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Original Research Article

BASELINE UNDERNUTRITION AND TREATMENT-RELATED TOXICITY IN PAEDIATRIC ACUTE LYMPHOBLASTIC LEUKAEMIA

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ABSTRACT

Background: Undernutrition is widespread among children in low- and middle-income countries and may compromise chemotherapy tolerance, yet its influence on early treatment-related morbidity in childhood acute lymphoblastic leukaemia (ALL) is poorly quantified in India. The objective is to determine the prevalence of undernutrition at diagnosis in newly diagnosed childhood ALL and its association with treatment-related toxicity and infection during induction and early consolidation chemotherapy.

Materials and Methods: This STROBE-compliant prospective observational study enrolled 48 consecutive children aged 0-12 years with newly diagnosed ALL at a tertiary paediatric haemato-oncology unit in northern Kerala, India, between January 2024 and January 2025. Nutritional status at diagnosis was classified by World Health Organization Z-scores for weight-for-age, height-for-age and weight-for-height or body mass index-for-age (undernutrition at or below -2 SD), plus serum albumin and 25-hydroxyvitamin D. Children were followed for eight weeks for CTCAE version 5.0-graded treatment-related toxicity and documented infection. Fisher's exact test and logistic regression were applied (SPSS version 26.0).

Results: Underweight, stunting and wasting affected 10 (20.8%), eight (16.7%) and 11 (22.9%) children respectively; hypoalbuminaemia 21 (43.8%) and vitamin D deficiency 14 (29.2%). Toxicity occurred in 18 children (37.5%) and infection in 26 (54.2%). Underweight children experienced more toxicity (70.0% versus 28.9%; unadjusted OR 5.73, 95% CI 1.25-26.28; P = 0.027), strengthening after adjustment for age (adjusted OR 10.73, 95% CI 1.79-64.31; P = 0.009). No nutritional index predicted infection.

Conclusion: Low weight-for-age at diagnosis independently predicts early treatment-related toxicity in childhood ALL. This inexpensive, universally available measurement should be embedded in routine risk assessment in resource-constrained paediatric oncology services.

Keywords: Precursor Cell Lymphoblastic Leukemia-Lymphoma; Child Nutrition Disorders; Nutritional Status; Drug-Related Side Effects and Adverse Reactions; Serum Albumin.

INTRODUCTION

Acute lymphoblastic leukaemia (ALL) is the commonest malignancy of childhood and accounts for approximately three-quarters of all paediatric leukaemias.[1] Risk-adapted multi-agent chemotherapy, coupled with advances in supportive care, has raised five-year event-free survival beyond 90% in high-income countries.[2] Outcomes in India remain considerably poorer, with contemporary multicentre data reporting overall survival of approximately 65%.[3] Only part of this gap is attributable to disease biology or protocol intensity; delayed presentation, treatment abandonment,

infection-related mortality and host characteristics that reduce tolerance of intensive therapy contribute substantially.[3,4]

Nutritional status at diagnosis is one such host characteristic, and it carries particular public health significance in India. The National Family Health Survey-5 (2019-21) reported that 35.5% of children under five years of age were stunted, 32.1% underweight and 19.3% wasted.[5] A child who develops leukaemia in this setting therefore frequently begins intensive cytotoxic therapy already nutritionally depleted, and the leukaemic process itself compounds that depletion through anorexia, hypermetabolism, systemic inflammation and disease-related catabolism.[6] Unlike disease biology, nutritional status is potentially modifiable, which makes it an attractive target for intervention within existing paediatric oncology services.

