



Nutritional status of HIV-infected women with tuberculosis in Dar es Salaam, Tanzania

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Setting: Tuberculosis (TB) treatment clinics in Dar es Salaam, Tanzania.

Objective: To quantify anthropometrics and intake of energy and protein among human immunodeficiency virus (HIV) positive women with TB.

Design: HIV-positive women with newly diagnosed TB were assessed on their anthropometric characteristics and dietary intake. Energy and protein intake were determined using Tanzania food composition tables and compared with standard recommendations. Patients were re-evaluated after 4–6 months of anti-tuberculosis treatment.

Results: Among 43 women, the baseline median CD4 count was 209 cells/ μ l (range 8–721); 19 (44%) had a CD4 count of <200 ; 20 (47%) were on antiretroviral therapy. Body mass index was <18.5 kg/m² in 25 (58%); the median food insecurity score was 6. The median level of kcal/day was 1693 (range 1290–2633) compared to an estimated need of 2658; the median deficit was 875 kcal (range –65–1278). The median level of protein/day was 42 g (range 27–67) compared to 77 g estimated need; the median protein deficit was 35 g (range 10–50). The median weight gain among 29 patients after 4–6 months was 6 kg.

Conclusion: HIV-positive women with TB have substantial 24-h deficits in energy and protein intake, report significant food insecurity and gain minimal weight on anti-tuberculosis treatment. Enhanced dietary education together with daily supplementation of 1000 kcal with 40 g protein may be required.

Malnutrition is common among patients with active tuberculosis (TB) disease and is exacerbated by concomitant human immunodeficiency virus (HIV) infection.^{1–4} Malnutrition in active TB represents the sum of previous malnutrition, which serves as a risk factor for TB, and new malnutrition, which develops as a consequence of active TB and its accompanying cytokine storm. Both malnutrition and HIV adversely influence the risk of TB disease and treatment outcome due to the impairment of T-lymphocyte-mediated immunologic defenses. Failure to gain weight during treatment of TB-HIV is associated with an adverse prognosis.^{5,6}

These findings suggest the need for studies to determine the effect of nutritional supplementation on the outcome of treatment for TB-HIV coinfection. We are not aware of previous studies that have attempted to quantify the specific deficits in energy and protein intake among patients with TB-HIV coinfection. In

order to design a macronutrient supplement for a controlled trial of nutritional supplementation for TB-HIV, we conducted a pilot nutritional study of patients with coinfection. The study was designed to focus specifically on women based on a World Health Organization Consultation on Nutrition and HIV/AIDS (acquired immune-deficiency syndrome) to identify gaps in the current understanding of nutrition in HIV.⁷

In the present study, we sought to determine the prevalence of low body mass index (BMI) in women with TB-HIV, quantify specific deficits in energy and protein intake, and assess food insecurity. We also assessed changes in nutritional status during treatment.

STUDY POPULATION, DESIGN AND METHODS

Subjects

HIV-positive women aged ≥ 18 years were recruited from four Tanzanian NTL (National Program on Tuberculosis and Leprosy) clinics (Mwananyamala, Temeke, Mbagala and Amana) in all three municipalities of Dar es Salaam between October 2009 and October 2010. Eligible subjects were within 2 weeks of being started on the standard four-drug treatment regimen with isoniazid, rifampin, pyrazinamide and ethambutol for pulmonary TB, and agreed to return for follow-up visits. All treatment for TB in Tanzania is provided free of charge by the public NTL clinics; the participating clinics were therefore considered representative. After providing informed consent, subjects underwent a single phlebotomy for confirmation of HIV status and determination of CD4 count. Subjects with two positive rapid HIV test results (Determine HIV-1/2, Inverness Medical, Tokyo, Japan; Uni-Gold HIV, Trinity Biotech, Bray, Ireland) were eligible for participation. NTL staff referred study subjects who were not already on antiretroviral therapy (ART) to a Ministry of Health HIV Care and Treatment Center (CTC) for HIV treatment.

