

# Research Journal of Pharmaceutical, Biological and Chemical Sciences

## Adverse Drug Reactions to Anti-tubercular Drugs in HIV/TB Co-infected Patients.

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### ABSTRACT

The medications used to treat HIV and TB can result in significant adverse effects and drug interactions which can adversely impact the disease management. The objective of this study is to determine the adverse reactions to anti-tubercular drugs in these HIV/TB co-infected patients. A retrospective study of case record files of HIV/TB co-infected patients on anti-tubercular treatment was carried out at a tertiary care teaching hospital and a district government hospital. Demographic details and adverse drug reactions were recorded. Data of 96 HIV/TB co-infected patients on anti-tubercular therapy was evaluated. Of these, 44 (45.8%) developed adverse drug reaction during the course of treatment. Rifampicin was considered to be responsible for 63.6% of adverse drug reactions. Hepatitis was the most common adverse reaction (31.8%). Almost half of the patient population with HIV/TB co-infection on anti-tubercular drugs experienced an adverse drug reaction. Early recognition and management of the adverse drug reactions is important to decrease morbidity and mortality.

**Keywords:** Adverse drug reaction, Anti-tubercular drugs, HIV, Hepatitis

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## INTRODUCTION

As per the World Health Organization data for the year 2014 the incidence of Human Immunodeficiency virus/tuberculosis (HIV/TB) co-infection per 100000 population was 8.3 (7.4-9.3) [1]. Both the diseases have been declared as global emergencies. The acquired immune deficiency syndrome (AIDS) caused by HIV weakens the immune system making patients susceptible to opportunistic infections. The risk of tuberculosis in HIV positive persons is twenty times higher as compared to HIV negative individuals [2]. Research has demonstrated that in resource-constrained settings, addition of prophylactic therapy for opportunistic infections can decrease the mortality proportion among patients with HIV without treatment but with concurrent tuberculosis from 50% to less than 10%. The benefits of concurrent treatment for HIV and TB is thus enormous [3]. As per the World Health Organization estimate, in the year 2014 approximately one third of deaths among HIV positive people were due to tuberculosis [1]. The National AIDS Control Organization (NACO), India, has classified the opportunistic infections in HIV-positive patients into 12 categories and provided guidelines for their prevention and treatment. The use of Revised National Tuberculosis Control Programme (RNTCP) guidelines is recommended for treatment of TB in these patients. Notwithstanding the possible morbidity due to disease progression, the medications used to treat HIV and TB can also result in significant adverse effects and drug interactions which can adversely impact the disease management. Antiretroviral drugs as well as the first line antitubercular drugs carry a significant risk of hepatotoxicity and yet need to be coadministered [4]. The objective of this study is to determine the adverse reactions to anti-tubercular drugs in these HIV/TB co-infected patients [5]. Determining the possible adverse effects in this population will help in early and better management which might ultimately decrease morbidity and mortality.

## METHODS

This was a retrospective study conducted at a tertiary care teaching hospital and a district government hospital in Mangaluru, Karnataka. The data of 96 HIV positive patients with tuberculosis who visited the ART centers of the above hospitals over a period of three years and were on anti-tubercular treatment was studied. Approval from the institutional ethics committee was obtained prior to initiation of the study. Data of patients who were not taking anti tubercular drug were excluded.

The retrospective data was collected from ART centers records as per the convenience of the investigators. Data was recorded on a case record form ensuring that no identifiable information is collected. The age, gender and adverse drug reaction details were collected for each patient. Data was entered into the Statistical package for social sciences SPSS version 16.0 and analyzed using descriptive statistics. Numbers are expressed as percentages.

## RESULTS

Data of 96 HIV/TB coinfecting patients who were on anti-tubercular treatment was evaluated. 45.8% (44/96) of the patients experienced an adverse drug reaction. Of these 44 patients, 75% were males. The mean age of the patients showing adverse reaction to anti-tubercular treatment was 43.42 years.

The anti-tubercular drugs likely to be responsible for the adverse drug reactions were as follows - Rifampicin (63.6% of the ADRs), Pyrazinamide (22.7% of ADRs) and Ethambutol (13.6% of ADRs). The details of the adverse drug reactions are shown in Table 1.

**Table 1: Adverse drug reactions to anti-tubercular drugs in HIV/TB co-infected patients**

Adverse drug reaction	Number of cases (%) [N = 44]
Hepatitis	14 (31.8)
Skin reaction (itching, rashes, drying, scaling)	11 (25%)
Gastrointestinal (gastritis, nausea, vomiting)	5 (11.3)
Diminished vision	3 (6.8)
Hyperuricemia	3 (6.8)
Others (neuropathy, allergic cough, rifampicin allergy)	5 (11.3)

## DICUSSION

The impact of the AIDS epidemic on the epidemiology of tuberculosis worldwide is being noted with growing concern. In a study done at a university teaching hospital in Nigeria the prevalence rate of pulmonary tuberculosis in HIV/AIDS patients was 13.9% [6]. The mean age of the patients was 22.9 years. In another study conducted at a tuberculosis research centre at Chennai, India the prevalence rate was estimated to be 6.9/100 person year [7].

In a study among intravenous drug users adverse effects to anti-tubercular drugs was associated with female gender, age over 60years, birthplace in Asia and positive human immunodeficiency virus status [8]. In our study, adverse reactions were more common in males and the mean age of the patients with adverse reactions was 43 years. A prospective single center study at a antiretroviral therapy center of a tertiary care hospital in Ahmedabad observed that 51% of the patients had adverse drug reactions to anti-tubercular drugs [9]. Majority of the adverse drug reactions were non-serious and did not warrant any therapy. During the study, one patient developed severe skin rashes progressing to peeling of skin. Rifampicin was suspected to be the causal drug. Gastrointestinal adverse effects were also frequent as most of the drugs are given orally. In our study, 45.8% patients showed adverse drug reactions. Among these, hepatitis (31.8%) was the most common side effect observed followed by skin reactions (25%).

Our study has limitations. The sample size was small and hence the results cannot be generalized. The adverse drug reactions could also have been due to the co-administered drugs. We did not determine the course of the adverse drug reaction once it occurred. This might provide valuable information on the progression of the adverse reactions in this patient population.

## CONCLUSION

In our study, almost half of the patient population with HIV/TB co-infection on anti-tubercular drugs experienced an adverse drug reaction. Adverse reactions such as hepatitis and skin rashes can lead to serious complications besides interfering with the pharmacotherapy of both HIV and TB. Also, since hepatotoxicity and dermatological reactions may also occur with antiretroviral drugs early recognition and management of such adverse drug reactions is important to decrease morbidity and mortality. Documenting the adverse drug reactions in these patients also helps the clinicians differentiate it from the natural course of the disease and opportunistic infection seen in AIDS.

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