

## A STUDY PROFILE ON ADVERSE DRUG REACTIONS TO FIRST-LINE ANTITUBERCULAR DRUGS IN EXTRA PULMONARY TB

Supriya Adiody<sup>1</sup>, Sivakumar P<sup>2</sup>, Jiji P. Saji<sup>3</sup>

<sup>1</sup>Professor and HOD, Department of Pulmonary Medicine, Jubilee Mission Medical College, Thrissur.

<sup>2</sup>Assistant Professor, Nehru College of Pharmacy, Thrissur.

<sup>3</sup>M Pharm Student, Nehru College of Pharmacy, Thrissur.

### ABSTRACT

#### BACKGROUND

Tuberculosis (TB) is an infectious disease caused by the organism *Mycobacterium tuberculosis*. It is one of the leading infectious causes of death worldwide. The aim of the study was to see the adverse drug reactions of the first line anti TB drugs in extra pulmonary tuberculosis (EPTB) population.

The aim of this study was to evaluate the adverse drug reactions to first line antituberculosis drugs in EPTB.

#### MATERIALS AND METHODS

The study was conducted in a tertiary care setting. It was a prospective, observational study. 60 patients suffering from EPTB were included. Patients were categorised to receive either category I, Category II DOTS or a private regimen. The data was analysed using SPSS version 20 software. Chi-square test were used for compared proportions.

#### RESULTS

Out of 60 patients, 22 (36.66%) developed ADR. The incidence of ADR's were found to be more in females (77.27%) as compared to males (22.72). Incidence of ADR's were maximum in the age group 21-40 years (63.63%).

#### CONCLUSION

A knowledge about ADR's is essential for effective management of any disease.

#### KEYWORDS

Pulmonary Tuberculosis, Adverse Drug Reaction, Extra Pulmonary Tuberculosis, Gastro Intestinal Tract.

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#### BACKGROUND

Tuberculosis is a major public health problem in India. It is the second leading infectious causes of death in the world wide. The world health organisation (WHO) declared TB as a global health emergency in 1996.<sup>1</sup>

As all drugs in clinical practice come with adverse drug reactions (ADR's), so also anti-TB drugs. Such events may cause additional cost by way of added outpatient visits, tests and sometimes even hospitalisation.<sup>2</sup> ADRs may be responsible for non-adherence to the treatment programme.

This study aims to observe the adverse drug reactions to first line anti TB drugs in extra pulmonary tuberculosis (EPTB). Non-compliance is cited as the major problem to the control of the tuberculosis at the level of public health.<sup>3</sup>

#### MATERIALS AND METHODS

The study was carried out in the Department of Pulmonary Medicine in a tertiary care hospital. It was a prospective and observational study. The study was carried out over a period of one year. Only patients with EPTB who were diagnosed

either clinically, radiologically or on histopathological grounds were included. The data such as demographic details, site of EPTB, blood investigations, ultrasound, computed tomogram, MRI (in relevant cases), FNAC/histopathological report were documented. Patients were categorised to receive category I DOTS (for newly detected cases) and category II DOTS (for patients who were previously treated). Most of the patients did not warrant extended treatment except for a few cases of spine and CNS involvement where total duration of treatment was 9 months to 1 year.

#### Statistical Analysis

The data was analysed using SPSS version 20 software. Chi-square test were used for compared proportions.

#### RESULTS

Of the 60 patients studied, 21 (35%) had lymph node tuberculosis followed by pleural effusion (16 in number i.e. 26.66%).

Sl. No.	Site of Extra Pulmonary Tuberculosis	Number of Patients (n=60)	Percentage (%)
1	Lymph node	21	35.00
2	Pleura	16	26.66
3	Bone and joints	8	13.33
4	Abdomen	6	10.00
5	Urinary	4	6.66
6	Meninges	3	5.00
7	Pericardial	2	3.33

**Table 1. Sites of Extra Pulmonary Tuberculosis**

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Corresponding Author:

Dr. Supriya Adiody,  
Professor and HOD,

Department of Pulmonary Medicine,  
Jubilee Mission Medical College,  
Thrissur-5.

