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A Study on Assessment of Adverse Drug Reactions in Patients with Tuberculosis in a Tertiary Care Teaching Hospital

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ABSTRACT

Tuberculosis is a chronic infectious disease caused by mycobacterium tuberculosis leading to increased morbidity and mortality. Adverse drug reactions associated with Anti-tubercular drugs can result in non-compliance and therapeutic failure. The present study was aimed to identify the adverse drug reactions caused by anti-tubercular drugs and their assessment by using causality, severity and preventability scales. All the patients with tuberculosis admitted during the study period who met the study criteria were included and monitored for adverse drug reactions and were then subjected to assessment of causality, severity and preventability. A total of 95 patients were followed during the study period, out of which 22 patients developed 33 adverse drug reactions. Higher incidence of adverse drug reactions was observed in females (54.5%) than males (45.4%). The most common system associated with adverse drug reactions was found to be gastrointestinal system (45.5%). On evaluation of the causality assessment of adverse drugs reactions, majority of them were found to be 'probable' by both WHO and Naranjo scales. The severity assessment of adverse drug reactions by using Hart wig *et al.* showed that 60.7% of the adverse drug reactions were 'moderate' and 36.4% were 'mild'. Preventability assessment showed that majority of the adverse drug reactions was 'probably preventable'. The present study shows that implementing a system for regular adverse drug reactions monitoring may help to minimize morbidity and improve patient compliance and achieve better therapeutic outcome.

INTRODUCTION

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". Like many other drugs, anti tubercular drugs also cause various types of adverse drug reactions and affects almost all the systems in the body mainly the gastrointestinal, liver, skin, nervous system and eyes (Honnaddi *et al*., 2016). These adverse drug reactions prove to be a challenge to successful treatment of active patients, as they are the prime factor of non-adherence to treatment, leading to therapeutic failure (Mishra *et al*., 2013). Adverse drug reactions are the leading cause of mortality and morbidity in health care and have a significant economic impact on health-care resources. Serious adverse drug reactions account for 6.7% of all hospital admissions and occur in 10–20% of hospitalized patients. 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 (Kinjal *et al.,* 2016; Ramnath *et al.,* 2012).

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 wherein the drug causing adverse drug reaction can be identified and appropriate therapeutic regimen can be tailored to the patient. Pharmacovigilance of anti-tubercular drugs is very much essential for successful treatment of tuberculosis and its elimination (Revanna *et al*., 2017; Verma *et al*., 2014; Sadiq *et al*., 2015).

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In the current scenario of high tuberculosis prevalence, involvement of clinical pharmacists in detecting and monitoring adverse drug reactions and in their management could be beneficial to achieving better therapeutic outcome. Information pertaining to patterns of observed Adverse drug reactions due to the wide spread use of anti-tubercular drugs is an avenue of pharmacovigilance which still requires plenty of attention in a country such as India, where reporting of such incidents is significantly less when compared to the number of occurrences. Thus it is of prime importance that a study such as this has to be conducted at the grass root level. For this purpose, this study was conducted with the aim on assessment adverse drug reactions in patients with tuberculosis in a tertiary care teaching hospital of Mangalore.

MATERIALS & METHODS

A prospective observational study was carried out in the departments of general medicine and pulmonary medicine of a tertiary care teaching hospital at Mangalore over a period of 8 months from August 2016 to March 2017.

Ethical approval

The study was approved by Institutional Human Ethics Committee (REF:INST.EC/EC/74/2016-17).

Study criteria

Inclusion criteria

All patients of either gender aged 18 years and above who are under the treatment of tuberculosis with anti tuberculosis drugs.

Exclusion criteria

Pregnant patients mentally challenged and who presented with hepatic dysfunction and subjects who were not willing to participate were excluded from the study.

