Contents lists available at UGC-CARE

International Journal of Pharmaceutical Sciences and Drug Research

[ISSN: 0975-248X; CODEN (USA): IJPSPP]

Available online at www.ijpsdronline.com

Research Article

Identification and Evaluation of Drug-Related Problems to First Line Therapy of Antitubercular Drugs among the Pulmonary Tuberculosis Patients in a Tertiary Care Hospital- A Randomised Controlled Study

Bandaru Y Raja*, Madiwalayya S Ganachari

Department of Pharmacy Practice, KLE college of Pharmacy, KLE Academy of Higher Education and Research, Belagavi, Karnataka, India

ARTICLE INFO

Article history:

Received: 20 October, 2023

Revised: 10 February, 2024

Accepted: 12 February, 2024

Published: 30 March, 2024

Keywords:

Drug-related problems, Adverse drug reactions, Antitubercular drugs, Tuberculosis.

DOI:

10.25004/IJPSDR.2024.160202

ABSTRACT

The standard treatment involves first-line antitubercular therapy for treating pulmonary tuberculosis (TB) in treating pulmonary tuberculosis (TB). This treatment is associated with many drug-related problems (DRPs) and adverse drug reactions (ADRs). A single-blind, randomized, controlled study was conducted on 250 patients to identify and evaluate the DRPs and ADRs among newly diagnosed pulmonary TB patients in a tertiary care hospital. The patients were classified as the usual care group (Control) and pharmaceutical care intervention group (Test). At the end of the follow-up study, the DRPs were assessed using PCNE classification V9.1. The causality assessment of ADRs was done with the Naranjo algorithm, the severity assessment was carried with a modified Hartwig and Siegel scale and the preventability of ADRs was assessed with a modified Schumock and Thornton scale. The statistical percentage analysis was done using Microsoft Excel 2019. Of 250 participants, 88% had DRPs and developed one or more ADRs. The DRPs of adverse drug event (possibly) occurring, unclear problem/complaint, duration of treatment too long, medication reconciliation problem and inappropriate timing or dosing intervals were found to be more. Around 94.55% of ADRs were mild, and 5.45% were moderate. The causality of ADRs around 94.09% were possible and 5.92% were probable, while the preventability of ADRs found around 89.55% definitely preventable and 10.45% were probably preventable. The study concludes the importance of clinical pharmacists in pharmaceutical patient care will contribute to understanding different DRPs and ADRs in managing TB.

Introduction

Tuberculosis (TB) remains a significant global health challenge, ranking among the deadliest infectious diseases.[1] The first-line treatment regimens for treating active TB encompass isoniazid (INH/H), rifampicin (RMP/R), ethambutol (EMB/E), and pyrazinamide (PZA/Z).[2] However, the prolonged use of these drugs in TB patients often results in medical issues and side effects, potentially leading to non-adherence. These adverse effects range from minor, such as abdominal pain, epigastric discomfort, nausea, vomiting, peripheral neuritis, itching, and joint pain, to major complications like hepatitis, seizures, jaundice, and optic neuritis. It is essential to note that while minor reactions do not necessitate discontinuation of antitubercular drugs, they can be managed by employing alternative medications to mitigate the adverse effects. Conversely, major adverse effects require the withholding or withdrawal of drug therapy for the well-being of the patient.[3]

Pharmaceutical care involves the clinical provision of medication therapy, focusing on identifying, resolving, and preventing drug-related problems (DRPs).[4] These problems encompass issues related to indications, safety, efficacy, and compliance, and addressing them is crucial for

***Corresponding Author:** Dr. Bandaru Y Raja

Address: Department of Pharmacy Practice, KLE college of Pharmacy, KLE Academy of Higher Education and Research, Belagavi, Karnataka, India.