Evaluation

Subjects were interviewed to obtain socio-demographic information, including age, residence, financial and employment status of both the patient and her partner, highest level of education, income spent specifically on food, and the number and ages of persons living in the same household.

Anthropometric measurements

Weight (kg), skin fold thicknesses (mm) at five different areas, including the triceps, subscapular, suprailiac,

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KEY WORDS

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abdomen and thigh, as well as the circumferences (cm) of the mid-upper arm, waist, hip and thigh, were determined using calibrated instruments.⁸

Body composition

Upper arm area (cm²), upper arm muscle area (cm²) and upper arm fat area (cm²) were calculated using methods described by Frisancho.⁹ Density (kg/m³) and body fat (%) were calculated using triceps, subscapular and suprailiac skinfold thickness measurements using methods described by Durnin et al.¹⁰

Macronutrient evaluation

Trained nutritionists or study nurses evaluated dietary intake using a multiple pass 24-h dietary recall method to list all beverages and foods consumed in the previous day.¹¹ Energy and protein intakes were then calculated utilizing the Tanzania food composition tables.¹² Daily protein and calorie deficits were estimated. The target intake was based on the World Health Organization recommendation of 2140 kcal for a moderately active adult woman, increased by 20% for TB-HIV coinfection to 2568 kcal; the protein target was 12% of total kcal, or 77 g.^{13–15} Deficits were calculated as the difference between the targets and the reported dietary intake. Nutritional education and counseling were provided for each woman based on dietary evaluation.

Food insecurity

The Household Food Insecurity Access Scale (HFIAS), which was adapted from the Food and Nutritional Technical Assistance II Project (FANTA-2) to determine the availability and accessibility of food in each woman's household, was administered among all subjects.¹⁵ An adapted questionnaire contained a total of nine yes or no questions followed by a 'frequency-of-occurrence' question. Some questions inquired about the subject's perception of food vulnerability, while other questions addressed the subject's behavioral responses due to food insecurity. Based on the answers given by the client, a score was assigned to each woman ranging from 0 (no insecurity) to 27 (maximum insecurity) using the HFIAS guideline.¹²

Follow-up

Subjects were requested to return every month during the 6 months of anti-tuberculosis treatment for repeat evaluation, including dietary intake and anthropometric measurements.

Quality assurance of data

All data were reviewed by two independent study personnel before entry into a computer database, and were reviewed by another investigator after computer entry.

Ethics approval

The study was approved by the Institutional Review Board at Dartmouth Medical School, Hanover, NH, USA, and the Research Ethics Committee of the Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania.

Statistical analysis

As this was a pilot study to prepare for an intervention, formal sample size was not calculated. Our main objective was to quantify energy and protein intake, and a sample size of 40 was considered adequate for the main analysis. Descriptive statistics were used to compare patient characteristics (Table 1) at baseline stratified by whether or not BMI was <18.5 or ≥18.5 kg/m², an accepted cut-off for moderate malnutrition.¹³ BMI groups were compared based on rank statistics (medians and interquartile ranges) and the Wilcoxon Mann-Whitney test, as the sample size was small and some results were skewed (e.g., CD4 counts in patients with and without ART).

RESULTS

Patient characteristics

A total of 334 consecutive women were screened to obtain 43 eligible subjects. The median age was 35 years. Table 1 depicts baseline clinical, nutritional and body composition data. The median CD4 count was 209 cells/μl (range 8–721); 19 (44%) patients had a CD4 of <200 cells/μl, and five had a CD4 of <50 cells/μl. A total of 20 women (47%) were on ART. BMI was <18.5 kg/m² in 25 (58%) and ≥18.5 in 18 (42%).