The biological pathways through which undernutrition might reduce treatment tolerance are well characterised. Protein-energy malnutrition depletes lean body mass and reduces serum albumin, altering the volume of distribution and protein binding of cytotoxic agents and thereby increasing free-drug exposure.[7] Impaired hepatic biotransformation and reduced renal reserve further modify drug clearance, while depleted antioxidant defences, compromised epithelial integrity and blunted cell-mediated immunity increase susceptibility to mucositis, gastrointestinal toxicity, hepatotoxicity and infection.[6,8] Micronutrient deficiencies, notably of vitamin D, have separately been proposed to influence innate immune competence during myelosuppressive therapy.[9]

Evidence linking nutritional status at diagnosis to outcome has accumulated largely from other low- and middle-income countries. Cohorts from Guatemala, Mexico and Nicaragua have reported higher induction mortality and greater treatment-related morbidity among undernourished children with cancer.[10-12] and a large Pakistani series described inferior event-free and overall survival among underweight children with ALL.[13] Indian data remain comparatively sparse, are frequently retrospective, and have concentrated on prevalence or on survival endpoints rather than on the early treatment-related morbidity that drives dose interruption, prolonged admission and out-of-pocket expenditure.[14-17]

The present study was therefore undertaken in a government tertiary referral centre in northern Kerala to determine the prevalence of anthropometric and biochemical undernutrition at diagnosis among children with newly diagnosed ALL, and to examine whether baseline nutritional status predicts treatment-related toxicity and infection during induction and early consolidation chemotherapy.

MATERIALS AND METHODS

Study design and setting: This prospective observational study was conducted in the Division of Haemato-Oncology, Department of Paediatrics, Government Medical College, Kozhikode, Kerala, India, between January 2024 and January 2025. The institution is a government tertiary care teaching hospital and the principal referral centre for paediatric oncology services in northern Kerala, providing care largely free at the point of delivery to a predominantly rural and semi-urban catchment population. The study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.

Participants: All children aged 0-12 years with newly diagnosed ALL who commenced treatment at the study centre during the study period were eligible for inclusion. The diagnosis was established by bone marrow morphology, cytochemistry and flow cytometric immunophenotyping according to institutional protocol, and treatment followed a modified Indian Childhood Collaborative Leukaemia Group regimen. Children requiring admission to the paediatric intensive care unit before baseline nutritional assessment could be completed were excluded, as critical illness precludes reliable anthropometry and confounds baseline biochemistry.

Sample size and sampling: Paediatric ALL is an uncommon disease and recruitment was bounded by a predefined 13-month enrolment window; a formal sample size calculation was therefore not undertaken, and the study should be regarded as exploratory with respect to statistical power. Consecutive sampling was used and every eligible child presenting during the study period was enrolled. Forty-eight children met the eligibility criteria and all completed the observation period; there were no losses to follow-up and no missing values for any exposure or outcome variable.

Data collection and nutritional assessment: Baseline demographic, clinical, anthropometric and laboratory data were recorded prospectively on a standardised pro forma by the investigating team. All nutritional measurements were obtained before the first dose of chemotherapy.

Weight was measured to the nearest 0.1 kg on a calibrated electronic scale with the child in minimal clothing, and length or height to the nearest 0.1 cm using an infantometer for children under two years and a stadiometer thereafter. Nutritional status was expressed as Z-scores derived from the World Health Organization Child Growth Standards.[18] Three indices were evaluated: weight-for-age, height-for-age, and weight-for-height for children under five years or body mass index-for-age for children aged five years and above. Undernutrition for each index was defined as a Z-score at or below -2 standard deviations (SD), corresponding conventionally to underweight, stunting and wasting respectively. Acute malnutrition was defined a priori as concurrent

weight-for-age and weight-for-height or body mass index-for-age at or below -2 SD.

Baseline serum albumin and serum 25-hydroxyvitamin D were measured on venous samples drawn at diagnosis in the institutional central laboratory. Hypoalbuminaemia was defined as serum albumin at or below 3.2 g/dL and vitamin D deficiency as serum 25-hydroxyvitamin D below 20 ng/mL.

Outcome measures: Children were followed prospectively through induction and into early consolidation, with a primary observation window of eight weeks from commencement of chemotherapy.

