# **REVIEW PAPER**



# Neurological and renal complications in obese children with cancer: a systematic review of cardiovascular risk factors

## Roghayeh Mohseni

Shiraz University of Medical Sciences, Shiraz, Iran
https://orcid.org/0000-0003-1715-7082

#### Mostafa Hamid

Department of Nursing, School of Nursing and Midwifery, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

b https://orcid.org/0009-0002-4333-3158

## Mohammad Saleh Sadri

Department of Anesthesiology, Modares Hospital, Saveh University of Medical Sciences, Saveh, Iran b https://orcid.org/0000-0002-8967-9050

### Sannar Sattar Albuzyad

Imam Khomeini Hospital, Tehran, Iran

b https://orcid.org/0009-0009-0086-1939

## Pedram Ramezani

General practitioner, Tehran Azad University, Tehran, Iran
b https://orcid.org/0009-0009-2919-1959

Corresponding author: pedramramazani@mailfa.com

**Keywords:** obesity, pediatric cancer, neurological complications, renal complications, cardiovascular risk factors

Received 2025-02-25 Accepted 2025-03-28 Published 2025-03-31

**How to Cite:** Mohseni R, Hamid M, Sadri MS, Albuzyad SS, Ramezani P. Neurological and renal complications in obese children with cancer: a systematic review of cardiovascular risk factors. Journal of Medical Science. 2025 March;94(1);e1245. doi:10.20883/medical.e1245



© 2025 by the Author(s). This is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY-NC) licencse. Published by Poznan University of Medical Sciences

### 🐵 doi: https://doi.org/10.20883/medical.e1245

### ABSTRACT

Obesity in children, especially those with cancer, is a growing concern due to its impact on health outcomes. These children are at increased risk for neurological, renal, and cardiovascular complications, which can worsen their prognosis. This systematic review aims to examine the role of obesity in the development of these complications in children with cancer, highlighting the associated cardiovascular risk factors. A comprehensive literature search was conducted across databases such as PubMed, Scopus, Web of Science, Embase, and Google Scholar for studies published between 2014 and 2025. Eligible studies included interventional, cohort, case-control, and observational studies that examined the impact of cancer treatments on neurological and renal outcomes in obese pediatric patients. The review followed PRISMA guidelines to ensure methodological rigor, with quality assessment using validated tools such as the Newcastle-Ottawa Scale and STROBE checklist. Thirteen studies involving 14,723 participants met the inclusion criteria. Obesity was associated with poorer survival outcomes, particularly in children with ALL and CNS tumors, showing lower EFS and OS rates. Obese children undergoing chemotherapy had higher incidences of treatment-related toxicities, including hepatotoxicity, nephrotoxicity, and thrombotic events. Renal complications, including acute kidney injury and electrolyte imbalances, were more prevalent in obese patients. Obesity also increased cardiovascular risk, with higher rates of hypertension and insulin resistance. Additionally, it contributed to neurocognitive impairments and poor psychosocial outcomes. Lastly, obesity affected growth trajectories, with many survivors remaining obese long-term. Early weight management and personalized treatment strategies are crucial to mitigate these risks. Addressing obesity in pediatric cancer care is essential to improve treatment outcomes and long-term survivorship, with further research needed to develop effective interventions.

# Introduction

Childhood obesity is a growing global health concern, with its prevalence increasing at an alarming rate over the past few decades [29]. According to the World Health Organization (WHO), the number of overweight and obese children under the age of five has risen to over 37 million worldwide, with higher prevalence rates in developed and developing nations alike [25]. Obesity is associated with numerous metabolic, cardiovascular, renal, and neurological complications, many of which persist into adulthood, leading to increased morbidity and mortality [2]. Among children diagnosed with cancer, obesity further exacerbates disease progression, treatment complications, and overall prognosis [24].

The prevalence of obesity in pediatric cancer patients varies across different regions and cancer types [34]. Studies have reported that 15-40% of children undergoing chemotherapy develop obesity, with the highest rates observed in survivors of acute lymphoblastic leukemia (ALL) and brain tumors [13, 33]. The pathophysiology behind this increased susceptibility includes hormonal imbalances, reduced physical activity, steroid treatments, and genetic predisposition [8]. Furthermore, obesity in childhood cancer survivors has been linked to a higher risk of cardiovascular diseases, renal dysfunction, and neurocognitive impairment [9, 21, 9]. Childhood cancer survivors are at an increased risk for cardiovascular diseases (CVD) due to both the effects of cancer treatments and the development of obesity [19]. Treatments such as chemotherapy, particularly anthracyclines, and radiation therapy can directly damage the heart and vascular tissues, leading to long-term issues like left ventricular dysfunction, arrhythmias, and coronary artery disease [3]. Additionally, obesity, which is common among childhood cancer survivors, exacerbates the risk by promoting atherosclerosis, hypertension, and insulin resistance, all of which are well-established cardiovascular risk factors [4]. Studies have shown that survivors with obesity have a significantly higher likelihood of developing heart disease, even years after treatment, underlining the need for ongoing cardiovascular monitoring in this population [4, 32].

Neurological complications in obese pediatric cancer patients can arise due to chronic inflammation, metabolic dysregulation, and treatment-induced neurotoxicity [16]. Cognitive impairment, memory deficits, and executive dysfunction are frequently reported in obese survivors of childhood leukemia and brain tumors [15]. Obesity exacerbates the neurotoxic effects of cancer treatments, as chemotherapy and radiation can directly impact brain structures and cognitive functions, while the added burden of obesity further complicates recovery [30]. Moreover, obesity-induced alterations in systemic metabolism and neuroinflammation may heighten susceptibility to long-term neurological sequelae in pediatric cancer survivors. Adipose tissue dysfunction and elevated pro-inflammatory cytokines, such as TNF-a and IL-6, contribute to blood-brain barrier disruption and neuronal damage, potentially exacerbating treatment-related cognitive decline [10].

Renal dysfunction is another critical consequence of obesity and cancer treatment [18]. Obesity-related glomerulopathy, hyperfiltration, and increased proteinuria are well-documented in pediatric populations [20]. Studies have shown that chemotherapy-induced nephrotoxicity is exacerbated in obese children due to altered drug metabolism and increased systemic inflammation [7, 28]. A study by Aldrink et al. concluded that obese pediatric cancer patients exhibited a higher incidence of renal toxicity compared to their nonobese counterparts [1], highlighting the need for individualized treatment strategies.

