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ORIGINAL ARTICLE

Anthropometric indices, plasma micronutrient levels and phagocytic factors associated with early sputum culture conversion among patients receiving treatment for multidrug-resistant tuberculosis

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ABSTRACT

Background: Sputum *Mycobacterium tuberculosis* (Mtb) culture remains an important indicator of treatment response and efficacy in multidrug-resistant tuberculosis (MDR-TB), however, sputum culture procedure is slow and often inaccessible in resource-limited settings. Consequently, there is a need for accessible surrogate indicators of sputum culture conversion to support treatment monitoring and clinical decision-making. **Aim:** This observational study assessed time to sputum culture conversion and explored anthropometric, nutritional, and phagocytic factors associated with early conversion among patients receiving MDR-TB treatment. **Methods:** Fifty consenting MDR-TB patients (mean age 34.8 ± 11.9 years) were recruited. Sputum culture was performed monthly, and culture conversion was defined as two consecutive negative cultures obtained at least one month apart. Anthropometric indices, plasma micronutrients, cytokines, and phagocytic and oxidative burst parameters were assessed at baseline and after two months of treatment and compared between patients who achieved sputum culture conversion by two months and those with delayed conversion. **Results:** Of the 50 participants enrolled, four (8%) died and one (2%) was transferred before two months of treatment, leaving 45 participants for conversion analyses. Culture conversion occurred in 30/45 (67%) participants by two months, 41/45 (91%) by three months, and 45/45 (100%) by four months. At two months of treatment, body weight, body mass index, percentage body fat, fat mass index, fat-free mass index, and plasma vitamin D concentrations were significantly higher among patients who achieved culture conversion by two months, whereas plasma vitamin E concentrations were significantly lower. No significant differences were observed in most circulating micronutrients, cytokines, phagocytic indices, or oxidative burst parameters between the groups. **Conclusion:** Early sputum culture conversion during MDR-TB treatment was associated with anthropometric recovery, whereas circulating micronutrient concentrations and phagocytic and oxidative burst parameters showed limited association with microbiological response. Anthropometric indicators may therefore have potential as accessible adjunctive markers of treatment response and warrant further evaluation in larger MDR-TB cohorts.

Keywords: Multidrug resistant tuberculosis, Nutritional recovery, Sputum culture conversion.

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1. INTRODUCTION

Tuberculosis (TB) caused by *Mycobacterium tuberculosis* (*Mtb*) remains a global public health challenge and currently ranks as the leading cause of death from a single infectious agent.[1] Multidrug-resistant tuberculosis (MDR-TB), which is caused by strains of *Mtb* that are resistant to both isoniazid (H, INH) and rifampicin (R, RMP) continues to represent a major public health and health-security challenge since it requires complex treatment, careful monitoring, sustained patient support, and is associated with higher mortality rates.[2, 3] Although implementation of shorter all-oral regimens for MDR/RR-TB has expanded rapidly since WHO endorsement,[4] global uptake and implementation remains incomplete across national TB programmes. [1] Furthermore, treatment monitoring continues to depend largely on sputum culture conversion, the most widely accepted interim indicator of treatment response. Understanding the temporal association between sputum culture conversion and observed improvement of the patients, could provide a comprehensive assessment of treatment response and inform patients monitoring strategies.

Sputum culture plays an important role in MDR-TB treatment monitoring with sputum culture conversion currently utilized as a clinical tool for assessment of treatment efficacy. Previous studies suggest that sputum culture conversion is associated with anti-TB treatment outcome in MDR-TB and may help identify patients who need intensified clinical review.[5-7] Nevertheless, culture is inherently slow, often requiring several weeks of incubation before results become available. While positive cultures may be detected within 2-8 weeks, confirmation of culture negativity may require up to 6-8 weeks of incubation, resulting in delays in establishing culture conversion and assessment of treatment response.[8] Additionally, culture is technically demanding and less accessible in many high-burden settings. Complementary clinical or laboratory indicators that can be measured more easily may therefore be useful for risk stratification and supportive care and could serve as surrogate indicators of treatment response while awaiting microbiological confirmation by culture. They may further provide insight into the factors underlying persistent culture positivity or delayed culture conversion, thereby supporting individualized patient management.

