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Original Research Article

Undernutrition or obesity: relationship with long-term survival in children with acute lymphoblastic leukemia in an upper-middle income country: a multicenter cohort study

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Abbreviations: ALL, acute lymphoblastic leukemia; BMAT, bone marrow adipose tissue; CDC, United States Centers for Disease Control and Prevention; CI, confidence intervals; CNS, central nervous system; CR, complete remission; HR, hazard ratios; IMSS, Instituto Mexicano del Seguro Social; MIGICCL, Mexican Interinstitutional Group for the Identification of the Causes of Childhood Leukemia; NCI, National Cancer Institute; OB, obese; OW, overweight; OS, overall survival; SES, socioeconomic status; SS, Secretaría de Salud; UN, undernourished; WBC, white blood cell.

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A B S T R A C T

Background: Long-term survival rates for children with acute lymphoblastic leukemia (ALL) have not improved in some countries, with undernutrition and obesity identified as potential contributing factors.
Objectives: To evaluate the relationship between undernutrition and obesity in long-term survival in Mexican children with ALL.
Methods: A cohort study included children <18 y, newly diagnosed with ALL between 2010 and 2013, treated at 8 public hospitals in Mexico City. Patients were followed from the diagnosis confirmation. Nutritional status at diagnosis was classified with body mass index (BMI) using the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC) criteria. The primary outcome variables were relapse and death >5 y of follow-up. Hazard ratios (HR) with 95% confidence intervals (CI) were reported using a Cox proportional hazards model adjusting for sex, socioeconomic status, immunophenotype, NCI risk classification, and treatment protocol.
Results: A total of 1254 children were diagnosed with ALL. Information was complete for the WHO classification in 1072 patients (85.5%) and for the CDC classification in 997 patients (79.5%). Using WHO criteria, 7% of patients were undernourished, and 13% were overweight or obese; with CDC criteria, the corresponding prevalences were 14.8% and 27.1%. A higher risk of relapse was observed among patients with overweight and obesity (aHR = 1.43; 95% CI: 1.02, 2.00) using the WHO classification. Following the CDC classification, patients with obesity also showed an increased risk of relapse (aHR = 1.33; 95% CI: 0.94; 1.89). Additionally, a higher risk of death was noted among patients with overweight or obesity (aHR = 1.65; 95% CI: 1.25, 2.19) using WHO criteria, whereas under the CDC classification, the increased risk of death was observed in patients with obesity (aHR = 1.65; 95% CI: 1.24, 2.20). No significant associations were found between undernutrition and either relapse or death.
Conclusions: Undernutrition was not associated with long-term survival in pediatric patients with ALL. However, overweight and obesity at diagnosis were associated with relapse and increased mortality, highlighting the importance of addressing these factors through interventions focused on nutritional optimization, especially regarding obesity prevention and management, at or prior to diagnosis, to improve outcomes in Mexican children with ALL.

Keywords: undernutrition, overweight, obesity, mortality, childhood leukemia, survival, childhood cancer, Mexico, latinos, BMI

Introduction

Acute lymphoblastic leukemia (ALL) is the most common childhood cancer worldwide [1]. In Mexico, incidence continues to rise [2], and mortality remains higher than in other countries [3], with no recent improvement [4]. Concurrently, Mexico ranks among the nations with the highest prevalence of childhood overweight and obesity [5]. Although several predictors of adverse outcomes in pediatric ALL are well established, including host characteristics, leukemia biology, treatment protocols, and treatment adherence [6], the prognostic significance of having overweight or obesity at diagnosis remains inconsistent. Some studies suggest that these conditions increase relapse risk and reduce event-free survival [7–10], whereas others do not confirm these associations [11–13]. In parallel, research on bone marrow adipose tissue (BMAT) has advanced considerably [14]. BMAT, which constitutes nearly 45% of marrow volume, is now recognized as a dynamic endocrine organ influencing hematopoiesis. Its effects are mediated by adipokines such as leptin, although evidence regarding their impact on B-lymphopoiesis remains conflicting [15,16]. Moreover, the bone marrow niche is increasingly understood as a protective sanctuary for leukemic cells, contributing to disease initiation, progression, and treatment resistance [14–20]. Adipocytes appear to support these processes by providing metabolic substrates and shielding leukemic blasts from chemotherapy-induced apoptosis through multiple mechanisms [21–24].

On the other hand, Mexico was among the first countries to demonstrate that children with undernutrition and ALL experience significantly poorer long-term survival than those with adequate nutritional status [25]. A second study reported that children with undernutrition had a 2.6-fold higher risk of death during remission induction (95% CI: 0.55, 11.89) compared with well-nourished counterparts [26]. More recently, the Mexican Interinstitutional Group for the Identification of the Causes of Childhood Leukemia (MIGICCL) evaluated undernutrition as a predictor of early mortality. Although undernutrition was not associated with mortality during remission induction, children with undernutrition and high-risk ALL had a significantly increased risk of death at 6 mo (HR 2.08; 95% CI: 1.08, 4.01) [27]. In another study, the same group reported that having overweight or obesity at diagnosis was associated with an increased risk of early death, although not with early relapse [28]. Together, these findings highlight that both undernutrition and excess weight may influence prognosis in pediatric ALL, particularly in resource-limited settings. However, heterogeneity across studies underscores the need for additional research to clarify the long-term impact of nutritional extremes.

Given these gaps, the present study aimed to evaluate the association between nutritional status at diagnosis, specifically undernutrition, overweight, and obesity, and long-term survival in children with ALL treated in an upper-middle income country. We hypothesized that overweight and obesity would be associated with higher long-term risks of relapse and death, whereas undernutrition would not significantly affect survival.

Methods

Study setting and participants

The MIGICCL conducted a multicenter retrospective cohort study across 8 public hospitals in Mexico City. The study included children diagnosed with ALL between January 1, 2010, and December 31, 2013, at any of the participating hospitals. Approval by the National Scientific Research and Ethics Committee of the Mexican Institute of Social Security was obtained with the number R-2015-785-070. Written informed consent for participation was obtained from the parents of the participants or their legal guardians.

The sample size was estimated based on an expected mortality rate of 24% in patients with obesity compared with 10.8% in patients without obesity, using a 2-sided test with 80% statistical power and a 95% confidence level. These estimates were informed by the study of Baillargeon et al. [29] in a cohort of predominantly Hispanic children with ALL. Based on these parameters, the minimum required sample included 83 patients with obesity and 330 patients without obesity to detect statistically significant differences in mortality between the

groups. Each child was followed for 60 mo from the time of diagnosis confirmation. The diagnosis of ALL was based on the morphological and immunophenotypic characteristics of leukemic cells. The participating institutions were the Instituto Mexicano del Seguro Social (IMSS), the Secretaría de Salud (SS), the Secretaría de Salud de la Ciudad de Mexico, and the Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado. All patients were treated according to the chemotherapy protocol of the hospital where they received medical care, including the St. Jude Total Therapy Study XIII-B protocol [30], the Modified ALL-BFM-95 protocol [31], and the DFCI-ALL Consortium Protocol 00-01 protocol [32], which will be analyzed in another manuscript.

