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FREQUENCY OF HYPERURICEMIA IN PATIENTS TAKING ANTI TUBERCULOSIS DRUGS AT A TERTIARY CARE HOSPITAL

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Abstract

Background
Hyperuricemia is a known side effect of anti-tuberculosis treatment, most commonly linked with pyrazinamide and other first-line drugs. Even though its clinical importance is undeniable, the extent of the syndrome in local populations is not fully understood and is not established in relation to demographic factors.

Objective
To determine the frequency of hyperuricemia in patients taking anti tuberculosis drugs at a tertiary care hospital.

Study Design
Cross-sectional observational study.

Duration and Place of Study
The study was conducted from December 2024 to April 2025 at the Department of Pulmonology, Ayub Teaching Hospital, Abbottabad.

Methodology
A total of 115 individuals between the ages of 18 and 65 years on conventional anti-tuberculosis treatment took part in the study. Hyperuricemia was taken to be serum concentration of uric acid of >7 mg/dl in men and >6 mg/dl in women. Uric acid was measured at the third month of treatment duration. Data on age, gender, BMI and residential and socioeconomic class was collected.

Results
The overall prevalence of hyperuricemia was 66.1%. Significant associations were found with age >50 years (100% prevalence), male gender (94.1%), BMI >25 (100%), rural residency (91.5%), and both low (85.2%) and high (100%) socioeconomic status groups ($p < 0.001$ for all).

Conclusion
Hyperuricemia is a common side effect of anti-tuberculosis treatment, especially in high-risk demographic groups.

INTRODUCTION

Tuberculosis (TB) is a chronic mycobacterial infection caused by Mycobacterium tuberculosis which predominantly causes infection in the lungs but may also affect other organs such as kidneys, spine, and

brain.[1] It is transmitted by air droplets that exit with a sneeze or a cough of the infected individual.[1] Despite the development of medicine, TB is a significant health issue in the entire globe and in low- and middle-income countries where it may result in significant morbidity and death.[2] In Pakistan, it is one of the significant causes of death and should be treated with early diagnosis and proper administration of medication with the aim of preventing further spread and complications.[3] For the curing of the infection and prevention of drug resistance, treatment of TB is typically multi-drug.[3]

Standard treatment of tuberculosis involves the administration of a regimen of first-line tuberculosis drugs like Rifampicin, Isoniazid, Pyrazinamide, and Ethambutol.[4] All these drugs are administered over a long period of time, usually spanning six months to ensure the removal of the tuberculosis bacterium from the body fully.[4] Rifampicin and Isoniazid form the backbone of the drug protocol with their bactericidal action against the tuberculosis bacterium being the aim of treatment.[5] While these medications are highly effective in treating tuberculosis, they do pose side effects that may range from mild to serious.[6]

Hyperuricemia is a condition of elevated concentration of uric acid in the circulation that is caused by imbalance between the synthesis and elimination of uric acid.[7] Uric acid is the natural byproduct of purine metabolism and is usually eliminated by kidneys in the form of urine.[8] However, in instances where the synthesis of uric acid is increased compared to excretion, it is trapped in the circulation.[9] It leads to deposition of crystals of urate in tissues which may accumulate in joints and cause painful conditions that have been known to be gout.[10]

In tuberculosis-treated individuals, particularly those treated with Pyrazinamide and Rifampicin, the side effect of hyperuricemia is one that is known to occur.[11] Pyrazinamide is itself a known cause of higher serum levels of uric acid due to its action of hindering the renal excretion of uric acid and promoting its build up in the circulation.[12] Rifampicin, indirectly so, may also be a contributory factor towards hyperuricemia due to interference with liver metabolism and clearance of uric acid.[13] Raised serum levels of uric acid during treatment in these subjects predisposes to gout in those who have risk factors of renal failure and also in those with a history of prior episodes of hyperuricemia.[14]

A study conducted by Shin HJ and colleagues demonstrated that the occurrence of hyperuricemia in patients receiving anti-tuberculosis drug treatment was 82.3%.[15]

Research of hyperuricemia in anti-tuberculosis drug-treated individuals is crucial in establishing the side effects of tuberculosis regimens in general and particularly because most regimens involve long-term administration of the drugs. Such research will guide the determination of the occurrence of high levels of uric acid in such individuals and early detection and management of gout and kidney calculi among other manifestations of hyperuricemia. By studying the cause of drug-induced hyperuricemia, the research may also assist in the optimal drug regimens to enhance outcomes in the patients and avoid side effects. It will also be important in enlightening health practitioners in closely monitoring and managing individuals on tuberculosis regimens.

