BMC Pediatrics

RESEARCH

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Birth weight and neonatal morbidity as early-life risk factors for childhood cancer: a nationwide cohort study

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Abstract

Background Childhood cancer is a significant public health issue, and growing evidence suggests that perinatal factors such as birth weight and neonatal complications may influence cancer risk. However, the potential impact of neonatal interventions on subsequent cancer development remains poorly understood. This study aimed to investigate the association between birth weight and childhood cancer risk, and how this relationship may be modulated by neonatal morbidities and interventions.

Methods We conducted a nationwide population-based cohort study using the National Health Insurance Service database in South Korea. All live births between 2008 and 2014 were included and categorized by birth weight. Cancer incidence was identified through 2018 using ICD-10 codes. Associations between birth weight, neonatal conditions, neonatal interventions, and cancer outcomes were analyzed.

Results Among over 2.9 million children, low birth weight (LBW) infants—particularly those weighing < 1.0 kg—had a significantly increased risk of childhood cancer (adjusted odds ratio [aOR], 4.03). Distinct cancer patterns were observed by birth weight category: hepatoblastoma was most common in infants < 1.5 kg, central nervous system malignancies in those 1.5–2.4 kg, and leukemia in those > 4.0 kg. In LBW infants, bronchopulmonary dysplasia (aOR, 2.21), sepsis (aOR, 1.56), oxygen exposure ≥ 4 days (aOR, 1.32), and ≥ 3 red blood cell transfusions (aOR, 4.03) were significantly associated with increased cancer risk. In contrast, phototherapy and radiography were not found to be associated with cancer development.

Conclusions These findings demonstrate that both birth weight extremes and neonatal exposures contribute to childhood cancer risk. In particular, conditions such as bronchopulmonary dysplasia and sepsis—and interventions including oxygen therapy and transfusions—may influence oncogenic pathways in LBW infants. Long-term follow-up in high-risk neonatal populations is warranted, along with further research into underlying biological mechanisms.

Keywords Birth weight, Bronchopulmonary dysplasia, Childhood cancer, Sepsis, Transfusion

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Background

Childhood cancer, a major area of pediatric research, poses a significant healthcare challenge, with an annual incidence of approximately 1 in 10,000 children and a rising trend [1, 2]. Notably, children under 5 years of age are at increased risk of cancer, with some cases diagnosed as early as the neonatal period. Despite ongoing research, the pathogenesis of childhood cancer remains poorly understood, emphasizing the need to examine determinants such as birth weight, sex, and genetic predisposition [3]. Growing evidence suggests an association between birth weight and childhood cancer risk, with studies reporting that higher birth weight is linked to increased incidence of leukemia and brain tumors [4–7]. In comparison, lower birth weight is associated with other cancers such as hepatoblastoma and retinoblastoma [8, 9]. Low birth weight (LBW, < 2.5 kg) infants may be particularly vulnerable to carcinogenesis due to factors such as impaired immune function, altered hormone levels, and genetic predisposition [10, 11].

Moreover, LBW infants often experience multiple morbidities stemming from prematurity and are subjected to potentially harmful interventions such as oxygen therapy, invasive ventilation, and blood transfusions in neonatal intensive care units. However, there is limited understanding of how LBW intersects with experiences in neonatal intensive care units. A case-control study using a population-based nationwide registry in Finland investigated the association between medical interventions and childhood cancer [12]. In that study, mechanical ventilation, resuscitation, antenatal steroids, and antibiotic therapy were associated with an increased risk of childhood cancer across various gestational ages, although these associations were not consistently observed in preterm infants. These findings highlight the importance of evaluating the relationship between postnatal exposures and childhood cancer risk, especially among LBW populations.

The National Health Insurance Service (NHIS) database in South Korea contains information on cancer diagnosis and treatment, while birth weight data can be retrieved from the National Health Screening Program for Infants and Children (NHSPIC) database. Linking these datasets enables large-scale, population-based studies. In this study, we utilized the NHIS and NHSPIC databases to investigate the association between birth weight and childhood cancer. Additionally, we aimed to identify cancer-related risk factors among LBW infants, offering insights into potential avenues for intervention and prevention.

