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Adverse Drug Reactions in Intensive / Initial Phase of Antitubercular Treatment in Patients of Tuberculosis

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Abstract: ***This study evaluated the incidence of adverse drug reactions ADRs during the intensive phase of antitubercular treatment ATT in tuberculosis patients. Over two years, 132 patients were monitored using Naranjos Algorithm and the Modified Hartwig and Siegel scale to assess ADR causality and severity. The results indicated that 37.88% of patients experienced ADRs, with hepatitis 38% and gastritis 32% being the most common. Extrapulmonary TB patients showed a higher ADR rate 55.26% compared to pulmonary TB patients 32.18%. DRTB patients had an ADR incidence of 88.89%, compared to 34.15% in DSTB. Most ADRs 48% occurred in the first week of treatment, emphasizing the need for early monitoring. The majority were moderate in severity, and 48% required treatment adjustments. Close monitoring during the early treatment phase is critical for managing ADRs and ensuring treatment adherence.***

Keywords: Adverse drug reactions, anti - tubercular treatment, tuberculosis, drug - resistant TB, drug - sensitive TB, hepatotoxicity, Naranjo's Algorithm, Modified Hartwig and Siegel scale.

1. Introduction

Tuberculosis (TB) remains a major global health issue, with India bearing the highest burden according to the World Health Organization's 2013 statistics, estimating around 2.1 million cases annually out of a global incidence of 9 million.[1] Notably, about 40% of India's population carries TB bacteria, predominantly in a latent state. The emergence of drug - resistant TB poses an increasing challenge, prompting the Indian government to declare TB a notifiable disease in 2012.[2- 3]

The National Tuberculosis Elimination Programme (NTEP) underscores the nation's commitment to eradicating TB by 2025, five years ahead of the global target. This shift highlights the critical need for research into the barriers preventing the elimination of the disease.[4]

With advances in medicine, TB is treatable with consistent and proper treatment. However, issues such as side effects from anti - TB drugs can lead to poor patient compliance, potentially fostering the development of multi - drug - resistant (MDR) TB and extensively drug - resistant (XDR) TB. Identifying and mitigating adverse drug reactions (ADRs) is crucial for improving patient compliance and reducing drug - resistant TB cases.[5 - 6]

Recent studies indicate that ADRs are prevalent among patients on the daily regime, underscoring the ongoing need for research into these reactions since the implementation of the new FDC - ATT under NTEP. The World Health Organization (WHO) defines ADRs as harmful and unintended responses to drugs that occur at normal doses used for disease prevention, diagnosis, or therapy. ADRs, a common reason for treatment interruptions, can be minimized through early recognition and management, thus enhancing treatment outcomes.[9 - 10]

The primary objective of the study was to assess the incidence of Adverse Drug Reactions (ADRs) during the Intensive/Initial phase of Anti - Tubercular Treatment in patients with Tuberculosis. The secondary objectives include evaluating the probability of ADRs using Naranjo's Algorithmic Scale and classifying the severity of ADRs by utilizing the Modified Hartwig and Siegel scale during the same treatment phase.

2. Material and Methods

This was a hospital - based descriptive study conducted to assess the incidence and nature of adverse drug reactions (ADRs) in patients undergoing anti - tubercular treatment (ATT) as per National Tuberculosis Elimination Program (NTEP) guidelines, which was conducted in the Department of Respiratory Medicine at a tertiary care hospital over a two - year period, from November 2022 to October 2024, following approval from the Institutional Ethics Committee.

Patients of all age groups and both genders who provided consent were included. The inclusion criteria for the study encompassed patients of any age and gender diagnosed with pulmonary, extrapulmonary, or both forms of tuberculosis

(TB), enrolled under the National Tuberculosis Elimination Program (NTEP) and receiving Anti - Tubercular Treatment (ATT). Patients who agreed to adhere to the prescribed TB treatment regimen, provided written informed consent, and committed to regular follow - up were included. Additionally, immune - compromised patients, such as those with HIV or diabetes mellitus, were part of the study. The exclusion criteria ruled out patients with pre - existing liver or kidney diseases, those suffering from other chronic conditions requiring concomitant medication, and individuals unwilling to provide informed consent or follow - up regularly. The study employed a prospective, observational, longitudinal descriptive clinical design for data collection and analysis.

