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Biochemical nutritional parameters and anthropometric measurements in Nigerian pulmonary tuberculosis patients before and during chemotherapy

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Abstract

Background: Epidemiological studies have demonstrated an overlap between malnutrition and tuberculosis (TB) in most developing countries, but reports of changes in nutritional status throughout TB treatment are scarce. The objective of this study was to determine the nutritional status of pulmonary TB patients before and during anti TB chemotherapy.

Materials and methods: This study comprised of sixty eight (68) participants, twenty-four (24) multi-drug-resistant TB (MDR-TB) patients, twenty-four (24) drug-sensitive TB patients(DS-TB) and 20 non-TB apparently healthy individuals. TB patients were followed-up throughout 6 months of anti-TB chemotherapy. Anthropometric measurements; mid-upper arm circumference(MUAC), weight, body mass index(BMI), percentage body fat(PBF), fat mass index(FMI), fat-free mass index(FFMI), waist circumference(WC), hip circumference(HC), waist-hip ratio(WHR), and plasma proteins(total protein, transferrin, retinol binding protein–RBP, pre-albumin and albumin) concentrations were determined.

Results: Under nutrition (BMI <18.5 kg/m^2) was observed in 65% and 23.1% of MDR-TB patients and DS-TB patients respectively. MUAC, weight, BMI, FFMI, WC and HC were significantly reduced before commencement- and at 2 months of chemotherapy in DS-TB patients compared with controls. Plasma transferrin and pre-albumin levels were significantly increased at 2 and 4 months of chemotherapy respectively, but plasma albumin levels were increased at 2 and 4 months of chemotherapy in DS-TB patients compared with controls. In MDR-TB patients, MUAC, weight, BMI, PBF, FMI and FFMI decreased significantly before and 2 months of chemotherapy compared with controls. Plasma albumin and HC decreased significantly before chemotherapy, while plasma TP and RBP increased before chemotherapy and 2 months of chemotherapy in MDR-TB patients compared with controls. At 4 months of anti-TB chemotherapy, MUAC was decreased while plasma total protein, pre-albumin and albumin increased significantly in MDR-TB patients compared with controls. Plasma transferrin and albumin increased significantly at 6 months of chemotherapy in MDR-TB patients compared with controls.

Conclusion: Protein-calorie under nutrition remains a major challenge in TB patients and nutritional support for TB patients during anti-TB chemotherapy could ensure quicker recovery.

Keywords: *Under nutrition; tuberculosis; chemotherapy, anthropometry; proteins*

Résumé

Contexte: Les études épidémiologiques ont démontré un chevauchement entre la malnutrition et la tuberculose (TB) dans la plupart des pays en voie de développement, mais les rapports d'évolution de l'état nutritionnel pendant le traitement de la tuberculose sont rares. L'objectif de cette étude était de déterminer l'état nutritionnel des patients tuberculeux pulmonaires avant et pendant la chimiothérapie anti-tuberculose.

Matériaux et méthodes: Cette étude comprenait soixante-huit (68) patients atteints de tuberculose, vingt-quatre (24) patients atteints de tuberculose multi-médicament-résistante (TB- MMR), vingt-quatre (24) patients atteints de tubercules sensibles aux médicaments (TB-SM) et 20 non tuberculeux apparemment en bonne santé. Les patients atteints de tuberculose ont été suivis pendant 6 mois de chimiothérapie antituberculeuse. Les mesures anthropométriques; la circonférence du milieu de l'avant-bras (CMAB), le poids, l'indice de masse corporelle (IMC), le pourcentage de graisse corporelle (PGC), l'indice de masse graisseuse (IMG), l'indice de masse sèche (IMS), le périmètre de la taille (PT), la circonférence de la hanche (CH), le rapport taille-hanche (RTH) et les concentrations de protéines plasmatiques (protéines totales, transferrine, protéines de liaison rétinol - PLR, pré-albumine et albumine) ont été déterminés.