TABLE 1 Demographic, clinical and body composition data on 43 human immunodeficiency virus positive women with tuberculosis at baseline

	All subjects (n = 43) median (25%–75%)*	BMI <18.5 (n = 25, 58%) median (25%–75%)*	BMI ≥18.5 (n = 18, 42%) median (25%–75%)*	P value
Age, median, years	35	32	39	0.04
CD4 count, cells/μl, median [range]	209 [8–721]	193.5 [8–721]	261 [19–588]	0.72
Completed primary school, %	72	76	67	0.52
Median number of persons in household	4	4	4	0.47
CD4 <200 cells/μl, n (%)	19 (44)	12 (63)	7 (37)	0.55
CD4 <50 cells/μl, n (%)	5 (12)	3 (60)	2 (40)	0.93
Patients on ART, n (%)	20 (47)	11 (55)	9 (45)	0.31
Weight, kg	43 (40–53)	42 (38–43)	55 (46–65)	<0.01
BMI, kg/m ²	18 (17–20)	17 (17–18)	21 (19–25)	<0.01
MUAC, cm	21 (20–24)	20 (19–21)	24 (23–29)	<0.01
Three-site skinfold thickness, mm	23 (18–32)	19 (17–23)	32 (26–51)	<0.01
UAMA, cm ²	27 (23–31)	25 (22–27)	32 (29–36)	<0.01
UAFA, cm ²	10 (7–16)	8 (6–10)	16 (11–24)	<0.01
Calculated % body fat three-site skinfold thickness	21 (17–25)	18 (16–21)	26 (21–36)	<0.01

*Quartiles.

BMI = body mass index; MUAC = middle upper arm circumference; UAMA = upper arm muscle area; UAFA = upper arm fat area.

TABLE 2 Reported dietary intake of study subjects at baseline

	All subjects (n = 43) median (25%–75%)*	BMI <18.5 kg/m ² (n = 25, 58%) median (25%–75%)*	BMI ≥18.5 kg/m ² (n = 18, 42%) median (25%–75%)*	P value†
Energy intake, kcal	1693 (1290–2633)	1761 (1490–2224)	1570 (1277–2633)	0.35
Energy deficit, kcal	875 (–65–1278)	807 (344–1078)	998 (–65–1291)	0.35
Protein intake, g	42 (27–67)	42 (33–59)	40 (24–69)	0.66
Protein deficit, g	35 (10–50)	35 (18–44)	37 (8–54)	0.66
Food insecurity score	6 (0–14)	8 (1–15)	4 (0–13)	0.47

*Quartiles.

†Wilcoxon Mann-Whitney test.

BMI = body mass index.

Anthropometry

The median body weight was 43 kg, and median BMI was 18 kg/m². The median upper arm circumference (MUAC) was 21 cm, and the median upper arm muscle area (UAMA) was 27 cm. Calculated body fat % using three-site skinfold thickness was 21% overall, 18% for BMI <18.5 kg/m² and 26% for BMI ≥18.5.

Macronutrient evaluation

Assessment of energy intake revealed an overall median daily intake of 1693 kcal/day for a median calculated energy deficit of 875 kcal/day. There was a trend toward higher median energy intake among women with a BMI of <18.5 kg/m², with a correspondingly lower kcal deficit (*P* = 0.35). The overall median daily protein intake was 42 g/day, for a calculated median deficit of 35 g. There were no significant differences in daily protein intake and

the corresponding daily protein deficit between the two BMI sub-categories (Table 2).

Follow-up at 1 month

Follow-up data at 1 month were available for 32 women (74%) (Table 3). Kcal energy and protein intake both increased compared to baseline, resulting in smaller deficits. The median weight gain was 1 kg for women with a BMI of <18.5 kg/m² and 0 kg for women with a BMI of ≥18.5. The number of subjects who failed to gain weight at 1 month was 9/32 (28%), of whom 7 had a BMI of ≥18.5 kg/m².

Follow-up at 4–6 months

Follow-up data at 4–6 months were available for 29 women (67%) (Table 4). Kcal energy intake and protein intake had continued to

TABLE 3 Patient characteristics at 1 month

	All subjects median (25%–75%)*	BMI <18.5 kg/m ² median (25%–75%)*	BMI ≥18.5 kg/m ² median (25%–75%)*	P value
Patients with available data, n (%)	32	18 (56)	14 (44)	
Weight, kg	47 (39–50)	42 (37–47)	51 (47–56)	<0.01
Weight gain, kg	1	1	0	0.07
BMI, kg/m ²	18 (17–20)	18 (17–18)	21 (20–22)	<0.01
Energy intake, kcal	2279 (1763–2779)	2325 (1756–2661)	2278 (1915–2745)	0.90
Energy deficit, kcal	289 (–177–805)	243 (–93–812)	289 (–177–653)	0.90
Protein intake, g	61 (43–78)	61 (36–68)	60 (52–78)	0.42
Protein deficit, g	16 (–1–34)	16 (9–41)	17 (–1–25)	0.42

*Quartiles.