Methods

Data source

Since achieving universal healthcare coverage in 1989, Korea has maintained a centralized database of all National Health Insurance and Medical Aid claims for insured services, accessible to all medical institutions. This database contains information on healthcare utilization, medical expenditures, and diagnoses, coded according to the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10). The NHIS offers screening for all children through the NHSPIC, which collects data on birth weight and assessments of growth and development. During the screening, parents provide birth weight as documented on the birth certificate issued by the delivering medical facility. The integrated use of NHIS and NHSPIC datasets has been validated for research purposes (https://nhiss.nhis.or.kr) [13]. We submitted our research plan and Institutional Review Board approval statement (K2021-2127-001) to the NHIS, which subsequently provided anonymized data to the research institutions participating in this study. The requirement for informed consent was waived due to the retrospective and anonymized nature of the study.

Study population

This study included all live births in South Korea between 2008 and 2014. Follow-up continued until December 31, 2018, allowing observation of cancer development from a minimum of 4 to a maximum of 11 years. Infants without documented birth weights (including those who died) and those weighing less than 0.4 kg at birth were excluded, under the assumption that neonatal resuscitation was not administered. Additionally, infants without parental income data and those diagnosed with chromosomal abnormalities (ICD-10 codes Q90-99) were excluded.

Birth weight ascertainment

Birth weight data were sourced from the NHSPIC database. Most children (94.6%) underwent at least one health examination in their lifetime, during which parents reported birth weight based on the birth certificate [14]. Infants were categorized into four birth weight groups: <1.5 kg, 1.5–2.4 kg, 2.5–4.0 kg (normal birth weight, NBW), and >4.0 kg. Given the extremely small number of infants weighing < 1.0 kg and corresponding cancer cases, this group was not designated as an independent category in the primary analysis. Nevertheless, exploratory subgroup analyses were conducted when data allowed to examine potential trends in this extremely low birth-weight population.

Cancer assessment

Cancer was defined based on the ICD-10 codes for malignant neoplasms and enrollment in the NHIS Beneficiary Program, in which most cancer patients are registered. The following cancers were classified as malignant neoplasms: leukemia (C91-95), lymphoma (C81-86), central nervous system (CNS) malignancies (C71-72), neuroblastoma (C30.0, C74.0, C74.9), retinoblastoma (C64), hepatoblastoma (C22.2), sarcoma (C38.0, C49, C40-41), and extracranial germ cell tumors (C38.3, C56.9, C62.9). Cancer diagnoses recorded between 2008 and 2018 were included in the analysis.

Other study variables

Demographic and socioeconomic data were collected from the NHIS database. Insurance premiums, which are based on income level and insurance type (National Health Insurance or Medical Aid), were used as proxies for household income. Income levels were categorized into four quartiles: Category 1 (lowest 25%), Category 2 (25%–50%), Category 3 (50%–75%), and Category 4 (highest 25%), with Medical Aid beneficiaries categorized as the lowest income group. Data were collected on neonatal conditions including respiratory distress syndrome (RDS, P22), bronchopulmonary dysplasia (BPD, P27.1), necrotizing enterocolitis (NEC, P77), sepsis (P36), and retinopathy of prematurity (ROP, H35.1). For diagnostic specificity, RDS was defined as requiring surfactant therapy, and ROP was defined as requiring laser treatment (S5121-2, S5130, S5160, and S5140) in addition to ICD-10 codes. Information was also collected on neonatal interventions within the first year of life, including oxygen therapy (M0040), while excluding brief oxygen use limited to immediate postnatal resuscitation, invasive mechanical ventilator support (M0850, M0857, M0858, M0860, M5850, M5857, M5858, and M5860), radiography examinations (G0501-G9901), red blood cell (RBC) transfusions (X2021, X2022, X2031, X2032, X2091, X2092, X2131, X2132, and X2512), and phototherapy (MM350). Oxygen therapy, invasive mechanical ventilation (IMV), and RBC transfusion were first analyzed as binary variables (any exposure vs. none) to assess their overall associations with childhood cancer. To further evaluate potential dose–response relationships, these exposures were re-categorized for an additional analysis according to duration or frequency: oxygen exposure (0, 1–3, or ≥4 days), IMV duration (0, 1–4, or ≥5 days), and RBC transfusions (0, 1–2, or ≥3 events). The cut-off points for each exposure were determined from the midpoints between the 1st–2nd and 3rd–4th quartiles of their respective distributions, corresponding to clinically meaningful thresholds that distinguish short versus prolonged respiratory support and single versus multiple transfusions.

