Original Research Article

PRESCRIBING PATTERN OF ANTI TUBERCULAR DRUGS IN PATIENTS OF TUBERCULOSIS IN TERTIARY CARE TEACHING HOSPITAL, HALDWANI, UTTARAKHAND

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Abstract

Background: Tuberculosis (TB) is a public health concern in India and its successful treatment can be procured by prescribing anti-TB drugs according to current Standard NTEP & PMDT guidelines for TB management which further may help in reducing the number of adverse drug reactions (ADRs) encountered & emergence of Drug Resistant TB. This study was aimed to evaluate the prescribing habits of anti-TB drugs. **Materials and Methods:** This was an observational open labelled cross sectional study conducted in the department of Pharmacology and department of Respiratory Medicine, GMC Haldwani, Uttarakhand from January 2023 to June 2024. The data regarding the prescription pattern was recorded in the structural proforma. The data was analyzed using the JASP software for Windows version 0.18.3. **Result:** Total number of 361 TB patients were included in the study out of 389 after meeting the inclusion criteria and written informed consent. The prescriptions were analyzed and compared to the standard NTEP & PMDT guidelines. Majority of the analyzed prescriptions followed the standard guidelines for the treatment of TB and WHO core prescribing indicators. The mean age was 40 years along with male preponderance. **Conclusion:** The analysis of prescribed regimens in 361 patients showed 97.5% adherence to NTEP and PMDT Guidelines for TB treatment highlighting the pronounced awareness among the public health sectors regarding the rational prescribing practices with better treatment outcomes of TB therapy.

INTRODUCTION

Tuberculosis (TB) is a communicable disease, usually caused by Mycobacterium tuberculosis. It is a major cause of infectious deaths worldwide.[1] According to the Global Tuberculosis Report 2023, an estimated 7.5 million new TB cases were diagnosed with 1.30 million deaths among TB patients in year 2022.[2] The National Tuberculosis Elimination Programme (NTEP) of India's Annual Status Report 2024 has reported an incidence of 199 new TB cases per lakh population with TB mortality of 23 per lakh population in India in year 2022.[3] Despite of the established treatment guidelines for TB management, significant number of medical practitioners deviate from these guidelines, resulting in wrong/missed diagnosis, treatment failures, drug side effects, and the development of drug-resistant TB (DR-TB). This non-compliance on the part of medical practitioners adversely impacts individual well-being and causes substantial socio-economic loss to the country. A systematic review done by Langendam MW et al. found that most TB prescriptions were written with inappropriate treatment regimens, contributing to drug resistance.[4] Another study conducted by Singh A et al. assessed tuberculosis treatment practices among health practitioners in North India, concluding that inappropriate practices highlight the need for awareness to ensure rational prescriptions and better

915

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treatment outcomes.[5] Udwadia ZF et al. have reported that limited knowledge about the National TB Elimination Program and its guidelines could result in incorrect prescriptions, further contributing to drug resistance and complicating TB treatment.[6] Due to the paucity of data and literature in the Kumaon Region of Uttarakhand regarding the prescription pattern of anti-tubercular drugs, this study was therefore undertaken to study the anti-TB prescription pattern of anti-tubercular drugs (ATDs) experienced by the patient treated at a tertiary care center of Kumaon region of State of Uttarakhand. The results of this study are expected to provide important feedback to the NTEP and Pharmacovigilance managers which in turn will help them in formulating the strategies directed at optimal management of TB in the country.

MATERIALS AND METHODS

This was an observational open labeled cross sectional study which was carried out from January 2023 to June 2024. After taking the approval from Institutional Ethical Committee (667/GMC/IEC/2022/Reg. No. 654/IEC/R-20-11-22) and obtaining the written informed consent from the patients, those meeting the inclusion criteria for the study were recruited. Sampling technique is shown in [Figure 1].