Nutrition is biologically and clinically relevant to TB incidence and treatment response.[9, 10] Undernutrition impairs cell-mediated immunity,[11] reduces TB treatment tolerance and has been associated with delayed culture conversion, mortality and unsuccessful outcomes among people with MDR-TB.[12-14] Anthropometric indicators such as weight and body mass index are commonly used to assess nutritional recovery during TB treatment. These indices primarily reflect macronutrient status and energy balance but may not adequately capture the status of essential micronutrients that play key roles in cell-mediated immunity. Consequently, there is a need to evaluate these indices concurrently to better understand their association with sputum conversion as indicators of treatment response during MDR-TB treatment.

In this study, we determined time to sputum culture conversion among adults receiving MDR-TB treatment in Ibadan, Nigeria, and compared selected anthropometric, plasma micronutrient and phagocytic markers between participants who achieved culture conversion by two months and those with delayed conversion.

2. PARTICIPANTS AND METHODS

Study design and setting

This was an observational study of adults receiving treatment for MDR-TB at the DOTS/MDR-TB treatment centre of the University College Hospital, Ibadan, Nigeria. Participants were admitted for pre-treatment evaluation and initiation of therapy. Study participants remained at the DOTS treatment centre throughout the intensive phase of treatment, where they received directly observed therapy and clinical monitoring. Study assessments were performed at baseline (before treatment initiation) and after 2 months of treatment.

Baseline and 2-month assessments were selected to capture early changes in microbiological and nutritional status during treatment. The first two months of anti-tuberculosis therapy represent a critical period during which substantial reductions in mycobacterial burden and early recovery are expected. Furthermore, sputum culture status after 2 months of treatment has been previously used as an interim indicator of treatment response,[5, 15] making this timepoint particularly relevant for evaluating the relationship between sputum culture conversion and changes in anthropometric, nutritional and phagocytic indices.

Participants

Fifty (50) consenting adults with MDR-TB were recruited for this study. MDR-TB was defined as tuberculosis caused by Mtb resistant to at least rifampicin and isoniazid. The cohort had a mean age of 34.8 years (SD 11.9); 32 participants (64.0%) were male and 18 (36.0%) were female. Four participants died before two months of treatment and one left the treatment facility, leaving 45 participants for analyses of sputum culture conversion.

Ethics statement

The study protocol was reviewed and approved by the University of Ibadan/University College Hospital Ibadan Ethics Committee (UI/EC/13/0340). Written informed consent was obtained from all study participants prior to enrolment. Participant confidentiality was maintained throughout the study with unique study identification numbers, and all data were anonymized prior to analysis.

Treatment and sputum culture monitoring

Participants received the standardized MDR-TB regimen in use at the study site during the period of recruitment (March 2023 to April 2025), which included kanamycin or amikacin, levofloxacin, prothionamide, cycloserine, pyrazinamide and pyridoxine. While participants were receiving MDR-TB treatment, they were supported by non-governmental organization which provided nutritional support 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 centre where this study was conducted. The supplement recommendation by this NGO was based on our previous observations in TB patients from this facility [17].

Sputum samples were collected monthly for culture. Culture conversion was defined as two consecutive negative cultures for M. tuberculosis obtained at least one month apart. Time to culture conversion was calculated from the date of MDR-TB treatment initiation to the date of the first negative culture in the pair.

Anthropometric measurements

Body weight (BW), mid-upper arm circumference (MUAC), waist circumference (WC), hip circumference (WC) and percentage body fat were measured using appropriate methods. Body mass index (BMI), fat mass index (FMI) and fat-free mass index (FFMI) were calculated using standard formulae. Body fat was assessed by bioelectrical impedance analysis using an IntelliScale BS0114 scale.