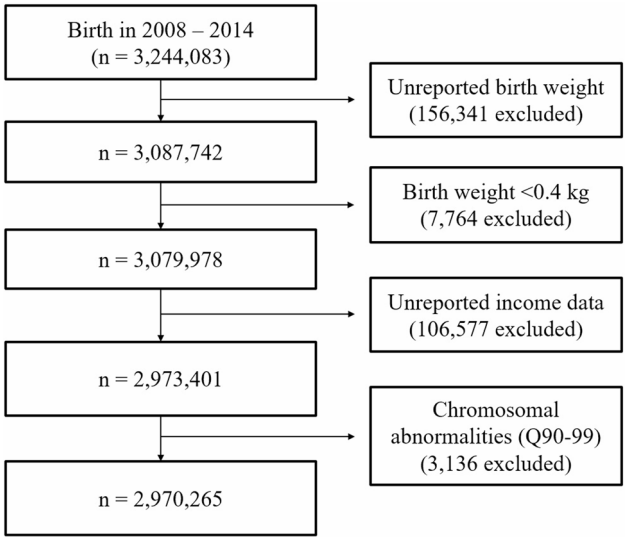

Fig. 1 Flow chart of the participant selection

Statistical analysis

Demographic differences among birth weight groups were analyzed using analysis of variance and Pearson's chi-square test. Logistic regression was used to analyze the association between birth weight and malignancy, with multivariable models adjusted for sex and income level. A subgroup analysis of LBW infants was conducted to determine the association between neonatal morbidities and subsequent cancer development. All analyses were conducted using SAS software (version 9.4; SAS Institute Inc., Cary, NC, USA). P-values < 0.05 were considered statistically significant. Odds ratios (ORs) with 95% confidence intervals (CIs) were reported to quantify associations.

Results

Study population and birth weight distribution

During the study period, 3,244,083 live births of infants who survived until discharge from their initial hospitalization were registered in the database. Of these, the following were excluded: 156,341 infants without documented birth weights, 7,764 with a birth weight < 0.4 kg, 106,577 with missing parental income data, and 3,136 with chromosomal abnormalities (Fig. 1). Each year, infants with a birth weight < 1.5 kg accounted for 0.5%–0.6% of live births, those with a birth weight of 1.5–2.4 kg accounted for 4.1%–5.1%, and those with a birth weight > 4.0 kg accounted for 2.1%–2.6% (Supplementary Table S1). The proportion of infants born to families with Medical Aid or in the lowest income quartile was lowest in the NBW group. Neonatal morbidities commonly observed in LBW infants, such as RDS, BPD, sepsis, NEC, and ROP, were most prevalent among those with a birth weight < 1.5 kg. The highest proportion of phototherapy

use was also observed in this group. Among the total of 2,970,265 live births, 4,641 children were diagnosed with cancer during follow-up, corresponding to an overall incidence of 0.16%.

Childhood cancer incidence by birth weight group

The incidence of cancer was highest among infants with a birth weight < 1.5 kg (0.36%), compared to those weighing 1.5–2.4 kg (0.19%) and the NBW group (0.15%) (Table 1). Leukemia was the most common childhood cancer (0.04%), followed by CNS malignancies (0.02%). Leukemia was most prevalent in the > 4.0 kg birth weight group (0.06%), while CNS malignancies (0.03%) were most common among infants weighing 1.5–2.4 kg. Hepatoblastoma was most prevalent in the < 1.5 kg birth weight group (0.05%). No significant differences were observed among the birth weight groups in the incidence of other childhood cancers.

