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Original Article

Multi-drug Resistant Tuberculosis: Experience in Bogra

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Abstract

This descriptive study was carried out from February 1995 to December 2004. Sputum positive tuberculosis patients who were not cured by re-treatment with Category–2 regimen under DOTS were included in this study. Information were collected from the patients, treatment cards and treatment registers.

Among 13633 sputum positive TB patients registered during study period, 12511 were new smear positive (NSP) TB patients and1122 were re-treatment smear positive (RSP) TB patients. RSPTB patients were found significantly (p<.001) decreased in respect to NSP TB in subsequent years. Percentage of Chronic TB patients in respect to total smear positive TB patients registered, in first three years, was higher (1.25%, 1.3% &1.5% respectively) and the percentage sharply decreased in the subsequent years and it remained near base line in last five years. There was no significant sex differences in Chronic TB cases. Age of Chronic TB patients was 37±12 years and 59%(23) were literate. All the Chronic TB patients were residing in their home and 44% from sador upazilla including Bogra town. 62% of Chronic TB patients were from economically in average group and 25% were poor. 85% Chronic TB patients had no associated diseases. Associated diseases of Chronic TB patients were diabetes, bronchiectasis and bronchitis. 56% Chronic TB patients were smoker but none of them had habit of drug abuse. 62% of them had history of incomplete Rifampicin containing anti TB treatment from general practitioners. About the reasons of discontinuation of treatment 50%(12) stated that they felt better and discontinued, 29%(7) stated that they could not afford treatment and 21%(5) stated that they did not get result from the treatment and discontinued. 23% of Chronic TB patients had history of Cat –I regimen relapse or failure under DOTS. During the study period 26%(10) died and duration of death from onset of declared MDR-TB was 22.4±17.5 months. Nearly half (57%) of Chronic TB patients had no information, 15% remain negative with treatment and 13% remain smear positive.

Age, sex, literacy, homelessness, associated diseases, poor economical condition, availability of treatment facility had less impact on irregular/ incomplete treatment. Unsupervised anti TB treatment with inadequate information and motivation prior to treatment starting is important cause of incomplete treatment. DOTS treatment for all TB patients with adequate motivation can check RSP-TB patients and thereby Chronic TB patients. Once MDR-TB is identified the patients should be isolated from the community and adequate treatment should be arranged for them.

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Introduction

Tuberculosis is becoming a high rising problem throughout the world for mainly two reasons: one is multi-drug resistant tuberculosis (MDR-TB) and world wide prevalence of AIDS. A person infected with both TB and HIV is up to 30 times more likely to become sick with TB than a person infected with only TB[1]. Mycobacterium tuberculosis is a hardy bacterium; it can acquire drug resistance[2]. Drugs resistant tuberculosis is a case of tuberculosis (usually pulmonary) excreting bacilli resistant to one or more anti tuberculosis drugs[3]. It is not only dangerous to the patients but also equally dangerous to the community. They will spread MDR-TB till death if adequate measures are not taken. The emergence of MDR-TB in different parts of the world is particularly worrisome, given the poor therapeutic outcomes when isolates are resistant to both isoniazid and rifampin[4]. Multi drug resistant tuberculosis is defined as resistant to isoniazid and rifampicin whether there is resistant to other drugs or not[5]. According to WHO/IUATLD Guidelines[6], The primary resistance is defined as the presence of drugs resistant *M. tuberculosis* in a patient with no or less than one month of previous anti TB drugs treatment. In patients with some record of previous treatment, the bacterial resistance is called acquired resistance[3]. Many factors were incriminated for drugs resistance like – inadequate regimen, unproven quality of drugs, lack of supervision of treatment, non adherence with treatment, irregular drugs supply of a programme, addition of a single drug to a failing regimen, HIV infection etc[7]. Prior but ineffective treatment is a strong predictor of drug resistance[7]. A history of anti tuberculosis therapy was the strongest predictor of the presence of resistant germ[8].

