

Pathway to care among inpatients with symptomatic Cryptococcal Meningitis in Johannesburg, SA

Lia F Edkins^{1,2}, Raphaela Berghammer-Bohmer³, Asha Thombrayil³, Jeremy Nel³, Merika Tsitsi⁴, Jack Adams⁵, Susan T Meiring^{6,7}, Vanessa C Quan⁶, Rudzani C Mashau⁸, David S Lawrence⁹, Kennedy Mupeli¹⁰, Shabbar Jaffar¹¹, Angela Loyse⁵, Duolao Wang¹², Joseph N Jarvis^{9,10}, Thomas S Harrison^{5,13,14}, Tom Boyles³, Nelesh P Govender^{5,8,14,15,16}, Rachel M Wake^{*,5,13,15}, Síle F Molloy^{*,5,15} *joint senior authors

BACKGROUND

Cryptococcal antigen (CrAg) screening and pre-emptive **treatment** reduces risk of HIV-associated cryptococcal meningitis (CM) and death¹.

Understanding the pathway to care following serum CrAg screening is crucial for improving screening practices for people with advanced HIV disease.

METHODS

Participants with HIV-associated symptomatic CM and CD4 count <100cells/μL were consented at two tertiary-level hospitals in Johannesburg, South Africa.

Data was collected through structured interviews and clinical notes. Prior serum CrAg results, if available, were obtained from the Laboratory Information Management System. Participants were asked about their pathway to care prior to presentation.

RESULTS

Among 205 participants with symptomatic CM, 29% (59/205) participants had ever undergone serum CrAg screening prior to hospital admission, of whom 54% (32/59) had a positive result.

Of those with available data, 71% (19/28) had no CM symptoms at the time of testing and the overall average delay until symptom onset was 43 days (Range 6 – 237, n=19).

Of those without symptoms, 94% (14/15) visited a healthcare provider following testing, however (in those with data) only 33% (3/9) had taken any fluconazole prior to hospitalisation.

Of those who did not take fluconazole, 17% (1/6) declined fluconazole, 17% (1/6) were referred for lumbar puncture without fluconazole, and 67% (4/6) were seen by a healthcare provider but neither fluconazole nor lumbar puncture were offered.

These results are from data collected as of February 2025 (data collection is ongoing).

Among 205 individuals with symptomatic CM, 19/205 (**9,3%**) were known to have had **asymptomatic cryptococcal antigenaemia**, prior to the onset of meningitis symptoms.

In this sub-group only **16%** (3/19) were confirmed to have **started pre-emptive fluconazole** following positive serum CrAg result. Those who did not take any fluconazole had an earlier onset of meningitis symptoms.

Within the cascade of care there were **multiple missed opportunities to prevent** symptomatic cryptococcal meningitis.

CONCLUSIONS

- Around a third of participants had ever had serum CrAg screening prior to presentation with symptomatic CM and just over half of these results were positive.
- The majority of participants who were serum CrAg positive did not have any symptoms of meningitis at the time of serum CrAg testing.
- Most people with asymptomatic cryptococcal antigenemia did not receive fluconazole or have a lumbar puncture despite accessing healthcare services.

This study highlights missed opportunities for reducing the incidence of CM and death in people with advanced HIV disease, despite the reflexive CrAg screening programme in South Africa.

Efforts to improve health worker and community understanding around CrAg screening and recommended management are essential.

ACKNOWLEDGEMENTS

We want to thank the study participants for their invaluable contributions to this research. We acknowledge the principal investigators and study teams from the EFFECT Clinical Trial consortium and the GERMS research team, for their role in this study.

This study is a sub-study of the subEFFECT study which is funded through the Academy of Medical Sciences (AMS) Springboard fellowship (awarded to S. Molloy) and supported by Wellcome Trust, Government Department of Business, Energy and Industrial Strategy (BEIS), British Heart Foundation, Diabetes UK and Global Challenges Research Fund (GCRF).

AFFILIATIONS

¹Mycology Division, Wits Health Consortium, South Africa. ²Department of Infectious Diseases, Nelson R Mandela School of Medicine, University of KwaZulu-Natal, South Africa. ³Division of Infectious Diseases, Helen Joseph Hospital, University of the Witwatersrand, South Africa. ⁴Department of Internal Medicine, Chris Hani Baragwanath Academic Hospital, University of the Witwatersrand, South Africa. ⁵Centre for Global Health, Institute for Infection & Immunity, St George's University of London, UK. ⁶Division of Public Health Surveillance and Response, National Institute for Communicable Diseases, National Health Laboratory Service, South Africa. ⁷School of Public Health, Faculty of Health Sciences, University of the Witwatersrand, South Africa. ⁸Centre for Healthcare Associated Infections, Antimicrobial Resistance and Mycoses, National Institute for Communicable Diseases, National Health Laboratory Service, South Africa. ⁹Department of Clinical Research, Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, UK. ¹⁰Botswana-Harvard AIDS Institute Partnership, Botswana. ¹¹Institute for Global Health, University College London, UK. ¹²Department of Clinical Sciences and International Public Health, Liverpool School of Tropical Medicine, UK. ¹³Clinical Academic Group, St George's Hospital NHS Trust, UK. ¹⁴MRC Centre for Medical Mycology, University of Exeter, UK. ¹⁵Mycology Division, School of Pathology in the Faculty of Health Sciences University of the Witwatersrand, UK. ¹⁶Institute of Infectious Disease and Molecular Medicine, University of Cape Town, South Africa.

CONTACT DETAILS

Dr Lia F Edkins, ledkins@witshealth.co.za

REFERENCES

1. Temfack E, Bigna JJ, Luma HN, Spijker R, Meintjes G, Jarvis JN, et al. Impact of Routine Cryptococcal Antigen Screening and Targeted Preemptive Fluconazole Therapy in Antiretroviral-naïve Human Immunodeficiency Virus-infected Adults With CD4 Cell Counts <100/μL: A Systematic Review and Meta-analysis. *Clinical Infectious Diseases*. 2019; 68(4):688–98.

