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Original Research Article

Analysis of Chronic Cases of Pulmonary Tuberculosis with Special Reference to causes in Hadoti Region Kota, Rajasthan, India

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Abstract: Tuberculosis (TB) is a specific infectious disease caused by *Mycobacterium tuberculosis*. The disease primarily affects lungs and causes Pulmonary TB (PTB).It can also affect intestine, meninges, bones and joints, lymph glands, skin and other tissues of the body. The disease is usually chronic with cardinal features like persistent cough with or without expectoration, intermittent fever, and loss of appetite, weight loss, chest pain and haemoptysis. This was an observational and analytical study, done with 50 cases of pulmonary tuberculosis failed on either Cat II regimen in RNTCP or retreatment under private sources were included in this study. This study was conducted in the Department of Respiratory medicine; Govt. Medical College and Hospital, Kota from 1 Oct. 2013 and completed on 30 Sep. 2014. The present study was carried out to know the factors that led to the development of chronic tuberculosis in patients of hadoti region. In our study, after one year study period we found that the Majority of chronic TB patients were chronic due to Default (60%), associated comorbidity (54%), Drug resistant (58%) either Mono or Multi drugs.
Keywords: Pulmonary Tuberculosis, Chest radiography, Multi-drug-resistant tuberculosis

INTRODUCTION

Tuberculosis (TB) is a specific infectious disease caused by *Mycobacterium tuberculosis*. The disease primarily affects lungs and causes Pulmonary TB (PTB).It can also affect intestine, meninges, bones and joints, lymph glands, skin and other tissues of the body. The disease is usually chronic with cardinal features like persistent cough with or without expectoration, intermittent fever, and loss of appetite, weight loss, chest pain and haemoptysis [1]. It is transmitted from person to person via droplets from the throat and Lungs of people with the active respiratory TB disease. TB is also called Koch's disease, after the scientist Koch. The bacillus causing TB, *Mycobacterium tuberculosis*, was identified and described on 24 March 1882 by Robert Koch [2]. The first genuine success in immunizing against tuberculosis was developed from attenuated bovine-strain tuberculosis by Albert Calmette and Camille Guerin in 1906. It was called "BCG" (Bacillus of Calmette and Guerin) [3]. In healthy people, infection with Mycobacterium Tuberculosis often causes no symptoms, since the person's immune system acts to "wall off" the Bacteria. Tuberculosis is one of the three primary diseases of poverty along with AIDS and malaria. A third of the world's population is thought to be infected with *M. tuberculosis*, and new infections occur at a rate of about one per second. Tuberculosis is treatable with a course of antibiotics. Two antibiotics most commonly used are rifampicin and isoniazid. Drug-resistant TB is a public health issue in many developing countries, as treatment is longer and requires more expensive drugs. Multi-drug-resistant tuberculosis (MDR-TB) is defined as resistance to the two most effective first-line TB drugs: rifampicin and isoniazid. Extensively drug-resistant TB (XDR-TB) is defined as resistance to at least INH and RMP (MDR-TB), plus resistance to any one of the fluoroquinolone drugs and to at least one of the three injectable second-line drugs (ie; amikacin, capreomycin, or kanamycin) [4]. The DOTS (Directly Observed Treatment Short course) strategy of tuberculosis treatment recommended by WHO was based on clinical trials done in the 1970s by Tuberculosis Research Centre, Chennai, India [4].

Defaulted- A patient who has not taken anti-TB drugs for 2 months or more consecutively after taking one month of treatment [5]. Default is one of the unfavourable outcomes for patients on DOTS and represents an important challenge for the control program. Inadequate treatment adherence is considered as a potential cause of drug resistance [6]. Studies in India and other developing countries have focused on various causes and risk factors for default. Gender, alcoholism, treatment after default, poor knowledge of tuberculosis, irregular treatment and socioeconomic status are some of the factors which have been found to be associated with higher default rates [7]. Other factors related to the disease, patients and service providers have also been identified as reasons for non-completion of treatment [8]. It has remained difficult to predict non-adherence to treatment.

MATERIAL AND METHOD

This was an observational and analytical study, done with 50 cases of pulmonary tuberculosis failed on either Cat II regimen in RNTCP or retreatment under private sources were included in this study. This study was conducted in the Department of Respiratory medicine; Govt. Medical College and Hospital, Kota from 1 Oct. 2013 and completed on 30 Sep. 2014. The present study was carried out to know the factors that led to the development of chronic tuberculosis in patients of hadoti region.