Blood sample collection

Five (5) milliliters of blood was drawn from the antecubital vein into lithium heparin tubes at baseline and at 2 months of anti-TB therapy. The sample was divided into two aliquots; one aliquot was used for cellular assays, while the other was centrifuged to obtain plasma for subsequent analyses.

Cellular assays

Percentage leukocyte migration (%LM) was determined using a leukocyte migration inhibition assay, and bacterially stimulated nitroblue tetrazolium dye reduction (%NBT) was measured as an indicator of phagocytic oxidative burst. These methods have been previously described.[16]

Plasma micronutrients, cytokines and oxidative burst components analyses

Plasma concentrations of vitamins A, C, D and E were measured by high-performance liquid chromatography while plasma iron (Fe), zinc (Zn) and copper (Cu) concentrations were measured by atomic absorption spectrophotometry as previously described.[17]

Plasma concentrations of interleukin (IL)-6 and IL-8 were determined by ELISA. The plasma concentrations of hydrogen peroxide and nitric oxide, as well as the activities of the enzymes superoxide dismutase (SOD), catalase (CAT) and myeloperoxidase (MPO) were measured using standard spectrophotometric methods as previously described.[16]

Statistical Analysis

Analyses were performed using SPSS version 25.0. For comparative analyses, study participants were stratified according to sputum culture conversion status after two months of treatment. Patients who achieved sputum culture conversion by two months were grouped as “Converted”, whereas those achieved sputum culture conversion by three and four months of treatment were grouped as “Non-converted”. Continuous variables were assessed for normality using the Kolmogorov-Smirnov test. Normally distributed variables are presented as mean and standard deviation and group comparison was performed using Student's t-test. Non-normally distributed variables are presented as median and interquartile range, and the groups were compared using the Mann-Whitney U test. Statistical significance was set at $p<0.05$.

3. RESULTS

Participant flow and time to sputum culture conversion

Of the 50 recruited MDR-TB patients, four (8.0%) died before two months of treatment and one (2.0%) left the treatment facility. None of the remaining participants attained sputum culture conversion at one month of treatment. At two months of treatment, 30 of 45 participants (66.7%) had achieved sputum culture conversion. By three months, 41 of 45 participants (91.1%) had converted, and all 45 participants included in the culture conversion analysis had converted by four months. (Figure 1)

