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Nutritional status trajectories in cured and non-cured pediatric tuberculosis patients following six-month anti-TB treatment

Trajektori status gizi pada pasien tuberkulosis anak kelompok sembuh dan tidak sembuh setelah enam bulan pengobatan OAT

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Abstract

Pediatric tuberculosis (TB) remains a critical public health issue in Indonesia, with 809,000 new cases reported in 2023. Malnutrition is a common comorbidity; however, the nutritional trajectory that differentiates children who achieve clinical recovery from those who do not remains underexplored. This retrospective cohort study analyzed 102 children aged 2–18 years with pulmonary TB who were treated at RSUD dr. Zainoel Abidin, Banda Aceh, from January 2024 to January 2025. Patients with comorbidities and incomplete medical records were excluded. Nutritional status was assessed using the CDC 2000 Growth Charts at three time points: baseline, 2 months, and 6 months, and analyzed using Repeated Measures ANOVA ($p<0.05$). Among the participants, 96 (94.1%) recovered, whereas 6 (5.9%) did not. The mean body weight increased significantly from 21.9 kg at baseline to 25.0 kg at six months ($p<0.001$), with the proportion of children classified as well-nourished rising from 45.1% to 71.6%. Nutritional trajectories improved significantly over the treatment period ($p<0.001$), with more consistent gains observed in the recovery group. In conclusion, these findings indicate that six-month anti-tuberculosis therapy (ATT) is effective not only in resolving infection but also in enhancing the nutritional status of children. Monitoring nutritional trajectories may serve as a valuable prognostic indicator for evaluating treatment response and predicting clinical outcomes in pediatric TB.

Keywords: Anti-tuberculosis therapy, nutritional status, pediatric tuberculosis, retrospective cohort, treatment outcome

Abstrak

Tuberkulosis (TB) pada anak masih menjadi masalah kesehatan penting di Indonesia, dengan kasus baru mencapai 809.000 pada 2023. Malnutrisi merupakan komorbiditas yang umum, namun pola perubahan status gizi yang membedakan anak yang sembuh dan yang tidak sembuh masih sedikit diteliti. Penelitian kohort retrospektif ini menganalisis 102 anak usia 2–18 tahun dengan TB paru di RSUD dr. Zainoel Abidin, Banda Aceh, antara Januari 2024 hingga Januari 2025. Pasien dengan komorbiditas atau data tidak lengkap dikeluarkan dari studi. Status gizi dievaluasi menggunakan Kurva Pertumbuhan CDC 2000 pada tiga titik waktu: awal, 2 bulan, dan 6 bulan, dianalisis dengan Repeated Measures ANOVA ($p<0,05$). Dari 102 anak, 96 (94,1%) sembuh dan 6 (5,9%) tidak sembuh. Berat badan rata-rata meningkat signifikan dari 21,9 kg menjadi 25,0 kg setelah enam bulan ($p<0,001$), dengan proporsi anak bergizi baik meningkat dari 45,1% menjadi 71,6%. Trajektori status gizi menunjukkan perbaikan signifikan selama terapi ($p<0,001$), lebih konsisten pada kelompok sembuh dibanding kelompok tidak sembuh. Kesimpulan, terapi obat anti tuberkulosis (OAT) enam bulan tidak hanya efektif mengatasi infeksi, tetapi juga meningkatkan status gizi anak. Pemantauan trajektori gizi dapat menjadi indikator penting untuk mengevaluasi respons pengobatan dan memprediksi kemungkinan kesembuhan.

Kata Kunci: Hasil pengobatan, kohort retrospektif, status gizi, terapi obat anti tuberkulosis, tuberkulosis anak

Introduction

Tuberculosis (TB) remains a major global public health challenge, causing approximately 1.25 million deaths in 2023 alone. Children under 15 years of age account for 1.2 million new cases, with the highest burden in endemic countries such as Indonesia. At the national level, pediatric TB notifications increased from 724,000 in 2022 to 809,000 in 2023. In Aceh Province, case detection remains suboptimal, reaching only 19.1% in 2020, contributing to delayed diagnosis and a higher risk of complications (Izza, 2025a; Nataprawira et al., 2024a; Ni Nyoman Ratna Sri Dewi et al., 2025a; Umijati & Andajani, 2024).