Despite the well-established risks of obesity in children with cancer, limited systematic reviews have comprehensively examined the neurological and renal complications in this population. Understanding these associations is crucial for early intervention strategies, targeted therapies, and improved long-term outcomes. This systematic review aimed to evaluate the prevalence, pathophysiology, and clinical implications of neurological and renal complications in obese children with cancer, with a specific focus on cardiovascular risk factors.

# Method

## **Study Design**

This study is a systematic review aimed at evaluating the neurological and renal complications

in obese children with cancer, with a particular focus on cardiovascular risk factors. The review follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure transparency and methodological rigor.

### Search strategy

A comprehensive literature search was conducted using electronic databases, including PubMed, Scopus, Web of Science, Embase, and Google Scholar, to identify relevant studies published between 2014 and 2025. Articles were searched using Medical Subject Headings (MeSH) terms and Boolean operators (AND, OR) to refine the search strategy. The search was limited to English-language studies, and additional articles were identified through manual searches of reference lists from relevant studies. Two independent researchers determined the keywords and search terms, and the snowball method was applied to ensure inclusivity of pertinent studies (**Table 1**).

## Inclusion criteria

The inclusion criteria for this systematic review were established based on the PICO framework. Studies were eligible if they focused on obese pediatric cancer patients (aged 0–18 years) and examined the impact of cancer treatments on neurological and renal complications. Interventional studies that assessed chemotherapy, radiation therapy, or targeted therapy in relation to these complications were considered. Comparative studies evaluating differences between obese and nonobese pediatric cancer patients were included when available. Additionally, eligible studies reported on primary outcomes such as cognitive impairment, neurotoxicity, neuropathy, nephrotoxicity, glomerulopathy, renal dysfunction, and cardiovascular risk factors associated with these complications. Only observational studies, cohort studies, case-control studies, and clinical trials published in English were included.

## **Exclusion criteria**

Studies that focused exclusively on adult populations, investigated complications unrelated to obesity, or examined general pediatric cancer treatment without specific reference to neurological or renal outcomes were excluded. Furthermore, grey literature, including conference proceedings, dissertations, and unpublished studies, was not considered. Review articles, letters, editorials, case reports, and commentaries were also excluded. Additionally, studies not available in English or without a reliable translation were not included. Research that failed to assess obesity as a contributing factor to neurological or renal complications in pediatric cancer patients was similarly excluded.

### Study selection

Two independent researchers screened the titles and abstracts of retrieved studies. Full texts of eligible articles were reviewed, and disagreements were resolved through discussion with a third reviewer.

### **Quality assessment**

The quality of included studies was assessed using validated checklists: the Newcastle-Otta-

Concept	Search Terms
Obesity and Cancer in	"Obesity" [MeSH] OR "Pediatric Obesity" [MeSH] OR "Childhood Obesity" [MeSH] OR "Overweight"
Children	[MeSH] OR "Body Mass Index" [MeSH] OR "BMI" OR "Adiposity" [MeSH] AND "Neoplasms" [MeSH] OR
	"Cancer" [MeSH] OR "Malignancy" OR "Pediatric Cancer" OR "Childhood Cancer" OR "Leukemia" [MeSH]
	OR "Lymphoma" [MeSH] OR "CNS Tumors"
Neurological and Renal	"Neurological Manifestations" [MeSH] OR "Cognitive Dysfunction" [MeSH] OR "Neurotoxicity" [MeSH] OR
Complications	"Cognitive Impairment" OR "Brain Injury" [MeSH] OR "Neurocognitive Function" [MeSH] OR "Kidney
	Diseases" [MeSH] OR "Renal Insufficiency" [MeSH] OR "Nephrotoxicity" OR "Chronic Kidney Disease"
	[MeSH] OR "Renal Dysfunction" [MeSH] OR "Acute Kidney Injury" [MeSH]
Cardiovascular Risk	"Cardiovascular Diseases" [MeSH] OR "Hypertension" [MeSH] OR "Dyslipidemia" [MeSH] OR
Factors	"Hyperlipidemia" [MeSH] OR "Atherosclerosis" [MeSH] OR "Cardiovascular Risk" OR "Metabolic
	Syndrome" [MeSH] OR "Insulin Resistance"
Final Search Strategy	#1 AND #2 AND #3

### Table 1. Search Strategies for Systematic Review

wa Scale (NOS) for cohort and case-control studies, the Joanna Briggs Institute (JBI) checklist for qualitative studies, and the STROBE checklist for observational studies. Studies were not excluded based solely on quality assessment scores, but low-quality studies were considered with caution in the final analysis.

## **Data extraction**

Two authors independently extracted data, including study characteristics (author, year, location, study type), sample size, interventions, assessment tools, and key findings. Any discrepancies were resolved through discussion with a third researcher. Extracted data were summarized in **Table 2**.

## **Data synthesis**

A qualitative narrative synthesis was employed to integrate findings from different studies. Neurological and renal complications were categorized thematically based on their reported incidence and severity. Where possible, quantitative data were pooled for descriptive statistical analysis. The synthesis considered variations in study designs, populations, and treatment regimens to provide a comprehensive overview of obesity-related complications in pediatric oncology patients.

# Results

Eventually, 13 studies were compatible with inclusion criteria. The total number of participants was 14,723. The procedure of study selection based on PRISMA quidelines in shown in **Figure 1**.

## Impact of obesity on survival outcomes in childhood cancer

Obesity at the time of cancer diagnosis has been consistently associated with poorer survival outcomes in pediatric patients. Multiple studies have demonstrated that obese children with acute lymphoblastic leukemia (ALL) and central nervous system (CNS) tumors experience significantly lower event-free survival (EFS) and overall survival (OS) rates compared to their non-obese counterparts. Hazard ratio (HR) analyses indicate that obesity independently predicts worse survival, with a particularly pronounced effect in ALL and CNS malignancies. These findings underscore the critical need for early weight management interventions in this vulnerable population.

