Poster #835

High Prevalence of Undiagnosed Cryptococcal Antigenuria at HIV Diagnosis across the CD4 Spectrum in Durban

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BACKGROUND

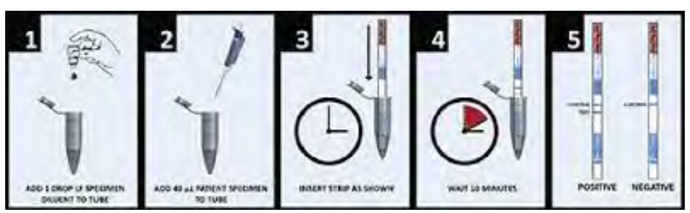
- Cryptococcal meningitis (CM) is a leading cause of HIV-related mortality and is responsible for approximately 600,000 annual deaths worldwide.
- World Health Organization (WHO) recommends cryptococcal antigen (CrAg) screening for HIV–infected patients with CD4 ≤100/mm^3 to identify cryptococcosis.
- Cryptococcosis causes many hospital admissions in South Africa, but the prevalence at HIV-diagnosis in the KwaZulu-Natal province is unknown.

OBJECTIVE

- To measure cryptococcal antigenuria prevalence among newly-diagnosed HIV-infected adults, irrespective of CD4 count, who presented for voluntary HIV testing and counseling at different outpatient clinics in Durban, South Africa.

METHODS

- We conducted a cross-sectional study of newly-diagnosed HIV-infected adults (≥18 years) who presented for voluntary HIV testing and counseling to 4 outpatient clinics in Durban from Oct 2011-May 2012.
- Urine samples were collected in sterile containers at the time of enrollment, and frozen at -20° until June 2013 when all samples were thawed and batch tested.
- Testing was performed using a WHO-endorsed rapid cryptococcal antigen lateral flow assay (Immy Inc., Norman, USA) according to the manufacturer's specifications (below).
- In primary analyses, cryptococcal antigenuria prevalence was stratified by CD4 above and below 100/mm^3, the current recommended threshold for cryptococcosis screening.
- In secondary analyses, cryptococcal antigenuria prevalence was stratified by CD4 above and below 200/mm^3, the current recommended threshold for stopping oral fluconazole prophylaxis.



FUNDING

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RESULTS

Table 1. Cohort Characteristics (N=806).

	N	*(%)*
Demographics		
Age mean (± SD)	34.4	± 9.8
Female	320	(39.7)
CD4 Count		
Total (Median, IQR)	210	80-358
>350	172	(21.3)
201-350	169	(20.1)
101-200	123	(15.2)
<100	196	(24.3)
<50	123	(14.0)

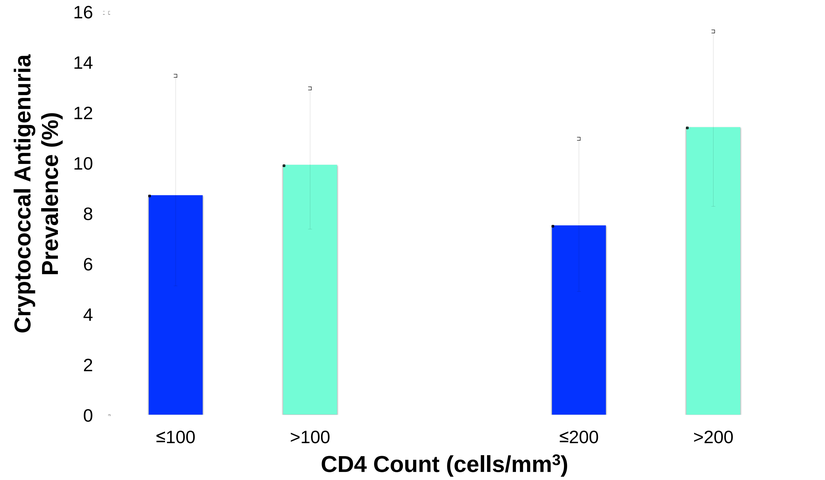
Table 2. Cryptococcal Antigenuria Prevalence (N=806).

Urine CrAg Testing	*N*	*(%)*
CrAg+	80	(9.9)
CD4 Count by CrAg Status	*Median*	*(IQR)*
CrAg+	249	83 – 445
CrAg-	203	80 – 352

Table 3. Cryptococcal antigenuria prevalence among HIV-infected adults stratified by CD4

	# Positive/ # Tested	*Prevalence (%) (95% CI)*
Total	80 / 806	9.9 (7.9 – 12.2)
Stratified by CD4 category		
CD4 >350/mm^3	21 / 172	12.2 (7.7 – 18.1)
CD4 201-350/mm^3	18 / 169	10.7 (6.4 – 16.4)
CD4 101-200/mm^3	7 / 123	5.7 (2.3 – 11.4)
CD4 <100/mm^3	17 / 196	8.7 (5.1 – 13.6)
CD4 <50/mm^3	14 / 113	12.4 (6.9 – 19.9)
Missing CD4 count	17 / 146	11.6 (6.9 – 18.0)

Figure 1. Cryptococcal antigenuria prevalence above and below CD4 100/mm^3 (WHO-recommended screening threshold) and above and below CD4 200/mm^3 (WHO-recommended prophylaxis threshold).



KEY POINTS

- Cryptococcal antigenuria prevalence was 9.9% among all newly-diagnosed HIV-infected adults in our study, irrespective of CD4 count, in Durban, South Africa.
- Cryptococcal antigenuria prevalence was not significantly higher using the WHO-recommended CD4 count threshold for CrAg screening or for stopping prophylaxis.

STRENGTHS & LIMITATIONS

- We included a large sample of newly diagnosed HIV-infected adults, which allowed for stratification across CD4 categories.
- CrAg concentration is 20-fold less in urine than in plasma or serum. We performed testing on thawed urine samples and did not perform laboratory reference standard testing on urine and/or blood samples. The use of urine samples may have underestimated the true burden of disease.
- Two studies have shown the rapid assay has 98% sensitivity (78/80), compared with latex agglutination (LA), gold standard for CrAg detection in serum.

CONCLUSIONS

- **Approximately 1 in 10 newly-diagnosed HIV-infected people in Durban, South Africa had evidence of cryptococcal antigenuria.**
- **Since the prevalence was similar for those with high and low CD4, current screening recommendations may miss HIV-infected people with cryptococcosis.**