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A STUDY OF ADR AMONG PULMONARY TUBERCULOSIS PATIENTS TREATED UNDER DOTS

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ABSTRACT

Introduction: Directly observed treatment strategy (DOTS) under RNTCP is the current treatment available for Pulmonary Tuberculosis. This mode of treatment shows a higher range of efficacy with minimal toxicity. The present study aims to determine prevalence and characteristics of patients with pulmonary tuberculosis and to study the ADRs caused by ATT and to assess the causality and severity of the reported ADRs. **Methods:** We studied cases of Pulmonary Tuberculosis diagnosed and treated under DOTS at Our hospital for the period of Six months (July 2014 to January 2015). Adverse effects observed during treatment course were recorded in standard 'Adverse Drug Event Reporting Form'. ADRs were also assessed for their causality and severity by using WHO-UMC criteria. **Results**: Pulmonary cases accounted for 61.2% of total TB cases. Among 217 cases of pulmonary tuberculosis 17 (7.8%) patients were defaulters; among them 5 cases were defaulters due to ADRs. In our study 47 patients developed 95 ADRs of various types and most of the ADRs noted within first 14 days after starting treatment. Gastritis was the most common ADRs (n=22)followed by anorexia (n=18). **Conclusions:** In our study 21.6% of patients developed ADRs. ADRs recorded in our study were categorised under 'probable' and 'possible' causes and severity assessment showed 39% are moderate and 61% are 'mild' in nature. Hence carrying out of good patient care programs are needed for early diagnosis and to reduce default rate and drug resistance.

KEYWORDS: Naranjo's causality assessment scale, Pulmonary Tuberculosis, DOTS.

INTRODUCTION

The World health Organisation has declared TB as a global health emergency in 1996.[1] Tuberculosis is one of the important public health problem in India. Our country bear the burden of 1/5th of the global TB cases.[2] Pulmonary tuberculosis is the most common presentation of tuberculosis disease, and commonest mode of spread being droplet inhalation. Mycobacterium may spread to any organ of the body through lymphatic or haematogenous dissemination and lie dormant for years at a particular site before causing disease. Manifestations may relate tothe system involved, or simply as prolonged fever and nonspecific systemic symptoms.

Treatment of Tuberculosis has been an arduous task for clinicians in the past. After many research experiments and studies it was concluded that multiple drug regimens and prolonged treatment is the key for successful management. Hence DOTS was introduced in 1993 in India as part of RNTCP.[3] One of the key component of DOTS therapy is the standard anti TB short course chemotherapy regimen, which requires continually taking drug combinations of Isoniazid (INH), Rifampicin (RFP), Pyrazinamide (PZA), Ethambutol (EMB), and/or Streptomycin (SM) every other day for 6-9 months.[4] Even though ATT has good beneficial effects, previous studiesdone have revealed these multidrug regimens can cause unwantedadverse drug reactions (ADRs) of varying degrees of severity, such as allergic reactions, gastrointestinal (GI) disorders, hepatotoxicity, neurological disorders, arthralgia.[5] None of the anti-TB drugs is safe but hardly these ADRs are life threatening. Close monitoring of adverse drug reactions and optimal treatment is needed. Pharmacovigilance activities can help in obtaining actual scenario of safety and effectiveness of medicines when they are being used in patients.[6] The present study aims to determine the prevalence and outcome of patients with pulmonary tuberculosis treated with DOTS and to identify the incidence and pattern of ADRs caused by ATT and to assess the causality and severity of the reported ADRs.

METHODS

All the details were collected from cases of Pulmonary TB from a tertiary care hospital for period of six months from July 2014 to January 2015 treated under DOTS. General characteristic of the patients was recorded. Treatment outcome was evaluated as cured, completed treatment, defaulted, failed, or died based on the definitions given by the WHO.Inclusion Criteria for this study includes all cases of Pulmonary TB of all age groups and both sexes. Exclusion Criteria includes any

cases of Drug resistant TB, Diabetes Mellitus, Ischemic Heart Disease, Chronic Kidney Disease and HIV co-infection. All the patients of pulmonary tuberculosis were enrolled after taking their informed consent and monitored for ADRs. Patient profile was maintained to incidence of ADRs, onset, management and outcome of the ADRs. Any adverse effects observed were recorded in the 'Adverse Drug Event Reporting Form' prepared by the CDSCO, Govt. of India. 217 cases were studied for ADR monitoring during the study period and causality was assessed using world Health Organization –Uppsala monitoring centre (WHO-UMC) and Naranjo's causality assessment scale. The study was conducted after obtaining ethical clearance from institutional ethical committee.

