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Hyperuricaemic Uveitis amongst Tuberculosis Patients taking Antituberculus Therapy; A Single Centre Study

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A B S T R A C T

Background: Around the world, among the top ten contributors to mortality is tuberculosis. People with asymptomatic hyperuricemia are typically ignorant of their illness and the potential repercussions, which include the possibility of diabetes, high blood pressure, kidney failure, cardiovascular disorders, and uveitis if they lack gouty symptoms.

Objective: This study aimed to evaluate the prevalence of hyperuricaemic uveitis amongst tuberculosis patients taking antituberculous therapy.

Methodology: The study was carried out at the Department of Pulmonology and Ophthalmology at Gajju Khan Medical College/Bacha Khan Medical Complex, Swabi, Khyber Pakhtunkhwa from January 2019 to October 2021. A total of 900 individuals who were taking 4 prescribed ATT drugs were enrolled. These were Ethambutal, Isoniazid, Rifampicin and Pyrazinamide. The independent sample t-test was used for statistical analysis.

Results: Out of 900 participants the male was 800 (88.8%) and female was 100 (11.1%). The age of the individual ranges from 20 to 60 years (mean 41 years). Based on age-wise distribution, 15% of patients were in the age group 20 - 30 years, 50% of patients were in the age group 31 - 40 years, 20% were in the age group 41-50 years while 5% of patientswere in the age group 51-60 years. The mean uric acid level was 19.325 ± 0.49 Mg /dl while the mean creatinine level was 0.80 ± 0.16 per mg. One patient had bands keratopathy involving refractile, yellow crystals on the Bowman membrane and deep corneal epithelial cells.

Conclusion: When ATT begins in tuberculosis patients, hyperuricaemic uveitis nearly always develops 8 weeks later. If this condition is not identified, it can have very dangerous consequences.

Keywords: Hyperuricaemia Uveitis; Tuberculosis; ATT

Introduction

In around the world, among the top ten contributors of mortality is tuberculosis. An estimated ten million persons contracted tuberculosis (TB) in 2017, of which 1.3 million people died in the HIV-negative population & an additional thirty thousand in the HIV-positive population.[1] Although it is a widespread illness in impoverished nations, its frequency is once again rising in developed nations.[2] For the first eight weeks of treatment, a conventional regimen of three or four medications is used. Antituberculosis therapy (ATT) frequently involves the use of the medi-cations such as (PZA), rifampicin, isoniazid (INH), ethambutol, and streptomycin.[3,4] Numerous medications used for tuberculosis therapy have a reputation for damaging the liver and kidneys. When renal functions are compromised, uric acid (UA) clearance is also impacted. Moreover, UA clearance varies depending on the circumstances. It has been shown that there is a negative correlation between tubular UA secretion and baseline metabolic index (BMI). PZA is a well-known modulator of proximal tubule-mediated UA transport.[5] A serum UA concentration in exceeding of urate solubility, or around 420 micromole/l for men and 360 micromole/l for women, is referred to as hyperuricemia.[6] Individuals with high uric acid levels but no signs of kidney stones, nephropathy, or gout are referred to as having asymptomatic hyperuricemia.[7] People with asymptomatic hyperuricemia are typically ignorant of their illness and the potential repercussions, which include the possibility of diabetes, high blood pressure, kidney failure, cardiovascular disorders, and uveitis, if they lack gouty symptoms.[8] In both rich and developing nations, increased urbanization, and economic growth have already significantly raised the level of UA globally. There have been reports of a rise in the prevalence of hyperuricemia recently. Uvetitis is a rare condition developed in patients treated with antituberculus drugs. Deposition of uric acid in the cornea, conjunctiva, and sclera are examples of ocular symptoms. Hyperuricaemia has been linked to chronic, recurring red eyes caused by scleritis, episcleritis, and iritis.[6] Gout patients have an increased risk of age-related macular degeneration (ARMD).The symptoms of acute uveitis include photophobia, abrupt onset unilateral discomfort, and redness that may be connected to lacrimation. The onset of chronic uveitis is subtle, and many individuals don't show any symptoms until difficulties start to arise.[7] The current study was conducted to find out Hyperuricaemic uveitis amongst tuberculosis patients taking antituberculus therapy

Objective

The objective of the study was to evaluate prevalence of hyperuricaemic uveitis amongst tuberculosis patients taking antituberculus therapy.

