

Factors Affecting Relapse of Tuberculosis-a hospital based study

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Abstract

Tuberculosis (TB) is a major health problem globally and India. Relapse rate in Indian new TB patients is about 12%. This study was carried to find out the factors affecting the relapse of TB in India. Source of data was relapse case of TB patients visiting the OPD of RL Jalappa Hospital and Research Centre, Kolar. Study design was a cross sectional study and patient who successfully completed ATT for pulmonary TB and was asymptomatic, but subsequently became sputum smear positive or developed clinical/radiographic features suggestive of active pulmonary TB were included. Each patient underwent detailed clinical evaluation, and review of investigations in order to note factors affecting TB relapse. With prevalence of relapse cases at 12%, error d as 6%, sample size calculated using open Epi software was 116.15. Quantitative variables were compared by t test and categorical by Chi2 or Fisher exact test wherever appropriate. P value <0.05 was considered significant. Age <40 years (57.1%), female gender (57.1%), over crowded residence (32.7%), urban (38.8%), illiteracy (55.1%), unoccupied (38%), no weight gain (93.9%), smoking (75%), alcohol (65%), ADR (44.9%) during previous ATT course were present in ≥30% patients. Significant gender based difference was notable in employment status and weight gain during previous ATT course only. The illiteracy, weight loss, residence, smoking, alcoholism and ADR are most frequently noted factors in TB relapse patients

Key Words: *Tuberculosis; Relapse; DOTS*

Introduction

More global efforts are needed to control the Tuberculosis as it still remains as a major public health problem. Even though we have been tackling this problem through Multidrug Therapy and DOTS (Directly Observed Treatment Short Course), previously treated patients are presenting again with disease, i.e. with the recurrent TB. The patient with the recurrent TB is the one who have been previously declared treatment completed or cured presenting again with symptoms of TB. It is also important to identify whether this recurrent TB patient is a case of true relapse (ie the person is presented with the infection from the same strain with

which he was previously affected – endogenous reactivation) or a reinfection(i.e. ,the person is getting infection from a new strain- exogenous infection). A true relapse indicates an unsuccessful treatment while reinfection indicates higher susceptibility to infection or chronic exposure.In high TB burden areas recurrent TB mostly will be a reinfection while a case of relapse may be due to unsuccessful treatment and Drug resistance[1].Globally, 20.5% (13.6–27.5%) of previously treated cases and 3.5% (2.2–4.7%) of new cases are estimated to have MDR-TB.Previous TB treatment is a known risk factor for MDR-TB [2-9].Patients with previous TB treatment are difficult to manage and might be infectious for a longer period of time[10] Previously treated recurrent TB is no longer a neglected area; rather, it is considered to be an important factor for TB control [11,12].Programmatic factors such as poor management of the patient, lack of directly observed treatment, limited or interrupted drug supplies, poor drug quality, widespread availability of anti-TB drugs without prescription, lack of uniformity between the public and private health sectors regarding the treatment regimens, and poorly managed and supported National TB Control Programmes (NTPs) were cited to be the factors related to development of MDR TB [13].

Tuberculosis (TB) is a major health problem India as well. Estimated annual incidence of all forms of TB in India is 2.640 million. 436,000 deaths are attributed to TB in India annually. Treatment success rate in Indian smear positive pulmonary TB is 88%. Relapse rate in Indian new TB patients is about 12%. Cure rates in relapse TB patients are less compared to newly diagnosed patients. Extensive cavitation, drug resistance, nutritional deficiencies, addictions, and poverty etc are considered contributory factors to relapse of TB [14].Now under NTEP the TB patients are followed up at 6,12,18 and 24 months for early detection of relapse of TB but Indian data focusing factors affecting TB relapse is sparse. This study was planned to note factors which may have role in relapse of TB. Even though the cases are to be followed up at 6,12,18 and 24 months after the completion of treatments the extent to which it is followed is unknown. This study aims to throw some light into this aspect.This hospital based study was conducted to find out the factors affecting the relapse of TB in India.