RESULTS

After strict scrutiny through inclusion and exclusion criteria 217 cases of Pulmonary TB cases were included in the study. Among them 134 (62%) were male and rest 83 (38%) were female patients and most of the patients were in the age group of 30-40 years (Table 1).

Table 1: Age and sex distribution of pulmonary TB cases.

AGE	MALE	FEMALE	TOTAL
<20 YRS	6	9	15
21-30 YRS	62	23	85
31-40 YRS	31	25	56
41-50 YRS	18	14	32
>50 YRS	17	12	29
TOTAL	134	83	217

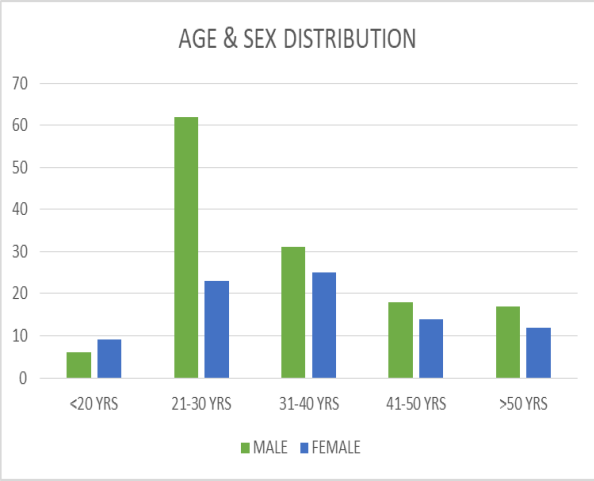

Chart 1: Age and sex distribution of pulmonary TB cases.

Among 217 cases of pulmonary tuberculosis who were on DOTS treatment, 184 (85%) patients completed treatment, 17 (7.8 %) patients defaulted, 6 (2.7%) patients died and rest were treatment failure (Table 3). Out of 17 defaulters, the most common reason for defaulting treatment was irregular treatment 10whereas in 5 patients it was due to ADRs (Table 2).

Table 2: Treatment outcome of total subjects.

Outcome	Number of patients	Percentage
Completed	184	85%
Defaulted	17	7.80%
Died	6	2.70%
Failure	10	4.50%
Total	217	100%

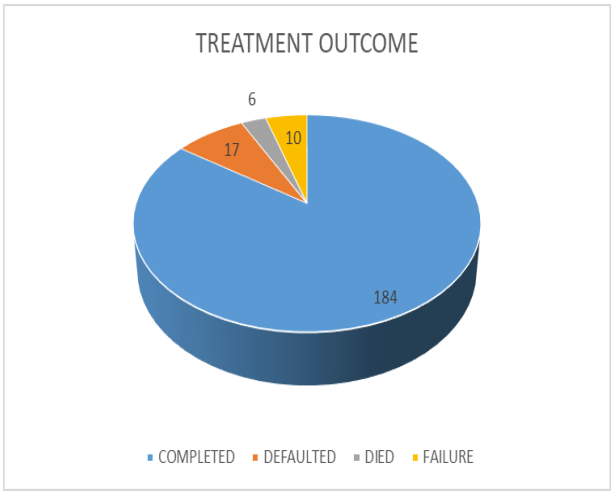

Chart 2: Treatment outcome of total subjects.

We studied onset of ADRs during the course of treatment. 6 (12.7 %) cases of the ADRs occurred on the first day of the treatment and 17 (36 %) ADRs occurred within a week of treatment, 21 (44 %) in the second week and rest 3 (7.3%) patients in the third week of the initiation of anti-tubercular therapy. Causality assessment of ADRs, revealed majority of them were found to be probable (59%) followed by possible (41%) (Assessed as per WHO-UMC and Naranjo's scales). The Naranjo algorithm is used widely in the causality assessment of ADRs. It is based on the score calculated on the basis of points assigned to each of the ten questions that comprises the table.

Our study revealed that out of 217 patients, 47 patients developed 95 ADRs of various types. Among them, most of ADRs were observed in males (n=31) and remaining (n=16) among females. The overall incidence of ADRs was 21.65%.We categorized ADRs according to the systems affected like gastrointestinal system, skin, nervous system and rest as other systems. Majority of ADRs were related to gastrointestinal system (67 cases) followed by central nervous system (20 cases), skin (9 cases) and other systems (27 cases). Gastritis was the most common ADR (n=22) followed by anorexia (n=18), Hepatitis (n=12), peripheral neuropathy (n=7) and skin reactions (n=6) (Figure 1). Among 97% of the cases, the suspected drug was continued in spite of the ADR, without any complications.

Table 3: Adverse drug reaction to Anti-Tubercular drugs.