Data collection

Information regarding child's sex, age at diagnosis, place of residence, white blood cell (WBC) count, immunophenotype (B or T lineage), weight, and height (or length when appropriate) at diagnosis, and treatment protocol was collected from the patient's clinical charts by previously standardized staff. Maternal education was used as a proxy for socioeconomic status (SES), categorized according to the strata previously applied in the Childhood Cancer & Leukemia International Consortium studies [33]: 0–9 y, 9.1–12.9 y, and ≥13 y. Risk classification was based on the criteria of the National Cancer Institute (NCI): standard risk (ages 1–9.99 y; WBC count $< 50 \times 10^9$/L) or high risk (age <1 y or ≥10 y, or WBC $\geq 50 \times 10^9$/L). Mortality was defined as the death of a patient at any time and from any cause, from the confirmation of diagnosis through 5 y of follow-up. Relapse in the bone marrow was defined as the presence of ≥25% lymphoblasts in a bone marrow aspirate after achieving complete remission (CR). Central nervous system (CNS) relapse was characterized by the presence of morphologically identified lymphoblasts in cerebrospinal fluid cytocentrifuge preparations with a mononuclear cell count ≥5/mL, cranial nerve paralysis, or any other extramedullary site, ≥ 60 mo following the first CR.

Assessment of nutritional status at diagnosis of ALL

BMI (in kg/m^2) at diagnosis was used in the analysis. In this study, undernutrition was defined specifically as low BMI-for-age (thinness), following international recommendations from the WHO and the Centers for Disease Control and Prevention (CDC). This operational definition corresponds to a BMI-for-age Z score below −2 SD (and <−3 SD for severe undernutrition) using WHO standards, and <5th percentile using CDC criteria [34]. It is important to note that in this context, undernutrition refers exclusively to thinness based on BMI-for-age and does not include other anthropometric dimensions, such as chronic stunting (low height-for-age) or acute wasting (low weight-for-height), which were not assessed due to data limitations. Using WHO Anthro and AnthroPlus for PC software (version 3.2.2, World Health Organization), the BMI-for-age *z*-scores were calculated for each patient. Using the WHO classification, patients were categorized as normal (−1.9999 to 0.9999), undernourished (−2 to −2.9999), severely undernourished (≥−3), at risk of overweight (1 to –1.9999), overweight (2–2.9999), and obese (≥3) [34]. In addition, the BMI percentiles cutoffs provided by the CDC were as follows: normal (p5 – 84.9999), undernourished (< p5), overweight (p85 – 94.9999), and obese (≥ p95). Children <2 y of age were excluded from the CDC BMI classification analysis, as BMI measurements are less reliable for this age group due to early childhood growth variations. Additionally, the CDC calculator used in this study reports BMI data for children and adolescents aged 2–19 [35]. This dual approach allowed us to conduct meaningful epidemiological comparisons using WHO *z*-scores, while also reporting findings in clinically interpretable terms using CDC percentiles. It also ensures consistency with prior literature and guidelines, which often report results using both systems for comparability [36–39].

The nutritional classification and validation of weight and height measurements recorded in clinical files to classify patients' nutritional status in the present study have been described elsewhere [27].

Statistical analysis

Data analyses were performed using SPSS version 30 (IBM Corp). Descriptive statistics were generated to summarize baseline demographic and clinical characteristics. Time-to-event outcomes (relapse and death) were evaluated using Cox proportional hazards models, and hazard ratios (HRs) with 95% confidence intervals (CIs) were estimated. An alpha level of 0.05 was used as the threshold for statistical significance. For all models, the reference group was defined using the BMI classification system applied. Under the WHO criteria, children with normal BMI-for-age values (−1.99 to +0.99 SD) served as the reference category. Under the CDC criteria, the reference group consisted of children whose BMI-for-age percentiles fell within the normal range (5th to <85th percentile). All HRs presented in the results represent comparisons between each nutritional status category and its respective reference group.

Survival analyses were conducted separately for relapse [disease-free survival(DFS)] and mortality events [overall survival, (OS)] over a follow-up period of >5 y. DFS was defined as the time from diagnosis to the earliest occurrence of relapse, death, or last follow-up. Patients who did not experience an event were right censored at the date of their last contact. OS was measured from diagnosis until death from any cause or last follow-up. Importantly, patients who experienced relapse remained in risk set for the OS analysis. Right-censoring was applied at the last known follow-up date for patients who were alive at the end of the study period. The covariates included in the multivariable models were selected a priori using a theory-driven approach, based on their well-established association with relapse and mortality in pediatric ALL, as documented consistently in the literature, including age, sex, socioeconomic status, immunophenotype, NCI risk classification, and treatment protocol. Gene rearrangements were excluded due to incomplete data in a large proportion of patients. A high correlation (0.64) was observed between age and NCI risk classification using correlation matrix analysis. Two Cox proportional hazards models were developed to address potential collinearity between age and NCI risk classification. In the first model, age was included; in the second, it was excluded. The hazard ratio for obesity was 1.647 with age in the model and 1.648 without it, a negligible difference of 0.06%. Given this minimal variation and to avoid multicollinearity, age was excluded from the final model. NCI risk classification was retained, as it already incorporates age and white blood cell count, providing a more comprehensive risk stratification. Interaction terms between nutritional status and each control variable (treatment protocol, immunophenotype, sex, maternal education, and NCI risk classification) were tested. To evaluate the relevance of including these interactions, the models were compared with and without interactions by estimating the difference in −2 log-likelihood values and degrees of freedom, which showed no significant improvement in model fit ($\chi^2 = 23.213$, df = 16, $P > 0.1$). As a result, the final model excluded interaction terms. To assess the proportional hazards assumption, the Schoenfeld residuals were calculated and plotted (data not shown). The analysis demonstrated that the

hazards associated with undernutrition and obesity remained stable over the 5-y follow-up period, under both WHO and CDC classifications. Consequently, the most parsimonious model included sex, SES, immunophenotype, NCI risk classification, treatment protocol, and nutritional status.

Results

During the study period, 1254 children were diagnosed with ALL at the participating hospitals; their baseline characteristics are shown in Table 1. Of these, 26 children (2.1%) were excluded due to Down syndrome, as their biological and clinical profiles require a separate analytical approach. An additional 113 children (9%) could not be included because they were nonresidents of Mexico City and lacked follow-up information, and 43 children (3.5%) were excluded due to missing weight and/or height measurements at diagnosis, which prevented BMI calculation. Consequently, 1,072 patients (85.5%) had complete anthropometric data for WHO BMI classification, and 997 patients (79.5%) had complete information for CDC BMI classification (Figure 1). A comparative analysis demonstrated significant differences in 3 baseline characteristics between patients included in the BMI analysis and those excluded due to missing BMI data: sex, age, and treatment protocol. Among patients without available nutritional status measurements, 13.5% were aged ≥15 y compared with 6.7% among those included ($P = 0.04$), 54.5% were female compared with 44.4% in the included group ($P = 0.02$), and 82.1% had received the St. Jude Total XIII-B regimen compared with 47.9% of those included ($P < 0.01$).

Among the 1,072 children eligible for WHO classification, 75 (7%) were younger than 24 mo and were therefore not included in the CDC classification, in accordance with CDC guidelines, which do not recommend BMI-for-age percentiles for children <2 y of age. For this age group, WHO charts are preferred. A comparison of demographic and clinical features between children ≥24 mo and those <24 mo showed no significant differences in sex distribution, immunophenotype, NCI risk status, parental education, or household crowding (data not shown). However, infants (<24 mo) exhibited significantly higher frequencies of adverse prognostic indicators, including leukocyte counts $>50 \times 10^9$/L, high-risk genetic rearrangements (e.g., MLL-AFF1, BCR-ABL1), CNS-3 involvement, and increased rates of relapse and death ($P < 0.01$).