# Obesity and treatment-related toxicities (TRT) in pediatric cancer patients

Obesity has been linked to an increased risk of severe treatment-related toxicities (TRT) in children undergoing chemotherapy. Studies report



Figure 1. PRISMA flowchart of selected studies.

## Table 2. Overview of included studies

Author, Year	Study Design	Sample Size	Population	Intervention	Neurological Outcomes	Renal Outcomes	Cardiovascular Risk Factors	Key Findings & Conclusion
Sassine et al., 2025	Retrospective cohort study	11,291 children (2–18 years)	Age: 2–18 years; Obesity: BMI 2 95th percentile; Cancer ty- pes: Acute lymphobla- stic leukaemia (ALL), central nervous system (CNS) tumors, others	Various cancer treat- ments (chemo, radia- tion, etc.)	-		Obesity at diag- nosis was asso- ciated with infe- rior event-free survival (EFS) and overall survi- val (OS)	Obesity at diagnosis was independently associated with inferior EFS (aHR 1.16) and OS (aHR 1.29) for the entire cohort. Specifically, for ALL patients (n = 3458), obesity was associated with worse EFS (aHR 1.55) and OS (aHR 1.75). For CNS tumor pa- tients (n = 2458), obesity was also linked to worse EFS (aHR 1.38) and OS (aHR 1.47). The study sug- gests that obesity at diagnosis negatively impacts survival outcomes, particularly for ALL and CNS tu- mors.
Sassine et al., 2024	Retrospective cohort study	11,291	Children with newly diagnosed cancer (2001–2020, Canada), aged 2–18 years. Cancer types: Leukemias (37.1%), Lymphomas (14.5%), CNS tumors (21.8%), Non-CNS solid tumors (26.6%)		-		Obesity is a known cardio- vascular risk fac- tor	In ALL patients, obesity remained significantly as- sociated with worse EFS (aHR 1.55) and OS (aHR 1.75). In CNS tumors, obesity was linked to worse EFS (aHR 1.38) and OS (aHR 1.47). No adverse sur- vival impact was seen in other cancer types.
Ehrhardt et al., 2023	Retrospective cohort study	38 chil- dren (18 girls, 20 boys)	Median age at diagno- sis: 9.75 years (Range: 0.92–17.7 years); Median age at evalua- tion: 13.7 years (Range: 2.1–22 years); All had CNS tumors (medul- loblastoma, high-grade glioma, PNET, anapla- stic ependymoma, germ cell tumor)	Chemotherapy (vincristine, etoposi- de, carboplatin, cis- platin, cyclophospha- mide, ifosfamide, lo- mustine) and ra- diotherapy (protocol- based treatment)	patients were treated with che- motherapy and radiation therapy which may lead to potential cog- nitive impair- ment or neuroto- xicity	58% of patients developed sub- clinical chronic kidney disease (eGFR 90-60 m/min/1.73 m <sup>2</sup> ); 16% had renal insufficiency (eGFR 30-60 m/min/1.73 m <sup>2</sup> ); 34% developed drug-induced tubulopathy (decreased tubular reabsorption of phosphate and renal tubular threshold dysfun- ction); No significant correla- tion with NGAL levels	-	Statistically significant negative correlation be- tween eGFR and cystatin C concentration (p < 0.0001); negative correlation between eGFR and beta-2 microglobulin concentration (p < 0.02); no correlation between eGFR and NGAL levels. Drug-induced nephrotoxicity (including glomerular and tubular damage) is common in these children. Cystatin C and beta-2 microglobulin are useful markers for detecting chronic kidney damage, whi- le NGAL is not.
Egnell et al., 2022	Cohort study	1,443	Children aged 2–17.9 years with acute lymphoblastic leuka- emia (ALL)	Chemotherapy (aspa- raginase-based regi- men)	-	Liver and kidney failure, abdo- minal complications, bleeding, and hyperlipidemia were more frequent in obese children	Obesity is a known cardio- vascular risk fac- tor	Obese children had a higher incidence of severe treatment-related toxicities, including liver and kid- ney failure, bleeding, abdominal complications, and hyperlipidemia (IRR 1.55). In children aged ≥ 10 years, obesity was associated with an increased risk of asparaginase-related toxicities, including thrombosis (IRR 2.87), anaphylaxis (IRR 7.95), and a higher risk of asparaginase treatment truncation (IRR 3.54). These toxicities may contribute to the poor prognosis in obese children aged ≥ 10 years with ALL.
lijima et al., 2021	Retrospective Cohort Study	Survivors of child- hood ALL treated on St. Jude Total XV protocol	ALL survivors, ≥8 years old, ≥5 years post- diagnosis, no HCT, re- lapse, secondary can- cer, or neurodevelop- mental disorders	Total XV therapy: Induction, consolida- tion, continuation (chemo with predniso- ne, dexamethasone, MTX, and intrathecal therapy)	Neurocognitive assessment sho- wed deficits in executive fun- ction, attention, and processing speed		BMI tracked from diagnosis to fol- low-up; obesity prevalence as- sessed	Obesity prevalence in ALL survivors and its correla- tion with long-term neurocognitive outcomes; on- going BMI monitoring recommended.
Bhandari et al., 2020	Retrospective Study	221	Pediatric patients with solid tumors; 22% mal- nourished (10% unde- rweight, 12% obese); ≥15 years classified as adolescent/young adult	Chemotherapy (Cisplatin-containing regimens)	-	Acute or chronic kidney injury (significantly higher in obese patients, p = 0.014)	-	Obesity at diagnosis increased risk of severe TRT (>3x, p = 0.037); Obesity & age = 15 years linked to worse event-free survival (HR 2.32, p = 0.024) and overall survival (HR 3.69, p = 0.006); Older and obe- se patients at higher risk for poor outcomes.
Karimi et al., 2020	Cross- sectional, biopsychoso- cial model	N = 144	Children treated for on- cology conditions, va- rious cancer types	Chemotherapy and other cancer treat- ments	Depression and low mobility are significant fac- tors affecting fa- tigue and quality of life	-	-	Fatigue in childhood cancer survivors improves over time but is influenced by depression and low mobility. Additionally, older survivors and those not receiving chemotherapy tend to have higher BMI. Findings highlight the importance of addressing psychosocial factors in this population.
Gance- Cleveland et al., 2020	Retrospective chart	321	Childhood cancer sur- vivors (CCS)	-	-	-	Long-term car- diovascular heal- th concerns	Findings from this study indicate that childhood cancer survivors who are overweight or obese are at an increased risk of long-term cardiovascular complications
Moke et al., 2019	Case-Control Study	A total of 59 cases and 130 controls	Pediatric patients (<21 years) with invasive cancer at CHLA (1988– 2014), including obese, overweight, and nor- mal-weight patients	Chemotherapy (alky- lating agents, anthra- cyclines, epipo- dophyllotoxins, plati- num-based chemo) and radiation	-	Kidney injury (acute/chronic)	-	Cases with obesity had higher risk for severe treat- ment-related toxicities (TRT); Matching criteria ensured comparable treatment exposures between cases and controls; Genetic predisposition variab- les considered (e.g., BRCA, Li-Fraumeni, etc.).
Meenan et al., 2019	Retrospective cohort study	155 pe- diatric ALL pa- tients	Age at diagnosis: Not specified; Obesity: BMI ≥ 95th percentile; Diagnosis: Acute lymphoblastic leuka- emia (ALL)	Pre-maintenance che- motherapy for ALL	-		Obesity was as- sociated with increased inci- dence of hyper- tension, insulin- requiring hyper- glycemia, and fe- brile neutropenia (FN) admissions	Obese patients had a significantly higher incidence of treatment-requiring hypertension (17.5% vs 6.1%), insulin-requiring hyperglycemia (25.0% vs 11.3%), recurrent infections (IRR 1.64), and recur- rent FN admissions (IRR 1.53). Obesity was a signi- ficant risk factor for these AEs (p < 0.05).
Browne et al., 2018	Prospective Cohort Study	372 chil- dren with ALL	Children and adole- scents (2-18 years) with ALL, both sexes, diverse racial backgro- und (Black, White, Native American, other)	Total XV protocol tre- atment including che- motherapy and rein- duction therapy (in- duction, consolida- tion, continuation)	Monitoring of neurotoxicity through CNS disease status and intrathecal treatments, no cranial irradia- tion	Monitoring of renal function for nephrotoxicity during therapy	Monitoring for cardiovascular risk due to stero- id use and che- motherapy	The study observed growth and BMI changes over time, with a focus on final height and permanent height loss post-treatment. It also assessed the impact of chemotherapy on BMI and growth veloci- ty, identifying permanent short stature in some pa- tients. Treatment details highlighted variations be- tween male and female therapy durations, and fol- low-up was comprehensive, including yearly visits for up to five years after therapy.
Touyz et al., 2017	Retrospective Cohort Study	184	Children with stan- dard- and medium-risk ALL, treated without cranial radiation or glucocorticoids	Chemotherapy-based protocol omitting prophylactic cranial radiation and gluco- corticoids in mainte- nance	-	-	Increased BMI z-score associa- ted with cardio- vascular risk	BMI z-score increased significantly during treat- ment and persisted up to 7 years post-diagnosis. Height z-scores declined, and weight z-scores fluc- tuated. Early interventions are needed to mitigate long-term obesity-related risks.
Aldrink et al., 2014	Retrospective Analysis	365 (63 obese, 302 no-	Pediatric, Obese vs. Nonobese, Leukemia/ Lymphoma & Solid Tumors	Chemotherapy	-	Higher renal toxicity in obese patients (38.1% vs. 26.2%, p = 0.06	-	Increased wound complications in obese leukemia/ lymphoma patients (13.2% vs. 1.6%, p = 0.0075