Study procedure

All the hospitalized patients with tuberculosis admitted under the general medicine and pulmonary medicine ward during the study period was reviewed on daily basis and monitored for adverse drug reactions by the pharmacist. When suspected Adverse drug reactions were detected, they were bought to the notice of the concerned physician and the relevant information including diagnosis, laboratory test, drugs used during the hospitalization, the type of reaction to the drug, and outcome of therapy of the patient were documented in the suitably designed patient data collection form and adverse drug reactions monitoring and reporting form as per the need of the study. The step taken towards the management of so reported adverse drug reactions such as withdrawal of the suspected drug, alteration in dose, treatment provided (specific, symptomatic) etc. were also documented in the adverse drug reactions reporting form. At the end of the study, the collected information in the adverse drug reactions monitoring and reporting form was used for assessing the causality, severity and preventability by using various scales. The adverse drug reactions were subjected to causality assessment using the WHO probability scale (Definite, probable, possible, unclassifiable, unlikely, conditional) and Naranjo's scale (Definite, probable, possible, unlikely). The Severity level was carried out by using the Hartwig's severity assessment scale (mild, moderate, severe) and the preventability assessment was done by using Modified Schumock and Thornton's Criteria (definitely preventable, probably preventable, not preventable).

Statistical analysis

The data obtained from the filled patient profile forms were entered in the Microsoft excel spread sheet and analyzed by using Statistical Package of Social Sciences (SPSS) for windows (version 16.0). Demographic details of the patients were analyzed by using descriptive statistics. Categorical variables such as age, gender, type of tuberculosis, drugs causing adverse drug reactions, type of adverse drug reactions, causality, severity and preventability are expressed in frequencies and percentages.

Table 1: Demographic details of the study populations.

Gender			
Sl. No	**Gender**	**Frequency (n = 22)**	**Percentage**
1.	Male	10	45.54
2.	Female	12	54.54
Age (years)			
Sl. No	**Age (years)**	**Frequency (n = 22)**	**Percentage**
1	18-29	6	27.27
2	30-39	5	22.72
3	40-49	2	9.09
4	50-59	2	9.09
5	60-69	5	22.72
6	70-79	2	9.09
Social habits			
Habits		**Frequency (n = 22)**	**Percentage**
Smoking	Yes	1	4.54
	No	21	95.45
Alcohol	Yes	2	9.09
	No	20	90.91
Smoking + Alcohol	Yes	1	4.54
	No	21	95.45

RESULTS

A total of 95 patient's case records were reviewed during the study period. Out of 95 patients, 22 (23.2%) patients developed a total of 33 adverse drug reactions to anti-tubercular drugs. Among 22 patients, eight patients (36.3%) developed two or more adverse drug reactions and 14 patients (63.6%) developed one adverse drug reactions to anti-tubercular drugs. Considering the gender wise distribution, female [12 (54.5%)] predominance was noted over males [10 (45.4%)]. The incidence of adverse drug reactions was more common in the age group of 18-29 years (27.27%) followed by age group of 30-39 years (22.7%). Among the total study subjects, only one patient had history of alcoholic intake, one patient with habit of smoking and one patient had history of both habits. The demographic characteristic of the study populations is shown in the following Table 1.

Table 2: Pattern of Tuberculosis among the study population.

Types of Tuberculosis	Frequency (n = 22)	Percentage
Pulmonary Tuberculosis	9	40.90
Extra Pulmonary Tuberculosis	10	45.45
Disseminated Tuberculosis	2	9.09
Multidrug resistant Tuberculosis	1	4.54

Table 3: Co-morbidities among patients with TB.

Co morbidities	Frequency (n = 55)	Percentage
Type 2 diabetes mellitus	12	21.81
Cardiovascular disorders	10	18.18
Blood disorders	7	12.72
Respiratory diseases	6	10.9
Infectious diseases	9	16.36
Thyroid diseases	3	5.45
Renal diseases	4	7.27
Psychiatric disorders	2	3.63
Gastrointestinal disorders	1	1.81
Lung Carcinoma	1	1.81

Table 4: Types of ADRs identified in the study subjects.

