Research Article

EXPLORATION OF HEPATIC FUNCTION IN PATIENTS UNDERGOING OR HAVING UNDERGONEANTI-LEPROSY TREATMENT AT OUIDAH (BENIN); WEST AFRICA

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ABSTRACT

Leprosy is a contagious infectious disease caused by Mycobacterium leprae (M. leprae) or Hansen's bacillus. This bacterium has a special affinity for the skin and peripheral nerves. Known since antiquity, this disease is still a public health problem in many countries around the world. However, much progress has been made in the fight against leprosy, including the advent of Multidrug Therapy (MDT) in 1982 for all leprosy patients. Benin and many African countries are in the process of eliminating the disease and MDT is available in all countries. Multidrug therapy has truly revolutionized leprosy control. The aim of our work is to see the impact of MDT on liver function in leprosy patients undergoing treatment and those who have finished treatment. In order to do this we took 80 lepers (those who had finished treatment and those who were in the process of treatment) to whom we made each one:

- The ASAT/ALAT transaminase assay
- The gamma-glutamyltransferase assay

This work represents the first extensive study of the impact of anti-leprosy drugs on liver function. It will be of great use to researchers in creating drugs that are less toxic to hepatocytes

Keywords: leprosy, Mycobacterium leprae, pathogen, contamination, therapy

INTRODUCTION

Leprosy, a contagious disease, has long been a dreaded scourge of humanity. This bacterium has a special affinity for the skin and peripheral nerves [1]. Some communities attributed its occurrence to a divine curse and others had had inhuman reactions towards the patients, who were driven out of their homes and even isolated in leprosaria [1]. The pathogen of this infection is *Mycobacterium* Leprae, discovered by ARMAUER HANSEN in 1873. Contamination is essentially familial. The reservoir of Mycobacterium Leprae is essentially human and the sources of contamination are nasal secretions of untreated lepers, the main sources of contamination, as well as ulcers, breast milk, faces. In view of the seriousness of the disease, because of the blow of its handicap and especially the social stigma attached to it, strategies to combat it have been organized in a number of countries. The global fight against leprosy is one of the most important achievements in the field of public health in recent years and the WHO has made it a key issue, hence the slogan "Eliminating leprosy as a public health problem" [2]. However, much progress has been made in leprosy control, including the advent of multidrug therapy (MDT) in 1982 for all leprosy patients [3]. Multidrug therapy has revolutionized leprosy control, reducing the prevalence of leprosy from 122 cases per 10,000 inhabitants in 1985 to less than 1 case per 10,000 inhabitants (WHO target) [4]. In BENIN, leprosy control started well before 1960 and was strengthened after independence by the creation of new areas of major endemics. Slowly the number of patients decreased from 20,000 cases in 1982 to 13771 in 1986 and 2256 in 1990. The prevalence of the disease

fell from 3.18% in 1986 to 0.47% in 1990 [5]. The Representative of the Minister of Health stated that 75% of the new cases detected are multibacillary forms and therefore highly contagious. Despite global progress, leprosy is still far from being eradicated and greater vigilance is required in leprosy control efforts [6]. Treatment of leprosy is long-term, from 6 to 12 months or more, and involves the use of drugs that can cause hepatotoxicity [7]. It is therefore important for patients undergoing treatment to explore liver function before, during and after treatment for possible liver damage. Our work consisted of "Exploring the liver function of subjects under treatment and those who have undergone anti-leprosy treatment at the Ouidah Anti-Leprosy Treatment Centre". In this work, our objectives are as follows:

Overall Target

To explore the consequences of leprosy treatment on liver function.

Specific Objectives

It's about:

- Transaminase (AST and ALT) determinations in both treated and untreated leprosy patients.
- Dosing for Gamma-Glutamyl-Transferase (GGT) in treated and untreated leprosy patients.

PATIENTS AND METHOD

Type of study

This is a three-month prospective study in collaboration with the Ouida centre to evaluate the impact of anti-leprosy drugs on the liver

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function of subjects under and those who have finished treatment.

