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ANTHROPOMETRIC–PHYSIOLOGICAL DECOUPLING IN SEVERE ACUTE MALNUTRITION: DIFFERENTIAL ASSOCIATIONS OF WEIGHT-FOR-HEIGHT Z-SCORE AND MID-UPPER ARM CIRCUMFERENCE WITH BIOCHEMICAL MARKERS

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ABSTRACT

Introduction: Severe acute malnutrition (SAM) induces profound metabolic and endocrine alterations. While weight-for-height Z-score (WHZ) and mid-upper arm circumference (MUAC) are standard diagnostic indices for severity assessment, their capacity to accurately reflect underlying physiological status at extreme levels of wasting remains unclear.
Objective: This study aimed to evaluate whether WHZ and MUAC differ in their associations with biochemical markers of physiological status in children with SAM, thereby exploring the hypothesis of anthropometric–physiological decoupling.
Materials And Methods: A retrospective secondary analysis was conducted on 68 children (aged 6–48 months) with non-edematous SAM. The study analyzed anthropometric measures (WHZ and MUAC) against biochemical markers, including free T3 (FT3), free T4 (FT4), and serum albumin. Associations were assessed using linear regression models, including multivariable adjustments for both anthropometric indices. Additionally, a categorical analysis compared severe (WHZ −3.0 to −5.0) and extreme (WHZ < −5.0) wasting groups.
Results: WHZ demonstrated no significant independent association with FT3, FT4, or serum albumin. Conversely, MUAC exhibited a significant positive association with FT3 and albumin, alongside a non-significant trend for FT4. Furthermore, categorical analyses revealed no significant differences in mean FT3, FT4, or albumin levels between the severe and extreme wasting groups.
Conclusion: In children with SAM, WHZ failed to associate with biochemical markers of physiological status, whereas MUAC maintained significant predictive value. These findings indicate anthropometric–physiological decoupling at extreme wasting levels, suggesting MUAC serves as a more reliable indicator of physiological reserve than WHZ in severely malnourished pediatric populations.

INTRODUCTION

Severe Acute Malnutrition (SAM) remains a critical driver of pediatric morbidity and mortality, threatening the lives of more than 19 million children globally (1). The clinical identification and management of SAM rely heavily on standardized anthropometric indices, primarily the weight-for-height Z-score (WHZ) and mid-upper arm circumference (MUAC) (2). While both metrics are validated for diagnosing severe wasting, they capture distinct dimensions of nutritional depletion (3,4). WHZ reflects acute changes in body mass relative to the skeletal frame, whereas MUAC serves as a more direct proxy for somatic muscle and subcutaneous fat reserves (5).

The pathophysiology of SAM involves profound, systemic metabolic adaptations designed to prolong survival during periods of severe caloric and protein deficit (6). Key among these adaptations is the modulation of the hypothalamic-pituitary-thyroid axis and the depletion of hepatic synthetic proteins, such as albumin (6). However, emerging evidence suggests that biologically active free thyroid hormones (FT3 and FT4) may be relatively preserved despite severe anthropometric deficits, reflecting a degree of physiological stabilization (7,8).

In our prior work, we observed a divergence in the clinical utility of anthropometric indices: while MUAC correlated significantly with both free thyroid hormones and somatic protein levels, WHZ demonstrated a lack of association with these biochemical parameters (7). This finding is consistent with previous studies (4). This finding raises the possibility that, within severe malnutrition, anthropometric variation as measured by WHZ may not reliably reflect underlying physiological status.

Previous studies suggest that in states of prolonged and severe wasting, children exhibit metabolic and endocrine adaptations that promote survival under conditions of nutrient deprivation (9,10). One potential explanation for the lack of association in our cohort is that, at advanced stages of wasting, adaptive mechanisms may attenuate further measurable changes in biochemical markers, resulting in a relative stabilization of physiological parameters. In such a context, incremental changes in WHZ may no longer correspond to proportional changes in metabolic or endocrine function, suggesting anthropometric–physiological decoupling.

Despite its potential implications for clinical assessment and risk stratification, this phenomenon has not been formally evaluated. Therefore, the present study aims to investigate whether, within severe acute malnutrition, WHZ loses its association with biochemical markers of physiological status, while MUAC retains predictive validity. We further examine whether this pattern is accompanied by stabilization of biomarker levels across increasing severity of wasting.