Email ✉**:** yashmohan2979@gmail.com

Tel.: +91-9490650260

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

delivering suitable treatment and preventing medication non-adherence. The delivery of pharmaceutical care is entrusted to a clinically trained pharmacist, proficient in pharmacotherapeutic oversight. The primary objective of these pharmacists is to attain well-defined therapeutic goals, including curing ailments, stabilizing disease processes, preventing diseases, and alleviating symptoms. Collaborating with other healthcare professionals, these pharmacists enhance patients' quality of life.[5]

Unresolved DRPs and ADRs can result in significant morbidity and impact TB treatment regimens.[6] Many patients experience a loss of follow-up upon discharge from the hospital, leading to therapy discontinuation, frequent changes in drug regimens, and insufficient patient counseling and education. These factors may contribute to the occurrence of DRPs or ADRs and unnecessary healthcare utilization. In this context, monitoring TB patients through a healthcare team is crucial to ensure treatment completion. In the current scenario, the comprehensive provision of pharmaceutical care by pharmacists is vital. This approach includes offering sufficient patient counseling to enhance medication compliance, positively influencing morbidity outcomes, detecting adverse events, correcting medication errors, promoting medication adherence, and ultimately contributing to an improved quality of life.[7,8] Therefore, the objective of the current study is to identify and assess DRPs and ADRs in individuals undergoing first-line therapy with antitubercular drugs through the implementation of pharmaceutical care.

Materials and Methods

Study Design and Settings

A randomized, controlled study with a single-blind design was conducted among tuberculosis (TB) patients visiting a tertiary-care teaching hospital in the Belagavi district of Karnataka state, India. The study spanned for 18 months, commenced in September 2021, and was completed in March 2023. Randomization was achieved through the use of a simple envelope method, resulting in two parallel branches (1:1 ratio): the usual care group (Control) and the pharmaceutical care intervention group (Test). The study participants opened the envelopes containing the group assignments in the presence of a clinical pharmacist. Participants in the test group received pharmaceutical care interventions administered by the clinical pharmacist in a designated room at the TB center within the hospital. On the other hand, the control group received standard care from other healthcare professionals within the usual care room in the hospital.

Study Participants

The study included individuals aged 18 years and above who were newly diagnosed with pulmonary tuberculosis (TB) and undergoing self-administered TB treatment, encompassing both antitubercular treatment (ATT) and fixed-dose combination therapy (FDC), obtained from private practitioners. Exclusion criteria comprised individuals below 18 years of age, those diagnosed with extrapulmonary TB, individuals with more than one comorbidity, and those unwilling to participate in the study. The participants were provided information about the study through a subject information sheet, and their consent was obtained after enrolling them.

Data Collection and Statistical Analysis

The participants underwent interviews using a data collection form that collected demographic details, including age, gender, marital status, religion, area, education level, and working experience. In adherence to the eligibility criteria, patients who did not meet the inclusion criteria were excluded. Through a single-blind randomization technique, the included patients were randomized into two groups: the test group (with pharmacist intervention) and the control group (with clinical care). Two regular intervals of participant follow-up followed enrollment at baseline. The first follow-up occurred at the third month, and the second follow-up occurred three months after the first follow-up. Data were collected and documented after the second follow-up. Statistical analysis was carried out using Microsoft Excel spreadsheet 2019. Descriptive statistics, such as frequencies and percentages, were calculated for the necessary data. Data visualization techniques were employed, including tabulations, bar graphs, and pie charts. The schematic consort flow chart outlining the materials and methods is depicted in Fig. 1.

The patient medication compliance, which are DRPs and ADRs was identified and evaluated. The DRPs were categorized using the Pharmaceutical Care Network

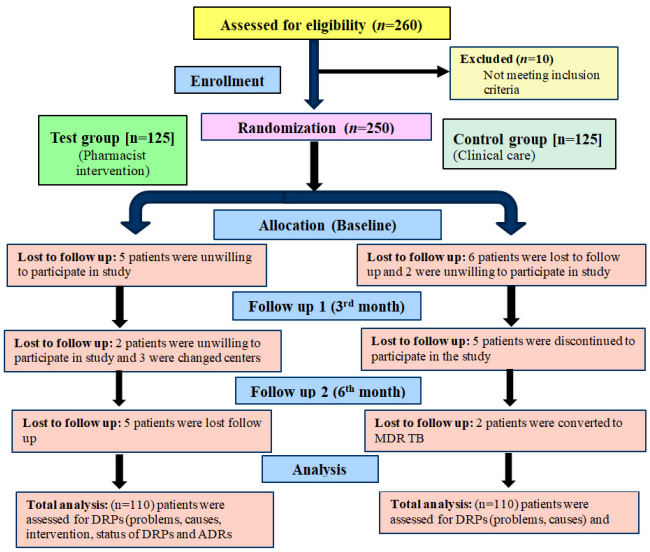

Fig. 1: The schematic consort flow chart representation of materials and methods

Europe's classification system (PCNE version 9.1).[9] The causality assessment of ADRs was conducted using the Naranjo algorithm, followed by the evaluation of severity using the modified Hartwig and Siegel scale. The preventability assessment was also performed using the modified Schumock and Thornton scale.[10-12]