Using the WHO BMI classification, 660 patients (61.6%) had a normal nutritional status, 197 patients (18.4%) were at risk of overweight (ROW), 95 patients (8.8%) had overweight (OW), and 45 patients (4.2%) had obesity (OB). Using the CDC classification, the distribution was as follows: 579 patients (58.1%) had a normal nutritional status, 148 patients (14.8%) had undernutrition, 129 patients (13%) had OW, and 141 patients (14.1%) had OB. Most patients classified as OW by WHO (92%) also met the criteria for OB using CDC BMI classification.

A total of 300 relapses (24.8%) occurred in the entire population. The primary sites of relapse were bone marrow (62.6%), followed by the central nervous system (4.7%). Furthermore, the overall mortality rate ≤5-y was 30.7% (n = 385) (Table 1). The variables associated with an increased risk of relapse or death are presented in Supplementary Table 1.

Table 2 shows the percentage and HRs for relapse in patients with ALL over a 60-mo follow-up, categorized by BMI using WHO and CDC criteria. Using the WHO classification, patients with

TABLE 1
Characteristics of pediatric patients with ALL diagnosed between 2010 and 2013 at participating hospitals in Mexico City (n = 1254)

Variable	n	(%)
Child's sex		
Female	570	(45.5)
Male	684	(54.5)
Age at diagnosis (age group in years)		
<1	34	(2.7)
1–4	486	(38.8)
5–9	354	(28.2)
10–14	286	(22.8)
≥15	94	(7.5)
Leukocyte count at diagnosis in peripheral blood (/μL)		
<50,000	978	(78.0)
>50,000	276	(22.0)
Immunophenotype		
T-lineage	116	(9.4)
B-precursor	1084	(86.4)
Mature B-cells	20	(1.6)
Biphenotypic	34	(2.8)
Gene rearrangements		
Performed	771	(61.5)
Detected	118	(15.3)
ETV6/RUNX1	55	(7.1)
TCF3/PBX1	37	(4.8)
BCR/ABL1	18	(2.3)
MLL/AFF1	8	(1.0)
Not detected	653	(53.1)
Not performed	483	(38.5)
Risk classification[1]		
Standard	691	(55.1)
High	563	(44.9)
Stacking level (Bronfmaṅs criteria)		
Not crowded	194	(15.5)
Semicrowded and crowded	1060	(84.5)
Place of residence		
Outside Mexico City	286	(22.8)
Residents of Mexico City	968	(77.2)
Mother's education level (years of schooling)		
0–9	314	(25.0)
9.1–12.9	749	(59.7)
≥13	191	(15.2)
Father's education level (years of schooling)		
0–9	330	(26.3)
9.1–12.9	690	(55.0)
≥13	234	(18.7)
Nonrespondents	324	(25.8)
Nutritional status using WHO criteria (85%, N = 1072)		
Severely undernourished (≥−3)	26	(2.4)
Undernourished (−2 to 2.99)	49	(4.6)
Normal (−1.99 to 0.99)	660	(61.6)
Risk of overweight (1–1.99)	197	(18.4)
Overweight (2–2.99)	95	(8.8)
Obese (≥3)	45	(4.2)
Nutritional status using CDC criteria (79.5%, N = 997)		
Undernourished (<p5)	148	(14.8)
Normal (5–84.99)	579	(58.1)
Overweight (p85–94.99)	129	(13.0)
Obese (p > 95)	141	(14.1)
Relapse within 60 mo		
No	909	(75.2)
Yes	300	(24.8)
Missing data	45	(3.6)
Sites of relapse		
Bone marrow (isolated)	194	(62.6)
Central nervous system (isolated)	59	(4.7)
Bone marrow + other site	41	(3.3)
Testicle/ovary	9	(0.7)

(continued on next page)

TABLE 1 (*continued*)

Variable	n	(%)
Parotid	7	(0.6)
Death within 60 mo		
No	824	(65.7)
Yes	385	(30.7)
Missing data	45	(3.6)

[1] Risk classification using the National Cancer Institute criteria.

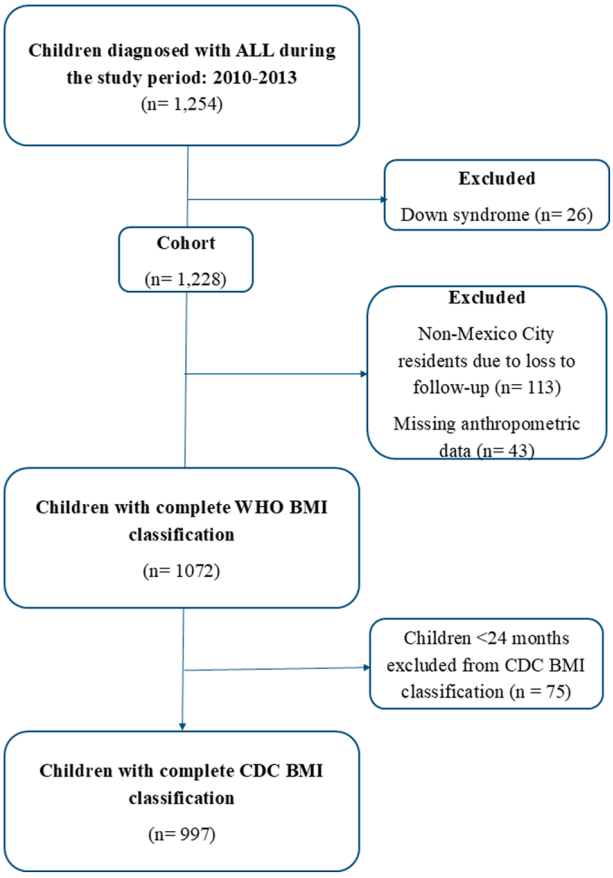

FIGURE 1. Children diagnosed with ALL, between January 1, 2010, and December 31, 2013. Distribution of cases analyzed using WHO criteria and CDC criteria.

undernutrition had a relapse HR of 0.62, which was not statistically significant. In contrast, patients with OW showed a significantly increased relapse risk (HR = 1.62; 95% CI: 1.11, 2.37), whereas OB was not significantly associated with relapse. Using the CDC classification, the HRs for relapse in patients with undernutrition and overweight were also not significant. However, obesity was significantly associated with relapse (HR = 1.41; 95% CI: 1.00, 2.01).

Table 3 presents the HRs for mortality, also over a 60-mo period and based on WHO and CDC BMI classifications. For the WHO-based analysis, groups with similar risk profiles observed in the separate analyses (Table 2) were merged: patients with normal BMI and those with risk of overweight were combined as the reference group, whereas patients with OW and OB were grouped together, as were patients with undernutrition and severe undernutrition. In this model, the group with OW and OB had a significantly higher mortality risk (HR = 1.65; 95% CI: 1.25, 2.19). The group with undernutrition and severe undernutrition had a lower, nonsignificant mortality risk (HR = 0.87; 95% CI: 0.53, 1.43). Based on the CDC classification, normal-weight and OW patients were grouped as the reference category. Patients with obesity had the highest mortality risk (HR = 1.65; 95% CI: 1.24, 2.20), whereas patients with undernutrition showed the lowest risk (HR = 0.80; 95% CI: 0.54, 1.17).

Survival curves (Figures 2 and 3) visually confirm that patients with OW or OB had the lowest survival probabilities. Using the WHO classification, patients with OW or OB showed a higher risk of relapse, whereas patients with undernutrition had a lower risk of relapse (Supplementary Figures 1 and 2). However, after adjusting for covariates, the HR associated with undernutrition and relapse was not statistically significant (aHR = 0.73; 95% CI: 0.49, 1.09; $P > 0.12$), indicating that the observed trend may be attributable to random variation rather than a true protective association (Table 3).

