



A STUDY ON FACTORS ASSOCIATED WITH HOSPITALISATION AMONG TUBERCULOSIS PATIENTS AND THEIR OUTCOME: A CROSS SECTIONAL STUDY IN DEPARTMENT OF PULMONARY MEDICINE IN A TERTIARY CARE CENTRE

Pulmonary Medicine

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ABSTRACT

Objectives: To investigate factors associated with hospitalization among TB patients, factors that lead to longer hospitalization time, outcome of hospitalized TB patients, the predictors of poor treatment outcomes and mortality in a cohort of hospitalized TB patients in the Department of Pulmonary Medicine, IPGME&R, Kolkata.

Methods: A cross-sectional study was conducted among 205 adult patients diagnosed with tuberculosis as per selection criteria were included in this study. Out of these participants, 106 patients are cases who are indoor TB patients in the Department of Pulmonary Medicine, IPGME&R and 99 patients are controls who are TB patients attending the outdoor of Department of pulmonary Medicine, IPGME&R.

Results: As per the case and control analysis, factors which are statistically significant in hospitalisation of TB patients are respiratory failure, hypotension, persistent fever, Hypoalbuminemia, hydropneumothorax, pneumothorax, Pyopneumothorax, Empyema, Anemia, low BMI <18 and pulmonary TB given in the table below in the order of significance as per p value, Odds ratio and 95% confidence interval.

Conclusion: Early case detection and effective treatment of tuberculosis and ensuring regularity of treatment adherence would probably lead to reduction of hospitalization and TB related mortality.

KEYWORDS

Factors, Hypotension, Respiratory failure, Persistent fever.

INTRODUCTION

Tuberculosis is one of the oldest diseases known to mankind. One third of the world's population is affected by TB. India accounts for more than 1/3rd of the global cases. In India, everyday more than 20,000 people become infected with TB, more than 5000 develop TB and more than 1000 die because of TB as per RNTCP statistics. India is the country with the highest burden of TB, with World Health Organisation (WHO) statistics for 2015 (global TB report 2015) giving an estimated incidence figure of 2.2 million cases of TB for India out of a global incidence of 9.6 million. The estimated TB prevalence figure for 2015 is given as 2.6 million. It is estimated that about 40% of the Indian population is infected with TB bacteria, the vast majority of whom have latent rather than active TB. Most of the national TB statistics for India come from the government Revised National Tuberculosis Control Programme (RNTCP) which was started in 1997, and which was then expanded across the country.

Improving TB treatment outcomes including reducing mortality is part of millennium development goals. Several recommendations to improve outcomes of patients with TB have been implemented such as early diagnosis and directly observed therapy (DOT), concurrent ART in HIV infected patients. WHO recommended outdoor treatment for tuberculosis. But in certain cases tuberculosis patients need hospitalization. In this study, we would like to aim to address the situation by evaluating the reasons and factors associated with hospitalization among TB patients, relevant comorbidities of tuberculosis along with assessment of outcome of treatment of hospitalized TB patients and predictors of poor treatment outcome. The study was a prospective study of hospitalized Tuberculosis patients in the DEPARTMENT OF PULMONARY MEDICINE,

IPGME&R, KOLKATA. The data was recorded in a pretested, semi-structured schedule and was analyzed in relation to their epidemiological profile using appropriate statistical tool.

We sought to investigate factors associated with hospitalization among TB patients, factors that lead to longer hospitalization time, outcome of hospitalized TB patients, the predictors of poor treatment outcomes and mortality in a cohort of hospitalized TB patients in the Department of Pulmonary Medicine, IPGME&R, Kolkata.

- Assessment of causes of hospitalization of TB patients, identifying the variables that lead to longer hospitalization time
- Assessment of various outcomes of treatment of hospitalized TB patients at the time of discharge or death as the case may be and predictors of poor treatment outcome

MATERIALS AND METHODS

STUDY SETTING: West Bengal and its neighbourhood.

TIMELINE: One & Half year (February 2016-August 2017)

1) DEFINITION OF PROBLEM: In certain cases, and complications, Tuberculosis patients require hospitalisation and mortality rates among them is high. So assessing the factors affecting the cause of hospitalisation of TB patients, factors that lead to increased hospital stay, and assessing their outcome at discharge and predictors of poor treatment outcome and mortality can help us in improving the treatment outcomes and better care.