Methodology

This was a single Centre study conducted at the Department of Pulmonology and Ophthalmology at Gajju Khan Medical Collage/Bacha Khan Medical Complex, Swabi, Khyber Pakhtunkhwa from January 2019 to October 2021. A total of 900 individuals who were taking 4 prescribed ATT drug were enrolled. These were Ethambutal, Isoniazid, Rifampicin and Pyrazinamide. In accordance with WHO recommendations, all medications were administered in fixed dosage combinations based on weight.[8,9] We employed a fixed dosage, authorized combination of four medications with established bio equivalency.

Individuals who had assessment by an ophthalmologist and were determined to have normal serum UA, creatinine, and no uveitis on slit laser inspection were included in the research. The research did not include any individuals receiving chemotherapy, having liver or renal disorders, or both. Serum UA and creatinine baseline values were obtained, and the results were repeated 8–12 weeks following the start of ATT. SERUM UA and creatinine specimens were processed using the fully automated SELECTRA - E (Merck) chemical analyzer. Employing Merck reagents for diagnostic purposes. An ophthalmologist used a slit lamp examination on each patient to detect uveitis. The independent sample t-test was used for statistical analysis.

Results

In the present study, a total of 900 participants were included. The age of the study cases range from 20 to 60 year (mean 41 years). Based on age wise distribution, 15% patients were in age group 20-30 years, 50% patients were in age group 31-40 years, 20% in age group 41-50 years while 5% patients were in age group 51-60 years (Figure 1). Among study cases 88.8% were male whereas remaining 11.1% were female (Figure 2). All study cases had a normal creatinine level and hyperuricemia. The mean uric acid level was 19.325±0.49 Mg /dl while the mean creatinine level was 0.80±0.16 per mg (Table 2). Yellow, refractile crystals were seen in the deep corneal epithelial cells at the level of the Bowman membrane in the eyes of a small number of individuals with band keratopathy. Within the intrapalpable regions, there were additional conjunctiva nodules with needle-like crystals, which in one patient was linked to a minor case of marginal keratitis. The epithelium was scraped off and crystals were removed in order to address cornea haze or foreign body feeling caused by epithelial breakdown, which causes visual blurring. Not a single patient had tenovitis or scleritis. Two individuals had Tophi, or uric

Table 1. Uric Acid and Creatinine mean levels in Serum

Age in years	Uric acid /Mg /dl(mean SD)	Creatinine/mg
20 to 30	18.6 ± 0.58	0.88 ± 0.12
31 to 40	21.2 ± 0.82	0.62 ± 0.11
41 to 50	16.9 ± 0.46	0.95 ± 0.21
51 to 60	20.6 ± 0.21	0.76 ± 0.21
Mean	19.325 ± 0.49	0.80 ± 0.16

acid nodules. In male the creatinine precipitate was observed in 1% patients while posterior synechae was observed in 0.20% patients. In female the creatinine precipitate was observed in 0.50% patients while posterior synechae was not observed in any patients. Ocular manifestations in the eye secondary to Uric Acid crystals within the ocular tissue presented in the figure 3.

Discussion

Uric acid is eliminated from the urine by glomeruli at rates filtered (8-12%). 98-100% of the urates are reabsorbed after filtering; around half of these urates are reabsorbed. released into the proximal tubules, and approximately 40% of it is reabsorbed.[7] Based on age wise distribution, 15% patients were in age group 20-30 years, 50% patients were in age group 31-40 years, 20% in age group 41-50 years while 5% patients were in age group 51-60 years. Every research participant had a normal creatinine level and hyperuricemia. The mean uric acid level was 19.325±0.49 Mg /dl while the mean creatinine level was 0.80±0.16 per mg. These findings are in accordance with the findings of Ahmad et al. which shows almost similar findings with our study.[6] Our research indicates that over the course of the trial, ATT considerably raised the blood level of UA, which is comparable to another study where