ADRs	Frequency (n = 33)	Percentage (%)
Abdominal pain	1	3.0
Decreased appetite	2	6.1
Diarrhea	1	3.0
Hearing loss	2	6.1
Hepatitis	3	9.1
Hyperuricaemia	2	6.1
Itchy lesions	2	6.1
Itchy rashes	1	3.0
Liver enzyme elevation	7	21.2
Nausea	3	9.1
Peripheral neuropathy	1	3.0
Severe gastritis	1	3.0
Vomiting	7	21.2

It was observed that out of 22 patients, 10 patients (45.4%) with extra pulmonary tuberculosis, 9 patients (40.9%) with pulmonary tuberculosis, 2 patients (9.09%) with disseminated tuberculosis and one patient (4.54%) with multidrug resistant tuberculosis developed different types of adverse drug reactions due to anti-tubercular therapy. The pattern of tuberculosis among the study populations is shown in the following Table 2.

A total of 55 co-morbidities were identified from 22 patients with tuberculosis during the study period. Among the co-morbidities, diabetes mellitus (21.81) was the most common co-morbidities identified among the study populations. Cardiovascular disorders including hypertension and ischemic heart diseases were reported in 10 (18.18%) patients followed by infectious diseases (16.36%). The different types of co-morbidities identified among the study populations are shown in the following Table 3.

Among the different types of adverse drug reactions, it was found that elevated liver enzyme levels (21.2%) was the most common adverse drug reaction identified during the study period. There were two cases reported of adverse drug reactions leading to hearing loss associated with the anti-tubercular drugs. The different types of adverse drug reactions identified with the antitubercular drugs in the study population are shown in the following Table 4.

Considering the system wise distribution of the adverse drug reactions, it was found that most common being gastro intestinal system related (45.5%) followed by hepatic system related (30.3%) which includes hepatitis and liver enzyme elevation... The system wise distribution of adverse drug reactions among the study population is shown in the following Table 5.

Table 5: System wise distribution of ADRs among the study subjects.

System wise	Frequency (n = 33)	Percentage
Auditory system	2	6.1
Skin and appendages	3	9.1
Hematological	2	6.1
Gastrointestinal	15	45.5
Hepatic	10	30.3
Peripheral nervous system	1	3.0

Table 6: Distribution of suspected drugs responsible for ADRs.

Suspected Drug(s)	Frequency	Percentage (%)
H	2	9.09
R	3	13.6
Z	2	9.09
E	1	4.54
S	1	4.54
Anti-tubercular therapy (H + R + Z)	7	31.8
H + R	6	27.2

(H - Isoniazid, R - Rifampicin, Z - Pyrazinamide, E - Ethambutol, S - Streptomycin, PAS - Para-aminosalicylate).

In the present study, 31.81% patients developed adverse drug reaction receiving triple anti-tubercular drug therapy (Isoniazid, rifampicin & pyrazinamide combination) followed by 27.2% patients receiving isoniazid with rifampicin combination therapy. Rifampicin alone was accounted for 13.6% of the adverse drug reactions. The anti-tubercular drugs involved in causing adverse drug reactions is shown in the following Table 6.

The causality assessment of the suspected adverse drug reactions were carried out by using WHO Probability scale and Naranjo's scale. The assessment by WHO scale showed that, majority of the ADRs were probable 26 (78.8%) followed by possible 7 (24.2%) reactions. As per Naranjo's scale, majority of the reactions were probable 75.8%, followed by 24.2% as possible. There were no definite reactions. The causality assessment of the adverse drug reactions as per Naranjo scale and WHO Probability scale is shown in the following Figure 1 and Figure 2.

