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# IMPACT OF ADR ON VARIOUS ORGAN SYSTEM WITHIN 30 DAYS AND 60 DAYS OF FIRST LINE ANTI-TUBERCULAR THERAPY IN DOTS CATEGORY-1PATIENTS

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**ABSTRACT:**

**INTRODUCTION:**

Pulmonary tuberculosis is respiratory infection caused by *M.tuberculosis* bacilli which occur via aerosol. First line drugs used in the treatment of TB are Isoniazid (H), Rifampicin (R), Pyrazinamide (Z) and Ethambutol (E). Use of multidrug regimens has been associated with increased incidence of adverse drug reactions, involving all the major organs. However the frequency of occurrence of ADRs to ATT involving major organs are not well known, so in this study we tried to find out the most commonly affected organ due to ATT.

**MATERIAL AND METHOD:**

This open, prospective, observational, non-comparative study was conducted from March 2015 to September 2016 in the Government Medical College, Amritsar. One hundred sputum positive patients of pulmonary tuberculosis on DOTS category I, of either sex, in the age group of 14 years to 65 years, from out-patient department and patients admitted in wards of the Department of TB and Chest Hospital were recruited. Follow up was done at 1$^{st}$ and 2$^{nd}$ month during which

patients were actively enquired of any adverse drug reactions and the organ system affected were evaluated.

**RESULTS:**

In present study, 118 ADRs were experienced by 84 patients. Among the 84 ADRs victims, 60 patients showed different ADRs. Out of 84 patients, 75 patients developed ADRs within 30 days of the start of treatment of which most common ADR was gastrointestinal (46.6%) followed by liver problems (33.3%).

**CONCLUSION:**

Gastrointestinal tract is most commonly affected with ATT followed by hepatobiliary system. Utmost care has to be taken of these adverse effects so as to increase compliance to ATT and improve efficacy

**KEYWORD:** Tuberculosis, DOTS, Gastrointestinal, Hepatobiliary, ADRs

## INTRODUCTION:

The term tuberculosis relates to the 'tubercles' which were first associated with the disease in 17th Century, in Holland, by 'Franciscus de la Boe', better known as Dr. Franciscus Sylvius. According to John Bunyan, 'Tuberculosis is Captain of all these men of Death.' In Ayurveda, TB is called as 'Rajayakshma'. The disease was called "consumption" in the past because of the way it would consume from within anyone who became infected.[1]

Tuberculosis infection occurs via aerosol, and inhalation of a few droplets containing M. tuberculosis bacilli. After infection, M tuberculosis pathogenesis occurs in two stages. The first stage is an asymptomatic state that can persist for many years in the host, called latent TB. When the immune system is weak, the bacteria begin replicating and cause characteristic symptoms such as cough, chest pain, fatigue and unexplained weight loss.[2] About one-third of the world's population (> 2 billion), are infected with TB bacilli. 10% of the people infected with TB bacilli will become sick with active TBA in their lifetime[3-4].

The first line drugs used in the treatment of TB are Isoniazid (H), Rifampicin (R), Pyrazinamide (Z) and Ethambutol (E). Use of multidrug regimens has been associated with increased incidence of adverse drug reactions, involving all the major organs.

The severity of adverse drug reactions may range from mild to fatal.[5] However the frequency of occurrence of ADRs to ATT involving major organs are not well known, probably due to lack of awareness, detection and under reporting.[6]

In this prospective study comprising of 100 patients on DOTS Category 1, we have tried to find out the incidence of various organs affected by ADRs due to anti-TB treatment.

## MATERIAL AND METHODS:

This open, prospective, observational, non-comparative study was conducted from March 2015 to September 2016 in the Government Medical College, Amritsar. One hundred sputum positive patients of pulmonary tuberculosis on DOTS category I, of either sex, in the age group of 14 years to 65 years, from out-patient department and patients admitted in wards of the Department of TB and Chest Hospital were recruited. The approval of thesis and institutional ethics

committee was taken before the start of study. Written informed consent was taken from patients in their vernacular language. After recruitment patients were monitored for adverse reactions. Follow up was done at 30 and 60 days during which patients were actively enquired of any adverse drug reactions and the same were recorded.

