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DOI:
Poor long-term outcomes for cryptococcal meningitis in rural South Africa

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Objectives. To explore linkage to and retention in HIV care after an episode of cryptococcal meningitis (CM) in rural South Africa.

Design. A retrospective case series of adult individuals (≥16 years old) with laboratory-confirmed CM from January - December 2007 at Hlabisa Hospital – a district hospital in northern KwaZulu-Natal.

Outcome measures. Inpatient mortality and associated risk factors were analysed. The proportion alive and on antiretroviral therapy (ART) at 2 years was determined by linkage to the HIV treatment programme.

Results. One hundred and four individuals were identified with laboratory diagnosis of CM; 74/104 (71.2%) with complete records were included in the analysis. Inpatient mortality was high (40.5%) and was significantly associated with reduced conscious level (aHR 3.09, 95% CI 1.30 - 7.33) and absence of headache (aHR 0.33 for headache, 95% CI 0.13 - 0.87). Only 8 individuals (10.8% of all study subjects) were alive and receiving ART 2 years after the CM episode.

Conclusions. Long-term outcomes of CM are poor in routine practice. Interventions to strengthen linkage to HIV treatment and care and continuation of secondary fluconazole prophylaxis are critical.

alone subsequently initiated ART. Only 8 (10.8% of all subjects, 95% CI 8.7 - 12.8) were alive and receiving ART 2 years after the CM episode. For the 10 confirmed deaths post-discharge, the median time to death was 133 days (IQR 43 - 230).

There was no evidence that included patients (N=74) differed from those excluded (N=30) in terms of sex (p=0.73), age (p=0.13), CSF protein (p=0.35), CSF glucose (p=0.31) or CSF lymphocyte count (p=0.26).

Discussion

These data from routine practice in a rural health district show poor long-term outcomes and highlight the challenges faced by overburdened health services in delivering comprehensive HIV care in high-prevalence settings. The short-term mortality is comparable with data from similar settings,1-3 but higher than reports from clinical trials or tertiary hospitals.4-6 About 1 in 10 of our patients were known to be alive on ART at 2 years, compared with: 60% at 12 months in a clinical trial in Cape Town; 74.0% at 12 months in a Ugandan clinical trial;10 and 27% at 3 years in a trial in Zimbabwe.11 Inpatient mortality was associated with more severe disease (reduced conscious level and absence of headache), as also suggested in a neighbouring hospital suggesting advanced disease at presentation.12 Sub-optimal induction therapy and management of CSF pressure might have contributed to high inpatient mortality, although we could not confirm this. Amphotericin B treatment was uncommon, mainly owing to drug supply problems, in accordance with national-level data showing that more than half of CM cases receive sub-optimal induction treatment.13

Not all patients had their HIV status confirmed during admission, possibly owing to patient refusals, health care worker uncertainty about consent for confused or unconscious patients, or inadequate provision of counselling and testing services. The most striking finding was the high rate of loss to follow-up after hospital discharge; almost half were not seen again, which suggests poor linkage between hospital inpatient services and PHC clinics providing ongoing HIV care and treatment. Continuation of fluconazole after the consolidation phase was also uncommon, similar to other findings in South Africa.14,15 While some patients might have accessed fluconazole and ART elsewhere, the majority probably died.

There are limitations to this analysis, including those inherent in retrospective investigations. Retrieval of hospital records was incomplete, although we found no evidence that bias was introduced by excluding those without case records. Our numbers were too small to explore factors associated with long-term survival. Since this study, aspects of care have been improved: improved supply of amphotericin B, clear protocols for managing CSF pressure, enhanced HIV counselling and testing service for inpatients, and better linkage systems between hospital and PHC clinics. However, numerous challenges remain with the increasing numbers of CM cases in South Africa.16 Practical, implementable local care pathways, that encompass acute management and early post-discharge community support and enhanced clinical follow-up, must be developed and evaluated. By strengthening health systems, we can realise the full benefits from the scale-up of comprehensive HIV treatment and care.

We thank Nomcbuthu Mwelase and Nombuso Xaba for their assistance with data retrieval, and the staff of Hlabisa Hospital and the Hlabisa HIV Treatment and Care Programme. This work was supported by the Wellcome Trust (grant numbers 050354 and 075393). TH was supported by the Centre for International Migration and Development (CIM), and Gesellschaft für Technische Zusammenarbeit (GTZ), Federal Ministry of Economic Cooperation and Development, Germany.

References