Tuberculosis at autopsy in inpatients at a tertiary referral centre in India: a prospective study

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ABSTRACT

Background: *India has the highest burden of TB in the world, an estimated 2 million cases annually, and accounting for approximately one fifth of the global incidence. It is also estimated by the World Health Organization (WHO) that 300,000 people die from TB each year in India. The diagnosis of tuberculosis may not be established during the inpatient stay due to many reasons (e.g. extra pulmonary TB, TB in immunocompromised host etc). We did an autopsy study to find out the prevalence of tuberculosis at post mortem in medical inpatients at a tertiary care hospital in Mumbai, India.*

Methods: *This is a prospective study and analysis of 112 consecutive medical autopsies of patients over a period of 12 months carried out at Grant Medical College and Sir JJ group of Hospitals, Mumbai, India. During this period, there were a total of 1558 deaths. A total of 112 medical autopsies were performed and included in this study .We did gross pathological and histopathological analysis. The primary outcome measure was specific disease or diseases. Secondary outcomes were missed tuberculosis, and co morbidities with tuberculosis.*

Results: *The median age of the 112 included patients was 32 years, 70 (63%) were men and 42 (37%) were females. 24 (21%) patients had tuberculosis, of whom 15 (62%) were infected with HIV. 13 (55%) of these 24 patients had disseminated tuberculosis. The risk of disseminated tuberculosis was higher among HIV infected patients than among uninfected patients with 11 of the 13 cases of disseminated tuberculosis diagnosed in HIV infected patients ($p<0.009$). 6 (33%) of 24 patients with tuberculosis were not diagnosed during their life.*

Conclusion: *Tuberculosis remains a major cause of death in India .Tuberculosis often remains undiagnosed and hence there is a need to increase awareness and actively screen for tuberculosis especially in HIV positive patients.*

Keywords: *Tuberculosis; Autopsy; HIV*

INTRODUCTION

Tuberculosis (TB) is second only to HIV/AIDS as the greatest killer worldwide due to a single infectious agent. Over 95% of TB deaths occur in low- and middle-income countries. TB is a leading killer of HIV-positive people causing one fourth of all HIV-related deaths. Accurate data on the incidence and prevalence of tuberculosis are not available as data are based on estimates from national tuberculosis returns and death certificate records, all of which are inaccurate. (1)

Autopsy has been called "the ultimate audit" and remains gold standard for identifying specific causes of death as it offers valuable insights into the accuracy of earlier clinical diagnoses and can identify previously un diagnosed disease burden.(2)

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Despite this, there is a trend of decline in autopsies due to a variety of reasons. (3,4,) We did a study of patients who died in the inpatient adult general medical wards at a tertiary care referral centre in Mumbai, India. The primary outcome measure was specific disease or diseases. Secondary outcomes were missed tuberculosis, and co morbidities with tuberculosis.

METHODS

Study design and setting: Between 14 January 2007, and 13 January 2008, we did a prospective autopsy study of patients aged at least 18 years who died in the adult medical wards at the Grant Medical College and Sir JJ group of hospitals which is the largest state government run hospital in the state of Maharashtra. The hospital receives referrals from Maharashtra and Western India. The study was approved by the hospital Institutional Ethics Committee. All patients who died after 24 hours of admission in the adult medical wards of J.J.hospital and where written informed consent by relatives was obtained for autopsy were included in the study. Cases where death occurred within 24 hours of admission and medico legal autopsies were excluded from the study.

Procedures

A full body post-mortem examination was undertaken as soon as possible after consent from the next of kin was obtained. First gross pathological examination was done, in which all organs were weighed and dissected. This was done by the residents and lecturers guided by the professor in-charge of autopsy. Samples for histopathology were taken from the lungs, brain, lymph nodes, thyroid, heart, liver, spleen, intestines, kidneys, bladder, and pancreas.Histopathological examination was done by histopathologists.

Tissue sections were examined after initial staining with haematoxylin and eosin, Ziehl-Neelsen, and Grocott-Gomori's methenamine silver stainsand special stains when required. Conventional mycobacterial cultures(LJ medium) were done for lung, lymph node and other tissues. Specific pathological abnormalities and diseases identified on examination were recorded. Patient case notes and death certificates were reviewed in a pre-designed, validated case report form.

This form included information regarding age, sex, duration of hospital stay, clinical presentation, antemortem investigation results, clinical diagnosis/differential diagnosis, treatment given, postmortem gross findings, provisional cause of death and final cause of death after histopathological tissue examination was recorded Outcomes. The primary outcome measure was specific disease or diseases. Secondary outcomes were missed tuberculosis, and co morbidities with tuberculosis.

STATISTICAL ANALYSIS

The data was evaluated using Microsoft Excel 2010 and Software Package for Statistical Sciences (SPSS). The association between various variables e.g. age, gender, antemortem diagnosis, HIV status and autopsy diagnosis was tested using tests as appropriate.

RESULTS

There were a total of 1558 deaths during the study period. A total of 112 medical autopsies were performed after taking due informed consent .Autospy rate was 7.2 %(112 out of 1558).

Median time from admission to death was 5 days. The median age of the 112 included patients was 32 years, 70 (63%) were men and 42 (37%) were females. 24 (21%) patients had tuberculosis, of whom 15 (62%) were infected with HIV.