Treatment-related toxicity, the primary outcome, was defined as any adverse event attributed by the treating team to chemotherapy and graded according to the Common Terminology Criteria for Adverse Events, version 5.0,[19] which was of sufficient severity to require modification of supportive care, interruption or delay of scheduled therapy, or unplanned hospitalisation. Events meeting these criteria included mucositis, gastrointestinal toxicity, hepatotoxicity, electrolyte disturbance and the syndrome of inappropriate antidiuretic hormone secretion, treatment-emergent hypertension, hyperglycaemia, cardiovascular events, haemorrhagic complications and hypersensitivity reactions to L-asparaginase.

Infection, the secondary outcome, was defined as any clinically or microbiologically documented infectious episode requiring systemic antimicrobial therapy or hospitalisation, and included febrile neutropenia, bloodstream infection, localised soft-tissue or oral sepsis, respiratory infection and invasive fungal disease. All-cause mortality within the observation window was recorded.

Ethical considerations: The study protocol was approved by the Institutional Ethics Committee of Government Medical College, Kozhikode (reference number GMCKKD/RP 2024/IEC/371, dated 6 January 2024). Written informed consent was obtained in the local language from the parent or legal guardian of every participant before enrolment, and assent was obtained from children aged seven years and above. The study was conducted in accordance with the Declaration of Helsinki.[20] No participant identifiers appear in this report or in the analysis dataset.

Statistical analysis: Data were analysed using IBM SPSS Statistics, version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were summarised as mean with standard deviation or as median with interquartile range (IQR) according to distribution, and categorical variables as counts with percentages. Associations between binary nutritional exposures and binary outcomes were tested using Fisher's exact test, which was preferred to the chi-squared test throughout because several cells contained fewer than five observations.

Unadjusted odds ratios (OR) with 95% confidence intervals (CI) were estimated by univariate binary logistic regression. Variables associated with the primary outcome at P less than 0.10 in univariate analysis, together with age group, were considered for a multivariable model. Given that only 18 toxicity events were observed, the multivariable model was deliberately restricted to two covariates to maintain approximately nine events per variable, and is presented as an exploratory adjusted analysis rather than as a definitive predictive model. All tests were two-sided and P less than 0.05 was considered statistically significant. Exact P values are reported throughout.

RESULTS

Baseline characteristics: Forty-eight children with newly diagnosed ALL were enrolled and all were included in the analysis. Twenty-eight (58.3%) were male. The median age was 4.0 years (IQR 3.0-6.0; range 1.0-12.0), and 29 children (60.4%) were under five years of age. B-cell ALL predominated, accounting for 40 children (83.3%), with the remaining eight (16.7%) having T-cell disease. Baseline characteristics are presented in [Table 1].

Anthropometric undernutrition was common. Ten children (20.8%) were underweight, eight (16.7%) were stunted and 11 (22.9%) were wasted; six children (12.5%) met the a priori definition of acute malnutrition, and 18 children (37.5%) were undernourished by at least one anthropometric index. Biochemical evidence of nutritional compromise was more frequent still: mean serum albumin was 3.33 (SD 0.40) g/dL and 21 children (43.8%) were hypoalbuminaemic, while mean serum 25-hydroxyvitamin D was 30.7 (SD 15.2) ng/mL and 14 children (29.2%) were vitamin D deficient.