Inclusion Criteria
- Patients with Drug Sensitive TB of 18 years and above age reporting to Respiratory Medicine Department
- Patients with Drug Resistant Tuberculosis of 18 years and above age reporting to Respiratory Medicine Department.
- Patients diagnosed with TB and registered at Nodal DR-TB Centre, situated in the Department of Respiratory Medicine, Government Medical College, Haldwani, Uttarakhand.

Exclusion Criteria
- Patients with age less than 18 years.
- Patients not willing to participate in the study.

- HIV 1 and 2 reactive patients.
- Patients with pre-treatment hemoglobin <8 gm%, myelosuppression, blood disorders, pancytopenia, thrombocytopenia, neutropenia, peripheral neuropathy or ocular disease.
- Pregnant females.
- Chronic bed ridden patients.

Study procedure: A total of 361 TB patients of either sex aged 18 years or above were included in the study. Detailed history / examination were evaluated. Details of medication, frequency, route, clinical diagnosis were recorded and prescriptions analysis was done on basis of WHO core prescribing indicators[7] and treatment regimen prescribed was compared with standard NTEP[8] and PMDT treatment regimen[9] for TB management.

Statistical Analysis: Data was collected and recorded in Microsoft Excel 2013 Spreadsheet and later checked for any possible errors in JASP (Jeffreys's Amazing Statistics Program.) for Windows version 0.18.3 (released on 12th January 2024 by University of Amsterdam). Analysis was also carried out using same software. Categorical data was presented as percentage (%). The descriptive analysis of data was presented in graphs and percentages.

RESULTS

A total of 361 TB patients were recruited and evaluated in the present study. Out of 361 patients, 210 (58.2%) were males and 151 (41.8%) were females as shown in [Figure 2]. The minimum and maximum age was evaluated and categorized into various age groups as depicted in [Figure 3]. The mean age came out to be 40 years. The demographic profile of selected patients is explained in [Table 1]. Majority were from rural areas (62.9%) and Most of them were students (27.4%) followed by housewives (21.1%). Positive family history of TB was found in 49 patients (13.6%).

Table 1: Demographic profile of patients.

Variable	Number of Patients (n)	Percentage (%)
Location		
Rural	227	62.9%
Urban	134	37.1%
Occupation		
Students	99	27.4%
Housewives	76	21.1%
Unemployed	45	12.5%
Positive Family history of TB		
Present	49	13.6%
Absent	312	86.4%

Table 2: Distribution of patients according to type of diagnosis

S.No.	Diagnosis	New case n (%)	Recurrent case n (%)	Total n (%)
1	Rifampicin Sensitive TB	163 (78%)	46 (22%)	209 (57.9%)
2	Rifampicin Resistant TB	91 (98.9%)	1 (1.1%)	92 (25.5%)
3	MDR Tuberculosis	21 (87.5%)	3 (12.5%)	24 (6.6%)
4	Pre XDR tuberculosis	15 (100%)	0	15 (4.2%)
5	XDR tuberculosis	0	0	0

6	Isoniazid Monoresistant TB	21 (100%)	0	21 (5.8%)
Total Patients		311	50	361 (100%)

Table 3: Different types of regimens used in TB patients:

S.No.	Diagnosis	Type of Regimen used	No. of patients (n)
1	Rifampicin Sensitive TB	FDC – HRZE	162
2	Rifampicin Resistant TB	Lfx + Bdq + Cfz + Lzd + Cs	67
3	MDR Tuberculosis	Lfx + Bdq + Cfz + Lzd + Cs	13
4	Isoniazid Monoresistant TB	R + Z + E + Lfx	20

Isoniazid (H), Rifampicin (R), Pyrazinamide (Z), Ethambutol (E), Levofloxacin (Lfx), Clofazimine (Cfz), Linezolid (Lzd) and Cycloserine (Cs).