The severity level of ADRs was assessed using Hart wig's scale. According to the scale, 20 (60.7%) ADRs were moderate, followed by 36.4% mild reactions. Only 1 ADR was found belonging to the Level 6 of severity scale. The severity level of assessment of ADRs by using Hart wig *et al.* scale is shown in the following Figure 3.

According to modified Schumock and Thornton's preventability scale, 2 (6.1%) reactions were found to be definitely

preventable, 30 (90.9%) reactions were probably preventable and only 1 reaction (3.0%) was found to be not preventable in nature. The preventability assessment of the ADRs is shown in the following Figure 4.

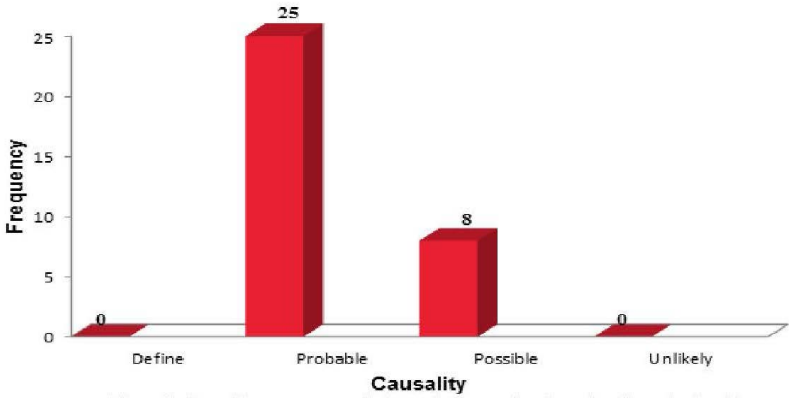

Fig. 1: Causality assessment of adverse drug reactions by using Naranjo algorithm.

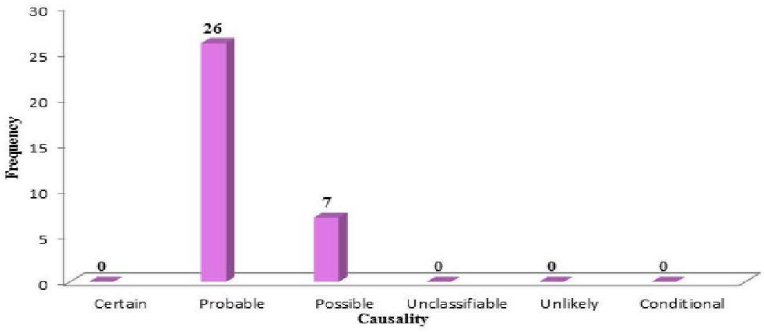

Fig. 2: Causality assessment of adverse drug reactions by using WHO Probability Scale.

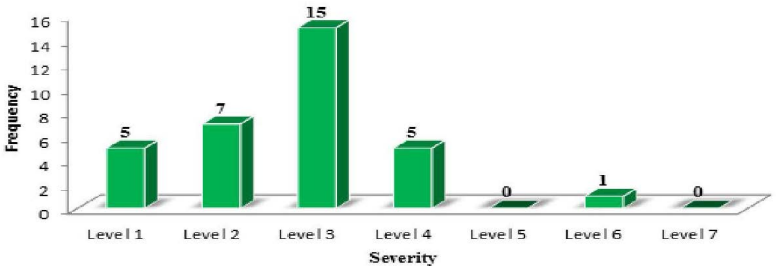

Fig. 3: Severity level assessment of adverse drug reactions by using Harvtwig *et al.*

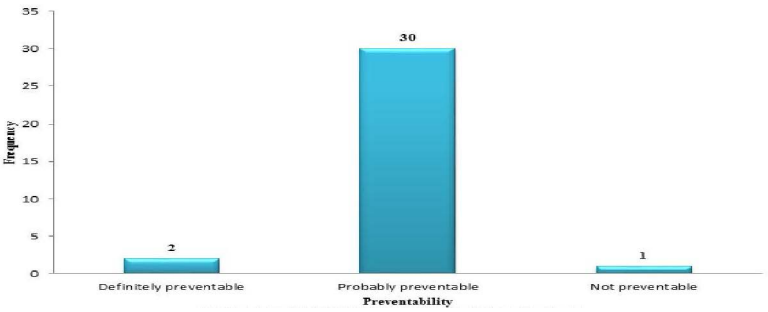

Fig. 4: Preventability assessment of adverse drug reactions.

