



Cryptococcosis in Gauteng: Implications for monitoring of HIV treatment programmes

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To the Editor: In South Africa, for reasons of confidentiality, difficulties with case definition and surveillance logistics, AIDS and AIDS-defining opportunistic infections are not notifiable. South African government authorities and non-governmental organisations have difficulty measuring the burden of disease due to HIV/AIDS, or obtaining objective evidence for effectiveness of interventions such as antiretroviral therapy (ART) to mitigate its impacts. Numbers of AIDS cases are inferred from mathematical models and population death rates. Data from a surveillance project for cryptococcosis (CC) in Gauteng,¹ and similar data from the pre-ART era in North America,² indicate that 1.4 - 6.6% of people with AIDS become ill with CC, an AIDS-defining illness and opportunistic infection that is preventable in the context of ART. In South Africa the introduction of ART may decrease deaths due to AIDS. We present incidence rates for CC, HIV seroprevalence data and number of deaths due to AIDS and propose that incidence rates of CC are good although crude markers of the effectiveness of HIV testing and treatment programmes.

Methods

Population-based surveillance for CC was conducted in Gauteng province, South Africa, from 1 March 2002 to 29 February 2004,¹ facilitating calculation of incidence rates and geographical

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distribution of cases. Demographic data for the population of Gauteng, including district and subdistrict population numbers, and numbers of health care facilities able to admit and treat CC in the province, were obtained from the October 2001 census (Statistics South Africa, Report No. 03-02-03 (2001) and the Health Information System, Gauteng Province). Estimated HIV denominators for the Gauteng population living with HIV/AIDS were obtained from the Actuarial Association of South Africa model.³ Age-related HIV seroprevalence estimates were obtained from the Nelson Mandela HSRC study of HIV/AIDS.⁴ Estimates of the number of deaths due to AIDS were obtained from the MRC report.⁵ Results from the Annual HIV and Syphilis Seroprevalence Survey of Women Attending Public Antenatal Clinics in Gauteng (unpublished survey) were used with permission.

Results

From 1 March 2002 to 29 February 2004, 2 753 incident cases of CC were identified. The incidence rate was 15.6/100 000 per annum (males 15.2/100 000, females 15.8/100 000) (Fig. 1). Using mathematically modelled data to obtain population sizes of people living with HIV and sick with AIDS, the incidence rate was 95/100 000 HIV-infected persons, and 14/1 000 people living with AIDS. Given the number of assumptions being made, these rates represent estimates of disease burden. During this period 4 - 17% of patients with CC resident in each district were admitted to a Gauteng hospital situated outside their district of residence, with the exception of Metsweding District Municipality, which has no public hospital capable of managing inpatients with CC. Death rates attributable to HIV/AIDS in Gauteng for 2000 and the age-adjusted incidence of CC peak in the same age category (35 - 44 years) (Fig. 2). The West Rand District Municipality had the highest HIV seroprevalence rate among antenatal clinic attendees in 1999, 2000 and 2003 (27.2%, 35.8% and 38.8%, respectively), as well as the highest incidence of CC during 2002 - 2004 (40.9%). Among men and women living with HIV, the incidence rates of CC differ by gender in the same way that HIV seroprevalence does, with the highest gender-related incidence in males (age category 35 - 39 years; incidence 39 cases/100 000 general population) occurring at an older age than females (peak at age category 30 - 34 years; incidence 36 cases/100 000 general population).

