

ASSESSMENT OF ANTIOXIDANTS AND NUTRITIONAL STATUS OF PULMONARY TUBERCULOSIS PATIENTS IN NIGERIA

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Aim: The aim of this study was to assess the nutritional and antioxidant status of pulmonary tuberculosis patients in Nigeria

Methods: Levels of total protein (TP), albumin (ALB.), triglyceride (TG), total cholesterol (TC), high density lipoprotein cholesterol (HDL), low density lipoprotein cholesterol (LDL), and total antioxidants (TAS) were determined in thirty-one Nigerian pulmonary tuberculosis patients and thirty-four controls using Spectrophotometric methods

Results: The mean levels of TP (7.13 ± 1.06 g/dl), ALB (3.27 ± 0.7 g/dl), TC (100.7 ± 23.6 mg/dl), HDL (28.6 ± 7.2 mg/dl), LDL (65.5 ± 15.1 mg/dl) and TG (61.6 ± 16.2 mg/dl) were significantly lower while the level of globulin (3.9 ± 0.84 g/dl) was significantly higher in pulmonary tuberculosis patients when compared with controls (TP= 7.6 ± 0.7 g/dl; ALB= 4.2 ± 0.48 g/dl; TC = 163.2 ± 40.1 mg/dl; HDL = 41.4 ± 5.4 mg/dl; LDL = 107.8 ± 27.5 mg/dl; TG= 101.5 ± 29 mg/dl; globulin = 3.4 ± 0.6 g/dl respectively).

Level of TAS (0.83 ± 0.34 mmol/l) was significantly lower when compared with controls (TAS= 1.65 ± 0.26 mmol/l). The significantly lower level of antioxidants observed in this study might be due to heavy load of free radicals released by the bacterial invaded macrophages.

Conclusion: The nutritional derangement and lower antioxidant status could call for prompt nutritional intervention in the management of pulmonary tuberculosis patients.

Key words: Pulmonary tuberculosis, antioxidants, nutritional status, Nigeria.

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INTRODUCTION

Tuberculosis is a highly infectious disease that is widely distributed throughout the world. The disease is influenced by economic and nutritional factors, although educational background, immunity and hormonal status have been associated with the prevalence (1,2). The economic and nutritional factors make the developing countries have the highest prevalent rate. The most popular causative agent is *Mycobacterium tuberculosis* although, *Mycobacterium bovis*, which affects cattles, can also be found in man (3).

It is commonly a disease of the lungs (pulmonary tuberculosis) where it forms a localized infection after inhalation (4,1). It can affect extra pulmonary regions like lymph nodes, bone and joints,

subcutaneous, meninges, eyes, the kidneys, and also the gastro-intestinal tract, where it causes an insidious disease that develops without any striking clinical evidence (5). It can also cause congenital tuberculosis transmissible from an infected mother to fetus following ingestion of the amniotic fluid containing *Mycobacterium tuberculosis* (6).

The mycobacteria activate the invaded macrophages resulting to free radical burst (7,8). High serum levels of these free radicals and high lipid peroxidation products are characterized by patients with advanced tuberculosis (9). The peroxidation could cause reduced concentration of serum lipids and tissue inflammation (10). Study also stressed that apart from tissue inflammation and oxidative stress observed in these patients,

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Table 1. Biochemical parameters of tuberculosis and control groups

	Control	Tuberculosis	t value	p value
n	34	31		
Age, years	33.21±11.4	31.5±10.0	-0.6	ns
Total protein, g/dL	7.6±0.7	7.1±1.1	-2.1	0.04*
Albumin, g/dL	4.2±0.5	3.3±0.7	-6.4	0.0*
Globulin, g/dL	3.4±0.6	3.9±0.8	2.7	0.0*
Total cholesterol, mg/dL	63.2±40.1	100.7±23.6	7.6	0.0*
Triglycerid, mg/dL	101.5±29.0	61.6±16.2	6.7	0.0*
HDL cholesterol, mg/dL	41.4±5.4	28.6±7.2	8.2	0.0*
LDL cholesterol, mg/dL	107.8±27.5	65.5±15.1	7.6	0.0*
TAS, mmol/L	1.7±0.3	0.8±0.3	10.9	0.0*

