**International Journal of Innovation Scientific Research and Review**
*Vol. 03, Issue, 02, pp.827-830, February, 2021*
*Available online at http://www.journalijisr.com*

IJISRR

**Research Article**

**ISSN: 2582-6131**

# EXPLORATION OF RENAL FUNCTION IN PATIENTS UNDER TREATMENT FOR TUBERCULOSIS

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**Received 11th December 2020; Accepted 14th January 2021; Published online 15th February 2021**

**ABSTRACT**

The objective of this study is to determine serum and urinary creatinine levels, hematies leukocytes per minute and the albuminuria/urinary creatinine ratio in tuberculosis patients at the National Hospital Center for Pneumo-phtisiology (CNHPP) in Cotonou. This is a prospective, descriptive and analytical study that included 42 patients over 15 years of age followed for 6 months at the National Center for Pneumo-Phtisiology (CNHPP) in Cotonou. Serum creatinine and urinary albumin levels were determined by the enzymatic method. The count of red and white blood cells in the urine was done under the microscope on Malassez cells. The results show that out of 29% of men and 71% of women, the majority age group is between 39 and 58 years old. The weight of the tuberculosis subjects according to the treatment at the beginning of the treatment is around 52.5Kg and at the end of the treatment is around 57.5Kg. White blood cell counts/min in TB patients on treatment at the end of the intensive phase ($p<0.03$) and at the end of treatment ($p<0.01$) were significantly lower compared to TB patients not yet on treatment. Urinary creatinine levels increased significantly in TB patients at the end of treatment ($p<0.05$) compared to TB patients not yet on treatment and at the end of the intensive phase. From these results, it is important to note that anti-TB drugs must be used with great care to ensure the proper functioning of the vital organ that is the kidneys. The impact of these anti tuberculosis drugs, which does not appear to be significant, can become so very quickly with the use of other molecules and in the worst case lead to dialysis.

***Keywords:*** Tuberculosis, hematuria, creatinine, renal clearance, renal failure.

## INTRODUCTION

Tuberculosis is an infectious, contagious disease caused by *Mycobacterium tuberculosis* (and sometimes by Mycobacteriumbovis and Mycobacteriumafricanum) [1]**.** It remains the leading fatal infectious disease despite effective treatment. The number of new cases of tuberculosis worldwide in 2012 is estimated at 8.6 million [2]. Incidence rates remain highest in developing countries [2]. Africa is the most affected region with an incidence rate of 27% [3]. In Benin, 4,075 cases of tuberculosis of all forms, including 3,454 (84.8%) cases of smear-positive pulmonary tuberculosis (new smear-positive cases, relapses, failures, and relapses after abandonment) were detected and treated in 2012 [4]. Tuberculosis is now curable with well-managed drug therapy [5]. While the efficacy of currently available drugs is undeniable, their complications are often the price to be paid for their therapeutic success [5]. All these drugs can sometimes cause side effects [6]. Some are excreted by the kidneys and can therefore be nephrotoxic [7]. In Benin, no studies on the renal toxicity of anti-tuberculosis drugs in patients under treatment have been conducted. For this reason, we felt it was important to explore the renal function of patients undergoing tuberculosis treatment. The overall objective of this study is to determine the impact of anti-tuberculosis drugs on kidney function in people with tuberculosis. The hypothesis guiding this study is that the use of anti-tuberculosis drugs results in damage to kidney tissue.

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## PATIENTS AND METHODS

The study took place at the Centre National Hospitalier de Pneumo-Phtisiologie (CNHPP) in Cotonou, which monitors adult tuberculosis patients. It was a prospective, descriptive, and analytical study of data collected over 6 months. For the conduct of this study, the informed and accepted consent of the patients is collected through a questionnaire following the scientific research procedure. Included in this study are all adult patients (over 15 years of age) with tuberculosis during the study period. Blood and urine (collected over 3 hours) were routinely collected from all patients included in the study. Patients' blood was collected in dry tubes (without anticoagulant) before, at the end of the intensive phase and at the end of treatment. Morning urine was collected over 3 hours in 500ml jars. Creatinine (Biolabo, France) and albumin (Ccromatest, Spain) were determined by enzymatic methods. The Hematies Leucocytes per Minute (HLM) was performed using the microscope. The treatment is based on a combination of ionized (H), rifampicin (R), pyrazinamide (Z), ethambutol (E) and streptomycin (S) for a period of 6 months. It consists of a first phase (called the intensive phase) with a combination of ERHZ for two months, followed by four months of RH. In case of recurrence, the treatment consists of a 3-month phase with 2 months of SERHZ followed by 1 month of ERHZ and 5 months of ERH for a total of 8 months.