3. Procedure

Patients were followed up at regular intervals every two months (day 0, 2 months, 4 months, 6 months, and 8 months) during the study period. At each follow - up visit, patients were asked about possible adverse drug reactions (ADRs) related to the Anti - Tubercular Treatment (ATT) they were receiving. In addition to in - person visits, telephonic follow - ups were conducted between visits to monitor any ADRs. These ADRs were recorded during regular outpatient department (OPD) visits or via telephone if necessary. Anticipated ADRs were identified, and their causality was assessed using Naranjo's Algorithm, while severity was determined using the Modified Hartwig - Siegel scale.

- **Data Collection:** Before inclusion in the study, participants provided written informed consent. Detailed clinical examinations and investigations, such as liver function tests (LFTs), kidney function tests (KFTs), and physical examinations, were performed to monitor ADRs.
- **Modified Hartwig - Siegel Scale:** This scale was used to assess the severity of ADRs and classify them into seven levels based on the need for treatment modification, hospitalization, and patient outcomes. Levels 1 and 2 represent mild ADRs, requiring no changes in treatment, while Levels 3 and 4 indicate moderate ADRs that may necessitate treatment modification or lead to hospitalization. Levels 5, 6, and 7 represent severe ADRs, ranging from intensive medical care to permanent harm or death.
- **Naranjo Adverse Drug Reaction Probability Scale:** This scale was used to determine the likelihood that an adverse event was drug - related, based on a series of weighted questions. The scale categorizes ADRs as definite, probable, possible, or doubtful based on the total score from questions related to timing, alternative causes, and dose - response relationships.
- **Data Analysis:** Data was analyzed using descriptive statistics, with results expressed as mean ± standard deviation (SD) and percentages.
- **Ethical Considerations:** The study was conducted with approval from the Institutional Ethics Committee. Written informed consent was obtained from all participants before inclusion. Adverse drug reactions were reported via NIKSHAY platform.

4. Results

Demographic information

The study included a total of 132 patients undergoing anti - tubercular treatment, with a gender distribution showing a higher prevalence among males. Specifically, 60.61% of the participants were male, while females constituted 39.39% of the study population. This indicates that tuberculosis and its subsequent treatment - related adverse drug reactions (ADRs) were more commonly observed in males in this cohort.

The age distribution of the participants reveals a diverse range of ages among those affected by tuberculosis. The largest age group was individuals less than 35 years, making up 40.15% of the subjects. This was followed by the 46 to 55 years age group, accounting for 19.70%, and those aged 36 to 45 years at 15.91%. Patients over 65 years represented 14.39% of the population, while the smallest group was the 56 to 65 years category, comprising 9.85%. (Table 1)

The occupational distribution of the participants highlights that tuberculosis predominantly affects unskilled workers, who made up 49.24% of the study population. Skilled workers accounted for 29.55%, while students and semi - skilled workers constituted 16.67% and 4.55%, respectively. This suggests a higher incidence of tuberculosis among individuals engaged in unskilled labor, possibly due to socioeconomic factors contributing to their vulnerability. (Table 1)

Table 1: Demographic information

Demographic information		Number	Percentage
Genderwise distribution	Females	52	39.39
	Males	80	60.61
Age distribution	Less than 35 years	53	40.15
	36 to 45 years	21	15.91
	46 to 55 years	26	19.7
	56 to 65 years	13	9.85
	More than 65 years	19	14.39
Occupation	Skilled	39	29.55
	Semi - skilled	6	4.55
	Unskilled	65	49.24
	Students	22	16.67
	Skilled	39	29.55

