(International Print/Online Journal)

SJIF IMPACT FACTOR: 5.565
PUBMED-National Library of Medicine ID-101739732

ISSN (Print): 2209-2870
ISSN (Online): 2209-2862

International Journal of Medical Science and Current Research (IJMSCR)
Available online at: www.ijmscr.com
Volume 4, Issue 5, Page No: 1366-1371
September-October 2021

IJMSCR

A study of pattern of adverse drug reactions in patients on ATT under RNTCP-DOTS reported from Tertiary care hospital, Bangalore.

Dr Shailaja M[1], Dr Mohammed Hafeez[1]*, Dr Fasheeh K M[1]. Dr Balwant Singh[1], Dr Pavan Raj N[1], Dr Midhila Gopinath[1],Dr Emad Mir Abbas[1], Dr Shyamala K K2, Dr Shivakumar B R[1]

[1]Department of General Medicine, Dr B R Ambedkar medical college, Bangalore, India
[2]Department of Pulmonary Medicine, Dr B R Ambedkar medical college, Bangalore, India

***Corresponding Author:**
Dr Mohammed Hafeez, Assistant Professor
Department of General Medicine, Dr B R Ambedkar medical college, Bangalore, India

Type of Publication: Original Research Paper
Conflicts of Interest: Nil

Abstract

Background and Objectives

Adverse Drug Reactions are a great cause of concern, can be mild or life threatening and thus, have to be observed, monitored, and managed properly. This is because that affect the compliance, contributes to development of MDR, XDR, TDR. Thus, this study was done analyze the onset and duration of ADRs, severity, haematological and biochemical parameters of ADRs started on DOTS.

Methods

An observational study was conducted among 100 TB patients reported in DR. BRAMCH registered under RNTCP(NTEP)-DOTS from November 2018 to May 2020. Data regarding pattern of ADRS was collected and evaluated with clinical data, haematological and biochemical investigations.

Results

Among 100 cases studied, 64 patients developed GI symptoms, 18 had generalized weakness, 8 developed hepatitis, 7 had arthralgia, developed cutaneous reactions, 6 had peripheral neuropathy, 5 had psychosis, 2 had retrobulbar neuritis, 13 had jaundice, 4 had anaemia, 9 had itching, 2 had nephrotoxicity., around 32 had more than one ADR and a total of 15 types of reactions were observed. The most common were GI symptoms. The mean onset time was observed within one week and mean duration time were seen up to 2 months after start of ATT.

Conclusion

Gastrointestinal upset, as an ADR was most common. Most ADRs were mild, but few were severe enough for discontinuation of the offending drug.

Keywords: Adverse drug reactions; Antitubercular treatment; Direct Observation treatment; Short course.

INTRODUCTION

Tuberculosis (TB) is one of the most prevalent chronic human infections and is the leading cause of mortality from a single infectious agent, ranking above HIV/AIDS. It is caused by the bacillus Mycobacterium tuberculosis and typically affects the lungs (pulmonary TB) but can also affect other sites (extrapulmonary TB). About a quarter of the world's population is infected with M. tuberculosis and so have a risk of developing TB disease.[1]

According to World Health Organisation (WHO) adverse drug reaction 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.[8] Studies have

shown that multidrug regimens can cause adverse drug reactions which are undesirable, such as gastrointestinal disorders, arthralgia, hepatotoxicity, neurological disorders, and allergic reactions [2,3].

The incidence of ADRs overall caused by anti-tubercular therapy ranges from 5.1% to 83.5% [4]. It may also increase morbidity and mortality of disease. The impact and the management of adverse drug reactions are complex as they may increase costs due to frequent hospitalization, prolongation of hospital stay, additional investigations, and drug therapy in more serious cases. Various studies have shown that adverse drug reactions to anti-tubercular drugs can negatively affect the compliance, discontinuation of treatment abruptly and indirectly contribute to multidrug resistance. Hence monitoring and reporting of adverse drug reactions is very much essential [5].

MATERIALS AND METHODS

Ethics

The study was conducted as per ethical laws stated by Institution Ethics Committee (IEC), DR B.R Ambedkar Medical College & Hospital. The appropriateness of the study design was seen to fulfil the objectives and norms of the ethical issues and all ethical standards were catered to during the study.