The study received approval from the Institutional Ethical Clearance (IEC) for human subjects under the reference number KAHER/EC/21-22/020, dated July 29, 2021, from KLE Academy of Higher Education and Research in Belagavi, India.

Results

Socio Demographic Details

In our study, a total of 250 patients were allocated and randomized into test and control groups. 30 patients were lost follow-up at the end of follow-up 2 (6^{th} month). We assessed a total number of 220 patients (n = 110 test & n = 110 control) DRPs and ADRs. As far as background information was concerned, the majority of the participants were males in both test and control (53.64% in test and 55.45% in control) and the majority belonged to the 26 to 35 years of age group (57.27% in test and 60% in control). Around 83.64% of the participants in both groups were literate and most were living in urban residential areas compared to rural areas in both groups. The marital status of the participants found that the majority of them got married (70% in test and 78.18% in the control). The participants' socioeconomic status found that the majority belonged to the lower middle (31.82% in test and 39.09% in control) followed by upper-lower and upper-middle-class groups. Most of the participants who were newly diagnosed for TB were taking ATT medication (59.09% in test and 55.45% in control). The social history of the participants found that most of them were non-alcoholic or smokers (45.45% in test and 50%in control) but there were few smokers (21.82% in the test and 23.64% in control) and smokeless tobacco chewing (23.64% in test and 17.27% in control). The majority of the participants were not have any comorbidities only a few of them had hypertension (5.45% in control and test) and diabetes (2.73% in test and 3.64% in control) (Table 1).

Table 1: Comparison of control group and test group with socio-demographic profile of TB patients

Socio-demographic profile	*Test (n = 110)*	*(%)*	*Control (n = 110)*	*(%)*
Age groups				
15–25	13	(11.82)	11	(10.00)
26–35	63	(57.27)	66	(60.00)
36–45	34	(30.91)	33	(30.00)
Gender				
Female	51	(46.36)	49	(44.55)
Male	59	(53.64)	61	(55.45)
Literacy				
Illiterate	18	(16.36)	18	(16.36)
Literate	92	(83.64)	92	(83.64)
Residency				
Rural	52	(47.27)	49	(44.55)
Urban	58	(52.73)	61	(55.45)
Marital status				
Unmarried	33	(30.00)	24	(21.82)
Married	77	(70.00)	86	(78.18)
Socioeconomic status				
Upper	3	(2.73)	4	(3.64)
Upper middle	23	(20.91)	16	(14.55)
Lower middle	35	(31.82)	43	(39.09)
Upper lower	35	(31.82)	29	(26.36)
Lower	14	(12.73)	18	(16.36)
TB drug treatment				
FDC	45	(40.91)	49	(44.55)
ATT	65	(59.09)	61	(55.45)
Social history				
Smoker	24	(21.82)	26	(23.64)
Smokeless tobacco	26	(23.64)	19	(17.27)
Alcohol	0	(0.00)	3	(2.73)
Alcoholic with smoking	10	(9.09)	7	(6.36)
Non-alcoholic/smoker	50	(45.45)	55	(50.00)
Comorbidities				
Hypertension	6	(5.45)	6	(5.45)
Diabetes	3	(2.73)	4	(3.64)
No comorbidities	101	(91.82)	100	(90.91)
Total	110	100.0	110	100.0

