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Impact of Rifampicin on Blood Pressure Control in Hypertensive Patients with Tuberculosis: A Study at a Tertiary Care Center

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ABSTRACT

Background: Hypertension and tuberculosis (TB) have an indirect relationship with each other. The anti-tuberculosis (Anti-TB) drug Rifampicin is an inducer agent. It is a potent liver enzyme inducer by inducing P450 and may have many drug interactions which reduces the therapeutical effects of many other drugs such as anti-hypertensive agents.

Objective: To know the role of rifampicin (RMP) on blood pressure (BP) control in hypertensive patients with tuberculosis.

Methodology: This prospective observational study was conducted at the Department of Cardiology, District Headquarters Teaching Hospital, Swabi, from January 2020 to Dec. 2021. In the present study, 200 patients with hypertension (HTN) who were on anti-hypertensive agents participated in this research. They all were diagnosed with tuberculosis as well as they were also treated with anti-tuberculosis drug rifampicin. Data were collected and entered into SPSS for analysis purposes. Blood pressure before starting the anti-TB drugs was recorded for all patients. During treatment for TB, the BP of all these patients re-check according to study rules.

Results: The majority of the patients (68.0%) were male under the age 55 years of age. Among study cases, 116 (58%) of the cases experienced HTN for less than four years, while the rest were facing the problem for almost eight to ten years. Before anti-tuberculosis therapy (ATT), blood pressure (BP) was recorded as 135/85 mmHg, but after starting ATT, BP was recorded as 155/95 mmHg even after taking multiple anti-hypertensive drugs. The BP was again under control after stopping ATT i.e., 135/85 mmHg.

Conclusions: Rifampicin weakens the effect of many blood pressure-lowering drugs, like calcium channel blockers, beta-blockers, and diuretics, by increasing liver enzymes that break down these drugs faster. So, their effective role in reducing the BP in hypertensive patients is reduced.

Keywords: Tuberculosis; Anti-TB drugs; Rifampicin

Introduction

Tuberculosis (TB) continues to pose a major health challenge worldwide, especially in low- and middle-income nations. According to the World Health Organization (WHO), around 10 million people contracted TB in 2020, with nearly 1.5 million deaths reported.[1] Concomitant with the TB epidemic, the prevalence of hypertension has been rising, contributing to the global burden of cardiovascular diseases.[2]

Blood pressure becomes high when the force of blood flowing through the blood vessels is too high for a longer period.[3] The main causes of Hypertension are environmental and genetic factors due to which primary hypertension develops, but the secondary causes of hypertension are renal, vascular, and endocrine factors.[4] Hypertension is one of the leading causes of the development of cardiovascular disorders and kidney diseases. According to recent studies, 90- 95% of cases were cases of Primary hypertension, whereas, 2-10% of the adult cases were cases of secondary hypertension.[5] However, some chronic inflammatory infections such as tuberculosis are also one of the causes of the development of hypertension by triggering various immunological factors.[6] According to many studies, there is no direct relation between tuberculosis and hypertension. The only relation between these two is the damage to the renal system i.e., renal tuberculosis and renal failure in hypertension. Besides these two, there is no possible link between tuberculosis and hypertension.

The anti-tuberculosis therapy (ATT) includes isoniazid, rifampicin, pyrazinamide, and ethambutol with fixed-dose combinations.[7] The duration of treatment ranges from six to eighteen months depending upon the location of TB i.e., whether it is pulmonary tuberculosis or extrapulmonary tuberculosis. Rifampicin is an antimicrobial drug used to treat various mycobacterial infections, including tuberculosis, as well as some gram-positive bacterial infections. It is also a first-line drug for tuberculosis. Rifampicin's ability to induce hepatic cytochrome P450 enzymes can significantly reduce the plasma levels of anti-hypertensive medications, potentially compromising their efficacy.[8] Drug interaction may result in poor blood pressure control in hypertensive patients undergoing anti-tuberculosis therapy (ATT), which may lead to an increased risk of cardiovascular complications in them.

