Determining biochemical parameters in patients under tuberculosis treatment

Abstract

Introduction: Tuberculosis (TB) is an infectious disease caused, in most cases, by *Mycobacterium tuberculosis* (KOCH's bacillus). It remains a major public health problem despite various therapeutic strategies implemented, such as first-line and second-line anti-tuberculosis drugs (in the case of MDR-TB) which can have dire effects on certain organs (liver, kidney, thyroid, etc.). This study was conducted to evaluate parameters such as transaminases, creatinine, uric acid, and ionogram in tuberculosis patients who are under treatment.

Methods: This is a retrospective study conducted from August 2021 to December 2023. It involves 172 patients with tuberculosis treated according to WHO recommendations at the National Tuberculosis Control Program (NTP). Renal transaminases and biomarkers were assayed using enzymatic and colorimetric methods with the A15® multiparametric analyzer (Biosystems). The analysis of the results and the correlation tests were performed with Excel 2013 software.

Results: The majority of patients involved in this study were male (sex ratio = 3.3). During treatment, an increase in mean aspartate amino transferase (AST) was observed (p=0.0036). For alanine amino transferase (ALT), this is a slight increase from the mean that was observed (p= 0.137). Unlike creatinine and uric acid, we found non-significant associations with p=0.897 and p=0.890, respectively.

Conclusion: Our study showed that the risk of hepatotoxicity and dysthyroidism should be monitored in patients on anti-tuberculosis treatment. However, it would be relevant to consider the nature of the drugs used.

Keywords : Tuberculosis, Anti-tuberculosis drugs, Toxicity, WHO, creatinine, uric acid

Introduction

Tuberculosis is an infectious disease caused, in most cases, by *Mycobacterium tuberculosis* (KOCH's bacillus) [1], [2]. It is transmitted from person to person [3]. Drug management is based on the combination of several specific antibiotics or anti-tuberculosis drugs, for at least six months. Contagiousness decreases rapidly at the start of treatment, but respiratory isolation measures may be necessary in some cases [1], [3].

Though Tuberculosis remains a global major public health problem and particularly in Africa [4], [5], it can be prevented and cured. Nonetheless, TB was the second leading cause of death from a single infectious agent in the world after the coronavirus (COVID-19). Until 2022 it was still causing almost twice as many deaths as HIV/AIDS. More than 10 million people continue to fall ill with tuberculosis each year. This highlights the importance of the implementation of effective therapeutic strategies and the renewed commitment of countries [6]. Directly observed treatment (DOT) is an important part of the WHO's recommended response to the disease [7]. Although effective, TB therapy faces several obstacles such as adherence to treatment, duration, adverse effects of anti-TB drugs, and management of latent dormant tuberculosis [1]. This study was conducted in this context and focuses on the evaluation of certain biochemical parameters during anti-tuberculosis treatment

Methodology

This is a retrospective study conducted from August 2021 to December 2023 on patients following anti-tuberculosis treatment. The study included 172 patients whose surveillance was carried out at the following frequencies:

- M0: Pre-therapeutic evaluation
- M1: Evaluation after one month of treatment
- M2: Evaluation after two months of treatment

- M6: Evaluation after six months of treatment etc.

this population is divided into two groups:

- Group 1: those who are at **M0**
- Group 2: those who are at **M1, M2, M6, M8, M16, M17.....**

A dry tube sample was taken from the crease of the elbow in fasted patients. Subsequently, centrifugation was performed at 3000 rpm for 5 minutes.

The parameters studied:

✓ sex

✓ Biological parameters: transaminases, creatinine, uric acid, sodium, potassium. The determination of these parameters was carried out with the A15® (Biosystems) and VIDAS (Biomérieux) PLCs.

Results

In our study population, we have a predominance of men with 133 males, (77%) and 39 females (23%.).