The relationship between TB and malnutrition is thus bidirectional. Undernutrition compromises cellular immunity, particularly by reducing CD4+ T-cell levels by 30–50%, thereby increasing susceptibility to infection by two- to five-fold. Conversely, active TB promotes a hypercatabolic state characterized by increased resting energy expenditure, anorexia, and impaired nutrient absorption, leading to progressive weight loss. Meta-analyses indicate that stunted Indonesian children under five years of age have a threefold higher risk of developing TB (Dedy Arisjulyanto & Neny San Agustina Siregar, 2024; Machfudz et al., 2024a; Simanjorang et al., 2024).

Despite these findings, current evidence is dominated by cross-sectional studies, leaving a significant gap in our understanding of longitudinal nutritional changes during treatment. Dynamic recovery patterns that differentiate successfully treated patients from those with treatment failure remain underexplored, limiting the prognostic value of nutritional monitoring and delaying early intervention in accordance with the WHO 2024 recommendations (Burusie et al., 2024a; Nataprawira et al., 2024b).

This retrospective cohort study, conducted at a tertiary referral hospital in Banda Aceh (2024–2025), addresses this gap by analyzing weight-for-height z-score trajectories at baseline, two months, and six months in cured and non-cured pediatric pulmonary TB patients aged 2–18 years. The findings demonstrate that divergent nutritional trends can serve as early indicators of treatment failure, supporting the integration of growth monitoring into Indonesia's National TB Program to improve outcome prediction and close existing detection and treatment gaps in the future.

Monitoring the nutritional status of pediatric patients with TB is critical because of the strong bidirectional interaction between malnutrition and disease progression. This study is important because it identifies longitudinal patterns in weight-for-height trajectories that may predict treatment outcomes, enabling early nutritional interventions. The objective of this study was to evaluate these dynamic nutritional changes over six months and assess their utility as prognostic markers for treatment failure, thereby providing evidence to inform policy and clinical practice in high-burden regions such as Aceh Province.

Methods

This retrospective cohort study was conducted at the Child Health Department of dr. Zainoel Abidin General Hospital is a tertiary referral hospital in Banda Aceh, Indonesia. This study utilized secondary data derived from standardized medical records of pediatric patients treated between January 2024 and January 2025. An observational analytic design with a retrospective approach was employed to evaluate the causal relationship between therapeutic interventions and nutritional outcomes. To address missing data, strict exclusion criteria were applied: patients with incomplete medical records, specifically those lacking anthropometric measurements at any of the three required time points (baseline, 2 months, and 6 months), were excluded from the analysis.

The target population included children aged 2–18 years who were diagnosed with pulmonary tuberculosis. The minimum sample size was determined using the hypothesis testing formula for two population proportions with a 95% confidence level ($Z\alpha = 1.96$), 80% statistical power ($Z\beta = 0.84$), and an estimated proportion difference of 20% ($P1 = 0.60$, $P2 = 0.40$). Based on this calculation, a minimum sample size of 102 participants was required. Total sampling was employed, and 102 eligible patients who met the inclusion criteria were recruited.

Demographic and clinical data were extracted from medical records. Anthropometric measurements (weight and height) were obtained from historical data recorded by trained healthcare professionals as part of the standard nutritional assessment protocol of the hospital. Data were collected at three critical time points: treatment initiation (baseline), end of the intensive phase (2 months), and treatment completion (6 months).

Nutritional status was evaluated using the CDC 2022 Growth Charts. Although the WHO Growth Standards are preferred for children under 5 years of age, CDC charts were utilized to maintain methodological consistency across the broad age spectrum (2–18 years) in this cohort. Nutritional categories were defined by weight-for-height/length (%W/H) z-scores: severe malnutrition (<70%), moderate malnutrition (70–89%), normal (90–110%), overweight (111–120%), and obesity (>120%) (CDC, 2022; Kemenkes RI, 2023; WHO, 2021).