Materials and Methods

Source of data was the relapse case of TB patients visiting the OPD of RL Jalappa Hospital and Research Centre,Kolar.The study conducted was a cross sectional study frompatient who successfully completed ATT for pulmonary TB and was asymptomatic, but subsequently became sputum smear positive or developed clinical/radiographic features suggestive of active pulmonary TB was included.Patients with newly diagnosed TB, treatment failure or treatment defaulters were not included.Detailed clinical evaluation and review investigations were done for each patient.The various sociodemographic factors such as age, gender, place of residence, overcrowding, educational status, occupation,monthly income and factors relating to relapse such as addiction and habits, history of contact with TB patients, body mass index (BMI), previous treatment related factors (radiological features, weight gain), and presence or absence of other diseases/conditions i.e. HIV, diabetes, asthma etc. were noted.Place of residence was categorized into urban and rural. Overcrowding was reported

when two or more people of opposite sex were sleeping in same room except when they were married or were less than ten years old. Educational status was assessed as literate or illiterate, based on person’s ability to read newspaper. Occupational status was assessed as employed and unemployed [15-21].Contact history was defined as a person who lives or comes into contact with an individual with infectious TB. BMI (weight in kilograms divided by the square of height in meters) of each subject was recorded as measure of nutritional status. BMI was categorized into underweight<19, normal (19-22.4), over weight (22.5-25). X-ray chest films obtained during previous course of therapy were reviewed to note; one or >one lobe involvement, cavitation, and presence or absence of residual lesions at end of the treatment. Regarding other factors pertaining to previous course of therapy patients were asked about; 1) weight gain, compared to previous weight record if available or feeling of tightness of cloth and, implementation status of DOTS. Diagnosis of asthma, diabetes mellitus, and COPD etc were based on standard criteria. Other medical and surgical illnesses which are associated with relapse like cirrhosis, malignancies, end-stage renal disease, jejunio-ileal bypass, gastrectomy, silicosis were also sought by clinical evaluation and investigations. The data was gathered with specifically designed proforma. With prevalence of relapse cases at 12%,error d as 6%,sample size calculated using open Epi software was 116.15.The study was started from Jan 2022.Purposive sampling was used to finds out the participants but because of the COVID 19 situation prevailing only 49 sample have been reached till date [22-27].All data was entered in excel and descriptive statistics is applied using Statistical Package for Social Sciences (SPSS version 12). Mean ± Standard Deviation were calculated for quantitative variables like age, BMI. Frequency and percentage of categorical variables like gender, place of residenceand addiction status etc was calculated.

RESULTS

Table1: Distribution of the participants under various sociodemographic Factors			
		Frequency	Percent
Age	<40	28	57.1
	>40	21	42.9
	Total	49	100.0
Sex	Male	41	83.7
	Female	8	16.3
	Total	49	100.0
Family size	Nuclear	41	83.7
	Joint	8	16.3
	Total	49	100.0
House	Pucca	46	93.9
	Katcha	3	6.1

	Total	49	100.0
Overcrowding	Yes	16	32.7
	No	33	67.3
	Total	49	100.0
Educational status	Literate	22	44.9
	Illiterate	27	55.1
	Total	49	100.0
Occupation	Occupied	46	93.9
	unoccupied	3	6.1
	Total	49	100.0
SES(modified BG prasad Classification	Classiii	19	38.8
	Class iv	30	61.2
	Total	49	100.0
urban residence	Yes	19	38.8
	No	30	61.2
	Total	49	100.0
Non-permanent residents	Yes	7	14.3
	No	42	85.7
	Total	49	100.0
Frequent travel	Yes	36	73.5
	No	13	26.5
	Total	49	100.0
Family history of TB	Yes	3	6.1
	No	46	93.9
	Total	49	100.0
Family support	Yes	31	63.3
	No	18	36.7
	Total	49	100.0
Facing social stigma	Yes	24	49.0
	No	25	51.0
	Total	49	100.0

About 57.1% of the participants belongs to <40 years age group.83.7% of total relapse cases were males.Majority(83.7%) of the cases were from nuclear families.32.7% of the cases are living in overcrowded houses.93.7% lives in kutchha houses.Illiteracy among the cases were

55.1% and 93.9 % are occupied.38.8% of cases lives in urban area and 14.3% are living in their non-permanent houses.73.5% of participants reported they will have frequent travelling [28-31].Only 6.1% of the cases are having positive family history of TB.36.7% of them reported they have no family support and 49 % are facing social stigma due to TB. (Table 1)

Table2: Distribution of the participants according to BMI and clinical presentations