Methodology:

This cross-sectional study was conducted between December 2024 and April 2025 at the Department of Pulmonology, ATH Abbottabad. The study aimed to assess the prevalence of hyperuricemia among patients undergoing treatment with anti-tuberculosis drugs. A total of 115 participants were included in the study, with sample size determination based on a 95% confidence level, a margin of error of 7%, and an expected prevalence of hyperuricemia of 82.3% in patients receiving anti-tuberculosis treatment.[15]

The inclusion criteria comprised individuals aged 18 to 65 years, of either gender, who were diagnosed with tuberculosis, defined as persistent cough lasting for at least two weeks, accompanied by fever, night sweats, weight loss, and a chest X-ray showing dense, homogeneous parenchymal consolidation in any lobe, along with a positive sputum smear microscopy test indicating the presence of acid-fast bacilli. The exclusion criteria included patients with a history of hepatic or renal dysfunction, gouty arthritis, use of uricosuric agents or diuretics, uncontrolled diabetes mellitus, substance or alcohol abuse, or pregnancy and lactation.

Demographic details such as age, gender, BMI, socioeconomic status, duration of symptoms, and

residential status were recorded. All participants were administered standard anti-tuberculosis medications, including isoniazid (5 mg/kg, maximum 300 mg), rifampicin (10 mg/kg, maximum 600 mg), pyrazinamide (25 mg/kg), and ethambutol (15 mg/kg, maximum 1.5 g), during both the initial and continuation phases of treatment. The doses were adjusted according to the individual characteristics, such as age and weight.

After three months of treatment, a blood sample of 5 ml was drawn from each patient using standard venipuncture techniques for serum uric acid measurement. The sample was sent to the laboratory for analysis. Hyperuricemia was defined as serum uric acid levels exceeding 7 mg/dl in males or 6 mg/dl in females. Data on hyperuricemia were recorded in a specially designed proforma by the researcher.

The data were analyzed using SPSS version 26. Descriptive statistics were employed for categorical variables such as gender, socioeconomic status, residential status, and hyperuricemia, expressed as frequencies and percentages. Continuous variables such as age, BMI, and duration of symptoms were summarized using mean ± standard deviation or median and interquartile range, with normality assessed using the Shapiro-Wilk test. Stratification of hyperuricemia was performed based on age, gender, BMI, socioeconomic status, duration of complaints, and residential status. The chi-square or Fisher's exact test was applied for post-stratification analysis, with a p-value of ≤0.05 considered statistically significant.

Results:

As shown in Table I, the mean age of patients was 43.70 ± 11.99 years, with a mean BMI of 22.17 ± 2.39 kg/m² and a mean duration of complaints of 6.17 ± 2.22 weeks. The gender distribution consisted of 76 male patients (66.1%) and 39 female patients (33.9%). Regarding residential status, 52 patients were from rural areas (45.2%), while 63 were from urban areas (54.8%). In terms of socioeconomic status, 52 patients were from poor backgrounds (45.2%), 41 from middle-class backgrounds (35.7%), and 22 from rich backgrounds (19.1%).

Table- I: Patient Demographics

Demographics	Mean ± SD
Age (years)	43.704 ± 11.99
BMI (Kg/m^2^)	22.172 ± 2.39
Duration of Complaints (weeks)	6.174 ± 2.22
Gender	Male n (%)
	Female n (%)
Residential Status	Rural n (%)
	Urban n (%)
Socioeconomic Status	Poor n (%)
	Middle n (%)
	Rich n (%)

As shown in Table II, the overall frequency of hyperuricemia in this sample was 66.1%, with 76 patients diagnosed with hyperuricemia and 39 patients without.

Table- II: Frequency of Hyperuricemia

Hyperuricemia	Frequency	% age
Yes	76	66.1%
No	39	33.9%

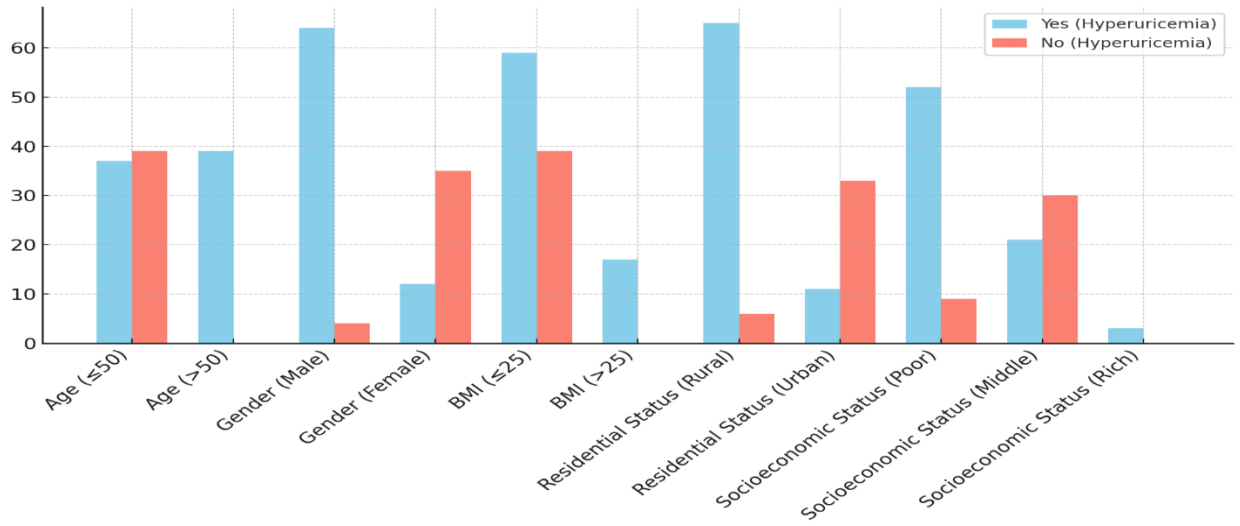
Hyperuricemia	Frequency	% age
Total	115	100%