In this study, the most common ADR symptoms was vomiting (13.64%) and weakness (12.88%). Nausea affected 7.58% of participants, while joint pain and swelling were seen in 5.30%. Other unspecified symptoms were reported by 18.94%. Comorbidities included post - TB sequelae (26.52%), hypertension (9.09%), and diabetes (6.82%), with 4.55% having other conditions. Smoking was reported by 5.30%, while 0.76% were chronic alcoholics, with no cases of tobacco or substance abuse. (Table 2)

ADR events occurred in 37.88% of subjects, while 62.12% had no ADRs. Pulmonary TB was present in 71.21% of cases, while 28.79% had extrapulmonary TB.

Table 2: Clinical Presentation

Clinical Presentation		Number of subjects	Percentage
Symptoms	Vomiting	18	13.64
	Weakness	17	12.88
	Nausea	10	7.58
	Joint Pain & Swelling	7	5.3
	Others	25	18.94
Comorbidities	Post TB Sequelae	35	26.52
	Hypertension	12	9.09
	Diabetes Mellitus	9	6.82
	Others	6	4.55
Addictions	Smokers	7	5.3
	Chronic Alcoholic	1	0.76
	Tobacco abuse	0	0
	Substance Abuse	0	0
TB sequele		35	26.52
Incidence of ADR events	ADR	50	37.88
	No ADR	82	62.12
PTB/EPTB	PTB	94	71.21
	EPTB	38	28.79

Incidence of ADR and types of TB: The incidence of ADRs was notably higher in patients with EPTB, where 55.26% experienced ADRs, compared to 32.18% of those with PTB and 14.29% of those with both PTB and EPTB. The chi - square test yielded a statistic of 7.7355 with a p - value of 0.020905, indicating that the difference in ADR incidence between these groups is statistically significant at the $p < 0.05$ level. This suggests that patients with EPTB are at a higher risk of developing ADRs during anti - tubercular treatment. (Table 3)

Table 3: Incidence of ADR and types of TB

Comparison of various parameters with occurrence of ADR		ADR		No ADR	
		Number	Percentage	Number	Percentage
Incidence of ADR and types of TB	PTB	28	32.18	59	67.82
	EPTB	21	55.26	17	44.74
	Both PTB+EPTB	1	14.29	6	85.71
	Total	50	37.88	82	62.12
	Significance	The chi - square statistic is 7.7355. The p - value is 0.020905. The result is significant at p <.05.			
DS - TB/ DR - TB Distribution	DS - TB	42	34.15	81	65.85
	DR - TB	8	88.89	1	11.11
	Significance	The chi - square statistic is 8.4807. The p - value is 0.00			
Type of DR - TB regimen	Longer (n=5)	4	80	1	20
	Shorter (n=4)	4	100	0	0
	H - Monotherapy	0	0	0	0
	Total	8	88.89	1	11.11

DS - TB/DR - TB Distribution: There is a strong link between ADR occurrence and TB type. Among DS - TB patients, 34.15% experienced ADRs, while 65.85% did not. In DR - TB patients, 88.89% had ADRs, with only 11.11% not affected. Overall, 37.88% of the 132 patients experienced ADRs. A chi - square test with Yates correction (chi - square value: 8.4807, p - value: 0.003589) shows a significant association between TB type and ADRs, with DR - TB patients more prone to ADRs due to complex treatments. (Table 3)

Type of DR - TB regimen: ADRs occurred in 80% of patients on the longer regimen (4 out of 5), while 100% on the shorter regimen (4 out of 4) had ADRs. There were no patients on H - monotherapy. Overall, 88.89% of DR - TB patients had ADRs.