Table 4: Different types of regimens used in Pre XDR TB patients

S. No.	Type of Regimen	No. of Patients n (%)	S. No.	Type of Regimen	No. of Patients n (%)
1	Cfz + Eto + Cs	2 (13.4%)	7	Bdq + Cfz + Am +Cs	1 (6.7%)
2	Z + Eto + Lzd + Cs	1 (6.7%)	8	Lfx + Bdq + Cfz + Eto + Cs	1 (6.7%)
3	E + Bdq + Cfz + Eto + Cs	2 (13.4%)	9	Z + Bdq + Cfz + Eto + Lzd + Cs	1 (6.7%)
4	Z + E + Bdq + Cfz + Eto + Cs	1 (6.7%)	10	Bdq + Cfz + Lzd	1 (6.7%)
5	Z + E + Cfz + Eto + Cs	1 (6.7%)	11	Z + Bdq + Cfz + Eto + Am + Cs	1 (6.7%)
6	Z + Bdq + Cfz + Eto + Am + Lzd + Cs	2 (13.4%)	12	Z + Bdq + Cfz + Lzd + Cs	1 (6.7%)

Pyrazinamide (Z), Ethambutol (E), Levofloxacin (Lfx), Ethionamide (Eto), Cycloserine (Cs), Amikacin (Am), Bedaquiline (Bdq), Clofazimine (Cfz), Linezolid (Lzd)

Table 5: Analysis of prescription using WHO core prescribing indicators

| S. No	WHO core prescribing indicators	Number or Percentage
1	Average number of drugs per counter	4.9
2	Percentage of drugs prescribed by Generic name	90.9%
3	Percentage of encounter with Anti-tubercular drugs (ATDs) prescribed	100%
4	Percentage of concomitant therapy prescribed	95.8%
5	Percentage of encounter with injections prescribed	21.4%
6	Percentage of drugs prescribed by essential list of formulary	77.1%
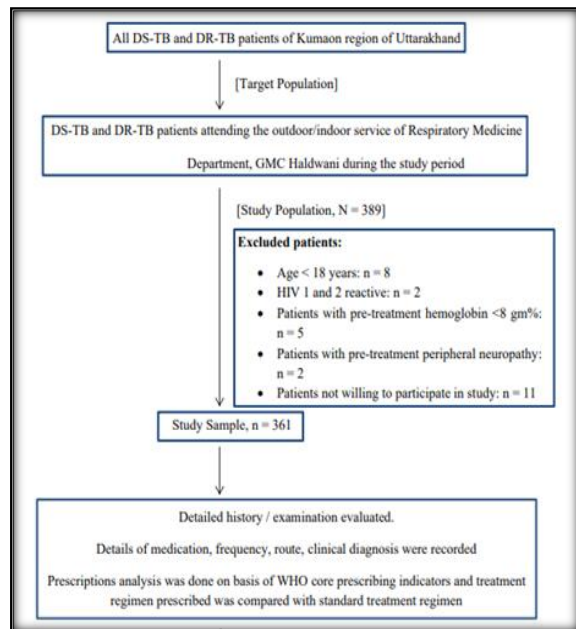
Figure 1: Sampling technique
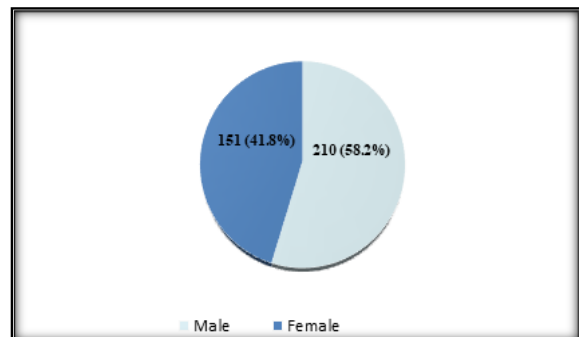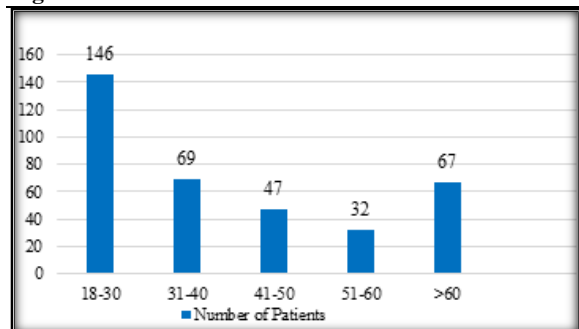

