A Targeted Pharmacovigilance Study on Antitubercular Drugs in the Department of Pulmonary Medicine at Tertiary Care Teaching Hospital in Rural Area

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Abstract

Tuberculosis (TB) is a chronic infectious disease caused by mycobacterium tuberculosis leading to increased morbidity and mortality. Adverse drug reactions (ADRs) are a global health problem and a leading cause of death, illness and injury in economically developed countries like India. ADRs associated with antitubercular drugs can result in non-compliance and therapeutic failure. The present study was aimed to identify the ADRs caused by anti-tubercular drugs and their assessment by using causality, preventability and severity assessment scales. This observational study was to identify the possible ways to improve the quality of the ADR reporting with a special focus on improving the aspect of ADR reporting that has to do with symptoms descriptions, ADR reporting also help to minimize morbidity and improve patient compliance and achieved the better therapeutic outcome.

Keywords: Causality Assessment; pharmacovigilance; symptoms; rifampicin; pulmonologist

Introduction

According to World health organisation, Tuberculosis is an infective bacterial disease caused by mycobacterium tuberculosis, which most commonly affects the lungs. TB is an age-old dreadful disease and it accounts up to 20% of total yearly cases in the world and about 0.4 million die every year. There were an estimated 10.4 million new TB cases with 1.8 million TB deaths in 2015 [1-7]. Most of the medicines used to treat TB today have been on the market for several decades [8]. Clinicians treating TB patients around the world know these medicines well, and are usually well aware of their associated ADRs. Antitubercular drugs also cause various types of ADRs and affects almost all the systems in the body mainly the gastrointestinal, liver, skin, nervous system and skin [9, 10]. ADRs is defined as 'Any response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis or therapy of disease or for the modification of physiological function'. ADRs is considered to be the sixth leading cause of death [11]. The incidence rate estimates approximately 2%of hospital admissions are due to ADRs. Drug attributed deaths are estimated to be 0.17% in all medical inpatients [12]. About 0.40% of ADRs identified were directly linked to high costs. ADRs not only increase the mortality and morbidity but also multiply the health care cost [13]. Post-marketing surveillance is also needed for these new drugs. ADRs are unfortunate burden of society both financially and in terms of human suffering. Systemized ADR monitoring and reporting helps physicians to rational prescribing of drugs [14-16].

Methodology

The prospective observational study was conducted in the Department of Pulmonary Medicine and Tuberculosis of Chhatrapati Shivaji Subharti Hospital, (Meerut) and its Pharmacology Department is a 1038 bedded tertiary care teaching hospital in rural area. This pharmacovigilance study has been approved by the Institutional Ethics Committee. All the patients visiting the medicine for pulmonary dysfunction in outdoor patient department which are taking anti-tubercular treatment were included in the study. The patients were treated by pulmonologist in medicines for pulmonary dysfunction data of these patients were recorded. Patient's demographic profile, characteristics, disease particulars, treatments, outcomes and adverse effects were recorded. The ADRs were recorded in the specified Performa designed by the National Pharmacovigilance Programme for this purpose. All suspected ADRs were recorded with the help of different investigational tests that was depended on the type ADRs. The patients were followed up till the study completed and any new change in prescription and status of each ADR was recorded.

Inclusion criteria

All patients of either sex aged 17 years and above who are under the treatment of tuberculosis with anti-tuberculosis drugs.

Exclusion criteria

1. Patients who were HIV Positive.

2. Patients with chronic illness such as Cirrhosis, chronic hepatitis and acute viral hepatitis.

3. Patients who are unwilling to participate in the study.

Ethics

The patient's data were recorded and privacy of identity was maintained. The study was approved by the Institutional Ethics Committee of Subharti Medical College and Hospital; file number is (SMC/IEC/2017/195).

Observations

There were ADRs in all the 22 cases on antitubercular drugs, but these were successfully managed by immediate measures taken. Symptomatic addition of adjuvant drugs for adverse symptoms could relieve the adverse symptoms. This helped in ensuring compliance with antitubercular drugs. No antitubercular drug had to be withdrawn as adverse effects could be managed with dose reduction or adjuvant treatment. The ADRs experienced by the tubercular patient were non-serious

and for the management of those ADR an add-on drug therapy was done and there was no need to withdraw the suspected drug showing in table 1.
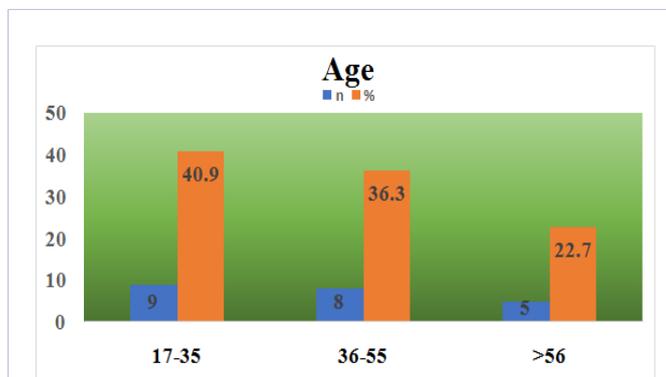

