



A STUDY ON THE ADVERSE EFFECTS IN DRUG SENSITIVE & MULTI DRUG RESISTANT TUBERCULOSIS PATIENTS IN A TERTIARY CARE CENTRE IN RAJASTHAN.

Pulmonary Medicine

Dr. Balram Chouhan	Junior Resident, Dept. Of Respiratory Medicine, Government Medical College Kota, Rajasthan.
Dr. Anil Saxena	Senior Professor, Dept. Of Respiratory Medicine, Government Medical College Kota, Rajasthan.
Dr. Babulal Bansiwal	Assistant Professor, Dept. Of Respiratory Medicine, Government Medical College Kota, Rajasthan.
Dr. Unnikrishnan R	Junior Resident, Dept. Of Respiratory Medicine, Government Medical College Kota, Rajasthan.
Dr. Santosh Kumar Bairwa	Junior Resident, Dept. Of Respiratory Medicine, Government Medical College Kota, Rajasthan.

ABSTRACT

Introduction: Tuberculosis (TB) is a preventable and curable infectious disease which is caused by *Mycobacterium tuberculosis* bacteria. Every year, 10 million people fall ill with tuberculosis (TB). The present study is intended to study the adverse effects of treatment in drug sensitive & multi drug resistant tuberculosis patients. **Materials And Method:** This prospective observational study was conducted in the Respiratory Medicine Department of Government medical college Kota Rajasthan July 2022 to December 2023. Two hundred patients were evaluated and followed up over the course of treatment, and the side effects were thoroughly inquired about. **Results:** The study reports various adverse effects experienced by tuberculosis patients at a tertiary care center, with gastric intolerance being the most common, affecting 6.5% of patients. Other adverse effects include hepatitis (3.5%), neuropathy (3%), arthralgia (2%), rash (1.5%), visual disturbances (1%), and nephrotoxicity (0.5%). **Conclusion:** To improve patient adherence and treatment outcomes, it is crucial to enhance communication between patients and healthcare providers and to actively manage side effects.

KEYWORDS

ADR-Adverse drug reactions, CBNAAT-Cartridge based nucleic acid amplification test, EPTB -Extra pulmonary tuberculosis, MTB- *Mycobacterium Tuberculosis*, PTB -Pulmonary tuberculosis

INTRODUCTION

Tuberculosis (TB) is a preventable and curable infectious disease which is caused by *Mycobacterium tuberculosis* bacteria. Every year, 10 million people fall ill with tuberculosis (TB). Despite being a preventable and curable disease, it is the leading cause of death from a single infectious agent. TB is curable if therapy is started immediately, appropriately and continues throughout the treatment period⁽¹⁾. However, high treatment default, adverse events, treatment interruption, non-adherence to medication, combined with a lack of knowledge about TB, contribute to poor treatment outcomes⁽¹⁾.

An adverse event is any untoward medical occurrence in a clinical study subject administered a medicinal (investigational or non-investigational) product. A patient who develops mild to moderate adverse effect may continue TB treatment with symptomatic treatment. If a patient develops severe to life-threatening side effect, the responsible drug or the entire regimen may need to be stopped and the patient should be immediately referred to an appropriate higher health facility for further assessment and treatment.

MATERIALS AND METHODS

This prospective observational study was conducted in the department of Respiratory medicine in Government medical college Kota in collaboration with the nodal DR-TB centre on MDR and XDR patients. During a study duration from July 2022- December 2023. After ensuring the completeness of the data, descriptive analysis was done. Measures of association was computed based on the type of variables. Categorical variables were compared using Chi-square (χ^2 test) and continuous variables were recorded as median and interquartile ranges. Linear and multiple Logistic regression analysis was performed to seek the predictors for faster sputum conversion rates. Interim and final outcomes were recorded and analyzed for factors predicting failure. P value < 0.05 was considered statistically significant. All statistical analysis was performed using The Statistical Package for Social Science (SPSS) software version 29.0. Ethical approval was obtained from institutional ethical committee. For follow-up, verbal consent from care givers of the patient were also obtained.

RESULTS:

We enrolled about 200 patients during the aforementioned study

period. Among the study population, 58% were males and 42% were females. Age group of the study population ranges from 18 to 85 years with a mean age of 53.02 ± 18.75 years. Age group of the study population ranges from 18 to 85 years with a mean age of 53.02 ± 18.75 years. 42.5% of the study population belongs to the age group of more than 60 years. Followed by 50 to 60 years (19%), 18 to 30 years (16%) and so on. The demographic and clinical details of the study population have been summarised in Table 1 and Figure 1,2.