Figure 2: Gender distribution
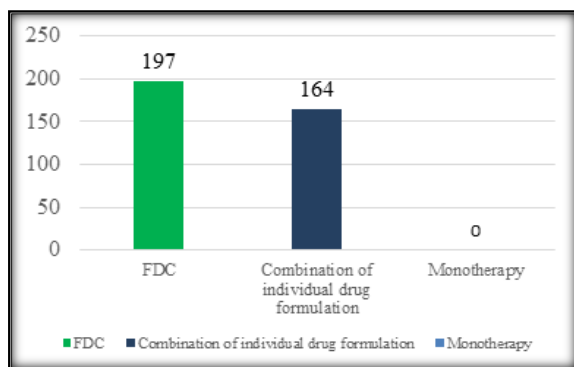

Figure 3: Age distribution

Figure 4: Type of Antitubercular therapy

The selected patients were divided according to their diagnosis as drug sensitive or drug resistant tuberculosis. Most common type of diagnosis was PTB (91.1%) which included majority of new cases of rifampicin sensitive tuberculosis (163). Details are explained in [Table 2].

Most commonly prescribed regimen of antitubercular drug was the fixed combination of isoniazid/rifampicin/pyrazinamide/ethambutol (HRZE) given in 162 patients for treatment of rifampicin sensitive TB. Most common regimen used for rifampicin resistant TB and MDR-TB patients was the combination of levofloxacin, bedaquiline, clofazimine, linezolid and cycloserine in 67 and 13 patients respectively. The regimen prescribed for isoniazid monoresistant TB patients included rifampicin, pyrazinamide, ethambutol and levofloxacin in 20 patients as explained in [Table 3 & 4]. 197 patients were prescribed with fixed dose combination (54.6%) and rest 164 was prescribed the combination of single drug formulations (45.4%) as shown in [Figure 4]. Most of the prescriptions analyzed followed the standard treatment guidelines for TB management (97.5%). The most common comorbidity encountered was Diabetes mellitus (12.7%). Most common concomitant drug prescribed was pyridoxine (273, 75.6%).

The WHO core prescribing indicators serve as an important parameter for the assessment of overall prescribing pattern and its rationality in a health care facility. The current study concludes that the drug prescribing practices were in concordance with WHO core prescribing indicators where 91.4% of the drugs were prescribed by their generic name which is almost identical with the WHO standard (100%) and 77.1% of the drugs prescribed were from essential drugs list or formulary. All prescriptions followed the national TB treatment guidelines provided by NTEP and PMDT Guidelines 2021 [Table 5].

DISCUSSION

The present study was done to evaluate the prescribing practices of anti-TB drugs in the public sector setting. In this study, males were more affected by TB (58.2%).[7-9] Krishnakanth K et al. have also reported male preponderance.[10] This male preponderance may be due to more outdoor activity and higher level of exposure to several risk factors such as smoking and alcohol.[11] It is important to note that 67 (31.9%) of the male subjects in our study were smoker & 31 (14.8%) were alcoholic, whereas only 3 (2%) of the females were smoker only. Majority of TB patients were aged between 18 to 30 years (40.4%), with mean age of 40 years. Majumdar P et al. have also reported that TB commonly affects young adults.[12] This highlights that TB affects the economically productive age group which may adversely impact the economy of the country. The present study also found that majority of TB patients was from rural areas (227, 62.9%). Sathiyamoorthy et al. in their meta-analysis have also observed higher prevalence of TB in rural populations which they associated with lack of awareness and close contact with infectious TB patients.[13] The most common comorbidity associated with TB was Diabetes Mellitus (12.7%). Carla M.A et al. have observed that increasing incidence of DM may be responsible for high TB incidence and prevalence.[14]

Prescription pattern analysis: Majority of patients (91.1%) were diagnosed with pulmonary TB, while 32 patients (8.9%) had extrapulmonary TB, with lymph node TB being the most common form (46.8%). Most patients were rifampicin-sensitive (57.9%), while 25.5% had rifampicin-resistant TB (RR-TB). There were 24 (6.6%) MDR-TB, 21 (5.8%) isoniazid monoresistant TB and 15 (4.2%) Pre XDR-TB patients.