Type of Drug Related Problems Identified

According to PCNE classification (V9.1), current study findings on drug related problems (DRPs) were identified among both test and control groups. We found that 03 (1.36%) patients were due to suboptimal drug treatment effects, while 42 (19.09%) patients had untreated symptoms or disease indication affecting treatment effectiveness. Adverse drug events potentially occurring were noted in 129 (58.64%) of patients, indicating concerns about treatment safety. Additionally, 46 (20.91%) of patients presented with unclear complaints or problems possibly arising from external factors (Table 2). The current study also identified various causes of DRPs among both test and control groups. These were due to polypharmacy which were unnecessarily prescribed in 4 (1.82%) patients, therapeutic duplication (excessively high doses of single active ingredients) were administered in 10 (4.55%) patients, complexity in dosage/treatment regimen

Table 2: Detailed drug related problems (PCNE)

The problems								
Primary domain	*Code*	*Problem*	*Frequency (N = 220)*		*Percentage (%)*		*Total (N = 220)*	*Total (%)*
			Test	*Control*	*Test*	*Control*		
1. Treatment effectiveness	P1.2	Effect of drug treatment not optimal	3	0	2.73	0	3	1.36
	P1.3	Untreated symptoms or indication	16	26	14.55	23.64	42	19.09
2. Treatment safety	P2.1	Adverse drug event (possibly) occuring	57	72	51.82	65.45	129	58.64
3. Other	P3.2	Unclear problem/complaint. Further clarification necessary	34	12	30.91	10.91	46	20.91
Total			110	110	100	100	220	100

Table 3: The causes for drug related problems (PCNE)

The causes								
Primary domain	*Code*	*Cause*	*Frequency (n = 220)*		*Percentage (%)*		*Total (N = 220)*	*Total (%)*
			Test	*Control*	*Test*	*Control*		
1. Drug selection	C1.6	Too many different drugs/active ingredients prescribed for indication	2	2	1.82	1.82	4	1.82
2. Dose selection	C3.2	Drug dose of a single active ingredient too high	6	4	5.45	3.64	10	4.55
3. Treatment duration	C4.2	Duration of treatment too long	30	27	27.27	24.55	57	25.91
4. Patient related	C7.1	Patient intentionally uses/takes less drug than prescribed or does not take the drug at all for whatever reason	16	8	14.55	7.27	24	10.91
	C7.7	Inappropriate timing or dosing intervals	27	29	24.55	26.36	56	25.45
5. Patient transfer related	C8.1	Medication reconciliation problem	29	40	26.36	36.36	69	31.36
Total			110	110	100	100	220	100

(longer duration of treatment) found in 57 (25.91%) patients, patient non-compliance (low dosage of prescribed drug intake or does not take the drug) was found among 24 (10.91%) patients, dosing timings or intervals were inappropriately administered among 56 (25.45%) patients and lack of transition care where the patients shift from hospital care to primary health care centres (medication reconciliation problem) were found among 69 (31.36%) patients (Table 3).

Acceptance of the Intervention Proposals, Planned Interventions & Status of the DRPs

As our study was an interventional RCT trial, we have implemented the interventional proposal to test group from the baseline. Among 110 patients in the test group, 94 (85.45%) patients were accepted pharmacist intervention and fully implemented it, 14 (12.73%) patients were accepted intervention but partially implemented, only 2 (1.82) patients accepted intervention but implementation of pharmaceutical care services was unknown (Fig. 2). Regarding the planned interventions, the test group was given with patient (drug) counseling on 83 (75.45%) patients, written information of provided on 12 (10.91%) patients who were unable to listen and on 15 (13.64%) counselling was given to family members (Fig. 3). After the follow-up, 2 (6^{th} month), at the end of the study, We found 74 (67.27%) patients in the test group the DRPs were totally solved and 36 (32.73%) patients the DRPs were partially solved.

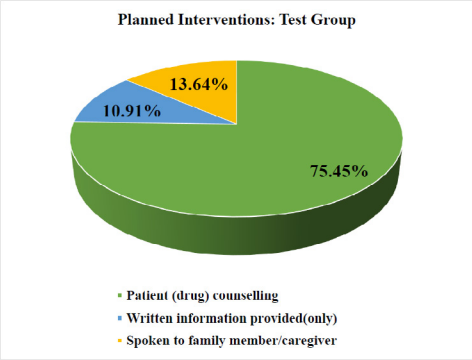

Fig. 2: The planned interventions

Table 4: Common adverse drug reactions observed in both test and control groups.