ns: non-significant

tuberculosis also leads to continuous production of these free radicals that may cause a resultant low level of antioxidant (7). Tuberculosis has been associated with malnutrition. Yamanaka et al (11) reported that serum cholesterol was significantly lower in tuberculosis patients and got worse in homeless patients who were prone to starvation. The available reports on the assessment of free radical load, antioxidants and lipid peroxidation products only dealt with non- Nigerians tuberculosis patients. This study is also necessary in Nigeria, since these nutritional and metabolic derangements could contribute to the complications and low success rate in the treatment associated with pulmonary tuberculosis. Therefore, the present work was designed to investigate the plasma levels of TP, ALB, TG, TC, HDLC, LDLC, and total antioxidants in pulmonary tuberculosis infection.

MATERIAL AND METHODS

Thirty-one subjects with active tuberculosis and were sputum smear-positive volunteered to participate in this study. The radiological examination also showed pulmonary inflammation. Patients suffering from other pulmonary diseases were excluded from this study. Thirty-four apparently healthy sputum smear-negative individuals selected from staffs of State Hospital Adeoyo Ring road, Ibadan, Nigeria served as controls. Ten milliliters (10ml) of blood was collected from these subjects into a lithium heparin container and spun within one hour. The plasma sample for total antioxidants, lipid profiles, total protein, and albumin estimations were stored at -20°C until ready for analysis.

Total antioxidant was measured using a standardized solution of Fe-EDTA complex that reacts with hydrogen peroxide to release a thiobarbituric reactive substance (12). Total protein was determined spectrophotometrically using alkaline solution of copper sulphate (13). The albumin concentration was determined by the brilliant cresol green solution supplied by Dialab Production and Vertrieb vonchemisch-technischen, Wien-Panikengasse. The globulin (GLOB) level was calculated by subtracting the value of albumin from that of total protein. TC, HDLC, LDLC and TG were measured spectrophotometrically using commercially prepared reagents purchased from Randox Laboratory Ltd, UK.

Statistical analysis

The results were expressed as mean \pm S.D. Comparison was made using student t-test while $p < 0.05$ was regarded as significant.

RESULTS

In table 1, there was no significant difference in the age range ($p > 0.05$) of patients with tuberculosis when compared with the controls selected for this study. The mean levels of TP ($7.13 \pm 1.06\text{g/dl}$), and ALB ($3.27 \pm 0.7\text{g/dl}$) were significantly lower in tuberculosis patients while the level of GLOB ($3.9 \pm 0.84\text{g/dl}$) was significantly higher when tuberculosis patients were compared with controls (TP= $7.6 \pm 0.7\text{g/dl}$; ALB= $4.2 \pm 0.48\text{g/dl}$; GLOB= $3.4 \pm 0.6\text{g/dl}$ respectively). TC ($100.7 \pm 23.6\text{mg/dl}$), HDLC ($28.6 \pm 7.2\text{mg/dl}$), LDLC ($65.5 \pm 15.1\text{mg/dl}$), TG ($61.6 \pm 16.2\text{mg/dl}$) and TAS ($0.83 \pm 0.34\text{mmol/l}$) were significantly lower in tuberculosis patients when compared

with the controls (TC=163.2±40.1mg/dl; HDLC= 41.4±5.4mg/dl; LDLC= 107.8±27.5mg/dl; TG= 101.5±29.6mg/dl; TAS= 1.65±0.26mmol/l).