		Frequency	Percent
BMI	Under weight	26	53.1
	Normal	22	44.9
	Over weight	1	2.0
	Total	49	100.0
Cough	Yes	43	87.8
	No	6	12.2
	Total	49	100.0
Fever	Yes	43	87.8
	No	6	12.2
	Total	49	100.0
Haemoptysis	Yes	4	8.2
	No	45	91.8
	Total	49	100.0
Loss of weight	Yes	46	93.9
	No	3	6.1
	Total	49	100.0
Breathlessness	Yes	9	18.4
	No	40	81.6
	Total	49	100.0
Sputum AFB	n/a	4	8.2
	Scanty	2	4.1
	1+	17	34.7

	2+	11	22.4
	3+	15	30.6
	Total	49	100.0
Resistance to anti tb drugs(mono/MDR)	Yes	3	6.1
	No	46	93.9
	Total	49	100.0
Pulmonary/extra-pulmonary TB	Pulmonary	45	91.8
	Extra pulmonary	4	8.2
	Total	49	100.0
X ray findings(past visit)	Present	0	0
	Absent	49	100
	Total	49	100
X ray findings(current visit)	Present	23	46.9
	Absent	26	53.1
	Total	49	100.0
Reported ADR during previous treatment	Yes	22	44.9
	No	27	55.1
	Total	49	100.0

53.1% of the participants are under weight. Most of them (>50%) had fever, cough and loss of weight during the evaluation. More than 90% of them were sputum AFB positive. Among the cases about 91.8 % are having pulmonary TB. 46.9% of them had positive findings in their X ray in the present visit. 44.9 % of them reported for ADR of anti TB medications. (Table 2)

Table3: Distribution of the participants according various comorbid conditions and substance abuse			
		Frequency	Percent
HIV co infection	Yes	3	6.1
	No	46	93.9
	Total	49	100.0
Diabetes	Yes	5	10.2
	No	44	89.8
	Total	49	100.0
Smoking	Yes	37	75.5
	No	12	24.5
	Total	49	100.0
Alcohol	Yes	32	65.3
	No	17	34.7
	Total	49	100.0

6.1% of the cases are having HIV co infection.10.2% are diabetics and 65.3% alcoholics.75.5% of them reported themselves as smokers (shown in Table 3)

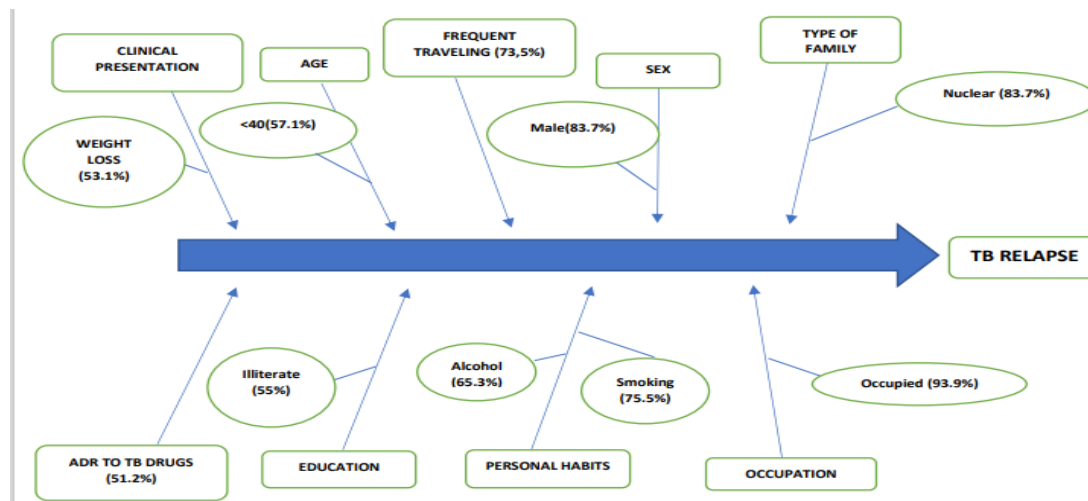


Figure 1:Fish bone analysis of the factors causing TB Relapse.