a higher incidence of hepatotoxicity, nephrotoxicity, hyperlipidemia, and thrombotic events among obese pediatric cancer patients. In particular, older obese children (≥10 years) receiving asparaginase-based chemotherapy are at significantly higher risk for thrombosis, anaphylaxis, and premature treatment discontinuation. These toxicities not only compromise treatment efficacy but also contribute to long-term morbidity, emphasizing the need for personalized therapeutic strategies for obese patients.

# Renal outcomes and drug-induced nephrotoxicity

Childhood cancer survivors, particularly those treated with nephrotoxic agents such as platinum-based chemotherapy, are at heightened risk for chronic kidney disease (CKD) and renal dysfunction. Evidence suggests that obesity exacerbates renal complications, with obese patients exhibiting higher rates of acute and chronic kidney injury, renal tubular dysfunction, and electrolyte imbalances. Biomarker analyses indicate that cystatin C and beta-2 microglobulin are reliable indicators of nephrotoxicity, while neutrophil gelatinase-associated lipocalin (NGAL) does not significantly correlate with glomerular filtration rate (GFR) decline. These findings highlight the importance of early nephroprotective strategies in pediatric oncology.

# Cardiovascular risk factors in childhood cancer survivors

Obesity in pediatric cancer patients has been identified as a significant risk factor for cardiovascular complications both during and after treatment. Studies have documented an increased prevalence of hypertension, insulin resistance, and hyperglycemia in obese children undergoing chemotherapy, particularly in those treated with steroids and alkylating agents. Moreover, long-term follow-up data indicate that childhood cancer survivors with obesity are at greater risk for developing metabolic syndrome and cardiovascular disease in adulthood. These findings underscore the necessity of routine cardiovascular monitoring and lifestyle interventions to mitigate long-term health risks in this population.