Drugs	*Common ADRs*	*Test (n = 110)*	*(%)*	*Control (n = 110)*	*(%)*
Isoniazid	Hepatotoxicity	6	(5.45)	4	(3.64)
	Peripheral neuritis	7	(6.36)	4	(3.64)
	GI disturbance	77	(70)	73	(66.36)
	Skin rashes	4	(3.64)	2	(1.82)
Rifampicin	Orange/red color urine	110	(100)	110	(100)
	Abdominal pain	25	(22.73)	27	(24.55)
	flu-like syndrome	11	(10)	6	(5.45)
	Nausea/vomiting	29	(26.36)	15	(13.64)
	Arthralgia	2	(1.82)	2	(1.82)
Pyrazinamide	Hepatotoxicity	6	(5.45)	4	(3.64)
	Malaise	4	(3.64)	3	(2.73)
	Anorexia	1	(0.91)	2	(1.82)
	Nausea/vomiting	29	(26.36)	15	(13.64)
	Ocular side effects	1	(0.91)	2	(1.82)
Ethambutol	Optic neuritis	0	(0)	2	(1.82)
	Pruritis	7	(6.36)	4	(3.64)
	GI disturbance	77	(70)	73	(66.36)
	Headache	27	(24.55)	18	(16.36)

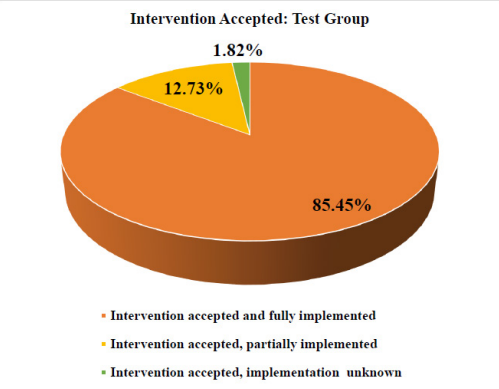

Fig. 3: Acceptance of the intervention proposals

Adverse Drug Reactions Assessment

Most adverse drug reactions (ADRs) (95.85%) occurred in the intensive phase, while only 4.15% occurred in the continuation phase in both test and control groups. Around 50% of ADRs occurred in the 1st week of treatment in the baseline. The majority of them were common ADRs, which were related to gastrointestinal disturbance, nausea or vomiting, abdominal pain, headache etc. The common ADRs that were observed in both test and control groups with four antitubercular drugs are listed in Table 4.

We have assessed the severity of ADRs by using a modified Hartwig and Siegal scale, and found that 102 (92.73%) in test and 106 (96.36%) in the control group of the ADRs classified as mild (Level 1 and 2), 8 (7.27%) in test and 4 (3.64%) in control as moderate (Level 3 and 4). None of the ADRs were classified as severe. According to the Naranjo algorithm causality assessment, 102 (92.73%) in the test and 105(95.45%) in the control group of the ADRs were classified as possible, 8 (7.27%) in the test and 5 (4.55%) in the control as probable. No ADRs were classified as definite. According to Schumock and Thorton preventability assessment scale, 95 (86.36%) in test and 102 (92.73%) in the control group of the ADRs were classified as definitely preventable, 15 (13.64%) in test and 8 (7.27%) in control as probably preventable. No ADRs were classified as not preventable.

Discussion

Pharmacists play a crucial role in ensuring the appropriate use of medications by identifying and addressing DRPs. As per the PCNE-DRP (V9.1) classification, a DRP is defined as an event or circumstance related to drug therapy that either actually or potentially interferes with the desired health outcomes. The standard treatment duration for newly diagnosed TB patients involves a six-month regimen with first-line antitubercular drugs.[13] During this extended therapy period, the potential for DRPs arises, posing a risk of treatment withdrawal and impacting the overall quality of life. Our present study underscores the significance of clinical pharmacist-led interventions in efficiently identifying and addressing DRPs. Similar findings were found from various studies that emphasize the positive impact of timely interventions in managing DRPs.[14-16]

This study specifically evaluates DRPs among TB patients attending the National Tuberculosis Elimination Program (NTEP) center at a tertiary care hospital, with subsequent follow-ups conducted at primary health care centers. Importantly, this study stands out as one of the few in India that systematically analyzes interventions targeting DRPs in TB patients, utilizing the PCNE classification, and assesses ADRs related to TB treatment.

