

A study on anti-tubercular drug-induced adverse reactions in South Indian district tuberculosis center

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ABSTRACT

Background: An adverse drug reaction (ADR) is any response to a drug which is noxious and unintended occurs at doses normally used in man for prophylaxis, diagnosis or therapy of disease or the modification of physiological function, anti-tubercular drugs can cause ADR and involving almost all systems in the body including the gastrointestinal (GI) tract, liver, skin, nervous system, and eyes.

Methods: A prospective observational study was conducted on tuberculosis (TB) patient. The suspected drug identified for ADRs and the type, nature, severity of reaction were recorded. A total of 239 patients were enrolled in the study. The patient was monitored the suspected ADRs were recorded and assessed for causality and severity.

Results: Out of 239 patients, 60 (25.11%) developed one and more than one ADR. A maximum number of tubercular patients were in age group of 21-40 years (44.4%). The majority of patients were males (69%). Incidence of ADRs based on affected organ was GI system disorders (30.33%), skin and appendages disorders (23.62%), central and peripheral nervous system disorders (15.28%), musculo-skeletal system disorders and liver and biliary disorder (9.72% each), hearing disorder (5.55%), and visual disorder accounts of (2.78%).

Conclusion: TB still becomes worldwide health problem not only on developing country but also in the developed country even the number of TB patients most large in the developing country. The importance of developing strategies to ameliorate ADRs both to improve the quality of patient care and to control TB safely.

Keywords: Tuberculosis, Directly observed treatment short course, Adverse drug reaction, Adverse drug event, Revised National Tuberculosis Control Programme

INTRODUCTION

Tuberculosis (TB) is one of the most common infectious diseases globally. According to the WHO reports, it causes ill-health among millions of people each year and ranks as the second leading cause of death from an infectious disease worldwide, after the human immunodeficiency virus (HIV). The latest reports estimated that there were almost 9 million new cases in 2011 and 1.4 million TB deaths (9,90,000 among HIV negative people and 4,30,000 HIV-associated TB deaths). Short course regimens of first-

line drugs that can cure around 90% of cases have been available since the 1980s.¹ India accounts for one-fifth of the global TB cases. Annually around 3,30,000 Indians die due to TB. India ranks first in the estimated number of TB cases and approximates to 1761 (thousands) cases per 10, 49, 549 population at the rate of 168 cases per 1,00,000 population.² In order to intensify the efforts to control TB, the Government of India gradually replaced National TB Programme by the directly observed treatment short course (DOTS) strategy/programme in 1993, now known as the Revised National TB Control Programme. The objective

of this revised strategy is to achieve a cure rate of 85% for infections and seriously ill patients through intermittent (3 days a week) supervised short course chemotherapy or the DOTS.³ Similar to other drugs even antitubercular drugs are not free from adverse drug reactions (ADRs). The added problem is that combinations of drugs are always used for prolonged periods of time and therefore, it is likely that the adverse reactions of one drug may be potentiated by the companion drugs used. Moreover, the ADRs to the drugs used are one of the major reasons for the patient default for treatment. A general knowledge of the various ADRs and their management is essential for the effective management of TB. All anti-tubercular drugs can cause ADRs and may result in ADRs involving almost all systems in the body including the gastrointestinal (GI) tract, liver, skin, nervous system, and eyes.⁴ The key component of DOTS strategy is the standard anti-TB short course chemotherapy regimen. The regimen which requires continually taking drug combinations of isoniazid (H), rifampicin (R), pyrazinamide (Z), ethambutol (E), and streptomycin (S) every alternate day for 6-9 months is recommended by WHO and currently used in the majority of high TB burden countries.^{5,6} Drugs in the therapy (H, R, Z, E, S), in addition to their role of killing and containing *Mycobacterium* effectively, could cause different kinds of adverse reactions, such as hepatotoxic reaction, gastro-intestinal discomfort, drug allergy, and arthralgia. Those ADRs are regarded as one of the major causes of noncompliance of anti-TB treatment. They may lead to final termination of TB treatment and severe ADRs outcomes like liver failure or death as well. As to the ADRs overall incidence, no consensus has been reached. Different studies may vary from 5.5% to 57.8% according to different populations and ADRs definitions.⁶⁻⁹

