Prevalence of *Cryptococcus* Antigenemia (CrAg) among HIV Infected Adults with Advanced Immunosuppression in Namibia

Presented at the African Society of Laboratory Medicine 2nd conference

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Background (1)

- Cryptococcal meningitis (CM) is common among severely immunosuppressed HIV-individuals and is associated with high mortality.
- The World Health Organization (WHO) recommends routine screening for cryptococcal disease in antiretroviral (ART)-naïve adults with a $CD4^+$ count <100 where CrAg prevalence is ≥3%.
- Several countries in sub-Saharan Africa (SSA), including South Africa have implemented routine screening programs.

Background (2)

- Namibia ranks among countries with the highest HIV prevalence in the world (18.2%).
- Namibia antiretroviral treatment (ART) program has achieved high coverage (>80% among people in need by 2014).
- Many HIV-infected patients still present at enrollment in HIV care with advanced immunosuppression:
  - Routine program data (2013) indicates that 16.7% of patients have $CD4^{+}$<100 at ART initiation.

Study Objective

- The objective of this study was to measure CrAg prevalence among HIV positive adults in Namibia with CD4<200 cells/uL

- Results were intended to guide development of routine CrAg screening strategies among HIV infected adults in Namibia.

Methods

- Cross-sectional study design
- Specimens sampled consecutively from patients receiving routine CD4+ testing at all MOHSS facilities providing routine HIV care.
  - Specimens with $CD4^+$ counts of <100 cells/uL and 100-200 cells/uL were identified and selected.
- CrAg testing performed on remnant specimens after routine $CD4^+$ testing using the IMMY® Lateral Flow Assay (LFA)
- Data analyzed using Stata/SE 12.1

Results (1)

Table 1. Demographic and clinical description of patient specimens

Patient samples included, #	836
Sex, #, [% (95% CI)] [a]	
Female	380, (46.1)
Age, median (IQR) years [b]	38 (32 - 46)
CD4 $^{+}$ result, median (IQR) cells/uL [c]	85 (51 - 114)
CD4 $^{+}$ strata, #, [% (95% CI)]	
< 100 cells/uL	520, [63.1 (59.7 -66.4)]
100 - 200 cells/uL	304, [36.9 (33.6 – 40.3)]

[a.] data on sex missing from 11 patients
[b.] data on age missing from 12 patients
[c.] data on CD4 result missing from 12 patients

Results (2)

Table 2. Prevalence of CrAg among HIV infected adults with advanced immunosuppression and factors associated with CrAg positivity

	CrAg prevalence (95% CI) [a]	AOR (95% CI) [b]	*P*-val.
Overall	3.4 (2.3 – 4.9)		
Sex			
Female	3.2 (1.6 – 5.5)	Ref.	
Male	3.6 (2.1 – 5.8)	1.20 (0.55 – 2.59)	0.65
Age [c]			
< 38 years	3.6 (2.1 – 6.2)	Ref.	
≥ 38 years	3.2 (1.8 – 5.5)	0.84 (0.39 – 1.80)	0.66
CD4⁺ count			
< 100 cells/uL	4.0 (2.5 – 6.1)	Ref.	
100 - 200 cells/uL	2.3 (0.1 – 4.7)	0.55 (0.23 – 1.31)	0.18

[a] 95% confidence intervals are binomial exact. [b] AOR, adjusted for all variables included in the table. [c] age strata defined by being < or ≥ the median age (38 years) of patients included.

Discussion (1)

- This is the first study to estimate the prevalence of CrAg among HIV-infected adults in Namibia
  - CrAg prevalence of $\geq$ 3.0% among patients with $CD4^{+}$<100 cells/uL justifies routine CrAg screening and preemptive treatment.
  - Given the high mortality associated with HIV-related CM, our results demonstrate that routine screening for CrAg and preemptive treatment has the potential to save lives in Namibia.