MDR-TB was first time reported in 80'S in USA among the HIV suffering TB patients. Subsequently MDR-TB was reported in non HIV/AIDS individual in USA and out side USA. In Bangladesh the prevalence of drugs resistant TB appear to be very high for several reasons. Even a village doctor can prescribe anti TB drugs and any body can buy anti TB drugs from pharmacies. Before the presence of National TB Control Programme (NTP), TB treatment were completely unsupervised. Even during an existing NTP, yet a large number of TB patients are receiving unsupervised anti TB treatment from General Practitioners. So, it is likely that the trend of incomplete and ineffective TB treatment exist in the country is responsible for acquired MDR-TB. There are very few studies on drug resistance in the country[8,9,10]. In a recent study in Bangladesh multidrug resistance was observed in 5.5% of isolates[11].

Category II regimen of ongoing national TB control programme contain all potent first line anti TB drugs (2RHZES +1 RHZE + 6 $H_3R_3E_3$)[12]. A Chronic case is a patient who remained smear positive after completing a directly observed re treatment (Cat-II) regimen[12]. A chronic case should also include a patient who has completed Cat –II regimen but became again smear positive within one year of treatment completion. Failure of Cat – II regimen to cure a re-treatment group patient is very likely to be a case of MDR-TB. Though logically the term MDR-TB should be applied only after culture and sensitivity test. At present MDR-TB / Chronic TB cases are serious problem in the field of tuberculosis control. So every aspect of these patients require further study to take adequate steps to stop this man-made serious problem.

Objectives

The main objective of the present study was to review the demographic profile of Chronic TB patients (MDR-TB).

Specific objectives of the present study were

- To find out number of New Smear Positive (NSP) and Re-treatment Smear Positive (RSP) TB patients diagnosed and registered in different years.
- To find out number of RSP-TB patients and Chronic TB patients diagnosed in different years
- To determine age and sex distribution of Chronic TB patients
- To verify literacy and economical status of Chronic TB patients

- To see the nature of residence of Chronic TB patients
- To find out smoking habit or history of drugs abuse among Chronic TB patients
- To find out associated disease/diseases among the Chronic TB patients
- To verify previous TB treatment including regimens and reasons for discontinuation of treatment.
- To find out the information about the subsequent life of Chronic TB patients.

Methods

It was a descriptive cases study and it was conducted in Bogra district where the present NTP started from February 1995 under GOB – BRAC (NGO) collaboration. Study period was February 1995 to December 2004.Inclusion criteria for Chronic TB patient was:

1. failure to cure (Failure and Relapse of Cat –II cured patients within 1 year)
2. a retreatment TB patient with Cat –II regimen of present NTP under DOTS.

All the Chronic TB patients (MDR-TB) during the study period were the study subjects.

Criteria of literacy in the present study was able to read and write Bangla (Whatever may be the academic degree).

Economical condition were classified in three groups:1. poor – the family could not afford daily food 2. average - the family could afford daily food but had no surplus money and 3. solvent – the family could afford normal life with surplus money.

Nature of residence was classified into two groups depending upon whether the patient residing in their home or had no residence/floating.

All the information were collected from the patients, from the treatment card and treatment registers. Follow up information were collected passively from the patients or from their relatives when they came to chest diseases clinic for their problems.

Results

During the study period total 13633 smear positive TB patients were registered in the district. New smear positive (NSP) and re treatment smear positive (RSP) TB patients in different years are shown in figure 1.

