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%) male 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. Ninet-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(95.4%), 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 | TBM and HIV |
|-----------|-----|-------------|
| 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
Gaysi 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 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 PB. 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 36.8 years (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 autopsies 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 | ✓ | ✓ | -- | -- | -- |

Acknowledgement
Our thanks go pathology colleagues as well as all technical staff of the Department of Pathology, Korle-Bu Teaching Hospital, Accra, Ghana, for their assistance and support.

Publication history
Editor: Han-Seung yoon, Iida Municipal Hospital, Japan.
EJC: Markus H. Frank, Harvard Medical School, USA.
Received: 24-Jan-2014 Revised: 13-Feb-2014
Accepted: 21-Feb-2014 Published: 04-Mar-2014

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