Criteria of inclusion

Patients of pulmonary tuberculosis with history of Cat I ATT and either taken Cat II ATT or now on Cat II ATT with persistent sputum positive (Any follow up sputum positive) and failed on retreatment (under private sources) cases.

Criteria of exclusion

1. Patients of extra pulmonary tuberculosis.
2. New cases of pulmonary tuberculosis.
3. Patients who did not give consent.

Data collection

Patients were enrolled after consent and full demographic profile were recorded including name, age, sex, education, occupation, marital status. Detailed past history of Antitubercular treatment, Clinical symptoms and any significant past history were also evaluated. A full set of routine blood investigation were carried out to all the study patients including complete blood count, liver function test, renal function test, HIV serology, thyroid profile, Blood sugar, ultra sonography of abdomen/chest, Body mass index and absolute lymphocyte count. Chest X-ray, sputum for Acid Fast Bacilli and line probe assay were done for all the study patients. Computerised tomography scan of chest/abdomen/ head was done as and where required.

The disease was assessed radiologically in term of extent of disease and cavitations.

Radiological classification of disease extent [9]

For clinical and research purpose the classification of the National Tuberculosis Association of the USA has proved useful.

1. **Minimal**
   Minimal lesions include those that are of slight to moderate density but which do not contain demonstrable cavitation. They may involve a small part of one or both lungs, but the total extent, regardless of distribution, should not exceed the volume of lung on one side that occupies the space above the second chondrosternal junction and the spine of the fourth or the body of the fifth thoracic vertebra.
2. **Moderately advanced**
   Moderately advanced lesions may be present in one or both lungs, but the total extent should not exceed the following limits: disseminated lesions of slight to moderate density that may extend through the total volume of one lung or the equivalent in both lungs; dense and confluent lesions limited in extent to one third the volume of one lung; total diameter of cavitation, if present, must be less than 4 cm.
3. **Far advanced**
   Lesions more extensive than moderately advanced.

Data management and statistical analysis

Editing of data was done after each interview and in the evening of the same day coding would be done to simplify the process of data entry. After correcting the error, the data was being transferred to variables as required and analysed. Summary output tables of percentage distributions were produced.

Ethical consideration

The study was approved by ethics committee of the Government Medical College, kota. The approval number is F3( ) /Acad/Ethicl comm./MCK/2014/1087.

Working definition

Following definitions were considered for study.

Pulmonary Tuberculosis

Smear-Positive

TB in a patient with at least one smear-positive for AFB out of the two initial sputum smear examination by direct microscopy.

Smear Negative

A patient with symptoms suggestive of TB with two smear examination negative for AFB, with

evidence of pulmonary TB by microbiological methods (culture positive or by other approved molecular methods) or Chest X-ray is classified as having smear negative pulmonary Tuberculosis.

Extra Pulmonary Tuberculosis

In any organ other than lungs (e.g. pleura, lymph nodes, intestine, genitor-urinary tract, joint and bones, meninges of the Brain etc).The diagnosis should be based on strong clinical evidence with the following investigations

- Smear/Culture from extra pulmonary sites
- Histopathological examination or
- Radiological examination or
- Biochemical and cytological examination including FNAC.

Diagnosis of tuberculosis

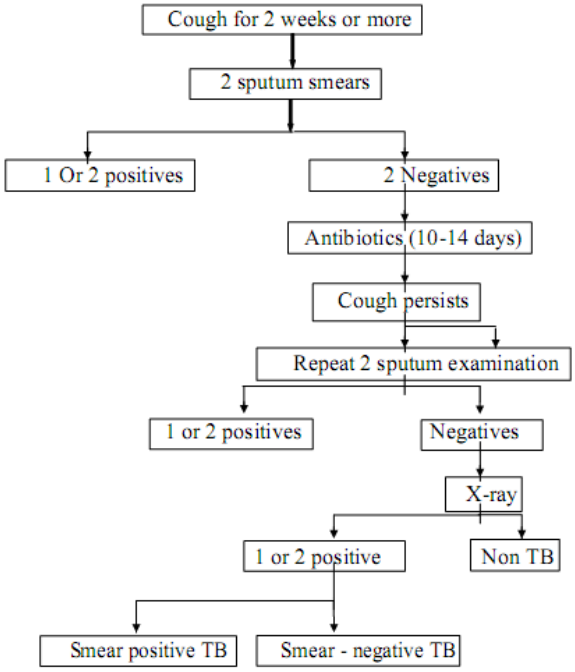

Fig-1: Diagnostic Algorithm for Pulmonary Tuberculosis [10]

RESULTS

Table no. 1 shows majority of patients were in the 26 to 45 age group, which is known to be the most economically productive period of life.