Discussion

We have demonstrated that the demographics of patients with CC match the demographics of South Africans living with HIV and dying from AIDS with respect to age, gender and



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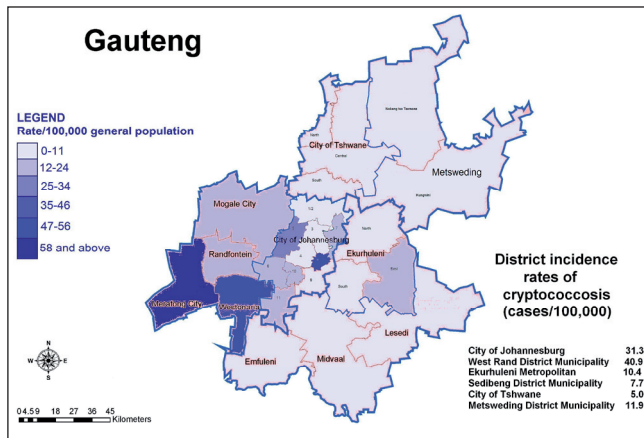


Fig. 1. Regions of Gauteng showing incidence of cryptococcosis by sub-district, 2002 - 2004.

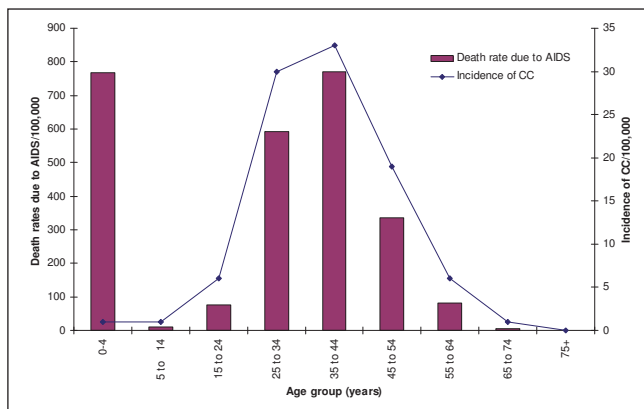


Fig. 2. Death rates attributable to HIV/AIDS in Gauteng, 2000,⁵ and age-adjusted incidence of cryptococcosis (CC) in Gauteng, 2002 - 2004.

geographical location within Gauteng. We propose that CC has the characteristics of an ideal opportunistic infection for monitoring the effectiveness of HIV testing and treatment programmes in South Africa, for the following reasons.

Firstly, laboratory-based surveillance programmes are likely to identify a substantial proportion of patients with CC because the predominant manifestation of meningoencephalitis is severe headache, which makes health-seeking behaviour by patients inevitable; the diagnosis of CC cannot be made clinically and lumbar puncture with laboratory testing is required; incident cases of cryptococcal meningitis are not treated empirically, unlike bacterial meningitis; and the inexpensive India ink test is readily available in all laboratories in South Africa and has excellent sensitivity in national surveillance compared with culture to identify cases of cryptococcal meningitis.

Secondly, in the context of the HIV/AIDS epidemic, there is sufficient burden of disease due to CC to ensure that surveillance is worth while and meaningful. CC has been

observed to be the third most common cause of death in South African ART treatment programmes (personal communication, Dr Andrew Boule, University of Cape Town, 3rd PACT Conference, Johannesburg, 16 - 18 October 2007).

Finally, population-based studies have demonstrated a significant reduction in the incidence of CC in the post-ART era,⁶ with one study demonstrating a 10-fold reduction in incidence among the general population from 4/100 000 to 0.4/100 000.²

In the context of providing comprehensive HIV/AIDS care and treatment, continued occurrence of CC points to patient failure or inability to access medical care for HIV, or inadequate monitoring of its progress and failure to initiate ART.⁶ CC will continue to occur in the context of immune reconstitution disease. However, these individuals commonly have CD4 counts under 100 cells/ μ l at the time of ART initiation, and may therefore still represent failure of timely initiation of ART. The incidence of CC in HIV-negative persons in the USA is less than 1/1 000 000 general population and has remained unaltered in the post-ART era.²

We anticipate substantial reductions in the incidence of CC in South Africa over the next decade. The Group for Enteric, Respiratory and Meningitis Surveillance of South Africa (GERMS-SA) of the National Institute for Communicable Diseases performs national laboratory-based surveillance for CC throughout South Africa (commenced January 2005), and is ideally placed to monitor changes in incidence of CC as the provision of HIV services expand.

The findings and conclusions in this article are those of the authors and do not necessarily represent the views of the CDC.

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