Table 1: Baseline demographic, clinical and nutritional characteristics of the study population (N = 48)

Characteristic	n	%
Sex		
Male	28	58.3
Female	20	41.7
Age group		
Under 5 years	29	60.4
5 to 9 years	14	29.2
10 years and above	5	10.4
Age, years: median 4.0 (IQR 3.0-6.0); range 1.0-12.0		
Immunophenotype		
B-cell ALL	40	83.3

T-cell ALL	8	16.7
Anthropometric nutritional status		
Underweight (weight-for-age ≤ −2 SD)	10	20.8
Stunting (height-for-age ≤ −2 SD)	8	16.7
Wasting (weight-for-height or BMI-for-age ≤ −2 SD)	11	22.9
Acute malnutrition*	6	12.5
Undernourished by at least one index	18	37.5
Biochemical nutritional status		
Hypoalbuminaemia (serum albumin ≤ 3.2 g/dL)	21	43.8
Vitamin D deficiency (25-hydroxyvitamin D < 20 ng/mL)	14	29.2
Serum albumin, g/dL: mean 3.33 (SD 0.40)		
Serum 25-hydroxyvitamin D, ng/mL: mean 30.7 (SD 15.2)		
Outcomes during observation period		
Treatment-related toxicity	18	37.5
Documented infection	26	54.2
Both toxicity and infection	8	16.7
Death within observation window	2	4.2

*Acute malnutrition was defined as concurrent weight-for-age and weight-for-height or body mass index-for-age at or below −2 SD. ALL: acute lymphoblastic leukaemia; BMI: body mass index; IQR: interquartile range; SD: standard deviation (Z-score).

Clinical outcomes during the observation period: Treatment-related toxicity occurred in 18 children (37.5%) and documented infection in 26 (54.2%); eight children (16.7%) experienced both. The spectrum of complications is shown in Figure 1. Bacterial sepsis or bloodstream infection was the single commonest event, recorded in 14 children (29.2%), followed by gastrointestinal toxicity in nine (18.8%), febrile neutropenia in eight (16.7%) and localised soft-tissue or oral infection in eight (16.7%). Multidrug-resistant Gram-negative organisms were isolated in five children (10.4%). Mucositis and treatment-emergent hypertension each occurred in five children (10.4%). Two children (4.2%) died during the observation window, both from refractory septic shock; neither was underweight nor hypoalbuminaemic at diagnosis.

Toxicity was more frequent in older children: 11 of 19 children aged five years and above (57.9%) developed treatment-related toxicity compared with seven of 29 younger children (24.1%) (P = 0.032). Neither sex (P = 0.226) nor immunophenotype (P = 1.000) was associated with toxicity.

Nutritional status and treatment-related toxicity

The association between baseline nutritional status and treatment-related toxicity is presented in Table 2. Underweight children experienced toxicity considerably more often than adequately nourished children: seven of 10 (70.0%) versus 11 of 38 (28.9%) (P = 0.027; unadjusted OR 5.73, 95% CI 1.25-26.28). The composite category of acute malnutrition showed a stronger association still, with five of six affected children (83.3%) developing toxicity compared with 13 of 42 (31.0%) (P = 0.022; unadjusted OR 11.15, 95% CI 1.18-105.24), although the confidence interval is very wide and rests on only six exposed children.

Hypoalbuminaemia was associated with a doubling of the observed toxicity proportion, 11 of 21 (52.4%) versus seven of 27 (25.9%), but did not reach conventional significance (P = 0.077; unadjusted OR 3.14, 95% CI 0.93-10.58). Neither stunting (P = 1.000) nor wasting (P = 0.724) was associated with toxicity. Vitamin D deficiency was, if anything, associated with less toxicity in this cohort, three of 14 (21.4%) versus 15 of 34 (44.1%), a difference that was not statistically significant (P = 0.196; unadjusted OR 0.35, 95% CI 0.08-1.47). Unadjusted odds ratios for all nutritional exposures are displayed in [Figure 2].