DISCUSSION

The present study shows significantly lower levels of total protein and albumin in subjects with pulmonary tuberculosis. Similar report was given by Sasaki et al (10), that albumin and total protein were significantly lower in pulmonary tuberculosis. Yamanaka et al (11) reported that the total protein, albumin, cholinesterase, hemoglobin and lymphocyte were significantly lower in homeless patients when compared with non-homeless tuberculosis patients and healthy men. Aily et al (14) also observed lower levels of albumin and hematocrite in tuberculosis. Lower levels of total protein and albumin in this study might have been caused by anorexia, malnutrition and mal-absorption commonly observed in tuberculosis. Albumin is an important component of plasma antioxidant activity that primarily binds free fatty acids, divalent cations and hydrogen oxochloride (HOCl) (15). It is a negative acute phase protein which the plasma value decreases during infection, injury or stress possibly as a result of increased metabolic need for tissue repair and free radical neutralization. The free radicals attack the cell membrane causing tissue damage and wasting disease in pulmonary tuberculosis patients with resultant high level of uric acid (a powerful antioxidant). The uric acid is endogenously produced as a compensatory mechanism for the neutralization of free radicals (16). The lower level of albumin may therefore be one of the complications associated with pulmonary tuberculosis.

Significantly high level of globulin observed in tuberculosis in our study might have arisen from combination of elevation of different globulin fractions previously observed. Arinola and Igbi (17) reported high levels of IgG and IgM in pulmonary tuberculosis. Nagayama et al (18) also stated that hyperglobulinaemia in tuberculosis is one of the predictive factors for the development of residual pleural thickening in tuberculous pleurisy. Gartner et al (19) reported higher levels of alpha-1-antitrypsin in pulmonary tuberculosis patients. The high level of

globulin observed in this study support the fact that humoral immune response is less affected and raises the possibility of polyclonal B cell activation in tuberculosis patients.

Lower levels of TC, TG, LDLC and HDLC were observed in this study. Kwiatkowska et al (9) and Reddy et al, (20) have reported high levels of lipid peroxidation in all categories of pulmonary tuberculosis patients, irrespective of treatment status and this might have caused reduction in the concentration of serum lipids as observed in our study. It was shown that total cholesterol was significantly lower in tuberculosis patients when compared with pulmonary tuberculosis-free controls (10, 11). Triglycerides and LDLcholesterol are the chief constituents of cell membranes (21), while the HDL cholesterol protects the arterial walls of the blood circulatory system (22). Lower levels of lipids noticed in these patients could be a factor that predisposes them to cell and tissue damage, cardiovascular problems and low cellular immunity (23, 24). The lower levels of total cholesterol, HDLC, LDLC and TG observed in this study could be the result of impaired rate of lipid production and enhanced lipid catabolic rate associated with tuberculosis.

Some previous workers have reported significantly low levels of total antioxidants, Zn and beta-carotene in pulmonary tuberculosis (7, 25). It was also reported that significantly lower levels of vitamin E and A were common in tuberculosis patients than in healthy Ethiopians (26). In our study, lower levels of total antioxidant were observed in pulmonary tuberculosis patients. This might be due to malnutrition and exhaustion in attempt to neutralize heavy load of free radicals in these patients.

The result of this study shows lower levels of antioxidants and nutritional profiles in pulmonary tuberculosis patients. This could be associated with heavy load of free radicals, oxidative stress and lipid peroxidation. Improved nutrition and supplementation with antioxidant therapy in the treatment of pulmonary tuberculosis may prevent the oxidative stress and further complications.