In the current study involving 220 participants, it was observed that the majority were males, constituting 53.64% in the test group and 55.45% in the control group, while females accounted for 46.36 and 44.55% in the test and control groups, respectively. This similar finding was seen in several other studies, indicating a higher risk of infection among males. [17,18] The study predominantly included adults aged 26 to 35 years, who had high risk of infection compared to the elderly and children, consistent with findings from other studies.[19,20] Furthermore, the present study revealed a notable prevalence of smokeless tobacco and smoker patients affected by TB, mirroring similar findings in other study, which highlighted the association between TB patients and smoking and smokeless tobacco habits.[20] Additionally, our study reported fewer patients without comorbidities compared to those with comorbidities, differing from another study that indicated a higher incidence.[21]

In our study, a total of 129 cases (58.64%) were identified as adverse events possibly occurring, followed by 46 cases (20.91%) with unclear problems/complaints, 42 cases (19.09%) related to untreated symptoms or indications, and only 3 cases (1.36%) where the effect of drug treatment was not optimal among the 220 patients. However, in the study by Tharanon V *et al*. revealed different categories of DRPs, including drug problems related to indications, excessively high or low drug doses, drug interactions, and patient failure to receive medication.[22] In our current study, the primary causes of DRPs were identified as medication reconciliation problems (31.36%), duration of treatment too long (25.91%), and inappropriate timing or dosing intervals (25.45%). These findings were attributed to the antitubercular drug treatment strategy, requiring patients to undergo a minimum 6-month therapy and refill their prescriptions weekly or monthly. Fauna Herawati *et al*. reported a similar trend, where TB patients faced challenges in adherence when admitted or transferred to different healthcare institutions, leading to treatment loss.[23]

Regarding ADRs, gastrointestinal disturbances were the most prevalent in our study. While in other study highlights gastritis as the most common ADR during anti-TB medication.[24] Our study reported low occurrences of hepatotoxicity, peripheral neuritis, flu, skin rashes, and malaise. The observation of orange/red-colored urine among all patients was attributed to a normal ADR associated with rifampicin. A higher frequency of ADRs was noted during the intensive phase (95.96%) compared to the continuation phase (5.04%), consistent with other studies indicating a higher incidence of ADRs in the early months of TB treatment.[25,26] our study did not affect the overall therapeutic outcome despite these ADRs.

In the current study, among the reported ADRs, 102 cases (92.73%) in the test group and 106 cases (96.36%) in the control group were categorized as mild (Level 1 and 2) on the modified Hartwig and Siegal scale. Additionally, 8 cases (7.27%) in the test group and 4 cases (3.64%) in the control group were classified as moderate (Level 3 and 4). Mild ADRs typically do not necessitate any changes in treatment, while moderate ADRs may require adjustments to the suspected drug dose or discontinuation of the drug. Regarding causality assessment using the Naranjo algorithm, the majority of ADRs, 102 cases (92.73%) in the test group and 105 cases (95.45%) in the control group, were classified as possible. Only 8 cases (7.27%) in the test group and 5 cases (4.55%) in the control group were categorized as probable. It's essential to note that the study did not conduct rechallenge tests to establish the causative agent, and there were no laboratory investigations to determine drug concentrations in tissues or body fluids. As a result, no reported ADRs were categorized as definite in this study.

The effective management of TB patients necessitates a multidisciplinary healthcare professional team strategy. Pharmacists play a vital role within such teams and can contribute at various stages in the value chain for TB control. The current study indicates that pharmacists significantly contribute to TB treatment by identifying DRPs and monitoring ADRs. This involvement proves instrumental in enhancing treatment adherence, assessing risk factors, managing disease control and prevention, and enhancing the safety and efficacy of TB treatment. Therefore, the provision of pharmaceutical care services in TB management, under the supervision of pharmacists, is a crucial element in contributing to controlling and preventing TB disease.