METHODOLOGY

Study Design and Setting

This study is a retrospective secondary analysis of a cross-sectional dataset originally collected at the pediatric ward of Deen Dayal Upadhyay Hospital, New Delhi, between February 2024 and March 2025 (7). The primary study evaluated thyroid hormone profiles and their association with nutritional status in children with severe acute malnutrition (SAM).

Study Population

The dataset comprises 68 children aged 6 to 48 months with a confirmed diagnosis of non-edematous SAM, recruited through consecutive sampling. Children with known thyroid disorders, chronic systemic illnesses (including tuberculosis and HIV), liver or renal disease, or malabsorption syndromes (such as celiac disease and protein-losing enteropathy) were excluded. Analyses were restricted to complete cases, and no imputation was performed.

Anthropometric and Biochemical Variables

Two anthropometric indices were used as primary predictors: Weight-for-Height Z-score (WHZ) calculated using WHO growth standards (11), analyzed both as a continuous variable and as a categorical variable to define severity strata; and Mid-Upper Arm Circumference (MUAC) measured to the nearest millimeter and analyzed as a continuous variable.

Biochemical markers reflecting physiological and metabolic status included: Endocrine markers: Serum Free T3 (FT3) and Free T4 (FT4); and Nutritional markers: Serum albumin. All biochemical measurements were obtained from venous blood samples and analysed using chemiluminescence-based immunoassay techniques as described in the primary study.

Statistical Analysis

All analyses were conducted using R software (version 4.5.3). The primary objective was to evaluate whether biochemical markers demonstrate reduced variability and loss of association with increasing severity of wasting, consistent with anthropometric–physiological decoupling.

Descriptive statistics were used to summarize baseline characteristics. Continuous variables were reported as mean ± standard deviation or median with interquartile range, depending on distribution. Normality was assessed using the Shapiro–Wilk test.

To evaluate the relationship between anthropometric indices and biochemical markers, linear regression models were constructed for each outcome (FT3, FT4, and albumin). For each biomarker, three models were specified: a univariable model using WHZ, a univariable model using MUAC, and a multivariable model including both WHZ and MUAC to assess their independent effects. Standardized regression coefficients with 95% confidence intervals were reported to facilitate comparison of effect sizes between predictors. Anthropometric–physiological decoupling was inferred when WHZ demonstrated no independent association with biochemical markers, while MUAC retained a statistically significant association, and when biomarker levels showed minimal variation across increasing severity of wasting.

To confirm the findings, a categorical analysis was performed by dividing the cohort into two groups based on WHZ: severe wasting (WHZ between −3.0 and −5.0) and extreme wasting (WHZ < −5.0). The −5 threshold was selected to explore anthropometric behavior beyond the conventional WHO-defined validity range (12). Comparisons between groups were performed using independent sample t-tests for normally distributed variables and Mann–Whitney U tests for non-parametric data. Effect sizes were reported using Cohen's d. Variance differences between groups were assessed using Levene's test, with reduced variance in the extreme wasting group interpreted as supportive of physiological stabilization rather than random heterogeneity.

Model diagnostics were conducted by assessing residual distributions using Q–Q plots and Shapiro–Wilk testing. Where violations of model assumptions were identified, heteroscedasticity-robust standard errors (HC3) were applied. Variance inflation factors were calculated to assess multicollinearity between WHZ and MUAC. Sensitivity analyses were performed by excluding observations with WHZ < −6.0 to evaluate the robustness of findings against potential measurement error at extreme anthropometric values.

Ethical Considerations

This secondary analysis utilized anonymized data from a previously approved study and was conducted under the original ethical clearance granted by the Institutional Ethics Committee (IEC) and Scientific Research Committee (SRC) of Deen Dayal Upadhyay Hospital.

RESULTS

A total of 68 children with non-edematous severe acute malnutrition were included in the analysis. All participants had weight-for-height Z-scores (WHZ) below −3.0. The anthropometric and biochemical characteristics of the population are summarized in table 1.

Table 1: Baseline Characteristics of the study population (N=68)

Characteristic	Median (IQR)	Mean ± SD
MUAC (in mm)	113 (110 to 119)	114.74 ± 6.13
WHZ (SD)	-3.98 (-4.43 to -3.35)	-4.05 ± 0.84
FT3 (pg/dL)	312 (298 to 343)	323.97 ± 41.37
FT4 (ng/L)	12 (9.8 to 14.38)	12.22 ± 3.27