In Table III, stratified analyses revealed that hyperuricemia was significantly associated with age, gender, BMI, residential status, and socioeconomic status. Specifically, patients aged over 50 years were more likely to have hyperuricemia, with 39 (100%) of those in this group affected, compared to only 48.7% of patients aged 50 years or younger. The p-value for age was <0.001, indicating a significant difference. Gender also showed a strong association, with 94.1% of males diagnosed with hyperuricemia, compared to only 25.5% of females, with a p-value of <0.001. Regarding BMI, 60.2% of patients with a BMI ≤25 had hyperuricemia, while all patients with BMI >25 were affected (p = 0.001). Residential status also showed a significant association, with 91.5% of rural residents diagnosed with hyperuricemia, compared to 25.0% of urban residents (p < 0.001). Lastly, socioeconomic status was also a significant factor, with 85.2% of patients from poor backgrounds affected, compared to 41.2% from middle-class backgrounds and 100% of those from wealthy backgrounds (p < 0.001). (Graph-I)

Table-III: Association of Hyperuricemia with Demographic Factors

Demographic Factors		Hyperuricemia		p-value
		Yes n(%)	No n(%)	
Age (years)	≤50	37 (48.7%)	39 (51.3%)	<0.001*
	>50	39 (100.0%)	0 (0.0%)	
Gender	Male	64 (94.1%)	4 (5.9%)	<0.001*
	Female	12 (25.5%)	35 (74.5%)	
BMI (Kg/m²)	≤25	59 (60.2%)	39 (39.8%)	0.001*
	>25	17 (100.0%)	0 (0.0%)	
Residential Status	Rural	65 (91.5%)	6 (8.5%)	<0.001
	Urban	11 (25.0%)	33 (75.0%)	
Socioeconomic Status	Poor	52 (85.2%)	9 (14.8%)	<0.001*
	Middle	21 (41.2%)	30 (58.8%)	
	Rich	3 (100.0%)	0 (0.0%)	

*Fischer Exact Test



Graph-I: Stratification of Hyperuricemia with Demographic Factors

Discussion:

The results show that the large percentage of 66.1% of the patients developed hyperuricemia during the treatment of anti-tuberculosis drugs. This is due to the known side effects of isoniazid, rifampicin and pyrazinamide drugs, which are typically employed in treating tuberculosis and which may increase serum levels of uric acid. These drugs inhibit excretion of uric acid and may lead to its accumulation to result in hyperuricemia.

The association of hyperuricemia with other population demographics also contributes to the complexity of the disorder. Patients over 50 years old were at higher risk of being affected by hyperuricemia due to age-related physiological factors also affecting elimination of uric acid, such as increasing renal impairments. Even the gender difference in large proportions of 94.1% being male and 25.5% being female is supported by recent studies that reveal that males stand at higher risk of having higher levels of uric acid and that this may be caused by differences in renal function and hormonal action that affect metabolism of uric acid.

The association with higher BMI is also seen here with a 100% prevalence of hyperuricemia among individuals with a BMI of greater than 25. Obesity as a risk factor for hyperuricemia is because of increased body fat that can result in decreased renal elimination of uric acid. In addition, the higher risk among rural dwellers compared to urban dwellers may be understood in the context of unequal access to health care, way of life and dietary habits. Last, the association of socioeconomic status with risk of getting affected with hyperuricemia indicates that individuals from lower socioeconomic strata stand at increased risk of getting affected due to poor diets, poor access to health care facilities and late diagnosis. The mean age of patients in our study was 43.70 ± 11.99 years, with a mean BMI of 22.17 ± 2.39 kg/m^2 and a mean duration of complaints of 6.17 ± 2.22 weeks. These demographic values are within a typical range for TB patients, which is similar to the characteristics described in other studies, such as the study by Sundas et al.[16] where the mean age was 38.2 ± 10.5 years. Furthermore, in terms of gender, our study found 66.1% male and 33.9% female patients, which aligns with other studies like those by Shin et al.[15] and Sasongko and Hasan [17] where male patients constituted a larger proportion of the sample, reflecting the higher incidence of TB in males globally.