Conclusion

This study appears to be first pharmaceutical care interventional study conducted on tuberculosis patients in India through a clinical pharmacist. A thorough understanding of the various DRPs and ADRs helped in effective TB management. Additionally, this study contributes to the assessment of the safe usage of antitubercular drugs, as the ADRs identified align with those previously reported in the literature. A noteworthy outcome of the study is the high acceptance and implementation of planned pharmacist interventions and recommendations among the test group patients. Furthermore, pharmaceutical care intervention in the test group resulted in resolving and improving DRP status. This study's findingshow that pharmaceutical care services' impactes in treating tuberculosis promotes better healthcare outcomes.

Acknowledgment

We would show our extreme gratitude to the Associate Professor & in charge of NTEP centre, Dr. Jyothi Hattiholi of KLE hospital, Belagavi, Karnataka who supported us in collecting cases in the hospital. We would like to acknowledge all patients who were participated and responded to our study.

References

1. World Health Organization (WHO): Global tuberculosis control, WHO report 2021. 2021. Available from: [http://www.who.int/gtb/publications].
2. National Tuberculosis Elimination Programme Annual Status Report. TB India 2016. New Delhi, India: Central TB Division, Ministry of Health and Family Welfare. Available from: [https://tbcindia.gov.in/WriteReadData/l892s/8337437943TOG-Chapter%204-Treatment%20of%20TB%20Part%201.pdf].
3. Forget EJ, Menzies D. Adverse reactions to first-line antituberculosis drugs. Expert opinion on drug safety. 2006;5:231-49. Available from: doi.org/10.1517/14740338.5.2.231.
4. Al-Quteimat OM, Amer AM. Evidence-based pharmaceutical care: The next chapter in pharmacy practice. Saudi Pharmaceutical Journal. 2016;24:447-51. Available from: doi.org/10.1016/j.jsps.2014.07.010.
5. Francis J, Abraham S. Clinical pharmacists: Bridging the gap between patients and physicians. Saudi Pharmaceutical Journal. 2014;22:600-2. Available from: doi.org/10.1016/j.jsps.2014.02.011.
6. Marra F, Marra CA, Bruchet N, Richardson K, Moadebi S, Elwood RK, et al. Adverse drug reactions associated with first line anti tuberculosis drug regimens. International Journal of Tuberculosis and Lung Disease. 2007;11:868 75.
7. Gillespie U, Al assaad A, Henrohn D, et al. A comprehensive pharmacist intervention to reduce morbidity in patients 80 years or older: a randomized controlled trial. Archives of Internal Medicine. 2009;169:894–900. Available from: doi:10.1001/archinternmed.2009.71.
8. Schnipper JL, Kirwin JL, Cotugno MC, et al. Role of pharmacist counseling in preventing adverse drug events after hospitalization. Archives of Internal Medicine. 2006;166:565–571. Available from: doi:10.1001/archinte.166.5.565.
9. Classification for Drug related problems [ebook] Pharmaceutical Care Network Europe Association, pp.1-10. 9th ed [cited Nov 21 2021]. Available from: [https://www.pcne.org/upload/files/417_PCNE_classification_V9-1_final.pdf].
10. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruis I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. Clinical Pharmacology and Therapeutics. 1981;30:239–45. Available from: doi.org/10.1038/clpt.1981.154.
11. Hartwig SC, Siegel J, Schneider PJ. Preventability and severity assessment in reporting adverse drug reactions. American Journal of Hospital Pharmacy. 1992;49:2229–32. Available from: doi.org/10.1093/ajhp/49.9.2229.
12. Schumock GT, Thornton JP. Focusing on the preventability of adverse drug reactions. Hospital Pharmacy. 1992;27:538. Avaliable form: http://europepmc.org /MED/10118597.
13. Conde MB, Lapa E Silva JR. New regimens for reducing the duration of the treatment of drug-susceptible pulmonary tuberculosis. Drug Development Research. 2011; 72:501-508. Available from: doi:10.1002/ddr.20456.