REFERENCES

1. Cruickshank R. *Mycobacterium tuberculosis*. Medical Microbiology Vol. 1; 12th edition Churchill Livingstone 1973;16:291-3
2. Halliwell B. Reactive oxygen species and the central nervous system. *J Neurochemistry* 1992;59:1609-23
3. Bates JH, Young IS, Galway L, Traub AI, Hadden DR. Antioxidant status and lipid peroxidation in diabetic pregnancy *Br J Nutr* 1997;78:4:523-32
4. Mohr JA, Killebrew L, Mushmore HG. Transfer of delayed hypersensitivity by blood transfusion in man. *JAMA* 1969;207:517
5. Hardy M A, Schumidek HH. Epidemiology of tuberculosis aboard a ship. *JAMA* 1968;203:175
6. Cantwell MF, Shehab ZM, Costello AM, et al. Brief reports. Congenital tuberculosis. *N Engl J Med* 1994;330 (15):1051-4
7. Wiid IS, Edmen T, Hoal EG, Benade AJ, Van Helden PD. Total antioxidants levels are low during active TB and rise with anti tuberculosis therapy. *IUBMB Life* 2004;56 (2):101-6
8. McGarvey J.A., Wagner D, Bermudez LE: Differential gene expression in mononuclear phagocytes infected with pathogenic and non-pathogenic mycobacteria. *Clin Exp Immunol* 2004;136(3):490-500
9. Kwiatkowska S., Piasecka G, Zieba M, Piotrowski D: Increased serum concentrations of concentrations of conjugated dienes and malondialdehyde in patients with pulmonary tuberculosis *Respir Med* 1999;93(4):272-6
10. Sasaki Y, Yamagishi F, Yasi T, Mizutani F. A case of pulmonary tuberculosis case with pancytopenia accompanied to bone marrow gelatinous transformation. *Kekkaku* 1999;74 (4):361-4
11. Yamanaka K, Sakai S, Nomura F, Akashi T, Usui T. A nutritional investigation of homeless patients with tuberculosis. *Kekkaku* 2001;76 (4):363-70
12. Koracevic D, Koracevic G, Djordjevic V, Andrejevic S, Cosic V.. Method for the measurement of antioxidant activity in human fluids. *J Clin Pathol* 2001;54:356-61
13. Reinhold J.G. Standard Methods of of Clinical Chemistry. Reiner M. ed, New York and London Academic press. 1953; :p. 88
14. Aily DC, Camargo SS, Paro HS, et al. Systemic mycobacterioses in AIDS patients as determined by blood cultures on biphasic medium. *Rev Argent Microbiol* 1999;31(2):53-7
15. Llesuy SF, Tomaro ML. Heme oxygenase and oxidative stress: Evidence of involvement of bilirubin as physiological protector against oxidative damage. *Biochem Biophys Acta* 1994;1223:9-4
16. Ames BN, Cathcart R, Scwiers E, Hochstein R. Uric acid provides an antioxidant defense in humans against oxidants and radicals caused ageing and cancer. A hypothesis. *Proc Nat Acad Sci USA* (1981):79:6858-62
17. Arinola OG, Igbi J. Serum immunoglobulin and circulating immune complexes in Nigerians with HIV and pulmonary tuberculosis infection. *Tropical J Med Res* 1998;2(2):41-8
18. Nagayama N. Tamura A. Kurashima A. Hayashi K. Parameters relating to the development of residual pleural thickening in tuberculous pleurisy. *Kekkaku* 1999; 74(2):91-7
19. Gatner EM, Anderson R. An invitro assessment of cellular and humoral immune function in pulmonary tuberculosis: correction of defective neutrophil motility by ascorbate, levamisol, metoprolol and propranolol. *Clin Exp Immunol* 1980;40(2): 327-36
20. Reddy YN, Murthy SV, Krishna DR, Prabhakar MC. Role of free radicals and antioxidants in tuberculosis patients. *Indian J Tubercul* 2004;5(4):213-8
21. Whitby LG, Smith A, Beckett GT. Disorders of plasma lipids . In: *Lecture notes of clinical Chemistry* (1988). 4th ed. P:223-61
22. Gordon T, Castelli WP, Hjortland MC, Kannel WB , Dawber TR. High density lipoprotein as a protective factor against coronary heart disease. The Framingham Study. *Am J Med* 1980;62:707-14
23. Hamosh M, Pleterson JA, Janderson TR, et al. Protective function of human. The milk fat globule. *Semin Perinatol* 1999;23(3):242-9
24. Das UN. Essential fatty acids as possible enhancer of a beneficial actions of probiotics. *Nutrition* 2002;18(9):786
25. Plit ML. Theron AJ, Fickl H, Vani Rensburge CE. Pendel S. Anderson R. Influence of antimicrobial chemotherapy and smoking status on the plasma concentrations of Vitamin C, Vitamin E, beta-carotene, acute phase reactants, iron and lipid peroxides in patients with pulmonary tuberculosis. *Int J Tuberc Lung Dis* 1998;2(7): 590-6
26. Madebo T, Lindtjorn B, Aukrust P, Berge RK. Circulating antioxidants and Lipid peroxidation products in untreated tuberculosis patients in Ethiopia. *Am J Clin Nutr* 2003;117-22