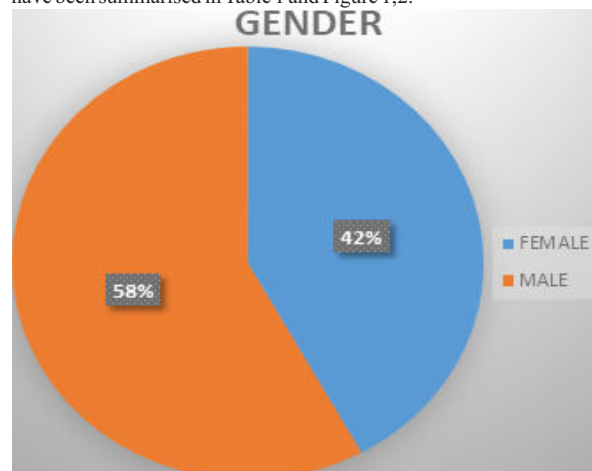


Figure-1: Gender Distribution

Table 1: Age Distribution

Age	Frequency	Percent
18-30	32	16.0
30-40	22	11.0
40-50	23	11.5
50-60	38	19.0
>60	85	42.5
Total	200	100.0

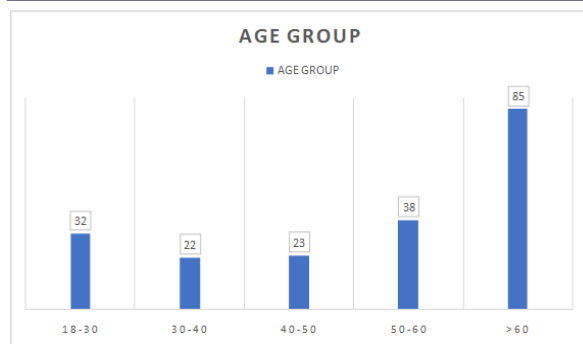


Figure-2: Age Distribution

Pulmonary tuberculosis (PTB) was diagnosed in nearly two thirds of the study participants, with extra-pulmonary tuberculosis (EPTB) accounting for the rest of the sample. Among the 134 pulmonary TB patients, 92% were drug sensitive TB (DSTB) and the remaining 8% were drug resistant TB (DRTB). Among extra-pulmonary TB patients 95.5% were drug sensitive whereas 4.5% were drug resistant cases (Figure 3,4).

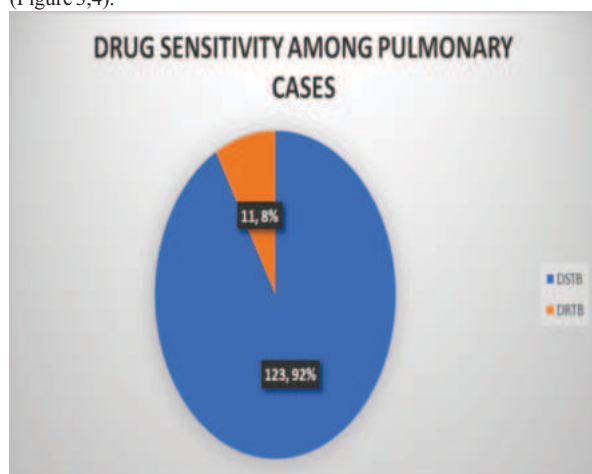


Figure-3: Drug Sensitivity Among Pulmonary TB

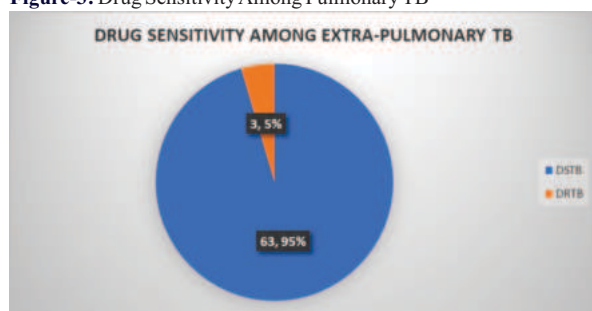


Figure-4: Drug Sensitivity Among Extra Pulmonary TB

When the side effects of anti-tubercular medications were analysed, the most common adverse effect was gastric intolerance (6.5%); followed by hepatitis (3.5%), neuropathy (3%), arthralgia (2%), rash (1.5%), visual disturbances (1%) and nephrotoxicity (0.5%). Similar results were obtained by studies which were conducted in different parts of India (Figure 5).



