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Original Research Article

Study on drug related problems in tuberculosis patients undergoing treatment

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ABSTRACT

Background: Tuberculosis is a chronic infectious disease caused by *Mycobacterium tuberculosis*. It is one of the leading causes of mortality and morbidity around the world. The aim of this study to identify and document the drug related problems in tuberculosis patients under anti-tubercular treatment (ATT) in an attempt to promote adherence, reduce the drug related problems and improve success rate in TB treatment. The main objective of the study to identify the drug related problems in tuberculosis patients on ATT and second objective measure the medication adherence and counsel patients to improve medication adherence.

Methods: A prospective observational study was conducted in Raja Muthiah Medical College Hospital for 6 months from November 2018 to April 2019. The study was approved by Institutional Human Ethics Committee (IHEC).

Results: Total 101 drug related problems have been identified in 70 patients using pharmaceutical care network of Europe classification. Drug interactions 41.58% was the most common drug related problems found, which was clinically significant in tuberculosis patients with co- morbidities. Insufficient awareness of health and disease 21.75% was the second most common drug related problems found, 16.83% drug choice problems found. Nearly 64% of the enrolled patients were found to be non-adherence during pre-patient counselling. After the patient counselling the adherent rate was improved 74%.

Conclusions: The study concludes that pharmacist provided patient counselling found to have significant influence on improvement in the patient's knowledge towards their disease and medication, and adherence to prescribed therapy which helps to improve the clinical outcome of TB patients.

Keywords: Drug related problem, Drug interaction, Medication adherence, Tuberculosis, Patient counselling

INTRODUCTION

Tuberculosis (TB) is a chronic granulomatous disease and a major health problem in developing countries. About 1/3rd of the world's population is infected with *Mycobacterium tuberculosis*, out of which 10-15% develop the disease over their life time. As per WHO statistics for 2014 there were 9.6 million new TB cases globally, to which India was the highest contributor with

2.2 million cases. India has the dubious distinction of being the highest TB burden country for the past many years.¹ Drug related problems are one kind of problem that appears in the using of the drugs or medicine therapy which was potentially or actual can influence the outcomes of the patient therapy, it's increasing the caring cost and also can block the attained of the therapy purposed. In order to improve the rational use of drugs, the pharmacist have an important role in identifying and

solving the problems which has correlation with the use of drugs and potential or actual drug related problems (DRPs). Medication adherence is defined as the extent to which a patient's medication-taking behaviour coincides with the intension of the health advice he or she been given. Medication adherence is one of the most important factors that determine therapeutic outcome, especially in patients suffering from chronic illness. Adherence is also defined by World Health Organization as the degree to which the person's behaviour corresponds with the agreed recommendations from a health care provider.²

The main objective of the study to identify the drug related problems in tuberculosis patients on ATT and second objective measure the medication adherence and counsel patients to improve medication adherence.

METHODS

Study design

The prospective observational study was carried out from November 2018 to April 2019 in Rajah Muthiah Medical College and Hospital, Annamalai University, Tamil Nadu. The study was approved by Institutional Human Ethics Committee (approval letter no IHEC/0398/2018).

Inclusion criteria

Inclusion criteria were tuberculosis patients of all age groups, with or without co-morbidities, who are undergoing anti-tubercular treatment (newly diagnosed and previously treated) according to revised national tuberculosis control program (RNTCP) guidelines.

Exclusion criteria

Exclusion criteria pregnant and lactating women, treatment completed patients, mentally ill persons, and subjects not willing to participate.

Study procedure

Informed consents were obtained from the patients prior starting the study. Data was collected from the total of 70 patients, who visited the department of Medicine and DOTs centre with tuberculosis during the study period. The data collection form was designed to collect the required demographic and clinical data of the patients. The data collection form contains particulars like name of patient, IP\OP No, age, medication history, present illness of the patient, category of drug and therapeutic management and treatment details. The patient demographics collected from patient case sheets and recorded into data collection forms. Collected data related to drugs prescribed, dose, duration etc., by observing the medication records of the enrolled patients. Found out the drug related issues and brought to the physician's attention. Analyzed the drug related problems by using

micro-medex and various text books along with interview from patients and evaluated as per PCNE classification. Adverse effect was documented using the form of national pharmacovigilance program. Medication adherence measured by using MAR scale. Counseled the patients-sensitizing them on need of medication adherence and using them to complete the course. Treatment outcome was measured.

