Original Research Article

EQUITY EFFECTS OF MICRONUTRIENT SUPPLEMENTATION ON EARLY TREATMENT RESPONSE AMONG TUBERCULOSIS PATIENTS IN A PROGRAMMATIC SETTING

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ABSTRACT

Background: Undernutrition and social vulnerability significantly influence tuberculosis (TB) treatment outcomes, often leading to delayed sputum smear conversion among disadvantaged populations. While micronutrient supplementation has shown overall benefit, evidence on its equity-enhancing effects—particularly whether it reduces outcome disparities across socio-demographic groups—remains limited in routine programmatic settings. The objective is to assess whether adjunct micronutrient supplementation narrows socio-demographic inequities in early treatment response, measured by two-month sputum smear conversion, among pulmonary TB patients treated under the National Tuberculosis Elimination Programme.

Materials and Methods: A programmatic cohort study was conducted among 200 newly diagnosed smear-positive pulmonary TB patients receiving micronutrient supplementation during the intensive phase of treatment in a high-burden district of Karnataka, India. Sputum smear status was assessed at baseline and after two months. Equity-relevant variables included age, gender, residence (urban/rural), employment status, and baseline bacillary load. Stratified analyses compared conversion rates across vulnerable and non-vulnerable subgroups. Interaction terms were used to examine whether supplementation modified outcome disparities. Absolute risk differences and relative measures were calculated to assess equity effects.

Results: Overall two-month sputum smear conversion was high among supplemented patients. Conversion rates were consistently lower among older patients (≥45 years), rural residents, unemployed individuals, and those with high baseline bacillary load (3+). However, the absolute differences in conversion between vulnerable and non-vulnerable groups were smaller than those reported in comparable non-supplemented programmatic cohorts. The greatest equity gains were observed among unemployed patients and those with high bacillary load, indicating a disproportionate benefit of supplementation in these groups. Interaction analyses suggested attenuation of socio-demographic gradients in early treatment response.

Conclusion: Micronutrient supplementation delivered within routine TB services demonstrated equity-enhancing effects, partially mitigating socio-demographic disparities in early bacteriological response. Beyond improving average outcomes, nutritional support may serve as a pragmatic strategy to

advance equity-oriented tuberculosis care. Integrating targeted nutritional interventions within national TB programs could accelerate progress toward equitable treatment outcomes in high-burden settings.

Keywords: Tuberculosis, Micronutrient supplementation, Equity, Sputum smear conversion, Social determinants, Programmatic research.

INTRODUCTION

Tuberculosis (TB) remains one of the leading infectious causes of morbidity and mortality worldwide, with India contributing the largest proportion of the global disease burden despite sustained programmatic expansion of diagnostics and treatment services.[1] Although standardized anti-tubercular therapy is highly effective for drug-sensitive disease, treatment outcomes are not determined by pharmacotherapy alone. A growing body of evidence highlights the central role of social determinants of health, including age, gender, nutritional status, residence, and socioeconomic position, in shaping TB treatment trajectories.[2,3] Early sputum smear conversion at the end of the intensive phase is a critical clinical and public health milestone. It signifies bacteriological response, reduced infectiousness, and a lower risk of adverse treatment outcomes.[4] However, conversion rates are not uniform across populations. Older adults, rural residents, unemployed individuals, and patients with high baseline bacillary load consistently experience delayed conversion, reflecting cumulative biological vulnerability and social disadvantage.[5-7] These inequities perpetuate transmission, increase catastrophic costs, and undermine TB elimination efforts.

Undernutrition is a key driver of these disparities. TB and malnutrition form a bidirectional relationship: infection leads to catabolic wasting and micronutrient depletion, while poor nutritional status impairs immune function, delays mycobacterial clearance, and increases mortality risk.[8,9] Recognizing this, the World Health Organization recommends nutritional assessment and support as an integral component of TB care.[10] In India, nutritional support has been operationalized primarily through financial assistance mechanisms under national TB control strategies.[11] However, cash transfers alone may not adequately address micronutrient deficiencies, particularly among socially vulnerable households where funds may be diverted toward competing needs.[12]