As regards the prevalence of hyperuricemia itself, according to the findings of previous studies, we noted that 66.1% of the patients developed hyperuricemia. Compared to Sasongko and Hasan[18] who noted 82.35% in their study with a notably higher prevalence of hyperuricemia, and in Sundas et al.'s [16] study with the same prevalence of 82.35%, these results may differ in studies in relation to sample size, the type of treatment used, and population

demographics being studied. In our study in particular, we noted that socioeconomic conditions, BMI, residential density, gender, and age were associated with the development of hyperuricemia in a significant way similar to what was also seen in studies by Sundas et al.[16] and Shin et al. [15]

By age, we saw that the over 50-year-old age group was more likely to be affected by hyperuricemia and that 100% of them were affected in comparison to 48.7% of the less than 50-year-old group ($p < 0.001$). This agrees with the findings in studies such as those by Sundas et al.[16] in which age was a good predictor of hyperuricemia. This association of increased age with hyperuricemia can be explained by the age-related renal function and the altered metabolism of uric acid that reduce the ability to excrete uric acid optimally.

Gender also showed a strong association in our study, with 94.1% of males diagnosed with hyperuricemia, compared to only 25.5% of females ($p < 0.001$). This is in line with other studies, such as Sundas et al.[16] and Sasongko and Hasan [17] where male patients were more likely to develop hyperuricemia. This gender disparity is likely due to differences in renal function, hormonal influences, and the overall metabolic processes between males and females, as observed in the broader literature.

BMI was another significant factor in our study, with 60.2% of patients with a BMI ≤25 having hyperuricemia, while all patients with BMI >25 were affected ($p = 0.001$). This is consistent with the study by Sundas et al.[16] where increased BMI was associated with a higher incidence of hyperuricemia. Obesity is known to impair the renal clearance of uric acid, leading to its accumulation in the blood, which could explain the increased prevalence of hyperuricemia among patients with higher BMI.

Residential status was significantly associated with hyperuricemia in our study, with 91.5% of rural residents affected, compared to 25.0% of urban residents ($p < 0.001$). This aligns with findings in studies such as those by Sasongko and Hasan [17] where socioeconomic and environmental factors likely play a role in the development of hyperuricemia. In rural areas, limited access to healthcare, differences in diet, and lifestyle factors could contribute to the higher prevalence of hyperuricemia.

Moreover, socioeconomic status was also closely linked to hyperuricemia in the current study, with 85.2% of individuals of poor socioeconomic status afflicted compared with 41.2% of those of middle socioeconomic status and 100% of those of high socioeconomic status ($p < 0.001$). This finding is in concurrence with that of studies by Sundas et al. [16] in which socioeconomic disparities in health outcomes such as hyperuricemia were also observed. Being of poor socioeconomic status is typically linked with malnutrition, deficiency of access to health care, and avoidance of good management of chronic illnesses and may therefore be implicated in the increased prevalence of hyperuricemia in such individuals.

These findings align with previous evidence and demonstrate the need to monitor the levels of urate regularly in tuberculosis treatment in the case of high-risk groups. Though most studies that include the current study evidence a high prevalence of hyperuricemia, the actual prevalence is a matter of geographic area, treatment protocols and in the population being treated and should be explored in further studies to promote risk-based monitoring and improved treatment adherence.

This research has several limitations which should be kept in mind upon interpreting the results. To begin with, it is one-center research conducted at a referral care center that may limit the generalizability of the results to other centers and populations. Second, there was no comparison group in the research that may have provided a sharper comparison of the TB patients who were treated with pyrazinamide and those who were not on the drug. Thirdly, the study duration of 3 months may not capture long-term effects of and complications resulting from hyperuricemia. Finally, owing to limited funds, dietary behaviors and other environmental determinants that may otherwise have provided additional information in the etiology of the development of hyperuricemia in the population were not fully measured.

Conclusion:

According to our study, hyperuricemia is a common and serious side effect of anti-tuberculosis treatment in tuberculosis patients. Hyperuricemia was observed to be closely associated with a number of demographic and clinical factors such as age, sex, BMI, residency, and socioeconomic class. These findings emphasize that regular monitoring of the concentration of uric

acid in persons at risk is indicated to prevent complications and to ensure optimal results of treatment. Further, the findings of the study corroborate with other evidence of metabolic derangement induced by pyrazinamide and illustrate the importance of personalized treatment of tuberculosis.

Conflict of interest: None

Disclaimer: None

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