Target population

It is leprosy patients under and those who have finished treatment who meet the criteria for inclusion and non-inclusion.

Criteria for inclusion

- Leprosy patients of both sexes
- Patients with up-to-date records i.e. regular follow-up

Exclusion criterion

- People not suffering from leprosy.
- People with hepatitis B or C
- Analytical method

Pre-analytical phase

- patients fasting or not
- venous sampling done on dry tube
- labeling of samples taken
- centrifugation of samples at 3000t/min.

Analytical phase

We had to do:
the determination of the transaminases ASAT/GOT and ALAT/GPT

ASAT/GOT dosing
Principle

Determination of aspartate aminotransferase (ASAT) activity :

L-Aspartate+ά-ketoglutarate $\xrightarrow{\text{ASAT}}$ oxaloacetate + L-glutamate

Oxaloacetate + NADH+H+ $\xrightarrow{\text{MDH}}$ L-Malate + NAD +
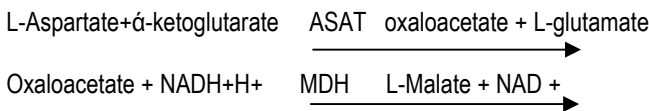
MDH: Malate dehydrogenase.

Method of operation

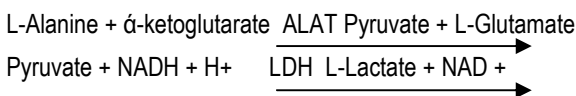| Reagent R1	200µL
Reagent R2	50µL

Mix, wait 25 seconds and add :

Sample	25µL

Reference value
Serum, plasma (37ºC): < 40 U/L

Dosing of ALAT/GPT
Principle

Determination of the activity of alanine aminotransferase (ALAT) :

L-Alanine + ά-ketoglutarate $\xrightarrow{\text{ALAT}}$ Pyruvate + L-Glutamate

Pyruvate + NADH + H+ $\xrightarrow{\text{LDH}}$ L-Lactate + NAD +

LDH: Lactate dehydrogenase.

Method of operation

Reagent R1	200µL
Reagent R2	20µL

Mix, wait 25 seconds and add :
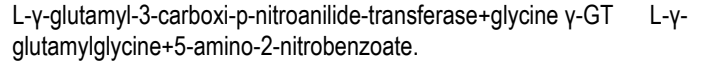
Sample	25µL

Reference value

Serum, plasma (37ºC): < 40IU/L

The dosage of GGT
Principle
The determination of the activity of γ-glutamyl-transferase is based on the following reaction:
L-γ-glutamyl-3-carboxi-p-nitroanilide-transferase+glycine $\xrightarrow{\text{γ-GT}}$ L-γ-glutamylglycine+5-amino-2-nitrobenzoate.

Method of operation

Dissolve one R.2 tablet in 15 ml of R.1 buffer. Cover with a cap and mix gently to dissolve the contents.
- Working solution 1.00ml
- Sample   0.10ml

Reference value

Woman	7 - 32UI/L
Man	11 - 50 IU/L

Post-analytical phase

After each dosing operation the values found are recorded on the bench record. Thus the transaminase and GGT values per sample are recorded.

Statistical analysis

The search for correlation between the different biochemical parameters considered is carried out by calculating the correlation coefficient "r" and a comparison of the averages was made according to the duration of treatment (between 6 months and 4 years and then more than 4 years) The data were processed with Microsoft Office Excel 2007. The essential statistical parameters which made it possible to carry out the various statistical tests are presented below.