ADR reported during: ADRs were most frequent during the admission period (22.73%), followed by follow - up visits (14.39%), and least during outpatient visits (0.76%). Table 11: ADR Reporting. (Table 4)

Table 4: ADR Reporting

ADR Reporting		Number of subjects (n=50)	Percentage
ADR reported during	Admission	30	22.73
	Follow Up	19	14.39
	OPD	1	0.76
ADR developed after	24 hrs	4	8
	7 days	24	48
	14 days	11	22
	28 days	6	12
	56 days	5	10
Course followed for ADR	Symptomatic treatment given with ATT being continued	26	52
	ATT Witheld, started after ADR resolution	24	48

ADR developed after: The onset of ADRs varied, with 48% occurring within the first week of treatment. Another 22% developed within two weeks, 12% within one month, and 10% within two months. A smaller proportion (8%) appeared as early as day one, underscoring the importance of close monitoring, especially in the early stages of treatment.

Course followed for ADR: Management of ADRs involved two main approaches. In 52.00% of cases (26 individuals), patients continued their anti - tuberculosis treatment (ATT) with symptomatic treatment for ADRs. However, 48.00% of patients (24 individuals) had their ATT regimen replaced with a safer alternative until the ADRs resolved.

Types of ADRs reported: Hepatitis was the most common ADR, affecting 38.00% of subjects (19 individuals). Gastritis followed at 32.00% (16 subjects), cutaneous reactions at 14.00% (7 subjects), arthralgia at 8.00% (4 subjects), peripheral neuropathy at 6.00% (3 subjects), and vertigo was the least frequent ADR at 2.00% (1 subject). . (Table 5)

Table 5: Details of ADRs reported

Details of ADRs reported		Number of subjects	Percentage
Types of ADRs reported	Hepatitis	19	38
	Gastritis	16	32
	Cutaneous	7	14
	Athralgia	4	8
	Peripheral Neuropathy	3	6
	Vertigo	1	2
Severity of ADR	Mild	18	36
	Moderate	29	58
	Severe	3	6
	Life threatening	0	0
Causality score	Definite (Score: 9 or higher)	3	6
	Probable (Score: 5 - 8)	43	86
	Possible (Score: 1 - 4)	4	8
	Doubtful (Score: 0 or less)	0	0
Culprit Drug	Isoniazid + Pyrazinamide + Rifampicin + Ethambutol (All drugs)	15	30
	Isoniazid + Pyrazinamide + Rifampicin	17	34
	Pyrazinamide	4	8
	Linezolid	3	6
	Pyrazinamide + Ethambutol	1	2
	Streptomycin	1	2
	Ethambutol	1	2

Severity of ADR: The Modified Hartwig and Siegel Scale was used to classify the severity of ADRs. Mild ADRs (Levels 1 - 2), which are easily managed and do not require hospitalization, affected 18 subjects (36.00%). Moderate ADRs (Levels 3 - 4), requiring more intervention like changing medication or hospitalization, were observed in 29 subjects (58.00%). Severe ADRs (Levels 5 - 7), which can lead to serious health consequences, were reported in 3 subjects (6.00%). There were no life - threatening ADRs in the study. (Table 5)

Causality Score: The study assessed the causality of adverse drug reactions (ADRs) using the Naranjo ADR Probability Scale. A score of 9 or higher indicates a "Definite" causality, meaning there is a very high probability that the ADR was caused by the drug. A score between 5 and 8 is considered "Probable, " suggesting the ADR is likely due to the drug, though other factors may contribute. A "Possible" score, ranging from 1 to 4, implies that while the ADR could be linked to the drug, alternative explanations are equally or more plausible. A score of 0 or less falls under "Doubtful, " indicating that the ADR is unlikely to be related to the drug**.** The Naranjo ADR Probability Scale determined that 43 subjects (86.00%) had a "Probable" score (5 - 8), indicating a likely link between the drug and the ADR. Four subjects (8.00%) had a "Possible" score (1 - 4), suggesting other explanations could be involved. Only 3 subjects (6.00%) scored "Definite" (9 or higher), confirming the drug as the cause of the ADR. No ADRs were classified as "Doubtful. ". (Table 5)

