

**How to Cite:**

Kumar, M., Kumar, P., Chandra, V., Choudhary, M. K., & Verma, N. K. (2022). A review on adverse drug reactions induced by anti-tubercular drugs. *International Journal of Health Sciences*, 6(S4), 11876–11880. <https://doi.org/10.53730/ijhs.v6nS4.11418>

## **A review on adverse drug reactions induced by anti-tubercular drugs**

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**Abstract**---Introduction: Tuberculosis is a chronic, highly contagious disease caused by the *Bacillus Mycobacterium tuberculosis* and spreads from person to person through air. Tuberculosis affects lungs majorly but also affects other parts of the body, such as brain, intestine, spine and kidney. The main cause for patient's non-adherence to anti-tuberculosis therapy is ADRs of varying degrees of severity such as hepatotoxicity etc. Aim: This study aimed to provide proper understanding of Adverse drug reactions resulted due to Anti-TB drug therapy in TB patients based on various studies done on Anti-TB agents induced ADRs. Conclusion: Anti-Tuberculosis drug (Anti-TB) could cause several ADRs both mild and severe types majority of ADR were wild, more attention is needed to prevent ADR and enhance current Anti-TB therapy. The study suggests that for more better in depth understanding and prevention of Anti-TB drug ADR many more studies with larger population is needed, also the current Anti-TB therapy requires some revision to prevent fatal hepatotoxicity.

**Keywords**---adverse drug reactions, anti-tubercular drugs, *Bacillus Mycobacterium*.

## Introduction

Tuberculosis is a chronic, highly contagious disease caused by the *Bacillus Mycobacterium tuberculosis* and spreads from person to person through air. Tuberculosis affects lungs majorly but also affects other parts of the body, such as brain, intestine, spine and kidney. The symptoms of tuberculosis are based on the body part affected such as chronic cough, pain in the chest, weakness, fatigue, weightlessness, fever are the symptoms of pulmonary TB. The matter of concern is the high frequency of anti-TB induced ADR's such as hepatotoxicity. In India RNTCP (Revised National Tuberculosis Control Program) was launched in 1997 and treatment guidance further revised in 2010. DOTS (Direct Observed Treatment Short-course) program is highly beneficial against TB, has been successful in reducing morbidity and mortality. Isoniazid (INH), Rifampicin (RFP), Pyrazinamide (PZA), Ethambutol (EMB) or Streptomycin combination is prescribed every other day for 6-9 months[1]. India accounted for one-fifth of the global TB burden, with 1.8 million developing the disease every year and of them about 800000 are infectious[2]. In 2018, India was able to achieve a total notification of 21.5 lakh TB cases of which 25% was from the private sector. Majority of TB burden is among the working age group. The 89% of TB cases come from the age group of 15-69 years. About 2/3 of the cases are males. India accounts 27% of global burden with estimated 27.5 lakhs patients as per Global TB report 2018[3].

Anti-tubercular treatment (ATT) exhibits greater level of efficacy with a satisfactory degree of toxicity; however, combination treatment, especially during the intensive phase of therapy may produce severe adverse events [4]. Adverse drug reactions (ADRs) results into decrease in patient compliance and obedience. Despite the positive therapeutic effects, studies have shown that utilization of multidrug regimens can cause undesirable adverse drug reactions (ADRs) of varying degrees of severity, such as hepatotoxicity, gastrointestinal (GI) disorders, allergic reactions, arthralgia, neurological disorders, and so on. Studies suggest that more than 5% of the patients on antitubercular drugs (ATD) develop ADRs. None of the antiTB drugs are without adverse reactions only rarely are the adverse reactions lifethreatening [5]. In this study, we aimed to get an overview study done on ADR's due to anti-TB agents.

## Discussion

In a study conducted by Kumarjit Sinha, they have evaluated 102 patients, majority of study cases (27.45%) were in the age group of 30-40 years. Incidence of ADRs was maximum in <20 years age group and minimum in 51-60 years age group of patients. Difference in ADRs among different age groups was statistically significant ( $P < 0.001$ ). Majority of female TB patients experienced ADRs when compared to male (91.67 vs 62.82%) and this difference was statistically significant ( $P < 0.001$ ).[5] Out Of total 102 patients, 71 patients (69.01%) showed one or more ADR. Majority of the patients (53.52%) suffered from GI symptoms, of

which anorexia was the most common (31.58%). Neurological symptoms and fever were the least common (2.82% each) ADRs. In the present study, 30.99% did not experience any ADRs [Pie chart 1]. Majority of ADRs were mild type (73.24%), out of which GI symptoms (73.08%) acquires major share, the only severe ADR is Liver dysfunction (15.49%).[5]

The study comprises males in major population 76.47% vs 23.53% females. The probable cause for this is that male is exposed more to smoking, alcoholism and drug addiction to get TB then females, while men are socially more active, visits public places more often, due to these factors may be men are more vulnerable for TB infection [6].