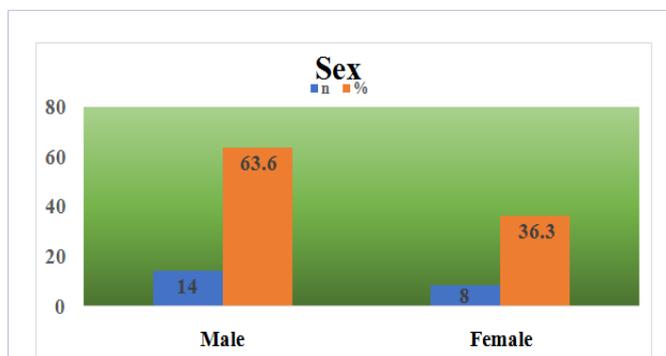**Figure 3:** Residency (rural/urban) wise distribution of patients

Figure 1: Age (in years) wise distribution of patients

Figure 2: Sex (male/female) wise distribution of patients

S. No.	Antitubercular drugs (combination dose and single dose)
**Table 1:** Antitubercular therapy used on 22 patients in department of pulmonary medicine and tuberculosis [17-19]
1	Rifampicin+isoniazid, Ethambutol, Pyrazinamide
2	Rifampicin+isoniazid, Ethambutol, Streptomycin
3	Rifampicin+isoniazid, Ethambutol, Streptomycin
4	Ethambutol, Rifampicin+isoniazid
5	Rifampicin+isoniazid, Ethambutol
6	Rifampicin+isoniazid, Ethambutol
7	Streptomycin, Isoniazid+rifampicin
8	Rifampicin+isoniazid, Ethambutol, Pyrazinamide
9	Isoniazid+rifampicin
10	Rifampicin+isoniazid, Ethambutol
11	Rifampicin+isoniazid, Ethambutol, Pyrazinamide
12	Streptomycin, Ethambutol+isoniazid+pyrazinamide+rifampicin
13	Isoniazid+ Ethambutol
14	Isoniazid+rifampicin
15	Rifampicin+isoniazid, Ethambutol
16	Rifampicin+isoniazid, Pyrazinamide
17	Rifampicin+isoniazid, Ethambutol, Pyrazinamide
18	Rifampicin+isoniazid, Ethambutol
19	Rifampicin+isoniazid, Ethambutol
20	Rifampicin+isoniazid, Ethambutol
21	Ethambutol, Rifampicin+isoniazid, Pyrazinamide
22	Rifampicin+isoniazid, Ethambutol, Pyrazinamide

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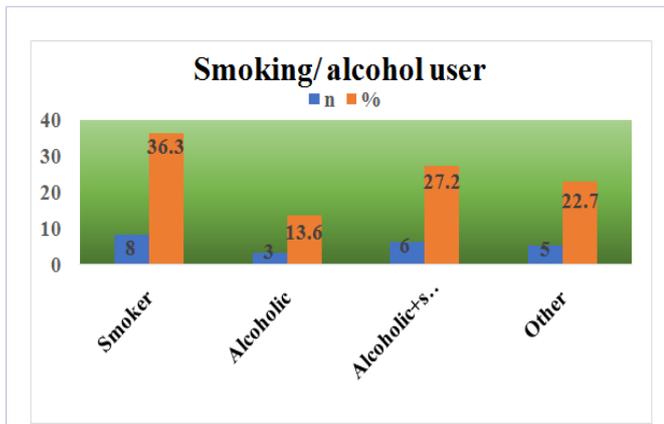
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Figure 4: Patients are smoker/alcoholic and nor consumed smoker/alcoholic
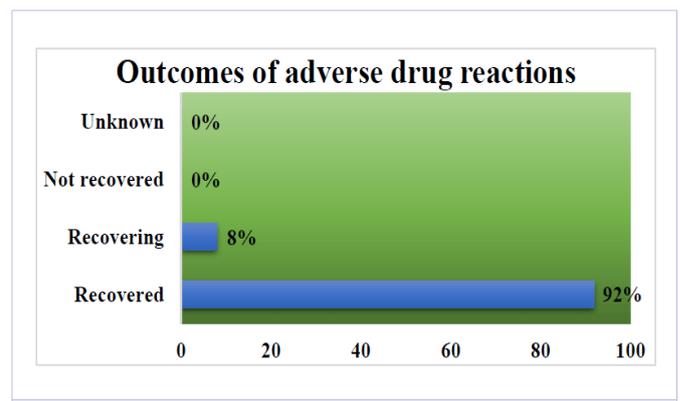