DISCUSSION

The current study analyzed the pattern of adverse drug reactions and its assessment among patients receiving anti-tubercular drug therapy. The incidence of adverse drug reactions among tuberculosis patients in our hospital during the study period was found to be 23.16%. Previous studies reported comparable incidence that ranged from 18.20% to 69.01% (Bai *et al*., 2017; Nanda *et al*., 2016; Athira *et al.*, 2016).

This discrepancy can be attributed to variations in the study settings and differences in the geographical and physical factors of the sample population. More over the number of patients enrolled in the study as well as the regimen followed by the study subjects could also have an effect on incidence. The methodology used to identify and classify the adverse drug reactions may induce significant changes in the occurrence of adverse drug reactions (Hassan *et al*., 2016; Zhan *et al*., 2013).

In the present study, female patients had the highest incidence of adverse drug reactions over males. These findings are consistent with the study results of previous studies (Maqussod *et al*., 2016; Nemagouda *et al*., 2014). Possible reasons for high prevalence of adverse drug reactions among female patients could be attributed to the various stages of life they pass through including pregnancy and menarche, which possibly could alter the drug response. Moreover, their reduced body size to body weight ratio, compared to males, also is an added factor to be considered. Because of these relevant factors, it is important to take proper steps of precaution to reduce adverse drug reactions among females while prescribing anti-tubercular drug therapy.

Considering the age wise categorization of the study population, patients aged between 18-29 years encountered maximum number of adverse drug reactions. These findings were similar to the previous study results which showed that the incidence of adverse drug reactions was found highest in age group of ≤ 20 years, followed by 31-40 years (Sinha *et al*., 2013). The high prevalence of tuberculosis infectious activities such as smoking and alcohol consumption and other activities that may result in the weakening of immunity could probably be the reason behind increased vulnerability of people of young age to tuberculosis as well as adverse drug reactions of tuberculosis regimen.

In this study, the prevalence of adverse drug reactions was more among non-alcoholics which is found to be similar to the previous study results (Mahendra Kumar *et al*., 2013; Chhetri *et al*., 2008). Susceptibility to drug hepatotoxicity is seen to be higher in alcoholics but it was not considered as a risk factor in the study. Most subjects who consumed alcohol did so only on an irregular basis for leisure, and thus cannot be defined as alcoholics, from a medical standpoint. The added factor that such subjects only comprised a minority of the study group could also justify the fact that these subjects did not show significant association with incidence of adverse drug reactions.

Various studies showed gastrointestinal tract and hepatic system with elevated level of liver transaminases as the organ system most commonly affected with adverse drug reactions associated with anti-tubercular drug therapy (Sood *et al*., 2016; Abideen *et al*., 2013; Kishore *et al*., 2008). Similarly in the present study, GI system was found to be the most commonly affected organ system, followed by hepatic system. A total of 15 adverse drug reactions affecting GI system were reported. The increased incidence of GI side effects could be attributed to multiple drug therapy which also can be considered as the as a major predisposing factor for the occurrence of adverse drug reactions.

Two cases of streptomycin induced sensor neural hearing loss was reported during the study period and the suspected drug was discontinued from patient drug therapy in both the cases. Confirmatory test of audiometry was done to assess ototoxicity in both patients. There are studies that reported streptomycin induced ototoxicity as adverse drug reactions with comparable incidence (Tak *et al*., 2009; Farazi *et al*., 2014).