Statistical analysis

Descriptive analysis was performed using microsoft excel and word 2007. For descriptive statistics, results were expressed in terms of percentage and presented using tables and diagrams according to the types of tool used.

RESULTS

A total number of 70 patients were enrolled in our study. All enrolled patients completed the study. The upcoming results were taken from the patients who successfully completed the study.

Table 1: Demographics of patients.

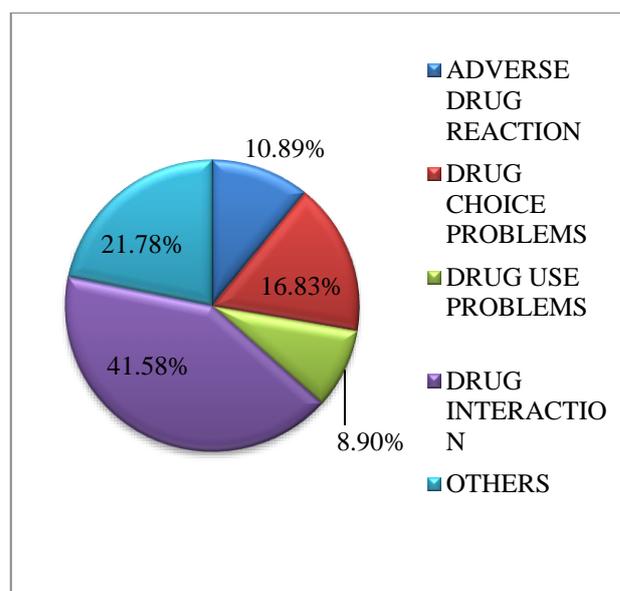
Characteristics	No. of patients	%
Gender		
Male	46	65.71
Female	24	34.28
Age distribution		
Pediatrics	3	4.28
Adults	56	80
Elderly	11	15.71
Comorbidities		
With co-morbidities	30	42.85
Without co-morbidities	40	57.14
Family history of TB		
Yes	39	55.71
No	31	44.28
Types of TB case		
New	53	75.71
Previously treated	17	24.28
Social habits		
Smoker	5	7.14
Alcoholic	9	12.85
Smoker and alcoholic	25	35.71
No social habits	31	44.28

Medication adherence

Medication adherence to anti-TB treatment is a major determinant of treatment outcome. Medication adherence measured by using MAR scale.

Table 2: Drug related problems (PCNE).

Code	Problems	No. of problems	Percentage
P1	Adverse drug reaction	11	10.89
P2	Drug choice problems	17	16.83
P2.1	Duplication of therapeutic group	5	4.95
P2.2	Inappropriate drug form	7	6.93
P2.3	No clear indication of drug	5	4.95
P3	Drug use problems		
P3.1	Drug overused/ over-administered	9	8.9
P4	Drug interaction	42	41.58
P5	Others		
P5.1	Insufficient awareness of health and diseases	22	21.75

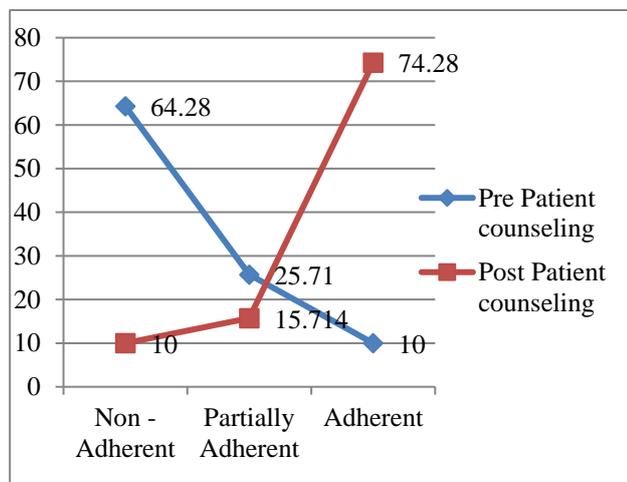
**Figure 1: DRPs classification.****Table 3: Detailed drug related problems.**