**Statistical analysis :**

The data were evaluated by the student test using the statistical analysis software Sigma Plot (Systat Software, Inc. San Jose, CA, USA). Quantitative data are expressed as mean ± standard deviation.

## RESULTS :

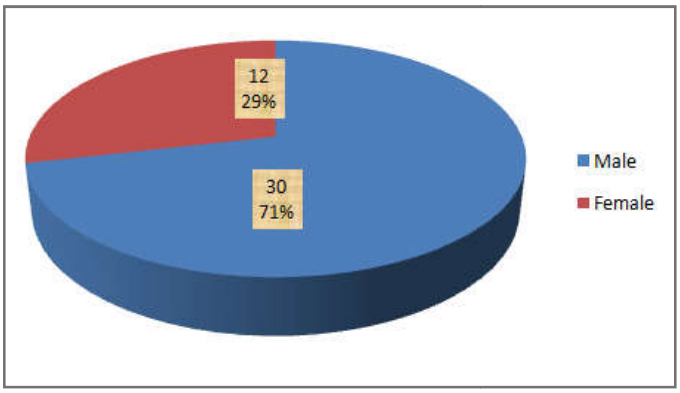


**Figure 1:** Gender Distribution of Patients

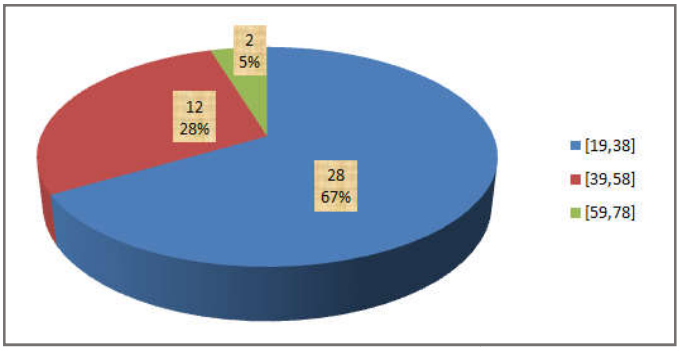


**Figure 2:** Distribution of Patients by Age 20 Years

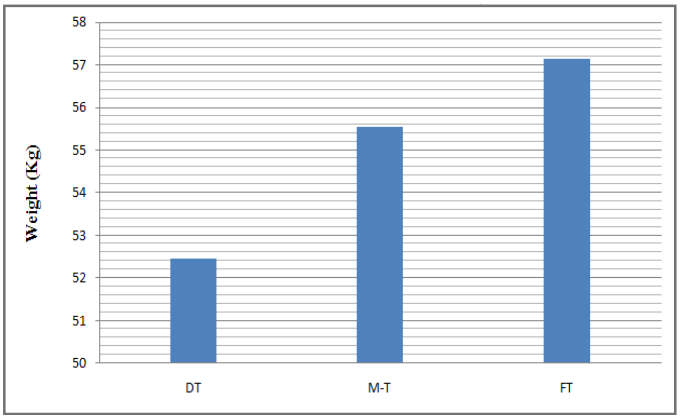


**Figure 3:** Weight variation in tuberculosis subjects as a function of treatment.

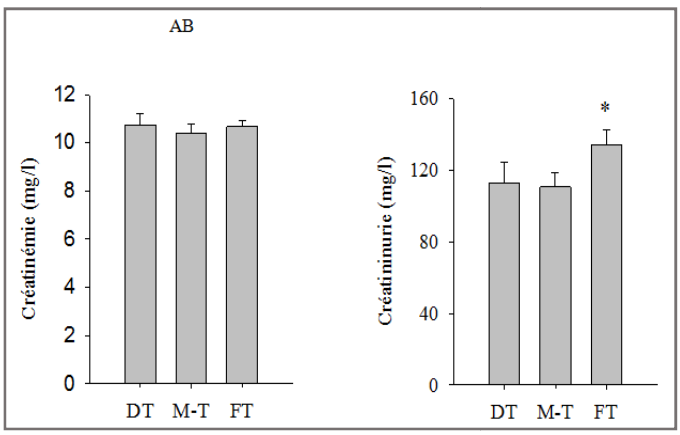


**Figure 4:** Creatinine (A) and creatinineuria (B) in TB patients who have not yet started treatment and in those on treatment at the start and end of treatment. (*p<0,05).

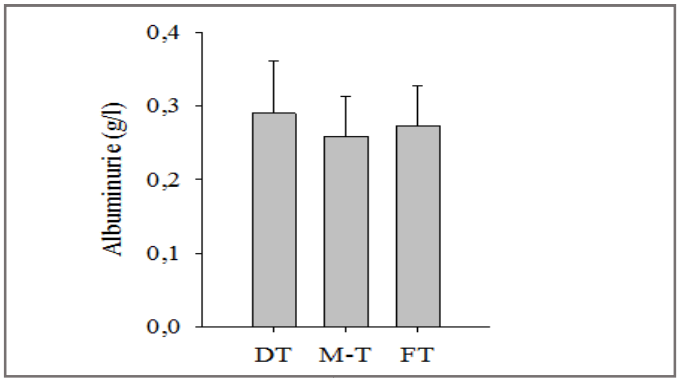