METHODS

A prospective observational study conducted in District tubercular center Chitradurga between November 2013 and April 2014. This study was approved by the “Institutional Human Ethical committee” of the S. J. M College of Pharmacy, Chitradurga (IEC/677 F/2013-14). The total of 239 patients diagnosed pulmonary TB of either sex and at least 18 years of age, undergoing DOTS regimen were enrolled in the study. HIV positive patients and multidrug-resistant TB patients were excluded. For monitoring therapeutic profile of patients, patient data collection form designed, it includes demographic details of the patients such as IP number, age, sex, date of admission, date of discharge, treatment chart, length of hospital stay, category of TB treatment, record of follow-up, and outcome of the patient’s treatment, during the follow-up, patients were questioned regarding occurrence of ADRs. The cases having ADR, full details of cases including patient name, age, sex, past and present medication details, and other relevant information brought into the self-designed data collection form. All the enrolled patients were monitored for the regards to drug therapy drug data such as drug name, dosage form,

route and duration of therapy, and the date on which the anti-TB therapy was instituted was collected. All decisions relating to the management of the patients including drugs and investigations were taken by DOTS center personnel. The investigator did not interfere in the management of the patient and only observed the proceedings.

RESULTS

A prospective observational study was conducted at district TB center Chitradurga. The total of 239 TB patients were included as the study subjects. The subjects were screened for the ADR caused by the anti-TB drugs. Among 239 (100%) patients on DOTS regimen about 60 (25.11%) patients developed one and more than one ADRs. In our study, maximum number of tubercular patients was in the age group of 21-40 years (44.4%). The majority of patients were males (69%). The majority of patients were from Category I (79.9%). Out of 239 patients, (31.4%) were alcoholics and (41.8%) having a habit of smoking. Baseline characteristics of study population shown in Table 1.

As shown in Figure 1, the most frequently occurred ADRs

Table 1: Baseline characteristics of study population.

Parameter	n (%)
Age group (years)	
<20	16 (6.7)
21-40	106 (44.4)
41-60	90 (37.7)
>60	27 (11.3)
Sex	
Male	165 (69)
Female	74 (31)
DOTS category	
Category I	191 (79.9)
Category II	48 (20.1)
Alcoholics	75 (31.4)
Smokers	100 (41.8)

DOTS: Directly observed treatment short course

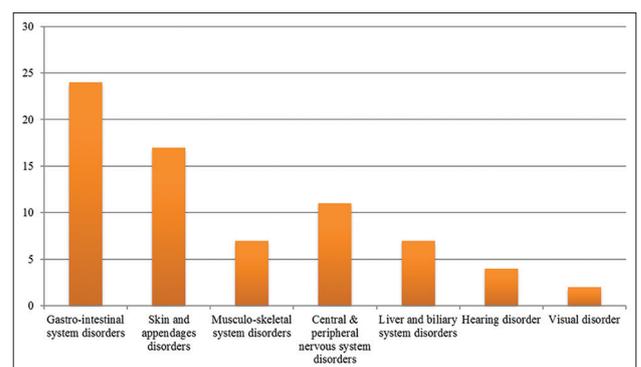


Figure 1: Incidence of adverse drug reactions as per system organ class.

were GI system disorders (30.33%), it was followed by skin and appendages disorders (23.62%), central and peripheral nervous system disorders (15.28%), musculo-skeletal system disorders and liver and biliary disorder (9.72% each), hearing disorder (5.55%), and visual disorder accounts of (2.78%).

Total 72 ADRs occurred in 60 patients. GI intolerance was most common frequently occurred ADR (30.33%). It was followed by skin disorder (23.62%), peripheral neuropathy/numbness and tingling (15.28), arthralgia and liver disorder (9.72% each).

Casualty assessment of ADR according to Naranjo algorithm revealed that out of 72 ADRs 50 (69.44%) were possible and 22 (30.56%) identified as probable (Figure 2).

Casualty assessment of ADR according to WHO probability scale shown that out of 72 ADRs 27 (37.5%) were possible and 19 (26.39%) were probable, 14 (19.44%) were certain, and 12 (16.67%) were unassessable/unclassifiable (Figure 3).

Hartwig and Seigels scale to take proper initiative toward the management of ADR is necessary to study the severity of ADR, modified Hartwig and Seigels scale was widely used for this purpose majority of cases were “mild (level 1 and level 2) was 59 (81.94%),” This was followed by “moderate” (level 3 and level 4A) only 13 (18.06%) patient (Figure 4).