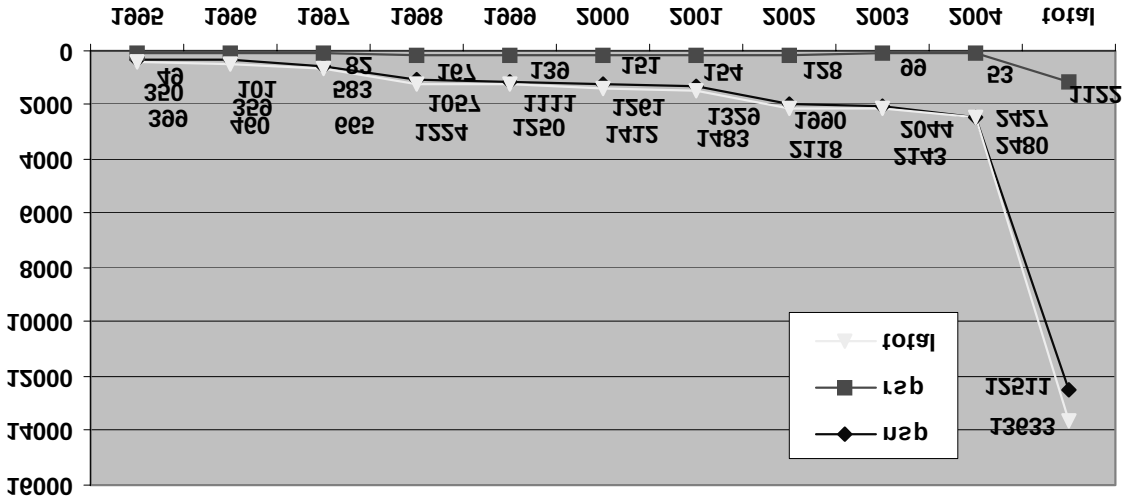
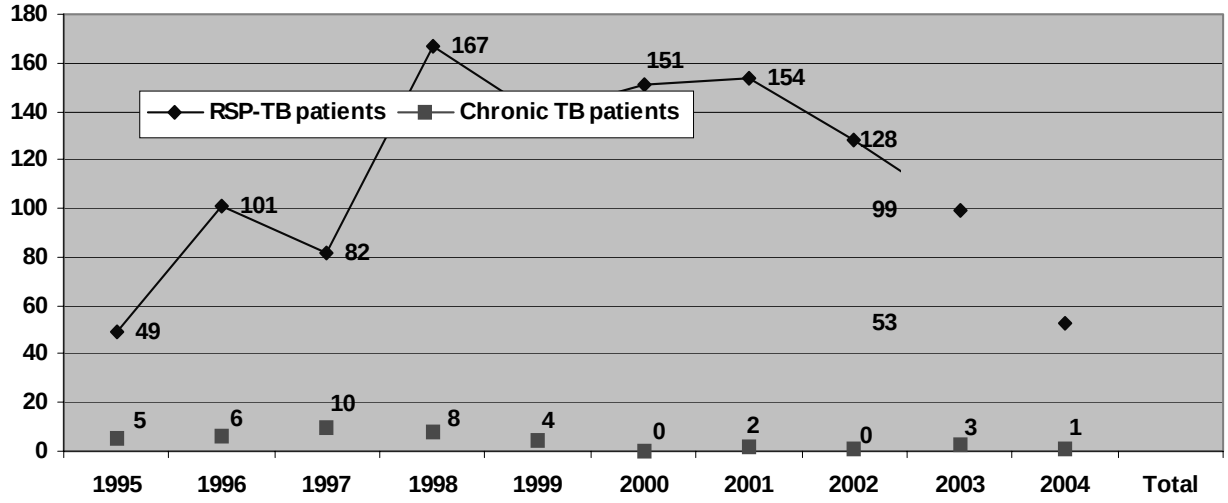


Figure 1: Shows smear positive (NSP & RSP)TB patients diagnosed and registered in different years

We have found significant difference (p<.001) of NSP-TB and RSP-TB patients diagnosed and registered in different years. RSP-TB patients were not proportionately increased as NSP-TB patients.

Number of RSP-TB patients and number of Chronic-TB patients in different years are shown in figure 2.

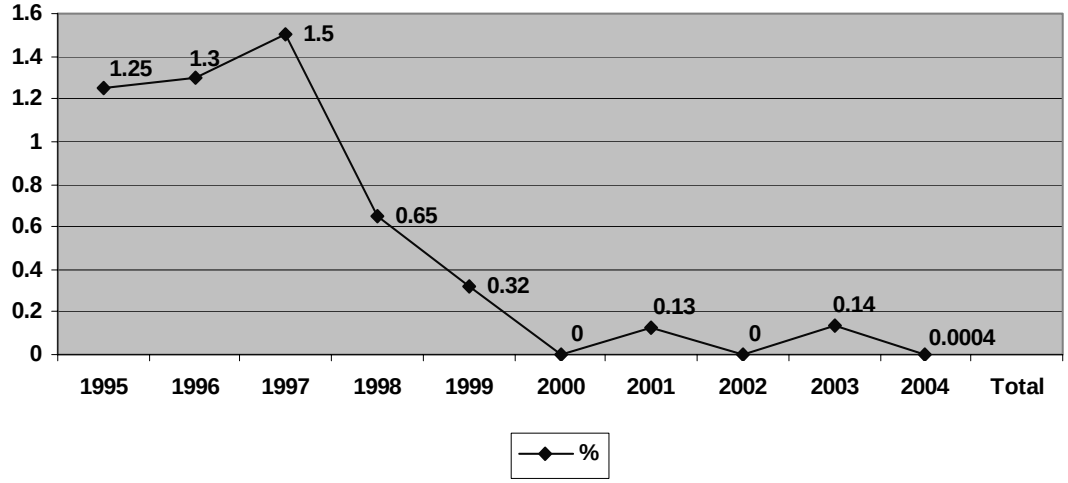
Figure 2: Shows RSP TB patients registered and Chronic TB patients converted in different years