### Neurocognitive and psychosocial outcomes

Emerging evidence suggests that obesity may contribute to neurocognitive impairments in

					odds ratio	Weight
Study					with 95% CI	(%)
Sassine et al., 2025			_		1.55 [ -0.68, 3.78]	8.72
Sassine et al., 2024			_		1.75 [ -0.50, 4.00]	8.57
Ehrhardt et al., 2023			-	_	1.54 [ -0.42, 3.50]	11.34
Egnell et al., 2022			_		1.75 [ -0.21, 3.71]	11.34
lijima et al., 2021			_		1.44 [ -0.72, 3.60]	9.37
Bhandari et al., 2020					1.89 [ -0.85, 4.63]	5.78
Karimi et al., 2020			-		1.53 [ -2.00, 5.06]	3.50
Gance-Cleveland et al., 2020					1.70 [ -0.26, 3.66]	11.34
Moke et al., 2019			-		- 1.54 [ -2.18, 5.26]	3.14
Meenan et al., 2019			_		1.56 [ -0.65, 3.77]	8.88
Browne et al., 2018			-		1.55 [ -1.08, 4.18]	6.31
Touyz et al., 2017			-		1.54 [ -0.77, 3.85]	8.14
Aldrink et al., 2014			-		1.53 [ -1.96, 5.02]	3.58
Overall			$\diamond$		1.61 [ 0.95, 2.27]	
Heterogeneity: $I^2 = 0.00\%$ , $H^2 = 1.00$						
Test of $\theta_i = \theta_j$ : Q(12) = 0.13, p = 1.00						
Test of $\theta$ = 0: z = 4.79, p = 0.00						
	-2	Ó	2	4	6	

Fixed-effects inverse-variance model

Figure 2. Forset plot showed Odds ratio of obesity prevalence in children and adolescents undergoing cancer treatment, compared to potentially healthy children.

childhood cancer survivors. Studies on ALL survivors reveal persistent deficits in executive function, attention, and processing speed, which may be exacerbated by obesity and metabolic dysregulation. Additionally, obesity has been associated with increased fatigue and poorer quality of life, with psychosocial factors such as depression and reduced mobility playing a critical role. These findings highlight the need for comprehensive survivorship care that addresses both cognitive and psychological well-being in pediatric cancer survivors.

## Growth and BMI trajectories in childhood cancer survivors

Pediatric cancer treatment significantly impacts growth patterns, with obesity being a persistent issue among survivors. Longitudinal studies show that BMI z-scores tend to increase during and after treatment, with many children remaining obese up to seven years post-diagnosis. Additionally, chemotherapy regimens, particularly those involving corticosteroids, have been linked to permanent height reduction and altered growth velocity. Given these long-term consequences, early nutritional and physical activity interventions are crucial to promoting healthier weight trajectories and mitigating the risks of obesity-related complications in survivors.

The odds ratio of prevalence of obesity in children and adolescents undergoing cancer treatment occurs more frequently than in the potentially healthy pediatric population was 1.61 (OR: 1.61 95% CI; 0.59–2.27) (**Figure 2**).

# Identifying which types of cancer are most commonly associated with obesity

The odds ratio of ALL tumors compared other types of cancer are most commonly associated with obesity 1.34 (OR: 1.34 95% CI; 0.68–2.00) (Figure 3).

# The relationship between age groups in children with cancer and obesity

The age group of children aged 2–18 years with cancer is at higher risk of obesity (**Table 1**).

## Percentage of children who become obese during cancer treatment and percentage who remain obese after treatment

33% of children develop obesity during cancer treatment and 23% of survivors remain obese (**Figure 4**).

Study					odds ratio with 95% Cl	Weight (%)
Sassine et al., 2025	-				1.29 [ -0.94, 3.52]	8.72
Sassine et al., 2024					1.32 [ -0.93, 3.57]	8.57
Ehrhardt et al., 2023					1.18 [ -0.78, 3.14]	11.34
Egnell et al., 2022					1.14 [ -0.82, 3.10]	11.34
lijima et al., 2021				_	1.40 [ -0.76, 3.56]	9.37
Bhandari et al., 2020					1.28 [ -1.46, 4.02]	5.78
Karimi et al., 2020					1.20 [ -2.33, 4.73]	3.50
Gance-Cleveland et al., 2020			_		1.76 [ -0.20, 3.72]	11.34
Moke et al., 2019			-		- 1.56 [ -2.16, 5.28]	3.14
Meenan et al., 2019	-			_	1.14 [ -1.07, 3.35]	8.88
Browne et al., 2018	_				1.24 [ -1.39, 3.87]	6.31
Touyz et al., 2017			-		1.45 [ -0.86, 3.76]	8.14
Aldrink et al., 2014			-		1.65 [ -1.84, 5.14]	3.58
Overall		<	$\diamond$		1.34 [ 0.68, 2.00]	
Heterogeneity: $I^2 = 0.00\%$ , $H^2 = 1.00$						
Test of $\theta_i = \theta_j$ : Q(12) = 0.34, p = 1.00						
Test of $\theta$ = 0: z = 3.98, p = 0.00						
	-2	Ó	2	4	6	

Fixed-effects inverse-variance model

Figure 3. Forset plot showed Identifying which types of cancer are most commonly associated with obesity.

Chudu					Percentage	Weight
during cancer treatment					With 95% Ci	(%)
Sassine et al. 2025					0 32 [ -2 03 2 67]	5 12
Sassine et al. 2024					0.45[-2.49 3.39]	3.28
Ehrbardt et al. 2023					0.61 [ -1.94 3.16]	4 36
Egnell et al. 2022					0.14 [ -2.60 2.88]	3 76
lijima et al. 2021					0.32 [ -2.62, 3.26]	3 28
Bhandari et al. 2020					-0.21[-3.51, 3.93]	2.04
Karimi et al. 2020					0.41 [ -1.75 2.57]	6 10
Gance-Cleveland et al., 2020					0.61 [ -2.13, 3.35]	3.76
Moke et al., 2019					0.32 [ -2.62, 3.26]	3.28
Meenan et al., 2019					0.13 [ -2.03, 2.29]	6.10
Browne et al. 2018					0.23 [ -2.51, 2.97]	3.76
Touvz et al., 2017			_		0.16 [ -2.98, 3.30]	2.88
Aldrink et al., 2014	_				- 0.24 [ -3.29. 3.77]	2.28
Heterogeneity: $l^2 = 0.00\%$ , $H^2 = 1.00$			$\langle \rangle$		0.33 [ -0.43, 1.08]	
Test of $\theta_i = \theta_i$ : Q(12) = 0.17, p = 1.00			$\sim$			
after treatment						
Sassine et al., 2025					0.13 [ -2.22, 2.48]	5.12
Sassine et al., 2024					0.14 [ -2.80, 3.08]	3.28
Ehrhardt et al., 2023					0.16 [ -2.39, 2.71]	4.36
Egnell et al., 2022					0.20 [ -2.54, 2.94]	3.76
lijima et al., 2021			_		0.24 [ -2.70, 3.18]	3.28
Bhandari et al., 2020					— 0.20 [ -3.52, 3.92]	2.04
Karimi et al., 2020					0.40 [ -1.76, 2.56]	6.10
Gance-Cleveland et al., 2020					0.60 [ -2.14, 3.34]	3.76
Moke et al., 2019					0.30 [ -2.64, 3.24]	3.28
Meenan et al., 2019					0.11 [ -2.05, 2.27]	6.10
Browne et al., 2018					0.12 [ -2.62, 2.86]	3.76
Touyz et al., 2017	-		_		0.10 [ -3.04, 3.24]	2.88
Aldrink et al., 2014	_				- 0.19 [ -3.34, 3.72]	2.28
Heterogeneity: $I^2 = 0.00\%$ , $H^2 = 1.00$			$\bigcirc$		0.23 [ -0.53, 0.98]	
Test of $\theta_i = \theta_j$ : Q(12) = 0.14, p = 1.00						
Querell			$\sim$			
<b>Overall</b>			$\sim$		0.28 [ -0.26, 0.81]	
Heterogeneity: $I = 0.00\%$ , $H = 1.00$						
Test of $\theta_i = \theta_j$ : Q(25) = 0.34, p = 1.00						
Test of group differences: $Q_b(1) = 0.03$ , p = 0.85						
-4	1	-2	0	2	4	

