ASSESSMENT OF BIOCHEMISTRY PROFILES OF TUBERCULOSIS AND TB-HIV COINFECTED PATIENTS RECEIVING TREATMENT AT THE NATIONAL TUBERCULOSIS REFERENCE CENTER, ZARIA, NIGERIA

[1]*Mohammed, N., [2]Taura, D. W., [2]Habibu A, U., [1]Ashafa A.M, and [1]Sanusi, S

[1]*Department of Microbiology, Federal University Gusau, Nigeria*
[2]*Department of Microbiology, Bayero University Kano, Nigeria*

*Author for correspondence: naibimohammad@fugusau.edu.ng

ABSTRACT

Tuberculosis (TB) remains a global health issue with high morbidity and mortality rates especially in the developing countries such as Nigeria. It is a multi-organ disease and can influence biochemical changes. This study sought to determine the effect of tuberculosis and its drug treatment on serum biochemical parameters in 238 patients assessing treatment at the National Tuberculosis and Leprosy Training Center (NTBLTC) Saye-Zaria, Nigeria. The study took place between May, 2021 and February, 2022, analysis was carried out at the baseline and after eight months of treatment with anti-tubercular and antiretroviral drugs, based on WHO guidelines with regular close monitoring. The values of sodium, potassium, albumin and creatinine are influenced during TB infection and its treatment. The percentage distribution of the parameters before and after treatment were statistically significant with P-value <0.05. Values recorded for serum creatinine levels in this study were lower among patients infected with only TB as compared to the values recorded for TB-HIV infected patients but the differences were not statistically significant. The research concludes that the values of biochemistry parameters are influenced during TB infection and its treatment. HIV status does not overtly affect the values of biochemistry parameters as observed from the result of the study, even though co-infection could increase the severity of the disease thereby increasing morbidity.

Keywords: Biochemistry, Coinfection, Tuberculosis, HIV, Treatment

INTRODUCTION

Mycobacterium tuberculosis causes the airborne disease Tuberculosis (TB), which typically affects the lungs and results in severe coughing, fever, and chest pains (Fogel, 2015). Though it is treatable and preventable, the morbidity of the disease is very high especially in settlements with poor hygiene and sanitary conditions due to poor economic conditions (Brett *et al.,* 2020). Several factors, such as Human Immunodeficiency Virus (HIV) co-infection and other co-morbidities contribute to the severity of the disease if not properly addressed. High TB prevalence, according to global health view, is reported in sub-Saharan Africa, Asia and India (WHO, 2020). These are regions with high rates of poverty and poor living conditions (WHO, 2020). The incidence of tuberculosis ranges from 9 to 11 million people worldwide, comprising 5.8 million men, 3.2 million women, and nearly a million children (Singh and Kabra, 2019).

Studies had indicated the association between TB infection and biochemical changes in human body (Gebreweld *et al*., 2024) comprising of low serum sodium, low serum albumin, low/high serum calcium, low/high serum potassium, among others (Jonaidi *et al.,* 2013; Memon *et al.,* 2014; Bhagyamma, 2016). Anti-TB agents administered to TB patients had been found

to also influence some of these biochemical changes (Sahin and Yıldız, 2013). There is paucity of data on the association of biochemical changes with TB infection in sub-Saharan Africa which includes Nigeria (Gebreweld *et al.,* 2024). This study sought to evaluate the influence of TB infection and its anti-TB medications on serum albumin, calcium, sodium and potassium, with a view to initiating measures to stem down adverse outcomes from these biological events

METHODS

The ethical clearance (HREC/NTBL/ZA/11-21/VOL.XII/005A) was obtained from the Research and Human ethics committee of National Tuberculosis and Leprosy Training Center Saye-Zaria, Nigeria. Five milliliters (5ml) of venous blood were collected from each of the two hundred and thirty-eight (238) consenting patients (HIV positive patients inclusive) by a trained clinician into a tube containing an anticoagulant and mixed thoroughly. Both the syringe and tube were properly labeled with patient s identification number as well as collection dates and stored at 2 to 8^0C before they were sent to laboratory for further processing.

