



HIV/AIDS and tuberculous meningitis: a five year retrospective autopsy study at the korle-Bu Teaching Hospital Accra Ghana

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Abstract

Background: There is paucity of autopsy data on tuberculous meningitis (TBM), even though it is an important cause of mortality, especially in HIV infected individuals. The objective of the study was to investigate HIV associated TBM mortality patterns, using a descriptive autopsy study.

Materials and methods: A retrospective review was carried out of all autopsy log books and hospital files in our institution for cases of TBM for which autopsies were performed during the period 2005 through 2009. Demographic data, category of death and HIV status were recorded. Data were entered and analyzed using SPSS software (version 18).

Results: Of the 719 meningitis deaths in our institution during the study period, 98(14.0%), were tuberculosis related. Of the 98 TBM deaths, 87(88.8%) were confirmed by histology, while 10(10.2%) were by brain smear. Ninety six (98.0%) maadelle@yahoo.com deaths occurred within the background of pulmonary tuberculosis (PTB); 78(79.6%) occurring within a health facility. Forty four (45.0%) of the TBM deaths had HIV co-infection, compared to 27(4.3%) of the 621 cases of purulent bacterial meningitis (PBM). The mean age of TBM cases with HIV co-infection was 36.8 (SD=10.7), and majority 29(66.0%), were males. Forty two (96.0%), out of the 44 HIV-related TBM deaths occurred in a health facility.

Conclusion: One out of every two TBM deaths that occurred in a health facility was HIV related and in young male adults. Autopsy studies could be useful in tracing contacts of both infections, for the initiation of early treatment in positive cases.

Keywords: Tuberculous meningitis, HIV/AIDS, autopsy, coroner, hospital

Introduction

The HIV/AIDS pandemic is now more than two decades old and the direct evidence of its impact on mortality pattern of tuberculous meningitis (TBM) can be described using retrospective autopsy studies. Globally and in Sub-Saharan Africa, clinical and laboratory studies have shown the association between HIV/AIDS and tuberculosis (TB) [1,2]. In 2007, it was estimated that 1 out of 4 TB deaths were HIV related [3]. HIV and TB are common in the 15-49 age group [4,5]. Available literature has shown divergent views on gender involvement. Some studies found females to be more at risk of both infections [6-9] others found males to be more at risk [10].

TBM is an important central nervous system (CNS) complication of pulmonary tuberculosis. Infection of the central nervous system is one of the most devastating clinical manifestations of tuberculosis. In a large scale epidemiological study of extrapulmonary tuberculosis in the United States, CNS involvement was noted in 5 to 10% of extrapulmonary tuberculosis cases [11]. The US center for disease control (CDC) data in 2005 indicated that 6.3% of extrapulmonary cases (1.3% of total tuberculosis cases) involve the CNS [12]. On the contrary, in the largest prospective epidemiological study on CNS tuberculosis, Phypers et al., [13] found that the chance

of developing CNS tuberculosis was 1.0% among 82,764 tuberculosis cases from 1970 to 2001 in a Canadian cohort.

The literature seems to suggest that, no study has been conducted in Ghana with regards to TBM and HIV co-infection. The aim of the study was to provide data on HIV and TBM co-infection in a Ghanaian population.

Materials and methods

Study site

The study was based in Korle-Bu Teaching Hospital, Accra Ghana. The hospital operates the largest mortuary in the country, which carries out, 3000 to 6,000 autopsies a year. This mortuary receives cases from Korle-Bu Teaching Hospital, the largest referral hospital in Ghana; as well as cases within the Accra Metropolis, neighbouring towns and district and in special circumstances cases from other regions across the country. It is important to note that not all deaths within the catchment area had autopsy done. Thus deaths that occurred in the communities and were not reported to the police did not have autopsy.