Albumin (g/dL)	3.4 (2.9 to 3.62)	3.26 ± 0.51

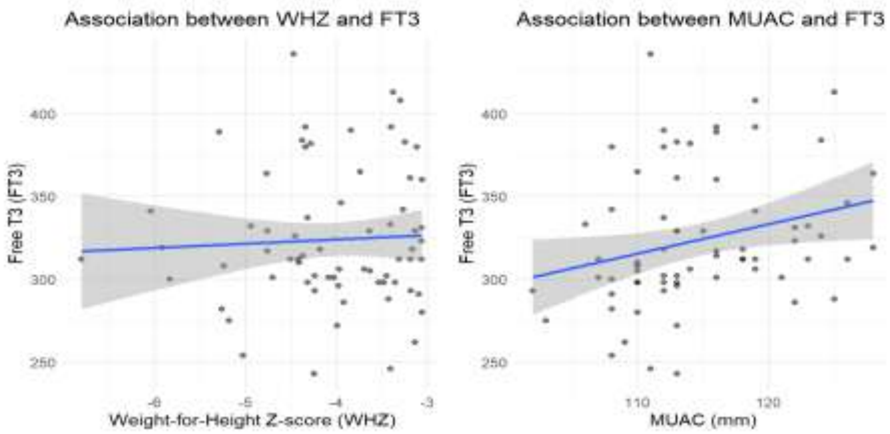
All variables deviated from normality based on Shapiro–Wilk testing; therefore, median (interquartile range) is presented as the primary measure of central tendency, with mean ± standard deviation provided for completeness. Overall, the cohort demonstrated uniformly low anthropometric indices consistent with severe wasting, with relatively preserved FT3 and FT4 .

Table 2: Multivariable linear regression analysis of anthropometric indices and biochemical markers.

Outcome	Predictor	Beta (standardized)	95%CI (standardized)	p-value
FT3	WHZ	0.090	-0.11 to 0.29	0.375
FT3	MUAC	0.276	0.05 to 0.50	0.016
FT4	WHZ	-0.007	-0.22 to 0.21	0.952
FT4	MUAC	0.220	-0.03 to 0.47	0.079
Albumin	WHZ	0.002	-0.27 to 0.27	0.990
Albumin	MUAC	0.346	0.10 to 0.60	0.007

Linear regression models were constructed to evaluate the association between anthropometric indices and biochemical markers. In multivariable analyses (Table 2), WHZ did not demonstrate a significant association with any of the outcomes, whereas MUAC retained a significant independent association with FT3 and albumin, with a positive but non-significant trend observed for FT4. Findings were consistent in univariable analyses. These relationships are visually illustrated in Figure 1, highlighting the absence of a meaningful association between WHZ and FT3 in contrast to the positive association observed with MUAC.

Figure 1: Association of Anthropometric Measurements and Free T3



Standardized regression coefficients were consistently greater for MUAC compared to WHZ across all models, indicating stronger predictive validity of MUAC for biochemical markers of physiological status. Based on the predefined analytical framework, this pattern is consistent with anthropometric–physiological decoupling.

To further examine this pattern, categorical analyses were performed by stratifying the cohort into severe wasting (WHZ −3.0 to −5.0) and extreme wasting (WHZ < −5.0). Comparisons of biochemical markers between groups demonstrated no statistically significant differences in central tendency. Mean FT3 levels were comparable between the extreme and severe groups ($p = 0.248$), as were FT4 ($p = 0.336$) and serum albumin ($p = 0.497$). Effect size estimates were small across all outcomes (Cohen's $d = -0.42$ for FT3, −0.28 for FT4, and −0.34 for albumin), with confidence intervals crossing zero.

Variance analysis using Levene's test did not demonstrate statistically significant differences in dispersion for FT3 ($p = 0.714$) or FT4 ($p = 0.157$). For albumin, a trend toward variance difference was observed ($p = 0.075$), although this did not reach statistical significance. Descriptive comparison of group-specific standard deviations showed no consistent reduction in variability within the extreme wasting group.

Overall, these findings indicate that biochemical markers remain largely stable across increasing severity of wasting, with no significant differences in mean levels and no clear evidence of variance compression between groups.

Model diagnostics were performed to assess the validity of regression assumptions. Residual analysis demonstrated deviation from normality in selected models, particularly for FT3 (Shapiro–Wilk $p = 0.002$), while residuals for FT4 and albumin did not show significant deviation ($p = 0.083$ and $p = 0.335$, respectively). To account for potential violations of model assumptions, heteroscedasticity-robust standard errors (HC3) were applied in all regression analyses.

Assessment of multicollinearity using variance inflation factors (VIF) demonstrated no evidence of collinearity between WHZ and MUAC (VIF ≈ 1.02 for both variables), indicating stable estimation of independent effects.