E-mail: supriyaadiody@yahoo.in

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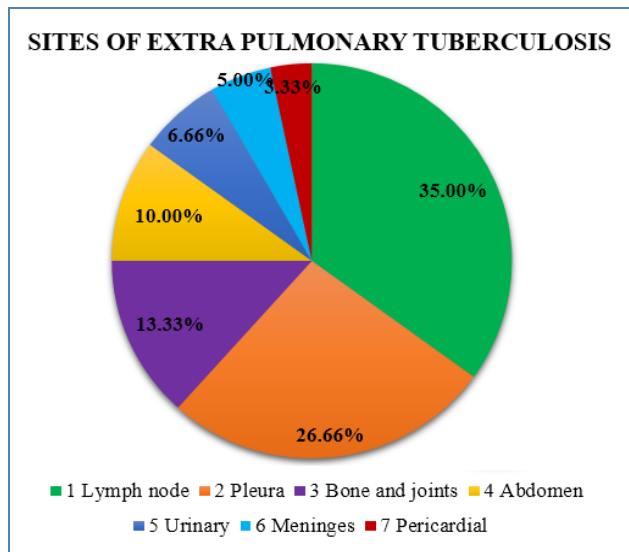


Figure 1

**Treatment Categories**

The treatment categories of the patients are as follows. 71.66% were newly detected EPTB cases whereas 10% in previously treated category II DOTS 18.33% of the patients were on a private regimen (AKT4).

Sl. No.	Treatment Categories	Number of Patients (n=60)	(%)
1	Cat I DOTS (HRZE)	43	71.66%
2	Cat II DOTS (HRZES)	6	10.00%
3	AKT <sub>4</sub> ( 1 tab E+H, 2 tab Z, 1 tab R)	11	18.33%

*Table 2. Treatment Categories*

H- Isoniazid, R- Rifampicin, Z- Pyrazinamide, E- Ethambutol, S-Streptomycin.

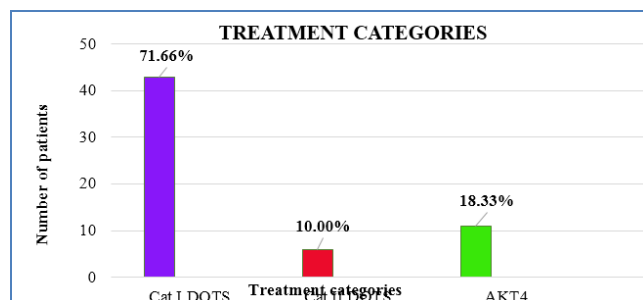


Figure 2

Sl. No.	Gender	Developed ADR (n=22)	Not Developed ADR (n=38)	P value
1	Males	5 (22.72%)	26(68.42%)	<0.001
2	Females	17 (77.27%)	12(31.57%)	

*Table 3. Sex Distribution of Adverse Drug Reactions among TB Patients*

Most of the ADR were seen in the females (77.27%).

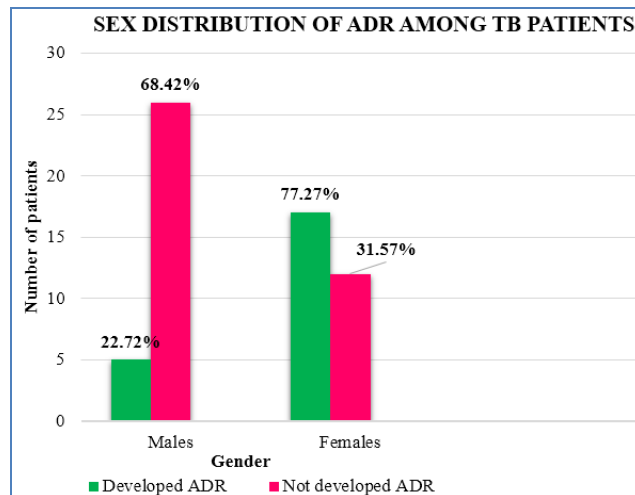


Figure 3

Sl. No.	Age Groups (Years)	Developed ADR (n=22)	Not Developed ADR (n=38)	P value
1	0-20 Yrs.	2 (9.09%)	10 (26.31%)	<0.001
2	21-40 Yrs.	14 (63.63%)	5 (13.15%)	
3	41-60 Yrs.	5 (22.72%)	11 (28.94%)	
4	61 Above	1 (4.54%)	12 (31.57%)	