Discussion

Consistent with prior evidence [40], children with overweight or obesity included in the present research experienced poorer outcomes in ALL. These observations align with broader evidence: meta-analyses by Orgel et al. [41] and Amankwah et al. [42] reported that higher BMI at diagnosis is associated with poorer survival and increased mortality in pediatric ALL. Similarly, Egnell et al. [43] observed greater relapse risk among children with low weight, OW, or

TABLE 2
Association between Nutritional Status Classification based on age-specific BMI categories per WHO and CDC and relapse risk during the first 60 mo after acute lymphoblastic leukemia diagnosis

	No relapse	Relapse	HR (95% CI)
	n (%)	n (%)	
WHO classification (n = 1072)			
Normal (−1.99 to 0.99) (ref.)	489 (74.1)	171 (25.9)	
Risk of overweight (1–1.99)	148 (75.1)	49 (24.9)	0.96 (0.70, 1.32)
Overweight (2–2.99)	63 (66.3)	32 (33.7)	1.62 (1.11, 2.37)
Obese (≥3)	35 (77.8)	10 (22.2)	1.04 (0.55, 1.97)
Undernourished (−2 to 2.99)	41 (83.7)	8 (16.3)	0.62 (0.30, 1.26)
Severely Undernourished (≥−3)	20 (76.9)	6 (23.1)	0.93 (0.41, 2.10)
CDC classification (n = 997)			
Normal (5–84.99) (ref.)	437 (75.5)	142 (24.5)	
Undernourished (<p5)	120 (81.1)	28 (18.9)	0.72 (0.48, 1.07)
Overweight (p85–94.99)	95 (73.6)	34 (26.4)	1.07 (0.74, 1.56)
Obese (p > 95)	101 (71.6)	40 (28.4)	1.41 (1.00, 2.01)

HR, hazard ratio; 95% CI, 95% confidence interval; CDC, Centers for Disease Control; Ref., reference group for all HRs.

TABLE 3
Association between nutritional status classification based on age-specific BMI categories per WHO and CDC and death and relapse risk during the first 60 months after acute lymphoblastic leukemia diagnosis

	n (%)	Death Risk		Relapse Risk	
		aHR (95% CI)	*P* value	aHR (95% CI)	*P* value
WHO (N = 1072)					
Normal/risk of OW (ref.)	857 (79.4)	———	———	———	———
OW/OB	140 (13.0)	1.65 (1.25, 2.19)	0.000	1.43 (1.02, 2.00)	0.037
UN/SUN	148 (14.8)	0.87 (0.53, 1.42)	0.578	0.73 (0.42, 1.27)	0.261
CDC (N = 997)					
Normal/OW (ref.)	708 (71.0)	———	———	———	———
OB	141 (14.1)	1.65 (1.24, 2.20)	0.001	1.33 (0.94, 1.89)	0.107
UN	148 (14.8)	0.80 (0.54, 1.17)	0.246	0.73 (0.49, 1.09)	0.124

Abbreviations: HR, hazard ratio; 95% CI, 95% confidence interval; aHR, adjusted hazard ratio; CDC, Centers for Disease Control; OW, overweight; OB, obesity; UN, undernourished; SUN, severely undernourished.
The model was adjusted for sex, socioeconomic status, immunophenotype, NCI, risk classification, and treatment protocol. Ref., reference group for all HRs.

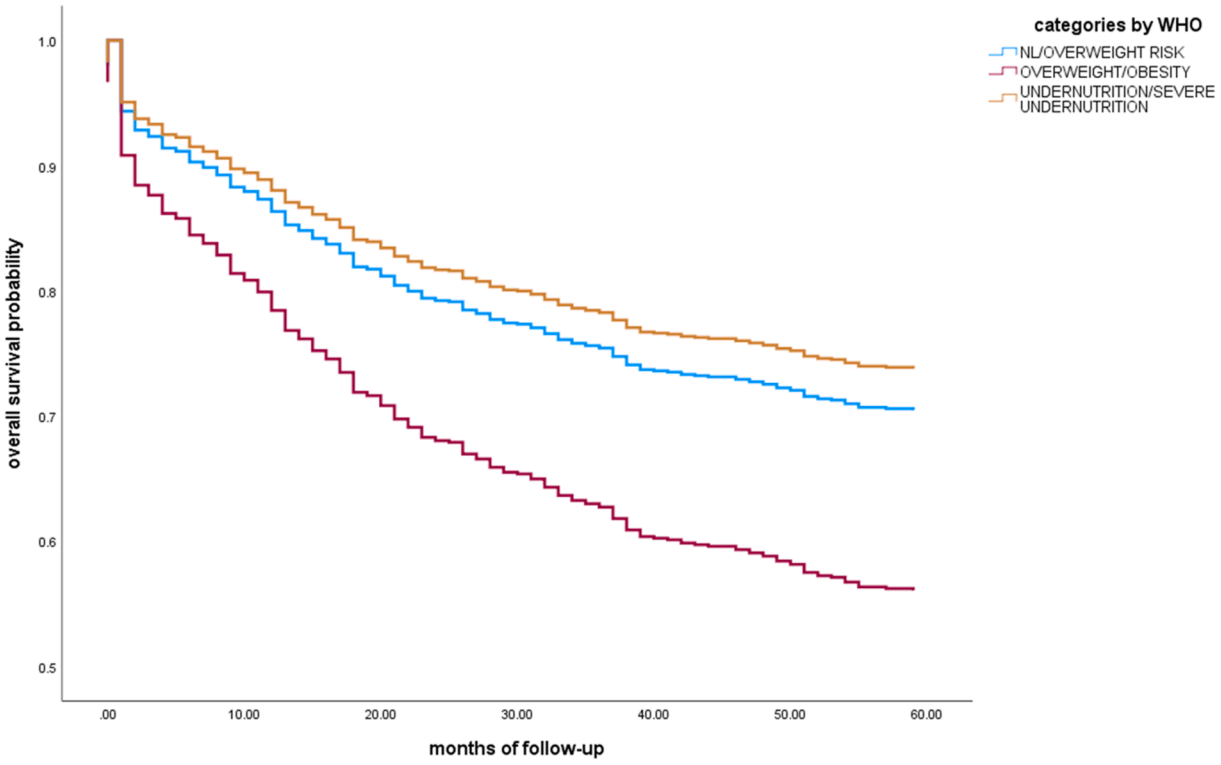

FIGURE 2. The overall survival curve was estimated using the Cox proportional hazards model. The curves are presented using the WHO categories. NL, normal.

OB compared with those with healthy weight, with age-stratified analyses suggesting that the adverse impact of high BMI may be more pronounced in adolescents than in younger children.