Résultats: La sous-nutrition (IMC <18,5 kg/m^2) a été observé chez 65% et 23,1% des patients TB-MMR et des patients TB-SM respectivement. La CMAB, le poids, l'IMC, l'IMS, le PT et la CH ont

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été considérablement réduits avant le début et à 2 mois de chimiothérapie chez les patients atteints de TB-SM par rapport aux témoins. Les concentrations plasmatiques de transferrine et de pré-albumine ont été significativement augmentées à 2 et 4 mois de chimiothérapie respectivement, mais les concentrations plasmatiques d'albumine ont été augmentées à 2 et 4 mois de chimiothérapie chez les patients atteints de TB-SM par rapport aux témoins. Chez les patients atteints de TB- MMR, la CMAB, le poids, l'IMC, le PGC, l'IMG et l'IMS ont diminué de manière significative avant et 2 mois de chimiothérapie par rapport aux témoins. L'albumine plasmatique et la CH ont diminué de manière significative avant la chimiothérapie, tandis que le plasma TP et PLR ont augmenté avant la chimiothérapie et 2 mois de chimiothérapie chez les patients atteints de TB- MMR par rapport aux témoins. À 4 mois de chimiothérapie antituberculeuse, la CMAB a diminué tandis que la protéine totale du plasma, la pré-albumine et l'albumine ont augmenté de manière significative chez les patients TB- MMR par rapport aux témoins. La transferrine plasmatique et l'albumine ont augmenté de manière significative à 6 mois de chimiothérapie chez les patients TB- MMR par rapport aux témoins.

Conclusion: La protéine calorique sous-nutrition reste un défi majeur chez les patients atteints de tuberculose et le soutien nutritionnel pour les patients atteints de tuberculose pendant la chimiothérapie anti-TB pourrait assurer une récupération plus rapide.

Mots-clés: *Sous nutrition; Tuberculose; Chimiothérapie, anthropométrie; Protéines*

Introduction

Malnutrition and tuberculosis are both problems of considerable magnitude in most developing countries, and epidemiological studies have demonstrated an overlap between these conditions in low income countries [1]. Among other risk factors, malnutrition has been reported to predispose to the development of active tuberculosis (TB). Also, active tuberculosis leads to aggravation of malnutrition due to reduced appetite, nutrient malabsorption, altered metabolism and increased excretion [2]. This accounts for the age-long link between consumption/wasting and active tuberculosis [3]. However, the nature of the interaction between these two conditions has been widely speculative and largely inconclusive [4]. Before the advent of anti tuberculosis chemotherapy, a diet rich in calories, proteins, fats, minerals and vitamins was generally considered an essential factor in treatment of tuberculosis. The introduction of anti-tuberculosis drugs, however has altered the management of tuberculosis and the role of diet is given little to no consideration in tuberculosis management. Malnutrition in tuberculosis patients may directly or indirectly affect treatment outcomes as it has been reported that malnourished TB patients have delayed recovery and higher mortality rates than well nourished patients [2, 5].

TB remains a major public health priority as worldwide 9.6 million people were estimated to have TB and 1.5 million died from *Mycobacterium tuberculosis* infection in 2014 [5]. Efforts towards eradication of TB have been hampered by emergence of drug resistant strains of *Mycobacterium tuberculosis*. A study reported a 90% cure rates of pulmonary tuberculosis cases using directly observed treatment short course (DOTS) strategy [6]. Treatment outcomes of TB are not entirely dependent on use of appropriate anti-TB drugs only, but also inefficient cellular immunity which may be a result of poor nutritional status [7].

Food insecurity and hunger are common in Africa due to a combination of climatic, economic, policy and political factors [8]. Analysis of multiple demographic and nutrition surveys estimated that 10-20% of African adults 20-49 years of age are malnourished, with protein-calorie malnutrition being reported as the common form of malnutrition [9-11]. It has been suggested that protein-calorie malnutrition, by reducing the expression of gamma interferon, tumour necrosis factor alpha, and other mycobactericidal substances may selectively compromise portions of the cell-mediated immune response that are important for containing and restricting *Mtb* [12,13]. Correlation of protein-calorie malnutrition and growth retardation allows assessment of individual nutritional status by measurement of growth indicators such as mid-upper arm circumference, weight and body mass index (BMI). Low BMI (<18.5 kg/m^2) and lack of adequate weight gain following TB treatment have been associated with increased risk of death [14,15] and TB relapse [16,17]. Also, waist circumference (WC), hip circumference (HC) and percentage body fat (PBF) are measures of bodily fat mass. These measures have been extensively employed in assessment of nutritional status in health and disease. Transferrin, retinol binding protein (RBP), pre-albumin and albumin are markers of protein nutritional status [4].