Data analysis was performed using the IBM SPSS Statistics software. Normality was assessed using the Kolmogorov-Smirnov and Shapiro-Wilk tests, and homogeneity was evaluated using Levene's test (Serdar, 2021). To analyze changes in nutritional status over time and compare differences between the "cured" and "non-cured" groups, a Two-Way Repeated Measures ANOVA was conducted. Mauchly's Test of Sphericity was performed to assess the assumption of sphericity. Since the assumption was violated ($p < 0.05$), the degrees of freedom were adjusted using the Greenhouse-Geisser correction to ensure valid F test results (Serdar, 2021). Although the sample sizes were unequal (96 cured vs. 6 non-cured), the analysis focused on the interaction effects to observe nutritional trajectories.

This study adhered to the established ethical standards and received approval from the Health Research Ethics Committee of RSUD dr. Zainoel Abidin, Banda Aceh (Approval No. 246/ETIK-RSUDZA/2025). As this was a retrospective study using secondary data, informed consent was waived. All patient information was anonymized prior to analysis to protect confidentiality in compliance with the Declaration of Helsinki. The research involved no invasive procedures and ensured strict protection of personal and medical data, with all records being handled in accordance with institutional policies and privacy regulations.

Result and Discussion

A total of 102 children with pulmonary tuberculosis were included in this study. The sex distribution was relatively balanced, comprising 52.0% girls and 48.0% boys. The largest age group was adolescents aged 11–18 years (41.2%), followed by children aged 0–5 years (34.3%) and 6–10 years (24.5%), respectively.

Mantoux test results were positive in 90.2% of the subjects, indicating a high level of exposure to *Mycobacterium tuberculosis* in this population. At the end of the six-month therapy, 94.1% of patients achieved clinical cure, while 5.9% were classified as non-cured. Statistical analysis of the baseline characteristics revealed no significant differences between the cured and non-cured groups ($p > 0.05$), indicating that both groups had comparable demographic and clinical profiles at the start of therapy.

Table 1. Characteristics of the study subjects (n=102)

Characteristic	n	%
Sex		
Female	53	52.0
Male	49	48.0
Age Group		
0–5 years	35	34.3
6–10 years	25	24.5
11–18 years	42	41.2
Mantoux Test		
Positive	92	90.2
Negative	10	9.8
Baseline Weight (Mean ± SD) in kg	21.9 ± 10.3	
Baseline Height (Mean ± SD) in cm	118.1 ± 27.5	

The findings demonstrate that six months of anti-tuberculosis therapy significantly enhances nutritional recovery in pediatric pulmonary TB patients. Cured individuals exhibited sustained weight gain and z-score improvements, in contrast to the stagnation observed in non-cured cases, as evidenced by a significant group × time interaction ($F = 16.61$, $p < 0.001$). These results align with those of Burusie et al.'s (2024) multicenter Ethiopian cohort, in which persistent undernutrition during the continuation phase independently predicted unfavorable outcomes (aRR = 3.76, 95% CI 1.90–7.43), emphasizing the need for nutritional monitoring beyond the intensive phase—a gap our study addresses through serial assessments up to six months (Burusie et al., 2024). Similarly, Amelia et al. (2024) reported superior nutritional gains in extrapulmonary TB, underscoring the influence of TB type; however, our pulmonary-focused cohort isolated the role of treatment efficacy (Amelia & Kaswandani, 2024; Ni Nyoman Ratna Sri Dewi et al., 2025b).