Childhood cancer risk by birth weight group

Univariate logistic regression analysis demonstrated that both low and high birth weights relative to NBW were associated with increased childhood cancer incidence (Table 2). In multivariate analysis, birth weight < 1.0 kg (adjusted odds ratio [aOR], 4.025; 95% CI, 2.644–6.127), 1.0–1.4 kg (aOR, 1.900; 95% CI, 1.355–2.664), and 1.5–2.4 kg (aOR, 1.227; 95% CI, 1.080–1.395) were associated with a higher incidence of childhood cancer. For cancers with incidence differences by birth weight—leukemia, CNS malignancy, and hepatoblastoma—multivariate analysis was adjusted for sex and income level. Infants weighing > 4.0 kg had a higher risk of leukemia, those weighing 1.5–2.4 kg had a higher risk of CNS malignancy, and those weighing < 1.5 kg had a higher risk of hepatoblastoma.

Neonatal conditions and childhood cancer in low birth weight infants

In the subgroup analysis of LBW infants, multivariate analysis revealed significant associations between childhood cancer and both BPD (aOR, 2.211; 95% CI, 1.423–3.434) and sepsis (aOR, 1.556; 95% CI, 1.162–2.084) (Table 3). Given that oxygen therapy and IMV are major interventions associated with BPD, their relationships with childhood cancer were further evaluated. After adjustment, oxygen exposure exceeding 4 days during the neonatal and infantile periods was significantly associated with childhood cancer (aOR 1.601, 95% CI 1.109–2.312; Fig. 2a), whereas the duration of IMV was not (Fig. 2b). Furthermore, the incidence of childhood cancer increased proportionally with the number of RBC transfusions—1–2 events (aOR 2.875, 95% CI 1.888–4.377) and ≥ 3 events (aOR 9.286, 95% CI 5.597–15.406) (Fig. 2c). Radiography and phototherapy were not associated with childhood cancer development.

Discussion

Utilizing a large-scale population-based dataset from the NHIS and NHSPIC in South Korea, we observed an increased risk of childhood cancer among LBW infants, with the greatest risk among infants weighing less than 1.0 kg. Certain cancer types showed specific associations: hepatoblastoma was linked to birth weights < 1.5 kg, CNS malignancy to birth weights of 1.5–2.4 kg, and leukemia to birth weights >4.0 kg. Among LBW infants, neonatal conditions such as BPD and sepsis, as well as exposure to oxygen and RBC transfusion, were associated with elevated cancer risk.

It is widely acknowledged that hepatoblastoma incidence is higher among LBW infants [8, 9, 15], while leukemia is more common in those with high birth weight [6, 7, 16, 17]. Although brain tumors are frequently associated with high birth weight [17–21], certain CNS malignancies have also been linked to LBW [19, 22],

Table 1 Incidence of childhood cancer by birth weight category

	Total	< 1.5 kg	1.5–2.4 kg	2.5–4.0 kg	> 4.0 kg	*p*-value
	(*N* = 2,970,265)	(*n* = 15,353)	(*n* = 133,568)	(*n* = 2,752,795)	(*n* = 68,549)	
All cancers	4,641 (0.16)	56 (0.36)	249 (0.19)	4,210 (0.15)	126 (0.18)	< 0.001
Leukemia	1,199 (0.04)	7 (0.05)	62 (0.05)	1,088 (0.04)	42 (0.06)	0.001
Lymphoma	273 (0.01)	1 (0.01)	9 (0.01)	256 (0.01)	7 (0.01)	0.174
CNS malignancy	604 (0.02)	4 (0.03)	41 (0.03)	546 (0.02)	13 (0.02)	< 0.001
Neuroblastoma	353 (0.01)	2 (0.01)	9 (0.01)	332 (0.01)	10 (0.01)	0.346
Retinoblastoma	190 (0.01)	2 (0.01)	13 (0.01)	172 (0.01)	3 (0.00)	0.310
Wilms tumor	144 (0.00)	0 (0)	4 (0.00)	134 (0.0)	6 (0.01)	0.822
Hepatoblastoma	105 (0.00)	7 (0.05)	7 (0.01)	86 (0.00)	5 (0.01)	< 0.001
Sarcoma	300 (0.01)	2 (0.01)	17 (0.01)	272 (0.01)	9 (0.01)	0.348
Extracranial GCT	177 (0.01)	1 (0.01)	3 (0.00)	165 (0.01)	8 (0.01)	0.421