Previous studies concentrated on anthropometric measurements as markers of macronutrient status in TB patients. In addition, studies [1, 4, 12] on changes in biochemical nutritional factors and anthropometric indices throughout treatment of either DS-TB patients, MDR-TB patients or both are scarce. This study assessed macronutrient status of drug sensitive and drug resistant pulmonary tuberculosis patients by combination of anthropometric measurements and plasma protein concentrations before and during anti-TB treatment.

Materials and methods

Study setting: University College Hospital, Ibadan, Nigeria

Study design: Case control

Study Instruments: Structured questionnaires and laboratory tests

Study variables: Anthropometric measurements (mid-upper arm circumference, weight, body mass index, percentage body fat, fat mass index, fat-free mass index, waist circumference, hip circumference, waist-hip ratio) and plasma proteins(total protein, transferrin, retinol binding protein–RBP, pre-albumin and albumin).

Study participants

Sixty eight (68) participants were enrolled for this study, this comprised of twenty four (24) multi-drug-resistant TB (MDR-TB) patients, twenty four (24) drug-sensitive TB patients (DS-TB) and twenty (20) non-TB apparently healthy individuals. MDR-TB patients had been previously diagnosed as being infected with isoniazid and rifampicin resistant strains of Mtb using clinical history, Chest X-ray and GENE Xpert. These patients were admitted into the MDR TB centre, University College Hospital (UCH) Ibadan, Nigeria for anti-TB treatment. DS-TB patients were recruited from the Medicine Out-patient Clinic, University College Hospital, Ibadan, Nigeria by a Consultant Chest Physician after confirmation with laboratory tests, chest X-ray and clinical history. The study protocol was reviewed and approved by the University of Ibadan/University College Hospital Joint Institutional Research Ethics Committee. Informed consent was obtained before data and samples collection from study participants.

Five (5) milliliters of blood was drawn from the anti cubital fossa vein into sterile lithium heparin tubes before commencement of chemotherapy, 2 months, 4 months and 6 months of anti-TB therapy. Blood samples were centrifuged and plasma obtained were analyzed.

Anthropometric measurements

Mid upper arm circumference (MUAC)

MUAC was measured using a measuring tape. Tape was extended around the mid upper arm of participant while the arm was straight and relaxed. Measurement was taken to the nearest 0.1cm and recorded.

Weight and Percentage body fat (PBF)

Weight and PBF were measured with a bioelectrical impedance analysis (BIA) scale (Intelli Scale BS0114, China) which was placed on a flat surface. Study participants wore light clothing and were without shoes before they stood on the scale.

Waist circumference (WC)

This was measured using a measuring tape. Participants were instructed to raise their cloth above waist and cross their arms at chest level while maintaining an upright posture. Measurements were taken by extending the measuring tape around the participants from the belly button.

Hip circumference (HC)

This was measured using a measuring tape extended around the hip of study participants while maintaining an upright posture.

Indices and Ratios

The following indices and ratios were calculated using their respective formulae;

$$\text{Body mass index (BMI)} = \frac{\text{Weight (kg)}}{\text{Height}^2\ (\text{m}^2)}$$

$$\text{Fat Mass Index (FMI)} = \frac{\text{Fat mass (kg)}}{\text{Height}^2\ (\text{m}^2)}$$

$$\text{Fat mass} = \text{PBF} \times \text{Body weight}$$

$$\text{Fat Free Mass Index (FFMI)} = \frac{\text{Fat free mass (kg)}}{\text{Height}^2\ (\text{m}^2)}$$

$$\text{Fat free mass} = \text{Body weight} - \text{Fat mass}$$

$$\text{Waist circumference to Hip circumference ratio (WHR)} = \frac{\text{Waist circumference (cm)}}{\text{Hip circumference (cm)}}$$

PTB Treatment protocol

All bacteriologically confirmed MDR-TB patients received intensive phase for 6-8 months in the hospital followed by 12 months of continuation phase in the community based on WHO updated guidelines in 2011 [18]. Standardized treatment regimen was done using five drugs namely: Kanamycin/Amikacin, Levofloxacin, Prothionamide, Cycloserine, Pyrazinamide and Pyridoxine). This present study was conducted during the intensive phase of treatment.

Patients admitted for MDR-TB treatment, received support from non-governmental organizations which provided nutritional assistance in the form of meals and micronutrient supplements. Vitamin C (Spartan C), Folic acid (Vitabiotics), Vitamin B complex (Vitabiotics), Vitamin B6 (Pauco) and multivit (Pauco) supplements were administered daily with anti-TB drugs as part of the treatment regimen at the study site .