Given the potential for rifampicin to interfere with the effectiveness of anti-hypertensive therapy, it is crucial to investigate the extent to which rifampicin influences blood pressure control in hypertensive patients receiving TB treatment. Understanding this interaction will provide valuable insights for clinicians managing these patients, guiding them in adjusting anti-hypertensive regimens to maintain effective blood pressure control during ATT.

Despite the critical importance of this issue, there is limited research on the impact of rifampicin on blood pressure control in hypertensive patients undergoing TB treatment. So, this study was planned to fill this gap by evaluating the effect of rifampicin on blood pressure levels in hypertensive patients with TB at a tertiary care center. Understanding these interactions is crucial for optimizing treatment protocols and improving clinical outcomes for this vulnerable patient population.

Objective

To find out the effect of rifampicin on hypertensive patients who were on anti-hypertensive drugs.

Methodology

This prospective observational study was conducted at the Department of Cardiology, District Headquarters Teaching Hospital, Swabi, from January 2020 to Dec. 2021. In this study, 200 patients with HTN who were on anti-hypertensive agents participated in this research. They all were diagnosed with tuberculosis as well as they were also treated with anti-tuberculosis drug rifampicin.

In this retrospective observational study, we included patients over 18 years of age who were diagnosed with tuberculosis (TB) and had hypertension managed with anti-hypertensive medications. Patients younger than 18 and those with other medical conditions such as liver disease, renal disease, coarctation of the aorta, pheochromocytoma, or any conditions other than TB and hypertension were excluded from the study.

We reviewed patient records and collected data on routine investigations performed before and during anti-tuberculosis therapy (ATT). These investigations included complete blood count, renal function tests (RFTs), liver function tests (LFTs), serum electrolytes, and imaging studies such as ultrasound of the kidneys and urinary bladder, as well as echocardiograms.

Blood pressure measurements were recorded at three stages: before the initiation of ATT (pre-ATT), during ATT, and after completing ATT (post-ATT). Blood pressure was monitored continuously for three days before starting ATT and regularly during the treatment period. We noted both systolic and diastolic blood pressure readings at these intervals.

To manage blood pressure during ATT, which interfered with the effectiveness of existing anti-hypertensive medications, additional anti-hypertensive drugs were prescribed. These included calcium channel blockers, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, beta-blockers, thiazide diuretics, loop diuretics, potassium-sparing diuretics, and alpha-1 blockers. All data were analyzed to assess the impact of rifampicin on blood pressure control in the study population.

Table 1. Baseline characteristics of study cases

Variables		Frequency	Percentage
Age group	<35	76	38
	36-45	70	35
	46- 55	25	12.5
	>55	29	14.5
Gender	Male	138	69
	Female	62	31
Hypertension duration (in years)	<4	112	56
	8-10	74	37
	>10	14	7

Results

Our study included 200 hypertensive patients. The majority of the patients were male (69%) under the age of 55 years (Figure 1). Among study cases, 112 (56%) of the patients were hypertensive for less than four years, while the rest were hypertensive for almost eight to ten years or more (Table 1).

These patients also have other comorbidities such as diabetes mellitus (34%) and cardiovascular diseases (29%) (Figure 2).

Before anti-tuberculosis therapy (ATT), BP was recorded as 125/82 mmHg, but after starting ATT, BP was recorded as 155/95 mmHg even after taking multiple anti-hypertensive drugs. The BP was again under control after stopping ATT i.e., 135/85 mmHg. The BP which was recorded before starting ATT was considered as baseline value. BP which was recorded during ATT was recorded in several intervals to compare. After discontinuation of ATT, BP was again recorded (Table 2).

Before starting anti-tuberculosis therapy (ATT), most patients (56.5%) effectively managed their blood pressure with just one anti-hypertensive medication. In contrast, 35% of the patients required a combination of two anti-hypertensive drugs, and 8.5% needed three different medications to achieve optimal blood pressure control. During ATT, the number of anti-hypertensive medications needed increased significantly, ranging from one to six drugs, to maintain a target blood pressure of 125/82 mmHg. After two weeks on ATT, 47% of patients could manage their blood pressure with only one anti-hypertensive drug. However, the remaining patients required between two to four anti-hypertensive medications to bring their blood pressure back to normal levels (Table 3).

