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Comparative studies on the side effect of anti-tuberculosis therapy on patients attending Coccin Rehabilitation Centre, Mangu

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Abstract

Comparative effect of anti-tuberculosis therapy was investigated .200 patients were used.100 TB patients on therapy, 50 TB not on therapy(positive control) and 50 apparently healthy individuals(negative control).Mean serum uric acid of TB patients on therapy, positive control and negative control were 463.39±134.41, 459.26±103.97 and 392.26±83.61. Comparism shows $p<0.05$ mean uric acid of TB patients on therapy with positive and negative control. Comparism shows $p>0.05$ mean uric acid of positive control with negative control. Mean urea for the three groups were 5.82±2.76, 3.71±2.22 and 6.04±0.45.Comparism shows $p<0.05$ mean urea level of TB patients on therapy with positive control and negative control.Comparism shows $p>0.05$ of urea of positive control with negative control .Mean creatinine for the three groups were 101.98±33.51, 69.52±21.32 and 96.41±4.59. Comparism shows $p<0.05$ creatinine of TB patients on therapy with positive control and with negative control. Comparism shows $p>0.05$ of creatinine of positive control with negative control. Alterations due to anti-tuberculosis therapy was observed.

Keywords: Anti-tuberculosis therapy, *Mycobacterium tuberculosis*, Uricacid, Creatinine, Urea

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1. Introduction

Tuberculosis, or TB, is an infectious bacterial disease caused by Mycobacterium tuberculosis, which most commonly affects the lungs and it is transmitted from person to person via droplets from the throat and lungs of people with the active respiratory disease (WHO, 2013). In healthy people, infection with Mycobacterium tuberculosis often causes no symptoms, since the person's immune system acts to "wall off" the bacteria, however, the symptoms of active TB of the lung are coughing, sometimes with sputum or blood, chest pains, weakness, weight loss, fever and night sweats . Tuberculosis is treatable with a six-month course of antibiotics (WHO, 2013).

Globally, there were an estimated 9.4 million incident (new) cases of TB in 2008. Most of the cases occurred in the WHO South-East Asia Region (55%) and the WHO African Region (30%), with small proportions of cases in the WHO Eastern Mediterranean Region (7%), the WHO European Region (5%) and the WHO Region of the Americas (3%). The five countries with the largest numbers of cases in 2008 were India (1.6–2.4 million), China (1.0–1.6 million), South Africa (0.38–0.57 million), Nigeria (0.37–0.55 million) and Indonesia (0.34–0.52 million). Of the 9.4 million new TB cases in 2008, an estimated 1.4 million (15%) were HIV positive; 78% of these HIV-positive cases were in the WHO African Region and 13% were in the WHO South-East Asia Region (CDC, 2006; WHO, 2007).

Infected patients of *Mycobacterium tuberculosis* are usually treated with a regimen of drugs taken for six months to two years depending on the type of infection in order to prevent drug resistance. However an effective control has been achieved by the wide spread use of anti-tuberculosis drugs in various combinations based on the activities against the organisms (CDC, 2006). The two major drugs used to treat tuberculosis are isoniazid and rifampin, which are the "first line" drugs that are potent and best tolerated of the anti-tuberculosis drugs, they are used to treat drug susceptible Mycobcterium tuberculosis. When a patient becomes drug-resistant to the "first line" drugs, other drugs often referred to as "second line" drugs such as cycloserine, ethionamide and several injectable drugs like streptomycin and capreomycin which are toxic and less effective are used but only when circumstances warrant them, for example during treatment failure with standard drugs and or multiple drugs resistance (Jasmer et al., 2002).

In Nigeria, it is estimated that about 200,000 of all types and 100,000 of new sputum positive tuberculosis occur each year with an estimated 2% annual risk of infection (FMOH.1998). Also 305 new cases per 100,000 populations in Nigeria in the year 2000 were estimated. The WHO TB report for 2007 says Nigeria has the fourth largest TB burden in the world and indeed, the largest in Africa. According to statistics obtained from the Nigerian Institute of Medical Research (NIMR) TB remains a serious public health problem in Nigeria. An estimated 390,000 Nigerian are infected with active TB yearly and over 170,000 people dies from the infection annually. Expectedly, this has place a huge burden on the shaky public health index in Nigeria (WHO, 2007&2009).

1.1. Justification

Tuberculosis is a disease of public health importance and as such treatment with anti-tuberculosis drugs is also important. However more public awareness on the side effects of these drugs on various organs and tissue are still necessary.