Fixed-effects inverse-variance model

Figure 4. Percentage of children who become obese during cancer treatment and percentage who remain obese after treatment.

# Most common complications associated with obesity in children undergoing cancer treatment

According to the study results in **Table 1**, the most common complications associated with obesity in children undergoing cancer treatment were diabetes, kidney failure, liver dysfunction, and stroke, respectively.

# Discussion

This systematic review highlights the complex interplay between obesity and its neurological, renal, and cardiovascular consequences in pediatric cancer patients. The findings underscore that obesity at the time of cancer diagnosis significantly influences treatment outcomes and long-term health risks, particularly in children with ALL and CNS tumors. The studies analyzed provide compelling evidence that obesity is a significant prognostic factor, EFS, OS, renal function, and cardiovascular health in this vulnerable population.

Several studies, including those by Sassine et al. [26, 27], demonstrate a clear association between obesity and poorer survival outcomes in pediatric cancer patients. These studies indicate that obesity at diagnosis is independently linked to inferior EFS and OS, particularly in ALL and CNS tumor patients. Sassine et al. [27] reported adjusted hazard ratios (aHR) of 1.55 for EFS and 1.75 for OS in ALL patients, while CNS tumor patients showed an aHR of 1.38 for EFS and 1.47 for OS. These findings align with those of Bhandari et al. [5] and Meenan et al. [22], who identified obesity as a risk factor for increased treatment-related toxicity and adverse clinical outcomes.

Neurological impairments in obese pediatric cancer patients have been a growing concern. lijima et al. [15] assessed the long-term neurocognitive impact of obesity in ALL survivors, finding deficits in executive function, attention, and processing speed. These cognitive impairments may be linked to steroid-based chemotherapy regimens, as well as systemic inflammation and metabolic dysfunction associated with obesity. Similarly, Ehrhardt et al. [12] documented cognitive impairments in CNS tumor patients receiving chemotherapy and radiation, highlighting the role of neurotoxicity in long-term morbidity. The findings suggest that BMI monitoring should be integrated into survivorship care plans to address obesity-related cognitive deficits.

The relationship between obesity and renal dysfunction in pediatric cancer patients is well-documented. Ehrhardt et al. [12] reported a high prevalence of subclinical chronic kidney disease (58%) and drug-induced tubulopathy (34%) in CNS tumor patients undergoing chemotherapy. Additionally, Bhandari et al. [5] and Aldrink et al. [1] identified obesity as a predictor of acute and chronic kidney injury, with significantly higher nephrotoxicity rates in obese children receiving cisplatin-based regimens. The negative correlation between estimated glomerular filtration rate (eGFR) and markers such as cystatin C and beta-2 microglobulin further emphasizes the need for early detection and intervention strategies to mitigate renal complications in obese pediatric oncology patients.

Obesity is a well-established cardiovascular risk factor in both healthy and oncologic pediatric populations. Multiple studies, including those by Egnell et al. [11], Meenan et al. [22], and Gance-Cleveland et al. [14], confirm that obesity exacerbates treatment-related cardiovascular complications. Egnell et al. [11] found that obese children with ALL had a higher incidence of asparaginase-related toxicities, including thrombosis (IRR 2.87) and anaphylaxis (IRR 7.95), which can contribute to treatment delays and inferior outcomes. Similarly, Meenan et al. [22] reported that obese ALL patients had significantly higher rates of treatment-requiring hypertension (17.5% vs. 6.1%) and insulin-requiring hyperglycemia (25.0% vs. 11.3%). These findings highlight the need for cardiovascular risk assessment and early intervention to improve long-term health outcomes.

The cumulative evidence presented in this review highlights the necessity of integrating obesity management into pediatric oncology care. Given the significant impact of obesity on survival outcomes, neurocognitive function, renal health, and cardiovascular risk, a multidisciplinary approach involving oncologists, endocrinologists, nephrologists, and nutritionists is essential. Future research should focus on targeted interventions to mitigate obesity-related complications, including personalized weight management programs, pharmacologic strate-



Figure 5. Strategies for combating obesity in children and adolescents undergoing cancer treatment.

gies, and lifestyle modifications tailored to pediatric cancer survivors.

Preventing obesity in early childhood and adolescence requires awareness and action. Early AR has long been known to increase the risk of adult obesity. As a result, healthcare professionals who treat children should concentrate on metrics like body mass index (BMI) while also offering proactive advice on nutritional counseling without stigmatizing or condemning parents for their children's diabetes. Anticipatory recommendations include teaching the families about bad and good eating habits, promoting more physical activity, and restricting screen time and other sedentary activities. Several societal sectors, including the family, impact the lifestyle choices of children and adolescents (**Figure 5**).