Study design

A cross-sectional, longitudinal observational study was performed to study the pattern of ADRs to antitubercular drugs in patients receiving DOTS under RNTCP (NTEP) at DR. B. R. Ambedkar Medical College Hospital and to assess severity of ADRs and referring them for consultations in respective departments.

Sample selection

A minimum of 100 participants were recruited using Systematic random sampling from November 2018 to May 2020.

Inclusion Criteria

All cases diagnosed as TB registered under RNTCP (NTEP) put on DOTS regimen and willing to participate in the study.

Exclusion Criteria

1. Patients who are not willing to participate in the study.
2. Patients under DOTS with no ADRs.

Data collection

The data was collected from TB Patients in DR B.R. Ambedkar Medical College Hospital registered under RNTCP (NTEP) -DOTS, patients with ADRs registered under RNTCP (NTEP)-DOTS, in OPD or admitted in hospital. Instructions were given to patients, to report any symptoms they would experience during the course of treatment.

Data analysis

Analysis Statistical Methods

Descriptive and inferential statistical analysis was used in the present study. Results on continuous measurements are presented on Mean-SD (Min-Max) and results on categorical measurements are presented in Number (%). Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups, non-parametric setting for Qualitative data analysis. Fisher Exact test used when cell samples are very small.

RESULTS

Adverse effects of anti-tuberculosis drugs were studied in 100 patients who were started on DOTS under Revised National Tuberculosis Control Programme (NTEP) in Dr. B.R. Ambedkar Medical College Hospital. Data was collected and analysed with the clinical findings, haematological and biochemical parameters. Results are as follows.

Out of the 100 patients studied, majority of patients were in the age group of 31-40 (24%) years, followed by 19 % in 21-30, 18% in 41-50, 15% in 11-20 and 12% each among 51-60 and above 60 yrs. Gender wise specification, 46% of female participants and 54 % of male participants demonstrated ADR, with more susceptibility in males. Additionally, weight-ADR relationship was also studied which depicted that ADR was most common in participants weighing 40-50 kgs. There existed no significance relationship between age, gender and weight with ADR outcomes. Out of all the participants, 78% had pulmonary tuberculosis and 22% had extrapulmonary TB. Nearly, 50% patients were sputum positive and 14 % were sputum negative. And the rest 36% were CBNAAT MTB detected or clinically diagnosed. This is probably because majority of the patients

Volume 4, Issue 5; September-October 2021; Page No 1366-1371

studied were pulmonary tuberculosis. It is also important to note that 5% of the patient included as participant were HIV positive. Another risk factor, use of alcohol was also studied which depicted that all 5 patients who consumed alcohol, developed ADR; indicating that alcohol consumption could be a strong risk factor for increased incidence of ADR.

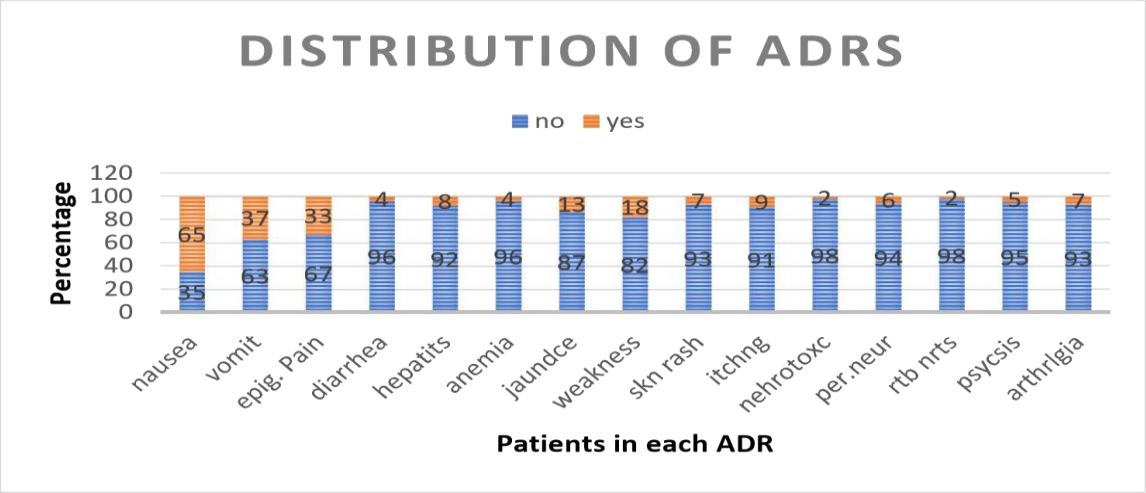

Figure No.1: Distribution of patients in each ADR

The most common symptom observed in this study was GI symptoms like nausea (65%), vomiting (37 %), epigastric pain (33%), diarrhoea (4%), Hepatitis (8%) jaundice (13%), Anaemia (4%) others were malaise (18%) and skin rash (7%), itching (9%), Nephrotoxicity (2%), Peripheral neuropathy (6%), Psychosis (5%), Retrobulbar neuritis (2%), Arthralgia (7%). Out of 100 patients, 24 participants developed severe ADRs.