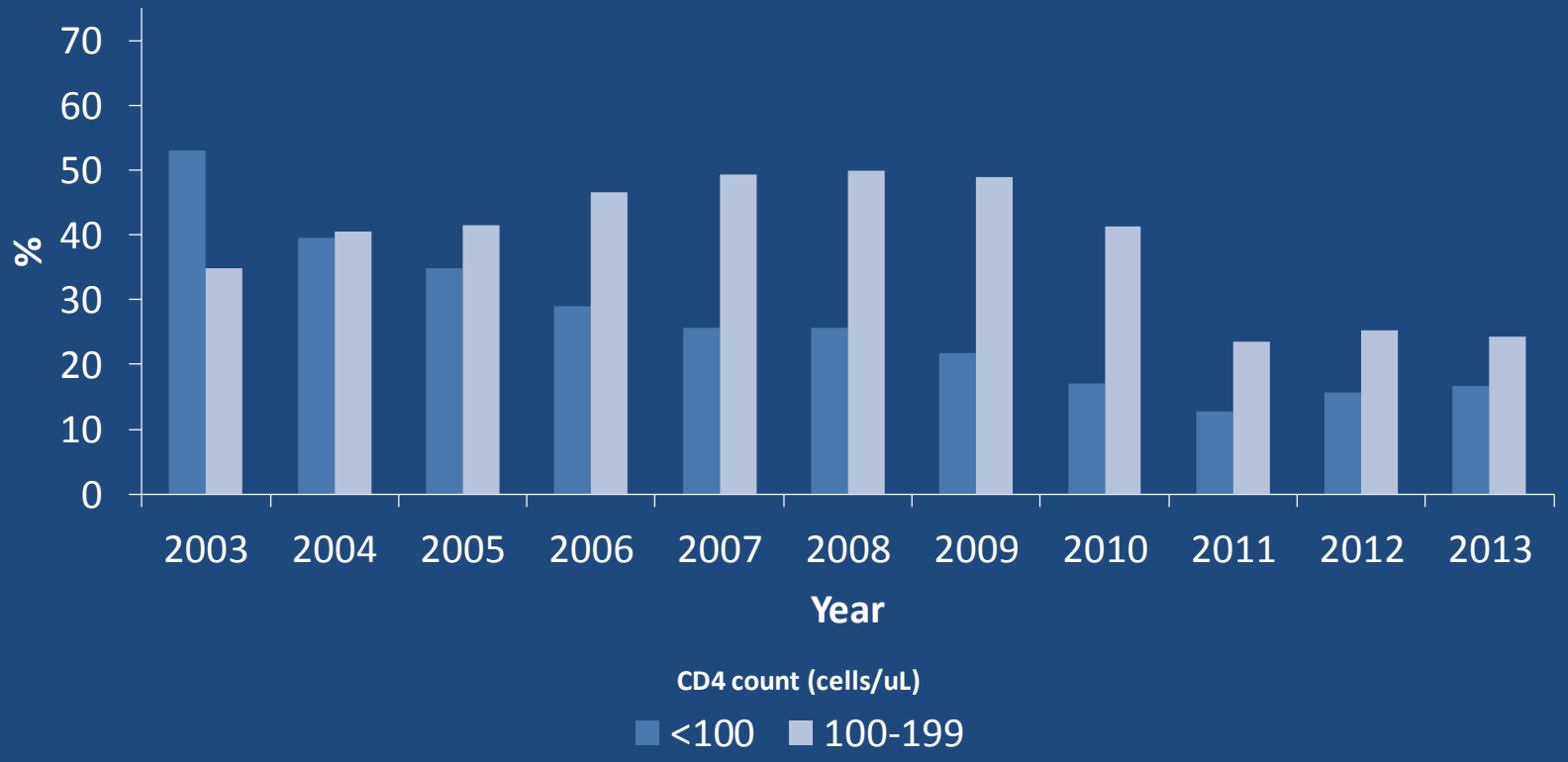
Discussion (2)

- CrAg prevalence estimated in our study was lower than estimates from other countries in the region. Reasons for varying may include:
  - different methodologies for assessing prevalence
  - differences in host factors or geographic variations in the epidemiology of CM within sub-Saharan Africa region.
  - inclusion of ART-experienced patients in our sample
- Our study found non-significant differences in prevalence between patients with $CD4^+ < 100$ and 100-200 cells/uL
  - potential benefits of including patients with $CD4^+$ 100-200 cells/uL in routine CrAg screening guidelines.

Discussion (3)

Many patients still present to ART with advance immunosuppression. The success of routine CrAg screening will still depend on improved strategies for earlier diagnosis and treatment of HIV infection.

Figure 1. Percentage of patients initiating ART in Namibia at CD4 + count <100 or 100 - 200 cells/uL by year of ART initiation.



Limitations

- Inclusion of ART experienced patients may have biased the estimated prevalence of CrAg downward.
- Failure to achieve the target sample size reduced the overall precision of prevalence estimates
  - external validity of statistical comparisons of CrAg prevalence between sub-groups is limited.
- Study was not powered to make sub-national estimates of CrAg prevalence.

Conclusions

- Theses results were used by the MOHSS and its partners in the revision of national ART guidelines (2014), which now include routine screening for CrAg and preemptive treatment for adults with CD4+ < 100 cells/uL.
  - Routine screening for ART-naïve and ART-experienced patients.
  - providers nationwide began implementing the new screening guidelines in Feb. 2014.
- Other national HIV programs should consider similar assessments and synthesis of the results into policy and guidelines.
- Benefit of CrAg screening will be maximized in Namibia and elsewhere if strategies to improve early initiation of ART can be strengthened.