P1 Adverse drug reaction					
S. no.	Drugs	ADR	Causality assessment	No. of cases	
1	H, R and Z	Gastritis	Probable	7	
2	H, R and Z	Gastritis with anemia	Probable	1	
3	H, R and Z	Anemia	Probable	1	
4	H and E	Flu like symptoms	Probable	1	
5	H, R, Z and E	Itching and rashes	Probable	1	
P2 Drug choice problems					
P2.1 Duplication of therapeutic group					
S. no.	Drugs	Therapeutic group	Classification	Consequence of drug duplication	No. of case
1	Injection amikacin	Injection streptomycin	Aminoglycoside	Amikacin was stopped	1
2	Injection pantoprazole	T. rabeprazole	PPI	Rabeprazole was stopped	1
3	Formoterol (inhaler)	Salbutamol	Bronchodilators	Formoterol was stopped	1
4	Injection streptomycin	Injection gentamicin	Aminoglycoside	Gentamicin was stopped	1
5	Budesonide and formoterol	Fluticasone	Corticosteroids	Budesonide was stopped	1
P2.2 Inappropriate drug form					
S. no.	Drug dosage form	Appropriate dosage form	Consequence of inappropriate drug form		No. of cases
1	Injection pantoprazole	Oral tablet	Informed to the physician then injection pantoprazole changed to tab pantoprazole		6
2	Injection ranitidine	Oral tablet	Informed to physician then changed to tab ranitidine		1
P2.3 No clear indication of drug					
S. no.	Drugs	Indication	Inappropriate use	No. of cases	
1	Chlorpromazine	Psychotic disorder	Patient does not have these symptoms	1	
2	Pantoprazole	Gastric ulcer/GERD	Patient does not have these symptoms	4	
3	Ranitidine	Gastric ulcer/GERD	Patient does not have these symptoms	1	
P3 Drug use problems					
P3.1 Drug overused/over-administered					
S. no.	Problem	Intervention			No. of cases
1	Patient taking drug too long period	Patient counselling			9

Table 3: Drug interactions (moderate) (ATT with concomitant drugs).

S. no.	Interacting drugs	Effect	No. cases	
1	Streptomycin and cefotaxime	Increased risk nephrotoxicity	2	
2	Streptomycin and amikacin	Increased risk nephrotoxicity and ototoxicity	1	
3	Rifampicin and antacid	Decrease the rifampicin absorption	2	
4	Isoniazid and paracetamol	Increase the paracetamol toxicity (H) Inhibit paracetamol metabolism	7	
5	Isoniazid and phenytoin	Decrease the phenytoin concentration	2	
6	Streptomycin and ceftriaxone	Increased risk of nephrotoxicity	2	
7	Isoniazid and prednisolone	Decrease the effect of isoniazid	1	
Clinically significant drug interactions (moderate/potential) of ATT drugs with hypertensive drugs and diabetic drugs				
S. no.	Interacting drugs	Effect	Intervention	No. of cases
1	Rifampicin and nifedipine	Decrease the anti-hypertensive effect	Monitor BP dose adjustment	5
2	Rifampicin and enalapril	Decrease the anti-hypertensive effect	Monitor BP dose adjustment	2
3	Rifampicin and losartan	Decrease the anti-hypertensive effect	Monitor BP dose adjustment	3
4	Isoniazid and metformin (oral anti-diabetics)	Interfere with glucose control	Monitor glucose level	9
5	Isoniazid and insulin	Interfere with glucose control	Monitor glucose level	6

H - Isoniazid, R - Rifampicin, Z - Pyrazinamide, E - Ethambutol, PPI - Proton pump inhibitors and GERD - Gastroesophageal reflux disease.