Figure-5: Adverse Effects Of ATT

DISCUSSION:

Among the study population, 58% were males and 42% were females. This data is consistent with the epidemiological trend of tuberculosis in India, where males are more affected than females. A study conducted by Sharma et al. reported the incidence of TB was higher among males as compared to females because males are more likely to also smoke and have alcohol and drug addictions compared to females, which increase their risk of contracting tuberculosis⁽²⁾.

Age group of the study population ranges from 18 to 85 years with a mean age of 53.02 ± 18.75 years. 42.5% of the study population belongs to the age group of more than 60 years. Followed by 50 to 60 years (19%), 18 to 30 years (16%) and so on. According to a study by Sharan Murali et al., the study participants mean (SD) age was 43.7 (14.6) years; the mean (SD) for the non-senior group was 40.2 (12) years, and the mean (SD) for the elderly group was 65.8 (6.2) years. The percentage of elderly TB cases was 15.6% (95%CI: 13.6%-17.6%), with almost 71% of cases occurring in the 60–69 age group⁽³⁾.

Pulmonary tuberculosis (PTB) was diagnosed in nearly two thirds of the study participants, with extra-pulmonary tuberculosis (EPTB) accounting for the rest of the sample. As per the India TB report of 2023, out of all diagnosed cases of TB, 76% were of pulmonary TB, with the rest cases being extra-pulmonary TB. In the state of Rajasthan, pulmonary tuberculosis accounts for 80.5% of all diagnosed tuberculosis cases⁽⁴⁾. Among the 134 pulmonary TB patients, 92% were drug sensitive TB (DSTB) and the remaining 8% were drug resistant TB (DRTB). Among extra-pulmonary TB patients 95.5% were drug sensitive whereas 4.5% were drug resistant cases. Within the 189 cases of extrapulmonary tuberculosis that were studied by Dusthacker A et al., 37 cases (19%) were multidrug resistant (MDR), and one case (XDR) was extremely drug resistant⁽⁵⁾.

ADRs can range from minor gastrointestinal disturbances to major hepatotoxicity, ototoxicity, nephrotoxicity, peripheral neuropathy, cutaneous ADRs, etc. and are influenced by a number of circumstances. The majority of ADRs are mild and manageable without stopping medication. Some ADRs can be serious or severe, resulting in potentially fatal events or changing or stopping a treatment plan if they are not identified and treated promptly.⁽⁶⁾

The most common adverse effect from this study was gastric intolerance (6.5%); followed by hepatitis (3.5%), neuropathy (3%), arthralgia (2%), rash (1.5%), visual disturbances (1%) and nephrotoxicity (0.5%). Similar results were obtained by studies which were conducted in different parts of India.

According to a different study by Laghari M. et al., out of 508 patients, 67 (13.2%) reported a total of 105 ADRs. The most common ADRs found were gastrointestinal disorders (65.7%), followed by arthralgia (24.8%). ADRs were classified as probable in about 65 cases (61.9%) and as mildly severe in 78 cases (74.3%) during the course of the research. Mild hepatotoxicity was noted in four patients in total. The results of multivariate analysis indicated that retreatment (OR; 22.32), absence of a BCG scar (OR; 17.84), and female (OR; 2.66) were the independent factors that showed a statistically significant association with ADRs.⁽⁷⁾

A similar study conducted in Himachal Pradesh by A Sood et al reported that adults with a mean age of 40.79 ± 16.79 years reported the highest ADRs. Regarding pulmonary and extrapulmonary tuberculosis cases, there were 62% MDR-TB patients on the DOTS-plus regimen, 35% on Cat1 ATT, and 3% of cases were XDR-TB. CNS-related ADRs accounted for 44 (27.5%) of all ADRs in patients receiving MDR therapy; they were followed in frequency by gastrointestinal system ADRs (19%), psychiatric ADRs (20 12.5%), otovestibular ADRs (8%) and ophthalmic ADRs (0.6%). In comparison, among patients on Cat 1 ATT, the most common adverse drug reactions (ADRs) included the gastrointestinal system (44%) and CNS (12%), with psychiatric and ADRs pertaining to otovestibular symptoms having the lowest incidence (1%)⁽⁸⁾.