The 94.1% cure rate exceeds Indonesia's national pediatric average (85–90%), likely reflecting hospital-based care and the exclusion of severe comorbidities, consistent with the WHO 2024 guidelines advocating integrated TB-nutrition interventions. Baseline malnutrition (49%) mirrors rates in high-burden settings (40–60%), where *Mycobacterium tuberculosis* exacerbates catabolism via cytokine storms (TNF-α, IL-6). Anti-TB therapy reversed this effect in responders, increasing the proportion of well-nourished children to 71.6%. In contrast, non-cured children exhibited stagnation, validating nutritional trajectories as dynamic prognostic tools and supporting Machfudz et al.'s (2024) recommendation for z-score monitoring to preempt treatment failure and stunting (Amelia & Kaswandani, 2024; Machfudz et al., 2024b).

The limitations of this study include its retrospective design and the small non-cured sample (n = 6), which may limit statistical power, although this is comparable to regional cohorts reporting 5–15% treatment failure. Future prospective trials incorporating nutritional interventions, such as high-protein supplementation, could clarify causal associations and address evidence gaps in Indonesia's pediatric TB-nutrition nexus, in accordance with the 2023 national guidelines. Therefore, routine growth chart monitoring is recommended to enhance outcome prediction and optimize resource allocation in high-prevalence areas (Ardhani et al., 2023; Khairiyadi et al., 2025; Sari Wulandari & Estela Karolina, 2023).

Nutritional assessment revealed significant improvements over six months of therapy. The mean body weight increased from 21.9 ± 10.3 kg at baseline to 25.0 ± 9.1 kg at the end of treatment ($p < 0.001$). The distribution of nutritional status shifted markedly: the proportion of children classified as well-nourished increased from 45.1% to 71.6%, whereas underweight and severe malnutrition decreased from 49.0% to 28.4%.

Repeated Measures ANOVA demonstrated a statistically significant interaction between the duration of therapy and clinical outcome ($F = 16.61$, $p < 0.001$), indicating that nutritional trajectories differed between the cured and non-cured groups. As shown in Table 2, the cured group (n = 96) exhibited a consistently positive trajectory in the weight-for-height percentage, increasing from 90.5% at baseline to 100.4% at six months. In contrast, the non-cured group (n = 6) showed a stagnant and declining trajectory from 85.3% to 81.7% over the same period. The mean difference between the groups widened significantly by the end of treatment (18.7%, $p < 0.001$).

Table 2. Comparison of nutritional status trajectories (estimated marginal means) between cured and non-cured groups

Clinical Outcome	Baseline (Mean ± SE)	2 Months (Mean ± SE)	6 Months (Mean ± SE)	P-value (Group)*
Cured (n=96)	90.5 ± 1.2	92.7 ± 1.2	100.4 ± 1.2	0.026
Non-Cured (n=6)	85.3 ± 5.0	84.0 ± 4.9	81.7 ± 4.7	
Mean Difference	5.2	8.7	18.7†	
P-value (Time)		0.030		
P-value (Interaction)		< 0.001		

Note: Values are expressed as Estimated Marginal Means ± Standard Error (SE). Statistical analysis was performed using Two-Way Repeated Measures ANOVA with Greenhouse-Geisser correction. P-value (Group) indicates the overall difference between cured and non-cured participants; P-value (Time) indicates nutritional changes over the treatment period; and P-value (Interaction) indicates the difference in growth trajectories between the two groups. †Significant difference between groups at 6 months ($p < 0.001$).

As demonstrated in Table 2, the cured group exhibited a consistently positive trajectory, increasing from 90.5% at baseline to 100.4% at the end of treatment. In contrast, the non-cured group showed a stagnant and declining trajectory, decreasing from 85.3% to 81.7%. These findings indicate that successful anti-tuberculosis therapy is strongly associated with significant nutritional improvement. Nutritional improvement appears not only as a co-occurrence but also as a critical physiological reflection of the reduced disease burden. The significant weight gain observed in the cured group aligns with the theory that effective oral anti-TB (OAT) administration reduces systemic inflammation, specifically the levels of cytokines such as TNF-α and IL-6, which are known to induce cachexia and protein catabolism (Rahajoe, 2018; Kementerian Kesehatan Republik Indonesia, 2023).