Discussion

The present study evaluated the impact of anti-tuberculosis therapy (ATT) on blood pressure (BP) control among 200 hypertensive patients. The findings highlight significant alterations in BP management during ATT, necessitating adjustments in anti-hypertensive therapy. Our cohort predominantly consisted of male patients (69%) under the age of 55. Additionally, 56% had been diagnosed with hypertension for less than four years, while the remaining patients had a longer history of hypertension (eight to ten years or more). Comorbid conditions included diabetes mellitus (34%) and cardiovascular diseases (29%).

The male predominance observed aligns with findings from Song et al (2020), Colafella et al (2018) and Doumas et al (2013) who reported a higher prevalence of hypertension among males in similar age groups.[10-12] Conversely, Maric-Bilkan and Manigrasso (2012), Singh et al (2011) noted a more balanced gender distribution in their hypertensive cohorts, suggesting possible regional or demographic variations.[13,14] The higher prevalence of hypertension in males may be attributed to lifestyle factors such as increased rates of smoking, alcohol consumption, and occupational stress, which are more common in males. The presence of comorbidities like

Table 2. Mean deviation of systolic blood pressure and diastolic blood pressure at different points of study

Bood Pressure	ATT	Follow-up	Mean	Standard deviation
Systolic blood pressure	Pre-ATT	Baseline	125.20	6.77
	During ATT	2 weeks	130.12	8.4
		2 months	135.87	7.33
		4 months	146.52	7.69
		6 months	154.67	6.91
	Post-ATT	2 weeks	132.11	6.77
		4 weeks	125.20	6.77
Diastolic blood pressure	Pre-ATT	Baseline	82.02	7.13
	During ATT	2 weeks	89.99	7.73
		2 months	93.21	7.89
		4 months	95.97	7.99
		6 months	96.56	8.46
	Post-ATT	2 weeks	85.21	7.13
		4 weeks	82.61	7.13

diabetes and cardiovascular diseases is consistent with the global trend of interconnected chronic conditions, as highlighted by the World Health Organization. Discrepancies in gender distribution across studies may result from differing population demographics, healthcare access, and cultural factors influencing health-seeking behaviors.

Baseline BP was recorded at 125/82 mmHg. Upon initiation of ATT, BP surged to 155/95 mmHg despite the administration of multiple anti-hypertensive drugs. After discontinuing ATT, BP stabilized at 135/85 mmHg. These findings are corroborated by Seegert et al. (2017), and Allwood et al. (2018) who observed a similar increase in BP among hypertensive patients undergoing ATT.[15,16] The increase in BP during ATT can be primarily attributed to the pharmacological effects of ATT drugs, such as rifampicin and isoniazid, which may interfere with anti-hypertensive medication metabolism. The normalization of BP post-ATT supports the hypothesis that ATT drugs are the causative agents for the observed hypertension. Differences in the magnitude of BP changes across studies might be due to variations in ATT regimens, patient adherence to medications, and baseline BP control.

Prior to ATT, 56.5% of patients managed their BP with a single anti-hypertensive drug, 35% required two drugs, and 8.5% needed three drugs. During ATT, the necessity for anti-hypertensive medications increased, with some patients requiring up to six drugs to maintain BP control. Initially Blood pressure was normal in majority of the patients, but the requirement of the anti-hypertensives increased from one to >5 based on the individual condition of patient after starting ATT in order to maintain normal. After ATT, blood pressure again got normalize with anti-hypertensive drug. After stopping of rifampicin-based ATT, serum level of rifampicin in patient decreases which result in lowering of blood pressure. Thus, the dose of anti-hypertensive drugs also decreases. In our study, we have found out that rifampicin may reduce the anti-hypertensive effects of dihydropyridine calcium channel blockers. Similar patterns of increased anti-hypertensive requirements during ATT have been documented by Parekh et al. (2020), who reported a need for additional BP medications in patients on ATT.[17] However, some other