Types of ADRs in DS - TB/DR - TB: The study compared ADRs between DS - TB (n=42) and DR - TB (n=8) patients. Hepatitis was reported by 38.10% of DS - TB and 37.5% of DR - TB patients. Gastritis occurred in 35.71% of DS - TB and 12.5% of DR - TB subjects. Cutaneous reactions were seen only in DS - TB patients (16.67%). Arthralgia was reported by 7.14% of DS - TB and 12.5% of DR - TB subjects. Peripheral neuropathy was absent in DS - TB but occurred in 37.5% of DR - TB patients. Vertigo was noted in 2.38% of DS - TB patients and none in the DR - TB group. The ADR profiles between DS - TB and DR - TB differed significantly, with peripheral neuropathy more common in DR - TB, and cutaneous reactions only in DS - TB (χ^2: 18.65, p - value: 0.00224). (Table 6)

Table 6: Types of ADRs reported with DS - TB/ DR - TB

Details of ADR		DS - TB (n=42)		DR - TB (n=8)	
		Number	Percentage	Number	Percentage
Types of ADRs reported	Hepatitis	16	38.1	3	37.5
	Gastritis	15	35.71	1	12.5
	Cutaneous	7	16.67	0	0
	Athralgia	3	7.14	1	12.5
	Peripheral Neuropathy	0	0	3	37.5
	Vertigo	1	2.38	0	0
	Significance	Chi - Square statistic (χ^2): 18.65, p - value: 0.00224			

Culprit drug: The most common combination causing ADRs was Isoniazid + Pyrazinamide + Rifampicin (34%, 17/50), followed by Isoniazid + Pyrazinamide + Rifampicin + Ethambutol (30%, 15/50). Pyrazinamide alone caused 8%, and Linezolid 6%. Less frequent combinations like Pyrazinamide + Ethambutol, Streptomycin, and Ethambutol alone each contributed 2%. . (Table 6)

Comparison of Types of Culprit Drug in DS - TB/DR - TB: In DS - TB, the most common culprit was Isoniazid + Pyrazinamide + Rifampicin (38.10%, 16/42), followed by the four - drug combination (33.33%, 14/42). Pyrazinamide (7.14%), Streptomycin (2.38%), and Ethambutol (2.38%) were less common. In DR - TB, Linezolid caused 37.5% of ADRs (3/8), while Isoniazid + Pyrazinamide + Rifampicin, the four - drug combination, Pyrazinamide, and Pyrazinamide + Ethambutol each accounted for 12.5% (1/8). The chi -

square statistic (χ^2 = 10.50, p = 0.0052) shows a significant association between TB type and culprit drugs. (Table 6)

Type of ADR vs Severity: Hepatitis was mostly moderate (16 cases), with 2 severe and 1 mild case. Gastritis was primarily mild (14 cases), with 1 moderate and 1 severe case. Cutaneous reactions were all moderate (7 cases). Arthralgia was mostly mild (3 cases), and Peripheral Neuropathy was moderate (3 cases). Vertigo was moderate in 1 case. The chi - square statistic (χ^2 = 37.71, p = 0.000043) indicates a significant link between ADR type and severity. (Figure 1)

Type of ADR vs Day of Onset: The timing of ADRs varied by type. Hepatitis occurred most frequently within the first 5 days (9 cases), followed by 5 cases between 16 - 30 days, 4 cases between 6 - 15 days, and 1 case after 30 days. Gastritis also showed early onset, with 10 cases within 5 days, 5 cases between 6 - 15 days, and 1 case after 30 days, but none between 16 - 30 days. Cutaneous reactions mostly occurred within 5 days (5 cases), with 1 case each between 6 - 15 days and 16 - 30 days. Arthralgia was spread across time periods, with 2 cases between 16 - 30 days, and 1 case each in the 6 - 15 day and over 30 day categories. Peripheral Neuropathy mostly occurred within 5 days (2 cases), with 1 case after 30 days. Vertigo had 1 case between 6 - 15 days. The chi - square statistic (χ^2 = 19.57, p = 0.189) shows no significant link between ADR type and the time of occurrence. (Table 7)

