PREVALENCE AND INCIDENCE OF ANTITUBERCULOSIS MEDICINE-INDUCED ADVERSE DRUG REACTIONS IN SIX DISTRICTS OF HARYANA AND DELHI

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Abstract

Pharmacovigilance studies are a cornerstone to ensure the safety of medicines. The awareness, training, and change in perception among healthcare professionals, patients, and other stakeholders can reduce the challenges of underreporting of adverse drug reactions. Isoniazid (INH), Rifampin (RIF), Pyrazinamide (PYZ), and Ethambutol (ETM) are prescribed as the first line of medicines for the treatment of tuberculosis. The common organ systems found to have adverse drug reactions due to first-line anti-tubercular medications are mainly gastrointestinal system (39%), musculoskeletal system (24%), skin disorders (21%), hepatobiliary system (46.9%), Central nervous system, and many others. The current study has focused on determining the Incidence and prevalence of adverse effects of the first-line medications used for treating tuberculosis in the six districts of Haryana and Delhi. The Incidence of ADRs in Gurgaon is 27.71 per 100,000 population, and 13.86 prevalence in a year. The Jhajjar district has a 7.86 incidence rate for adverse effects and a 3.93 prevalence rate for adverse effects. New antituberculosis drugs are needed to improve treatment outcomes and reduce the Incidence of adverse effects of drugs

Keywords: Pharmacovigilance, tuberculosis, adverse drug reactions, ADR.

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1. Introduction

Globally, Pharmacovigilance studies are a cornerstone to ensure the safety of medicines. The medicines used for treating pulmonary tuberculosis are being studied and kept under a pharmacovigilance program for a long time, but they will continue to be monitored throughout their life cycle as with any other drug. Isoniazid (INH), Rifampin (RIF), Pyrazinamide (PYZ), and Ethambutol (ETM) are prescribed as the first line of medicines for the treatment of tuberculosis during the Intensive phase of treatment, which is of two months. The Continuation phase lasts four months, following a regimen of INH and RIF. As used for treatment, these drugs also show adverse effects on the patient. No drug can be labeled Safe without pharmacovigilance studies. As we know today, safety is a relative term in the healthcare system, and the outcome of pharmacovigilance studies supports the clinical decision based on drug safety profile for better patient care. In the previous studies conducted so far, the common organ systems found to have adverse drug reactions due to first-line anti-tubercular medications are mainly gastrointestinal system (39%), musculoskeletal system (24%), skin disorders (21%), hepatobiliary system (46.9%), Central nervous system, and many others. (1)(2)(3)(4)(5)

Reporting adverse drug reactions (ADRs) is a global challenge. A systematic review by Hazell et al. concluded that underreporting is 94 percent through spontaneous reporting systems compared to occurred ADRs. The awareness, training, and change in perception among healthcare professionals, patients, and other stakeholders can reduce the challenges of underreporting of adverse drug reactions. Early detection, management, and reporting of adverse drug reactions can improve the health outcomes of patients. Lack of data on adverse drug reactions due to underreporting affects the patient's hospital stay, causes delays in the management of the clinical condition, and increases the cost of treatment for the patient or the insurance agencies and government.

The data to provide insight into the challenges mentioned above and the scenario is lacking for the Haryana state of India region. The current study has focused on determining the Incidence and prevalence of adverse effects of the first-line medications used for treating tuberculosis in the six districts of Haryana and Delhi.

2. Methodology

All the patients diagnosed with tuberculosis were enrolled in the study through convenience sampling in the In-patient department of pulmonology, a peri-urban area of Haryana state of India, for One year. The Patients diagnosed with MDR-TB or XDR-TB were excluded from the study as they were referred to the regional center.

The patient's demographic details, treatment chart, daily progress, Adverse effects, and associated details were collected.

The Naranjo's Score was used for causality assessment of the Adverse drug reactions since it is easy to use and implement. (6)

Statistical Analysis

All demographic and clinical features were reported using frequency and descriptive analyses in MS Excel 365.

3. Results and Discussion

A total of 94 patients were enrolled in the study through convenience sampling. The demographic details of the patients are shown in Table 1, and ADRs based on location are shown in Table 2.

Table 1. Demographic Details Of The Enrolled Patients

Age	n (%)	Location	n (%)
<20	9 (9.57)	Gurgaon	69 (73.4)

21-40	38 (40.43)	Jhajjar	2 (2.13)
41-60	28 (29.79)	Faridabad	2 (2.13)
>60	19 (20.21)	Palwal	1 (1.06)
Sex	**n (%)**	Kurukshetra	1 (1.06)
Male	47 (50)	Rohtak	2 (2.13)
Female	47 (50)	Delhi	17 (18.09)

Table 2. ADRs in the Six Districts of Haryana and Delhi

Location	ADR	Number	Location	ADR	Number
Gurgaon	Fever	36	**Jhajjar**	Vomiting	2
	Anxiety	28		Hemetesis	2
	Peripheral Neuropathy	24		Itching	1
	Discoloration of Body Fluids	23		Fever	1
	Abdominal Pain	21		Anxiety	1
	Vomiting	21	**Faridabad**	Vomiting	2
	Disturbed Menstrual Cycle	8		Disturbed Menstrual Cycle	1
	Constipation	7		Cough	1
	Cough	7		Discoloration of body fluids	1
	SOB	6		Sleep Disturbed	1
	Chest Pain	6	**Rohtak**	Discoloration of body fluid	2
	Headache	6		Fever	2
	Hemoptysis	6		Anxiety	1
	LFT Elevated	5		Vomiting	1
	Rashes	5		Loose stools	1