**Figure 5:** Albuminuria in untreated tuberculosis patients and in patients on treatment at the beginning and end of treatment.

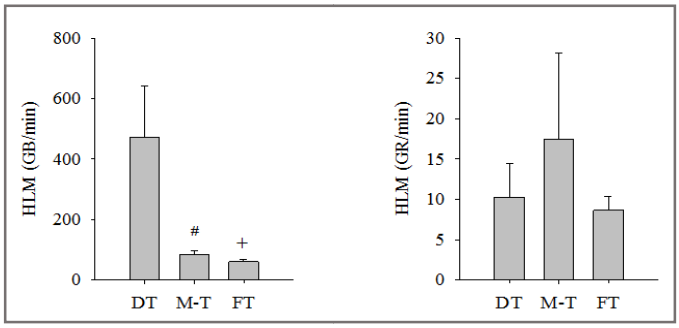


**Figure 6:** Leukocyte Red Blood Cells per Minute (LBC) in tuberculosis patients not yet on treatment and in patients on and off treatment.

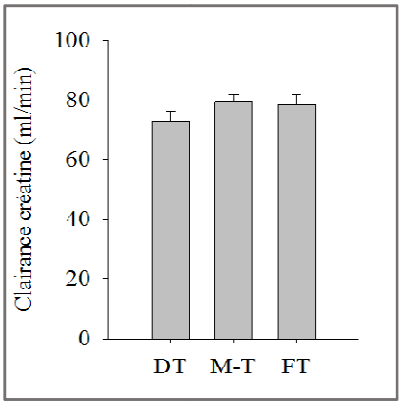


**Figure 7:** Creatinine Clearance in Treatment-naïve TB Subjects and Treatment-Mature and End-of-Treatment Subjects.

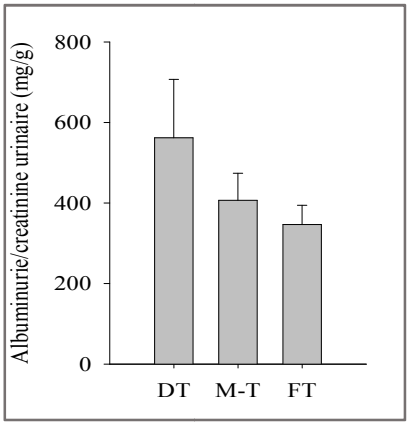


**Figure8:** Albuminuria /urinary creatinine in untreated tuberculosis patients and in patients on treatment at the start and. end of treatment.