DEFINITION OF POPULATION: Tuberculosis patients who are admitted in the Department of Pulmonary Medicine, IPGME&R are

cases and Tuberculosis patients attending the outdoor of Department of Pulmonary Medicine are controls.

SAMPLE SIZE:

205 adult patients diagnosed with tuberculosis as per selection criteria were included in this study. Out of these participants, 106 patients are cases who are indoor TB patients in the Department of Pulmonary Medicine, IPGME&R and 99 patients are controls who are TB patients attending the outdoor of Department of pulmonary Medicine, IPGME&R. Informed consent was taken from all patients along with approval from institutional Ethics committee.

SAMPLE DESIGN: As per selection criteria.

INCLUSION CRITERIA:

CASES

- 1) Hospitalised Tuberculosis patients with age 12 years and above, either sex, who are on Antitubercular treatment.
- 2) Patients admitted as suspected Tuberculosis cases and diagnosed as TB (either clinicoradiologically or bacteriologically), but require hospitalization even after the making of diagnosis of TB and starting of ATT, due to complications like Miliary TB, TB meningitis, skeletal TB, pneumothorax or empyema etc.

CONTROLS

- 1) Tuberculosis cases attending the outdoor with age 12 years and above

EXCLUSION CRITERIA:

- 1) Age less than 12 years
- 2) Patients who were admitted as suspected TB, but proved as not a case of TB after evaluation.
- 3) Patients who are already a diagnosed case of multidrug resistant tuberculosis before admission.

STUDY DESIGN:

Analytical observational study (cross sectional)

RESULT AND DISCUSSION

Tuberculosis is a disease that is present ever since the existence of mankind. Improving tuberculosis (TB) treatment outcomes, including reducing mortality is part of the Millennium Development Goals¹. Although TB-associated mortality was estimated to have decreased by 41% in 2011 from that reported in 1990, substantial morbidity and mortality is still recorded worldwide especially in low and middle income countries². With our constant efforts we have succeeded in reducing the incidence and mortality since then, but still TB is one among the most common cause of mortality among infectious disease. And India accounts for one forth of global burden of TB patients with an incidence of 2.2 million per year and 2.2 lakhs death per year (Global TB report 2015). India is the largest country with both TB and MDR TB and second largest country with HIV coinfecting TB cases³. Even though TB is curable with standardised outdoor basis treatment, certain cases of TB require hospitalisation and show higher rates of mortality. These include complications of TB (like respiratory failure, empyema, pneumothorax, pyopneumothorax, hemoptysis, constrictive pericarditis etc), associated comorbidities (like uncontrolled DM, chronic renal failure, HIV), antitubercular drug intolerance, TB failure and cases like TB meningitis, miliary TB etc.

The present study shows that there is no sex predilection in the hospitalisation rate among TB patients when compared with the sex distribution of controls (p value 0.481). In this study the mean age group of hospitalisations of TB patients is 40.20 years with a SD of 16.918. And 76.2% hospitalised patients belong to the age group 20-40 years. The study concludes that age is not a factor affecting the hospitalisation rate of TB patients (p value 0.877).

The present study shows that smoking and alcoholism do not increase the hospitalisation rate of TB patients (p value 0.888, p value 1.000 respectively). A prospective cohort study of 1493 patients conducted in US in 2000 to evaluate the costs and length of stay of TB patients found that alcoholism increases the risk of hospitalisation during the treatment course of TB.

In this study 90.5% of the cases are admitted while already diagnosed with tuberculosis and taking antitubercular drugs. The mean duration of antitubercular drug intake before getting admitted during the course of TB infection is 8.56 weeks with an SD of 0.900.

In this study among 106 cases, 68.86% cases are pulmonary TB (including 2.8% cases miliary TB), 25.47% cases are extra pulmonary TB and 5.6% cases of disseminated TB. The study reveals that Pulmonary TB is associated with more hospitalisation rate than extrapulmonary or disseminated TB (p value 0.003). This may be because the study is conducted in the Department of pulmonary medicine and hence more PTB cases are admitted than extrapulmonary TB cases.