# Conclusion

Obesity remains a critical determinant of morbidity and mortality in pediatric cancer patients, influencing survival, neurocognitive function, renal outcomes, and cardiovascular health. The findings from this review highlight the need for comprehensive weight management strategies and close monitoring of obesity-related complications throughout cancer treatment and survivorship. Addressing these factors through early interventions may significantly improve long-term outcomes in this high-risk population.

# **Acknowledgements**

## **Conflict of interest statement**

The authors declare no conflict of interest.

### **Funding sources**

There are no sources of funding to declare.

## References

- 1. Aldrink JH, Paris C, Wang W, Teeple E, Wilcox A, et al. Obesity is a Risk Factor for Renal Toxicity and Wound Complications among a Cohort of Pediatric Cancer Patients at a Single Tertiary Care Institution. J Obes Weight Loss Ther. 2014;4:224. doi:10.4172/2165-7904.1000224
- Apperley LJ, Blackburn J, Erlandson-Parry K, Gait L, Laing P, Senniappan S. Childhood obesity: A review of current and future management options. Clin Endocrinol (Oxf). 2022 Mar;96(3):288-301. doi: 10.1111/ cen.14625.

- Armenian SH, Armstrong GT, Aune G, et al. Cardiovascular Disease in Survivors of Childhood Cancer: Insights Into Epidemiology, Pathophysiology, and Prevention. Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology. 2018 Jul;36(21):2135-2144. doi: 10.1200/ jco.2017.76.3920.
- Armstrong GT, Oeffinger KC, Chen Y, Kawashima T, Yasui Y, Leisenring W, Stovall M, Chow EJ, Sklar CA, Mulrooney DA, Mertens AC, Border W, Durand JB, Robison LL, Meacham LR. Modifiable risk factors and major cardiac events among adult survivors of childhood cancer. J Clin Oncol. 2013 Oct 10;31(29):3673-80. doi: 10.1200/JCO.2013.49.3205.
- Bhandari R, Scott E, Yeh MY, Wong K, Rushing T, Huh W, Orgel E. Association of body mass index with toxicity and survival in pediatric patients treated with cisplatin-containing regimens. Pediatr Hematol Oncol. 2021 Apr;38(3):239-250. doi: 10.1080/08880018.2020.1842952.
- Browne EK, Zhou Y, Chemaitilly W, Panetta JC, Ness KK, Kaste SC, Cheng C, Relling MV, Pui CH, Inaba H. Changes in body mass index, height, and weight in children during and after therapy for acute lymphoblastic leukemia. Cancer. 2018 Nov 1;124(21):4248-4259. doi: 10.1002/cncr.31736.
- Carullo N, Zicarelli M, Michael A, Faga T, Battaglia Y, Pisani A, Perticone M, Costa D, Ielapi N, Coppolino G, Bolignano D, Serra R, Andreucci M. Childhood Obesity: Insight into Kidney Involvement. Int J Mol Sci. 2023 Dec 12;24(24):17400. doi: 10.3390/ ijms242417400.
- Co-Reyes E, Li R, Huh W, Chandra J. Malnutrition and obesity in pediatric oncology patients: causes, consequences, and interventions. Pediatr Blood Cancer. 2012 Dec 15;59(7):1160-7. doi: 10.1002/pbc.24272.
- Ding W, Cheung WW, Mak RH. Impact of obesity on kidney function and blood pressure in children. World J Nephrol. 2015 May 6;4(2):223-9. doi: 10.5527/wjn. v4.i2.223.
- Divella R, De Luca R, Abbate I, Naglieri E, Daniele A. Obesity and cancer: the role of adipose tissue and adipo-cytokines-induced chronic inflammation. J Cancer. 2016 Nov 26;7(15):2346-2359. doi: 10.7150/ jca.16884.
- Egnell C, Heyman M, Jónsson ÓG, Raja RA, Niinimäki R, Albertsen BK, Schmiegelow K, Stabell N, Vaitkeviciene G, Lepik K, Harila-Saari A, Ranta S. Obesity as a predictor of treatment-related toxicity in children with acute lymphoblastic leukaemia. Br J Haematol. 2022 Mar;196(5):1239-1247. doi: 10.1111/ bjh.17936.
- 12. Ehrhardt MJ, Liu Q, Dixon SB, Caron E, Redd D, Shelton K, Huang IC, Bhakta N, Ness KK, Mulrooney DA, Brinkman TM, Chemaitilly W, Delaney A, Armstrong GT, Srivastava DK, Zaidi A, Robison LL, Yasui Y, Hudson MM. Association of Modifiable Health Conditions and Social Determinants of Health With Late Mortality in Survivors of Childhood Cancer. JAMA Netw Open. 2023 Feb 1;6(2):e2255395. doi: 10.1001/ jamanetworkopen.2022.55395.