Undernutrition was not associated with poorer prognosis in our cohort, with outcomes resembling those of children with normal weight or at risk of overweight, consistent with some studies [40–43] but differing from reports showing adverse effects [25,26,41]. This null finding may reflect the urban setting, where undernutrition is less prevalent and less severe than in other Mexican regions [44] and many LMIC/UMIC contexts. Additional explanations include potential differences in supportive care for undernourished patients, the lack of data on duration or severity of undernutrition during follow-up, and possible survivor bias if the sickest children died before diagnosis. Although unadjusted analyses suggested a protective pattern, this was not statistically significant after adjustment. Given that Mexico City shares characteristics with other major urban centers, these results may apply to similar settings but warrant caution when extrapolated to rural or underserved populations. In contrast, substantial mechanistic and clinical evidence links obesity with adverse outcomes in pediatric ALL [45]. Leukemic blasts can migrate into adipose tissue, where mediators such as Galectin-9 enhance survival [19]. Obesity-driven increases in insulin, IGF-1, IL-6, TNF-α, and IL-1β activate PI3K/AKT and mTOR pathways, promoting leukemic proliferation, angiogenesis, and genomic instability [45,46]. Additional mechanisms include STAT3/NF-κB–mediated methotrexate resistance [47], adipocyte sequestration and metabolism of chemotherapeutics through AKR1C3 and CBR1 [48,49], and adipocyte-induced blast quiescence that reduces sensitivity to cytotoxic therapy [50]. Adipocytes also

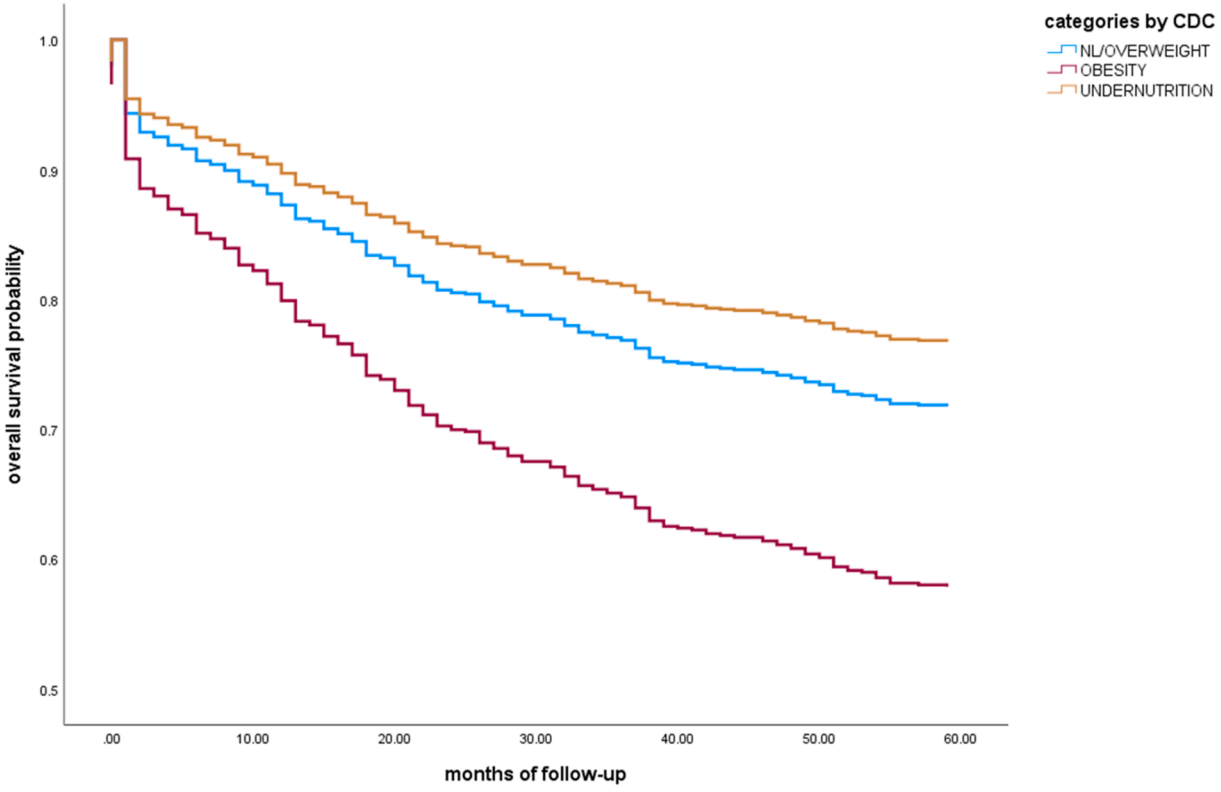

FIGURE 3. The overall survival curve was estimated using the Cox proportional hazards model. The curves are presented using the United States Centers for Disease Control and Prevention (CDC) categories. NL, normal.

supply metabolic substrates that reduce responsiveness to agents such as L-asparaginase [49]. Moreover, chronic low-grade inflammation and leptin-driven immune dysregulation further weaken antileukemic immunity [51–53]. These effects may be amplified in Mexican children, particularly in marginalized or semirural settings where OB often coexists with metabolic dysfunction, inflammation, excess adiposity, and micronutrient deficiencies [54].

Given this evidence, understanding how treatment exposures interact with nutritional status is essential. Although the 3 protocols used in this cohort have comparable overall survival, they differ in the intensity, timing, and type of glucocorticoids and other agents administered. The Modified ALL-BFM-95 protocol delivers the highest cumulative dexamethasone dose during maintenance [31], whereas DFCI-ALL 00-01 incorporates repeated prednisone pulses and prolonged L-asparaginase exposure, both of which may influence weight gain and metabolic parameters over time [32]. The St. Jude Total XIII-B protocol also includes scheduled dexamethasone during maintenance [30]. These pharmacologic differences may shape nutritional trajectories during therapy and should be considered when interpreting BMI-related risks. In our study, the nutritional status was assessed exclusively before chemotherapy initiation. This approach minimizes confounding from treatment-related weight fluctuations and allows a more precise estimation of the prognostic impact of baseline obesity and undernutrition.

Study limitations

A primary limitation of this study is the use of BMI as the only indicator of nutritional status. Although widely applied in pediatric oncology, BMI cannot differentiate between lean and fat mass and may not fully capture the components of body composition most relevant to prognosis in children with ALL [55]. Moreover, nutritional status was assessed exclusively at diagnosis; therefore, changes in BMI or weight trajectories during treatment, which may influence treatment tolerance, metabolic responses, and overall prognosis, were not evaluated [56]. Longitudinal assessments are required to clarify how dynamic nutritional and metabolic alterations during therapy affect outcomes.

In addition, discrepancies between the WHO and CDC growth standards warrant consideration, as they generated markedly different prevalences of children classified as having undernutrition in our cohort (7% vs. 14.8%). The CDC 2000 charts, derived from a more heterogeneous reference population, tend to identify a higher proportion of children with undernutrition, particularly around 2 y of age when the transition from WHO to CDC charts produces abrupt shifts in growth percentiles [57]. These differences are further influenced by methodological factors, including the change from recumbent length to standing height and the absence of smoothing between reference datasets. Although recently developed smoothed transition charts substantially reduce these inconsistencies, minor misclassification may persist in certain age groups [57]. Nevertheless, these discrepancies are expected and do not compromise the interpretation of our findings.

Another limitation is missing BMI measurements. Children without BMI data differed in age, sex, and treatment protocol. Although adolescents were more frequent among excluded cases, this group also had a higher proportion of females, linked to more favorable outcomes in childhood ALL [58]. Furthermore, sensitivity analyses using both worst-case and best-case imputation scenarios demonstrated consistent directions of association across WHO and CDC classifications, with only minor variations in effect size, reinforcing the robustness of our conclusions (data not shown).

It is also important to note that children <24 mo were excluded from the CDC BMI-for-age classification. Although this exclusion did not introduce systematic differences in baseline characteristics, these infants exhibited higher-risk clinical features and poorer outcomes, patterns consistent with the aggressive biology of infant ALL, including MLL rearrangements, leukocytosis, and early CNS involvement [59–61]. Their exclusion does not compromise the validity of BMI-related results; instead, it highlights the need for age-tailored therapeutic approaches in this particularly vulnerable subgroup.