Table 3. Distribution of anti-hypertensive drugs required for patients at different point of study

Number of anti-hypertensives required	1	2	3	4	>5
Pre-ATT	56.5	35	8.5	-	-
During ATT					
2 weeks	51	27.5	21.5	-	-
2 months	41.5	30.5	16	12	-
4 months	16.5	49.5	21.5	7	5.5
6 months	4	24	44	17	11
Post-ATT					
2 weeks	47	37	10	6	-
4 weeks	56	38	6	-	-

studies found that only a subset of patients required escalation in anti-hypertensive therapy, suggesting variability in response. The escalation in anti-hypertensive therapy during ATT is likely due to drug-drug interactions, where ATT agents induce hepatic enzymes that metabolize anti-hypertensive drugs more rapidly, reducing their efficacy. The variability in the need for additional medications across studies may stem from differences in the types and doses of anti-hypertensive drugs used, genetic factors influencing drug metabolism, and the presence of comorbidities that affect BP regulation.

The present study underscores the significant impact of anti-tuberculosis therapy on blood pressure control in hypertensive patients, highlighting the need for careful monitoring and management of BP during ATT. The observed fluctuations in BP and the increased requir-

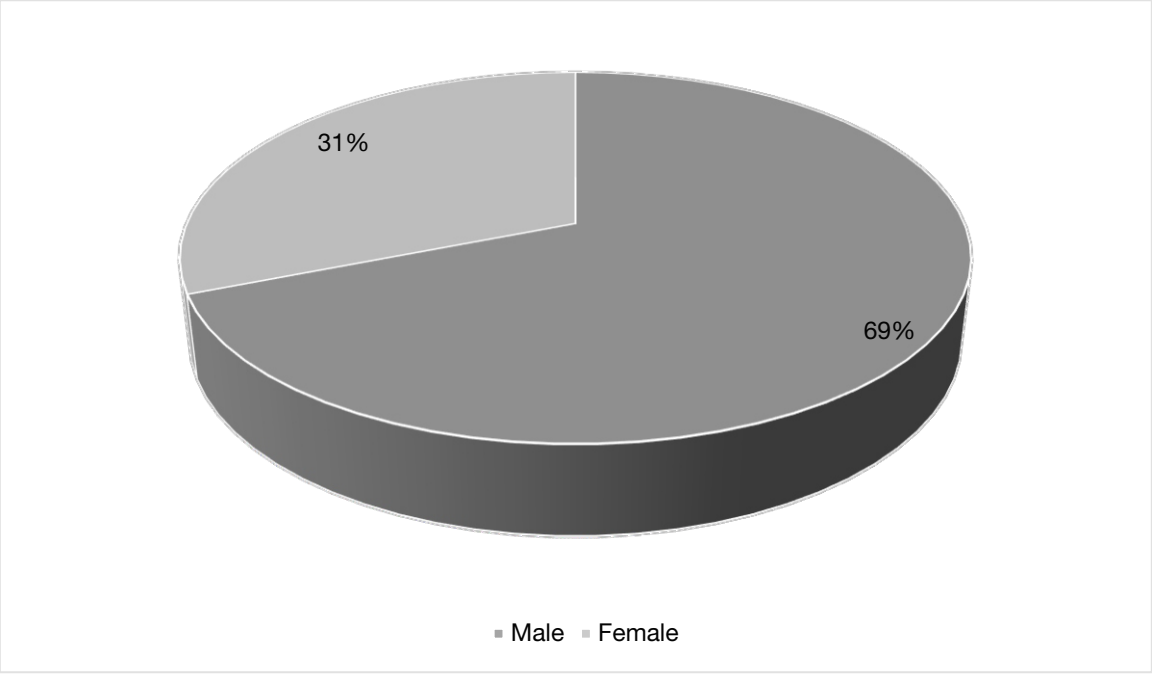

Figure 1. Gender base distribution of study cases

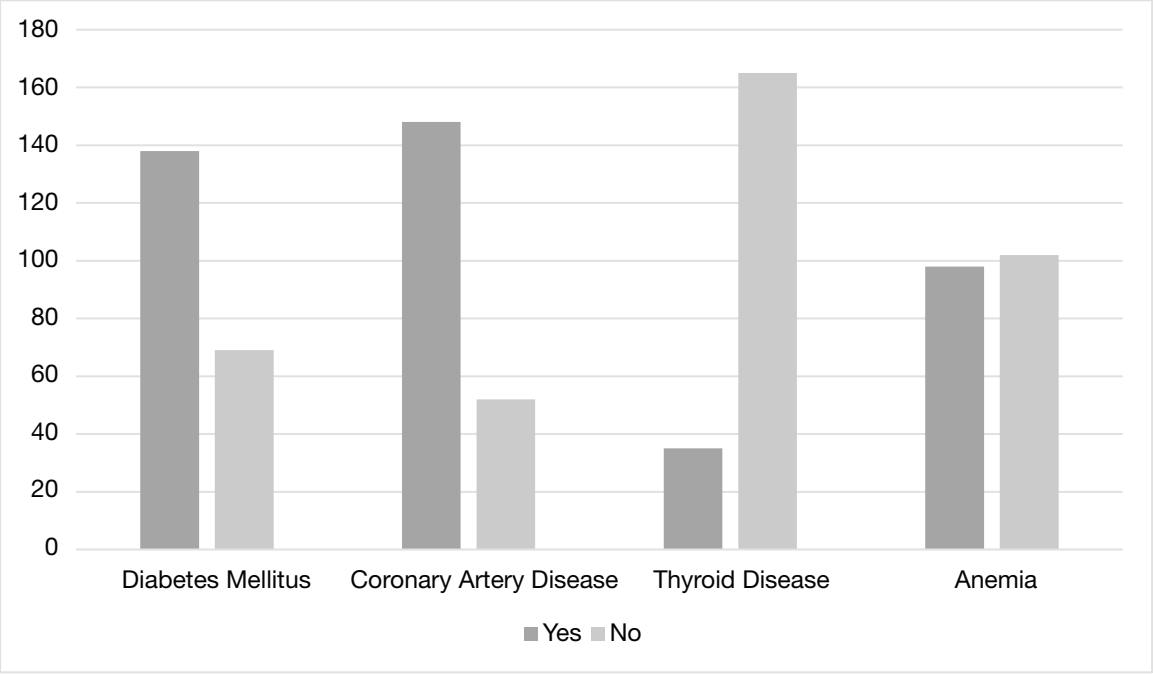

Figure 2. Frequencies of comorbidities found in study cases