Biochemistry profiles of *Mycobacterium tuberculosis* infected patients and TB/HIV patients was analyzed at the Clinical Biochemistry laboratory of NTBLTC Saye - Zaria between May, 2021 and February, 2022 using Clinical Chemistry Auto-Analyzer (Rayto RT1904C). Five milliliters (5mls) of blood were collected from each of a total of Two hundred and thirty-eight (238) TB patients (HIV co-infected patients inclusive). The analysis was carried out at the baseline and after treatment with anti-tubercular (Rifampicin, Isoniazid, Ethambutol, Streptomycin and Pyrazinamide) and antiretroviral (Tenofovir, Lamivudine and Efavirenz) drugs, for a period of eight months, based on the internationally recognized WHO guidelines, with regular close monitoring. In this study Creatinine, Albumin, Sodium, Potassium, Calcium, Glucose and T-Bilirubin in patients who are infected with MTB only and those coinfected with HIV were analyzed. After the blood samples were loaded in the device, it was connected to a power source and turned on, the required reagents (A Calibration Reagent, B Standard Reagent, Agape reagent and Reaction Reagent) within their shelf lives were added; and then the instrument was calibrated according to Manufacturer s instructions using the calibration standards. The cations and anions of blood samples were measured to determine the specific alterations in various biochemical markers associated with TB infection in order to provide information about the disease status, progression and response to treatment. After the analysis was completed, the instrument provided the obtained result on the analyzer s display screen in the form of an output report which was reviewed for accuracy and quality before interpreting. At the end of analysis, the spills and residues from the samples were cleaned and biohazardous wastes were appropriately disposed.

RESULTS

Generally, the result for percentage cases of biochemistry parameters were higher before treatment and lower after treatment of the patients as presented in Table I. The percentage distribution of the parameters before and after treatment were statistically significant with P-value <0.05. The mean values recorded for patients biochemistry status is presented in Table II. The mean serum sodium levels were within the normal range for both groups; however, it was lower among patients who have not received treatment (132.2±16.03mmol/l) compared to patients who had already received treatment (135.9±23.9mmol/l).

Table I: Percentage Occurrence of Abnormal Biochemistry levels among patients infected with only TB before and after Treatment

Biochemistry Parameters	Reference Range	Before treatment Case (%)	After treatment Case (%)	Chi Square (P-value)
Sodium (mmol/L)	136-145	196 (82.35)	25 (10.50)	246.98 (0.0001)
Potassium (mmol/L)	2.25-2.75	226 (94.96)	26 (10.92)	337.3 (0.0001)
Albumin (g/dL)	35-47	202 (84.87)	13 (5.46)	303.0 (0.0001)
Calcium (mmol/dL)	2.25-2.75	224 (94.12)	26 (10.92)	334.1) (0.0001)
T-bilirubin (mmol/L)	0-20.5	96 (40.34)	18 (7.56)	70.18 (0.0001)
Creatinine (mmol/L)	9-126	73 (30.67)	3 (1.26)	76.72 (0.0001)
Glucose (mmol/L)	3.5-8.5	202 (84.87)	13 (5.46)	303.0 (0.0001)

Table II: The mean Values of Biochemistry Parameters among TB Patients before and after Treatment

Biochemistry Parameters	Reference Range	Before treatment Mean ± SD	After treatment Mean± SD	P-value
Sodium (mmol/l)	136-145	132.2±16.03	135.9±23.9	0.1907
Potassium (mmol/l)	2.25-2.75	4.28±0.99	2.46±0.48	0.0001
Albumin (g/dL)	35-47	32.66±2.66	36.85±7.11	0.0001
Calcium (mmol/dl)	2.25-2.75	2.13±0.10	2.32±0.42	0.0001
T-bilirubin (mmol/L)	0-20.5	17.3±7.5	14.7±6.1	0.0001
Creatinine (mmol/L)	9-126	62.2±56.2	57.1±44.3	0.2711
Glucose (mmol/L)	3.5-8.5	8.73±1.06	5.62±1.64	0.0001