Majority of DS-TB patients were prescribed potentially curative regimen that conformed to NTEP recommendations, i.e. DOTS FDC in 196 (93.8%) patients. Non FDC or single drug formulations of H, R, Z and E were prescribed in 13 (6.2%) patients due to intolerance to ATT and in context to adverse effects of anti-TB drugs experienced by the patients such as hepatotoxicity, hyperuricaemia, reversible vision loss etc. The most common regimen prescribed for DR-TB patients was that recommended in the PMDT 2021 guidelines, i.e. a combination of levofloxacin, bedaquiline, clofazimine, cycloserine, and linezolid followed by combination of Lfx, Lzd, Cfz & Cs. This regimen was used in 67 cases (72.8%) of RR-TB and 13 cases (54.2%) of MDR-TB patients.

Of the analyzed prescriptions for DS-TB and DR-TB, 97.5% were conforming to the standard NTEP and PMDT 2021 guidelines for the management of TB in our study. A cross-sectional study by Nautiyal RG and Singh RK found that most of the health professionals in private sector did not follow the NTEP guidelines for TB treatment.[15] A systemic review by Langendam MW et al. found the inappropriate TB treatment regimens being prescribed which further contributed to development of drug resistance and poor treatment outcome which was not observed in our study.[4] Limited knowledge about NTEP may result in incorrect prescriptions for TB treatment as concluded by

918

Udwadia ZF et al. study.[6] Krishnakanth et al. explained that following the national treatment guidelines for the management of TB and regular monitoring of patients may result in better treatment outcome, improvement in patient's compliance to therapy, early detection and management of ADRs and minimal risk of development of drug resistance.[10]

The average number of all drugs prescribed was 4.9 drugs per prescription. Of these, 64 drugs were prescribed using generic names, consistent with WHO guidelines. All 15 antitubercular drugs (100%) were prescribed by their generic name. Among concomitant drugs, 49 out of 55 drugs were prescribed by generic name. Prescribing medications by their generic names is crucial for promoting rational prescribing practices among health professionals. This approach can reduce dispensing errors, lower prescription costs, and enhance overall treatment efficiency. Educating healthcare professionals about rational prescribing practices and familiarizing them with national TB treatment guidelines can further support this practice. Overall, 77.1% of all prescribed drugs were from NLEM 2022, indicating predominant adherence to national formulary. In contrast, Joshi R et al. found that only 47.6% of their evaluated prescriptions with generic names, falling short of WHO prescribing guidelines 16. Similarly, Yilma Z et al. noted that prescribing practices among health professionals often deviated from WHO guidelines, highlighting the need for enhanced training and awareness to promote rational prescribing practices.[17] Our study's findings suggest rational prescribing practices, likely due to the setting in a government tertiary care hospital where chest specialists are well-versed in WHO and NTEP guidelines for TB treatment resulting in increased patient compliance with ATT, better treatment outcomes and a minimized risk of developing drug resistance and minimizing the risk of prescription errors.

CONCLUSION

In the present study on prescribing pattern of antitubercular drugs in patients of TB, we conclude that majority of the analyzed prescriptions followed the current NTEP and PMDT 2021 standard treatment guidelines for TB management which might be due to conduction of our study at a tertiary care public sector setting where doctors are well-versed with the guidelines contributing to better treatment outcomes and a minimized risk of developing drug resistance. The findings of the present study highlights that the public sectors have better treatment outcome of TB. This message has to be spread among the TB treatment seekers, so that better compliance, optimum TB care and minimization of TB related deaths may be achieved.

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919

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