

Prevalence and Relative Evaluation of Adverse Drug Reactions in Tuberculosis Patients undergoing DOTS in Karad region

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Abstract:

Tuberculosis (TB), a multisystemic disease with myriad presentations and manifestations, is the most common cause of infectious disease-related mortality worldwide. To find out adverse drug reactions induced due to Directly Observed Treatment, Short-course (DOTS), a study was undertaken to assess the prevalence rate and pattern of adverse drug reactions (ADR) in DOTS with focus on Human immunodeficiency virus (HIV) non reactive cases in Karad region, Maharashtra state. The incidence of adverse drug reactions was prospectively observed in 202 individuals treated for TB, all were HIV non reactive cases. 202 tuberculosis infected individuals received DOTS therapy. Adverse drug reactions were recorded in 21. The result of our study showed that the adverse drug reactions appeared in 10.39% of the patients. Patients experienced skin Hypersensitivity, Gastritis, Nausea, Vomiting, Arthralgia, Fever, Abdominal Pain, Constipation, Vertigo and Restlessness. Adverse drug reactions decreases patient adherence to treatment; it is a high risk factor for treatment discontinuation and Multi-drug-resistant tuberculosis (MDR-TB).

Keywords: *Adverse Drug Reactions, DOTS, India, Karad, Tuberculosis*

Introduction:

In continuation of our previous study “Prevalence and comparative assessment of adverse drug reactions in DOTS with focus on HIV negative patients in Karad region” ^[1]. We planned to study more patients in addition to suburban area in Karad region.

Tuberculosis (TB), a multisystemic disease with myriad presentations and manifestations, is the most common cause of infectious disease-related mortality worldwide. The World Health Organization (WHO)

has estimated that globally, in 2009, the disease killed 1.7 million people ^[2]

WHO recommends DOTS strategy that emphasizes the use of the most effective standardized, short-course regimens, and of fixed-dose drug combinations (FDCs) under observation so as to facilitate the adherence to treatment and to reduce the risk of drug resistance development ^[3]

Long duration of treatment for Tuberculosis patients with drugs like Isoniazid, Pyrazinamide, Rifampin, Ethambutol and Streptomycin – the drugs used above are potential to cause adverse drug reactions like Arthralgia, Headache, Skin Rashes etc ^[4]. Patients under multiple drug therapy are prone to develop adverse drug reaction due to alteration of drug or by synergistic effect. Multiple / intercurrent disease and multiple drug therapy are responsible for increased risk of developing an ADR ^[5]. Anti-TB chemotherapy exhibit greater level of efficacy with an acceptable degree of toxicity, however combination treatment may produce severe adverse events. Important adverse effects are Hepatitis, Skin rash, Gastrointestinal Upset, Hyperuricemia, Peripheral Neuropathy, Visual Disturbances ^[6].

Few studies have been reported on adverse effects of anti-TB drugs related to specific regimen of drug and risk factors for those adverse effects. So, we aimed to study the adverse drug reaction in DOTS treatment in patients without HIV. Tuberculosis in HIV is having high prevalence rate. HIV patients receive several multiple drug therapies like antiretroviral therapy (ART) as well as the regular symptomatic treatment. Due to such combinations drug interactions occur. To avoid this confusion we have targeted only DOTS patients with HIV negative cases.

In this context the present study was carried out with an objective to assess the adverse drug reactions in tuberculosis patients with HIV negative cases in Karad region.

Materials and Methodology:

Site of study: The study was conducted on the patients of DOTS with HIV non reactive cases at urban, suburban and rural hospitals providing and monitoring DOTS in Karad region. Karad is the largest tehsil in Maharashtra state. Total population of Karad is 1630272.

Period of study: From 31st March 2010 to 30th September 2012, a prospective evaluation of DOTS in people was undertaken. A total of 202 newly diagnosed tuberculosis patients, who were tested for HIV at Venutai Chavan Hospital Karad, the patients with HIV non reactive reports were participated in the study. 90 were attending Venutai Chavan Sub-district Hospital, Karad, 63 patients attending Primary Health Centre Vadgaon and 49 attending Krishna Hospital, Malkapur were included in the present study.