BMI = body mass index.

TABLE 4 Patient characteristics at 4–6 months

	All subjects median (25%–75%)*	BMI <18.5 kg/m ² median (25%–75%)*	BMI ≥18.5 kg/m ² median (25%–75%)*	P value
Patients with available data, n (%)	29	17 (59)	12 (41)	
Known deaths, n (%)	1 (3)	0	1 (8)	0.18
Patients on ART, n/N (%)	19/29 (66)	11/17 (65)	8/12 (67)	
Median weight, kg	48	46	55	0.04
Median weight gain, kg	6 (2–7)	6 (5–8)	3 (2–5)	0.09
Change in BMI	2 (1–3)	2 (2–3)	1 (1–2)	0.06
Energy intake, kcal	2370 (2069–2868)	2340 (1925–3327)	2391 (2072–2868)	0.87
Energy deficit, kcal	198 (–300–499)	228 (–759–643)	177 (–300–496)	0.87
Protein intake, g	54 (46–78)	52 (40–80)	56 (48–78)	0.54
Protein deficit, g	23 (–1–32)	25 (–3–37)	21 (–1–29)	0.54
Change in CD4, median [range]	105 [–425–866]	99 [–425–866]	137 [–52–407]	0.57
Days to CD4, median [range]†	183 [35–233]	186 [61–233]	180 [35–220]	0.31

*Quartiles.

†Interval between the tests.

BMI = body mass index; ART = antiretroviral therapy.

increase compared to baseline and 1 month. The median weight gain after 4–6 months was 6 kg. Women with a BMI of <18.5 kg/m² gained a median of 6 kg vs. 3 kg for women with a BMI of ≥ 18.5 . The number of subjects who failed to gain weight at 4–6 months was 2/32 (6%), all of whom had a BMI of ≥ 18.5 kg/m². The median change in CD4 count after 6 months of follow-up was 105 cells/ μ l: 99 in the BMI <18.5 group and 137 in the BMI ≥ 18.5 group. The median change in MUAC was 0 mm. The median change in BMI was 2 kg/m² in the BMI <18.5 group and 1 in the BMI ≥ 18.5 group. Modest energy and protein intake deficiencies persisted up to the end of the anti-tuberculosis treatment, both overall and when segregated by BMI. There was one reported death: a patient with a baseline BMI 21 kg/m² and CD4 120 cells/ μ l who had gained 4 kg at 4 months, but remained sputum-positive, died at 5 months due to an undiagnosed febrile illness.

DISCUSSION

This study shows that energy and protein undernutrition is common among women with TB-HIV coinfection in a developing country. Almost 60% of women with TB-HIV were found to have a BMI of <18.5 kg/m² and macronutrient deficits were substantial. To our knowledge, this is the first study to quantify specific deficiencies in dietary energy and protein intake in women with TB-HIV coinfection. We also found that, despite expert nutritional counseling, weight gain at 4–6 months was modest and the proportion of women with a BMI of <18.5 kg/m² did not change from baseline among women who were not lost to follow-up.