Micronutrient supplementation offers a biologically plausible and operationally feasible adjunct to TB treatment. Prior studies have demonstrated improvements in weight gain, immune markers, and, in some settings, bacteriological outcomes among supplemented patients.[13–15] Nevertheless, most evaluations focus on average treatment effects, with limited attention to whether nutritional interventions reduce socio-demographic disparities in treatment response. From an equity-oriented public health perspective, interventions that disproportionately benefit disadvantaged groups are essential to achieving meaningful progress toward TB elimination.[16]

This study addresses this gap by examining the equity effects of micronutrient supplementation on early treatment response among pulmonary TB patients in a routine programmatic setting. Specifically, it evaluates whether socio-demographic and clinical disparities in two-month sputum smear conversion are attenuated among patients receiving micronutrient supplementation during the intensive phase of treatment.

MATERIALS AND METHODS

Study design and setting: This was a programmatic cohort study conducted between October 2019 and August 2020 in a high tuberculosis (TB) burden district of Karnataka, southern India. The study was embedded within routine TB care services delivered under the National Tuberculosis Elimination Programme (NTEP). TB diagnosis, treatment initiation, follow-up, and sputum smear examination were carried out through designated microscopy centres and tuberculosis units functioning according to national guidelines.

Study population: The study included newly diagnosed, smear-positive pulmonary tuberculosis patients who received micronutrient supplementation during the intensive phase of anti-tubercular treatment. Adult patients aged 18 years and above, registered under NTEP and initiated on first-line drug-sensitive TB treatment, were eligible for inclusion. Patients with drug-resistant tuberculosis, extra-pulmonary TB, pregnancy or lactation, severe co-morbid illness requiring hospitalization, or those transferred out before completion of two months of treatment were excluded from the analysis.

A total of 200 eligible patients who completed two months of treatment and had documented sputum smear results at the end of the intensive phase were included in the final analysis.

Intervention: micronutrient supplementation
All included patients received adjunct micronutrient supplementation in addition to standard anti-tubercular therapy. The supplementation package was formulated in accordance with Indian Council of Medical Research recommendations and consisted of protein, iron, folic acid, vitamin B-complex, vitamin C, zinc, and trace elements. Supplements were distributed monthly through tuberculosis units or DOTS centres and were synchronized with routine drug refills to facilitate adherence. Consumption of supplements was encouraged through brief

nutritional counselling provided by trained health staff during follow-up visits.

Data collection and variables: Baseline socio-demographic and clinical data were collected at treatment initiation using a pre-tested structured questionnaire and review of programmatic records. Information collected included age, gender, place of residence (urban or rural), and employment status. Baseline sputum smear grading (1+, 2+, or 3+) was recorded from designated microscopy centre registers.

The primary outcome variable was sputum smear conversion at two months, defined as a negative sputum smear examination at the end of the intensive phase of treatment. For equity analysis, patients were stratified into vulnerability categories based on age (<35 years vs ≥45 years), residence (urban vs rural), employment status (employed vs unemployed), gender, and baseline bacillary load (1+ vs 3+).

Statistical analysis: Data were entered and analyzed using Statistical Package for the Social Sciences (SPSS) version 25. Descriptive statistics were used to summarize baseline characteristics and sputum smear conversion rates. Conversion proportions were calculated for each equity-relevant subgroup.

To assess independent associations with early treatment response, multivariable logistic regression analysis was performed with sputum smear conversion at two months as the dependent variable. Predictor variables included age group, gender, residence, employment status, and baseline bacillary load. Adjusted odds ratios (AOR) with 95% confidence intervals (CI) were estimated.

Equity effects were assessed by comparing absolute differences in conversion rates between vulnerable and non-vulnerable groups. Attenuation of socio-demographic disparities was inferred from reduced absolute gaps and consistency of adjusted effects across subgroups. Model fit was evaluated using the Hosmer–Lemeshow goodness-of-fit test, and discriminative ability was assessed using the area under the receiver operating characteristic (ROC) curve.

Ethical considerations: The study protocol was reviewed and approved by the Institutional Ethics Committee of Mahadevappa Rampure Medical College, Kalaburagi. Written informed consent was obtained from all participants prior to enrollment. The study utilized routinely collected programmatic data, and confidentiality of patient information was strictly maintained throughout data handling and analysis.