## DISCUSSION

Our study involved 42 tuberculosis subjects followed at the CNHPP. Blood and urine samples used for testing are collected from patients in three stages: before treatment (TD), at the end of the intensive phase of treatment (MT) and at the end of treatment (FT). A major characteristic of tuberculosis, demonstrated in many parts of the world, is that it is predominantly male. The difference between males and females is most notable in Asia and sub-Saharan Africa [8]. This is confirmed by the present study. Of all the tuberculosis subjects who participated in our study, 71% were male compared to 29% female (Figure 1). According to Vinod K Diwan, Anna Thorson. 1999, each year more than 70% of new cases of tuberculosis are diagnosed in men [9]. Iffat et al. (2005) reported that out of every 100 TB patients, 67% were male versus 33% female [10]. Nkoghe et al (2005) estimated the male prevalence of tuberculosis to be 60% in a study in Gabon [11]. This result is similar to that of Cissé and Domoua in Côte d'Ivoire and Mabiala in Congo [12, 13, 14]. In Benin, Gninafon et al. (2010) reported that out of 2973 national tuberculosis cases, 65% were male [15]. Similarly, Akpovi et al (2013) reported that out of 83 TB patients, 71% were male and 29% female [16]. There is no clear explanation for this unequal distribution of tuberculosis. According to a 1998 WHO report, men tend to report their disease more often than women, suggesting that the prevalence of tuberculosis is underestimated in women [2]. However, this reason alone cannot explain the observed difference. Barely 10% of *M. tuberculosis* infections progress to active tuberculosis, which is the form generally reported to clinicians [17]. Some authors believe that the progression from infection to disease is influenced by biological differences between men and women [8,18,19]. In addition, 67% of patients are between 19 and 38 years of age. Adults aged 39 to 58 years are affected at 28%. Persons aged 59-78 years (5%) were the least infected with *M. tuberculosis in the* population (Figure 2). There was an increase in body weight among individuals with M. tuberculosis who were on treatment at the start and end of treatment (Figure 3). The same observation was made by Ouédraogo in Burkina Faso on age and weight increase [20]. 20] This study showed that TB drugs significantly lowered WBC levels in subjects on treatment at baseline ($p<0.03$) and at the end of treatment ($p<0.01$) compared to subjects not yet on treatment. No cases of decreased WBC counts were reported in the literature. The progressive decrease in WBCs observed is therefore not due to an alteration in renal function caused by the *antituberculosis* drugs but to the efficacy of the latter on *Mycobacteriumtuberculosis*. The fact that the RBC level does not vary significantly despite the progressive decrease in WBC in the urine supports this explanation. The albuminuria/urinary creatinine ratio did not vary significantly between the three groups. Our results disagree with those of Oyedeji et al (2013) [21]. We showed that the increase in GB levels in TB patients before treatment was an infection. The latter is the basis of the transient increase in the albuminuria/urinary creatinine ratio observed in pre-treatment patients [22]. Blood creatinine in TB patients on treatment at the end of the intensive phase and at the end of treatment was not significantly different from the results obtained in pre-treatment TB patients. This result does not confirm those of Edalo and colleagues (2012) [23]. Serum creatinine is a marker that accounts for glomerular filtration rate [24]. Less sensitive and not very specific, it is necessary for the renal impairment to be advanced for its values to change significantly [24].

## CONCLUSION

In this study, we analyzed the effect of anti-tuberculosis drugs on kidney function in subjects with tuberculosis using commonly used biochemical tests. The results of this study showed that anti-TB drugs must be used with great care to ensure the proper functioning of the vital organ of the kidney. The impact of these anti tuberculosis drugs, which does not appear to be significant, can become significant very quickly with the use of other molecules and lead in the worst case to dialysis. We strongly suggest that a more in-depth study be carried out. This will involve selecting a large number of patients suffering from tuberculosis and following them rigorously in their treatment. In addition to the biological parameters measured in this study, other more specific tests such as NGAL (Neutrophil PolynuclearGelatinase-Associated Lipocalin), renal CT scan and renal Doppler ultrasound should be performed.

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