Table: 1

Group	Number of cases	Percentage (%)
Infections	61	55
Cancer related deaths	12	11
Cirrhosis of liver	3	2
Kidney disease	1	<1
Cardiac diseases	12	11
Perforative peritonitis	4	4
Brain pathology	5	5
Miscellaneous	14	12
TOTAL	112	100

Table 1 shows the major findings at autopsy.

The major causes of death in our study were infections followed in order by cardiac deaths and cancer related deaths etc.(Refer Table 1). Tuberculosis as a major cause of death was seen in 24 cases while bacterial pneumonia, meningitis and malaria/dengue make up for rest of the deaths. (Table 1). Mycobacterial cultures were positive in 16 of the 24 cases (66%).

Disseminated TB was the most common form of TB (seen in 13 out of 24 cases) followed by pulmonary TB(6) and extra pulmonary TB (3 cases of TB Meningitis and 2 cases of GI Tuberculosis). The risk of disseminated tuberculosis was higher among HIV infected patients than among HIV uninfected patients with 11 of the 13 cases of disseminated tuberculosis diagnosed in HIV infected patients ($p<0.009$). There were 20 cases of non-tubercular pneumonia out of which 4 were lobar pneumonia and 16 were bronchopneumonia. In the present study, lung pathology was detected in 93% of the patients who were HIV infected (11 cases had TB and 3 cases had bacterial pneumonia).

Fungal infections (aspergillosis and cryptococcosis) were seen in 5 patients. The three patients who had cryptococcal meningitis were HIV positive. Parasitic diseases like malaria are a major health problem in our country. We had 6 deaths due to malaria and dengue each in our series. Out of 12 cancer related deaths the diagnosis of malignancy was made antemortem in 10 cases. It remained undiagnosed till autopsy in 2 cases. In Cardiac causes, out of 12 cases, majority i.e. 9 had acquired cardiac pathology due to hypertension, atherosclerosis or Ischemic heart disease. 3 patients had rheumatic heart disease. All cases of perforative peritonitis were postoperative deaths. Out of four cases in our series, three perforations were in small intestine and one was in sigmoid colon.

Out of 5 cases in which brain had the primary pathology, bleed was found in 4 cases and pineal cyst in one case. The attending physician noted pulmonary or disseminated tuberculosis as a cause of death in 18 (66%) of 24 patients. 6 (34%) of 24 patients were not suspected of having tuberculosis on

admission and were undiagnosed and untreated. Admission diagnoses for the six missed patients with tuberculosis were: suspected meningitis (three), bacterial pneumonia (two), and fever without focus in one. Of the 15 HIV infected patients 11 were on ART and 8 were on cotrimoxazole prophylaxis. Common co morbidities within patients with tuberculosis were anaemia in 20 (83%), pyogenic pneumonia in 4 patients (16%) and pyogenic meningitis in two (8%).

DISCUSSION

Our study shows that infectious diseases, most commonly TB, are still commonest cause of death in our part of the country. Cases of undiagnosed and untreated tuberculosis that were missed by physicians constitute a challenge. Disseminated TB is very common, especially among the HIV infected patients. About 20 percent of patients with tuberculosis who were co-infected with HIV were receiving antiretroviral therapy and about 50 percent were not on cotrimoxazole prophylaxis.

Several other studies have studied TB lesions at autopsy in India with a varying prevalence from 2% to 8%. These; however, were forensic autopsies which typically study sudden, unexplained deaths.(5,6) Our study has several limitations. Facilities for detection of MDR TB were not available at that time in our institute. We could autopsy only 7% of all deaths leading to less number of deaths studied. Because this study was done at a tertiary referral centre, it may not represent the real burden of disease in other health care set ups. Tuberculosis remains a common disease in India and there are many challenges in its diagnosis and treatment. Many patients with underlying pulmonary tuberculosis, extra pulmonary tuberculosis, and subclinical tuberculosis are easily missed. Poor diagnostic facilities add to the problem.

Our finding that disseminated tuberculosis is more common in HIV co-infected adults is in keeping with other studies.(7) Pulmonary involvement has been reported in 80-94% of patients with AIDS-associated diseases.(8,9) In the present study, lung pathology was detected in 93% of the HIV infected patients. Despite availability of ART, TB and other infections remain a common cause of death in HIV infected patients. Anaemia and pyogenic infections are common co morbidities in HIV positive patients in our study.

All patients admitted to hospitals should be screened for TB irrespective of the admitting diagnosis. In patients who are at high risk of TB(e.g. HIV infection), every effort should be made to rule out TB. Newer diagnostic methods like GenXpert will help in diagnosis and have an advantage of rapid availability of results compared to traditional culture methods.(10)

There is an urgent need to sensitize clinicians for the need of autopsy especially in teaching institutes. More autopsy studies with advanced techniques for diagnosis of tuberculosis and other infections(especially in HIV infected patients) are necessary to find out the true prevalence of diseases.

CONCLUSION

Our study shows that Tuberculosis remains a common cause of death in India. Tuberculosis often remains undiagnosed and hence there is a need to increase awareness and actively screen for tuberculosis especially in HIV positive patients.

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