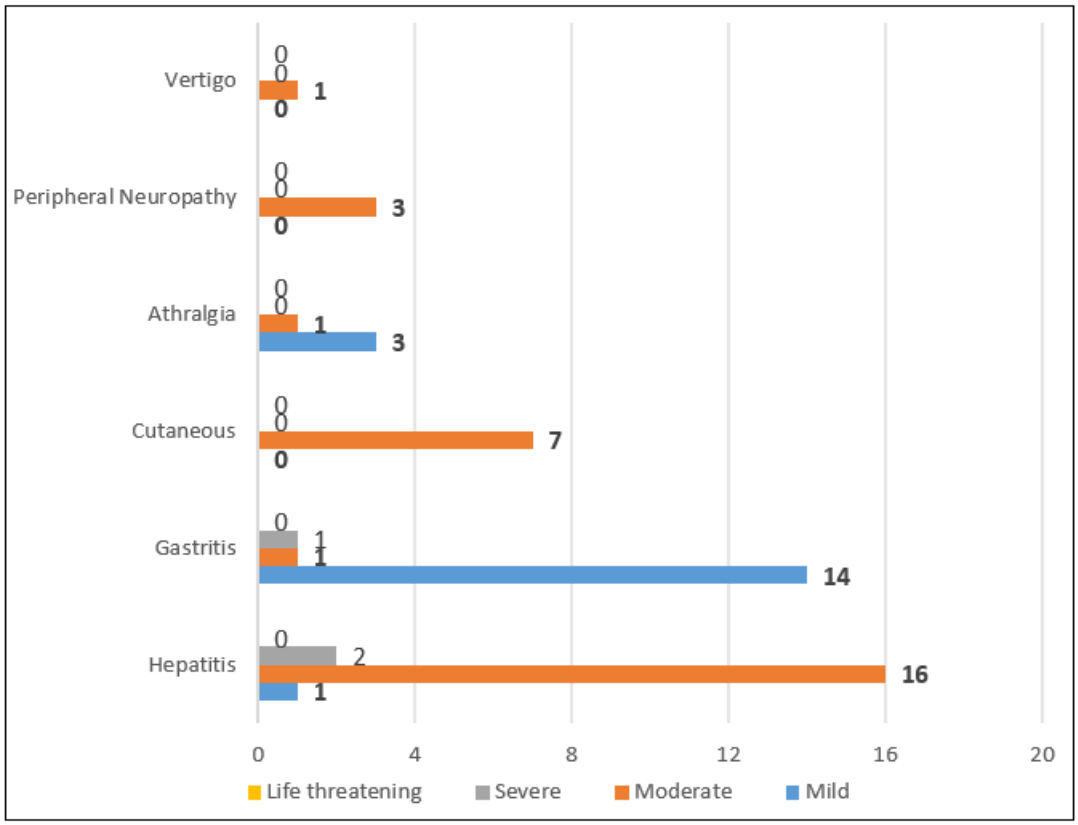

Figure 20: Type of ADR Vs severity of ADR

Table 7: Type of ADR Vs Day of ADR

Type of ADR Vs Day of ADR	Less than 5 days	6 to 15 days	16 to 30 days	More than 30 days
Hepatitis	9	4	5	1
Gastritis	10	5	0	1
Cutaneous	5	1	1	0
Athralgia	0	1	2	1
Peripheral Neuropathy	2	0	0	1
Vertigo	0	1	0	0
Significance	Chi - Square statistic (χ^2): 19.57, p - value: 0.189, Degrees of Freedom (df): 15			

5. Discussion

The primary aim of this study was to evaluate the incidence of adverse drug reactions (ADRs) during the intensive phase of anti - tubercular therapy (ATT). Understanding the frequency and severity of these reactions is crucial as they can significantly impact treatment adherence and patient outcomes. ADRs can lead to discomfort, interruption of therapy, or even treatment failure if not appropriately managed. Therefore, by assessing the incidence of ADRs, healthcare providers can better anticipate potential complications, allowing them to implement preventive or management strategies that not only minimize patient discomfort but also enhance compliance. This is especially critical during the intensive phase of treatment, which typically involves more aggressive drug regimens.