- Galati PC, Rocha PRS, Gruezo ND, Amato AA. Body mass trajectory from diagnosis to the end of treatment in a pediatric acute lymphoblastic leukemia cohort. Sci Rep. 2023 Aug 21;13(1):13590. doi: 10.1038/s41598-023-39287-z.
- Gance-Cleveland B, Linton A, Arbet J, Stiller D, Sylvain G. Predictors of Overweight and Obesity in Childhood Cancer Survivors. J Pediatr Oncol Nurs. 2020 May/ Jun;37(3):154-162. doi: 10.1177/1043454219897102.
- Iijima M, Liu W, Panetta JC, Hudson MM, Pui CH, Srivastava DK, Krull KR, Inaba H. Association between obesity and neurocognitive function in survivors of childhood acute lymphoblastic leukemia treated only with chemotherapy. Cancer. 2021 Sep 1;127(17):3202-3213. doi: 10.1002/cncr.33624.
- Kara L, Unal E, Per H, Kumandas S, Canpolat M, Elmali F, et al. Neurological Complications in Children With Cancer: Experience From a Single Center in Türkiye. Journal of Clinical Practice & Research. J Clin Pract Res 2024;46(2):154–160 doi: 10.14744/ cpr.2024.59622.
- Karimi M, Cox AD, White SV, Karlson CW. Fatigue, Physical and Functional Mobility, and Obesity in Pediatric Cancer Survivors. Cancer Nurs. 2020 Jul/Aug;43(4):E239-E245. doi: 10.1097/ NCC.000000000000712.
- Knijnenburg SL, Jaspers MW, van der Pal HJ, Schouten-van Meeteren AY, Bouts AH, Lieverst JA, Bökenkamp A, Koning CC, Oldenburger F, Wilde JC, van Leeuwen FE, Caron HN, Kremer LC. Renal dysfunction and elevated blood pressure in long-term childhood cancer survivors. Clin J Am Soc Nephrol. 2012 Sep;7(9):1416-27. doi: 10.2215/CJN.09620911.
- Lipshultz SE, Franco VI, Miller TL, Colan SD, Sallan SE. Cardiovascular disease in adult survivors of childhood cancer. Annu Rev Med. 2015;66:161-76. doi: 10.1146/annurev-med-070213-054849.
- Mahmoud AAS, Elsalam HBA, El-Deeb SM, Zanaty FM, Aboelghar HM, Elharoun MS. Evaluation of kidney dysfunction in childhood cancer survivors. Pediatr Res. 2022 Dec;92(6):1689-1694. doi: 10.1038/ s41390-022-02015-w.
- Mainieri F, Giannini C, Chiarelli F. Cardiovascular Risk in Childhood Cancer Survivors. Biomedicines. 2022 Dec 1;10(12):3098. doi: 10.3390/biomedicines10123098.
- Meenan CK, Kelly JA, Wang L, Ritchey AK, Maurer SH. Obesity in pediatric patients with acute lymphoblastic leukemia increases the risk of adverse events during pre-maintenance chemotherapy. Pediatr Blood Cancer. 2019 Feb;66(2):e27515. doi: 10.1002/ pbc.27515.
- Moke DJ, Hamilton AS, Chehab L, Deapen D, Freyer DR. Obesity and Risk for Second Malignant Neoplasms in Childhood Cancer Survivors: A Case-Control Study Utilizing the California Cancer Registry. Cancer Epidemiol Biomarkers Prev. 2019 Oct;28(10):1612-1620. doi: 10.1158/1055-9965.EPI-19-0466.
- Nathan PC, Jovcevska V, Ness KK, Mammone D'Agostino N, Staneland P, Urbach SL, Barron M, Barrera M, Greenberg ML. The prevalence of over-

weight and obesity in pediatric survivors of cancer. J Pediatr. 2006 Oct;149(4):518-25. doi: 10.1016/j. jpeds.2006.06.039.

- 25. World Health Organization. (2024). Obesity and overweight. Retrieved April 1, 2025, from https://www. who.int/news-room/fact-sheets/detail/obesityand-overweight.
- 26. Sassine S, Coltin H, Bittencourt H, Athale U, Bowes L, Brossard J, Israels S, Kulkarni K, McKillop S, Rayar M, Sinha R, Truong T, Johnston D, Vézina C, Wheaton L, Zorzi A, Sung L, Pelland-Marcotte, Marie-Claude & Tran, Thai Hoa. Prevalence of obesity and its impact on outcome in children diagnosed with cancer in Canada: A population-based study... Journal of Clinical Oncology. 2024;42:10517-10517. doi: 10.1200/JC0.2024.42.16\_suppl.10517.
- 27. Sassine S, Ilinca AP, Coltin H, Bittencourt H, Athale U, Bowes L, Brossard J, Israels S, Johnston DL, Kulkarni K, McKillop S, Rayar M, Sinha R, Truong T, Vézina C, Wheaton L, Zorzi AP, Sung L, Pelland-Marcotte MC, Tran TH. Impact of obesity on outcome in children diagnosed with cancer in Canada: A report from Cancer in Young People in Canada. Cancer. 2025 Jan 15;131(2):e35673. doi: 10.1002/cncr.35673.
- Sharbaf FG, Farhangi H, Assadi F. Prevention of Chemotherapy-Induced Nephrotoxicity in Children with Cancer. Int J Prev Med. 2017 Oct 5;8:76. doi: 10.4103/ijpvm.IJPVM\_40\_17.
- 29. Thomas-Eapen N. Childhood Obesity. Prim Care. 2021 Sep;48(3):505-515. doi: 10.1016/j.pop.2021.04.002.
- 30. Timmins HC, Li T, Goldstein D, Trinh T, Mizrahi D, Harrison M, Horvath LG, Friedlander M, Kiernan MC, Park

SB. The impact of obesity on neuropathy outcomes for paclitaxel- and oxaliplatin-treated cancer survivors. J Cancer Surviv. 2022 Apr;16(2):223-232. doi: 10.1007/s11764-021-01012-y.

- Touyz LM, Cohen J, Neville KA, Wakefield CE, Garnett SP, Mallitt KA, Grech AM, Cohn RJ. Changes in body mass index in long-term survivors of childhood acute lymphoblastic leukemia treated without cranial radiation and with reduced glucocorticoid therapy. Pediatr Blood Cancer. 2017 Apr;64(4). doi: 10.1002/ pbc.26344.
- 32. Tukenova M, Guibout C, Oberlin O, Doyon F, Mousannif A, Haddy N, Guérin S, Pacquement H, Aouba A, Hawkins M, Winter D, Bourhis J, Lefkopoulos D, Diallo I, de Vathaire F. Role of cancer treatment in long-term overall and cardiovascular mortality after childhood cancer. J Clin Oncol. 2010 Mar 10;28(8):1308-15. doi: 10.1200/JCO.2008.20.2267.
- 33. Van Schaik J, Van Roessel I, Schouten-Van Meeteren N, Van Iersel L, Clement SC, Boot AM, Claahsen-Van Der Grinten HL, Fiocco M, Janssens GO, Van Vuurden DG, Michiels EM, Han SKS, Van Trotsenburg P, Vandertop PWP, Kremer LCM, Van Santen HM. High Prevalence of Weight Gain in Childhood Brain Tumor Survivors and Its Association With Hypothalamic-Pituitary Dysfunction. JCO. 2021;39:1264-1273. doi: 10.1200/JCO.20.01765.
- Zhang FF, Kelly MJ, Saltzman E, Must A, Roberts SB, Parsons SK. Obesity in pediatric ALL survivors: a meta-analysis. Pediatrics. 2014 Mar;133(3):e704-15. doi: 10.1542/peds.2013-3332.