System	Adr	No of patients
Git	Hepatitis	12
	Gastritis	22
	Anorexia	18
Skin	Skin allergies	6
Cns/pns	Peripheral neuropathy	7
	Dizziness	3
	Psychosis	4
Others	Weakness	15
	Arthralgia	8

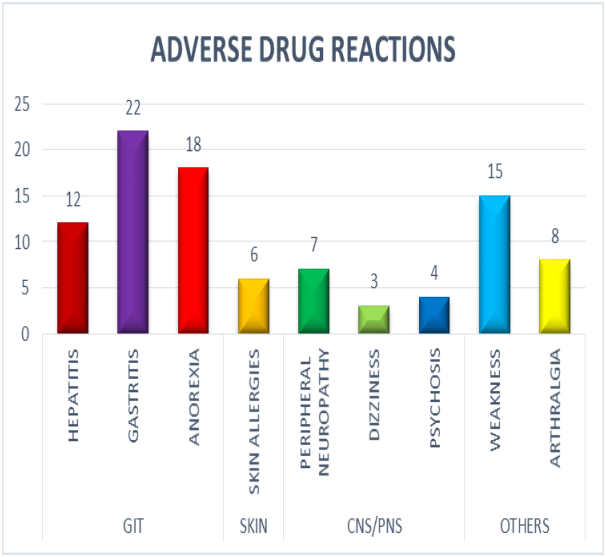

Chart 3: Adverse drug reaction to Anti-Tubercular drugs.

DISCUSSION

We did a study in around 217 pulmonary tuberculosis cases. Coming to age distribution male were most commonly infected than female patients.Our study is in accordance with study done by Chandir et al.[7]However one study done by Azam Khanreported equal number of cases in both sex.[8] Among 217 cases of Pulmonary tuberculosis studied, 184 (85%) patients completed treatment, 17 (7.8%) patients defaulted, 6 (2.7%) patients died and there was 10 (4.5%) case of treatment failure. Similar study conducted by Chandir et al showed higher Default rate (34.5%) and only 59.8% patients had completed treatment and more treatment failures (5.2%) compared to our study.[7]

The most common reason for default in our study was irregular treatment and ADRs were the reason for default in 5 cases. The study by Tekle reported that default was 11.3%, the reason being lack of family support, inadequate knowledge of treatment duration and side effects of medication.[9] Out of 217 patients enrolled in the study, 47 patients developed 95 ADRs. The highest number of ADRs was observed in males which are in contrast to the study by Yee and Shakya et al which showed female gender as a risk factor for the occurrence of ADRs due to anti-TB drugs.[10] But in the study, by D.K. Tak et al, males developed more ADRs, which could be due to majority of males included in the study.[11]

In our study most of the patients who developed ADR were between 30-40 years which is in contrast to the study by Yee et al where age over 60 years was associated with increased incidence of ADRs due to anti TB drugs. A study conducted by Daphne et al showed that ADRs due to anti tubercular drugs occurred in patients above the age of 60 years. But in our Study, majority of ADRs were observed in patients below 40 years of age. This may be due to less number of patients in above 60 yrs age group in our study.

In our study we studied onset of ADRs during the course of treatment. 6 (12.7 %) cases of the ADRs occurred on the first day of the treatment and 17 (36 %) ADRs occurred within a week of treatment, 21 (44 %) in the second week and rest 3 (7.3%) patients in the third week of the initiation of anti-tubercular therapy. Most of the ADRs were noted before 2 weeks of initiation of treatment. So thorough monitoring for ADRs required during first two weeks of treatment. The highest reported ADR was gastritis which is in accordance to the study by Dhingra et al[11], where it was around 53%. Anorexia was the second common ADR noted. A study conducted by Sainul Abideen et al reveals that, GI system, liver and biliary system is the most frequent organ system affected by ADRs.[6] Multiple drug therapy was noticed to be a major predisposing factor for developing GI side effects.

Other ADRs noted were generalised weakness, Hepatitis and Peripheral neuropathy in our study population, whose occurrence was comparable to that found in the study conducted by Dhingra et al.[11] On evaluation of the causality of ADRs, a majority of the reactions were probable (59%), followed by possible (41%). There were no definite reactions. Gholami et al also supported the same findings that the probable reaction was the more.[12]

CONCLUSION

This study was conducted to analyse Pulmonary TB cases and to look for ADRs of ATT in our hospital. Our study revealed 7.8% default rate. The side effects may steer the patient to make a judgment for stopping the medications and finally the occurrence of drug resistance and leading to amplified health care cost. In majority of the cases, ATT was continued in spite of the ADRs, without any complications. Most of the ADRs were noted within 2 weeks of initiation of treatment. So intensive monitoring for ADRs required during first two weeks of treatment. Hence implementation of good patient care oriented program is need of the hour and arrange for a follow up visit before 2 weeks of initiation of treatment.

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