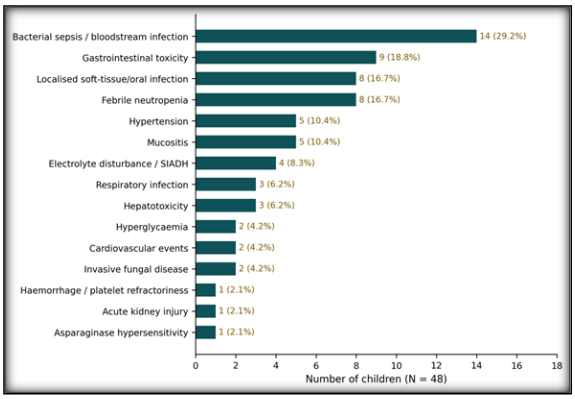

Figure 1: Spectrum of treatment-related toxicity and infectious complications recorded during induction and early consolidation chemotherapy (N = 48). Individual children may contribute to more than one category.

Table 2: Association between baseline nutritional status and treatment-related toxicity (N = 48)

Baseline nutritional exposure	Toxicity present, n (%)	Toxicity absent, n (%)	P value
Weight-for-age			
> −2 SD (n = 38)	11 (28.9)	27 (71.1)	0.027
≤ −2 SD (n = 10)	7 (70.0)	3 (30.0)	
Height-for-age			
> −2 SD (n = 40)	15 (37.5)	25 (62.5)	1.000
≤ −2 SD (n = 8)	3 (37.5)	5 (62.5)	
Weight-for-height or BMI-for-age			

> −2 SD (n = 37)	13 (35.1)	24 (64.9)	0.724
≤ −2 SD (n = 11)	5 (45.5)	6 (54.5)	
Acute malnutrition*			
Absent (n = 42)	13 (31.0)	29 (69.0)	0.022
Present (n = 6)	5 (83.3)	1 (16.7)	
Serum albumin			
> 3.2 g/dL (n = 27)	7 (25.9)	20 (74.1)	0.077
≤ 3.2 g/dL (n = 21)	11 (52.4)	10 (47.6)	
Serum 25-hydroxyvitamin D			
≥ 20 ng/mL (n = 34)	15 (44.1)	19 (55.9)	0.196
< 20 ng/mL (n = 14)	3 (21.4)	11 (78.6)	

P values by Fisher's exact test. *Acute malnutrition was defined as concurrent weight-for-age and weight-for-height or body mass index-for-age at or below −2 SD. BMI: body mass index; SD: standard deviation (Z-score).

Because toxicity was also more frequent in older children, an exploratory multivariable model containing weight-for-age category and age group was fitted [Table 3]. Both covariates remained independently associated with toxicity, and the estimated effect of underweight status increased after adjustment (adjusted OR 10.73, 95% CI 1.79-64.31; P = 0.009), as did that of age five years and above (adjusted OR 7.41, 95% CI 1.65-33.32; P = 0.009). The model was significant overall (likelihood ratio P = 0.001). A parallel model substituting acute malnutrition for underweight status yielded a consistent result (adjusted OR 18.33, 95% CI 1.65-203.17; P = 0.018).

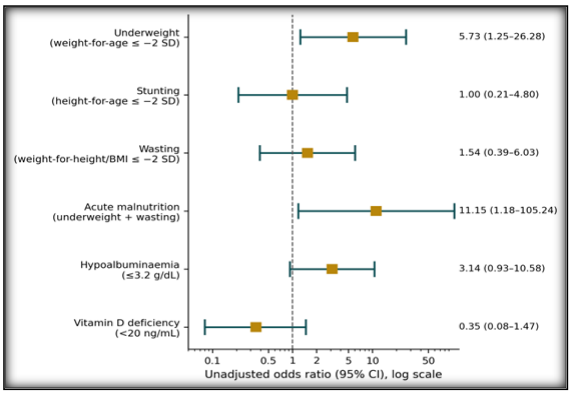

Figure 2: Unadjusted odds ratios with 95% confidence intervals for treatment-related toxicity according to baseline nutritional status (N = 48). Squares denote point estimates and horizontal lines 95% confidence intervals; the dashed vertical line indicates the null value. The x-axis is on a logarithmic scale.