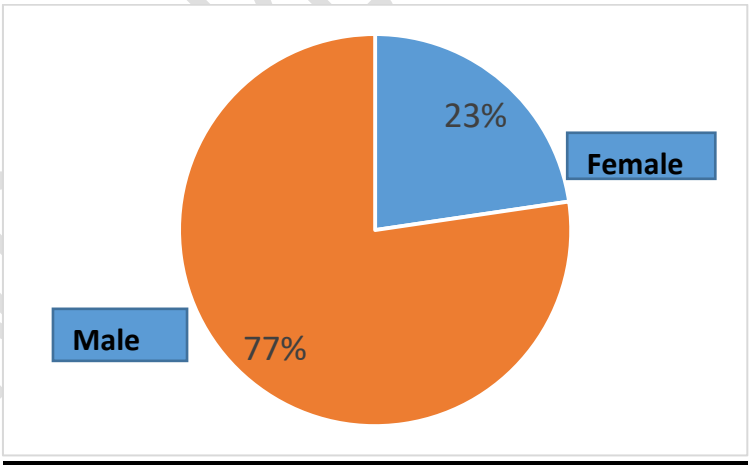


Figure 1: Gender distribution

The averages are 33.67 uI/l for ALT, 40.94 uI/l for AST, 9.22 for creatinine and 66.07mg/l for uric acid

Table 1: Means and Standard Deviation of Parameters

PARAMETERS	AVERAGE	TYPICAL GAP
ALT (IU/l)	33,67	25,77
AST (IU/L)	40,94	31,24
U A (mg/l)	66,07	27,10
CREATED (mg/l)	9,22	2,32
T4 (pmol/l)	18,67	12,46
NA+ (mmol/)	138,30	8,06
K+ (mmol/)	4,44	0,71
CL- (mmol/)	101,27	7,77

In group 1, 26 patients had an increase in AST and 14 patients had an increase in ALT level. And for group 2, 67 patients had an increase in AST levels and 47 patients had an increase in ALT levels.

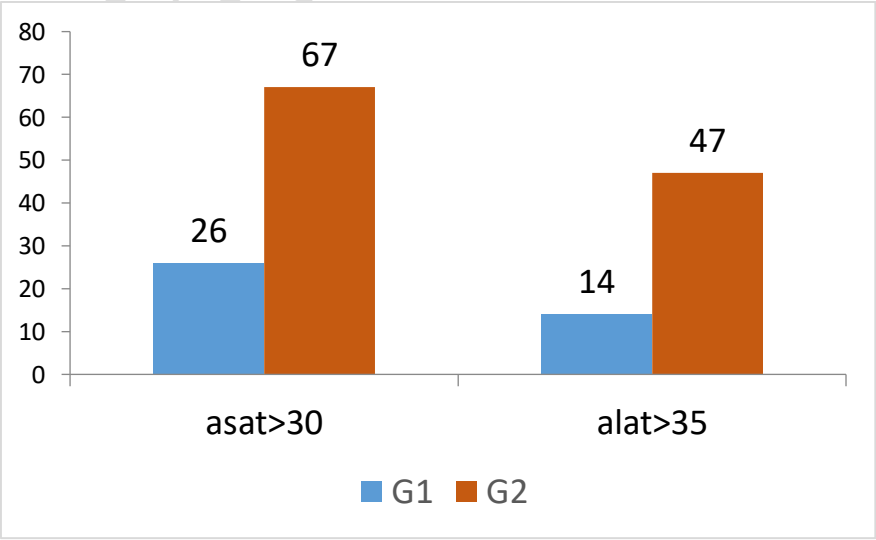


Figure 2: Number of patients with increased transaminases

A correlation equal to 0.22 with p-value equal to 0.0036 was found between the increase in AST and the use of medications. And for the ALT, we found a correlation equal to 0.11 with p-value equal to 0.137.