*Table 4. Age Distribution of ADR among Tb Patients*

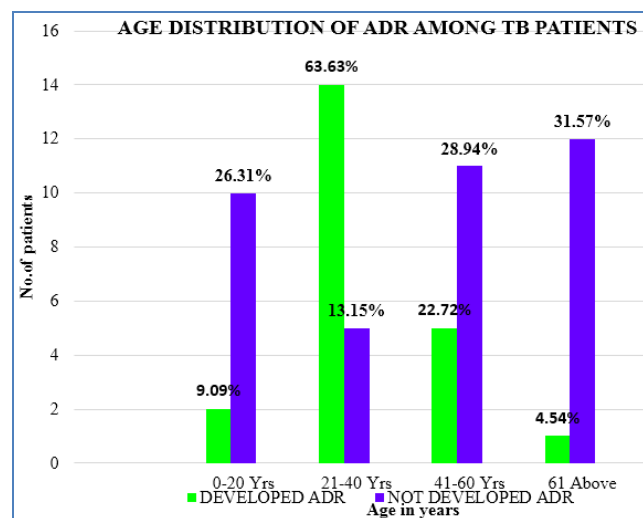


Figure 4

Most of the ADRs were common in the age group of 21-40 years (63.63%).

Sl. No.	Type of ADR	Number of Incidence (n=34)	Percentage (%)
1	Gastritis	8	23.52
2	Weakness or fatigue	6	17.64
3	Anorexia	5	14.70
4	LFT deranged	5	14.70
5	Joint pain	4	11.76
6	Skin reactions	3	8.82
7	Peripheral neuritis	1	2.94
8	Optic neuritis	1	2.94
9	Redness in eye	1	2.94

*Table 5. Distribution of Adverse Drug Reactions*

Gastritis was the commonest ADR seen in 8 patients (23.52%), followed by Weakness (17.64%).

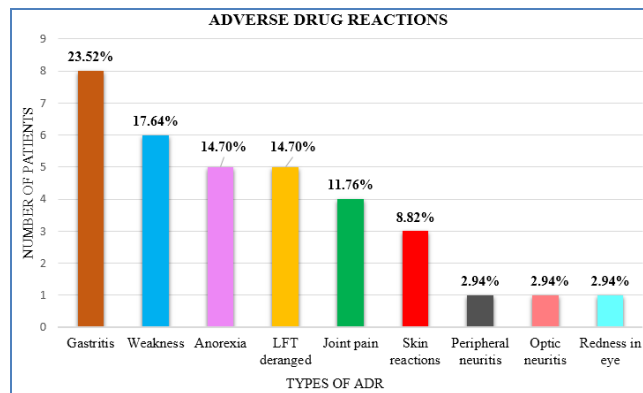


Figure 5

## DISCUSSION

An adverse drug reaction is a response to a drug that is noxious and unintended and occurs at doses normally used in man for prophylaxis, diagnosis or therapy of disease, or for modification of physiological function.<sup>4,5</sup> A general knowledge about ADRs is essential for effective management of any disease.

Tuberculosis requires prolonged treatment and some of the drugs may cause ADRs involving the GIT, liver, skin, nervous system, otovestibular apparatus and eyes.

Out of 60 patients included in our study (22) developed ADR's. 17 females (77.27%) and 5 males (22.72%) were who developed ADR's. Most of the ADRs were in the age group of 21-40 years (63.63%) followed by 41-60 years (22.72%). Gastritis was the commonest ADR (23.52%), followed by weakness or fatigue (17.64%), deranged LFT (14.70%), anorexia (14.70%). Reena Varma et al, found that hepatitis and biliary dysfunction were most observed ADR.<sup>6</sup> In our study, 4 patients (11.76%) developed joint pain and skin reactions were observed in 3 cases (8.82%). Devesh Kumar et al, also found in their study that GI disturbance was the common ADR (30.33%).<sup>7</sup> Only one patient had peripheral neuropathy and optic neuritis were observed in one patient as well. In the patient with optic neuritis, ethambutol had to be stopped permanently. Of the 5 patients who developed deranged LFT, drugs were modified after temporary cessation of the regular ATT which was later again reintroduced after LFT normalised. All other patient with ADR were managed symptomatically. The exact reason why females had more ADR's is not exactly known though some

studies have shown increase incidence of hepatitis with elderly age, female sex, slow acetylators, malnutrition, alcoholism, low serum albumin levels.

## CONCLUSION

Anti-tubercular drugs may cause ADR's just like other drugs used in management of other diseases. A knowledge about ADR's is essential as also an increased awareness because they may result in default, prolonged hospital stay and rarely, even death.

Our sample size though small and limited to just a single hospital, is enough to implicate that larger comparative studies are essential. Regular monitoring of ADR's is essential for management of any disease, especially tuberculosis where prolonged treatment is required. The activity of the pharmacovigilance needs to be strengthened.

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