In the current study, combination of HRZE was found responsible for many of the adverse drug reactions. Since it is very difficult to evaluate the toxicity of a given drug from a combination regimen given, it is often not easy to distinguish the role played by the simple drug. Factors including the category of regimen, dose of the drugs as well as genetic differences of the study population could also affect the number of Adverse drug reactions caused by drugs (Golami *et al.,* 2006; Hema *et al*., 2013).

The causality assessment of the suspected adverse drug reactions were evaluated by using Who Causality assessment and Naranjo causality algorithm scale. According to WHO Causality assessment, majority of the reported adverse drug reactions belonged to the probable category and the rest of the adverse drug reactions were found as possible. As per Naranjo's scale, majority of the reactions were probable, followed by possible reactions.

In order to take proper management steps towards adverse drug reactions, it is essential to carry out the severity assessment. The severity level of assessment was carried out by using the by using Hartwig's *et al.* scale which is categorized into mild, moderate and severe levels. Such categorization ultimately helps to decide whether hospitalization is required or not for an adverse drug reactions developed. Majority of the reactions were found to be moderately severe as a proper treatment measure was required even after the suspected drug was held, discontinued or changed.

Preventability assessment carried out by using modified Schumock and Thornton's preventability scale revealed that most of the adverse drug reactions were probably preventable.

CONCLUSION

The current study shows the incidence of adverse drug reactions in patient receiving anti-tubercular drug therapy. Gastrointestinal system was the most common system involved in causing adverse drug reactions. The severity level of assessment of the adverse drug reactions observed in the study showed that most of them were 'moderate' in nature as per the Hart wig *et al.* scale. The causality assessment by using Naranjo's and WHO scale showed majority of the adverse drug reactions had a 'probable' relationship with the suspected drug(s). The study results provide an insight to the healthcare providers on the importance of monitoring and reporting of adverse drug reactions in patients with tuberculosis who might suffer significant deleterious effects associated with the drugs. The clinical pharmacists involvement helps in detecting and monitoring of adverse drug reactions that might help to improve the patient adherence, minimize drug resistance and achieving better therapeutic outcome.

CONFLICT OF INTEREST

The authors have declared no conflict of competing interest.

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REFERENCES

Athira B, Manju CS, Jyothi E. A study on adverse drug reactions to first line antitubercular drugs in DOTS therapy. Int J Pharmacol and Clin Sci, 2016; 4:7-11.

Abideen P, Chandrasekharan K, Maheshwaran U, Kumar V, Kalaiselvan V, Mishra P *et al.* Implementation of Self Reporting Pharmacovigilance in Anti Tubercular Therapy using Knowledge Based Approach.J Pharmacovigil, 2013; 1(1):1-5.

Bai GP, Ravikumar P, Salma U.A study of adverse drug reactions among pulmonary tuberculosis patients treated under dots in a tertiary care hospital.IJBCP, 2017; 6(4):1-4.

Chhetri AK, Saha A, Verma SC, Palaian S, Mishra P, Shankar PR.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.J Pak Med Assoc, 2008; 58(10):531-536.

Farazi A, Sofian M, Jabbariasi M, Keshavarz S.Adverse Reactions to Antituberculosis Drugs in Iranian Tuberculosis Patients. Tuberculosis Research and Treatment, 2014; 1-6.

Gholami K, Kamali E, Hajiabdolbagh M, Shalviri G. Evaluation of anti-tuberculosis induced adverse reactions in hospitalized patients. Pharmacy Practice, 2006; 4(3):134-138.

Hema NG, Bhuvana KB, Virupaksha HM.Critical Assessment of Adverse drug Reactions to Antitubercular Drugs in a Government Teaching Hospital. IJBMS, 2013; 4(2):60-67.

Hassan MK, Siddique A, Karadiya RK, Chakraborty A.Incidence of Adverse Drug Reactions Among the Tuberculosis Patients Treated Under Directly Observed Treatment Short course (DOTS) regimen in North India.Indian Journal of Applied Research, 2016; 6(7):598-600.