ement for anti-hypertensive medications during treatment emphasize the potential for drug-drug interactions, particularly with rifampicin-based regimens, which can reduce the efficacy of standard anti-hypertensive therapies. These findings suggest that individualized treatment plans, including possible adjustments to anti-hypertensive regimens, should be considered for patients undergoing ATT to mitigate the risk of uncontrolled hypertension. Further research is warranted to explore the long-term cardiovascular outcomes of hypertensive patients treated with ATT and to develop optimized strategies for managing BP in this population. Ultimately, a multidisciplinary approach, involving collaboration between pulmonologists and cardiologists, is essential to ensure comprehensive care and improve patient outcomes in this complex clinical scenario.

Conclusions

This study highlights the significant impact of rifampicin, a key anti-tuberculosis drug, on blood pressure control in hypertensive patients. Rifampicin's induction of hepatic enzymes accelerates the metabolism of various anti-hypertensive drugs, leading to increased blood pressure despite ongoing treatment. The observed normalization of blood pressure after discontinuing rifampicin underscores its role in diminishing the efficacy of anti-hypertensive therapies. These findings emphasize the importance of careful monitoring and potential adjustments to anti-hypertensive regimens in patients undergoing rifampicin-based TB treatment. Clinicians should be aware of these interactions and consider alternative strategies to maintain optimal blood pressure control during TB therapy. Further research is warranted to explore methods for mitigating these drug interactions and improving clinical outcomes in this population.

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