The need for epidemiological data on HIV-related CNS infections in low-income and middle-income settings

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Globally, in 2023, 39·9 million people were living with HIV, 1·3 million were newly infected with HIV, and 630 000 died from HIV-related illnesses. Sub-Saharan Africa and the Asia-Pacific regions are disproportionally affected.[1] In adults and adolescents, WHO defines advanced HIV disease as CD4 cell count below 200 cells per µL or WHO stage 3 or 4 in both persons presenting to care who are antiretroviral therapy (ART) naive and those returning to care after interrupted treatment.[2,3] The WHO package of care for advanced HIV disease targets cryptococcal meningitis and tuberculosis through recommendations on screening, treatment, and prevention strategies. Additionally, co-trimoxazole, recommended for the prevention of *Pneumocystis jirovecii* pneumonia, might also prevent toxoplasmosis and some bacterial infections. Despite these recommendations and access to tolerable, effective ART and despite more than three quarters of people living with HIV accessing combination ART, opportunistic infections of the CNS remain drivers of morbidity and mortality. Cryptococcal meningitis contributes to about 15–20% of all AIDS-related deaths, and tuberculosis meningitis accounts for about 4%. Other important opportunistic infections include pneumococcal meningitis, cerebral toxoplasmosis, progressive multifocal leukoencephalopathy, and cytomegalovirus.[4]

Diagnosis and management of CNS-infections in resource-limited settings is challenging and often hampered by poor access to special investigations and imaging, lumbar puncture refusal, insufficient knowledge and skills in providers, and lack of access to the best therapeutic interventions. The DREAMM project previously highlighted how health-system engineering, education, social science, clinical mentorship, and laboratory-capacity building act as catalysts to reducing mortality within routine-care services.[5] In this further analysis of data from the DREAMM project, Cecilia Kanyama and colleagues[6] provide insights into the prevalence and cause of these CNS infections in hospitalised people living with HIV from Cameroon, Malawi, and Tanzania. These localised epidemiological insights are key to identifying gaps in care, set priorities, tailor care packages, and inform local health policy, which in many low-income and middle-income countries (LMICs) are complex and evolving.

Key findings are that most people living with HIV hospitalised with CNS infection were already on ART and had a lower CD4 count (median 61 cells per µL [IQR 25–137] *vs* 282 cells per µL [101–468]; p<0·0001), and higher viral load (p<0·0001) than people living with HIV without CNS infection. As expected, cryptococcal meningitis was the most important pathogen in the full cohort, with all-cause 2-week mortality of 23% (34 of 147) and all-cause 10-week mortality of 45% (66 of 146), but the study highlights the importance of toxoplasmosis in Cameroon, where the disease accounted for 39 (43%) of 90 cases. The study raises several important questions on the implementation of advanced HIV disease guidelines and prevention of CNS infections in people living with HIV.

Among those with CNS infection receiving ART, time on ART before hospitalisation for participants with cryptococcal meningitis was 21 months (IQR 3–68), for bacterial meningitis 45 months (9–90), and for cerebral toxoplasmosis 56 months (16–80). The median CD4 count was less than 200 cells per µL in all groups. Although Kanyama and colleagues do not report the viral suppression rate in participants on ART or comment on interrupted ART care, these data suggest missed opportunities to ensure viral suppression and immune recovery. Similarly, the analysis does not provide data on the uptake of cotrimoxazole in Cameroon or among the participants in the study.

Additionally, to understand the broader impact of interventions beyond mortality, it is necessary to examine the geographical variance of long-term outcomes for survivors of CNS infections, including cognitive function, rehabilitation, quality of life, and health-system impact. Although Kanyama and colleagues highlight regional differences in the prevalence of specific CNS infections, the study does not explore the underlying socioeconomic, health-care access, health-care worker training, care co-ordination, or behavioural determinants of health. Achieving Sustainable Developmental Goal target 3.3 to end the epidemic of AIDS and the morbidity and

mortality associated with CNS co-infection by 2030, requires addressing gaps in HIV diagnosis, prevention of opportunistic infections, and access to improved diagnosis and treatment.[7] Equitable health-care provision, informed by local knowledge, is essential to close these gaps. Local factors such as health-care infrastructure, access to early diagnosis, HIV treatment coverage, and health-care-seeking behaviour must be understood to construct tailored care packages.

Kanyama and colleagues contribute valuable insights into (1) regional variation in the cause of HIV-related CNS infections, highlighting the need for context-specific approaches to care; (2) the importance of early diagnosis and treatment to reduce mortality and improve outcomes for HIV-associated CNS infections, reinforcing the importance of improved access to diagnostics and upskilling health workers; (3) deficiencies in chronic and rehabilitative care; and (4) the essential need for region-specific epidemiological data to guide effective design of health systems, especially in African and LMIC settings.

We declare no competing interests.

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