Edoh and Adjei, also found 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 [7]. This is probably because the people in this age group are involved in TB infectious activities like smoking, large alcohol intake, etc., which results in the weakening of immunity [8]. The most common ADRs were GI symptoms (53.52%). The drugs, which are responsible for these side effects, may be PZA and RFP. 15.49% patients developed hepatic dysfunction as ADRs. The drugs that are responsible for this side effect may be PZA, RFP, and INH [9]. Female cases are more commonly affected by ADRs when compared with their male counterparts and this difference was statistically significant ( $P < 0.001$ ). In general, females are at higher risk of developing ADRs [10]. It might be because they pass through life stages like pregnancy, menarche, etc., which modify the drug response [11].

In another study conducted by Tak, et al. on "Safety evaluation of anti-tubercular therapy under revised national tuberculosis control program in India" in which the incidence of ADRs was found to be 17.02% [12], while in a study by Athira et al., out of 511 patients studied, 93 patients (18.20%) developed adverse drug reactions, majorly GI problems, skin allergy and hepatotoxicity [13]. In a similar study by Gillani, et al., out of 653 patients, 103 (15.8%) patients had an experience of adverse drug reactions [14]. While discussing the severe ADR i.e., Liver toxicity timely diagnosis of liver toxicity caused by Anti-TB drugs will reduce the rate of mortality of patients. The death rate due to liver damage will be about 50% if the drug is continued after increasing transaminase enzymes up to 3 times of base line. But with on time discontinuation of drug regimen, this rate could be decreased to 10%. Increase serum level of transaminases mainly is due to Isoniazid. In the other hand Rifampin usually causes cholestasis, which leads to raise alkaline phosphatase and bilirubin. Liver toxicities can be the major side effect of all three main anti-TB drugs, Isoniazid, Rifampin and Pyrazinamid. [4]

## **Conclusion**

In conclusion, Anti-TB agents causes several ADRs mostly mild type except few severe such as hepatotoxicity, common ADRs are GI symptoms, skin allergy, liver dysfunction, hepatotoxicity, visual problems, hearing problems etc. it is found that TB was more prevalent in the age group 30-40 years and more prevalent among females. The study suggests that for more better in depth understanding and prevention of Anti-TB drug ADR many more studies with larger population is

needed, also the current Anti-TB therapy requires some revision to prevent fatal hepatotoxicity.