The mean serum Albumin level among the group not yet treated was 32.66±2.66g/dL as compared to the group of patients who had taken their treatments (36.85±7.11g/dL). The differences in mean values of serum albumin among the three groups was statistically significant, $p<0.05$. The mean calcium level was slightly lower among the group yet to receive any treatment (2.13±0.10mmol/L) as compared to the group that have received treatment (2.32±0.42 mmol/L). The mean differences among the three groups were statistically significant ($p<0.05$). Total bilirubin levels recorded among the patients before treatment was higher than among patients after treatment (17.3±7.5mmol/L and 14.7±6.1mmol/L respectively). The difference in the two groups were not statistically significant ($p>0.05$). Serum creatinine level was slightly higher among the population not yet treated (62.2±56.2mmol/L) as compared to the population who were already treated

(57.1±44.3mmol/L) while and serum glucose level was higher among the population not yet treated (8.73±1.06mmol/L) as compared to the population who had already received treatment (5.62±1.64mmol/L). Comparison of means indicated that mean values obtained for creatinine and sodium were the only ones not statistically significant (P≥0.05) when compared before and after treatment. Other mean values obtained had statistically significant difference among the two groups compared (P≤0.05).

Results obtained from this study indicated that the mean values for serum Sodium and serum Potassium were higher among patients infected with only TB (132.2±16.07 and 4.28±1.0 mmol/L respectively) compared to TB-HIV co-infected patients (132.0±16.21 and 4.26±1.0mmol/L respectively). Serum albumin mean values among patients infected with only TB were 32.61±2.65g/dL while TB-HIV co-infected patients had 32.59±2.63g/dL. Serum

calcium and Total bilirubin levels were 2.13±0.1mmol/L and 17.24±7.49mmol/L respectively for patients infected with only TB while 2.12±0.1mmol/L and 17.34±7.58mmol/L respectively were values recorded for TB-HIV co-infected patients.

Values recorded for serum creatinine levels in this study were lower among patients infected with only TB (61.9±56.2mmol/L) as compared to the values recorded for TB-HIV co-infected patients (63.0±56.4mmol/L). Serum glucose mean value was 8.75±1.02mmol/L for patients with only TB and 8.75±1.03mmol/L for TB-HIV co-infected patients. Comparison of the means of the independent samples indicated that none of the difference in the mean values recorded for all test parameters was statistically significant (p≥ 0.05).

The result from the present study indicated a rise in the serum potassium and serum glucose. All other tested parameters fell within the normal range as shown in Table III below.

Table III: The Mean Values of Biochemistry Parameters for Tuberculosis and tuberculosis-HIV Co-infected Patients after Treatment

Biochemistry Parameter	Reference range	TB Mean±SD	TB/HIV Mean±SD	P-value
Sodium (mmol/l)	136-145	132.2±16.07	132.0±16.21	0.8938
Potassium (mmol/l)	2.25-2.75	4.28±1.0	4.26±1.0	0.8294
Albumin (g/dL)	35-47	32.61±2.65	32.59±2.63	0.9350
Calcium (mmol/L)	2.25-2.75	2.13±0.1	2.12±0.1	0.2816
T-bilirubin (mmol/L)	0-20.5	17.24±7.49	17.34±7.58	0.8863
Creatinine (μmol/L)	9-126	61.9±56.2	63.0±56.4	0.8333
Glucose (mmol/L)	3.5-8.5	8.75±1.02	8.75±1.03	1.0000

DISCUSSION

Biochemical changes were observed in serum sodium, serum potassium, serum calcium and serum albumin levels among