FACTORS ASSOCIATED WITH HOSPITALISATION OF TB PATIENTS

As per the case and control analysis, factors which are statistically significant in hospitalisation of TB patients are respiratory failure, hypotension, persistent fever, Hypoalbuminemia, hydropneumothorax, pneumothorax, Pyopneumothorax, Empyema, Anemia, low BMI <18 and pulmonary TB given in the table below in the order of significance as per p value, Odds ratio and 95% confidence interval.

Risk factor	P value	Odds ratio (Case : Control)	95% Confidence Interval of OR
RespFail	<0.001	222.64	13.468 to 3680.6
LowBP	<0.001	206.58	12.497 to 3414.8
PerFever	<0.001	90.701	5.464 to 1505.5
Hypoalb	<0.001	22.870	7.839 to 66.722
HydPNTX	0.003	19.390	1.112 to 337.97
PNTX	0.007	17.173	0.977 to 301.80
PyoPNTX	0.014	15.000	0.845 to 266.38
Empyema	0.030	12.871	0.715 to 231.70
Anemia	0.099	9.097	4.827 to 17.145
LowBMI	<0.001	7.090	3.323 to 15.128
PTB	0.003	1.999	1.131 to 3.535

The most significant factor associated with hospitalisation of TB patients in this study is respiratory failure (p value <0.001). 52.83% cases have respiratory failure. This respiratory failure in TB can be due to TB infection per se, TB infection in a post TB sequelae lung or complications of TB like pneumothorax, hydropneumothorax or empyema. In the present study Pneumothorax is seen in 7.55% cases, hydropneumothorax is seen in 8.49% cases, Empyema is seen in 5.66% cases, pyopneumothorax is seen in 6.60% cases, hemoptysis seen in 11.32% cases of which 3 patients had massive hemoptysis requiring blood transfusion. In this study 25.47% cases have a post TB damaged lung including 13.21% cases of post TB bronchiectasis. Long term follow up of a TB patient can help us in identifying patients with post TB lung sequelae and regular follow up of such patients with adequate counselling can help in early detection of a TB recurrence and thus reduction of complications and hospitalisation rates later. One should be very careful to prevent iatrogenic hydropneumothorax, as an underlying diseased lung in a TB patient may not expand well with an intercostal drainage and may require surgical treatment later and increased morbidity. In patients with hemoptysis, adequate control of hemoptysis with proper medication and correction of associated anemia reduce the complication and duration of hospital stay. It is also important to exclude complications of TB like mycetoma and post TB bronchiectasis which can cause hemoptysis.

Among the cases, 55.6% cases have low BMI <18, 76.42% cases have anemia with Hb <8 mg/dl, 50.94% cases have hypotension and 49.06% cases have hypoalbuminemia. And all the four above mentioned factors are statistically associated with increased hospitalisation rates of TB patients. This suggests the utmost importance of maintenance of adequate nutrition of a TB patient. A careful supervised high protein diet can improve the nutritional status of TB patients and henceby reduce the morbidity and hospitalisation rates as well as duration and cost of hospital stay. Proper nutrition and adequate fluid balance can thus reduce hospitalisation rates.

Among the patients afflicted with TB and DM, DM is reported to be associated with poor treatment outcomes^{4,5}. DM increases the risk of the combined outcome of treatment failure, death, and relapse. The risk of death has been reported to be 6.5-6.7 times higher in TB patients with DM. A study was performed in Ethiopia in smear positive pulmonary TB among diabetic patients, 52% were males and 48% were females⁶. It has been reported that patients with TB and diabetes are older, more likely to have haemoptysis, pulmonary cavitations, be smear positive at diagnosis, and remain positive at the end of the first or second month of treatment⁷. They found out Diabetes is one of the most

serious health challenges resulting in significant morbidity and mortality rates. In the present study, Diabetes mellitus is more common among non hospitalised TB patients (41.41%) than hospitalised patients (23.58%) and hence Diabetes Mellitus is not a factor associated with hospitalisation of TB patients (pvalue 0.007). The increased awareness of Diabetes mellitus among the study population and the proper glycemic control may have led to this result in this study.