## OBSERVATIONS AND RESULTS

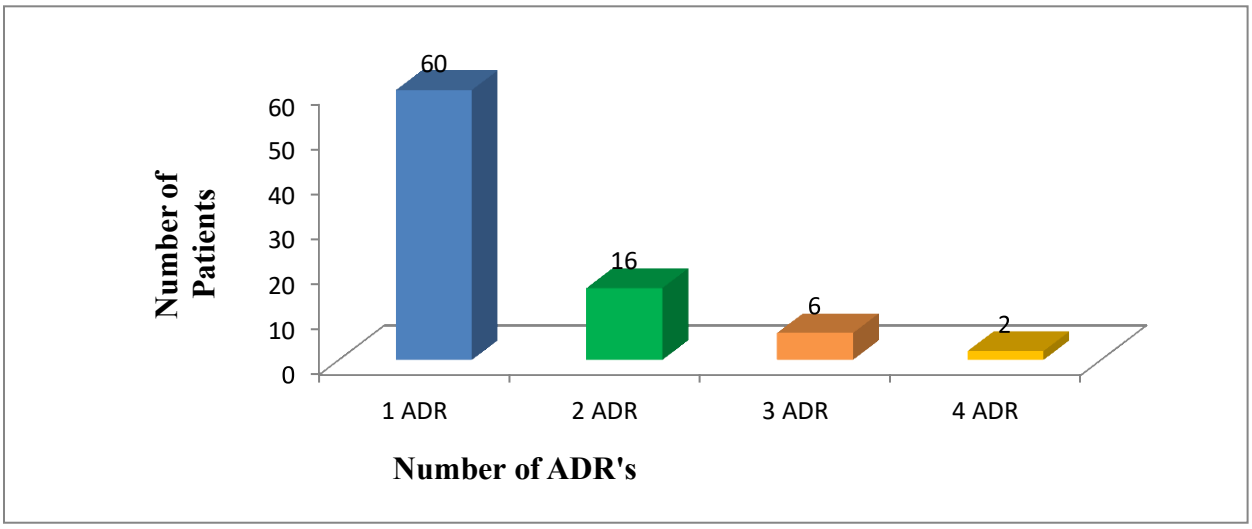
Out of 100 patients recruited in our study, 81 developed a total of 118 ADRs. In the majority of the patient (60) only one ADR has been reported

**TABLE 1: NUMBER OF ADRs PER PATIENT**

| Number of ADRs | Number of patients (N) | Percentage (%) |
|---|---|---|
| 1 ADR | 60 | 71.42 |
| 2 ADR | 16 | 19.04 |
| 3 ADR | 6 | 7.14 |
| 4 ADR | 2 | 2.38 |

A total of 118 ADRs were experienced by 84 patients. Among the 84 ADRs victims, 60(71.42%), 16 (19.04%), 6 (7.14%), 2 (2.38%) patients showed one, two, three and four different ADRs respectively.

**FIGURE 1: NUMBER OF ADRs PER PATIENT**




Most common organ affected by First line ATT is Gastrointestinal followed by hepatobiliary, CNS and skin as shown in Table 2 and Fig 2