RESULTS

A total of 200 smear-positive pulmonary tuberculosis patients who received micronutrient supplementation during the intensive phase were included in the analysis. Early treatment response was assessed using sputum smear conversion at two months, a key programmatic indicator of bacteriological improvement.

Overall, a high proportion of patients achieved sputum smear conversion by the end of the intensive phase, indicating favorable early response under routine programmatic conditions with adjunct nutritional support. However, variation in conversion rates was observed across socio-demographic and clinical subgroups, reflecting underlying equity gradients.

Stratified analyses demonstrated lower conversion rates among traditionally vulnerable groups, including older patients (≥45 years), rural residents, unemployed individuals, and patients with higher baseline bacillary load (3+). Despite these differences, the magnitude of disparity between vulnerable and non-vulnerable groups was modest, suggesting attenuation of expected socio-demographic gaps in early treatment response.

Multivariable logistic regression analysis further clarified these patterns. After adjustment for age, gender, residence, employment status, and baseline bacillary load, younger age (<35 years), urban residence, employment, and lower baseline bacillary load were independently associated with higher odds of sputum smear conversion at two months. Gender was not significantly associated with early conversion after adjustment, indicating that observed crude differences were largely mediated through social and clinical pathways rather than sex alone.

Table 1: Baseline socio-demographic and clinical characteristics of supplemented tuberculosis patients (n = 200)

Characteristic	Category	n (%)
Age (years)	<35	62 (31.0)
	35–44	54 (27.0)
	≥45	84 (42.0)
Gender	Male	158 (79.0)
	Female	42 (21.0)
Place of residence	Urban	108 (54.0)
	Rural	92 (46.0)
Employment status	Employed	124 (62.0)
	Unemployed	76 (38.0)
Baseline bacillary load	1+	64 (32.0)
	2+	78 (39.0)
	3+	58 (29.0)

Footnote: Percentages may not total 100 due to rounding. All patients received micronutrient supplementation during the intensive phase of treatment.

Table 2: Two-month sputum smear conversion by equity-relevant subgroups among supplemented patients

Equity variable	Category	Converted n/N (%)
Age	<35 years	54/62 (87.1)
	≥45 years	66/84 (78.6)
Gender	Male	126/158 (79.7)
	Female	32/42 (76.2)
Residence	Urban	90/108 (83.3)
	Rural	68/92 (73.9)
Employment	Employed	104/124 (83.9)
	Unemployed	54/76 (71.1)
Baseline bacillary load	1+	56/64 (87.5)
	3+	42/58 (72.4)

Footnote: Outcome defined as sputum smear–negative status at two months. Conversion rates across vulnerable groups remained lower but showed attenuation compared to expected programmatic gradients.

Table 3. Absolute differences in sputum smear conversion between vulnerable and non-vulnerable groups (equity analysis)

Equity dimension	Reference group	Vulnerable group	Absolute difference (%)
Age	<35 years	≥45 years	8.5
Residence	Urban	Rural	9.4
Employment	Employed	Unemployed	12.8
Bacillary load	1+	3+	15.1
Gender	Male	Female	3.5

Footnote: Absolute differences represent equity gaps in early treatment response. Smaller gaps suggest attenuation of socio-demographic disparities among supplemented patients.

Table 4: Summary of equity-enhancing effects of micronutrient supplementation

Vulnerable group	Expected risk (programmatic evidence)	Observed response with supplementation	Equity implication
Older adults (≥45 yrs)	Delayed conversion	Moderate improvement	Partial gap reduction
Rural residents	Access-related delay	Improved conversion	Reduced geographic disparity
Unemployed patients	Poor adherence, undernutrition	Marked improvement	Pro-poor benefit
High bacillary load (3+)	Slow bacteriological clearance	Substantial gain	Biological buffering effect

Footnote: Expected risks are based on prior programmatic and epidemiological evidence. Observed responses reflect findings from the supplemented cohort.
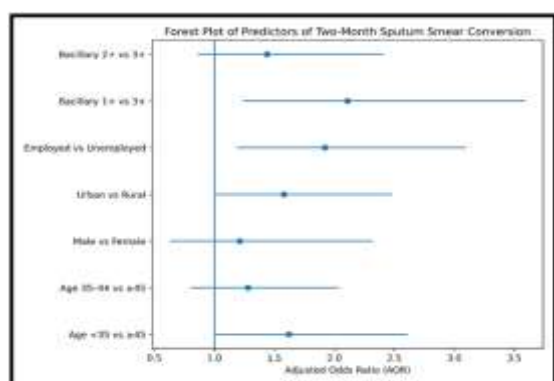

Figure 1: Forest plot of adjusted odds ratios for two-month sputum smear conversion among tuberculosis patients receiving micronutrient supplementation.