Sensitivity analyses excluding observations with WHZ < −6.0 yielded results consistent with the primary analysis. WHZ remained non-significant across all models, while MUAC retained a significant association with FT3 ($p = 0.016$) and albumin ($p = 0.007$), with a similar non-significant trend observed for FT4 ($p = 0.079$). These findings confirm the robustness of the observed associations and indicate that results were not driven by extreme anthropometric values.

DISCUSSION

This study evaluated the relationship between anthropometric indices and biochemical markers in children with severe acute malnutrition (SAM), with a specific focus on the hypothesis of anthropometric–physiological decoupling at extreme levels of wasting. The findings demonstrate a consistent pattern in which weight-for-height Z-score (WHZ) fails to show an independent association with biochemical markers of endocrine and somatic status, whereas mid-upper arm circumference (MUAC) retains significant predictive validity. This divergence was observed across multiple analytical approaches, including continuous regression models, categorical comparisons, and sensitivity analyses, suggesting that the findings are robust and not driven by statistical artifacts or extreme values.

The absence of association between WHZ and biochemical markers, despite substantial variability in WHZ values, suggests that at severe levels of wasting, further reductions in WHZ may not correspond to proportional physiological deterioration. In contrast, MUAC demonstrated consistent associations with both FT3 and albumin, indicating that it continues to reflect underlying metabolic and somatic reserve even in advanced stages of malnutrition. This pattern supports the concept of anthropometric–physiological decoupling, wherein WHZ loses its ability to capture biologically meaningful variation in severely wasted children, while MUAC retains clinical relevance (13).

The categorical analysis further reinforces this interpretation. The absence of significant differences in mean FT3, FT4, and albumin levels between severe and extreme wasting groups suggests stabilization of biochemical markers across increasing severity of anthropometric deficit. Although formal evidence of variance compression was not statistically significant, the lack of meaningful differences in central tendency suggests that biochemical parameters may reach a functional plateau in advanced malnutrition. Together, these findings are consistent with a model of physiological adaptation, in which endocrine and metabolic systems stabilize at a reduced but sustainable level to preserve essential function under conditions of chronic energy deficit (6,14,15).

These findings align with existing understanding of adaptive responses in SAM. Previous studies have demonstrated alterations in thyroid hormone dynamics characterized by reductions in total hormone levels with relative preservation of free hormone fractions, reflecting a state of metabolic downregulation. The present analysis supports this concept by demonstrating that anthropometric indices do not uniformly capture this adaptive physiology (16). Specifically, WHZ while effective for identifying acute wasting may have limited utility in reflecting ongoing physiological status at extreme deficits, whereas MUAC appears to better correlate with markers of metabolic and somatic reserve (5).

From a clinical perspective, these results have important implications for assessment and monitoring of children with SAM. Current diagnostic frameworks rely heavily on WHZ thresholds to define severity(2); however, the present findings suggest that within the severe range, WHZ may not provide meaningful stratification of physiological risk. In contrast, MUAC may offer a more reliable indicator of underlying metabolic status and could play a greater role in guiding clinical decision-making, particularly in severely wasted populations. These findings only suggest limitations in the ability of WHZ to stratify physiological status within the severe range in the context of existing diagnostic frameworks and do not negate the diagnostic utility of WHZ

This study has several limitations. The sample size was modest, which may limit the power to detect subtle differences in variance or small effect sizes. The cross-sectional design precludes causal inference and limits the ability to assess dynamic changes over time. Additionally, biochemical markers were limited to thyroid hormones and albumin, and may not fully capture the complexity of metabolic adaptation in SAM. Despite these limitations, the consistency of findings across multiple analytical approaches strengthens the validity of the observed patterns.

In conclusion, this study provides evidence that WHZ may become relatively decoupled from physiological status in severe acute malnutrition, while MUAC retains meaningful associations with endocrine and somatic markers. These findings are consistent with the presence of a physiological plateau at extreme levels of wasting and highlight the need to reconsider the relative roles of anthropometric indices in the assessment of severely malnourished children. Further studies with larger cohorts and longitudinal designs are required to confirm these findings and to better define the clinical implications of anthropometric–physiological decoupling.