1.2. Aims and objectives

- To determine the serum uric acid, urea and creatinine levels in tuberculosis patients on therapy, those not on therapy and apparently healthy individuals.
- To compare the effect of ATT (anti-tuberculosis therapy) among TB patients on therapy with those not on therapy and apparently healthy individuals.
- To make recommendations where necessary

2. Materials and method

A total of two hundred (200) samples were collected from pulmonary tuberculosis patients with age range from 18-70years from COCIN Rehabilitation Hospital Mangu, Plateau state. The samples were collected from both sexes, their consent was sought for and questionnaires was used to determine inclusion and exclusion criteria and also adjust for other risk factors for renal functions such as alcohol, diets, cigarette and concomitant use of paracetamol. 100 samples were collected from TB patients on therapy, 50 samples from TB patients not on therapy and 50 samples from apparently healthy individuals.

2.1. Inclusion criteria

Inclusion criteria were confirmed TB patients on ATT for at least two weeks and above with know other known ailment and not on any drug other than ATT, confirmed TB patients who are not on any drug including ATT (positive control), apparently healthy people who are neither TB nor Hiv infected and having no any known sickness (negative control).

2.2. Exclusion criteria

Exclusion Criteria Includes all patients who have any known ailment, patients who are alcoholics, patients on any drug other than ATT, patients on ATT drug for less than two weeks.

2.3. Blood sample collection

5ml of veinous blood was collected from ante-cubital vein using evacuated blood tubes i.e. serum tubes with non-additives, after sterilizing the cubital Fossa with methylated spirit and avoiding venous stasis. The blood was allowed to clot and centrifuge for 3-5mins at 3000 revolution per minutes (RPM) within 3hours of collection, the serum was collected into a clean separate sterile bottle with labels corresponding to the initial blood sample and stored at -20^0C. The following parameters in the samples were determined, serum uric acid, creatinine and urea levels. Determination of creatinine was by jaffe reaction, while determination of serum urea was by modified berthelot method and that of serum uric acid was estimated by enzymatic colorimetric method.

3. Discussion, conclusion and recommendation

3.1. Discussion

The serum uric acid level of TB patients on therapy when compared statistically with the TB patients not on therapy (positive control) was found to be statistically significant ($p<0.05$) and with apparently healthy individuals was also found to be significant ($p<0.05$). Also there was a statistical significant difference ($p<0.05$) between the serum urea and creatinine of TB patients on anti-tuberculosis therapy when compared with those of TB patients not on any drug(positive control) and with apparently healthy individual(negative control). This was found to be in agreement with the study carried out by (Adebisi et al., 2000; Cammalleri et al., 2007; Ghulam et al., 2007) in which they stated that pyrazinamide increases the levels of serum uric acid, BUN significantly during the course of the therapy. Pyrazinamide affects the serum uric acid early and affects handling of urate, urea and creatinine by the kidneys. It was also reported in Nigeria that among TB patients on ATT with pyrazinamides, 51.6% developed hyperuricaemia (Adebisi et al., 2000). This work was also in agreement with the study carried out by (Julia and Bhurgri et al., 2010), who reported that renal side effects in TB patients on ATT have included elevations in BUN, serum uric-acid, and creatinine in TB patients on ATT. This difference which may be due to the drug may be further understood if the three group of subjects are carefully evaluated thus, since there was a significant statistical difference ($p<0.05$) between the serum uric acid, urea and creatinine level of TB patients on therapy and TB patients not on treatment, this difference must have been due to the drug since all other factors applies to both groups. Furthermore it was observed that there was no statistical difference ($p>0.05$) between TB patients that are not on any treatment (positive control) with apparently healthy individuals (negative control), a situation which may be inferred to be due to the fact that the disease have not spread to other organs and particularly the kidney(Harris et al., 2004).

However, there was a statistical difference ($p<0.05$) between TB patients on therapy and apparently healthy individual which further confirms that antituberculosis therapy may have effect on the three parameters under investigation. In addition since the TB is primarily a disease of the respiratory tract, kidney as well as other organs only becomes affected in the course of spread of the disease. In people with a fully functioning immune system, active tuberculosis is usually limited to the lungs (pulmonary tuberculosis) (Cedars-Sinai, 2013).Tuberculosis that affects other parts of the body (extrapulmonary tuberculosis) comes from pulmonary tuberculosis that has spread from the lungs through the blood (Cedars-Sinai, 2013). As in the lungs, the infection may not cause disease, but the bacteria may remain dormant in a very small scar.(Cedars-Sinai, 2013). Dormant bacteria in these scars can reactivate later in life, leading to symptoms related to the organs involved (Cedars-Sinai, 2013). Dormant bacteria in these scars can reactivate later in life, leading to symptoms related to the organs involved (Culleton et al., 1999; Vinary et al*.,* 2007).

Anti-TB chemotherapy exhibit greater level of efficacy with an acceptable degree of toxicity, however combination treatment may produce severe adverse events. Important adverse effects are hepatitis, rash, gastrointestinal upset, hyperuricemia, peripheral neuropathy, visual, as well as increased blood creatinine and urea disturbances (Bass et al., 1994; Sharkya et al., 2004).