Table 3: Logistic regression analysis of predictors of treatment-related toxicity (N = 48; 18 events)

Variable	Unadjusted OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Weight-for-age ≤ −2 SD	5.73 (1.25-26.28)	0.025	10.73 (1.79-64.31)	0.009
Age ≥ 5 years	4.32 (1.24-15.02)	0.021	7.41 (1.65-33.32)	0.009
Acute malnutrition*	11.15 (1.18-105.24)	0.035	—	—
Serum albumin ≤ 3.2 g/dL	3.14 (0.93-10.58)	0.065	—	—
Weight-for-height or BMI-for-age ≤ −2 SD	1.54 (0.39-6.03)	0.536	—	—
Height-for-age ≤ −2 SD	1.00 (0.21-4.80)	1.000	—	—
25-hydroxyvitamin D < 20 ng/mL	0.35 (0.08-1.47)	0.149	—	—

Adjusted estimates are from a two-covariate multivariable model containing weight-for-age category and age group (likelihood ratio P = 0.001). Variables not entered into the multivariable model are shown as an em dash. In a parallel model substituting acute malnutrition for weight-for-age, the adjusted odds ratio for acute malnutrition was 18.33 (95% CI 1.65-203.17; P = 0.018). *Acute malnutrition was defined as concurrent weight-for-age and weight-for-height or body mass index-for-age at or below −2 SD. CI: confidence interval; OR: odds ratio; SD: standard deviation (Z-score).

Nutritional status and infection: No baseline nutritional index was significantly associated with documented infection (Table 4). Infection proportions were similar in underweight and adequately nourished children (50.0% versus 55.3%; P = 1.000), and in hypoalbuminaemic and normoalbuminaemic children (57.1% versus 51.9%; P = 0.776). Stunting (P = 0.710), wasting (P = 0.302) and acute malnutrition (P = 0.392) were likewise unassociated with infection. Vitamin D deficient children experienced infection more often than vitamin D replete children, 10 of 14 (71.4%) versus 16 of 34 (47.1%), but the association did not reach significance (P = 0.202; unadjusted OR 2.81, 95% CI 0.74-10.75).

Table 4: Association between baseline nutritional status and documented infection (N = 48)

Baseline nutritional exposure	Infection present, n (%)	Infection absent, n (%)	P value
Weight-for-age			
> −2 SD (n = 38)	21 (55.3)	17 (44.7)	1.000
≤ −2 SD (n = 10)	5 (50.0)	5 (50.0)	
Height-for-age			
> −2 SD (n = 40)	21 (52.5)	19 (47.5)	0.710
≤ −2 SD (n = 8)	5 (62.5)	3 (37.5)	
Weight-for-height or BMI-for-age			

> −2 SD (n = 37)	22 (59.5)	15 (40.5)	0.302
≤ −2 SD (n = 11)	4 (36.4)	7 (63.6)	
Acute malnutrition*			
Absent (n = 42)	24 (57.1)	18 (42.9)	0.392
Present (n = 6)	2 (33.3)	4 (66.7)	
Serum albumin			
> 3.2 g/dL (n = 27)	14 (51.9)	13 (48.1)	0.776
≤ 3.2 g/dL (n = 21)	12 (57.1)	9 (42.9)	
Serum 25-hydroxyvitamin D			
≥ 20 ng/mL (n = 34)	16 (47.1)	18 (52.9)	0.202
< 20 ng/mL (n = 14)	10 (71.4)	4 (28.6)	

P values by Fisher's exact test. *Acute malnutrition was defined as concurrent weight-for-age and weight-for-height or body mass index-for-age at or below −2 SD. BMI: body mass index; SD: standard deviation (Z-score).

DISCUSSION

In this prospective cohort of 48 children commencing treatment for ALL at a government tertiary centre in Kerala, roughly one child in five was underweight at diagnosis, more than two in five were hypoalbuminaemic and almost one in three were vitamin D deficient. The principal finding is that low weight-for-age at diagnosis was independently associated with treatment-related toxicity during induction and early consolidation, with an adjusted odds ratio in excess of 10 after accounting for age. Baseline nutritional status was not associated with documented infection over the same period.