REFERENCES

1. UNICEF, World Health Organization, & World Bank Group. Levels and trends in child malnutrition: UNICEF/WHO/World Bank Group Joint Child Malnutrition Estimates: Key findings of the 2025 edition [Internet]. New York: United Nations Children's Fund; 2025. Report 2025 Edition. Available from:
2. https://data.unicef.org/resources/jme/
3. WHO Guideline on the Prevention and Management of Wasting and Nutritional Oedema (acute Malnutrition) in Infants and Children under 5 Years. 1st ed. Geneva: World Health Organization; 2024. 1 p.
4. Garretson S, Walton S, Alier KK, Grounds S, Khattak Q, Mohamoud SA, et al. Analysing concordance between MUAC, MUACZ, and WHZ in diagnosing acute malnutrition among children under five in Somalia. J Glob Health. 2025 Dec 12;15:04258. doi:10.7189/jogh.15.04258 PubMed PMID: 41383165; PubMed Central PMCID: PMC12699285.
5. Grellety E, Golden MH. Weight-for-height and mid-upper-arm circumference should be used independently to diagnose acute malnutrition: policy implications. BMC Nutr. 2016 Feb 5;2(1):10. doi:10.1186/s40795-016-0049-7
6. Nsima L, Nkongolo BK, Bosonkie M, Nahimana D, Mayavanga JB, Kimpanga P, et al. Comparison of the prevalence of acute malnutrition in children aged 6-59 months by mid-upper arm circumference and weight-for-height index in Democratic Republic of the Congo from 2020 to 2022. Journal of Global Health Economics and Policy. 2025 Dec 18;5. doi:10.7189/001c.151307
7. Dipasquale V, Cucinotta U, Romano C. Acute Malnutrition in Children: Pathophysiology, Clinical Effects and Treatment. Nutrients. 2020 Aug 12;12(8):2413. doi:10.3390/nu12082413

8. Rubanbalaji G, Kumar DA, Prajapati DJ. Free Thyroid Hormone Profile and Its Association with Nutritional Status in Children with Severe Acute Malnutrition: A Cross-Sectional Study. International Journal of Medical and Pharmaceutical Research. 2026 Mar 27;7:1453–9.
9. Chandrashekaraiah S, Ratageri VH, Kamath L. Thyroid status in children with severe acute malnutrition. Karnataka Paediatr J. 2021 Mar 8;36(4):165–8. doi:10.25259/KPJ_13_2021
10. Müller O, Krawinkel M. Malnutrition and health in developing countries. CMAJ. 2005 Aug 2;173(3):279–86. doi:10.1503/cmaj.050342 PubMed PMID: 16076825; PubMed Central PMCID: PMC1180662.
11. Page L, McCain E, Freemark M. Adaptive Responses in Severe Acute Malnutrition: Endocrinology, Metabolomics, Mortality, and Growth. Nutrients. 2025 Sep 4;17(17). doi:10.3390/nu17172864
12. World Health Organization. Length/height-for-age, weight-for-age, weight-for-length, weight-for-height and body mass index-for-age; methods and development. Onis M de, editor. Geneva: WHO Press; 2006. 312 p. (WHO child growth standards).
13. WHO/UNICEF Technical expert advisory group on nutrition monitoring (TEAM). Recommendations for data collection, analysis and reporting on anthropometric indicators in children under 5 years old [Internet]. New York: World Health Organization; 2019 [cited 2026 Apr 3]. Available from: https://www.who.int/publications/i/item/9789241515559
14. Briend A, Maire B, Fontaine O, Garenne M. Mid-upper arm circumference and weight-for-height to identify high-risk malnourished under-five children. Matern Child Nutr. 2012 Jan;8(1):130–3. doi:10.1111/j.1740-8709.2011.00340.x PubMed PMID: 21951349; PubMed Central PMCID: PMC6860828.
15. Mudibo EO, Sande C, Ngari MM, Jenkins B, Singa BO, Lancioni CL, et al. Biological landscape of acute illness in children in sub-Saharan Africa and South Asia [Internet]. Systems Biology; 2025 [cited 2026 Apr 3]. Available from: http://biorxiv.org/lookup/doi/10.1101/2025.09.01.672585 doi:10.1101/2025.09.01.672585
16. Turkay S, Kus S, Gokalp A, Baskin E, Onal A. Effects of protein energy malnutrition on circulating thyroid hormones. Indian Pediatr. 1995 Feb;32(2):193–7. PubMed PMID: 8635781.
17. Kanani SM, Bharani SN. A comparison of mid-upper arm circumference and weight-for-height Z score of world health organization growth standards in detecting moderate and severe acute malnutrition in children aged 6-60 months. International Journal of Contemporary Pediatrics. 2024;11(1):38–44. doi:10.18203/2349-3291.ijcp20233957