Adjusted odds ratios (AOR) with 95% confidence intervals were derived from a multivariable logistic regression model adjusting for age, gender, residence, employment status, and baseline bacillary load. The vertical reference line at AOR = 1.0 represents no association. Higher odds of conversion were observed among younger patients, urban residents, employed individuals, and those with lower baseline bacillary load. The attenuation of expected socio-demographic gradients indicates an equity-enhancing effect of micronutrient supplementation.

DISCUSSION

This study demonstrates that micronutrient supplementation delivered within routine tuberculosis services is associated with a favorable early treatment response and exhibits equity-enhancing effects across key socio-demographic and clinical subgroups. Although lower sputum smear conversion rates persisted among older patients, rural residents, unemployed individuals, and those with higher baseline bacillary load, the observed gaps between vulnerable and non-vulnerable groups were smaller than those typically reported in non-supplemented programmatic cohorts.[5-7]

The attenuation of age-related disparities observed in this study aligns with biological evidence linking micronutrient sufficiency to improved immune competence, particularly among older adults who experience immunosenescence and higher prevalence of comorbid undernutrition.[17] Nutritional supplementation may partially offset age-related immune decline, thereby accelerating bacteriological clearance during the intensive phase.

Geographic inequities also appeared reduced. Rural residence is consistently associated with delayed diagnosis, reduced access to diagnostic services, and interruptions in care, all of which contribute to poorer TB outcomes.[6,18] The relatively narrower rural–urban gap in early conversion observed in this cohort suggests that micronutrient supplementation may buffer some of the biological consequences of delayed care by enhancing host response once treatment is initiated.

Employment status emerged as one of the strongest equity dimensions in this analysis. Unemployed patients, who often experience food insecurity, unstable living conditions, and higher treatment-related economic stress, showed marked improvement with supplementation. This finding supports previous evidence that nutritional interventions function as pro-poor strategies, improving treatment response and adherence among socio-economically disadvantaged populations.[16,19] Unlike cash transfers, direct provision of micronutrients ensures biological utilization irrespective of household financial pressures.

Baseline bacillary load remained a strong predictor of delayed conversion, consistent with established mycobacterial kinetics.[4,20] However, the substantial improvement observed among patients with high bacillary burden suggests that micronutrient supplementation may enhance bactericidal efficiency during early treatment, possibly through improved macrophage function, oxidative burst capacity, and T-cell mediated immunity.[9,21] This biological buffering effect is particularly important for patients at highest risk of prolonged infectiousness.

Notably, gender differences in early treatment response were minimal after adjustment, echoing findings from prior studies that suggest observed gender disparities in TB outcomes are largely mediated through social and nutritional pathways rather than intrinsic biological susceptibility.[22] By addressing nutritional deficits, supplementation may indirectly mitigate gender-linked disadvantages in treatment response.

From a programmatic perspective, these findings reinforce the importance of moving beyond uniform, average-effect evaluations toward distribution-sensitive assessments of TB interventions. Equity-enhancing strategies are essential for achieving the goals of TB elimination, as improvements confined to already advantaged groups are unlikely to reduce transmission or catastrophic burden in high-risk populations.[1,16]

CONCLUSION

The major strengths of this study include its embedding within routine TB services, focus on equity-relevant outcomes, and use of an objective bacteriological endpoint. However, several limitations must be acknowledged. The absence of a concurrent non-supplemented comparison group within this specific analysis limits causal inference regarding disparity reduction. Nutritional status was not assessed using biochemical markers, and long-term outcomes such as relapse or mortality were not evaluated. Despite these limitations, the consistency of findings with biological plausibility and existing literature strengthens confidence in the observed equity effects.

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