We have found significant (p<.001) difference of RSP-TB patients registered for treatment and Chronic TB patients converted in different years. Chronic TB patients were found decreased in respect to RSP-TB patients in the subsequent years.

Percentage of Chronic TB patients among total smear positive TB patients registered in different years shown in figure 3.

Figure -3: Shows percentage of Chronic TB patients in respect to total smear positive TB registered in different years



Number of Chronic TB patients were higher in earlier three years of NTP in the district. Then the percentage of Chronic TB patient sharply came down and remain near base line in last five years.

Gender distribution of total RSP-TB patients registered and total Chronic TB patients converted are shown in table 1.

Table I: Shows gender distribution of RSP-TB patients registered and Chronic TB patients converted

Gender	Total RSP TB patients registered	Number of patients converted to Chronic TB	Percentage (%)
Male	880	31	3.52
Female	242	8	3.30
Total	1122	39	3.48

We have no significant (p = NS) difference of conversion of chronic TB patient among total male and female RSP-TB patients registered.

Mean age of Chronic TB patient was 37±12 years.

Among the Chronic TB patients 59%(23) were literate and 41%(16) were illiterate.

All the Chronic TB patients were residing in the home and non were homeless.

23% of Chronic TB patients were from Bogra town and 44% were from Bogra sador thana including Bogra town.

Among the ChronicTB patients 62%(24) were in the economically average group. 13%(5) were solvent and 25%(10) were in poor group.

Most (85%) of the Chronic TB patients had no associated diseases. Associated diseases were diabetes mellitus (8%), bronchiectasis (5%) and bronchitis (2%).

56%(22) of Chronic TB patients were smoker. There found no history of drugs abuse among the Chronic TB patients.

Previous treatment history of Chronic TB patients are shown in table II.

Table II: Shows previous treatment history of Chronic TB patients(N=39)

Previous treatment	Relapse to Cat-I regimen of NTP	Cat – I regimen failure	Cat – I regimen dropout	Incomplete treatment with regimen containing Rifampicin from GPs	Relapse to complete treatment with regimen containing Rifampicin from GPs	Relapse to Cat–III regi-men of NTP previously given to NSPTB patients	Failure to Rifampicin containing 6 month regimen from GP	Total
Number	7	2	1	24	2	2	1	39
Percentage (%)	18	5	2.5	62	5	5	2.5	100

From the previous treatment history it was found that nearly 62% of the Chronic TB patients had history of previous incomplete TB treatment from general practitioners (GPs). Few patients had history of more than 3 – 4 times incomplete anti TB treatment. History of relapse and failure to Cat –I regimen of NTP was 23%(9). Among the previous incomplete treatment (24) patients from GPs, 50%(12) stated that they discontinued treatment as they felt remission of symptoms, 29%(7) stated that they discontinued as they could not afford the treatment and 21%(5) stated that they did not get result from treatment so they discontinued treatment.

Last information available about Chronic TB patients of the district are shown in table III.

Table III Shows last information about the MDRTB patients of the district

Died	Remain smear positive	Remain smear negative with treatment	No information	Total patients
10	5	6	18	35
26%	13%	15%	46%	100%

Nearly 26% of the Chronic TB patients had died during the study period. Duration of time from the onset of declaration as chronic TB patient to death was 22.4±17.5 months. Nearly half (46%) of the Chronic cases no information were available. Of them few might be dead but it is apprehended that most of them are alive and discharging resistant TB bacilli in the community.