DISCUSSION

The present study was undertaken to find out the ADRs of anti-TB drugs due to DOTS therapy among the TB patients in a hospital setting. The males constitute the major population of the study group, that is, 76.47% against 31% females. It may be due to the fact that the males are having higher risk factors such as smoking, alcoholism, and drug addiction to get TB than females, and men are socially more active and visit public places more often. These risks make them more vulnerable for TB infection.¹⁰

It has been found that TB was more prevalent in the age group 21-40 years 106(44.4) Edoh and Adjei, also found a higher incidence of TB in the age group of 21-40 years with the highest peak of 29.7% in the group of 31-40 years.¹¹ Another study conducted by Sinha et al., TB was more prevalent in the age group 31-40 years (27.45%).¹² This is probably because the people in this age group are involved in TB infectious activities such as smoking, and large alcohol intake, which results in the weakening of immunity.¹³

In our study total, 72 ADRs occurred in 60 patients. GI intolerance was most common frequently occurred ADR (30.33%). It was followed by skin disorder (23.62%), peripheral neuropathy/numbness and tingling (15.28), in another study conducted by Dalal et al., Total 35 ADRs occurred in 29 patients. GI intolerance was most frequently occurred ADR (12.67%). It was followed by arthralgia (2.67%) and hepatotoxicity (2%).¹⁴

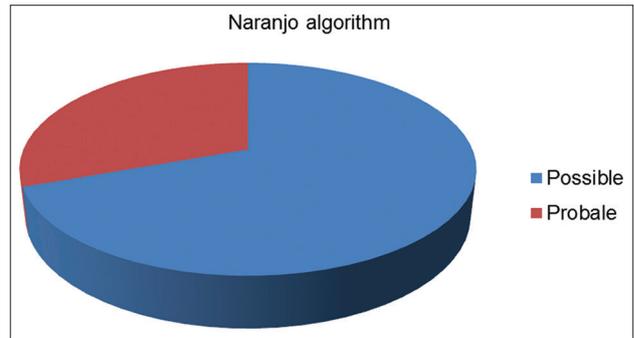


Figure 2: Casualty assessment of adverse drug reaction according to Naranjo scale.

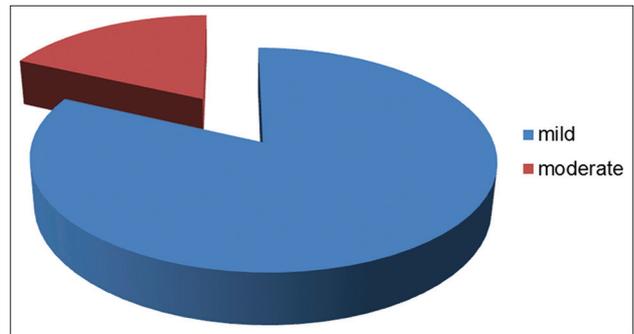


Figure 3: Severity of adverse drug reaction, modified Hartwig and Seigels scale.

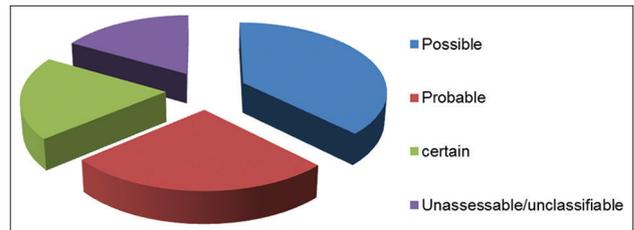


Figure 4: Casualty assessment of adverse drug reaction according to the WHO probability scale.

In our study, casualty assessment of ADR according to Naranjo algorithm revealed that out of 72 ADRs 50 (69.44%) were possible and 22 (30.56%) identified as probable. In another study conducted by Dalal et al., Naranjo algorithm revealed that out of 35 ADRs 32 (91.43%) were “possible” and 3 (8.57%) were “probable.” The “probable” ADRs included two cases of hepatotoxicity and one case of ototoxicity.¹⁴

In our study, the majority of cases were “mild was (81.94%),” this was followed by “moderate” (18.06%) patient. In another study conducted by Dalal et al., the severity assessment showed that majority of ADRs (17, 48.57%) were “moderate,” followed by “mild” (15, 42.86%). Only 3 (8.57%) were “severe” ADRs.¹⁴

Limitations

This study could review a small percentage of patient’s undergone TB treatment in district TB center due to shorter

duration of study period regular biochemical investigations were not carried out. So, our incidence may not be a true reflection of the entire population.

CONCLUSION

This study showed that 25.11% of TB patients who received DOTS therapy developed one or more ADRs. ADRs may result in an increase in health care services and affect the anti-TB treatment pattern. Patients with ADRs were more susceptible to develop unfavorable anti-TB outcomes. The study shows that TB was more prevalent in the age group 21-40 years 106 (44.4) and among the males. Most common ADR was GI symptoms, but most were mild this highlighted the importance of developing strategies to ameliorate ADRs both to improve the quality of patient care and to control TB safely.

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