Honnaddi UC, Honnaddi MU, Tharangini SR, Hossain T, Somani R. Adverse Drug Reactions to First Line Anti-Tubercular Drugs-A Pharmacovigilance Study. IJPR, 2016; 6(2):51-54.

Kinjal P, Mira D, Samidh S, Jigar P, Kapadia J, Dikshit R. An analysis of serious adverse drug reactions at a tertiary care teaching hospital. Perspect Clin Res 2016; 7(4):81-86.

Kishore PV, Palaian S, Ojha P, Shankar PR.Pattern of adverse drug reactions experienced by tuberculosis patients in a tertiary care teaching hospital in Western Nepal.Pakisthan journal of pharmaceutical sciences, 2008; 21(1):140-143.

Mishra S, Jena M, Jena B, Mishra SS. A study of Anti-tubercular drug induced adverse drug reactions in patient's pulmonary medicine department of a tertiary care teaching hospital. Int J Pharm Sci Rev Res, 2013; 21(2):308-311.

Maqussod M, Khan FA, Swaroop A.A Study on Incidence of Adverse Drug Reaction of Anti-Tubercular Drugs in New Cases of Pulmonary Tuberculosis in a Tertiary care Teaching Hospital.IJMRP, 2016; 2(3):53-56.

Mahendra Kumar BJ, Mathew S, Ramesh S, Maheshwari DM, Hymavathi R, Srikanth MS.Causality Assessment of Adverse Drug Reactions in Tuberculosis Patients who are on Directly Observed Treatment Short Course Strategy in Mysore District. Indian Journal of Pharmacy Practice, 2013; 6(4):22-26.

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.

Nemagouda S. The Antitubercular Drug Induced Adverse Effects in Registered Cases under RNTCP – Dots Programme in Bijapur.Journal of Evolution of Medical and Dental Sciences, 2014; 3(19):5255-5262.

Ramanath KV, Ramesh.S. A study on assessment of Adverse Drug Reactions in Tuberculosis patients. American Journal of Pharmtech Research, 2012; 2(2):584-592.

Revanna S, Harish CK, Amol G. Adverse drug reaction monitoring of anti-tubercular drugs at tertiary care medical college hospital: prospective study. Int J Basic Clin Pharmacol, 2017; 6(11):2738-2742.

Sadiq S, Khajuria V, Vishal RT, Mahajan A, Singh JB. Adverse drug reaction profile in patients on Anti-tubercular treatment alone and in combination with highly active antiretroviral therapy. Journal of Clinical and Diagnostic Research, 2015; 9(10):FC01-FC04.

Sinha K, Marak ITR, Singh WA. ADR 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.The journal of association of chest physicians, 2013; 1(2):50-53.

Sood A, Bansal R, Sharma A, Himani, Bhagrs S, Kansal D. Profile of adverse drug reactions in patients on anti-tubercular drugs in a sub Himalayan rural tertiary care teaching hospital. Int J Res Med Sci, 2016, 4(10):4465-4471.

Tak DK, Acharya LD, Gourinath K, Rao Padma GM, Subish P. Safety evaluation of Anti tubercular therapy under Revised National Tuberculosis Control Programme in India.Journal of Clinical and Diagnostic Research, 2009; 3:1395-1401.

Verma R, Mahor GR, arun KS, Prashant P. Adverse drug reactions associated with first line anti-tubercular drugs in a tertiary care hospital of central India: A study of clinical presentations, causality and severity. Asian J Pharm Clin Res, 2014; 7(5):140-143.

Zhan S, Lv X, Tang S, Xia Y, Wang X, Yuan Y *et al.* Adverse Reactions Due to Directly Observed Treatment Strategy Therapy in Chinese Tuberculosis Patients: A Prospective study. PLoS ONE, 2013; 8(6):e65037.

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