Average

$$\bar{x}=\frac{1}{n}\sum_{i=1}^{n} xi \; ; \qquad \bar{y} = \frac{1}{n}\sum_{i=1}^{n} yi$$

Variance

$$V(x)=\frac{1}{n}\sum_{x=1}^{n}(xi - \bar{x})^2 \; V(y)=\frac{1}{n}\sum_{x=1}^{n}(yi - \bar{y})^2;$$
$$\sigma(x) = \sqrt{V(x)} \; \sigma(y) = \sqrt{V(y)} \; ;$$

Covariance

$$Cov(x, y)=\frac{1}{n}\sum_{i=1}^{n}(xi - \bar{x})(yi - \bar{y}) \; ;$$

Correlation

$$r=\frac{Cov(x,y)}{\sigma(x)\sigma(y)}$$

RESULTS

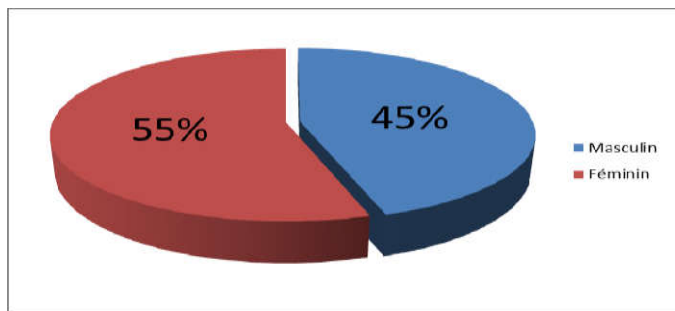Our study involved a population of 80 subjects divided into two groups according to gender.

Figure 1: Distribution of the study population by gender.

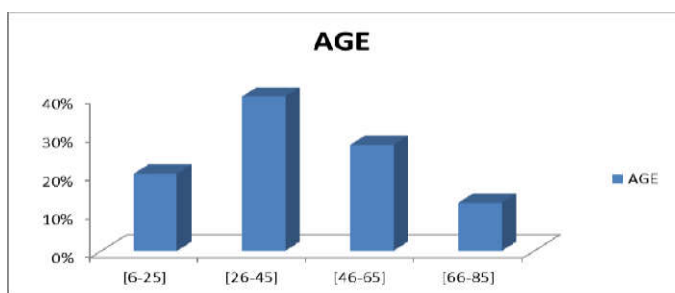Of the 80 subjects in our study population, 45% are male and 55% female.

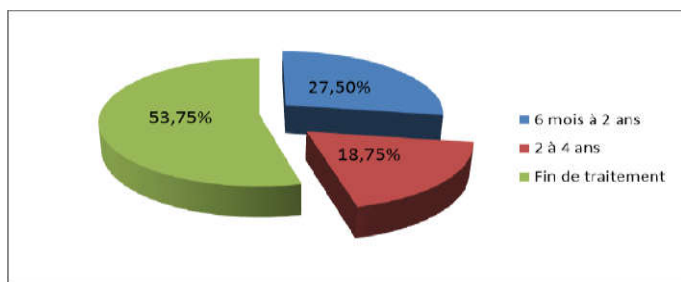**Figure 2:** Age distribution of the study population.

Figure 3: Distribution of the study population by duration of treatment.

Table 6: Some statistical parameters considered for the collection of GER, GPT and GGT values in patients on and off treatment.

Statisticalparameters	TGO	TGP	GGT
average	29,81	20,66	30,61
Standard deviation	19,85	14,07	36,92
variance	394,23	198,02	522,26
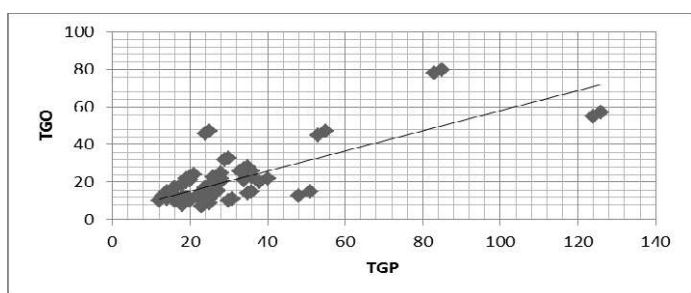
Figure 4: Correlation between TGO and TGP