Naranjo's Algorithm is a valuable tool for establishing the causality link between a drug and the observed ADR. This helps clinicians make informed decisions about whether to continue, modify, or discontinue treatment. The Modified Hartwig and Siegel scale categorizes the severity of ADRs, helping healthcare professionals prioritize interventions based on the intensity of the reactions. Mild reactions may be managed symptomatically, whereas moderate to severe

reactions may require more aggressive management, including the temporary cessation of drugs.

In terms of demographics, the majority of participants in this study were male, accounting for 60.61% of the total sample, while females represented 39.39%. This gender disparity could be attributed to the higher exposure of males to environmental and occupational risk factors for tuberculosis (TB), particularly in developing regions. Men are often engaged in more physically demanding work environments, where exposure to dust, chemicals, and crowded conditions increases their risk of contracting TB. Studies such as Navelkar et al.[12] have reported similar findings, where males made up 63.97% of the study population suggesting that the higher prevalence of TB among males is a consistent trend, potentially linked to lifestyle and occupational hazards.

The age distribution in this study revealed that the largest group of TB patients was under 35 years of age (40.15%), followed by those aged 46 - 55 years (19.70%). This indicates that TB affects both younger and middle - aged adults, with possible explanations including increased exposure to social interactions for younger individuals and weakened immune systems or comorbidities in older patients. The data suggests that TB is not confined to older populations but also impacts younger adults, who may face heightened susceptibility due to social and environmental factors. The high incidence in the younger age group is consistent with global TB trends, where the disease often strikes during the most productive years of life, further highlighting the public health impact of TB.

In terms of occupation, 49.24% of the study population were unskilled workers, followed by 29.55% who were skilled workers. This occupational distribution reflects the higher risk of tuberculosis among individuals engaged in physically demanding jobs with poor working conditions. Unskilled workers are often more likely to live and work in overcrowded environments, which increases their exposure to TB. These findings are in line with studies like Mishra et al.[14], who reported that socioeconomic factors and employment type significantly influence TB prevalence, particularly in marginalized communities such as the Saharia tribe, where poverty and limited access to healthcare exacerbate the TB burden. This underscores the need for targeted TB interventions among low - income and unskilled laborers, who may face significant barriers to early diagnosis and treatment.
Coexisting comorbidities, such as hypertension (9.09%) and diabetes mellitus (6.82%), were also observed in the study population. Managing TB in patients with additional chronic conditions presents a unique challenge, as comorbidities like diabetes can accelerate TB progression and complicate treatment regimens. Although only a small percentage of patients had addictions such as smoking (5.30%), such habits can increase susceptibility to TB and impair recovery.

The incidence of ADRs in this study was 37.88%, highlighting the significant risk of side effects during anti - tubercular treatment, particularly in the intensive phase. Given that nearly 40% of patients experienced ADRs, it is essential to monitor patients closely during this phase and implement proactive management strategies to ensure treatment adherence and patient safety. Mishra et al.[14] reported an even higher ADR incidence of 89.6% in a tribal population, emphasizing the variability of ADR incidence depending on patient populations and treatment regimens. In this study, ADR occurrences were more common during hospital admissions (22.73%) compared to follow - up visits (14.39%) or outpatient visits (0.76%). The higher incidence during admission may be attributed to more intensive drug administration and closer monitoring, allowing for early identification and management of ADRs.

The study also found that pulmonary tuberculosis (PTB) accounted for 71.21% of cases, while extrapulmonary tuberculosis (EPTB) represented 28.79%. PTB is the more common form of TB due to its airborne transmission, but ADRs were significantly higher in patients with EPTB (55.26%) compared to those with PTB (32.18%). This statistically significant difference (p - value = 0.020905) suggests that patients with EPTB are more prone to developing ADRs, possibly due to the more complex and prolonged nature of their treatment, which often involves a broader spectrum of drugs. Managing ADRs in EPTB patients may require more intensive monitoring and adjustments to therapy to minimize adverse outcomes.