TB patients before and after treatment as shown in Table I. The subgroup of patients with TB before treatment had significantly lower serum sodium than those after

treatment. Low serum sodium levels in TB may be caused by any of these mechanisms: local invasion to the adrenals, hypothalamus, and pituitary gland or by syndrome of inappropriate anti-diuretic hormone (ADH) secretion if there is TB meningitis (Verbalis *et al.,* 2013; Ye *et al.,* 2022). This finding is similar to the finding of Nematollah *et al.* (2015) after they reviewed 200 cases of TB which demonstrated lower serum sodium levels than those on treatment and controls. Chinyelu *et al.* (2021) in Anambra State, Nigeria reported a similar finding. This study was however in contrast to the findings of Olalekan *et al.* (2015) in Southwestern Nigeria who observed that serum sodium was significantly lower among those on treatment than those not yet receiving treatments. This could be as a result of treatment-related side effects like vasopressin resulting in hyponatremia, inappropriate antidiuretic hormone secretion, fluid shifts, increased sodium excretion or underlying condition progression (Lu *et al.,* 2022). Difference in study population size may have also affected their results (Shu, *et al.*, 2018).

Higher serum potassium among TB patients before treatment as compared to those that have received treatment is in line with the findings of Chinyelu *et al.* (2021) in Anambra State, Nigeria where mean values obtained were 4.604±0.937 among TB only patients as compared to 4.163±0.886 among TB-HIV patients. This finding was not in agreement with that of Olalekan *et al.* (2015) in Southwestern Nigeria and Bhagyamma *et al.* (2016) in India where TB patients not yet treated had lower serum levels of potassium as compared to those treated. It is reported that *M. tuberculosis* has a unique transcriptional response to changes in potassium levels both intra-mycobacteria and extra-mycobacteria (MacGilvary, 2019). Tuberculosis have also

been reported to swing the human physiology of the infected patient into an hypercatabolic state that is associated with cell and tissue destruction as a result of movement of potassium into the serum (Friedland, 2008).

This study did not show any variation in blood glucose among only TB patients and TB-HIV co-infected patients, although some researchers have observed that diabetes and tuberculosis association have being more significant among TB-HIV co-infected patients, it is not consistently reproduced in different populations (Sama, *et al.*, 2023).

Conclusion

The finding of this research shows that the values of sodium, potassium, albumin and creatinine are influenced during TB infection and its treatment. It could also be concluded from this research that HIV status does not overtly affect the values of biochemistry parameters, even though this co-infection could increase the severity of the disease thereby increasing morbidity.

Recommendation

The study recommends monitoring of biochemistry parameters of TB and TB-HIV coinfected patients during and after treatment as treatment regimen could also affect the values of biochemistry parameters.

Acknowledgment

The research team acknowledges the contribution of the research subjects in agreeing to participate in the research.

Conflict of Interests

The research team declares that there is no conflicting interest among the researchers.

References

Bhagyamma, S.N., Sreeenivasulu, U. and Anuradha, R. (2016). Study of Electrolyte Changes in Tuberculosis and Human Immune Deficiency Virus (HIV) Co Infected with Tuberculosis Patients: A Hospital Based Study. *IOSR-JDMS*, 15(9X):28-31.

Brett, K., Dulong, C. and Severn, M. (2020) *Prevention of Tuberculosis*: A Review of Guidelines. Ottawa (ON): Canadian Agency or Drugs and Technologies in Health; PMID: 3048484

Chinyelu, U.U., Chidimma, A.O., Victor, A.M., Chidimma, I.M., Shirley, N.C., Chukwudi, C.U., Iloduba, N.A., Simon, N.U., Arthur, E.A., Emeka, H.E., Ernest, N.A. and Prince, U.E. (2021). Biochemical changes in tuberculosis. *Pan Afr. Med. J. Conf. Proc.,* 38(66). 10.11604/pamj.2021.38.66.21707

Fogel, N. (2015). Tuberculosis: A Disease Without Boundaries. *(Edinb)* 95:527 531.