HIV coinfection generally increase the morbidity and mortality of TB patients^{8,9,10}. Previous studies have attributed this to HIV/AIDS disease progression, delayed diagnosis of TB and/or HIV, drug-resistant TB (DR-TB) (22) and a lack of immediate access to effective treatment. In this study 4.72% cases have HIV coinfection and HIV is not a factor associated with hospitalisation or mortality (p value 1.000). The small sample size of HIV patients may have led to this contradictory result. A prospective cohort study conducted in Kampala, Uganda in 2014 by Kirenga et al on TREATMENT OUTCOMES OF HOSPITALISED TUBERCULOSIS PATIENTS¹¹ concluded that advanced HIV disease and no use of ART is associated with increased morbidity and mortality of TB.

In the present study 4.72% patients have chronic renal failure, and the study reveals that chronic renal failure does not increase the hospitalisation rate of TB patients (p value 1.000).

In this study 16.03% cases required hospitalisation due to ATD intolerance like hepatitis, ATD induce rash, psychosis and uncontrolled GI sideeffects. And this study shows ATD intolerance is not a significant factor associated with hospitalisation when compared with the control group (pvalue 1.000).

In this study 82.07% cases are drug sensitive TB cases, 15.19% cases are diagnosed as multidrug resistant TB cases after admission and 0.94% cases are diagnosed as extensive drug resistant TB cases. This study shows drug resistant TB cases have an increased risk of hospitalisation (p value <0.001) than sensitive TB cases. A previous study conducted in US in 2000 also have a similar finding. A prospective cohort study of 1493 patients conducted in US to evaluate the costs and length of stay of TB patients found that MDR TB cases were at an increased risk of hospitalisation during the treatment course of TB.¹²

This study shows, higher the sputum bacteriological index, higher the risk of complications and hospitalisation (p value 0.005).

DURATION OF HOSPITAL STAY

The mean duration of hospital stay for hospitalised TB patients is 3.6 weeks with a SD of 0.214. Empyema accounts for maximum duration of hospital stay (mean duration 6.3 weeks) followed by constrictive pericarditis (mean duration 6.2 weeks). Pneumothorax, hydropneumothorax and pyopneumothorax patients have a mean duration of hospital stay 4.4 weeks, 4 weeks and 3.8 weeks respectively. The mean duration of hospital stay in case of antitubercular drug intolerance is 3 weeks and patients with BMI <18 have a mean hospital stay of 2.9 weeks.

OUTCOME ANALYSIS

The various outcome in this cohort of patients include a favourable outcome which includes patients discharged with normal ATD regime, patients discharged with modified ATD regime, patients who required major surgical procedures and patients who are died during hospital stay.

55.54% cases in this study have a favourable outcome who are discharged with a normal ATD regime. Out of this 16.03% cases required major surgical procedures, decortications and BPF correction being the most common surgery required. There is no post surgical mortality reported in this study. 16.03% cases required modification of ATD regime because of intolerance like hepatitis, rash, psychosis or comorbidities like renal failure.

In this study, mortality rate of hospitalised TB patients is 12.3% during the hospital stay. Respiratory failure is the leading cause of mortality among hospitalised patients followed by constrictive pericarditis and TB meningitis. 61.5% of died TB cases are pulmonary TB cases, 23.07% are extra pulmonary TB cases and 15.3% cases are disseminated TB cases. 23.07% of expired TB patients are diagnosed

as drug resistant Tuberculosis after admission. Anemia and hypoalbuminemia are present in 84.6% of died TB cases and hypotension is present in 69.23% of died TB cases. From this study, we conclude that Diabetes mellitus, HIV and older age doesn't increase the mortality rate of TB patients where as smear positivity, smoking and alcoholism, anemia, hypoalbuminemia and hypotension increases the risk of mortality. A study conducted by C Kolappan, R Subramani et al in 2000 on 'MORTALITY OF TUBERCULOSIS PATIENTS IN CHENNAI, INDIA' found that younger patients, men, patients with Category II disease, patients who defaulted on, or failed courses of treatment, and male smokers who were alcoholics, all had higher mortality ratios when compared to the rest of the cohort.¹³ Another study conducted in US in 2000 by Hansel NN et al on HOSPITALISATION OF TUBERCULOSIS PATIENTS- PREDICTORS OF IN HOSPITAL MORTALITY found that old age and associated comorbid illness increases the duration of hospital stay and mortality rate of TB patients.¹⁴

The mortality rate of this cohort of TB patients is 12.3%. As per WHO Global TB Report 2015 mortality rate of TB in India is 36 per 1 Lakh population. The mortality rate is high in this study which is because the study population includes hospitalised TB patients in a tertiary care centre who are gravely sick TB patients referred from different primary and secondary centres.