These findings are consistent with data from other studies that have demonstrated energy and protein deficits in patients with TB-HIV and an adverse prognosis in patients with such deficits. In a previous study from Tanzania, women with TB-HIV were found to have a median BMI of 19 compared to one of 23 in a general population of women in Dar es Salaam.^{16,17} A study in Burundi showed that low BMI was common in TB-HIV patients and worse than in non-HIV-infected patients with TB.¹⁸ A study in Malawi among patients with a high rate of HIV showed that a BMI of <17 in patients with TB was associated with an increased risk of early death.¹⁹ Another study from Tanzania showed that early mortality was increased two-fold among patients with a baseline BMI of <17 or MUAC of <25 .²⁰ Other studies have shown an increased mortality in TB-HIV for patients with BMI values of <17 – 18.5 kg/m².^{3,19,21}

Low BMI in patients with TB-HIV is characterized by a decrease in lean body mass and fat mass and increased risk of mortality.²² A decreased MUAC was found to be a predictor of incident TB among HIV-1-infected women in Tanzania.²³ Among women with TB in Uganda, both low baseline BMI and low lean tissue mass were associated with an increased risk of death.²⁴

Failure to gain weight at 1 month of anti-tuberculosis treatment has been shown to be a risk factor for mortality in HIV-associated TB,⁶ and failure to gain weight at 2 months has been shown to be risk factor for unsuccessful treatment in HIV-negative subjects.⁵ Our finding that 28% of patients with follow-up data at 1 month failed to gain weight is thus particularly noteworthy.

Patients in the present cohort had a high level of moderate malnutrition and evidence of food insecurity. We are not able to assess the extent to which incipient TB itself caused or worsened malnutrition or the extent to which poverty and lack of nutrition education were the principal cause of malnutrition. However, deficits in recommended levels of energy and protein intake were widespread, suggesting that the high level of poverty in Tanzania was a contributing factor. It has been reported that high food prices and the global financial crisis have resulted in reduced ac-

cess to nutritious food and worsened nutritional status and health in the world.²⁵ Both the social disadvantage of women in Tanzanian culture and the stigma attached to HIV and TB may play a role in the low BMIs observed here.²⁶

We found a trend toward greater energy and protein intake among women in the BMI <18.5 kg/m² subgroup. Women in both subgroups had increased energy intake by approximately 30% and protein intake by approximately 50% at 1 month; however, deficits from recommended intakes had not been erased. Energy intake was similar at 1 and 6 months, but protein intake had fallen at 6 months. The proportion of women in the BMI <18.5 kg/m² subgroup was unchanged between baseline and 6 months.

Data have shown that initiation of ART is critical for optimal treatment of TB-HIV coinfection²⁷ and may influence weight gain. Our findings indicate the need for controlled studies of nutritional supplements to further improve treatment outcomes of patients with TB-HIV coinfection. Several studies have suggested potential benefit from adjunctive protein energy supplementation during anti-tuberculosis treatment.^{28–31} However, inadequate sample sizes, insufficient levels of supplementation and modest clinical effects have led to a consensus that the benefits of macronutrient supplementation in TB have yet to be proven.³²

Our study has several limitations. The sample size is modest, limiting our ability to test multiple associations or to provide confidence intervals for the prevalence of malnutrition, and our study was restricted to women. The energy and protein targets used were applied to all women, regardless of age or activity level, although these are specified for a moderately active adult woman. Not all patients in this cohort were started on ART during the first 8 weeks of anti-tuberculosis treatment, as is currently recommended. Furthermore, loss to follow-up and the likelihood of death among some lost patients prevented us from performing an analysis of risk factors for mortality. Data on change in CD4 count and weight at 4–6 months must also be interpreted with caution, as one third of the patients were lost to follow-up. The nutritional counseling received by subjects in this study may have been more extensive than typically offered in public clinics; our weight gain findings on treatment may thus represent a best case scenario in the absence of a program that provides direct supplements. The substantial number of patients lost to follow-up during treatment may have had poorer outcomes.

In summary, we have shown that undernutrition is common among women with TB-HIV in Tanzania and that it persists throughout anti-tuberculosis treatment. Reported energy intake is typically 33% below estimated needs and protein intake 45% below estimated needs. Further controlled trials of nutritional supplementation in TB-HIV coinfection are indicated. Our estimates of specific deficiencies in energy and protein intake suggest that investigational supplements should provide approximately 1000 kcal and 40 g protein/day.

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Contexte : Dispensaires de traitement de la tuberculose (TB) à Dar es Salam, Tanzanie.