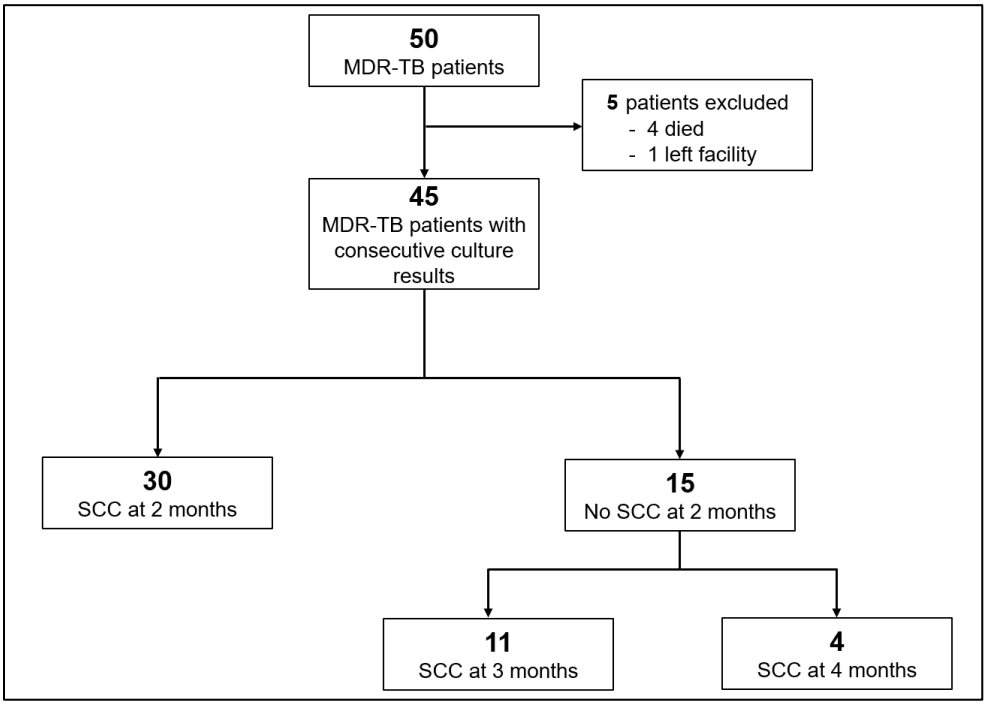

Figure 1. Flow diagram of study participants and timing of sputum culture conversion (SCC) during MDR-T treatment.

Anthropometric characteristics of study participants based on sputum culture-conversion status at 2 months of treatment

At baseline, there were no statistically significant differences in anthropometric indices between the converted and non-converted groups. Measurements of MUAC, weight, BMI, PBF, FMI, FFMI, WC, and HC were comparable between the two groups ($p > 0.05$). (Table 1).

Table 1. Baseline and 2-months anthropometric measurements of MDR-TB patients by sputum culture-conversion status after two months of treatment.

Variables	Baseline			After 2 months		
	Converted (n=30)	Non-converted (n=15)	*P*-value	Converted (n=30)	Non-converted (n=15)	*P*-value
MUAC *(cm)*	20.61±2.95	22.37±3.07	0.090	22.61±2.57	23.19±2.82	0.490
Weight *(kg)*	47.07±10.06	50.25±7.20	0.302	51.70±9.31	41.77±4.92	<0.001*
BMI *(kg/m²)*	17.11±3.18	17.52±2.81	0.694	18.84±2.91	14.58±2.08	<0.001*
PBF *(%)*	15.34±1.66	11.37±1.31	0.089	19.96±1.59	8.43±1.16	<0.001*
FMI *(kg/m²)*	2.82±0.43	2.09±0.30	0.204	3.94±1.28	1.29±0.84	<0.001*
FFMI *(kg/m²)*	14.29±1.78	15.43±1.89	0.074	14.90±1.50	13.30±1.56	0.002*
WC *(cm)*	70.14±7.52	72.43±5.25	0.313	77.14±8.25	74.91±6.70	0.362
HC *(cm)*	81.91±6.82	84.82±4.56	0.168	86.68±7.56	87.44±6.33	0.736

Values are mean±SD. *Significant at $p<0.05$. MUAC, mid-upper arm circumference; BMI, body mass index; PBF, percentage body fat; FMI, fat mass index; FFMI, fat-free mass index; WC, waist circumference; HC, hip circumference.

At two months of treatment, the converted group had significantly higher weight (51.70 ± 9.31 kg vs 41.77 ± 4.92 kg, p < 0.001), BMI (18.84 ± 2.91 kg/m² vs 14.58 ± 2.08 kg/m², p < 0.001), PBF (19.96 ± 1.59% vs 8.43 ± 1.16%, p < 0.001), FMI (3.94 ± 1.28 kg/m² vs 1.29 ± 0.84 kg/m², p < 0.001), and FFMI (14.90 ± 1.50 kg/m² vs 13.30 ± 1.56 kg/m², p = 0.002) than the non-converted group. No significant differences were observed for MUAC, WC, or HC (p>0.05). (Table 1)

Plasma micronutrient levels of study participants based on sputum culture-conversion status at 2 months of treatment

At baseline, plasma iron concentrations were significantly lower among participants in the converted group compared with non-converted (84.39 ± 7.32 µg/dL vs 95.47 ± 9.45 µg/dL, p = 0.049). Plasma copper concentrations were significantly higher among the converted group than the non-converted (105.48 ± 2.39 µg/dL vs 94.33 ± 9.54 µg/dL, p = 0.039). No significant baseline differences were observed for zinc, vitamins A, C, D, or E (p>0.05). (Table 2)

At two months of treatment, plasma vitamin D concentrations were significantly higher among the converted than non-converted group (72.25 ± 29.12 pg/mL vs 54.35 ± 14.60 pg/mL, p = 0.027). Also, plasma vitamin E concentrations were substantially lower among the converted than non-converted group (0.36 ± 0.13 mg/dL vs 1.06 ± 0.19 mg/dL, p < 0.001). No significant differences were observed for iron, zinc, copper, vitamin A, or vitamin C (p>0.05). (Table 2).