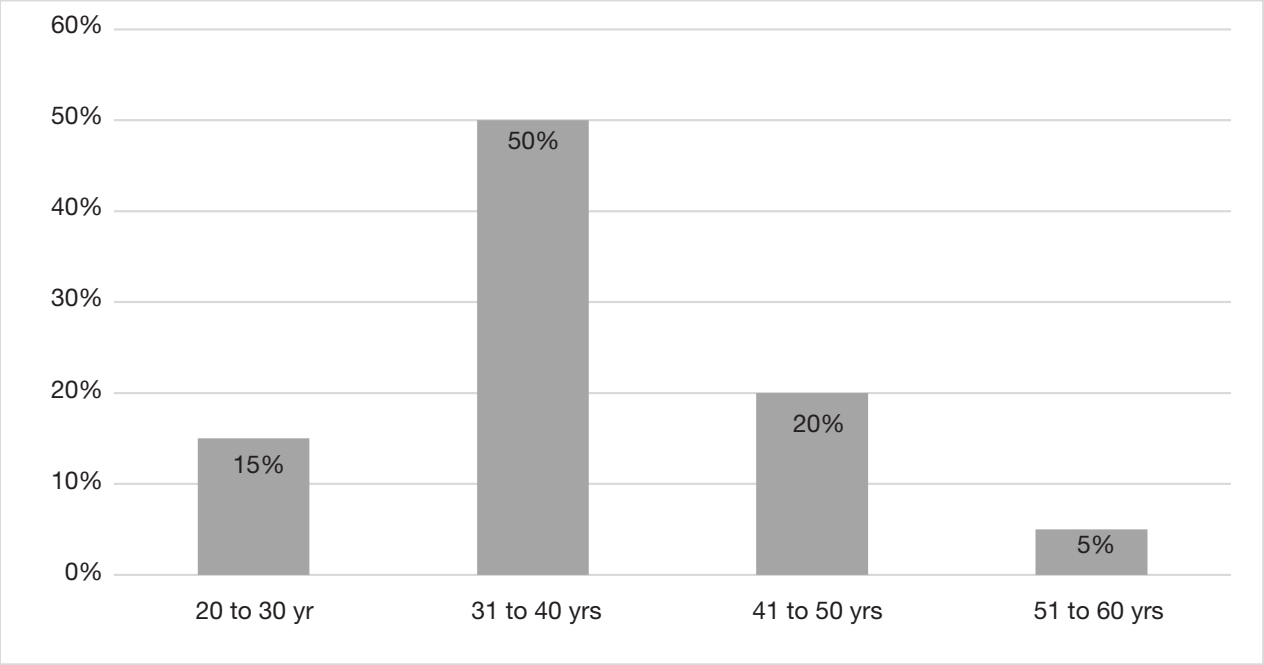

Figure 1. Age wise distribution of study cases

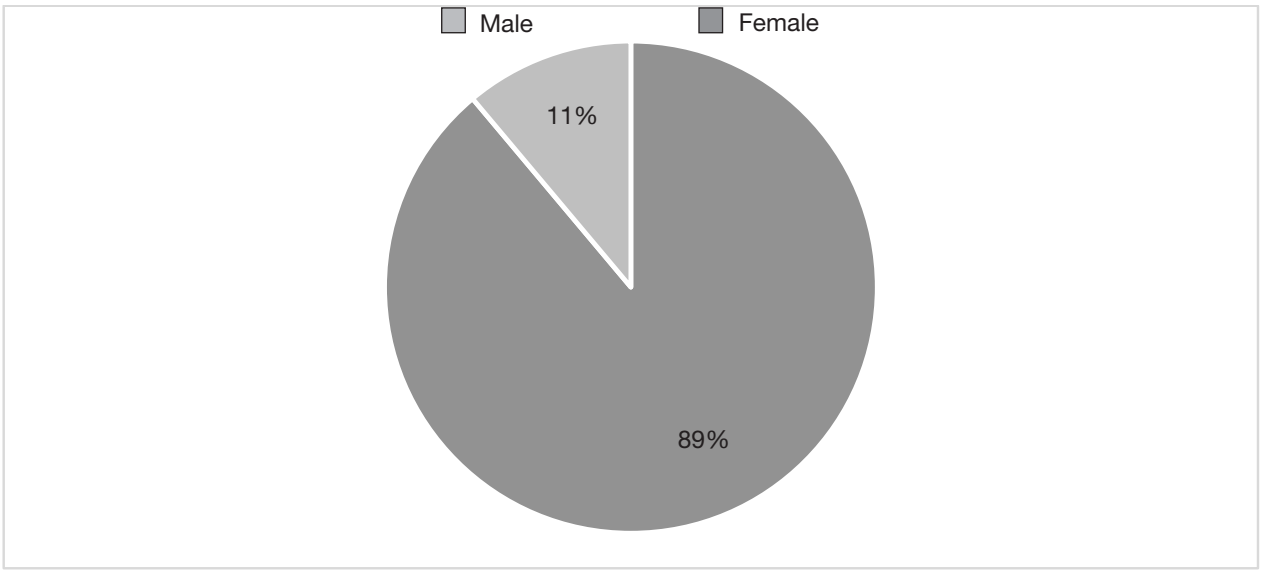

Figure 2. Gender base distribution of the study cases

hyperuricemia developed following the start of anti-TB medication.[5] In male the creatinine precipitate was observed in 1% patients while posterior synechae was observed in 0.20% patients. In female the creatinine precipitate was observed in 0.50% patients while posterior synechae was not observed in any patients. These findings are in accordance with the findings of Ahmad et al. which shows almost similar findings with our study.[6] Compared to our investigation, another study on kids using PZA produced different findings for blood uric acid levels following ATT.[10] The rationale is because, in our trial, PZA was administered in split doses, whereas in ours, we employed fixed dosage combination pills for therapy. Perhaps could have been the cause of our study's exceptionally high blood UA level. The fact that our study focused more on the adult population than the study on children might be another factor contributing to the elevated UA in our analysis when compared to the

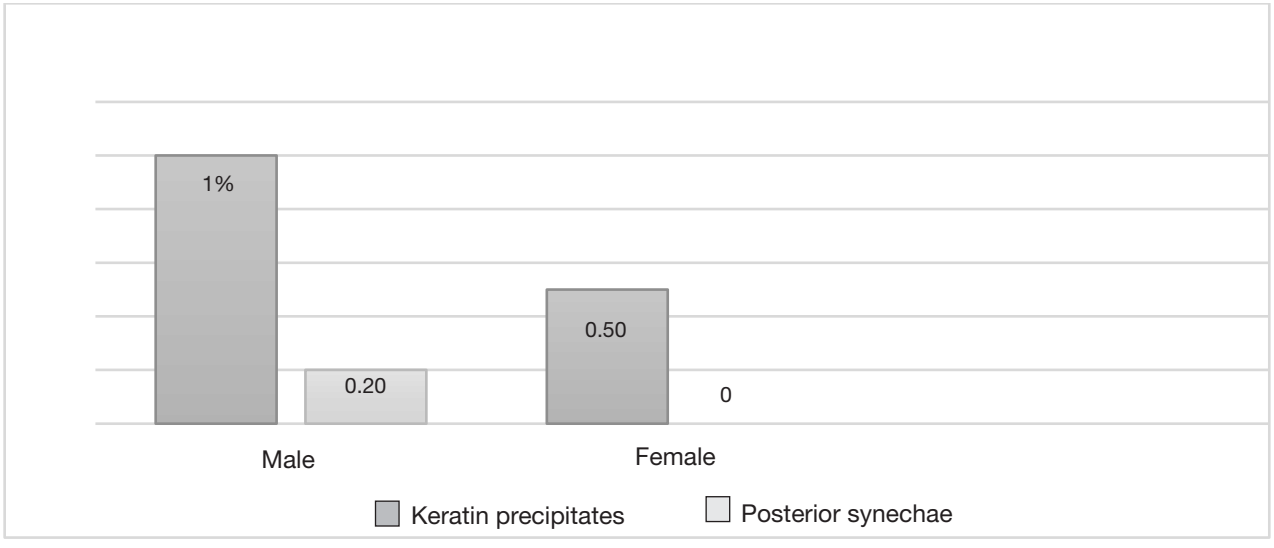

Figure 3. Ocular manifestations in the eye secondary to Uric Acid crystals within the ocular tissue

previously stated study. Our investigation yielded nearly identical results to that of study,[11] with the exception that our trial's proportion of keratin precipitates significantly higher. This might be because more recent, more advanced ophthalmological slit lights with higher sensitivity and ability to diagnose provide greater visualization. In one such trial, 50% of patients experienced escalating hyperurecemia between weeks 6 and 8 of therapy; in our study, however, 100% of patients experienced hyperurecemia. This discrepancy could be explained by the fact that only PZA was utilized as monotherapy in our investigation, which had 850 study individuals compared to 50 in the comparison trial. Moreover, compared to the previously described study, a greater proportion of ocular tissue manifestations linked to elevated UA was discovered.[6] This might be because we treated TB with combination therapy and looked at a bigger group. When the research's findings for blood creatinine and hyperuricaemic levels following ATT are compared to those from a study done in Nigeria, they are almost identical.[12] Our research generates results that are consistent with a recent study conducted by Alberti and his co-workers.[13]

Conclusion

Despite relatively minor side effects like hyperuricemic uveitis, which must be promptly recognized to minimize sight-threatening side effects, combination therapy is still a valuable treatment for people with pulmonary TB.

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