Discussion

It was found that smear positive TB patient's diagnosis gradually increases in the subsequent years in the district. However, RSP-TB patients were not proportionately increased in respect to NSP-TB patients. These two findings indicates that a good quality microscopic diagnosis and an effective NTP running in the district.

Significant decrease of Chronic TB patient among RSP-TB patients and sharp decrease of Chronic TB patients in subsequent years establishes the importance of DOTS to combat MDR-TB. we have no significant difference (p=NS) of Chronic TB patients among male and female, indicating that gender has no role in conversion of MDR-TB.

Mean age of Chronic TB patients was 37±12 years; it indicates that most of these patients were in younger age group. In this active part of life they became incurable patients. Not only that they became dangerous for their family and the community for discharging MDR-TB bacilli till death.

Majority (59%) of the Chronic TB patients were literate. So it is reflected that literacy has less influence in conversion of Chronic TB patients. Chronic cases were mostly due to previous irregular anti TB treatment

100% of the Chronic TB patients were residing in their home and none of them were homeless. Homelessness or floating people were incriminated for dropout from treatment, was not proved by the present study. It was found in the present study that nearly one fourth (23%) of the Chronic TB patients were from Bogra town where treatment facilities were available. Nearly half (44%) of Chronic cases were from Bogra sador upazilla where treatment facilities were not far from their home. So, availability of treatment was not a factor for completion of anti TB treatment.

It was found that 62% of the MDR-TB patients were in economically average group and only 25% were poor. From this finding it can not be said that poor economic condition was an important factor for incomplete treatment and thereby MDR-TB patients.

Most (85%) of the Chronic TB patients had no associated diseases. Associated diseases like diabetes, bronchiectasis and bronchitis might have some role in conversion to Chronic TB patients. More than half (54%) of the chronic TB patients were smoker and none of them had habit of drug abuse. The smoker suffers TB more than non smoker due to impaired lung innate immunity. However, it's impact on chronic TB is not clear.

Of the total 62% of MDR-TB patients had history of incomplete treatment. Few patients had history of more than 3 – 4 times anti TB treatment. About the reason of incomplete treatment: 50% discontinued when they felt better, 21% discontinued as they did not get result of treatment (may be due to side effect of drugs) and only 29% stated that they could not afford treatment cost. This picture revealed that lack of adequate motivation before starting treatment was an important cause of incomplete treatment and leads to MDR-TB specially in unsupervised anti TB treatment.

Chronic TB cases among the relapse and failure to previous Cat –I regimen under DOTS strategy of NTP is very difficult to explain. One explanation may be wrong categorization and prescribing Cat – I to TB patients with history of previous anti TB treatment instead of Cat – II. Another explanation might be previous Cat – I regimen (2HREZ+6HT)

where in continuation phase INH and Thiacetazone were given. However, no study is available to support this hypothesis.

According to last information 26% of the MDR-TB patient had death and duration of death from onset of chronic TB patients was 22.4±17.5 years. That is before death, these MDR-TB patients had much time to discharge drugs resistant bacilli in the family and in community. Nearly 15% remained noninfectious but 15% of the Chronic TB patients remain smear positive. Nearly half (46%) of the Chronic TB patients had no information and it is very likely that they remain infectious and spreading resistant TB in the community and will continue to spread till death. Undoubtedly it is a serious situation.

Conclusion

Age, sex, literacy, homelessness, associated diseases, poor economical condition, availability of treatment facility has less impact on irregular/incomplete treatment and thereby conversion to Chronic TB. Unsupervised anti TB treatment with inadequate motivation prior to treatment is important cause of incomplete TB treatment which is the main cause of MDR-TB. Widespread supervised (DOTS) treatment for all TB patients and adequate motivation to the patient before treatment starting can prevent MDR-TB patients. NTP of a country with fully covered good quality microscopic service and only DOTS strategy treatment can check RSP-TB patients and thereby MDR-TB in this country. MDR-TB patients usually do not die in short time and they will spread drugs resistant TB bacilli in the community. So once a MDR-TB patient is identified, the patient should be isolated from the community and adequate treatment should be arranged for him.

Recommendations

***** Widespread use of sputum microscopy for diagnosis of TB patients

* Ensure DOTS treatment for all TB patients and treatment facility should be decentralized.

* Identified MDR-TB patients should be isolated and effective treatment should be given after culture sensitivity test.

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