Table 2. Baseline and 2-months plasma levels of micronutrients in MDR-TB patients by sputum culture-conversion status after two months of treatment

Variables	Baseline			After 2 months		
	Converted (n=30)	Non-converted (n=15)	*P*-value	Converted (n=30)	Non-converted (n=15)	*P*-value
Fe *(µg/dl)*	84.39±7.32	95.47±9.45	0.049*	92.78±12.87	87.55±7.82	0.144
Zn *(µg/dl)*	65.19±4.32	61.56±4.06	0.144	69.68±4.49	67.79±4.54	0.188
Cu *(µg/dl)*	105.48±2.39	94.33±9.54	0.039*	101.22±4.08	99.98±5.27	0.389
Vit A *(µg/dl)*	49.28±14.97	50.60±11.72	0.855	57.77±11.94	53.51±8.52	0.217
Vit C *(mg/dl)*	4.18±0.73	4.97±1.16	0.224	1.96±0.49	2.21±0.48	0.109
Vit D *(pg/ml)*	49.16±8.64	58.50±13.74	0.224	72.25±29.12	54.35±14.60	0.027*
Vit E *(mg/dl)*	1.99±0.39	2.28±0.67	0.434	0.36±0.13	1.06±0.19	<0.001*

Values are mean±SD. *Significant at p<0.05.

Phagocytic indices, plasma cytokine levels and oxidative burst components of study participants based on sputum culture-conversion status at 2 months of treatment

There were no statistically significant differences in %LM, %NBT, IL-6, IL-8, SOD activity, CAT activity, MPO activity, H_2O_2 concentration, or NO concentration at baseline or at two months of treatment between the converted and non-converted group (p > 0.05). (Table 3).

Table 3. Baseline and 2-months indices and mediators of phagocytosis of MDR-TB patients by sputum culture-conversion status after two months of treatment.

Variables	Baseline			After 2 months		
	Converted (n=30)	Non-converted (n=15)	*P*-value	Converted (n=30)	Non-converted (n=15)	*P*-value
%LM	[a]80.44±10.62	[a] 82.61±9.38	0.506	[a] 81.60±9.27	[a] 85.14±4.85	0.164
%NBT	[a]87.15±12.69	[a] 84.73±10.66	0.529	[a] 90.64±7.13	[a] 86.55±9.49	0.113
IL-6 *(pg/ml)*	0.01 (0.006-0.02)	0.23 (0.09-0.32)	0.060	0.01 (0.003-0.03)	0.04 (0.02-0.05)	0.062
IL-8 *(pg/ml)*	223.6 (161.7-764.3)	1011.0 (729.7-1890.5)	0.170	470.6 (385.1-871.8)	795.8 (489.0-1432.4)	0.171
SOD *(U/ml)*	0.11 (0.08-0.19)	0.17 (0.12-0.31)	0.435	0.15 (0.11-0.21)	0.17 (0.12-0.25)	0.252
CAT *(U/mg protein)*	0.02 (0.01-0.06)	0.02 (0.02-0.03)	0.112	0.04 (0.02-0.07)	0.02 (0.02-0.04)	0.157
MPO *(U/ml)*	7.58 (6.18-8.46)	7.03 (6.45-7.88)	0.614	8.00 (7.35-8.57)	8.05 (7.51-8.95)	0.721
H_2O_2 *(µmol/l)*	308.33 (288.1-311.6)	315.8 (273.4-327.8)	0.975	315.62 (293.9-324.9)	319.1 (305.6-357.2)	0.185
NO *(µmol/l)*	7.53 (6.70-10.33)	9.80 (6.12-11.45)	0.249	11.54 (7.64-17.13)	11.18 (9.42-15.71)	0.572