Finally, although formal testing confirmed that the proportional hazards assumption was met, the possibility of residual bias due to unmeasured confounding or subtle violations of model assumptions cannot be entirely excluded. We also evaluated potential interactions between nutritional status and covariates, which were not statistically significant. These analyses strengthen the robustness of our findings; however, inherent limitations of observational survival analyses remain.

Public health and clinical implications

OW and OB at diagnosis were strongly associated with higher relapse and mortality, highlighting their importance for both clinical care and population health. Nutritional interventions should prioritize preventing and managing obesity at diagnosis to improve survival in pediatric ALL. Although undernutrition warrants clinical attention, our data indicate it is less influential on survival than obesity in this setting. In Mexico, where childhood obesity continues to rise, early weight-focused strategies could mitigate treatment complications and long-term cardiometabolic risks among survivors.

Conclusions

In this pediatric population with ALL, undernutrition was not associated with long-term survival, whereas OW and OB at diagnosis were strongly linked to higher relapse and mortality. These results identify obesity as a key modifiable factor in ALL prognoses. Early recognition and targeted weight management at or before diagnosis may improve survival and reduce long-term health burdens, particularly in settings, such as Mexico with rising childhood obesity rates.

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Author contributions

The authors' responsibilities were as follows – EJH and JFL: concept and study design, data curation, analysis and data interpretation, investigation, writing – original draft, writing – review & editing; AMS, EMDA, LEEH, RAS, JGPG, BVG, JRTN, RMEE, LVFV, MLPS, KASL, HRV, MMR, JAMT, SJM, MGJ, MMZT, JAG, JMZ, and FVFP: writing – original draft, writing – review & editing, analysis and data interpretation, investigation; JCNE and JMMA: concept and study design, data curation, analysis and data interpretation, funding acquisition, investigation, project administration, resources, supervision, writing – original draft, writing – review & editing; and all authors: have read and approved the final version of the manuscript.

Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article.

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Data availability

Data described in the article will be available upon request pending application and approval.

Patient consent statement

Written informed consent for participation was obtained from the parents of the participants or their legal guardians.

Ethics statement

Approval by the National Scientific Research and Ethics Committee of the Mexican Institute of Social Security was obtained with the number R-2015-785-070. The study was conducted in accordance with the local legislation and institutional requirements as well as the ethical standards outlined in the Declaration of Helsinki.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ajcnut.2025.101180.

References

[1] E. Steliarova-Foucher, M. Colombet, L.A.G. Ries, F. Moreno, A. Dolya, F. Bray, et al., International incidence of childhood cancer, 2001-10: a population-based registry study, Lancet Oncol 18 (2017) 719–731, https://doi.org/10.1016/S1470-2045(17)30186-9.

[2] J. Flores-Lujano, D.A. Duarte-Rodríguez, E. Jiménez-Hernández, J.A. Martín-Trejo, A. Allende-López, J.G. Peñaloza-González, et al., Persistently high incidence rates of childhood acute leukemias from 2010 to 2017 in Mexico City: a population study from the MIGICCL, Front. Public Health. 10 (2022) 918921, https://doi.org/10.3389/FPUBH.2022.918921.

[3] L. Chatenoud, P. Bertuccio, C. Bosetti, F. Levi, E. Negri, C. La Vecchia, Childhood cancer mortality in America, Asia, and Oceania, 1970 through 2007, Cancer. 116 (21) (2010) 5063–5074, https://doi.org/10.1002/CNCR.25406.

[4] P. Muñoz-Aguirre, M. Zapata-Tarrés, P. Espinosa-Tamez, H. Sánchez-Blas, M. Brochier, H. Lamadrid-Figueroa, Childhood acute lymphoblastic leukemia in Mexico: mortality trend analysis, 1998-2018, Salud Publica Mex 64 (1) (2022) 26–34, https://doi.org/10.21149/13210.

[5] T. Shamah-Levy, L. Cuevas-Nasu, E.B. Gaona-Pineda, D.G. Valenzuela-Bravo, I. Méndez Gómez-Humarán, M.A. Ávila-Arcos, Childhood obesity in Mexico: influencing factors and prevention strategies, Front. Public Health 10 (2022) 949893, https://doi.org/10.3389/FPUBH.2022.949893.

[6] A.L.H. Pai, M.E. Mcgrady, Assessing medication adherence as a standard of care in pediatric oncology, Pediatr, Blood Cancer 62 (Suppl 5) (2015) S696–S706, https://doi.org/10.1002/PBC.25795.

