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Rapid semi-quantitative antigen testing and mortality in cryptococcal meningitis

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BACKGROUND

Mortality rates in individuals with HIV-associated cryptococcal meningitis (CM) remain high in sub-Saharan Africa, with 25-50% of individuals dying within 10 weeks of diagnosis despite antifungal therapy.

Stratifying patients with CM into higher and lower risk groups could help guide management and target at-risk individuals for more intensive care.

The BIOSYNEX® CryptoPS is a semi-quantitative, lateral flow immunochromatic test designed for the detection and quantification of cryptococcal antigen (CrAg) in bloods and cerebrospinal fluid (CSF), and may have value as both a diagnostic and a prognostic tool.

We performed a study to determine the utility of BIOSYNEX® CryptoPS testing in individuals presenting with CM in Botswana and Malawi.

METHODS

From January 2018 to February 2021, EDTA whole blood specimen were collected from patients admitted with CM and included in the AMBITION-cm clinical trial in Botswana (Princess Marina Hospital, Gaborone) and Malawi (Queen Elizabeth Hospital, Blantyre).

CrAg detection and quantification were performed using the BIOSYNEX® CryptoPS according to manufacturer's instruction, with individuals classified as negative, low titer, or high titer.

We determined associations between CryptoPS titers and baseline variables, and used Cox regression to explore the relationship between CryptoPS titer and 10-week mortality.

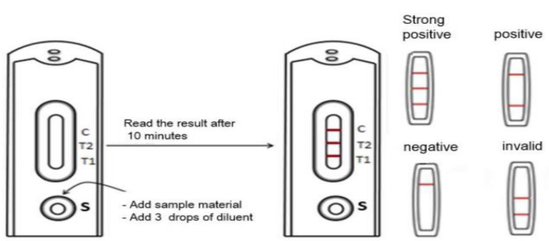


Figure 1: Interpretation of the BIOSYNEX® CryptoPS results

The BIOSYNEX® CryptoPS semi-quantitative CrAg assay provides useful prognostic information in individuals presenting with HIV-associated cryptococcal meningitis. Individuals with high blood CryptoPS titers were almost twice as likely to die as those with low titers.

RESULTS

We tested 187 individuals presenting with CM using the BIOSYNEX® CryptoPS on whole blood. 181 of 187 (97%) were CryptoPS positive; 79/181 (44%) had a low titer, and 102/181 (56%) had a high titer.

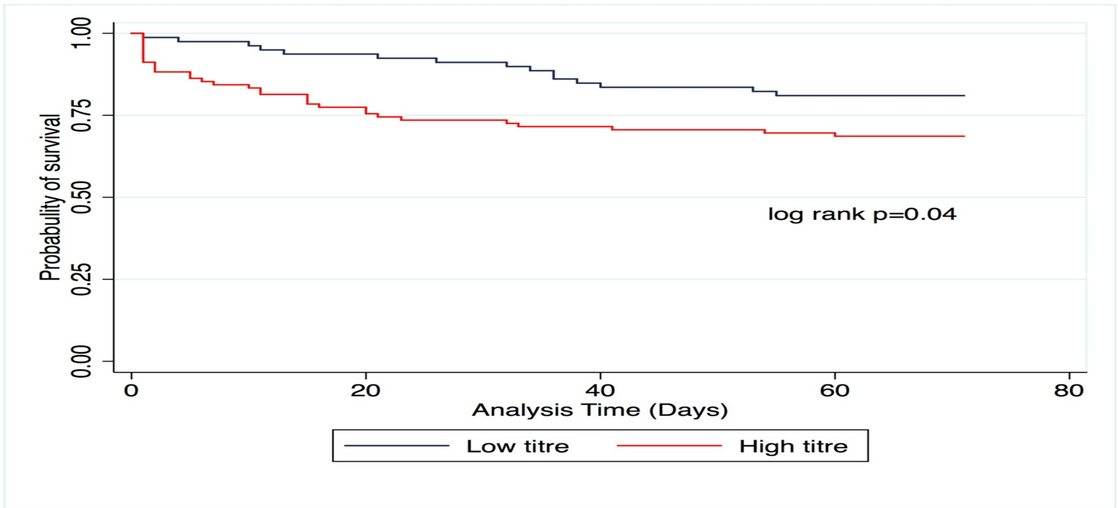


Figure 2. – Kaplan Meier curves showing the probability of survival among patients with HIV-associated cryptococcal meningitis with high CrAg titer levels compared to those with low titer levels.

RESULTS (cont.)

Over 10 weeks of follow-up, 32/102 (31%) of those with high titers died compared to 15/79 (19%) with low titers [HR 1.88, 95% confidence interval 1.02-3.47, p=0.04]. This mortality difference remained significant after adjustment for age, sex, and treatment group.

Table 1: Factors associated with CrAg titer levels

	Low CrAg titer	High CrAg titer	P-value
Median Age, years (IQR)	38 (33-44)	37 (32-42)	0.46
Median CD4 (IQR) cells/uL	44 (26-89)	32 (14-56)	0.02
Median CSF fungal burden (IQR) CFU/ml	2,500 (100-41,500)	310,000 (31,00-1,150,000)	<0.0001

CONCLUSIONS

The BIOSYNEX® CryptoPS semi-quantitative CrAg assay provides useful prognostic information in individuals presenting with HIV-associated cryptococcal meningitis. Individuals with high blood CryptoPS titers had higher baseline fungal burdens in the CSF and were almost twice as likely to die as those with low titers.

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