

Uric Acid Levels in Patients on Antituberculosis Drugs in the Southwest Region of Cameroon

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Abstract

Background: Antituberculosis drugs (ATDs) efficiently combat *Mycobacterium tuberculosis* either through direct molecular interactions or those of its metabolites. However, a variety of adverse effects have been reported, leading to frequent interruptions of treatment. To investigate the possible metabolic disturbances resulting from antituberculosis (TB) treatment, the uric acid (UA) level of patients on ATDs was measured in the southwest region of Cameroon. **Methods:** This hospital-based cross-sectional study involved 96 TB patients on ATDs and 32 controls who were neither on ATDs nor any other treatment that could increase UA levels. The hospital records of consenting participants were reviewed for medical history and questionnaires were issued. About 2 ml venous blood was collected and analyzed using spectrophotometers to determine UA levels. **Results:** Hyperuricemia was observed in 56/96 (58.3%) of the studied group as compared with 4/32 (12.5%) in the control group ($P < 0.001$). Our results indicated that treatment duration was significantly associated with hyperuricemia ($P = 0.0016$) while gender ($P = 0.1275$) was not. **Conclusion:** Hyperuricemia is associated with ATDs, with treatment duration being a significant factor. The disorder should be closely monitored, especially during the intensive phase of treatment.

Keywords: Antituberculosis drugs, Cameroon, hyperuricemia, intensive phase, southwest region

INTRODUCTION

Tuberculosis (TB), a highly infectious disease, remains a major global public health challenge. An effective control of TB has been achieved by the recommended WHO directly observed treatment, short-course (DOTS) strategy and the widespread use of first-line antituberculosis drugs (ATDs) such as isoniazid, rifampicin, pyrazinamide (PZA), ethambutol, and streptomycin.^[1] Although they efficiently combat the microorganism either due to the active principle itself or their metabolites,^[2] ATDs have been shown to induce various adverse drug reactions (ADRs) or side effects, which may lead to nonadherence with the risk of treatment failure.^[3,4]

The data on global prevalence of ADRs with first-line antitubercular drugs are scarce, and the antituberculosis therapy (ATT)-induced ADRs have become a clinical concern.^[5,6] Thus, this study was carried out in the four major TB centers of the southwest region of Cameroon, to assess

the level and risk of high uric acid (UA) levels in patients on first-line ATT.

METHODS

Study area and design

This hospital-based cross-sectional study, including 96 TB patients on ATDs between 1 and 3 months and 32 control individuals, was carried out at the four major TB/DOTS centers in the southwest region of Cameroon and including two regional hospitals (Limbe and Buea) and two general hospitals (Kumba and Mamfe). The inclusion criteria for the study grouped included TB patients on ATD between 1 and

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3 months and without any diseases (HIV, hepatic, kidney) or drug that could affect UA level while the control group included any apparently healthy individual neither on ATT nor any drug that could affect their UA level or metabolism.

Consenting participants' hospital records were reviewed for medical history, and a structured questionnaire was administered by trained personnel to collect clinical information, dietary habits, and sociodemographic characteristics.

About 2 ml of venous blood was collected from the participants by direct puncture to a vein located at the antecubital area of the arm and analyzed using spectrophotometer to determine their UA levels. Data were analyzed using the IBM Statistical Package for the Social Sciences (SPSS), Statistics for Windows, Version 20.0.

Ethical considerations

The ethical approval of the study was obtained from the Ethical Review Committee of the Faculty of Health Sciences Institutional Review Board of the University of Buea and the administrative clearance from the Southwest regional delegation for public health and directors of the various hospitals concerned. Written informed consent was gotten from each recruited study participant from 21 years and above with participation being voluntary.

RESULTS

Age distribution and mean uric acid of studied participants

Of the 96 studied participants on ATT enrolled, 50 (52.08%) were between the ages of 21 and 30 years, 14 (14.58%) between 31 and 40 years, 23 (23.96%) between 41 and 50 years, and 9 (9.38%) between 51 and 80 years. In the 32 control group, the mean age was 30.26 years ranging between 21 and 42 years.

The mean \pm standard deviation for UA level in the studied and control groups was 129.2 ± 461.6 mg/l and 56.7 ± 21.9 mg/l, respectively ($P < 0.001$) [Table 1].