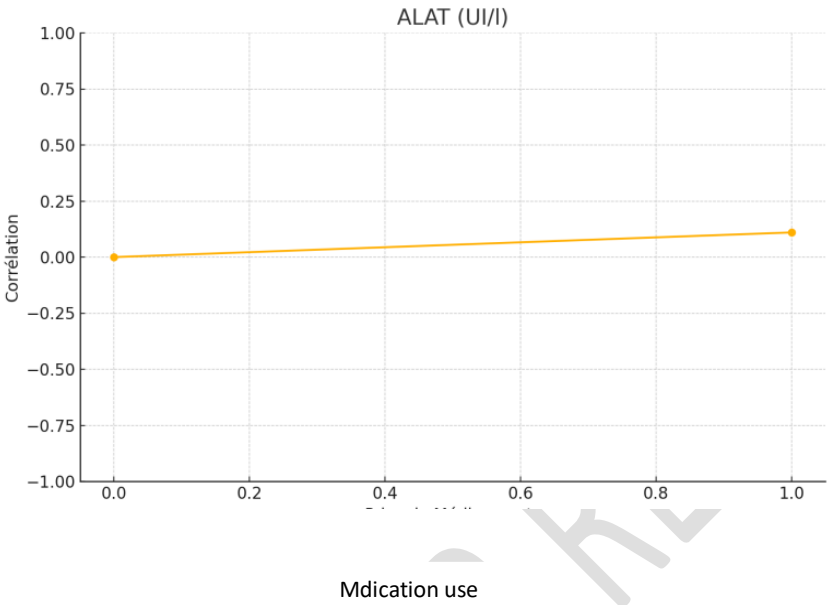


Figure 3: Correlation between ALT increase and medication use

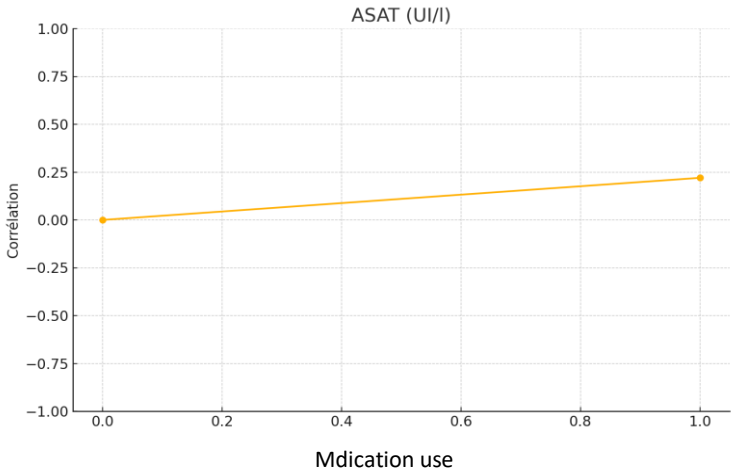


Figure 4 : Correlation between increased AST and medication use

In group 2, we noted that 7 patients had an increase in serum creatinine, whereas in group 1, we did not find pathological findings.