Sputum smear positive DSTB patients received DOTS intensive phase for 2 months and 4

months continuation in the hospital, as recommended in the 2011 WHO updated guidelines [18]. Standardized treatment regimen with fixed drugs containing; Rifampicin, Isoniazid, Pyrazinamide and Ethambuthol during intensive phase, and Rifampicin and Isoniazid in continuation phase, were used. Drug sensitive TB patients were treated at Out-Patient Clinic and did not benefit nutritional support during the period of anti-TB treatment.

Biochemical analysis

Enzyme-linked immuno sorbent assay (ELISA) was used to measure transferrin (Transferrin; Assayprolnc, USA), retinol binding protein (RBP; Lot #-15C1, Part #-E-80RBP, Immunology Consultants Laboratory Inc, Portland), albumin (Albumin; Lot #-17, Part #-E-80AL, Immunology Consultants Laboratory Inc, Portland) and prealbumin (Prealbumin, Lot #-11Q1, Part #-E-80PRE, Immunology Consultants Laboratory Inc, Portland). Assay protocol was as specified by the manufacturer and the absorbance of all the assays was measured at 450nm with an ELISA reader (Spectra Max Plus 384, Molecular Devices LLC, USA). The procedure was carried out as previously described [19].

Statistical analysis

Data obtained was analyzed using statistical package for social sciences (SPSS) version 17.0. Independent Student t-test was used to compare the mean values of PTB patients and controls, while paired t-test was used to compare the mean values of PTB patients before commencement of chemotherapy, 2 months, 4 months and 6 months of anti-TB chemotherapy. Values were considered significant at $p<0.05$.

Results

Under-nutrition was observed in 65% and 23. MDR-TB and DS-TB patients respectively t commencement of chemotherapy while, co were all normal weight individuals. In MD patients, the percentage of underweight pa increased to 70% after 2 months of ant chemotherapy and declined to 15% and 5.6% months and 6 months of anti-TB chemoth respectively. In DS-TB patients on the other the percentage of underweight patients decrea 20% at 2 months of anti-TB chemotherapy an at 4 months and 6 months of anti-TB chemoth (Table 1)

Drug-sensitive TB

The anthropometric measurements MUAC, w BMI, FFMI, WC and HC were significantly re in DS-TB patients before anti-TB chemothera 2 months of anti-TB chemotherapy when com with control. Plasma concentrations of trans and albumin of DS-TB patients were signific increased at 2 months of anti-TB chemotherapy compared with controls. Significant increas plasma concentrations of pre-albumin and alb of DS-TB patients at 4 months of anti chemotherapy when compared with controls also observed. There were also significant incr in weight and plasma concentration of pre-alb of DS-TB patients at 4 months of chemothe

Table 1: Proportion of participants with undernutrition (BMI <18.5 kg/m²)

Group	No of participants	BMI <18.5 kg/m² (%)	BMI <18.5 kg/m² (%) – MDR-TB	BMI <18.5 kg/m² (%) – DS-TB
Control	20	0		
Before chemotherapy	48		65.5	23.1
2 months of chemotherapy	48		70.0	20.0
4 months of chemotherapy	48		15.0	0.0
6 months of chemotherapy	48		5.6	0.0

when compared with their levels before anti- chemotherapy. Plasma concentration of transfe of DS-TB patients was reduced significantly, w weight was increased at 6 months of anti- chemotherapy when compared with the values be commencement of chemotherapy. (Table 2).

Multi-drug resistant TB

Anthropometric measurements MUAC, weig BMI, PBF, FMI and FFMI were significantly redu in MDR-TB patients before and at 2 months of a TB chemotherapy when compared with contr

Table 2: Anthropometric measurements and plasma concentrations of markers of nutritional status in DS-TB patients before and during chemotherapy and in healthy controls