Table no. 2 shows most of the patients (72%) were either illiterate or educated up to or below primary.

Table no. 3 show distribution of chronic case patients according to the type of treatment taken, Most of them i.e. 52% had DOTS treatment under RNTCP followed by 40% patients had both type of treatment i.e. DOTS under RNTCP and Non DOTS under Private.

Table no. 4 show Distribution of chronic cases of PTB Based on previous category of treatment:

- 41 (82%) patients took Cat 1st ATT in first time treatment episode
- 2 (4%) patients took Cat3rd ATT in first time treatment episode
- 4 (8%) patients took Non DOTS HRZE in first time treatment episode
- 3 (6%) patients took Non DOTS other drugs in first time treatment episode
- 35 (70%) patients took Cat2nd ATT in Second time treatment episode
- 10 (20%) patients took Non DOTS HRZES in Second time treatment episode
- 5 (10%) patients took others like, SHERZL, SHERZM, SHERZO in Second time treatment episode
- 19 (38%) patients took ATT under Non DOTS in third time treatment episode

Majority of Patients 82% took Cat1 in first time treatment episode and 70% took cat 2 ATT in second time treatment episode.

Table no. 5 show 26% patients had contact history with known TB patient while 12% patients had contact with MDR TB patient.

Table no. 6 show majority of patients (54%) on sputum for AFB examination were found to be 3+.

Table no. 7 Show majority of patients (52%) had severe disease on Chest X- ray followed by (34%) had moderate disease.

Table no. 8 shows Majority of chronic TB patients were chronic due to Default (60%), associated comorbidity (54%), Drug resistant (58%) either Mono or Multi drugs.

Table no. 9 shows

- 18 (36%) patients did not consider regular treatment.
- The long duration of treatment come out to be a reason for treatment interruption by 17 (34%) patients.
- Financial constrain in the family happened to be a reason for treatment interruption in 26% patients.
- Side effect due to TB drugs was reported 26% patients to be a reason for treatment interruption.
- 18% patients not complete their treatment due to symptomatic relief.

- 12% patients left treatment before complete due to social stigma.
- 8% patients mentioned that their treatment was delayed or interrupted due to non-availability or irregular supply of ATT drugs.
- Small percentage (6%) patients reported that due to a negative attitude of Health worker, they were irreluctant to continue regular treatment.

Table 1: Distribution of Patients according to Age

S.N.	Age	No. Of cases	Percent
1	16 to 25	8	16%
2	26 to 35	17	34%
3	36 to 45	13	26%
4	46 to 55	6	12%
5	56 to 65	6	12%

Table 2: Distribution of Patients According to Educational status

S.N.	Education	No. of Cases	Percent
1	Illiterate	17	34%
2	Literate	5	10%
3	Primary	14	28%
4	Middle	4	8%
5	Secondary	3	6%
6	Senior Secondary	3	6%
7	Graduate	3	6%
8	Post Graduate	1	2%

Table 3: History of TB Treatment according to Under RNTCP or PRIVATE or BOTH

S.N.	H/O TB Treatment	No. of cases	Percent
1	RNTCP	26	52%
2	PRIVATE	4	8%
3	Initial Private than RNTCP	3	6%
4	Initial RNTCP than Private	17	34%

Table 4: Type of TB Treatment according to Category

Treatment episode	Type of TB treatment	No. of cases	present
I	Cat I	41	82%
	Cat III	2	4%
	Non DOTS HRZE	4	8%
	Non DOTS others HREL HRZES HRZEL	3	6%
	Total Case	50	100%
II	Cat II	35	70%
	Non DOTS HRZES	10	20%
	Non DOTS Others HRZESL HRZESM HRZESO	5	10%
	Total Case	50	100%
III	Under DOTS(Cat II)	4	8%
	Under Non DOTS	19	38%
	Total Case	23	46%