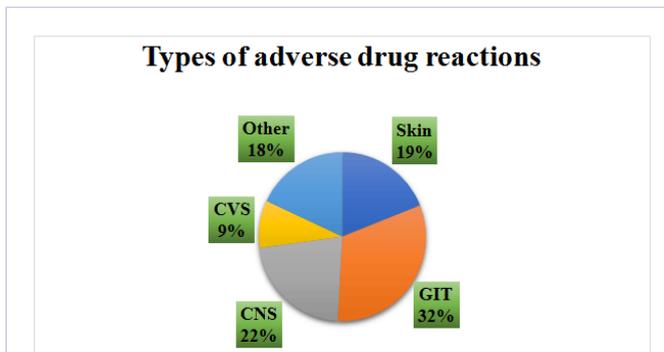**Figure 7:** Outcomes of ADRs induced by anti-TB drugs

Figure 5: Types of ADRs induced by anti-TB drugs
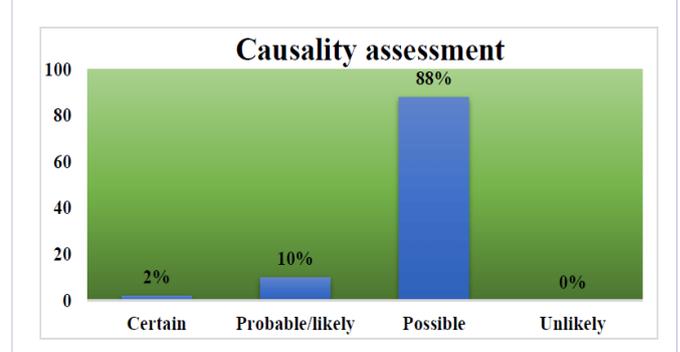
Figure 8: Causality assessment of ADRs according to WHO-UMC scale [20]

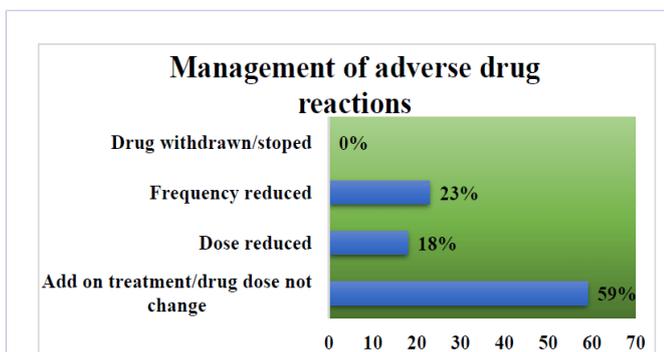**Figure 6:** Management of ADRs induced by anti-TB drugs
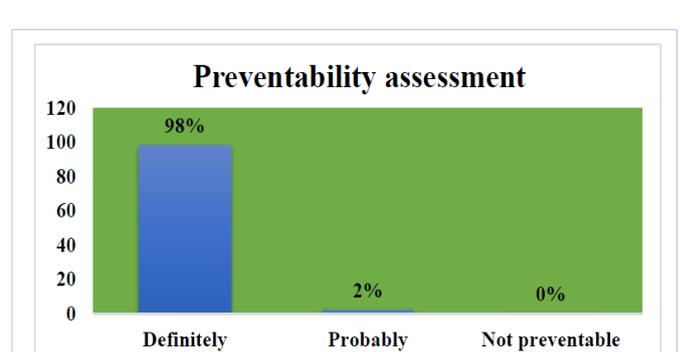
Figure 9: Preventability assessment of ADRs by Schumock and Thornton scale [21]

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Figure 10: Severity assessment of ADRs by Hartwig and Seigel scale [22]