Parameters	Control (n=20)	Before chemotherapy (n=24)	2months (n=24)	4months (n=24)	6months (n=24)
MUAC *(cm)*	27.4±2.3	24.6±3.3*	25.2±2.6*	27.0±3.9	26.8±3.0
Weight *(kg)*	67.0±14.1	56.5±10.4*	59.6±8.3*	65.9±10.9"	65.9±8.0"
BMI *(kg/m²)*	22.9±3.4	20.4±3.8*	20.4±2.2*	23.1±4.8	22.9±2.5
PBF *(%)*	24.2±8.5	22.0±10.3	21.0±8.9	25.5±10.8	20.4±9.0
FMI *(kg/m²)*	5.7±2.6	5.2±4.4	4.6±2.4	4.7±1.9	4.4±2.4
FFMI *(kg/m²)*	17.2±2.1	15.8±1.9*	15.9±1.8*	16.1±1.9	16.5±1.7
WC *(cm)*	75.0±23.7	72.0±9.5*	71.9±5.5*	78.6±9.8	75.3±6.3
HC *(cm)*	92.8±15.2	89.2±8.3*	91.2±5.3*	94.3±6.5	94.5±6.8
WHR	0.8±0.2	0.86±0.06	0.84±0.03	0.88±0.06	0.85±0.03
Total Protein *(g/L)*	59.8±8.9	58.9±6.3	60.6±3.9	56.5±6.5	58.7±2.3
Transferrin *(g/L)*	167.6±39.5	187.0±40.7	188.6±29.8*	167.0±9.0	151.3±17.0"
RBP *(mg/L)*	55.1±7.0	53.6±14.0	50.6±6.8	57.0±7.6	50.7±8.9
Pre-albumin *(mg/L)*	272.3±87.1	261.0±78.8	313.9±78.2	339.2±33.0*"	339.5±113.5
Albumin *(g/L)*	37.0±22.0	45.5±10.9	53.2±6.2*	55.5±17.3*	52.7±27.4

**Significantly different from Control (p<0.05)*
"Significantly different from before commencement of chemotherapy (p<0.05)

Table 3: Anthropometric measurements and plasma concentrations of markers of nutritional status in MDR-TB patients before and during chemotherapy and in healthy controls

Parameters	Control (n=20)	Before chemotherapy (n=24)	2months (n=24)	4months (n=24)	6months (n=24)
MUAC *(cm)*	27.4±2.3	23.0±2.7*	24.0±2.0*	24.6±2.5*	25.3±2.6"
Weight *(kg)*	67.0±14.1	50.9±8.3*	47.1±10.4*	60.4±8.5"	64.2±7.9"
BMI *(kg/m²)*	22.9±3.4	17.8±3.1*	16.5±4.0*	21.1±3.1"	22.5±3.2"
PBF *(%)*	24.2±8.5	13.4±7.5*	13.6±11.2*	20.5±9.4"	22.5±10.1"
FMI *(kg/m²)*	5.7±2.6	2.6±1.9*	2.6±2.9*	4.5±2.7"	5.3±3.0"
FFMI *(kg/m²)*	17.2±2.1	15.3±1.9*	13.9±1.8*"	16.6±1.8"	17.2±1.8"
WC *(cm)*	75.0±23.7	73.6±6.1	78.3±8.4	78.2±7.7	81.5±7.7"
HC *(cm)*	92.8±15.2	84.7±5.7*	90.2±7.3"	91.6±6.7"	93.9±7.2"
WHR	0.8±0.2	0.9±0.04	0.9±0.05	0.9±0.05	0.9±0.05
Total Protein *(g/L)*	59.8±8.9	75.9±3.3*	76.6±6.6*	70.1±8.2*"	65.5±9.4"
Transferrin *(g/L)*	167.6±39.5	198.8±42.6	122.7±63.7"	233.6±132.8	354.0±53.0*"
RBP *(mg/L)*	55.1±7.0	66.4±9.9*	70.1±17.4*	55.3±10.7"	63.0±18.8
Pre-albumin *(mg/L)*	272.3±87.1	247.2±54.7	264.0±28.5	332.1±63.9*"	303.9±43.6"
Albumin *(g/L)*	37.0±22.0	16.3±3.6*	45.9±17.3"	69.9±13.6*"	64.1±9.2*"

**Significantly different from Control (p<0.05)*
"Significantly different from before commencement of chemotherapy (p<0.05)

Mean HC and plasma albumin concentration of MDR-TB patients decreased significantly after 2 months of anti-TB chemotherapy, while plasma RBP of MDR-TB patients increased significantly at 2 months and 4 months of anti-TB chemotherapy when compared with controls. Though MUAC of MDR-TB patients decreased significantly at 4 months of anti-TB chemotherapy, plasma pre-albumin and albumin concentrations in MDR-TB patients increased significantly at 4 months and 6 months of anti-TB chemotherapy respectively when compared with controls. Plasma TP was significantly raised before, at 2 months and 4 months of chemotherapy in MDR-TB patients compared to controls. (Table 3)