14. Abu Ruz S, Jaber D, Basheti I, Sadeq A, Arafat M, Al Ahmad M, et al. Impact of pharmacist interventions on drugrelated problems in general surgery patients: A randomised controlled trial. European Journal of Hospital Pharmacy. 2021; 28:728. Available from: doi:10.1136/ejhpharm-2020-002206.
15. Song YK, Jeong S, Han N, Na H, Jang HY, Sohn M, et al. Effectiveness of clinical pharmacist service on drugrelated problems and patient outcomes for hospitalized patients with chronic kidney disease: A randomized controlled trial. Journal of Clinical Medicine. 2021;10:1788. Available from: doi:10.3390/jcm10081788.
16. Sagita VA, Bahtiar A, Andrajati R. Evaluation of a clinical pharmacist intervention on clinical and drugrelated problems among coronary heart disease inpatients: A preexperimental prospective study at a general hospital in Indonesia. Sultan Qaboos University Medical Journal. 2018;18:817. Available from: doi:10.18295/squmj.2018.18.01.013.
17. Shivaraj G, Murali krishnan, Nijeesh. Study on drug related problems in tuberculosis patients with co morbidities in a tertiary care teaching hospital. European Journal of Pharmaceutical and Medical Research. 2017;4:756-67. Available from: https://www.ijbcp.com/index.php/ijbcp/article/view/4208.
18. Fei C M, Zainal H, Ali I, Ali H. Evaluation of adverse drug reactions induced by anti-tuberculosis drugs in hospital pulau pinang. Malaysian Journal of Medical Sciences. 2018;25:103-14. Available from: doi:10.21315/mjms2018.25.5.10.
19. Krishna G K, Ananthakrishnan S, Reddy T. Study on adherence to anti tuberculosis drugs under DOTs and Non-DOTs and factors affecting adherence. World Journal of Pharmacy and Pharmaceutical Sciences. 2020; 6:1973-86. Available from: https://www.ijbcp.com/index.php/ijbcp/article/view/4208.
20. Gube A A, Debalkie M, Seid K, Kiberlem. Assesment of anti-TB drug nonadherence and associated factors among TB patients attending TB clinics in Arba Minch government health institution. Tuberculosis Research and Treatment. 2018:1-7. Available from: doi:10.1155/2018/3705812.
21. Nowinski A, Wesołowski S, Korzeniewska-Koseła M. The impact of comorbidities on tuberculosis treatment outcomes in Poland: a national cohort study. Frontiers in Public Health. 2023; 11:1253615. Available from: doi:10.3389/fpubh.2023.1253615.
22. Tharanon V, Putthipokin K, Sakthong P. Drug-related problems identified during pharmaceutical care interventions in an intensive care unit at a tertiary university hospital. SAGE Open Medicine. 2022;10:20503121221090881. Available from: doi:10.1177/20503121221090881.
23. Herawati F, Fahmi EY, Pratiwi NA, Ramdani D, Jaelani AK, Yulia R, Andrajati R. Oral anti-tuberculosis drugs: An urgent medication reconciliation at hospitals in Indonesia. Journal of Public Health Research. 2021;10:1896. Available from: doi:10.4081/jphr.2021.1896.
24. Hema NG, Bhuvana KB, Virupaksha HM. Critical assessment of adverse drug reactions to antitubercular drugs in a government teaching hospital. International journal of basic science in medicine. 2013;4:607. Available from: doi.org/10.1136/bmjgh-2020-003979.
25. Ormerod LP, Horsfield N. Frequency and type of reactions to antituberculosis drugs: Observations in routine treatment. Tuberculosis and Lung Disease. 1996;77:3742. Available from: doi:10.1016/s0962-8479(96)90073-8.
26. Schaberg T, Rebhan K, Lode H. Risk factors for sideeffects of isoniazid, rifampin and pyrazinamide in patients hospitalized for pulmonary tuberculosis. European Respiratory Journal. 1996;9:202630. Available from: doi:10.1183/09031936.96.09102026.

HOW TO CITE THIS ARTICLE: Raja BY, Ganachari MS. Identification and Evaluation of Drug-Related Problems to FirstLine Therapy of Antitubercular Drugs among the Pulmonary Tuberculosis Patients in a Tertiary Care Hospital- A Randomised Controlled Study. Int. J. Pharm. Sci. Drug Res. 2024;16(2):142-148. **DOI:** 10.25004/IJPSDR.2024.160202