Early diagnosis and regular follow up of patients with monitoring of nutritional status, liver and renal function tests, control of comorbidities like DM, chronic kidney disease, COPD etc can reduce the complication rate and hospitalisation rate. In case of TB patients who are not responding, early advocacy of tests like CBNAAT/LPA/ AFB culture and drug sensitivity helps in detection of resistant TB can help in reduction of morbidity and mortality. Ensuring regularity of treatment by strictly adhering to the DOTS strategy would reduce mortality by minimizing treatment defaulters and failures.

CONCLUSION

The study shows that anemia, low BMI, hypoalbuminemia and hypotension increase morbidity and hospitalisation rates of TB patients and this suggests the utmost importance of maintenance of adequate nutrition of a TB patient. Once hospitalized, TB patients have higher rate of requirement of surgical management and mortality rate compared to nonhospitalised TB patients. Early case detection and effective treatment of tuberculosis and ensuring regularity of treatment adherence would probably lead to reduction of hospitalization and TB related mortality.

REFERENCES

- Steingart KR, Sohn H, Schiller I, Kloda LA, Boehme CC, et al. (2013) Xpert(R) MTB/RIF assay for pulmonary tuberculosis and rifampicin resistance in adults. *Cochrane Database Syst Rev* 1: CD009593.
- Mosimaneotse B, Talbot EA, Moeti TL, Hone NM, Moalosi G, et al. (2003) Value of chest radiography in a tuberculosis prevention programme for HIV-infected people, Botswana. *Lancet* 362: 1551-1552.
- www.who.int/tb/data. Tuberculosis country profiles. Burden in India.
- Dooley KE, Chaisson RE (2009) Tuberculosis and diabetes mellitus: convergence of two epidemics. *Lancet Infect Dis* 9: 737-746.
- Dooley KE, Tang T, Golub JE, Dorman SE, Cronin W (2009) Impact of diabetes mellitus on treatment outcomes of patients with active tuberculosis. *Am J Trop Med Hyg* 80: 634-639.
- Amare H, Gelaw A, Anagaw B, Gelaw B (2013) Smear positive pulmonary tuberculosis among diabetic patients at the Dessiere referral hospital, Northeast Ethiopia. *Infectious Diseases of Poverty* 2:6.
- Restrepo BI, Fisher-Hoch SP, Crespo JG, Whitney E, Perez A, et al. (2007) Type 2 diabetes and tuberculosis in a dynamic bi-national border population. *Epidemiol Infect* 135: 483-491.
- Corbett EL, Marston B, Churchyard GJ, De Cock KM (2006) Tuberculosis in sub-Saharan Africa: opportunities, challenges, and change in the era of antiretroviral treatment. *Lancet* 367: 926-937.
- Lawn SD, Wood R (2006) The epidemic of HIV-associated tuberculosis in sub-Saharan Africa: does this also impact non-HIV-infected individuals? *Aids* 20: 1787-1788.
- Gandhi NR, Shah NS, Andrews JR, Vella V, Moll AP, et al. HIV coinfection in multidrug- and extensively drug-resistant tuberculosis results in high early mortality. *Am J Respir Crit Care Med* 181: 80-86.
- Kirenga BJ, Levin J, Ayakaka I, Worodria W, Reilly N, Mumbowa F, et al. (2014) Treatment Outcomes of New Tuberculosis Patients Hospitalized in Kampala, Uganda: A Prospective Cohort Study. *PLoS ONE* 9(3): e90614.
- Taylor Z, Marks SM, Rios Burrows NM, Weis SE, Stricof RL, Miller B. Causes and costs of hospitalization of tuberculosis patients in the United States. *The International Journal of Tuberculosis and Lung Disease*. 2000 Oct 1;4(10):931-9.
- Kolappan C, Subramani R, Karunakaran K, Narayanan PR. Mortality of tuberculosis patients in Chennai, India. *Bulletin of the World Health Organization*. 2006 Jul 10;84:555-60.
- Hansel NN, Merriman B, Haponik EF, Diette GB. Hospitalizations for tuberculosis in the United States in 2000: predictors of in-hospital mortality. *Chest*. 2004 Oct 1;126(4):1079-86.