The similarities in study outcomes concerning defaulting and adverse drug reactions (ADRs) among tuberculosis (TB) patients in Rajasthan compared to other studies with the same objective may stem from several common factors. Firstly, adherence to standardized treatment protocols and guidelines, such as the Directly Observed Treatment Short-course (DOTS) strategy, across different regions can lead to

consistent outcomes in TB management. Similarities in patient demographics, including age, gender distribution, and socio-economic status, may also contribute to comparable rates of treatment adherence and ADR occurrences. These shared elements underscore the robustness and generalizability of findings across diverse geographic settings, enhancing our understanding of effective TB management strategies globally.

These factors underscore the importance of contextualizing findings within the specific regional context and considering the nuanced interplay of healthcare delivery, patient behaviors, and research methodologies when interpreting study outcomes in TB management.

CONCLUSION

The study identifies various adverse effects experienced by tuberculosis patients at a tertiary care center, highlighting gastric intolerance as the most prevalent issue, affecting 6.5% of patients. Other reported adverse effects include hepatitis (3.5%), neuropathy (3%), arthralgia (2%), rash (1.5%), visual disturbances (1%), and nephrotoxicity (0.5%). To improve patient adherence and treatment outcomes, it is crucial to enhance communication between patients and healthcare providers and to actively manage side effects. Implementing customized support and educational initiatives can significantly reduce treatment default rates and improve results for both drug-sensitive and multi-drug resistant TB cases. This approach ensures that patients are better informed and supported throughout their treatment journey, ultimately leading to more effective management of tuberculosis.

LIMITATIONS

The generalizability of the study's findings may be restricted by regional disparities in healthcare facilities and access throughout Rajasthan. Issues with the study's methodology, such as the reliance on retrospective data, small sample sizes, and incomplete patient histories, may compromise the accuracy of the results. Additionally, cultural and behavioral differences across the region could introduce biases, affecting the applicability of the conclusions. Therefore, it is essential to approach the interpretation of these findings with caution and consider context-specific factors when formulating broader healthcare policies and tuberculosis treatment strategies.

REFERENCES

- [1] Conradie F, Meintjes G, Hughes J, et al. Clinical access to Bedaquiline Programme for the treatment of drug-resistant tuberculosis. *S Afr Med J* 2014;104: 164-166
- [2] Sharma N, Malhotra R, Taneja DK, Saha R, Ingle GK. Awareness and perception about tuberculosis in the general population of Delhi. *Asia Pacific Journal of Public Health*. 2007 Jun;19(2):10-5.
- [3] Murali S, Krishnamoorthy Y, Knudsen S, Roy G, Ellner J, Horsburgh CR, Hochberg N, Salgame P, Prakash Babu S, Sarkar S. Comparison of profile and treatment outcomes between elderly and non-elderly tuberculosis patients in Puducherry and Tamil Nadu, South India. *PLoS One*. 2021 Aug 27;16(8):e0256773. doi: 10.1371/journal.pone.0256773. PMID: 34449817; PMCID: PMC8396735.
- [4] Global tuberculosis report 2023. Geneva WHO Global tuberculosis report 2023 (who.int)
- [5] Dusthacker A, Sekar G, Chidambaram S, Kumar V, Mehta P, Swaminathan S. Drug resistance among extrapulmonary TB patients: Six years experience from a supranational reference laboratory. *Indian Journal of Medical Research*. 2015 Nov 1;142(5):568-74
- [6] Sarpal SS, Goel NK, Kumar D, Janmeja AK. Reasons for interruption of anti-tubercular treatment among the retreatment patients in category II of RNTCP in Chandigarh, north India. *Indian J Tuberc*. 2014 Apr;61(2):121-8. PMID: 25509934
- [7] Laghari M, Talpur BA, Sulaiman SA, Khan AH, Bhatti Z. Adverse drug reactions of anti-tuberculosis treatment among children with tuberculosis. *The International Journal of Mycobacteriology*. 2020 Jul 1;9(3):281-8.
- [8] Sood A, Bansal R, Sharma A, Himani H, Bhagra 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 Oct;4(10):4465-71