Data collection and analysis

All autopsy log books and hospital files were reviewed for the

5-year period, January 2005 through December 2009, and all deaths due to meningitis were recorded. Data was collected and cross-checked to prevent double entry. For each case of meningitis death, data was collected on age, sex, category of autopsy (Coroner's request or hospital), and HIV status. Available data of all cases confirmed by histology and brain smear were also collected. Coroner's cases are deaths that occurred in the community, or within 24-hours of admission at a health facility, where no definitive diagnosis was arrived at before death. Hospital deaths, on the other hand, are deaths that occurred in a health facility while the patient was being managed for a given diagnosis. The diagnosis of TBM was based on the clinical history, macroscopic (autopsy) findings and microscopic study. The microscopic diagnosis of TBM was based on features (Necrotizing granulomatous inflammation) identified on Hematoxylin and Eosin (H&E) and confirmed by Ziehl-Neelsen (Z-N) stain. HIV status was based on ante-mortem/postmortem laboratory test results, using the rapid test, confirmed by the ELISA (Enzyme Linked Immunosorbent Assay) in some cases. The data were entered into a computerized spreadsheet and analyzed using SPSS software (Version 18). Frequency distributions and descriptive statistics were calculated for each variable. Given the descriptive nature of this study, no multivariate analyses were attempted.

Inclusion criteria

All were preserved bodies that had meningitis.

Exclusion criteria

All cases of Cryptococcus meningitis.

Results

During the study period a total of 24,787 autopsies were performed at the Korle-Bu teaching hospital mortuary. Of this number 719(2.90%) were diagnosed as meningitis. Ninety-eight (13.6%), out of the 719 deaths due to meningitis were (TBM). The remaining 621(86.4%), were purulent meningitis. Ninety six (98.0%) of the TBM had background pulmonary tuberculosis (PTB) at autopsy. Eighty-seven (88.8%) of the 98 TBM cases were confirmed by histology and 10(10.2%) by brain smear. Seven-eight (79.6%) of the TBM deaths occurred in a health facility, while 20(20.4%) were deaths in the community. Sixty four (65.3%) of the TBM deaths were males and 34(34.7%) females. The highest frequency of the TBM deaths (36.7%) occurred in the 30-39 years age group, with no TBM death among infants (**Table 1**). The mean age of the TBM related deaths was 34.7 years (SD=14.5).

Out of the 98 cases of TBM, 44(44.9%), had HIV co-infection, compared to much lower value of 27(4.3%) out of the 621 cases of acute purulent bacterial meningitis (PBM). Of the 44 TBM with HIV co-infection, 42(95.45%), deaths occurred in a health facility and most were in the 30-39 years and 40-49 years age groups (68.2%). The mean age for the HIV/TBM cases was 36.8

years (SD=10.7). There were no deaths in the under 5 years, age group from TBM and HIV co-infection (**Table 1**). Twenty-nine (65.9%) of the 44 cases of the TBM with HIV were males, and 15(34.1%) were females.

Table 1. Comparison between tuberculous meningitis with and without HIV.

Age/years	TBM n (%)	TBM and HIV n(%)
1-4	1(1.0)	0(0.0)
5-19	15(15.3)	2(4.7)
20-29	12(12.2)	5(11.4)
30-39	36(36.7)	20(45.5)
40-49	17(17.4)	10(22.7)
50-59	14(14.3)	7(15.9)
≥60	3(3.1)	0(0.0)
Total	98(100.0)	44(100.0)