Legend: This figure shows the correlation between GER and GPT values in patients on and off treatment (r=0.75 and y=0.67x+0.53).
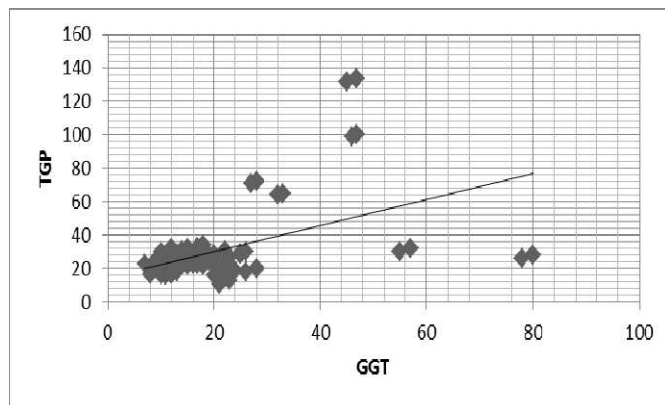

Figure 5: Correlation between TGP and GGT

Legend: This figure shows the correlation between TGP and GGP values in patients on and off treatment (r=0.47 y=0.66x+0.17).
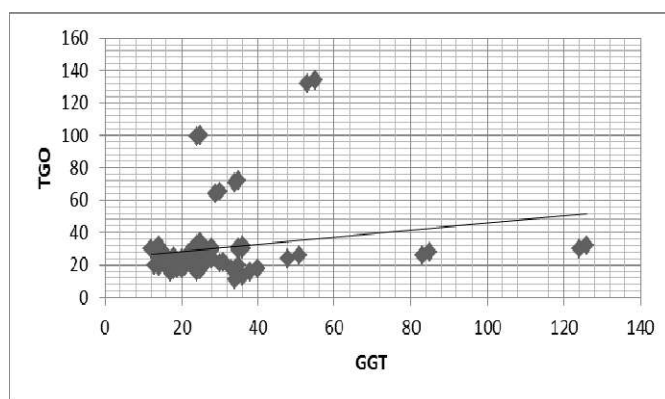

Figure 6: Correlation between TGO and GGT

Legend: This figure shows the correlation between TGO and GPM values in patients under and over treatment (r=0.19 and y=0.96x+0.27).
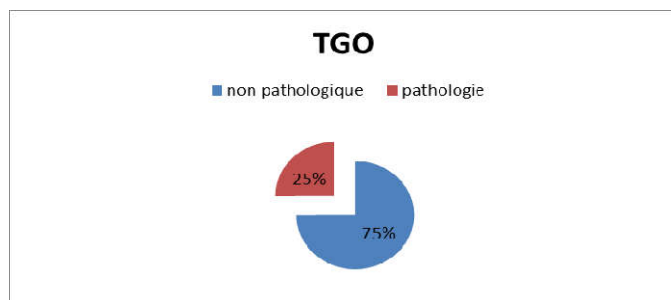

Figure 7: Percentage of pathological and non-pathological GERD values in patients 6 months to 4 years of treatment.
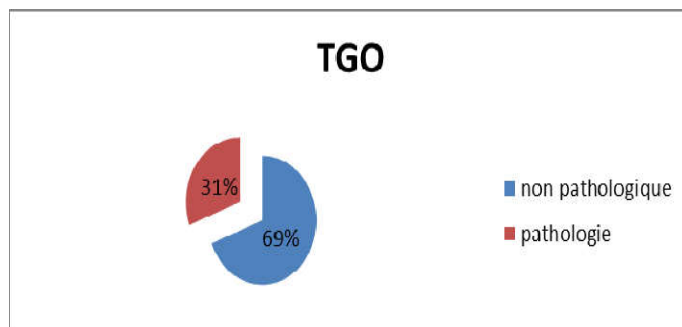