The prevalence of anthropometric undernutrition observed here is lower than that reported from several other Indian centres. Sonowal et al. described acute malnutrition in 52.5% of children with ALL during induction.[16] Jain et al. found undernutrition by weight-for-age in 56.8% of children with newly diagnosed malignancy,[14] Tandon et al. reported baseline undernutrition in approximately two-thirds of children with ALL,[15] and Radhakrishnan et al. documented a prevalence of 44% at a tertiary cancer centre in Chennai.[17] The comparatively lower figures in the present cohort are plausibly explained by Kerala's distinctive nutritional epidemiology: the state has among the lowest burdens of child undernutrition in India, and a well-developed primary care and public distribution infrastructure. This observation is itself of public health interest, since it suggests that the effect of undernutrition on treatment tolerance is detectable even in a relatively well-nourished Indian population, and would be expected to be more pronounced in states with a higher baseline burden.

The association between low weight-for-age and treatment-related toxicity is consistent with a substantial international literature. Murphy et al. reported that anthropometric and body composition measures predicted toxicity in children with ALL,[7] and systematic review evidence has repeatedly identified malnutrition at diagnosis as a determinant of adverse treatment outcome in childhood cancer.[8] Cohorts from Guatemala, Mexico and Nicaragua have described higher induction mortality and greater treatment-related morbidity among undernourished children,[10-12] while a Pakistani series of over 500 children with ALL reported inferior event-free and overall survival in those who were underweight.[13] The present study extends these observations by demonstrating that the effect is detectable at the level of early, non-fatal treatment morbidity, which is the point at which clinical intervention is still feasible.

It is notable that weight-for-age, but neither height-for-age nor weight-for-height, predicted toxicity. Stunting reflects chronic nutritional deprivation that is largely historical by the time of diagnosis and may have little bearing on current physiological reserve. Wasting, conversely, is a purely contemporaneous index that in leukaemia is confounded by organomegaly, tumour mass and fluid retention, all of which inflate measured weight relative to height and may mask true tissue depletion. Weight-for-age integrates both chronic and acute deficits against a chronological reference and may therefore represent the more faithful proxy for cumulative nutritional reserve at the moment therapy begins. This interpretation is supported by the further strengthening of the association when acute malnutrition, which requires deficits on two indices simultaneously, was substituted as the exposure. From a service delivery perspective the finding is fortunate, since weight-for-age is the simplest, cheapest and most universally recorded anthropometric index in Indian paediatric practice and requires no additional equipment, training or expenditure.

Age emerged as an independent predictor of toxicity, with children aged five years and above experiencing more than twice the toxicity of younger children. This is biologically plausible: older children receive higher absolute cumulative doses, are more likely to be assigned to higher risk strata, and have greater capacity to report subjective toxicity such as mucositis pain. Importantly, adjustment for age strengthened rather than attenuated the estimated effect of underweight status, indicating negative confounding, since underweight children in this cohort were somewhat younger than adequately nourished children. Analyses that fail to adjust for age may therefore underestimate the true contribution of nutritional status to treatment morbidity, and this may partly explain the modest effect sizes reported in some earlier unadjusted series.

Hypoalbuminaemia showed a consistent but statistically non-significant association with toxicity. Serum albumin is a composite marker reflecting protein reserve, hepatic synthetic function and the acute-phase response, and pretreatment hypoalbuminaemia is an established adverse prognostic marker across adult and paediatric oncology.[21] The direction and magnitude of the association observed here, together with the width of the confidence interval, are more consistent with inadequate statistical power than with absence of biological effect, and the finding warrants formal evaluation in an adequately powered cohort.