## References

- Adnyana, I. G. A. P., Sukarasa, I. K., & Adi, W. A. (2020). Rare earth ion contribution in barium hexaferrite structure to a change of magnetocrystalline anisotropy to improving its magnetic properties. *International Journal of Physical Sciences and Engineering*, 4(2), 1–13.  
<https://doi.org/10.29332/ijpse.v4n2.433>
- Central TB Division, Directorate of General Health Services Ministry of Health and Family Welfare, Nirman Bhavan, New Delhi, India.
- Chhetri Anupa Khatri, et al. A study of adverse drug reactions caused by first line anti-tubercular drugs used in Directly Observed Treatment, Short course (DOTS) therapy in western Nepal, Pokhara. *JPMA*, 2008; 58(10): 531-6.
- Edoh D, Adjei R. Rapid assessment of a National Tuberculosis (TB) Control Programme in Eastern Ghana. *Afr J Health Sci* 2002; 9:15964
- Estevez, A. G., Espinosa, A. H. R., Rodriguez, D. L., & Leyva, T. F. (2019). Current approaches and controversies: legalization and non-legalization of drugs. *International Journal of Health & Medical Sciences*, 2(1), 26-32.  
<https://doi.org/10.31295/ijhms.v2n1.85>
- Gholami K, Kamali E, Hajiabdolbagh Mi, Shalviri G. Evaluation of antituberculosis induced adverse reactions in hospitalized patients. *Pharmacy Practice*, 2006; 4: 134-8.
- Horne N. Tuberculosis and other mycobacterial disease. In: Cook G, editor. *Manson's tropical diseases*. London: W.B. Saunders; 1996. p. 9711015.
- India Tb Report [HYPERLINK "https://tbcindia.gov.in/index1.php?lang=1&level=2&sublinkid=5358&lid=3450"](https://tbcindia.gov.in/index1.php?lang=1&level=2&sublinkid=5358&lid=3450) [HYPERLINK "https://tbcindia.gov.in/index1.php?lang=1"](https://tbcindia.gov.in/index1.php?lang=1) [HYPERLINK "https://tbcindia.gov.in/index1.php?lang=1&level=2&sublinkid=5358&lid=3450"](https://tbcindia.gov.in/index1.php?lang=1&level=2&sublinkid=5358&lid=3450) & [HYPERLINK "https://tbcindia.gov.in/index1.php?lang=1&level=2&sublinkid=5358&lid=3450"](https://tbcindia.gov.in/index1.php?lang=1&level=2&sublinkid=5358&lid=3450) level=2 [HYPERLINK "https://tbcindia.gov.in/index1.php?lang=1&level=2&sublinkid=5358&lid=3450"](https://tbcindia.gov.in/index1.php?lang=1&level=2&sublinkid=5358&lid=3450) & [HYPERLINK "https://tbcindia.gov.in/index1.php?lang=1&level=2&sublinkid=5358&lid=3450"](https://tbcindia.gov.in/index1.php?lang=1&level=2&sublinkid=5358&lid=3450) & [HYPERLINK "https://tbcindia.gov.in/index1.php?lang=1&level=2&sublinkid=5358&lid=3450"](https://tbcindia.gov.in/index1.php?lang=1&level=2&sublinkid=5358&lid=3450) sublinkid=5358 [HYPERLINK "https://tbcindia.gov.in/index1.php?lang=1&level=2&sublinkid=5358&lid=3450"](https://tbcindia.gov.in/index1.php?lang=1&level=2&sublinkid=5358&lid=3450) & [HYPERLINK "https://tbcindia.gov.in/index1.php?lang=1&level=2&sublinkid=5358&lid=3450"](https://tbcindia.gov.in/index1.php?lang=1&level=2&sublinkid=5358&lid=3450) lid=3450" [HYPERLINK "https://tbcindia.gov.in/index1.php?lang=1&level=2&sublinkid=5358&lid=3450"](https://tbcindia.gov.in/index1.php?lang=1&level=2&sublinkid=5358&lid=3450) 2019: [HYPERLINK "https://tbcindia.gov.in/index1.php?lang=1&level=2&sublinkid=5358&lid=3450"](https://tbcindia.gov.in/index1.php?lang=1&level=2&sublinkid=5358&lid=3450) [HYPERLINK "https://tbcindia.gov.in/index1.php?lang=1"](https://tbcindia.gov.in/index1.php?lang=1) [HYPERLINK "https://tbcindia.gov.in/index1.php?lang=1&level=2&sublinkid=5358&lid=3450"](https://tbcindia.gov.in/index1.php?lang=1&level=2&sublinkid=5358&lid=3450) & [HYPERLINK "https://tbcindia.gov.in/index1.php?lang=1&level=2&sublinkid=5358&lid=3450"](https://tbcindia.gov.in/index1.php?lang=1&level=2&sublinkid=5358&lid=3450) level=2 [HYPERLINK "https://tbcindia.gov.in/index1.php?lang=1&level=2&sublinkid=5358&lid=3450"](https://tbcindia.gov.in/index1.php?lang=1&level=2&sublinkid=5358&lid=3450)

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 0" Central TB Division (tbcindia.gov.in)
- Kurniawati F, Sulaiman SAS, Gillani SW. Adverse Drug Reactions of Primary Anti-tuberculosis Drugs Among Tuberculosis Patients Treated in Chest Clinic. *International J of Pharmacy and Life Sciences*, 2012; 3: 1331-8
- Lönnroth K, Williams BG, Stadlin S, Jaramillo E, Dye C. Alcohol use as a risk factor for tuberculosis a systematic review. *BMC Public Health* 2008; 8:289.
- Nanda GS, Singh H, Sharma B, Arora A. Adverse Reactions Due to Directly Observed Treatment Short Course Therapy: An Indian Prospective Study. *IAIM*, 2016; 3(1): 6-12.
- Puavilai S, Timpatanapong P. Prospective study of cutaneous drug reactions. *J Med Assoc Thai* 1989; 72:16771.
- Sinha K, Marak IR, Singh WA. Adverse drug reactions in tuberculosis patients due to directly observed treatment strategy therapy: Experience at an outpatient clinic of a teaching hospital in the city of Imphal, Manipur, India. *J Assoc Chest Physicians* 2013; 1:50-3.
- Steele MA, Burk RF, DesPrez RM. Toxic hepatitis with isoniazid and rifampin. A metaanalysis. *Chest* 1991; 99:46571.
- Suryasa, I. W., Rodríguez-Gámez, M., & Koldoris, T. (2021). Get vaccinated when it is your turn and follow the local guidelines. *International Journal of Health Sciences*, 5(3), x-xv. <https://doi.org/10.53730/ijhs.v5n3.2938>
- Tak DK, Acharya LD, Gowrinath K, Rao Padma GM, Subish P. Safety Evaluation of Antitubercular Therapy Under Revised National Tuberculosis Control Programme in India. *Journal of Clinical and Diagnostic Research*, 2009; 3: 1395- 401.
- Wilson K. Sexrelated difference in drug disposition in man. *Clin Pharmacokinet* 1984; 9:189202.