[7] A.M. Butturini, F.J. Dorey, B.J. Lange, D.W. Henry, P.S. Gaynon, C. Fu, et al., Obesity and outcome in pediatric acute lymphoblastic leukemia, J. Clin. Oncol. 25 (2007) 2063–2069, https://doi.org/10.1200/JCO.2006.07.7792.
[8] C.B. Gelelete, S.H. Pereira, A.M.B. Azevedo, L.S. Thiago, M. Mundim, M.G. P. Land, et al., Overweight as a prognostic factor in children with acute lymphoblastic leukemia, Obesity (Silver Spring). 19 (2011) 1908–1911, https://doi.org/10.1038/OBY.2011.195.
[9] M.C. Ethier, S. Alexander, O. Abla, G. Green, R. Lam, L. Sung, Association between obesity at diagnosis and weight change during induction and survival in pediatric acute lymphoblastic leukemia, Leuk. Lymphoma 53 (2012) 1677–1681, https://doi.org/10.3109/10428194.2012.664843.
[10] E. Orgel, R. Sposto, J. Malvar, N.L. Seibel, E. Ladas, P.S. Gaynon, et al., Impact on survival and toxicity by duration of weight extremes during treatment for pediatric acute lymphoblastic leukemia: a report from the Children's Oncology Group, J. Clin. Oncol. 32 (13) (2014) 1331–1337, https://doi.org/10.1200/JCO.2013.52.6962.
[11] N. Hijiya, J.C. Panetta, Y. Zhou, E.P. Kyzer, S.C. Howard, S. Jeha, et al., Body mass index does not influence pharmacokinetics or outcome of treatment in children with acute lymphoblastic leukemia, Blood 108 (2006) 3997–4002, https://doi.org/10.1182/blood-2006-05-024414.
[12] F.K. Aldhafiri, J.H. McColl, J.J. Reilly, Prognostic significance of being overweight and obese at diagnosis in children with acute lymphoblastic leukemia, J. Pediatr. Hematol. Oncol. 36 (2014) 234–236, https://doi.org/10.1097/MPH.0000000000000056.
[13] H.M. Eissa, Y. Zhou, J.C. Panetta, E.K. Browne, S. Jeha, C. Cheng, et al., The effect of body mass index at diagnosis on clinical outcome in children with newly diagnosed acute lymphoblastic leukemia, Blood Cancer J 7 (2017) e531, https://doi.org/10.1038/BCJ.2017.11.
[14] B. Lecka-Czernik, S. Baroi, L.A. Stechschulte, A.S. Chougule, Marrow fat-a new target to treat bone diseases? Curr. Osteoporos Rep. 16 (2018) 123–129, https://doi.org/10.1007/S11914-018-0426-Z.
[15] B.D. Bennett, G.P. Solar, J.Q. Yuan, J. Mathias, G.R. Thomas, W. Matthews, A role for leptin and its cognate receptor in hematopoiesis, Curr. Biol. 6 (9) (1996) 1170–1180, https://doi.org/10.1016/S0960-9822(02)70684-2.
[16] P. Żelechowska, E. Brzezińska-Błaszczyk, A. Kusowska, E. Kozłowska, The role of adipokines in the modulation of lymphoid lineage cell development and activity: an overview, Obes. Rev. 21 (10) (2020) e13055, https://doi.org/10.1111/OBR.13055.
[17] D. Duarte, E.D. Hawkins, C. Lo Celso, The interplay of leukemia cells and the bone marrow microenvironment, Blood 131 (2018) 1507–1511, https://doi.org/10.1182/BLOOD-2017-12-784132.
[18] A.M. Hughes, V. Kuek, R.S. Kotecha, L.C. Cheung, The bone marrow microenvironment in B-cell development and malignancy, Cancers (Basel) 14 (2022) 2089, https://doi.org/10.3390/CANCERS14092089.
[19] R. Pramanik, X. Sheng, B. Ichihara, N. Heisterkamp, S.D. Mittelman, Adipose tissue attracts and protects acute lymphoblastic leukemia cells from chemotherapy, Leuk. Res. 37 (2013) 503–509, https://doi.org/10.1016/j.leukres.2012.12.013.
[20] J.C. Balandrán, J. Purizaca, J. Enciso, D. Dozal, A. Sandoval, E. Jiménez-Hernández, et al., Pro-inflammatory-related loss of CXCL12 niche promotes acute lymphoblastic leukemic progression at the expense of normal lymphopoiesis, Front. Immunol. 7 (2017) 666, https://doi.org/10.3389/FIMMU.2016.00666.
[21] X. Sheng, J. Tucci, J.H. Parmentier, L. Ji, J.W. Behan, N. Heisterkamp, et al., Adipocytes cause leukemia cell resistance to daunorubicin via oxidative stress response, Oncotarget 7 (2016) 73147–73159, https://doi.org/10.18632/ONCOTARGET.12246.
[22] M.C. Delahaye, K.I. Salem, J. Pelletier, M. Aurrand-Lions, S.J. C. Mancini, Toward therapeutic targeting of bone marrow leukemic niche protective signals in B-cell acute lymphoblastic leukemia, Front. Oncol. 10 (2021) 606540, https://doi.org/10.3389/FONC.2020.606540.
[23] J. Tucci, T. Chen, K. Margulis, E. Orgel, R.L. Paszkiewicz, M.D. Cohen, et al., Adipocytes provide fatty acids to acute lymphoblastic leukemia cells, Front. Oncol. 11 (2021) 665763, https://doi.org/10.3389/FONC.2021.665763.
[24] M.S. Shafat, T. Oellerich, S. Mohr, S.D. Robinson, D.R. Edwards, C. R. Marlein, et al., Leukemic blasts program bone marrow adipocytes to generate a protumoral microenvironment, Blood 129 (2017) 1320–1332, https://doi.org/10.1182/BLOOD-2016-08-734798.
[25] E. Lobato-Mendizábal, G.J. Ruiz-Argüelles, A. Marín-López, Leukaemia and nutrition I: malnutrition is an adverse prognostic factor in the outcome of treatment of patients with standard-risk acute lymphoblastic leukaemia, Leuk. Res. 13 (1989) 899–906, https://doi.org/10.1016/0145-2126(89)90043-X.
[26] J.M. Mejía-Aranguré, A. Fajardo-Gutiérrez, N.I. Reyes-Ruíz, R. Bernáldez-Ríos, A.M. Mejía-Domínguez, S. Navarrete-Navarro, et al., Malnutrition in childhood lymphoblastic leukemia: a predictor of early mortality during the induction-to-remission phase of the treatment, Arch. Med. Res. 30 (1999) 150–153, https://doi.org/10.1016/S0188-0128(98)00026-8.
[27] J.A. Martín-Trejo, J.C. Núñez-Enríquez, A. Fajardo-Gutiérrez, A. Medina-Sansón, J. Flores-Lujano, E. Jiménez-Hernández, et al., Early mortality in children with acute lymphoblastic leukemia in a developing country: the role of malnutrition at diagnosis. A multicenter cohort MIGICCL study, Leuk. Lymphoma 58 (2017) 898–908, https://doi.org/10.1080/10428194.2016.1219904.
[28] J.C. Núñez-Enríquez, A.E. Gil-Hernández, E. Jiménez-Hernández, A. Fajardo-Gutiérrez, A. Medina-Sansón, J. Flores-Lujano, et al., Overweight and obesity as predictors of early mortality in Mexican children with acute lymphoblastic leukemia: a multicenter cohort study, BMC Cancer 19 (2019) 708, https://doi.org/10.1186/s12885-019-5878-8.
[29] J. Baillargeon, A.M. Langevin, M. Lewis, J. Estrada, J. Mullins, A. Pitney, et al., Obesity and survival in a cohort of predominantly Hispanic children with acute lymphoblastic leukemia, J. Pediatr. Hematol. Oncol. 28 (2006) 575–578, https://doi.org/10.1097/01.MPH.0000212985.33941.D8.
[30] C.H. Pui, J.T. Sandlund, D. Pei, D. Campana, G.K. Rivera, R.C. Ribeiro, et al., Improved outcome for children with acute lymphoblastic leukemia: results of total therapy study XIIIB at St Jude Children's Research Hospital, Blood 104 (2004) 2690–2696, https://doi.org/10.1182/BLOOD-2004-04-1616.
[31] A. Möricke, M. Zimmermann, A. Reiter, G. Henze, A. Schrauder, H. Gadner, et al., Long-term results of five consecutive trials in childhood acute lymphoblastic leukemia performed by the ALL-BFM study group from 1981 to 2000, Leukemia 24 (2010) 265–284, https://doi.org/10.1038/LEU.2009.257.
[32] E. Jiménez-Hernández, E.Z. Jaimes-Reyes, J. Arellano-Galindo, X. García-Jiménez, H.M. Tiznado-García, M.T. Dueñas-González, et al., Survival of Mexican children with acute lymphoblastic leukaemia under treatment with the protocol from the Dana-Farber Cancer Institute 00-01, Biomed. Res. Int. 2015 (2015) 576950, https://doi.org/10.1155/2015/576950.
[33] M. Talibov, A. Olsson, H. Bailey, F. Erdmann, C. Metayer, C. Magnani, et al., Parental occupational exposure to low-frequency magnetic fields and risk of leukaemia in the offspring: findings from the Childhood Leukaemia International Consortium (CLIC), Occup. Environ. Med. 76 (2019) 746–753, https://doi.org/10.1136/OEMED-2019-105706.
[34] T.J. Cole, K.M. Flegal, D. Nicholls, A.A. Jackson, Body mass index cut offs to define thinness in children and adolescents: international survey, BMJ 335 (2007) 194–197, https://doi.org/10.1136/BMJ.39238.399444.55.
[35] WHO child growth standards: training course on child growth assessment [Internet]. [cited November 13, 2025]. Available from: https://www.who.int/publications/i/item/9789241595070.
[36] A. Meyers, K. Joyce, S.M. Coleman, J.T. Cook, D. Cutts, S.E. Ettinger de Cuba, et al., Health of children classified as underweight by CDC reference but normal by WHO standard, Pediatrics 131 (2013) e1780–e1787, https://doi.org/10.1542/PEDS.2012-2382.
[37] R.J. Kuczmarski, C.L. Ogden, L.M. Grummer-Strawn, K.M. Flegal, S.S. Guo, R. Wei, et al., CDC growth charts: United States, Adv. Data. 314 (2000) 1–27. Available from: https://pubmed.ncbi.nlm.nih.gov/11183293/.
[38] K.M. Flegal, T.J. Cole, Construction of LMS parameters for the Centers for Disease Control and Prevention 2000 growth charts [Internet]. [cited November 13, 2025]. Available from: https://www.researchgate.net/publication/263743696_Construction_of_LMS_parameters_for_the_Centers_for_Disease_Control_and_Prevention_2000_growth_charts.
[39] World Health Organization, Use of World Health Organization and CDC growth charts for children aged 0–59 months in the United States [Internet]. [cited November 13, 2025]. Available from: https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5909a1.htm.
[40] P.C. Galati, C.M. Ribeiro, L.T.G. Pereira, A.A. Amato, The association between excess body weight at diagnosis and pediatric leukemia prognosis: a systematic review and meta-analysis, Blood Rev 51 (2022) 100870, https://doi.org/10.1016/j.blre.2021.100870.
[41] E. Orgel, J.M. Genkinger, D. Aggarwal, L. Sung, M. Nieder, E.J. Ladas, Association of body mass index and survival in pediatric leukemia: a meta-analysis, Am. J. Clin. Nutr. 103 (2016) 808–817, https://doi.org/10.3945/ajcn.115.124586.
[42] E.K. Amankwah, A.M. Saenz, G.A. Hale, P.A. Brown, Association between body mass index at diagnosis and pediatric leukemia mortality and relapse: a systematic review and meta-analysis, Leuk. Lymphoma 57 (2016) 1140–1148, https://doi.org/10.3109/10428194.2015.1076815.
[43] C. Egnell, S. Ranta, J. Banerjee, A. Merker, R. Niinimäki, B. Lund, et al., Impact of body mass index on relapse in children with acute lymphoblastic leukemia treated according to Nordic treatment protocols, Eur. J. Haematol. 105 (2020) 797–807, https://doi.org/10.1111/EJH.13517.
[44] T.S. Levy, Resultados de la Encuesta Nacional de Salud y Nutrición (ENSANUT) estado de nutrición en la CDMX 2024 [Internet]. [cited November 13, 2025]. Available from: https://semujeres.cdmx.gob.mx/storage/app/media/JuevesEstadisticasGenero/2024/Estado_nutricion_CDMX_EVALUA.pdf.