Friedland, J.S. (2008) Tackling tissue destruction in tuberculosis. *Trans R Soc Trop Med Hyg.;* 102(10):953-4

Gebreweld, A., Fiseha, T., Kebede, E., Tamir, Z., Gebremariam, B., Miruts, F. and Haileslasie, H. (2024) Immuno-Hematological and Biochemical Changes in Patients with Tuberculosis in Dessie Comprehensive Specialized Hospital, Dessie, Ethiopia. *J Blood Med.* Doi: 10.2147/JB. S445857. PMID:38532889, PMCID: PMC10964777

Jimenez-Corona, M.E., Cruz-Hervert, L.P. and Garc´ıa-Garc´ıa, L. (2013). Association of diabetes and tuberculosis: impact on treatment and post-treatment outcomes. *Thorax*, 68(3):214-220.

Jonaidi, J.N, Izadi, M., Sarrafzadeh, F., Heidari, A., Ranjbar, R., Saburi, A. (2013). Hyponatremia due to pulmonary tuberculosis: Review of 200 Cases. *Nephrourol Mon.* Winter; 5(1):687 91.

Lu, J.,Yi,W., Mei, L., Jiahua, L., Tao, Li., Lei, Wu., Qifeng, W. and Jinyi, L. (2022). Pretreatment Low Serum Sodium as a Prognostic Factor for Patients with Esophageal Cancer Treated with Radiotherapy or Chemoradiotherapy; *J. Oncol.* 4586729.PMID: 35356251, PMCID: PMC8959962

MacGilvary, N.J., Kevorkian, Y.L. and Tan, S. (2019). Potassium response and homeostasis in Mycobacterium tuberculosis modulates environmental adaptation and is important for host colonization. *PLoS Pathog*, 15(2): e1007591.

Morris, C.D, Bird, A.R, Nell, H. (1989) The Hematological and Biochemical Changes in Severe Pulmonary Tuberculosis. *QJM*,73(272):1151 9.

Nematollah, M. M., Yaghobi, F. Paykan, H. and S. Dorafshan (2015). Serum Biochemical Changes and Acute Stress Responses of the Endangered Iridescent Catfish (Pangasianodon hypophthalmus) Supplied with Dietary Nucleotide, *JAST*, 17: 1161-1170
Olalekan, A.W., Oluwaseun, F.A., Oladele, H.A. and Akeem, A.D. (2015). Evaluation of electrolyte imbalance among tuberculosis patients receiving treatments in Southwestern Nigeria. *Alex. J. Med.*, 51(3):1-7.

Sahin. F, Yıldız P. (2013). Distinctive biochemical changes in pulmonary tuberculosis and pneumonia. *AMS,* 30;9(4):656-661.

Sama, L.F., Sidoine, S., Thibau, F.T., Slange, D. and Georges, F.K. (2023) Diabetes Mellitus and HIV Infection among Newly Diagnosed Pulmonary Tuberculosis Patients in the North West Region of Cameroon: A Cross-Sectional Study, *Int J Clin Pract.* https:/doi.org/10.115/2023/5998727

Shu, Z., Tian, Z., Chen, J., Ma, J., Abudureyimu, A., Qlan, Q. and Zhuo, L. (2018). HIV/AIDS-related Hyponatremia: An Old but still serious problem. Ren Fail, 40(1):68-74

Singh, V., Kabra, S.K. (2019). Advances in Tuberculosis: diagnostics. *Indian J. Pediatr.* 86:439 440.

Verbalis, J.G., Goldsmith, S.R., Greenberg, A., Korzelius, C., Schrier, R.W. and Sterns, R.H. (2013) Diagnosis, evaluation and treatment of hyponatremia: Expert panel recommendations. *Am J Med;*126 (Suppl 10):S1-42

World Health Organization. Global tuberculosis reports. Accessed on 8th January 2020. www.sciencedirect.com/article/pii

Ye, Q., Peng, X., Zhang, X., Cao, Q., Tao, K. and Wang, L. (2022) Clinical analysis of 103 cases of tuberculous meningitis complicated with hyponatremia in adults. *Neurol Sci*; 43(3):1947-1957