	Weakness/ Fatigue	4	**Delhi**	Discoloration of body fluids	12
	Itching	4		Anxiety	3
	anemia	3		Fever	8
	Uric Acid Elevated	3		Peripheral Neuropathy	7
	Gastritis	3		Vomiting	9
	Insomnia	2		Hepatitis	1
	Leg/ Knee Pain	2		Abdominal pain	2
	Loose Stool	2		Gastritis	1
	Nausea	2		Rashes	2
Palwal	Discoloration of body fluids	1		Itching	1
	Loss of Appetite	1		Cough	2
	Constipation	1		Loss of appetite	1
Kurukshetra	Discoloration of body fluids	1		Elevated Uric Acid	2
				Hydropneumothorax	1
				Weakness	1

Table 3. Incidence and Prevalence of ADRs in Six Districts of Haryana and Delhi

Locations	**ADRs**	**Incidence[#]**	**Prevalence[$]**
Gurgaon	243	27.71	13.86
Jhajjar	7	7.86	3.93
Faridabad	6	0.43	0.21
Palwal	3	2.98	1.49
Kurukshetra	1	0.09	0.05
Rohtak	7	1.87	0.94
Delhi	53	0.54	0.27

[#]Incidence Rate: (Total No. of New Cases/ Total Population at risk) * 100,000
[$]Prevalence Rate: (Incidence rate) * (disease duration in years)

The Incidence and prevalence of adverse drug reactions due to first-line medicines used in tuberculosis treatment are calculated using the standard formula mentioned in table 3. The Incidence of ADRs in Gurgaon is 27.71 per 100,000 population, and 13.86 prevalence in a year. These include fever, anxiety, peripheral neuropathy, discoloration of body fluids,

abdominal pain, and vomiting being the common adverse effects. The Jhajjar district has a 7.86 incidence rate for adverse effects and a 3.93 prevalence rate for adverse effects.

4. Conclusions

The development of newer antituberculosis drugs in the mid of 20th century has improved the complete treatment of tuberculosis, but at the same time, it has adverse effects on the patient. First-line drugs are used in the treatment for six months and have a highly successful treatment. Even though the Incidence and prevalence of tuberculosis and the adverse effects of medications used for tuberculosis are also significant, this study found a significant incidence and prevalence rate of adverse drug reactions due to medicines used in tuberculosis at Gurgaon. New antituberculosis drugs are needed to improve treatment outcomes and reduce the Incidence of adverse effects of drugs.

Ethical Disclosures

The Institutional Ethics Committee - SGT Dental College, Hospital and Research Institute (IEC-SGTDCHRI) approved the study.

The patients gave Informed consent to enroll in the study. The identity of the enrolled patients is kept confidential.

Conflicts of Interest

The authors declare no conflicts of interest.

5. References

1. Ravichandran M, Rajaram M, Munusamy M. Pharmacovigilance of Antitubercular Therapy in Tuberculosis. Cureus. 2022;14(2):1–7.
2. Krishnappa L, Gadicherla S, Chidambaram P, Anuradha H V., Somanna SN, Naik PR, et al. 'Have we missed reporting adverse drug reactions under Revised National TB Control Programme?' - A mixed method study in Bengaluru, India. Indian J Tuberc [Internet]. 2020;67(1):20–8. Available from: https://doi.org/10.1016/j.ijtb.2020.01.003
3. Imam F, Sharma M, Khayyam KU, Al-Harbi NO, Rashid MK, Ali MD, et al. Adverse drug reaction prevalence and mechanisms of action of first-line anti-tubercular drugs. Saudi Pharm J [Internet]. 2020;28(3):316–24. Available from: https://doi.org/10.1016/j.jsps.2020.01.011
4. Krasniqi S, Neziri B, Jakupi A, Shurdhaj I, Daci A, Jupolli-Krasniqi N, et al. Tuberculosis drug safety and pharmacovigilance in health system of Kosova: A cross-sectional analysis. Pharmacoepidemiol Drug Saf. 2020;29(9):1037–45.
5. Castro AT e., Mendes M, Freitas S, Roxo PC. Incidence and risk factors of major toxicity associated to first-line antituberculosis drugs for latent and active tuberculosis during a period of 10 years. Rev Port Pneumol [Internet]. 2015;21(3):144–50. Available from: http://dx.doi.org/10.1016/j.rppnen.2014.08.004
6. Pradhan P, Lavallée M, Akinola S, Raphael F, Gimenes E, Bérard A, et al. Causality assessment of adverse drug reaction : A narrative review to find the most exhaustive and easy-to-use tool in post-authorization settings. J Appl Biomed [Internet]. 2023;21(2):59–66. Available from: https://doi.org/10.32725/jab.2023.010