Values are median (interquartile range) unless otherwise stated. [a] Values are mean±SD. LM, leukocyte migration; NBT, nitroblue tetrazolium reduction; IL, interleukin; SOD, superoxide dismutase, CAT, catalase; MPO, myeloperoxidase; H_2O_2, hydrogen peroxide; NO, nitric oxide.

4. DISCUSSION

Sputum culture conversion is considered an important interim indicator of the efficacy of anti-tuberculosis treatment, and has been shown to be predictive of treatment outcome in drug-resistant TB.[5] The present study observed a sputum culture conversion rate of 67% among MDR-TB patients after 2 months of anti-TB treatment. This increased to 91% at 3 months and reached 100.0% at 4 months of anti-TB treatment. These findings are consistent with those of Ige and Oladokun, who reported that 90% of MDR-TB patients achieved sputum culture conversion by the end of 3 months of treatment. [15] However, the 2-month culture conversion rate observed in the present study was higher than 49% reported among MDR-TB by Balay and colleagues.[18] The variation in time to sputum culture conversion observed among patients suggests heterogeneity in treatment response and may reflect differences in Mtb strain, disease severity and host factors. Previous studies have identified several determinants of sputum culture conversion and treatment outcomes in MDR-TB, with evidence suggesting that both host-related and disease-related factors contribute to variability in treatment response.[6, 19]

The present study recorded a mortality rate of 8% during the first 6 months of MDR-TB treatment, with all deaths occurring within the first 8 weeks of therapy. Although lower than mortality rates reported in other MDR-TB cohorts,[20] this finding could reflect variations in study population. Notably, no HIV-infected patients were enrolled during the study period, whereas previous studies have consistently identified HIV co-infection as an important predictor of mortality and poor treatment outcomes among patients with MDR-TB, likely owing to impaired immune function and increased disease severity.[20, 21] The concentration of deaths during the early treatment phase further underscores the importance of identifying patients at increased risk of poor outcomes and highlights the continued role of host immunity in determining treatment response and prognosis.

The well-established relationship between malnutrition and tuberculosis continues to highlight the potential value of nutritional assessment in disease prognosis and treatment monitoring, although it remains underutilized in routine clinical practice. Anthropometric markers of nutritional status such as body weight, WC, HC, BMI, PBF, FMI and FFMI are readily accessible measures that may serve as indicators of treatment response in patients with MDR-TB. In this study we evaluated the association between anthropometric indices, micronutrient status, phagocytic activity and sputum culture conversion during the early phase of MDR-TB treatment. Although baseline anthropometric characteristics were largely comparable between MDR-TB patients who achieved sputum culture conversion at two months of treatment and those who converted later (at three and four months), substantial differences emerged between these groups of patients at two months of treatment. The choice of micronutrient supplementation with vitamins C, B6, B complex, folic acid was based on our previous observations in TB patients from the same hospital setting [17]. The differences in the micronutrient levels of our present TB patients as treatment progressed was likely due to physiological response to anti-TB therapy because first-line anti-TB medications (such as Rifampin, Isoniazid, and Pyrazinamide) frequently cause gastrointestinal disturbances, malabsorption, and altered lipid metabolism.[1] In addition, daily adherence to the use of supplementation was monitored by nurses since the patients were on hospital admission. The supplements were counted and recorded daily to ensure strict compliance. Finally, participants with gastrointestinal related complaints were excluded and not recruited from the beginning of the study.