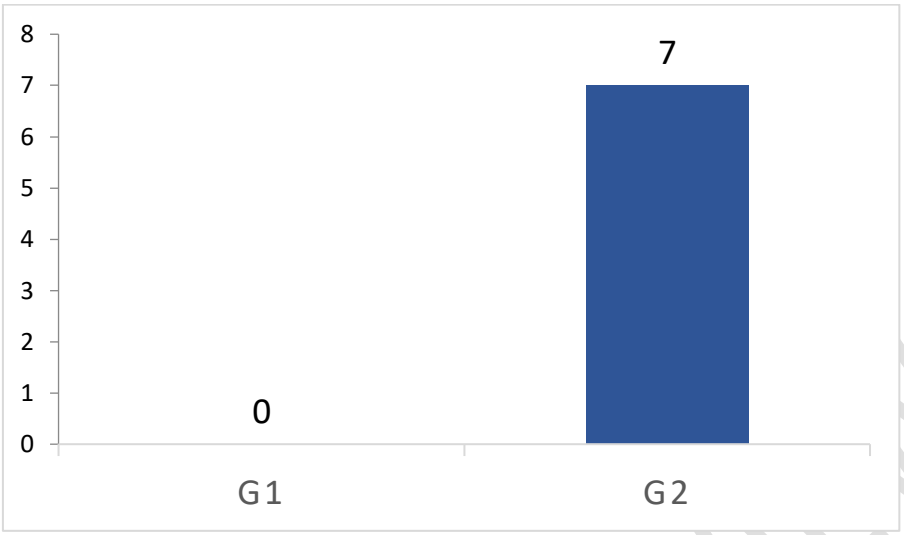
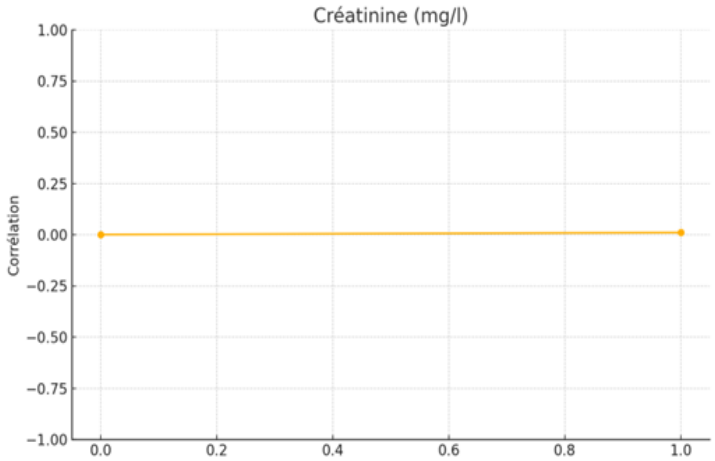


Figure 5 : Number of patients with increased serum creatinine

For this same parameter, a positive correlation was found between its increase and the use of drugs with ***R*** which is equal to 0.01.



Mdication use

Figure 6 : Correlation between creatinine levels and medication use

The results also showed that 14 patients had an increase in uric acid in group 1 while in group 2, 45 patients had hyperuricemia

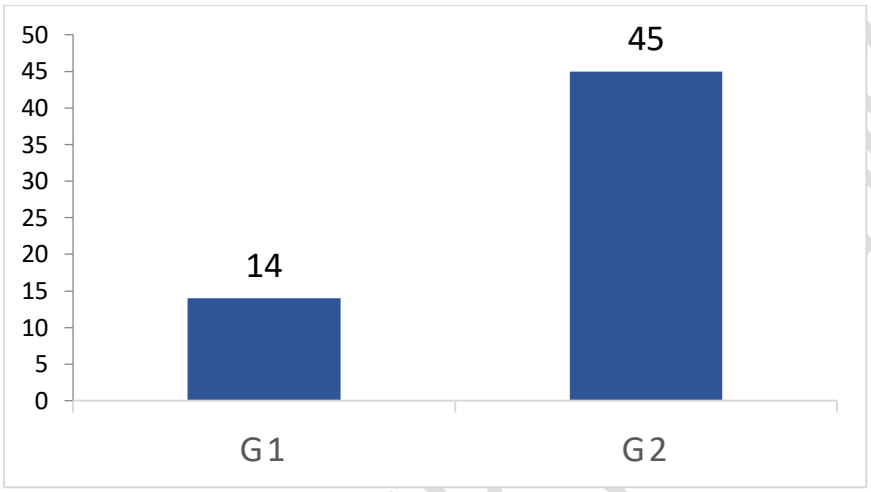


Figure 7: Number of patients with increased urate

Concerning this hyperuriemia, we noted a positive correlation with r equal to 0.01 and a p-value equal to 0.897