**Figure 2: Medication adherence score.**

DISCUSSION

The gender distribution of study population showed that among 70 patients, 65.71% were male and 34.28% were female. This data showed that males are at more risk to get infection than female patient; this similar result shows many studies.^{3,5,6,9} In this study shows more adult people were exposed to risk factors\infections compared to elderly and children this result was similar to the other studies.^{3,10} The present study shows without co morbidities patient was more than with co morbidities patient, another study shows more no of TB with co

morbidities patients.⁶ In this study shows patients with family history of TB was found more as compared to No family history TB, Krishna et al shows similar results but another study result patients are mostly in no family history of TB.^{3,10} More no of newly treated TB patients in present study, these similar study result showed by Shivaraj et al and Krishna et al.^{3,10} Study result shows more no smoker and alcoholic patients affect with TB, Fei et al shows less no of TB patient had smoking and alcoholic habits.⁶ A substantial proportion of hospitalized patients experience medication-related problem that is preventable. Total 101 DRPS have been identified in 70 patients. The present study shows more number of DRPs occurred in TB patients with co-morbidities 43% as compared to TB alone, as similar to the study conducted by Raj et al shows DRPs in TB patients with co morbidities are more due to drug interactions of ATT with concomitant drugs which are clinically significant in case of hepatic impairment, DM, COPD, and hypertension.³ Gastritis was found to be the most frequent ADR by anti-tubercular drugs in the present study. Some study shows gastritis most common ADR with intake of anti TB drugs.^{5,6,8} Anemia, flu like syndrome and itching was less in the study. Total 16.83% DCP were identified in the study, another study shows more no of DCP; they are studied in more sample size.³ This study found to be 4.95% of no clear indication of drug used. 19.05% drugs used without indication; this result studied by Ramatillah et al.⁷ Study found to be 4.95% of duplication of therapeutic group and 6.93% inappropriate drug form. Similar result by Shivaraj et al.³ 8.9% drug use problems identified due to drug overused/over administered. 1.8%

overdose of drug dose problem studied.⁸ In this study, a total of 41.58% drug interactions were found shown in (Table 2 and 3). Drug-drug interactions having significant impact on TB patients with co-morbid disease conditions like DM, hypertension and COPD etc. were the chronic illness patients on regular medications. Management of DM in TB should be aggressive. The efficacy of insulin and other anti-diabetic agents may be diminished by isoniazid.⁴ Caution is advised when anti diabetic drugs prescribed for DM with TB patients. Clinical monitoring is recommended following initiation or discontinuation of anti-diabetic drugs, and the dosages of concomitant anti-diabetic agents adjusted as necessary. In this study 21.78% patients showed insufficient awareness of health and disease as it comes under “others” category of DRPs. Patients are discriminated by using separate utensils for food or drink due to the misapprehension about transmission of disease. Increase anxiety/tension, fear of loss of wage/earning, and stigma threatening self-esteem and quality of life are associated with diagnosis of TB. Psychosocial reactions towards TB as divulged in this study should be addressed through counselling and communication during treatment in the DOTS centre. These may contribute the success rate of TB control program.^{3,10} Non adherent 24.7% less in this study.⁹ Present study shows 64.28% of non-adherent. Adherent rate was improved by patient counselling shown in Figure 2. The present study assessed the impact of pharmacist assisted patient counselling in improving medication adherence in TB patients. Non-adherence can affect the success rate of TB treatment. Reason identified for non-adherence. In the present study, the main reason for non-adherence forgetting to take medication, physical difficulty, social habits, lack of support from family and friends, co-morbidity, side effects. These problems of the non-adherence would be reduced by good communication between the patient and health provider as well as by patient counselling. The similar findings were observed in the study conducted by Krishna et al shows pharmacist assisted patient counselling had a statistically significant impact in improving medication adherence and QOL in TB patients.¹⁰

CONCLUSION

The study concludes that pharmacist provided patient counselling found to have significant influence on improvement in the patient’s knowledge towards their disease and medication, and adherence to prescribed therapy which helps to improve the clinical outcome of TB patients. The study shows necessity of clinical pharmacy service in health care system. Clinical pharmacist work directly with physician, other healthcare professionals, and patients to ensure that the medications

prescribed for patients contribute to the best possible health outcomes.

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Ethical approval: The study was approved by Institutional Human Ethics Committee (IHEC/0398/2018)

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