[45] D. Tsilingiris, N.G. Vallianou, N. Spyrou, D. Kounatidis, G. S. Christodoulatos, I. Karampela, et al., Obesity and leukemia: biological mechanisms, perspectives, and challenges, Curr. Obes. Rep. 13 (2024) 1–34, https://doi.org/10.1007/S13679-023-00542-Z.

[46] R. Higos, K. Saitoski, M. Hautefeuille, G. Marcelin, K. Clément, N. Varin-Blank, et al., The critical role of adipocytes in leukemia, Biology (Basel). 14 (2025) 624, https://doi.org/10.3390/BIOLOGY14060624.

[47] J.A.G. Hamilton, M. Lee, G.R. Talekar, C.J. Henry, Obesity-induced chemoresistance in B-Cell acute lymphoblastic leukemia cells is mediated by reduced chemotherapy uptake and interleukin-9 signaling, Blood 136 (2020) 37–38, https://doi.org/10.1182/BLOOD-2020-143164.

[48] X. Sheng, S.D. Mittelman, The role of adipose tissue and obesity in causing treatment resistance of acute lymphoblastic leukemia, Front. Pediatr. 2 (2014) 53, https://doi.org/10.3389/FPED.2014.00053.

[49] E.A. Ehsanipour, X. Sheng, J.W. Behan, X. Wang, A. Butturini, V.I. Avramis, et al., Adipocytes cause leukemia cell resistance to L-asparaginase via release of glutamine, Cancer Res 73 (2013) 2998–3006, https://doi.org/10.1158/0008-5472.CAN-12-4402.

[50] X. Sheng, J.H. Parmentier, J. Tucci, H. Pei, O. Cortez-Toledo, C.M. Dieli-Conwright, et al., Adipocytes sequester and metabolize the chemotherapeutic daunorubicin, Mol. Cancer Res. 15 (2017) 1704–1713, https://doi.org/10.1158/1541-7786.MCR-17-0338.

[51] J. Maaskant, A.J. Ross, K.A. Haynes, A.N. Evans, E.C. Sullivan, E. P. Weinzerl, et al., Obesity attenuates CAR T-cell function in pediatric B-Cell acute lymphoblastic leukemia, Blood 144 (2024), https://doi.org/10.1182/BLOOD-2024-212050, 4807–4807.

[52] C.J. Andersen, K.E. Murphy, M.L. Fernandez, Impact of obesity and metabolic syndrome on immunity, Adv. Nutr. 7 (2016) 66–75, https://doi.org/10.3945/an.115.010207.

[53] C.K. Meenan, J.A. Kelly, L. Wang, A.K. Ritchey, S.H. Maurer, Obesity in pediatric patients with acute lymphoblastic leukemia increases the risk of adverse events during pre-maintenance chemotherapy, Pediatr. Blood Cancer 66 (2019) e27515, https://doi.org/10.1002/PBC.27515.

[54] N. Bistre, S. Guillén-López, I. Medina-Vera, M.E. Reyna-Fabián, N. L. Hernández-Martínez, L. Castro-Monroy, et al., Identifying early metabolic risks of obesity in Mexican children and adolescents from a semi-rural community in Mexico: beyond BMI and into biochemical and nutritional markers, Nutrients 17 (2025) 2195, https://doi.org/10.3390/NU17132195/S1.

[55] J. Budzyński, B. Szukay, BMI as a biomarker in patients' nutritional assessment, in: V.B. Patel, V.R. Preedy (Eds.), Biomarkers in Nutrition. Biomarkers in Disease: Methods, Discoveries and Applications, Springer, Cham, Switzerland, 2022. Chapter 36, https://doi.org/10.1007/978-3-030-81304-8_36-1.

[56] J.J. Reilly, M. Brougham, C. Montgomery, F. Richardson, A. Kelly, B.E. S. Gibson, Effect of glucocorticoid therapy on energy intake in children treated for acute lymphoblastic leukemia, J. Clin. Endocrinol. Metab. 86 (2001) 3742–3745, https://doi.org/10.1210/JCEM.86.8.7764.

[57] C. Daymont, W. Hwang, I.M. Paul, N. Shur, D.S. Freedman, Creation and evaluation of new growth charts with a gradual transition from WHO to CDC values, Pediatrics 156 (2025), https://doi.org/10.1542/PEDS.2025-070697.

[58] S. Gupta, D.T. Teachey, Z. Chen, K.R. Rabin, K.P. Dunsmore, E.C. Larsen, et al., Sex-based disparities in outcome in pediatric acute lymphoblastic leukemia: a Children's Oncology Group report, Cancer 128 (2022) 1863–1870, https://doi.org/10.1002/CNCR.34150.

[59] J. Bartram, P. Ancliff, A. Vora, How I treat infant acute lymphoblastic leukemia, Blood 145 (2025) 35–42, https://doi.org/10.1182/BLOOD.2023023154.

[60] D. Deak, N. Gorcea-Andronic, V. Sas, P. Teodorescu, C. Constantinescu, S. Iluta, et al., A narrative review of central nervous system involvement in acute leukemias, Ann. Transl. Med. 9 (2021), https://doi.org/10.21037/ATM-20-3140, 68–68.

[61] M. Kulczycka, K. Derlatka, J. Tasior, M. Sygacz, M. Lejman, J. Zawitkowska, Infant acute lymphoblastic leukemia-new therapeutic opportunities, Int. J. Mol. Sci. 25 (2024) 3721, https://doi.org/10.3390/IJMS25073721.