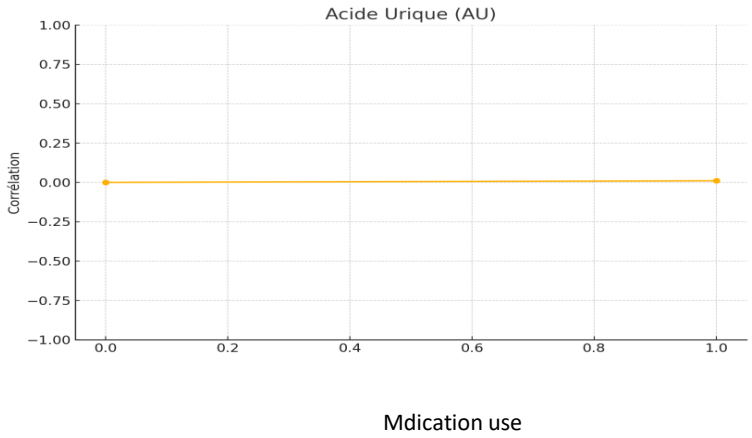


Figure 8 : Correlation between hyperuricemia and medication use

For sodium, we noted a decrease in 12 patients in group 1 and 7 patients in group 2

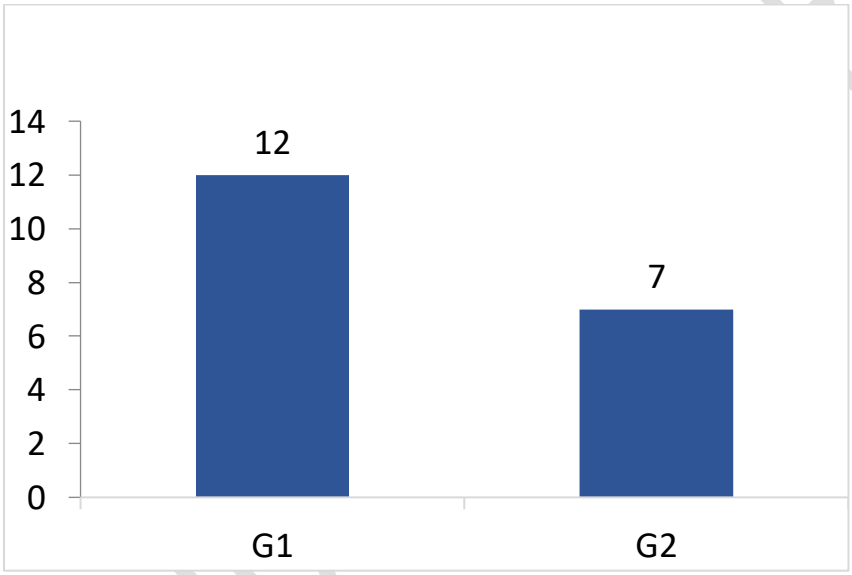


Figure 9 : Number of patients with decreased Na+

As for potassium, the number of patients with high potassium is greater in group 2 than in group 1

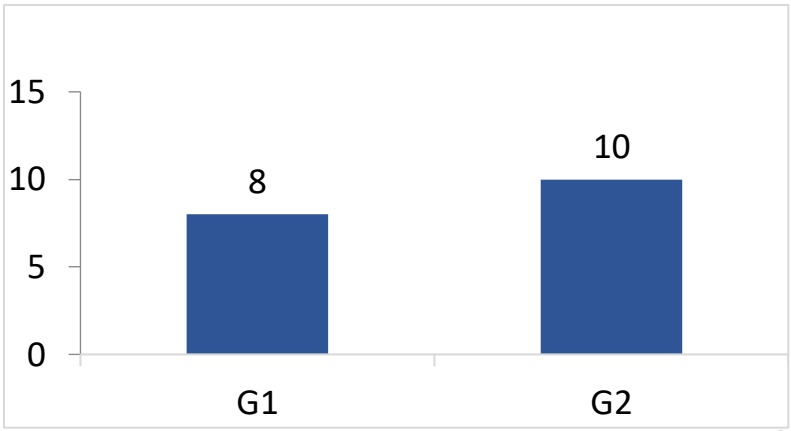


Figure 10 : Number of patients with high K+

Discussion

Tuberculosis is a common disease, especially in developing countries. Currently, it is a real public health problem. The management of TB involves several strategies, including the taking of anti-tuberculosis products by patients for a somewhat long period of time. This treatment is often accompanied by side effects that must also be managed both clinically and biologically. This requires an exploration of certain organs such as liver, kidney.... This exploration step involves the determination of a number of parameters, including transaminases, creatinine, uric acid, ionogram, etc.