Most ADRs (48%) developed within the first week of treatment, with 22% occurring by the second week. This early onset of ADRs highlights the importance of vigilant monitoring during the initial phase of treatment. Early detection of ADRs allows for timely interventions, such as adjusting the drug regimen or managing symptoms, which can prevent more severe complications and improve treatment adherence. In 52% of cases, patients were able to continue their anti - tubercular treatment (ATT) while receiving symptomatic treatment for ADRs. However, in 48% of cases, ATT had to be withheld, and a safer regimen was initiated until the ADR resolved. This underscores the importance of balancing effective treatment with the management of ADRs to avoid treatment interruption, which can lead to drug resistance.

Hepatitis (38%) and gastritis (32%) were the most frequently reported ADRs in this study, followed by cutaneous reactions (14%). Hepatotoxicity is a well - known complication of TB drugs, particularly regimens that include isoniazid and rifampicin. This finding highlights the need for regular liver function monitoring during treatment to prevent severe outcomes such as drug - induced liver injury. Similar findings were reported by Ramakrishnan et al., [13] who found that hepatitis and gastrointestinal disturbances were among the most frequent ADRs in their study. Navelkar et al.[12] also identified gastrointestinal reactions as the most common ADR, occurring in 39.39% of cases.

Most ADRs in this study were classified as moderate (58%), with 36% being mild and 6% severe. No life - threatening reactions were observed. The predominance of moderate ADRs suggests that while many patients experience side effects, these are manageable with appropriate interventions. The absence of life - threatening reactions is encouraging, indicating that with proper monitoring and management, severe toxicity can be avoided.

Using Naranjo's Algorithmic Scale, 86% of ADRs were classified as probable, and 6% were deemed definite. This high percentage of probable ADRs indicates a strong likelihood that the ADRs were directly related to the anti - tubercular drugs. Accurate causality assessment is vital for making informed decisions regarding treatment continuation or modification, ensuring patient safety while maintaining therapeutic efficacy. These findings are consistent with other studies, such as those by Ramakrishnan et al.[13] and Navelkar et al., [12] which similarly found that the majority of ADRs were classified as probable.

The data further revealed a significant relationship between the occurrence of ADRs and the type of tuberculosis (TB) a patient had, whether drug - sensitive (DS - TB) or drug - resistant (DR - TB). Among DS - TB patients, 34.15% experienced ADRs, while 65.85% did not. In contrast, the majority of DR - TB patients (88.89%) experienced ADRs. The higher incidence of ADRs in DR - TB patients is likely due to the more complex and toxic treatment regimens required for managing drug - resistant tuberculosis.

Among DR - TB patients, Linezolid was the most common culprit drug, responsible for 37.5% of ADRs, while in DS - TB patients, the combination of Isoniazid + Pyrazinamide + Rifampicin was the leading cause, responsible for 38.10% of ADRs. This aligns with findings from studies by Mishra et al.[14] and Ramakrishnan et al., [13] which reported that second - line drugs used in DR - TB, such as Linezolid, tend to be more toxic, resulting in a higher incidence of ADRs.

In conclusion, the study underscores the importance of close monitoring during the intensive phase of TB treatment, particularly in patients receiving more complex DR - TB regimens. Early detection and management of ADRs are essential to minimize treatment disruptions and improve patient outcomes.

6. Conclusions

The study highlights the high incidence of adverse drug reactions ADRs during the intensive phase of antitubercular treatment, particularly in drug resistant TB patients. Hepatitis and gastritis were the most common ADRs, with early onset in many cases, emphasizing the need for vigilant monitoring during the initial treatment phase. Ensuring timely detection and management of ADRs is essential for improving treatment adherence and preventing drug resistance.

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