While there were significant increases in weight, BMI, PBF, FMI, FFMI and plasma pre-albumin concentration of MDR-TB patients at 4 months and 6 months of anti-TB chemotherapy, there were significant decreases in PBW and TP of MDR-TB patients at 4 months and 6 months of anti-TB chemotherapy when compared with mean values before commencement of chemotherapy. Mean HC and plasma albumin concentrations of MDR-TB patients increased significantly at 2 months, 4 months and 6 months of anti-TB chemotherapy when compared with mean values before anti-TB chemotherapy. Although plasma RBP concentration of MDR-TB patients decreased significantly at 4 months of anti-TB chemotherapy, MUAC, WC and plasma transferring concentrations of MDR-TB patients increased significantly at 6 months of anti-TB chemotherapy when compared with mean values before anti-TB chemotherapy. (Table 3)

There were significant decreases in BMI, PBF, FMI and albumin whereas TP and RBP were significantly increased in MDR-TB patients when compared to DS-TB patients before chemotherapy. (Table 4).

Zachariah *et al* [15] who reported under-nutrition in 42%, 51% and 57% of TB patients in Uganda, Ghana and Malawi respectively. It is however lower than 71.6% reported by Kennedy *et al* [22] in Tanzanian TB patients. Under-nutrition has been associated with alterations in immune function which increases susceptibility to infection and may also aggravate development and progression of active TB infection [12]. It is also suggested that under-nutrition alters effectiveness of medication, vaccine efficacy and increases mortality of TB patients [23-26]. Due to the viscous cycle of TB and under-nutrition, it is difficult to establish if under—nutrition results in active TB or active TB results in under-nutrition, but the high prevalence of under nutrition in TB patients reported in this present study indicates that under-nutrition is still a major concern in TB patients. Hence, there is a need for assessment of nutritional status of TB patients at diagnosis.

Anthropometric indicators are regularly measured and interpreted to assess malnutrition [16]. This study found reduced anthropometric measures of nutritional status in DS-TB and MDR-TB patients before commencement of anti-TB chemotherapy when compared to healthy controls. Lower mean mid-upper arm circumference, weight, BMI and hip

Table 4: Anthropometric measurements and plasma concentrations of markers of nutritional status in DSTB and MDR-TB patients before chemotherapy.

Parameters	DS-TB before Chemotherapy (n=24)	MDR-TB before Chemotherapy (n=24)	t	P value
MUAC *(cm)*	24.6±3.3	23.0±2.7	-1.994	0.055
Weight *(kg)*	56.5±10.4	50.9±8.3	-2.027	0.051
BMI *(kg/m²)*	20.4±3.8	17.8±3.1	-2.052	0.049*
PBF *(%)*	22.0±10.3	13.4±7.5	-2.545	0.017*
FMI *(kg/m²)*	5.2±4.4	2.6±1.9	-2.352	0.026*
FFMI *(kg/m²)*	15.8±1.9	15.3±1.9	-0.672	0.507
WC *(cm)*	72.0±9.5	73.6±6.1	-1.065	0.295
HC *(cm)*	89.2±8.3	84.7±5.7	-1.912	0.065
WHR	0.86±0.06	0.9±0.04	1.183	0.246
Total Protein *(g/L)*	58.9±6.3	75.9±3.3	9.504	0.000*
Transferrin *(g/L)*	187.0±40.7	198.8±42.6	0.845	0.405
RBP *(mg/L)*	53.6±14.0	66.4±9.9	3.311	0.002*
Pre-albumin *(mg/L)*	261.0±78.8	247.2±54.7	-0.858	0.397
Albumin *(g/L)*	45.5±10.9	16.3±3.6	-9.733	0.000*