Objectifs : Quantifier les données anthropométriques ainsi que les besoins énergétiques et protéiques chez les femmes séropositives pour le virus de l'immunodéficience humaine (VIH) atteintes de TB.

Schéma : On a évalué les femmes séropositives pour le VIH atteintes d'une TB nouvellement diagnostiquée au sujet de leurs caractéristiques anthropométriques et de leur consommation alimentaire. On a déterminé la consommation énergétique et protéique au moyen des tableaux de composition alimentaire de Tanzanie et on les a comparées aux recommandations standard. On a réévalué les patients après 4 à 6 mois de traitement de la TB.

Résultats : Au début, parmi les 43 femmes, les décomptes médians de CD4 ont été de 209 cellules/ μ l (extrêmes 8–721) et un CD4 < 200 cellules/ μ l a été observé chez 19 d'entre elles (44%). Vingt (47%) étaient sous traitement antirétroviral. L'indice de masse corporelle est

< 18,5 kg/m² chez 25 femmes (58%). Le score médian d'insécurité alimentaire est de 6. La quantité médiane de kcal/jour est de 1693 (extrêmes 1290–2633) par comparaison avec les besoins estimés à 2.658 ; le déficit moyen est de 875 kcal (–65–1278). Le nombre médian de g de protéines par jour est de 42 (extrêmes 27–67) par comparaison à un besoin estimé de 77 ; le déficit médian de protéine est de 35 g (extrêmes 10–50). Le gain de poids médian parmi 29 patientes a été de 6 kg après 4 à 6 mois.

Conclusion : Les femmes séropositives atteintes de TB subissent un déficit substantiel au cours de 24 heures en matière de consommation énergétique et protéique, signalent une insécurité alimentaire significative, et leur poids n'augmente que de façon minimale sous traitement antituberculeux. Un renforcement de l'éducation diététique associé à des suppléments de 1000 Kcal avec 40 g de protéines pourrait être indispensable.

Marco de referencia: Los consultorios de atención de la tuberculosis (TB) de Dar es Salaam, en Tanzania.

Objetivo: Cuantificar las características antropométricas y el contenido energético y de proteínas de la ingesta alimentaria de las mujeres con un examen serológico positivo frente al virus de la inmunodeficiencia humana (VIH) y diagnóstico de TB.

Métodos: Se evaluaron las características antropométricas y la ingesta alimentaria cotidiana de mujeres con serología positiva frente al VIH y diagnóstico reciente de TB. La ingesta de energía y proteínas se

determinó mediante las tablas de composición de los alimentos de Tanzania y se comparó con las normas recomendadas. Se practicó una nueva evaluación de las pacientes entre 4 y 6 meses después del tratamiento antituberculoso.

Resultados: En las 43 mujeres que participaron en el estudio, el recuento inicial de células CD4 fue 209 células/ μ l (entre 8 y 721) y 19 pacientes presentaron un recuento <200 células/ μ l (44%); 20 mujeres recibían el tratamiento antirretrovírico (47%). El índice de masa corporal fue <18,5 kg/m² en 25 pacientes (58%); la mediana del índice

de inseguridad alimentaria fue 6; la mediana de la ingestión energética diaria fue 1693 kcal (entre 1290 y 2633), frente a unas necesidades estimadas de 2658; la mediana del déficit energético fue de 875 kcal (de -65 a 1278); la mediana de la ingesta proteica fue 42 g/día (de 27 a 67), en comparación con un requerimiento calculado en 77 g/día; la mediana del déficit de proteínas fue 35 g/día (de 10 a 50). La mediana de la ganancia de peso en 29 pacientes de 4 a 6 meses después del tratamiento antituberculoso fue de 6 kg.

Conclusión: Las mujeres con serología positiva frente al VIH y diagnóstico de TB presentan déficits apreciables en el contenido energético y proteico de su ingesta en 24 horas, informan una considerable inseguridad alimentaria y logran una ganancia mínima de peso después del tratamiento antituberculoso. Puede ser necesario reforzar la educación alimentaria y al mismo tiempo ofrecer un complemento a la ingesta, que aporte 1000 kcal y 40 g de proteína diarios.