The absence of significant baseline differences in anthropometric measures suggests that nutritional status at treatment initiation may be less informative than changes in nutritional status during treatment. Although baseline anthropometric characteristics were comparable between groups, patients who achieved sputum culture conversion by two months exhibited significantly higher body weight, BMI, percentage body fat, fat mass index, and fat-free mass index than those with delayed culture conversion. These findings suggest that improvements in anthropometric status may occur alongside favourable microbiological responses during MDR-TB treatment and may reflect recovery from the catabolic effects of active disease. The observed associations are consistent with previous studies that identified weight gain as a useful predictor of treatment response and favourable outcomes in patients with tuberculosis. [22, 23] Collectively, these findings support further investigation of anthropometric indicators as potential adjunctive markers of treatment response in MDR-TB, including evaluation of their predictive performance and clinical utility for incorporation into routine treatment monitoring protocols.

The exhibition of significantly higher body weight, BMI, percentage body fat, fat mass index, and fat-free mass index in patients that achieved sputum culture conversion from 2 months compared with those having delayed culture conversion might be due to hospitalisation of the patients throughout the study period. A protective, highly standardized hospital environment was found to promote accelerated anthropometric recovery of tuberculosis patients by minimizing chronic energy drain, mitigating infection-driven catabolism, and ensuring optimal nutrient absorption. This supportive setting optimizes metabolic function, enabling a faster restoration of body weight, lean muscle mass, and BMI. Active TB increases the body's resting energy expenditure, leading to wasting. But during hospitalization, physical exertion is regulated and total daily caloric expenditure is reduced. Also, a protected settings limit exposure to indoor air pollution, tobacco smoke, and secondary infections, which historically exacerbate systemic inflammation and catabolism. [28] Hospitalised patients are provided with strictly medication adherence with precise caloric and protein intake,

structured nutritional support, personalized meal timing, and other medical management to circumvent barriers to eating which is foundational for reversing TB-induced weight loss and rebuilding lean muscle mass. [29]. During hospitalization, patients' treatment is not delayed and the emergence of resistant strains is prevented. This is to achieve successful pathogen clearance that halts the progression of TB-associated wasting. [28, 29]

Interestingly, despite substantial differences in anthropometric recovery, no significant differences were observed in iron, zinc, copper, vitamins A and C, leukocyte migration, nitroblue tetrazolium reduction, IL-6, IL-8, myeloperoxidase, nitric oxide, hydrogen peroxide, superoxide dismutase, or catalase between patients who achieved sputum culture conversion at two months and those with delayed culture conversion. These findings suggest that the association between nutritional recovery and sputum culture conversion may not be mediated through marked differences in circulating micronutrient levels and may not be accompanied by significant changes in the phagocytic or oxidative burst parameters measured in this study. One possible explanation is that all participants received standardized meals and routine micronutrient supplementation throughout the study period, which may have minimized inter-individual variability in micronutrient status and reduced the likelihood of detecting differences between groups. Although the present study was not designed to evaluate the effectiveness of nutritional supplementation, these findings are consistent with the growing recognition that nutritional support constitutes an important component of tuberculosis care and may contribute to improved nutritional recovery, treatment adherence, and clinical outcomes among patients receiving anti-tuberculosis treatment.[24]

This study observed higher mean plasma vitamin D level while mean plasma vitamin E level was lower in MDR-TB patients that achieved sputum culture conversion at two months of treatment and those who converted later. Vitamin D has recognized immunomodulatory effects in tuberculosis, including enhancement of macrophage antimicrobial activity, induction of the antimicrobial peptide cathelicidin (LL-37), promotion of autophagy, and improved intracellular killing of Mtb.[25, 26] Although causal inferences cannot be drawn from the present study, the findings suggest that improved vitamin D status may accompany or contribute to favourable microbiological responses during MDR-TB treatment. As a lipid-soluble antioxidant, vitamin E may be utilized during the resolution of inflammation and tissue remodeling accompanying recovery from active tuberculosis.[27] Lower vitamin E concentration observed in this present study is consistent with our previous report that demonstrated decreased vitamin E concentration among MDR-TB patients during anti-TB treatment. [17] This finding may also reflect alterations in vitamin E distribution associated with changes in body composition, since patients who achieved sputum culture conversion at two months of treatment also demonstrated greater gains in anthropometric indices.