Table 5: Distribution of Patients According to the history of contact with TB/MDR patient

S.N.	Contact With	No. of Patients	%
1	TB Patient	13	26
2	MDR Patient	6	12

Table 6: Distribution of Patients According to the Grading of Sputum for AFB

S.N.	Sputum Grading	No. of Patients	%

1	3+	27	54
2	2+	9	18
3	1+	14	28

Table 7: Severity of Disease on CXR

Severity	MDR	DR	Sensitive	Total
Minimum	1	2	4	7
Moderate	5	5	7	17
Far advanced	9	7	10	26

Table 8: Cause of Chronicity

S.N.	Cause of chronicity	No. of Patients	Percent
1	Drug Resistant	14	28%
2	Multi Drug Resistant	15	30%
3	Inadequate Regime	15	30%
4	Associated Comorbidity	27	54%
5	Default	30	60%

Table 9: Causes of Default

S.N.	Cause Of Default	No. Of Patients	%
1	Took treatment less seriously	18	36%
2	Drug regime too long	17	34%
3	Financial problem	13	26%
4	Side effect of drugs	13	26%
5	Symptomatic relief	9	18%
6	Social Stigma	6	12%
7	Poor supply of drugs	4	8%
8	Negative attitude of drug provider	3	6%

DISCUSSION

The present study was carried out to know the factors that led to the development of chronic tuberculosis in patients of hadoti region.

Out of 50 study patients 36 (72%) were male and 14 (28%) were female. Male being a predominant earning member of the family in this region, this increased prevalence of chronic tuberculosis in male patient had an adverse impact on the socio economic status of the family leading to burden on the other earning members increasing dependency.

This gender distribution in this study shows similar findings to earlier studies.

A study by R K Kotokey *et al.* [11] also found male predominant 44 (74.5%) in comparison to females 15 (25.5%).

Similarly a study conducted by Chadha SL *et al.* [12] showed that males67.6% were predominantly affected in comparison to females 32.4%.

In another study Goyal BM *et al*. [13] on Drug default among 262 Pulmonary Tuberculosis patients, found that 73.4% patients were males and common age group was (21-50 yrs).

In present study 60% of study patients were in the age group of 26 to 45 years, which is known to be the most economically productive period of life. Apart from physical suffering and social stigma, TB has the potential to place a considerable financial stress on the family. This age distribution in this study shows similar findings to earlier studies.

A study conducted by R K Kotokey *et al.* [11] found the median age of study population to be 35 years, with maximum of 75 years and minimum of 15 years. Most of the patients in their study belonged to the age group of 21-40 years.

Another similar study conducted by Henry D. Meriki *et al.* [14] found that the majority (55.9%) of the participants were between the ages of 30-45 years.

34% of study population was illiterate and 38% of patients were educated below primary level. Only 38% of patients were educated more than primary level.

Similarly Chadha SL *et al* [12] also observed in their study that maximum patients 39% were illiterate. R K Kotokey *et al*. [11] also observed that maximum (42.4%) patient swere illiterate. 18.6% of patients each had primary and middle school level of education respectively.

In present study most of patients 52% had DOTS treatment under RNTCP followed by 40% patients had both type of treatment i.e. DOTS under RNTCP and Non DOTS from Private source.

In present study most of patients (82%) took Cat IATT in their first time treatment episode, 70% patients had Cat IIATT when he/she took treatment second time, 38%patients took treatment as Non DOTS from various sources in third time treatment episode.

Rajeswari R *et al*. [15] concluded from their study that factors associated with health system delay when private providers were consulted first, and from a long patient delay when government providers were consulted first.

In present study majority of male patients (61.11%) were smoker and majority of female patients (92.86%) were Non-smokers.

Thomas A. *et al*. [16] also observed that 68% of men from their study population were smoker and were thrice as likely to relapse as those who did not smoke, associating smoking with relapse of pulmonary tuberculosis.

On radiological evaluation of our study population majority of chronic tubercular patients (52%) had far advance disease on X- ray chest and 66% patients had cavitatory lesion on X-ray chest.