Discussion

Seven hundred and nineteen, 3.0% of the total of 24,787 deaths were due to meningitis 98(14.0%), of which were due to tuberculous meningitis. This percentage (14.0%) of TBM deaths is lower than the 20-40% found in some studies [14,15]. Seventy-eight (80.0%) of TBM deaths in this study occurred in a health facility, in patients who had some form of treatment before death. This finding emphasizes the point that TB, with TBM is a chronic infection and patients will eventually find themselves in a health facility either for confirmation of the diagnosis or for treatment. Also, because of difficulties associated with TBM diagnosis and the emergence of multi-drug resistant TB, appropriate treatment is often initiated late, resulting in the poor outcome, as found in this study. Ninety six (98.0%) of the TBM deaths in this study at autopsy, also had pulmonary tuberculosis (PTB). Available records (from the autopsy log books) indicate that, 87(88.8%) out of the 98 TBM cases were confirmed by histology and 10(10.2%) by brain smear. This means that, the source of the TBM infection in majority of the cases was a spread from the lung primary Gyasi et al., [16], in Accra, found TBM to be the third most common form of extrapulmonary tuberculosis. We found TBM to be common in adults, particularly the 30-39 years age group (36.7%), with the lowest frequency of 1% in the 1-4 years age group. In contrast, some previous clinical studies have found children under five years to be at greater risk of TBM [17-19]. Our findings, however, agree with Karstaedt, et al., [22] who found TBM to be more common in adults in a South African urban population. In our opinion, a possible explanation for the low figure for the under 5 years age group in our study, could be the high nationwide BCG immunization coverage in Ghana. There is thus the need for a more comprehensive

clinical study of TBM in Ghana. Our study also found 64(65.3%) of the TBM deaths to be in males, and 34(34.7%) females. Our findings are not in accord with those studies that found females to be more commonly affected by TBM [8,9]. Thus, our findings simply add to the ongoing discussion with regard to sex preference of TBM.

We found that, a large proportion, 44/98(45%) of the TBM deaths were associated with HIV infection, compared to a much lower 27/621(4.3%) cases of acute PBM. Studies have found HIV co-infection to be a poor prognostic factor for TBM [24-27]. Our finding therefore, tends to support the findings of these earlier studies. This further emphasizes the point that, the interaction between HIV and *M. tuberculosis* may be synergistic, each increasing the pathogenicity of the other. With progressive immunodeficiency, extrapulmonary involvement becomes increasingly common. Available literature indicates that up to 60% of HIV-infected patients with low CD4⁺ T cell counts (200/ul) who develop tuberculosis have involvement of one or more extrapulmonary sites, particularly the CNS, leading to TBM [28,29].

The study also found that, nearly 50% of the TBM/HIV patients were young adults with a mean age of 36.8years (SD=10.7). The association of pulmonary tuberculosis with TBM and HIV in this age group is in line with the known characteristics of *M. tuberculosis* and HIV co-infection. Both diseases affect the sexually active section of the population. Nearly 100% (42/44) of the HIV associated TBM deaths, that had autopsy performed in our institution, occurred in a health facility. This finding is similar to the findings of Hesse et al., [30] in their study on HIV infection in pulmonary tuberculosis patients admitted to the Korle-Bu hospital, between 1996 and 1997. In our study, 66% of HIV related TBM deaths were males. There were no deaths due to TBM and HIV co-infection in children under 5 years and adults above 60 years. The exact reasons for our findings of no TBM and HIV related deaths in these age groups are unclear at present, since there is no previous autopsy study on the association between HIV and TBM mortality pattern in Ghana. Furthermore, our search at the National Tuberculosis Control Unit (NTBC), Infectious Disease Control unit (MOH), the Department of Medicine and the Chest Clinic, all located within Korle-Bu Teaching Hospital in Accra Ghana, seems to suggest that, there is limited data on the clinical incidence of TBM and HIV co-infection in Ghana during the period of our study (2005-2009). Our finding however, reflects the distribution pattern of HIV infection in most communities.

Conclusion

One out of every two TBM deaths that occurred in a health facility in this study was HIV associated and a young male adult. Looking at the public health importance of both infections, we recommend a prospective study that will follow up all HIV cases to determine the mortality patterns and specifically, the incidence of TBM among this group. Furthermore, we think

results of autopsy studies could be useful in tracing contacts of both infections, for the initiation of early treatment and monitoring of progress.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Authors' contributions	EMD	JBKD	EKW	RKG	JTA
Research concept and design	✓	✓	--	✓	--
Collection and/or assembly of data	✓	--	--	--	--
Data analysis and interpretation	✓	✓	✓	--	--
Writing the article	✓	--	✓	✓	✓
Critical revision of the article	✓	--	✓	✓	✓
Final approval of article	✓	--	--	--	✓
Statistical analysis	✓	✓	--	--	--

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