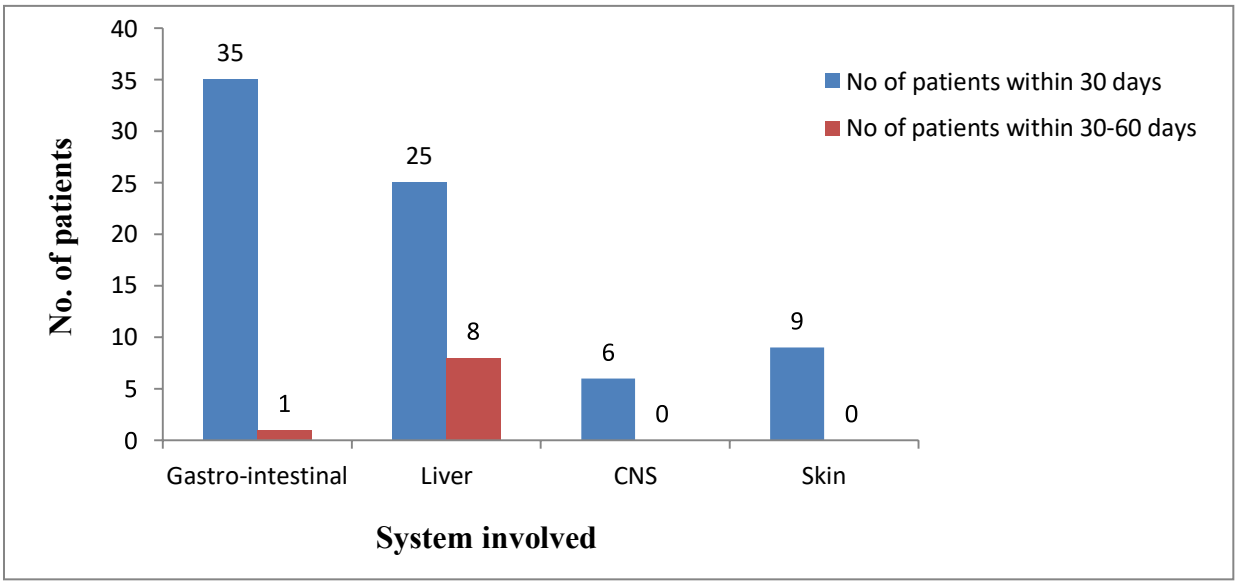
**TABLE 2: DISTRIBUTION OF ORGAN SYSTEM INVOLVED WITHIN 30 AND 60 DAYS**

| System involved | No of patients within 30 days N (%) | No of patients within 30-60 days N (%) |
|---|---|---|
| **Gastro-intestinal** | 35 (46.66) | 1 (11.11) |
| **Liver** | 25 (33.33) | 8 (88.88) |
| **CNS** | 6 (8.00) | 0 (0) |
| **Skin** | 9 (25.71) | 0 (0) |
| **Total** | 75 (100%) | 9 (100%) |

Above table shows that most of ADRs occur within 30 days of the start of treatment. Out of 84 patients, 75 developed ADRs within 30 days of the start of treatment, of which 35 (46.66%) suffered from gastrointestinal, 25 (33.33%) liver, 6 (8.00%) CNS and 9 (25.71%) skin problems. Within 30-60 days, nine patients developed ADRs of which 1 (11.11%) suffered from gastrointestinal and 8 (88.88%) from liver problems.

Most common organ affected by First line ATT is Gastrointestinal followed by hepatobiliary, CNS and skin as shown in Fig 2

**FIGURE 2: DISTRIBUTION OF ORGAN SYSTEM INVOLVED WITHIN 30 AND 60 DAYS**




This is in accordance to the study by Sahithi et al.[7] done in Andhra Pradesh, published in July 2016 which showed incidence of gastrointestinal side effects to be 30.90%. Other studies conducted by Honnaddi et al.[8] and Sinha et al.[9] showed comparatively higher incidence of gastro-intestinal problems i.e 32(51%) and 38 (53.52%) respectively. In contrast to our study, the study done by Sankar et al[10] in 2017-20 states that hepatobiliary is the most common organ affected (46.9%) followed by eye, skin and GI system.

## DISCUSSION

Anti-TB drugs could cause significant adverse effects both in magnitude and severity.[11] The results of this study indicated that ADRs due to DOTS therapy is a problem which should be highlighted. The high incidence of ADRs in Tuberculosis may steer the patient to make a judgment for interrupting the medication leading to emergence of drug resistance and an amplified health care cost. Hence it is important to monitor these reactions at early stages and treat them simultaneously.

In the study conducted by Gholami et al.[11] at Imam tertiary teaching hospital in Iran for a period of 8 months, the most prominent ADR was hepatotoxicity (37%), which is comparable to incidence of hepatotoxicity in our study (35.59%). In other studies conducted by Chandrasekaran et al.[12] at Coimbatore, Tamilnadu, and Lv X, et al.[13], in Chinese population, hepatotoxicity was

the most prominent ADR, with incidence being 22.97% in former and 6.34% in the later study, both of which are lower than incidence of hepatotoxicity in our study.

Study by Kurniawati et al[14] in Malaysia on 653 patients, concluded that majority of adverse drug reactions were skin reactions, followed by hepatotoxicity. Unlike our study which is prospective, this study was retrospective study.

**CONCLUSION:**

Anti-TB drugs are like double edge sword which have beneficial as well as adverse effect, so monitoring of these drugs are highly required, with prime focus on Gastrointestinal system as this is the most commonly affected followed by Hepatobiliary.

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