DISCUSSION

The present study shows that 57.1% of the cases belong to less than 40 years age group.Similar results have been obtained in a multicentric prospective study conducted in India by BhanurekhaVelayudam et al [24] which showed that 58% of the relapse cases

belongs to the < 40 age group category. Similar results have been obtained in a study in Korea by Hayungmin Lee et al which showed more than 50% of the relapse cases belonging to less than 40 years. This may be because the age group less than 40 includes the age groups 20-24 and 25-29 years which accounts for 15.47% and 13.73% of total TB burden in India [25].

83.7% of the cases are males in the current study which will go along with the findings of studies done elsewhere on being by Bhanurekha et al²⁴ showing 72% of cases being male. Another study done by Sandeep Singh Sarpal et al²⁶ at the northern India shows that the retreatment percentage was higher in females compared to males below the age of 20 years. But as the age progresses the males were having the highest percentages. Also the treatment outcomes are more favourable in men compared to the women. Biological and various other socio cultural factors might have contributed to this gender disparity which needs further research studies to establish the same.

32.7% of the cases reported to be having overcrowding in their houses. The importance of the inadequate housing in TB infection has been highlighted in the study done by Ju Yeun Lee et al [27] which shows that inadequate housing has been related to the 8 steps in TB development that is exposure, detection, incidence, transmission, treatment adherence, drug resistance, treatment success and recurrence.

53.1% are illiterate and 61.2% belongs to class IV in BG Prasad's classification in our study. A review by R Duarte et al [28] states that socioeconomic status can influence all stages of TB pathogenesis. Once the MTB infection has occurred, increased susceptibility to disease can be related to co-morbidities such as infection with human immunodeficiency virus (HIV), diabetes, silicosis or rheumatoid arthritis and other chronic illnesses or immunosuppressive therapies but also to malnutrition, alcohol or tobacco abuse. In the present study 75% of the cases are smokers and 65% alcoholic. Also 61% were having HIV and 10% diabetes mellitus. An analysis that included the 22 High TB Burden Countries estimated the population attributable fraction of malnutrition (27%), smoking (23%), HIV (19%), diabetes (6%) and alcohol abuse (13%). The role of these factors in TB can also be related to its relapse [29]. 53.1% of the cases are under weight. This highlights the role of malnutrition in the progression of the disease.

93.9% cases are occupied which make us to think the relapse is more among the working group and it is more of an occupational exposure. But this is in contradiction to the various studies and literatures like the one done by S Y Ouakim which shows few occupational groups demonstrated a relatively elevated risk of contracting TB infection per reported exposure event. These included employment counsellors, x-ray technicians, nurses and home support workers. Other occupational groups that may have an increased risk per exposure event include correction officers, LPN and healthcare aids. But none of our cases belongs to the particular occupational groups and hence is just a coincidence in our study. The annual incidence of active TB in the affected occupational groups ranges from 1 to 4/100,000 person-years. These rates are lower than the observed annual incidence for the BC population, 6.5–9.6/100,000 person-years over the decade from the British data.

61.2% of the cases have their residence in the rural area vs 38.8% in urban which is consistent with the study done by Sophie Huddart et al [32] in Patna which shows 21.9% having residence in rural area vs 15% in the urban.

44.9% reported ADR to anti TB drugs. This is similar to the observation by Abhijith Singh et al [33] in their study showing the overall prevalence of ADRs with first-line anti-tuberculosis drugs is estimated to vary from 8.0% to 85%. They are observed more commonly in the intensive phase and do not differ with intermittent or daily intake of anti-tuberculosis drugs.

The present study focused on factors associated with TB relapse, but the confounding limitations noted during this study are: 1) number of patients, 2) lack of drug sensitivity testing, 3) lack of microbiological data specifically genotyping of mycobacteria which would explain relapse or reinfection, 4) interruption in previous TB treatment and its side effects, and 5) follow up. The various factors present in more than 50% of the cases have been highlighted through the qualitative method of fish bone analysis and it includes occupation, gender, personal habits, education, age, clinical presentations and ADR to anti TB drugs. Nevertheless all of these factors could not be attributed to the relapse of TB either through this study.

Conclusion

The illiteracy, weight loss, residence, smoking, alcoholism and ADR are most frequently noted factors in TB relapse patients. Further studies conducted in the future, yet it is worthy to undertake a community based multi-centric study especially in India as India aspires for ending the TB earliest by 2025.

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