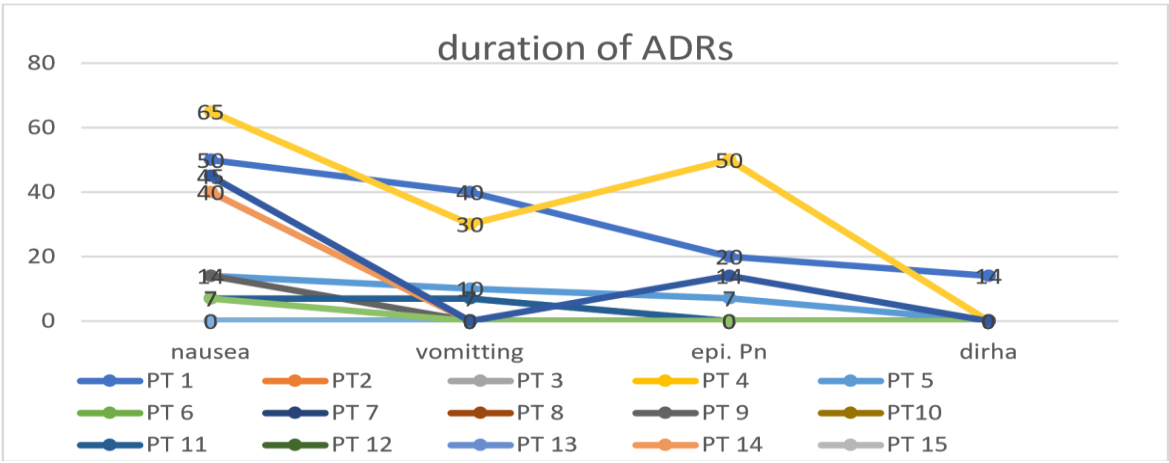

Figure No. 2: Mean duration time of ADR

The Fig 2 depicts that majority of the participants reported subsiding of symptoms within two months after initiation of ATT however, adverse events like malaise lasted up to 4 months.

Out of the 100 patients who developed ADR, 37% of patients required symptomatic treatment with antacids, antiemetics, analgesics, multivitamins, protein supplements, antihistamines in order to sustain therapeutic effects of ATT. It was seen that out of 100 patients who developed ADR, 74 had OPD visits, out of that 45-patients had 1 OPD visit, 20 patients had 2 OPD visits, and 7 patients had 4 OPD visits. The reasons noted in this study for

Volume 4, Issue 5; September-October 2021; Page No 1366-1371

increasing OPD visits were increase in severity of GI intolerance and jaundice followed by generalised weakness, hepatitis, skin rashes, itching etc. Out of the 100 patients who developed ADR, 74 patients did not require any admission to hospital, 26 patients required 1 admission and 1 patient required 2 admissions. The reasons noted in this study for increasing admissions were increase in severity of GI intolerance and jaundice and nephrotoxicity. Considering mortality, group 2 patients (2%) lost lives who developed ADR. Out of them, 1 patient expired due to extensive involvement of tuberculosis and poor general condition of the patient developing nephrotoxicity.

It was observed that there was significant increase in the Total Bilirubin, SGOT, SGPT in the first week after the onset of treatment. The pair wise comparison done among the pre-treatment values, 1st week, 1st month and 4th month values also showed that there was significant increase in the Total Bilirubin, SGOT, SGPT in the first week after the onset of treatment. The pair wise comparison of other haematological and biochemical investigations did not show any significant difference.