Method: Informed consent was taken from each patient enrolled in this study. After taking the consent of the patient, Case record form was filled. Patients were kept under observation during their whole treatment period. Patients were instructed to report any signs and symptoms; which they come across during the treatment period. Physicians also observed the adverse drug reactions. The patients with any kind of adverse drug reactions were focused and recorded into the adverse drug reaction form.

Results:

A total of 202 cases during 31st March 2010 to 30th September 2012 for the period of 30 months were included in the study. Among the studied 202 cases of tuberculosis mean average age was found to be 39.24 years (Fig. 2), 119 males were included with the mean average age of 40.11 years and 83 females with mean average age of 38 years (Fig. 1,2).

Fig. 1. Sex ratio

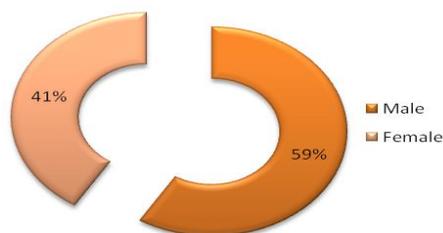
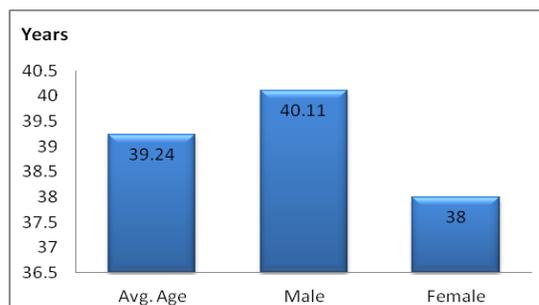


Fig. 2. Female-Male average age

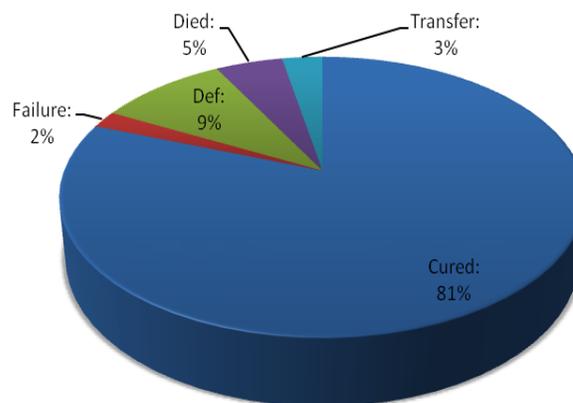


Total No. of patients participated in the study were 202. In between those 163 were cured successfully. 19 patients were dropped from the study without completion of the treatment so they are named as defaulter from study. 10 patients died during the study period. 4 patients could not be cured due to treatment. 6 patients were transferred to other places (Table1)

Table 1. Outcome of treatment

Total patients	202
Cured	163
Failure	4
Defaulter	19
Died	10
Transfer	6

Fig. 3. Percentwise outcome of treatment

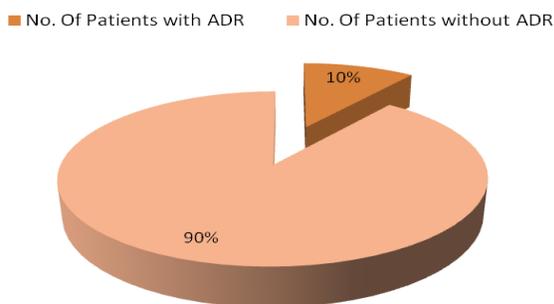


Adverse drug reactions were recorded in 21 patients (Table 2). The study showed that 10.39% of patients reported at least one type of adverse drug reaction. However, most of the reactions were minor and required no modification of treatment. The results of our study showed that the adverse drug reactions appeared in 10.39% of the patients (Fig. 4).

