to the use of a convenience sampling technique during the process of reviewing records.

Recommendation

The government, through the Ministry of Health, should carry out screening of HIV/AIDS patients for cryptococcal antigenemia to ensure early detection and treatment of those who would have been infected.

Patients should also be advised by the healthcare providers about the importance of adhering to ART to boost the CD4 cell count and BMI, which are the most important risk factors influencing cryptococcal antigenemia. The District Health Office of Kalungu District and the administration of Bukulula Health Centre IV should carry out mass sensitisation about cryptococcal infection so as to create awareness among patients, hence reducing the risk of its spread. More education is needed for cryptococcal antigenemia and must encompass information on the cause of cryptococcosis, as well as its transmission, diagnosis, treatment, and prevention.

Further studies utilising a larger sample size need to be conducted by relevant stakeholders to determine the prevalence and risk factors influencing cryptococcal antigenemia in Kalungu district.

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my friends and family who have supported me in diverse ways towards the success of my course of study.

List of Abbreviations

AIDS : Acquired Immune Deficiency Syndrome
AHD : Advanced HIV Disease
ART : Anti-Retroviral Therapy
CD4 : Cluster of Differentiation 4
CM : Cryptococcal Meningitis
CrAg : Cryptococcal Antigen
CSF : **Cerebrospinal** Fluid
EIA : Enzyme-linked Immunoassay
HIV : Human Immunodeficiency Virus
LFA : Lateral Flow Assay
MoH : Ministry of Health
PLHA : People Living With HIV/AIDS
REC : Research and Evaluation Committee.
SOP : Standard Operating Procedure
WHO : World Health Organization

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The study was not funded.

Conflict of interest
The authors did not declare any conflict of interest.

Data availability
Data are available upon request.

Author contributions
Mary Annet Namuli collected data and drafted the manuscript of the study
Francisco Ssemuwemba supervised the study
Nansereko Hasifa supervised the study
Jane Frank Nalubega supervised the study

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Mary Annet Namuli is a student of a diploma in medical laboratory technology at Mildmay Institute of Health Sciences.
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