Table 1. Shows the mean, standard deviation of Serum Uric Acid, Urea and Creatinine level of tuberculosis patients on therapy, not on therapy and apparently healthy individuals

	TB patients on therapy			TB patients not on therapy			Apparently healthy individuals		
Parameter	**N**	**Mean**	**S.D**	**N**	**Mean**	**S.D**	**N**	**Mean**	**S.D**
Uricacid (µmol/L)									
Male	54	486.73	131.65	19	463.13	94.47	21	398.10	84.91
Female	46	435.79	133.80	31	456.89	110.84	29	386.12	81.73
TOTAL	**100**	**463.29**	**134.41**	**50**	**459.26**	**103.97**	**50**	**392.26**	**83.61**
Urea (mmol/L)									
Male	54	5.63	2.18	19	4.10	2.50	21	6.18	0.51
Female	46	6,05	3.32	31	3.48	2.03	29	5.95	0.39
TOTAL	**100**	**5.82**	**2.76**	**50**	**3.71**	**2.22**	**50**	**6.04**	**0.45**
Creatinine (µmol/L)									
Male	54	105.89	30.14	19	72.52	16.23	21	96.55	4.15
Female	46	97.40	36.88	31	67.67	23.99	29	96.32	4.96
TOTAL	**100**	**101.98**	**33.51**	**50**	**69.52**	**21.32**	**50**	**96.41**	**4.59**

Table 2. the statistical Comparison of the mean and standard deviation of Serum Uric Acid, Urea and Creatinine of tuberculosis patients on therapy and those not on therapy

	TB patients on therapy			TB patients not on therapy			
Parameter	**N**	**Mean**	**S.D**	**N**	**Mean**	**S.D**	**P-value**
Uric-acid (µmol/L)	100	463.29	134.41	50	459.26	103.97	0.000
Urea (mmol/L)	100	5.82	2.76	50	3.71	2.22	0.000
Creatinine (µmol/L)	100	101.98	33.51	50	69.52	21.32	0.000

Based on the questionnaire used, overcrowding was observed as well as the nutritional diet of pulmonary TB patients was poor and it is well known that this is a strong risk factor for becoming unwell with TB apart

from the fact that TB is itself a risk factor for malnutrition and that malnourished patient with TB is at an increase risk of death even with appropriate antibiotic therapy (Ranjendram.2006).Concomitant use of paracetamol could also be a risk factor. This is supported by (Hussain, 2003; Herwig et al., 2009) that ATT in combination with alcohol and concomitant use of paracetamol in TB patients serve as a predisposing risk factor.

This study also reveals that males were more affected 54% TB patients on therapy that are tending towards hyperuricaemia compared with females 46%. This is in agreement with the reported of Rajendram and Sivapathasundharam (2006) and Vasudevan and Sreekumari (2007) which states that males are more affected than females because of their bread winner status in the society and also because women and children excrete less creatinine than men and creatinine clearance is altered by body muscle mass, drugs, and age.

As was observed in this study, the fact that pulmonary TB patients not on treatment (positive control) showed no significant difference ($p>0.05$) when compared statistically with apparently healthy individuals(negative control) even at active stage of the infection for the three parameters whereas comparism between TB patients on therapy and apparently healthy individual (negative control) and TB patient not on therapy(positive control) was ($p<0.05$),probably indicate on one hand that there was increased serum uric acid, urea and creatinine due to the ATT and on the other hand this may also indicate that these TB patients on therapy are responding to treatment, thus withdrawal of the drug may probably lead to reduction of the drug induced blood uric acid, urea, and creatinine.

Table 3. The Comparison of Serum Uric Acid, Urea and Creatinine level of tuberculosis patients on therapy and apparently healthy individuals

	TB patients on therapy			Apparently Healthy Individuals			
Parameters	**N**	**Mean**	**S.D**	**N**	**Mean**	**S.D**	**P-value**
Uric acid(µmol/L)	50	459.26	103.97	50	392.26	80.61	0.000
Urea(mmol/L)	50	3.71	2.22	50	6.00	0.50	0.000
Creatinine(µmol/L)	50	65.52	21.32	50	96.40	4.60	0.000

Table 4. the Statistical Comparison of Serum Uric Acid, Urea and Creatinine level of tuberculosis patient not on therapy and apparently healthy individual

	TB patients not on therapy			Apparently Healthy Individuals			
Parameters	**N**	**Mean**	**S.D**	**N**	**Mean**	**S.D**	**P-value**
Uric acid(µmol/L)	100	463.29	134.41	50	492.26	101.61	0.822
Urea(mmol/L)	100	5.82	2.76	50	6.04	0.45	0.269
Creatinine(µmol/L)	100	101.98	33.51	50	96.41	4.59	0.225

3.2. Conclusion

We conclude therefore that there was a drug-induced hyperuricaemia, increased serum creatinine and urea associated with anti-tuberculosis therapy used in the treatment of pulmonary tuberculosis patients.

3.3. Recommendation

We recommend that TB patients should be monitored during treatment in case of any adverse effects which should be detected promptly and managed properly.

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