Results

The present study was envisaged to study pattern of pulmonary medicine and tuberculosis cases, treatment given and asses the ADRs to first line antitubercular drugs prescribed to tuberculosis patients attending outpatient to department of pulmonary medicine and tuberculosis of a tertiary care teaching hospital. It was observed in this stu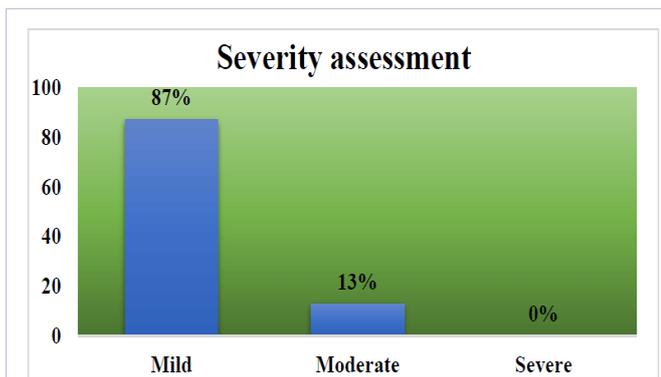dy total 22 ADRs were reported, the study was conducted in pulmonary medicine and tuberculosis department at chhatrapati shivaji subharti hospital (Meerut) that is a 1038 bedded tertiary care teaching hospital in rural area. In this observational study we found that the age of patients ranged from 17 to >56 years. That there were more male 63.6% patients as compared to female 36.3%. More than 77% patients were smokers or consumed alcohol. Whereas a less number of patients 23% were neither smoker nor-consumed alcohol, Male predominance and a more number of smokers are in agreement with aetiology of respiratory diseases. Smoking and alcohol consumption are risk factors for respiratory diseases. There were adverse events in all the 22 cases on antitubercular drugs, but these were successfully managed by immediate measures taken. Symptomatic addition of adjuvant drugs for adverse symptoms could relieve the adverse symptoms. This helped in ensuring compliance with antitubercular drugs. No antitubercular drug had to be withdrawn as adverse effects could be managed with dose reduction or adjuvant treatment. Total 22 ADRs were reported in 22 patients who experienced the ADR of outpatient to department of pulmonary medicine and tuberculosis. The majority of cases of the adverse drug reactions were related to the central nervous system such as sedation, vertigo, severe headache and sleeping disturbance it happened in 22% mostly due to the first line antitubercular drug like rifampicin, isoniazid, ethambutol and pyrazinamide followed by gastrointestinal reactions such as nausea, vomiting, gastritis and abdominal pain 32%, skin reaction such as erythematous rash, urticaria and skin dryness 19%, cardiovascular such as palpitation and increased heart rate 9%, and other adverse drug reaction were reported 18%. The adverse drug reactions experienced by the tubercular patient were non-serious and all were managed by the add-on drug therapy. On the basis of the risk benefit ratio of the drug therapy for treatment of tuberculosis drug withdrawn of the suspected drug was not required.

However, the management of the adverse drug reaction occurrence in tubercular patient were done with add-on therapy 59%, then followed by drug permanently withdrawn 0%, dose reduced 18%, frequency of dose schedule reduced 23% cases. The Causality of each ADR was assessed by using WHO-UMC causality assessment scale. On the basis of scale nearly 2% of the ADR were classified as certain, 10% probable, 88% possible and 8% of the ADR were unlikely. The severity assessment of each ADR was assessed by the modified Hartwig and Siegel scale. As per this assessment highest number of ADR i.e. 87% of the ADR comes on the level 1-2 and classified mild ADR, 13% of the ADRs were on level 3 i.e. moderate ADR and there was no any ADR were come on the level 4 and above i.e. severe ADR. For the preventability assessment of each ADR Schumock and Thornton scale were used, which showed that 98% of the ADRs were definitely preventable, 2% of ADRs were probably preventable and no any ADR were come under the not preventable class.

Conclusion

The present evaluation has revealed opportunities or interventions especially or avoidable ADRs which will help in promoting safer drug use, information to the healthcare professionals. Improve the quality of patient care and educate to increase awareness. The adverse drug reaction monitoring and reporting programmes or pharmacovigilance programme aim is to identify the risks associated with the use of the drugs. This information may be useful to identify and to minimize the preventable ADRs. Many time patients discontinue their treatment because of the suffering of the adverse drug reaction. Some time it may be very dangerous for the patient as well as society e.g. if the patient discontinues their antitubercular therapy the risk of the failure of the tubercular treatment increased and it may be the chance of resistance tuberculosis. So now the time has come to aware the general public too for the reporting the adverse drug reaction to nearest hospital or ADR monitoring centre or to the healthcare professionals. They may directly report the ADR through government. Toll-free number 18001803024, ADR application, email and other method like social media [23-25].

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