**Significant at p<0.05*

Discussion

This present study reports under-nutrition in 48.5% of the TB patients before commencement of anti-TB chemotherapy. This finding is in consonance with the reports of Mupere *et al* [20], Dodor [21], and

circumference in DS-TB and MDR-TB patients, WC and PBF in DS-TB and MDR-TB patients respectively compared with controls represent loss of both fat and fat-freemass in these patients as

shown by decreases in FMI and FFMI. This could be a result of a shift in metabolism in favour of increased catabolism and increased protein loss (negative nitrogen balance), or decreased nutrient supply due to anorexia and/or malabsorption. Studies of protein and energy metabolism in infection previously demonstrated metabolic changes in acute, sub-acute and chronic infectious diseases [27]. Increased energy demand and expenditure determined by increased oxidation of fat and breakdown of lean tissue for energy were reported in several infectious diseases including TB [28]. Macallan *et al* [28] further hypothesized that there is a block to the anabolic response to nutrition in TB patients thereby hampering utilization of exogenous nutrient supply in these patients. These may explain the loss of fat and fat-free mass in TB patients observed in this study. Moreso, it also supports the age-long association between tuberculosis and wasting as well as previous reports of protein-caloric malnutrition in TB patients [1,21,29-31].

Conventional TB treatment involves the use of combinations of anti-TB therapeutic drugs for at least 6 months. The length of treatment and side-effects of the drugs have been identified among factors responsible for patients' non-compliance with treatment, which has largely resulted in the emergence of drug resistant strains of Mtb. In DS-TB, only weight increased significantly at 4 months and 6 months of anti-TB chemotherapy when compared with before chemotherapy. In MDR-TB on the other hand, MUAC, weight, BMI, PBF, FMI, FFMI, WC and HC were increased at 4 months and 6 months of chemotherapy when compared with before chemotherapy. The differences observed between DS-TB and MDR-TB patients may be as a result of nutritional support received by MDR-TB patients.

This study therefore proposes that a balanced diet and micronutrient supplementation can be added to conventional anti-TB drugs. This is particularly necessary in developing regions of the world where poverty and food insecurity are endemic. Improved nutritional status of TB patients could also lead to immunologic changes that may enhance Mtb clearance and reduce infectiousness of patients. However, there is a need for further studies to determine the optimal amount and combinations of nutrients for better nutritional, immunological and treatment outcomes in these patients. The present finding is in consonance with the study of Paton *et al* [27] where increased body weight and lean mass of TB patients on energy-protein supplement compared to a non-supplemented group was reported.

Components of plasma protein are altered in different physiological and pathological conditions. This study found decreased plasma albumin with increased total protein and RBP concentrations in MDR-TB patients before commencement of anti-TB chemotherapy when compared with controls. Decreased plasma albumin with increased plasma total protein concentration in MDR-TB patients before chemotherapy might be an indication of electrophoretic pattern of plasma proteins seen in chronic inflammation which is characterized by reduction in the albumin band and a marked increase in gamma globulin band. Inflammation is a phenomenon in TB patients as shown by the results of this study. Elevated gamma-globulins with concomitant reduced albumin in TB patients have been previously reported [32,33]. The increase in gamma-globulins represents increased production of immunoglobulin classes in TB patients, though the roles of immunoglobulins in defence against Mtb are largely unclear. Reduced albumin in MDR-TB patients before chemotherapy on the other hand may be suggestive of either malnutrition or an acute phase response. However, in acute phase response, a decrease in plasma RBP is expected but we found increased plasma RBP with reduced plasma albumin. This is plausible since most of the MDR-TB patients in this study were not severely ill before commencement of chemotherapy. Reduced plasma albumin may be due to reduced albumin synthesis or increased albumin utilization. Paton *et al* [27] previously suggested an anabolic block in TB. Our study goes further to propose that this anabolic block may affect synthesis of selected proteins but not all proteins in TB patients. In addition, reduced plasma albumin before chemotherapy might be due to utilization of albumin in scavenging free radical as previously demonstrated in TB patients [34-36].

Proper TB treatment helps restore nutritional status. However, the time of nutritional recovery may be long and many TB patients remain undernourished after TB treatment is completed [37]. This present study found significant increases in the concentrations of plasma proteins albumin, pre-albumin and transferrin in MDR-TB patients at 4 months and 6 months of anti-TB chemotherapy, whereas pre-albumin alone was significantly increased at 4 months of anti-TB chemotherapy in DS-TB patients. This further supports the need for provision of nutritional support for TB patients on anti-TB chemotherapy to ensure early recovery.

In conclusion, protein-caloric under nutrition remains a major challenge in TB patients and nutritional support in the form of controlled diet and micronutrient supplements should be given to TB patients during anti-TB chemotherapy to ensure quick recovery.

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