The dramatic and abrupt drop in vitamin E levels at two months in patients who achieved culture conversion might be due to the fact that vitamin E is a fat-soluble antioxidant which could be depleted in the bloodstream during the initial intensive phase of therapy.[17] While the patient's sputum culture was converting to negative, the body might still be repairing lung tissue and controlling systemic inflammation. To neutralize the high levels of free radicals generated by inflammatory response, the body rapidly utilized circulating antioxidants such as vitamin E. This systemic demand for vitamin E to protect against ongoing inflammation must have outpaces both liver reserves and dietary replenishment at this 2 months post-treatment period.

The significant increase in plasma vitamin D observed in tuberculosis patients who convert early might be explained thus: As patients respond to treatment and recover from the systemic effects of TB, overall nutritional intake and metabolic functions improve, physical activities and exposure to sunlight naturally raising plasma vitamin D concentrations. Also, tuberculosis causes profound systemic inflammation, which can temporarily impair the transport and storage proteins of vitamin D. However, successful early treatment reduces the inflammatory burden, making plasma level of vitamin D recovers. [30] Finally, during active TB, immune cells (macrophages and monocytes) utilize vitamin D to generate antimicrobial peptides like cathelicidin, which kill the bacteria. This localized immune response can lower systemic plasma vitamin D levels, but as the bacterial load drops during successful treatment and sputum conversion, this localized demand for vitamin D decreases, allowing plasma level of vitamin D to increase. [30, 31]

Lower baseline plasma iron in sputum-converted TB patients compared to non-converted patients observed in this study reflected a healthier, more robust early immune response. The body actively sequesters iron into macrophages (via hepcidin and ferritin) to starve the bacteria, which suppresses bacterial replication and leads to faster, more effective sputum conversion.[32] *Mycobacterium tuberculosis* bacteria relies heavily on host iron to grow and replicate. During active TB, the host immune system triggers an innate response to withhold iron from the bacteria. Patients who successfully and quickly clear the bacteria (sputum-convert) mount a stronger initial inflammatory response, driving plasma iron into storage proteins inside cells where the bacteria cannot access it. Also during active TB-induced systemic inflammation, liver produces high levels of hepcidin that blocks iron release and traps iron inside macrophages and the liver. Baseline iron deficiency impairs T-cell immunity and effector cell activity that paralyses the adaptive immune system, reduces *M. tuberculosis* clearance leading to delayed sputum conversion. [33]

Our finding of higher baseline plasma copper levels in patients who achieved early sputum conversion than in non-converted TB patients is in contrast to a report by [34] During active TB, the body triggers an acute-phase inflammatory response which prompts liver to release caeruloplasmin and causing a rise in plasma copper levels.[35]

A major strength of the present study is the comprehensive assessment of anthropometric, micronutrient, phagocytic, and oxidative burst parameters in relation to sputum culture conversion, an important microbiological indicator of treatment response in MDR-TB. In addition, all participants remained admitted at the treatment facility throughout the study period and received standardized clinical care, nutritional support, and treatment monitoring, thereby minimizing variability in patient management.

In conclusion, sputum culture conversion during early phase of MDR-TB treatment was associated with anthropometric recovery but showed limited association with circulating micronutrient levels and phagocytic and oxidative burst parameters. These findings support the importance of nutritional assessment and suggest that anthropometric recovery may be a useful adjunct indication of treatment response.

Limitation of the study

The major limitation of the study is the relatively small sample size of patients recruited. This was due to strict selection criteria and appreciable number of un-consenting patients due to non-readiness for bleeding. Future study should include many centers to increase patient population. Furthermore, all participants received standardized meals and micronutrient supplementation, which may have reduced inter-individual variability in nutritional status and attenuated differences between groups. Finally, no HIV-infected patients were enrolled during the study period, which may limit the generalizability of the findings to settings with a high burden of HIV/MDR-TB co-infection.

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