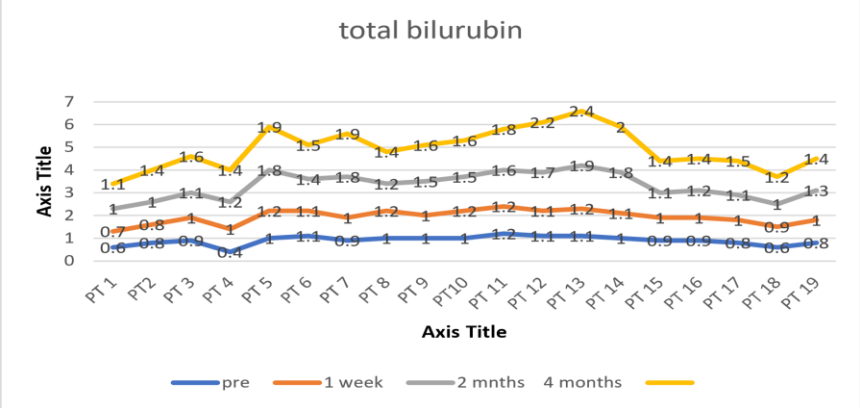

Figure No. 3: Pattern of rise of total bilirubin (in mg/dl) during the course of RX.

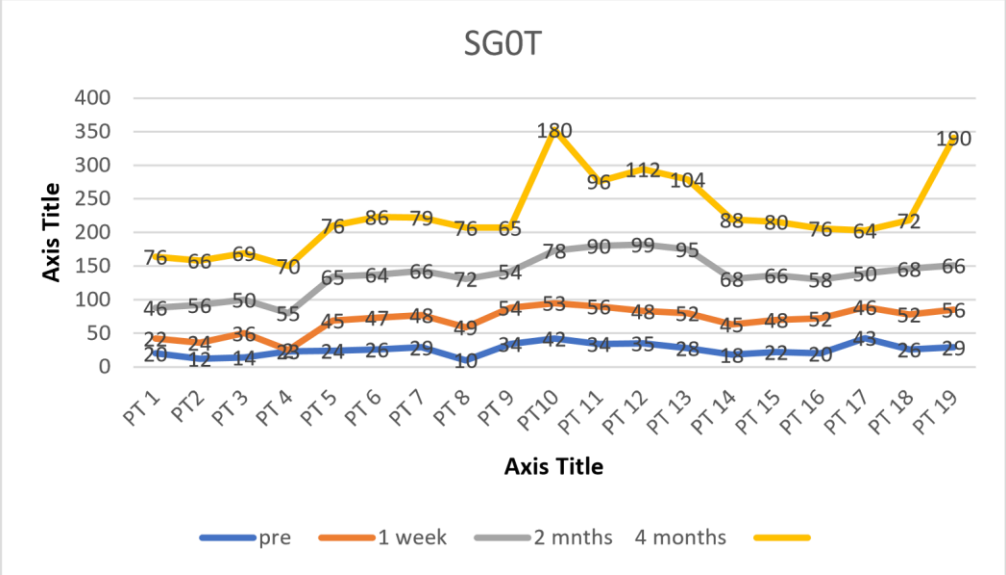

Figure No. 4: Pattern of rise of SGOT (in Units/ml) during the course of RX

Volume 4, Issue 5; September-October 2021; Page No 1366-1371

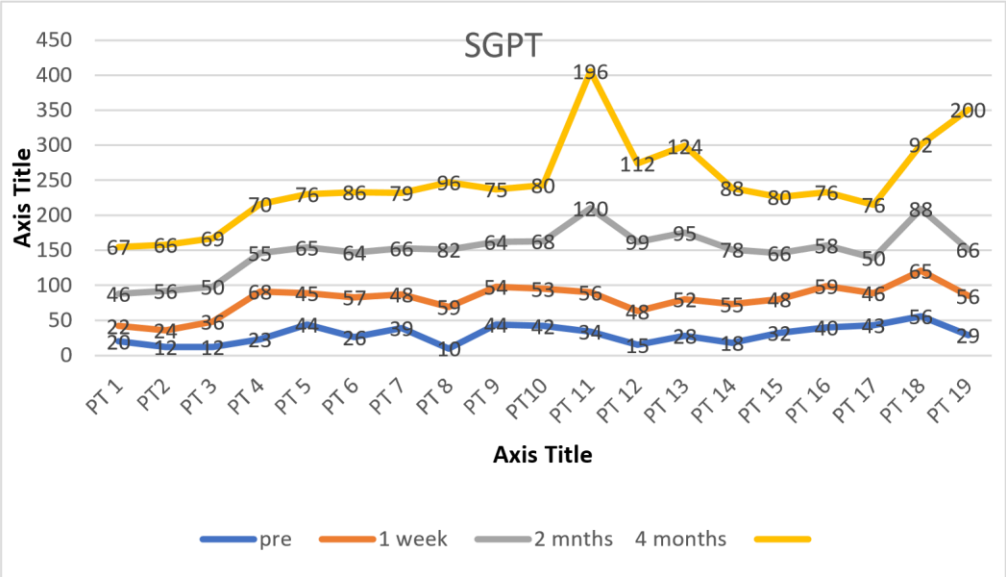

Figure No. 5: Pattern of rise of SGPT (in Units/ml) during the course of RX

DISCUSSION

Anti-tubercular therapy, identifying adverse drug reactions, treating them and improving compliance is a very important aspect in the treatment of tuberculosis. Directly observed treatment, short course (DOTS) is a very effective treatment strategy adopted by Revised National Tuberculosis Control Programme (RNTCP). - now NTEP Anti-tuberculosis drugs are one of the most common drugs causing ADR [6].

The study designed to find out the anti-TB drug ADRs in TB patients at BIDAR hospital upon DOTS therapy. The findings from the study suggest that males constitute the major population than females. Drug addiction, alcoholism and smoking are the major causative factors in males to get TB compared to females and also males have more social activities and visit public places more often. Due to involvement of activities such as smoking, use of tobacco products, high alcohol intake, 31-40 years and 21-30 years aged group cases have been found increased prevalence of TB, because these activities deteriorate the immune system.[7]

In a study done in King George's Medical University, Lucknow, Uttar Pradesh, India, pulmonary cases constituted 67.83% (78 out of 115) while extrapulmonary cases formed 32.17% (37 out of 115). in the study the incidence of adverse drug reaction in pulmonary cases came out to be 57.69% (45 out of 78 pulmonary TB patients) while this incidence in extra-pulmonary cases came out to be 56.75% (21 out of 37 patients with extrapulmonary TB). Thus, out of the total patients who developed ADR (N= 67) 67.16% (i.e., 45 out of 67) were pulmonary cases while 32.84% (21 out of 67) were extrapulmonary cases [8].

CONCLUSION