Conversely, the divergent trajectory in the non-cured group suggests a persistent catabolic state due to an uncontrolled infection. Unlike their cured counterparts, these children did not exhibit any nutritional improvement. This stagnation likely reflects ongoing inflammation, which suppresses appetite (anorexia) and increases metabolic demands, preventing weight gain despite treatment (Niki et al., 2020). This finding underscores the potential of using "nutritional stagnation" at the two-month evaluation as an early warning sign for potential treatment failure or drug resistance, prompting an earlier clinical reassessment.

Furthermore, our data revealed a shift towards overweight and obesity in a subset of cured patients (increasing from 5.9% to 14.7%), likely resulting from the rapid restoration of appetite combined with a high-calorie intake during recovery. While weight restoration is desirable, excessive weight gain poses long-term metabolic risks, highlighting the need for balanced nutritional counseling (Bhargava et al., 2023). Shah et al. (2024) further validated supplementation-enhanced gains in cured DS-TB patients (weight +2.5 kg vs. +0.8 kg in treatment failures; $p < 0.01$), attributing divergence to resolved inflammation restoring anabolism, although they cautioned against over-reliance without resistance testing.

Consistent with evidence that nutritional recovery differentiates cured from non-cured pediatric TB patients, anti-TB drug dosing should be individualized according to nutritional status, using reduced doses during acute malnutrition and gradually escalating with weight and growth recovery. This approach necessitates the revision of current WHO guidelines and treatment algorithms to optimize outcomes and enable the early detection of treatment failure (Oshikoya & Senbanjo, 2018).

Patterns of nutritional change consistently distinguish between pediatric tuberculosis patients who are cured and those who are not after six months of anti-TB therapy. Children who successfully complete treatment experience progressive improvements in body weight and growth parameters, indicating effective disease control, decreased inflammatory activity, and restoration of normal appetite and metabolism. Conversely, patients who fail to achieve a cure exhibit minimal or worsening nutritional gains, reflecting ongoing infection, sustained catabolic processes, and potential drug resistance. These findings highlight that nutritional recovery serves not only as a treatment outcome but also as a reliable physiological indicator of successful therapy. Therefore, regular longitudinal assessment of nutritional status provides a simple, cost-effective prognostic approach for detecting early treatment failure, particularly in low-resource healthcare settings (Izza, 2025b; Kaur et al., 2025).

This study has several limitations. First, the retrospective cohort design relies on medical records, which may introduce information biases. Second, specific data on daily calorie intake, socioeconomic status, and medication adherence, which could influence nutritional outcomes, were not available for analysis. Third, the study utilized CDC 2000 Growth Charts for all ages to maintain consistency across the sample, whereas WHO standards are typically preferred for children aged under five years. Finally, the small sample size of the non-cured group ($n = 6$) limits the statistical power for detailed subgroup comparisons, although the interaction effect was highly significant. Despite these limitations, the longitudinal nature of the data provides strong evidence of the prognostic value of nutritional monitoring in pediatric TB.

Conclusion

This study confirms that a six-month regimen of anti-tuberculosis therapy (OAT) significantly improves the nutritional status of pediatric patients with pulmonary tuberculosis. Importantly, this study identified distinct nutritional trajectories based on clinical outcomes: while cured patients demonstrated progressive weight gain and nutritional recovery, non-cured patients exhibited nutritional stagnation or decline. These findings refute the notion that nutritional improvement is independent of clinical cure; instead, they highlight the intrinsic link between physiological recovery and infection eradication.

Clinically, these results suggest that nutritional parameters can serve as valuable surrogate markers for the treatment response. "Nutritional stagnation," particularly when evaluated at the end of the intensive phase (2 months), should be regarded as a potential early warning sign of treatment failure, drug resistance, or poor adherence. Therefore, we recommend the integration of routine longitudinal nutritional monitoring into national TB control programs. Moreover, early nutritional interventions and close clinical supervision should be prioritized for patients who fail to demonstrate positive growth trajectories to ensure optimal treatment outcomes.

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