Contrary to prior expectation, vitamin D deficiency was not associated with greater toxicity and was, numerically, associated with less. This result should be interpreted with considerable caution. Only 14 children were deficient, the confidence interval is wide and includes clinically important effects in both directions, and serum 25-hydroxyvitamin D at diagnosis is influenced by season, sun exposure, skin pigmentation and duration of symptomatic illness before presentation, none of which was captured. The literature on vitamin D and outcome in childhood ALL is itself inconsistent.[9] The present data are best read as showing no demonstrable relationship between vitamin D status at diagnosis and early treatment toxicity in this cohort, rather than as evidence of a protective effect of deficiency.

No nutritional index predicted infection, despite infection being the commoner outcome and despite the well-established relationship between malnutrition and immune competence in the general paediatric population. Infection during induction is overwhelmingly driven by the depth and duration of chemotherapy-induced neutropenia, and is further modified by leukaemic burden, central venous access, environmental exposure, antimicrobial prophylaxis and institutional supportive care practice. Against this dominant iatrogenic background, any independent contribution of baseline nutritional status is likely to be modest and would require a considerably larger cohort to detect. The high proportion of bacterial sepsis observed here, together with multidrug-resistant Gram-negative isolates in one child in 10, is a reminder that antimicrobial resistance is now a first-order determinant of infectious outcome in Indian paediatric oncology and may plausibly overwhelm host nutritional factors.

This study has a number of strengths. Recruitment was consecutive and prospective, with complete follow-up and no missing data for any exposure or outcome. Nutritional status was classified against internationally standardised WHO references, and exposure was ascertained before any treatment was administered, which excludes reverse causation. Outcomes were defined a priori and graded against a standard instrument. The setting, a government referral hospital serving a largely rural population with care free at the point of delivery, is representative of where most Indian children with leukaemia are actually treated.

Several limitations must be acknowledged. The study was conducted at a single centre with a small cohort, and the resulting confidence intervals are wide; the point estimates should be regarded as imprecise even where statistically significant. With 18 toxicity events, multivariable adjustment was necessarily restricted to two covariates, and residual confounding by risk stratum, protocol intensity and comorbidity cannot be excluded. Nutritional status was assessed only at diagnosis, so nutritional trajectory during therapy, which may itself mediate outcome, was not captured. Mid-upper arm circumference, triceps skinfold thickness and formal body composition assessment were not performed, and these may detect tissue depletion masked by organomegaly more reliably than weight-based indices. Dietary intake, inflammatory markers and functional nutritional assessment were not recorded. Finally, follow-up was limited to eight weeks, so the influence of baseline nutrition on relapse, event-free survival and overall survival could not be evaluated.

The clinical and public health implications are nonetheless reasonably direct. Weight-for-age at diagnosis identifies a subgroup of children at materially higher risk of early treatment morbidity, and does so using a measurement that every paediatric unit in India already records. Embedding formal nutritional classification into the diagnostic workup, and linking an abnormal result to a defined pathway involving dietetic assessment, structured nutritional support and intensified toxicity monitoring, is achievable without additional diagnostic infrastructure. Whether such an intervention reduces toxicity, shortens admission or improves survival remains to be demonstrated, and is the appropriate subject of a multicentre prospective study with serial nutritional assessment and longer follow-up.

CONCLUSION

Among children commencing treatment for acute lymphoblastic leukaemia at a tertiary centre in Kerala, undernutrition at diagnosis was common and low weight-for-age was independently associated with treatment-related toxicity during induction and early consolidation. No baseline nutritional index predicted infection over the same period. Weight-for-age is a simple, inexpensive and universally available measurement, and its incorporation into routine risk assessment at diagnosis offers a practical means of identifying nutritionally vulnerable children for early supportive intervention. Adequately powered multicentre studies with serial nutritional assessment and longer follow-up are required to establish whether early nutritional optimisation translates into reduced treatment morbidity and improved survival.

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