This study shows that DOTS treatment is an effective and safe treatment strategy as most of the adverse drug reactions noted were of a mild variety and were managed with symptomatic medications. Gastrointestinal symptoms were the most common observed symptoms and most of the symptoms subsided within the intensive phase of the treatment. The most common laboratory abnormality seen was rise in liver enzymes and bilirubin. The health care professionals have to be vigilant during the intensive phase of the treatment, identify symptoms at the earliest and hence help in minimising morbidity. Awareness needs to be created among the doctors treating TB patients for timely recognition and

Volume 4, Issue 5; September-October 2021; Page No 1366-1371

treatment of ADRs with minimum modification of treatment regimen. Equal attention should be showed during DOTS therapy without ADR cases to raise over all cure rate.

REFERENCES

1. Global tuberculosis report 2018. Geneva: World Health Organization; 2018
2. World Health Organization, International https://www.who.int/medicines/technical_briefing/tbs/04-PG_Dug-Safety_final-08.pdf?ua=1
3. R. Singla, S. K. Sharma, A. Mohan et al., "Evaluation of risk factors for antituberculosis treatment induced hepatotoxicity," Indian Journal of Medical Research, vol. 132, no. 7, pp. 81–86, 2010.
4. Kathmandu university journal of science, engineering and technology 2005; 1(1): 1-2
5. Koju D, Rao BS, Shrestha B, Shakya R, Makaju R. Occurrence of Side Effects from Anti-tuberculosis Drugs in Urban Nepalese Population Under Dots Treatment.
6. Revised National Tuberculosis Programme Training Module For Medical Practitioners. Central TB Division, Directorate General of Health Service/ Ministry Of Health and Family Welfare Niaman Bhawan, New Delhi, 2005.
7. Pasha SS, sabiha N, Naseeruddin S. Adverse drug reactions impact on DOTS therapy courses in tuberculosis patients at bidar institute of medical sciences, Indian J Pharm Pharmacol 2019;6(2):42-4.
8. IJPSR (2009), Issue 1, Vol- International Journal of Pharmaceutical Sciences and Research. University, Lucknow-, Uttar Pradesh, India, Feb 18, 2018.

Volume 4, Issue 5; September-October 2021; Page No 1366-1371