Uric acid levels and gender

Comparison of the UA as shown in Figure 1 between the genders in the studied group shows that of the 59 males on

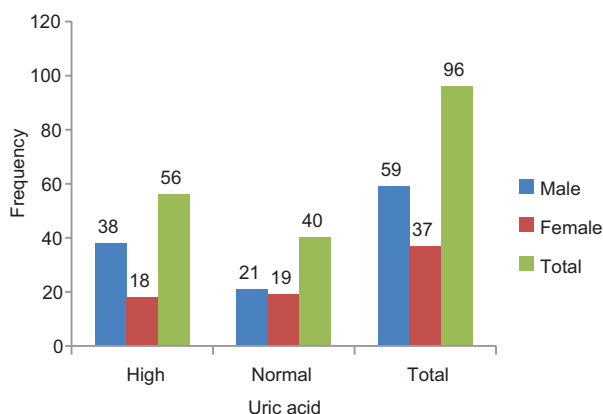


Figure 1: Uric acid levels by gender of the studied participants

ATT, 38 (64.4%) had high UA level, while of the 37 females, 18 (48.6%) developed high UA level ($P = 0.1275$).

Uric acid and treatment phase

The level of UA at the intensive (≤ 2 months) and continuation (> 2 months) phase among the studied patients is compared in Table 2. Forty-four (69.8%) of the 63 patients at the intensive phase against 12 (36.4%) of the 33 patients at the continuation phase had a high level of UA level ($P = 0.0016$).

DISCUSSION AND CONCLUSION

The hyperuricemia observed in the studied group is most likely a consequential effect of the ATT taken by the patients. This goes further to buttress the fact that ATT has the potential of inducing hyperuricemia as indicated in an earlier study.^[7] It has been shown that PZA increases the level of UA significantly during the course of therapy, with the mean concentration of UA significantly increasing after 1 month of ATT with PZA and falling 1 month after it was stopped.^[8]

Likewise the treatment regimen of patients involved in our study consisted of ethambutol and PZA, various studies corroborate our results with reports of prevalence ranging from 13% to 73.7% in patients treated with combination therapy or single therapy with either ethambutol or PZA.^[6,9-12] Ethambutol has been known to increase the production of UA by decreasing renal clearance.^[10]

Combination therapy has been shown to result in progressive hyperuricemia in about 50% of the patients between the 6th and 8th weeks of treatment.^[8,13] This is the likely explanation while the treatment duration was significantly associated with hyperuricemia, especially during the initial phase of treatment (≤ 2 months), and it most probably due to the effects of isoniazid, ethambutol, and PZA^[5,8-11] while its decrease altogether, at the continuation phase (> 2 months), might be due to the uricosuric of rifampicin and absence of both ethambutol and PZA.^[11,13]

Table 1: Uric acid level comparison between control and studied groups

Group	Uric acid level		Total	Mean \pm SD	P
	High (%)	Normal (%)			
Control	4 (12.5)	28 (87.5)	32	56.7 \pm 21.9	<0.001
Studied	56 (58.3)	40 (41.7)	96	129.2 \pm 461.6	
Total	60	68	128		

SD: Standard deviation

Table 2: Uric acid level according to treatment duration of patients on antituberculosis drugs

Duration on treatment	Uric acid level		Total	P
	High (%)	Normal (%)		
≤ 2 months	44 (69.8)	19 (30.2)	63	0.0016
> 2 months	12 (36.4)	21 (63.6)	33	
Total	56	40	96	

Higher UA level in male participants compared to females in our study, as shown in a similar study,^[11] is most likely related to their difference in metabolism. The lower serum urate in adult women than in men of a similar age has been thought to be due to the higher renal clearance of urate in women, as a result of higher plasma estrogen levels.^[14]

This study showed that TB patients who received standard treatment with ATDs developed high UA levels. The most affected being male and those at the intensive phase of treatment. This high UA could lead to other serious issues such as gout and kidney stones. Therefore, patients should be closely monitored during the intensive phase of the treatment to prevent the side effects of hyperuricemia as well as the monitoring of the therapeutic doses for high-risk patients.

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Conflicts of interest

There are no conflicts of interest.

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