Figure 8: Percentage of pathological and non-pathological GERD values in patients with a treatment duration of more than 4 years.
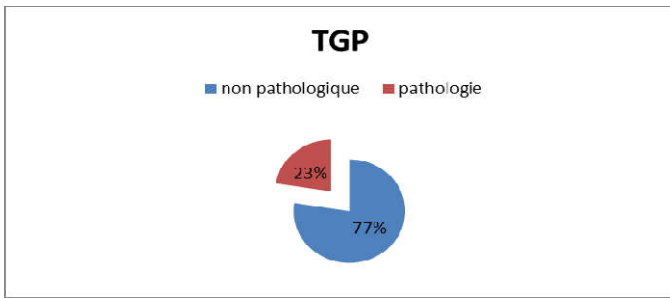
Figure 9: Percentage of pathological and non-pathological TGP values in patients with a treatment duration between 6 months and 4 years.
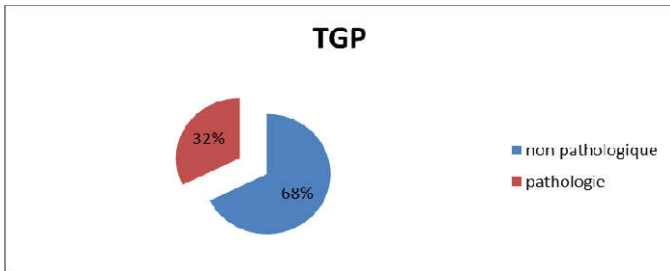

Figure 10: Percentage of pathological and non-pathological TGP values in patients with a treatment duration of more than 4 years.
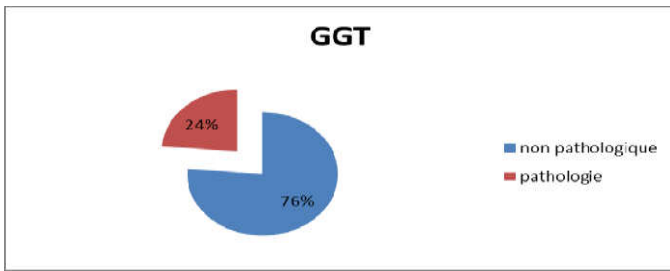

Figure 11: Percentage of pathological and non-pathological GGT values in patients with a treatment duration between 6 months and 4 years.
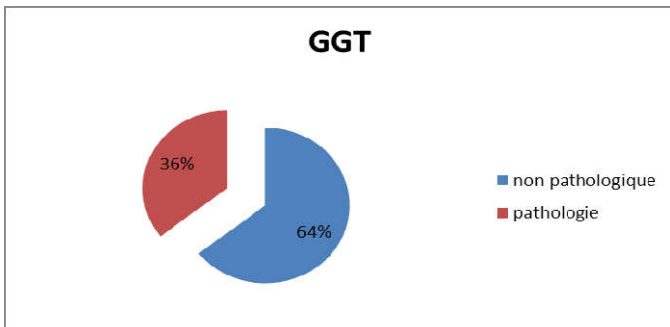

Figure 12: Percentage of pathological and non-pathological GGT values in patients with a treatment duration of more than 4 years.

DISCUSSION

Looking at the data in Table 6 of the subjects we notice that there is an alteration in liver function. Similarly, taking into account figures 7, 8, 9, 10, 11 and 12, we clearly see very significant percentages of pathological forms. However, we are aware that any increase in serum transaminase and GGT levels reflects liver damage. Given that during treatment, the intake of alcoholic beverages is prohibited, this increase in enzyme activity would be due either to the toxicity of the drugs administered (which is revealed in the liver), on the one hand, or to a lesion of other organs (kidney, pancreas, heart, etc.....)

occurring during treatment, on the other hand. Excluding the second condition, our work focuses on whether taking the drugs during treatment has no impact on liver function. Moreover, the literature tells us that some drugs have major hepatotoxic side effects, including anti-leprosy drugs such as Rifampicin, Dapsone....., etc. This also supports our data found above: The hepatotoxicity would be due to the anti-leprosy medication.

CONCLUSION

In terms of age, we can say that leprosy is more prevalent in relatively young people (40% between 26 and 45 years of age) than in adolescents (20% between 6 and 25 years of age). As for the results obtained after dosage, a clear increase in certain transaminases and certain gamma-GGT has been noted. This increase is due to the leprosy medication. We can admit that our main objective has been achieved because it was to assess the impact of anti-leprosy drugs on liver function.

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