Similarly Yagi T et al. [17] also observed that 88.4% patients of their study population had cavitory lesion on X-ray chest.

Katou M *et al.* [18] concluded that among chronic excretor of mycobacteria bacilli patients (chronic tuberculosis), many patients showed far advance disease on X-ray chest. Chronic patients had extensive cavitary lesion on X-ray chests.

In present study among chronic tubercular patients associated comorbidities which included alcoholism (18%), Diabetes mellitus (16%), pyothorax (16%) and Hepatic dysfunction (12%) also played a significant role in developing cases of chronic tuberculosis.

Similar observation found by Tsuchiya T *et al.* [19] who found that among chronic excretors of mycobacterium tubercular bacilli patients (chronic tuberculosis) 12.4% were complicated with Diabetes mellitus, followed by 10.1% were pyothorax, 10.1% alcoholics and 6.7% hepatic disorders.

Drug resistance was most probably reason for chronicity of tuberculosis majority 58% of chronic tubercular patients were either mono or multi drug resistant, ultimately leading to chronic excretors (chronic tuberculosis).

Similar observation also found by Vasanthkumari R *et al.* [20] who noted that 63% patients of their study population were either mono or multi drug resistant.

Yoshiyama T *et al.* [21] also found that 22% patients were either H or R resistant and 25.4% patients were MDR tuberculosis.

Hanif M *et al*. [22] found 52% patients from study cohort to be either mono or multi drug resistant. Mendoza MT *et al.* [23] also found that incomplete anti-TB treatment taken for longer than 3 months increased the likelihood of MDR-TB and thus leading to development of chronic tuberculosis until treated with proper ATT.

On further investigation in present study patient related factors were main culprits for discontinuation of therapy. Most common factor leading to their discontinuation was that the patients were not serious enough to take treatment regularly (36%), 34% patients defaulted because drug regime was of too long duration. 26% patients defaulted because of side effect of anti tubercular drugs. 26% patients left treatment because of feeling of well-being after start of therapy/ taking only few doses. Other factor of defaulter were social stigma (12%), financial problem in (20%), poor supply of anti-tubercular drugs (8%) and negative attitude of drug (DOT) provider (6%).

Sweta Gupta, Sanjay Gupta *et al.* [24] concluded that early improvement and high cost of treatment were found to be the two most common reasons, leading to treatment interruption. Continuous health education should be provided to all tubercular patients emphasizing the need to continue treatment despite early improvement in symptoms.

Md. Salahuddin Ansari *et al*. [25] concluded that Patients who suffered from adverse drug reaction and toxicity of drug contributed the highest rate (40%) of default.

CONCLUSIONS

From the present study we conclude that following factors play vital role in development of chronic pulmonary tuberculosis.

1. Low education status of the population may lead to lower awareness about tuberculosis its

diagnosis and adequate treatment, consequences of treatment interruption, which lead to development of chronic tuberculosis.

2. Apart from this, population of labour and farmer occupation, due to their lower gross/per capita income may interrupt treatment prematurely due to financial concerns if taking treatment from Non DOTS (Private sources) making such patients chronic excretors of mycobacterium bacilli.
3. The probable major factors accountable to the development of chronic cases of pulmonary tuberculosis were
   (1) Drug resistance either Mono or Multi Drug Resistant.
   (2) Associated comorbidity
   (3) Inadequate drugs/Doses/Regimen
4. Out of these drug resistance was most significant cause of chronicity in these cases. Drug default was probably the most important factor for this drug resistance. On further evaluation of default we found that
   (1) Patient took tuberculosis treatment less seriously and defaulted.
   (2) Long duration of treatment and financial problem of the patient also lead to default.
   (3) Sometime early symptomatic relief by anti tubercular therapy. And feeling of social stigma of tuberculosis by patient also caused early interruption of anti tubercular therapy.
   (4) Even from programme side, poor drug supply also lead to development of drug default.
5. We would like to recommend to RNTCP
   (1) Increase awareness regarding symptomatology, freely available diagnosis and treatment of tuberculosis. So that early identification adequate treatment without default can be provided to remote end of the population.
   (2) By treating adequately without default and decreasing the chances of drug resistance we can decrease the incidence of chronic pulmonary tuberculosis.
   (3) Early identification of drug resistance by various means, chances of chronicity in pulmonary tuberculosis can be decreased.

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