Table 2. Comparative assessment of ADR against Non ADR cases

Skin Hypersensitivity	6
Gastritis	5
Joint Pain and inflammation	2
Fever	4
Constipation	2
Vertigo	1
Restless	1

Fig. 4. Percentwise comparative assessment of ADR against Non ADR cases

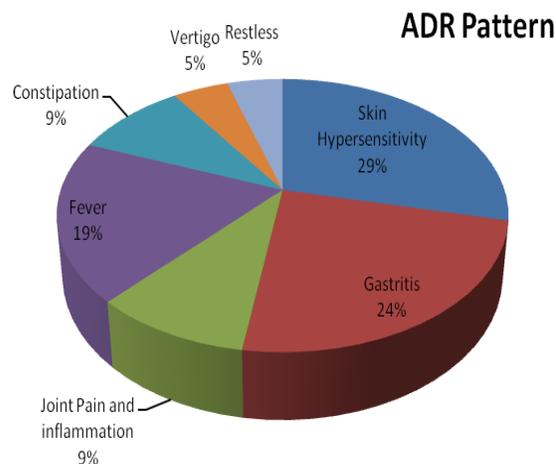


In this study, 6 patients (28.5%) experienced skin hypersensitivity. 5 patients (23.8%) experienced gastritis, nausea, vomiting. 2 patients (9.5%) experienced joint pain and inflammation (arthralgia). 4 patients (19%) experienced fever. 2 patients (9.5%) experienced abdominal pain and constipation. Also vertigo was experienced by 1 patient (4.7%). Restlessness was experienced by 1 patient (4.7%) (Table.3, Fig.5).

Table 3. Various pattern of ADR in DOTS

Total No. Of Patients	202
No. Of Patients with ADR	21
No. Of Patients without ADR	181

Fig. 5. Percentwise pattern of ADR in DOTS



Discussion :

Highlights of extended study

This study was conducted with an increase in the sample with the inclusion of the sub-urban area in Karad region. ADR rate is reduced and ADR pattern is changed significantly compared to our previous study with limited samples. Number of ADR patients with Skin Hypersensitivity, Gastritis, Fever and Constipation has increased. Other ADR patterns like Joint Pain and Inflammation, Vertigo and Restlessness did not change significantly. Whereas the sex ratio of the patients remains the same.

Prevalence rate of ADR in Karad region

In previous study, of the 99 patients, 4 patients (31%) experienced Skin Hypersensitivity. 2 patients (15%) experienced Gastritis; Nausea Vomiting. 2 patients (15%) experienced Joint Pain and Inflammation (arthralgia). 2 patients (15%) experienced Fever. 1 patient (8%) experienced Abdominal Pain and Constipation. Also Vertigo was experienced by 1 patient (8%). Restlessness was experienced by 1 patient (8%).

In the current study of the 202 patients, 6 patients (28.5%) experienced Skin Hypersensitivity- the drugs, which are responsible for this side effect, may be Pyrazinamide, Rifampicin and Isoniazid. 5 patients (23.8%) experienced Gastritis, Nausea, Vomiting- the drugs, which are responsible for these side effects, may be Pyrazinamide and Rifampicin. 2 patients (9.5%) experienced Joint Pain and

Inflammation (arthralgia) - the drug, which are responsible for these side effects, may be Pyrazinamide, Ethambutol. 4 patients (19%) experienced Fever- the drug, which is responsible for this side effect, may be Rifampicin. 2 patients (9.5%) experienced Abdominal Pain and Constipation- drugs, which are responsible for these side effects, may be Pyrazinamide, Rifampicin and Isoniazid. Also Vertigo was experienced by 1 patient (4.7%) - drug, which is responsible for this side effect may be Streptomycin. Restlessness was experienced by 1 patient (4.7%) - the drug, which is responsible for this side effect, may be Isoniazid^[7, 8].

Conclusion:

The study shows that the HIV negative DOTS patients are having high incidence rate of adverse drug reaction, which is 10.39%. Due to adverse drug reactions, patient adherence to the treatment decreases. ADR is a major cause and high risk factor for treatment discontinuation and Multi-drug-resistant tuberculosis (MDR-TB). In future it is necessary to monitor patients under DOTS with special reference to ADR's occurred during their due course of treatment.

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