The results of our study confirmed that 77% are male, with a gender ratio of 3.3. This result is consistent with the data in the literature, as many studies show a male preponderance. This is corroborated by the results of the studies conducted by UD Kombila [8], and Karima KARNAMI [9] which found a male predominance of 53.8%, and 65% respectively. At the Adjamé Anti-Tuberculosis Center, the study conducted on 89 cases of tuberculosis miliaria also showed that the disease was more common in men [10].

Regarding the results of transaminases, we found that the number of patients with high level of transaminase is higher at the level of group 2**.** This result could be explained by the use of drugs, which seems to have a slight positive influence on AST levels (p-value: 0.0036),

although the correlation is weak (0.22). Similarly, a non-significant correlation (0.11), indicating a probably negligible effect of the drugs on the ALT level with p-value = 0.137 was recorded. In the same line, LARACHI Hadjer, in a case study, collected 11 pharmacovigilance reports related to anti-tuberculosis treatment, 9 of which were related to hepatotoxicity problems [11]. According to Bouchentouf, et al; The risk of symptomatic hepatitis related to isoniazid is estimated to be between 2.5 and 6% [12]. Likewise, the study of Kombila, on the difficulties and obstacles in the management of multidrug-resistant tuberculosis at the Libreville University Hospital and Center, found 2 cases of severe hepatic cytolysis linked after investigation to an association of second-line treatment with phytotherapy [13]. The results of C. Altman, in the study of hepatic toxicity of antituberculosis drugs, showed that in 199 cases, liver damage appeared significantly earlier in the case of the combination of isoniazid and rifampicin [14].

For creatinine, the results showed that hypercreatinine is noted only in patients on anti-tuberculosis treatment. Although the mean serum creatinine (9.22mg/l) is within normal values and the association is not significant (p-value = 0.897), the use of anti-tuberculosis drugs may have an effect on creatinine levels. This is in line with the results of Devriese study in Belgium, where out of 48 cases, Rifampicin was found to be responsible for kidney failure [15]. Other results such as Webmaster's showed that out of 637 patients treated with anti-TB drugs, 23 or 3.6% had treatment-related kidney damage [16].

For the determination of uratemia, the results showed a mean of (66.07mg/l) which is within the range of its normal value and the p-value was equal to 0.890, indicating that there is no significant association. Authors such as Narang RK found that out of 52 cases treated with ethambutol, 22 cases (42%) showed no increase in uric acid [17]. According to Solangi, Ghulam

Akbar et al., anti-tuberculosis treatment with pyrazinamide affects uric acid levels early, but this change is reversible after removal of the pathogen [18].

The results of the serum sodium level show that the average value was 138.30 mmol/l and there is a slight decrease. But this decrease remains within the range of usual values. It could be remembered that hyponatremia can often be due to other underlying diseases and not to treatment. Authors such as Jonaidi Jafari N, F. Belhimer and F. Chentli confirmed these results in their work [19], [20]. And for the study by Jan F et al in Pakistan, on a series of 179 patients treated for multidrug-resistant tuberculosis, aimed at discovering the effect of amikacin on serum electrolytes in patients with MDR-TB, serum sodium remained in the steady state. This is to some extent similar to our work [21].

For serum potassium, the average (4.44 mmol/l) is slightly higher than the usual average value of 4.25 mmol/l. This result is controversial. They are in line with the work of Hong Ki Min et al [93]. On the other hand, the results of Yimer Seid on serious adverse effects associated with drugs against multidrug-resistant tuberculosis in patients of the ALERT hospital in Ethiopia; found hypokalemia of 49.3% [21].

Conclusion

The results of this study showed that anti-tuberculosis treatment in general can be associated with biological disorders such as liver and kidney damage. Hence the importance of biological monitoring of patients.

Disclaimer (Artificial intelligence)

Option 1:

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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