Variables are expressed as: number of cases (percentage of cancer incidence in each birth weight category)

CNS Central nervous system, *GCT* Germ cell tumor

Table 2 Logistic regression analysis of childhood cancer by birth weight category

		N	%	OR (95% CI)	Adjusted* OR (95% CI)
All cancers	< 1.0 kg	22	0.61	3.995 (2.624–6.081)	4.025 (2.644–6.127)
	1.0–1.4 kg	34	0.29	1.897 (1.353–2.660)	1.900 (1.355–2.664)
	1.5–2.4 kg	249	0.19	1.219 (1.073–1.386)	1.227 (1.080–1.395)
	2.5–4.0 kg	4210	0.15	Ref.	
	> 4.0 kg	126	0.18	1.202 (1.007–1.436)	1.182 (0.990–1.412)
Leukemia	< 1.5 kg	7	0.05	1.154 (0.549–2.426)	1.157 (0.550–2.433)
	1.5–2.4 kg	62	0.05	1.175 (0.909–1.517)	1.183 (0.916–1.528)
	2.5–4.0 kg	1088	0.04	Ref.	
	> 4.0 kg	42	0.06	1.551 (1.139–2.111)	1.519 (1.115–2.068)
CNS malignancy	< 1.5 kg	4	0.03	1.314 (0.491–3.513)	1.316 (0.492–3.520)
	1.5–2.4 kg	41	0.03	1.548 (1.127–2.126)	1.553 (1.131–2.134)
	2.5–4.0 kg	546	0.02	Ref.	
	> 4.0 kg	13	0.02	0.956 (0.552–1.657)	0.956 (0.551–1.658)
Hepatoblastoma	< 1.5 kg	7	0.05	14.603 (6.758–31.553)	14.547 (6.732–31.438)
	1.5–2.4 kg	7	0.01	1.678 (0.776–3.625)	1.683 (0.779–3.638)
	2.5–4.0 kg	86	0.003	Ref.	
	> 4.0 kg	5	0.007	2.335 (0.948–5.752)	2.277 (0.923–5.617)

OR Odds ratio, *CI* Confidence interval, *Ref* Reference, *CNS* Central nervous system

*Adjusted for sex and income

The < 1.0 kg category was analyzed only for all cancers because the number of cancer cases in this group was too small for type-specific analyses

consistent with our findings. Since certain cancers show higher rates in both high and low birth weight categories, overall cancer risk estimates should be interpreted with caution. Most prior research—primarily from Western countries—has reported increased overall cancer risk in high birth weight children [6, 7, 16]. Notably, our findings contrast with these studies, showing an inverse association between birth weight and overall cancer risk. This divergence may reflect population-specific factors, such as genetic predisposition, environmental exposures, or differences in perinatal care, which warrant further investigation.

To our knowledge, this is the first study to identify BPD and sepsis in LBW infants as risk factors for subsequent childhood cancer. BPD, defined as more than 28 days of oxygen supplementation or mechanical ventilator support [23], can lead to chronic inflammation via oxidative stress and mechanical ventilation-induced injury. This inflammation may promote cancer development through mechanisms such as precancerous mutations, apoptosis resistance, angiogenesis stimulation, and DNA damage by reactive oxygen species [24]. Previously, two large studies using registry data from Sweden and the United States reported that exposure to oxygen during

Table 3 Subgroup analysis of low birth weight infants: association between neonatal conditions and childhood cancer

		Childhood cancer *N* %		OR	Adjusted* OR (95% CI)
Birth weight	< 1.5 kg	56	0.36	1.960 (1.466–2.621)	1.950 (1.458–2.607)
	1.5–2.4 kg	249	0.19	Ref.	
Neonatal condition	RDS	47	0.34	1.766 (1.294–2.411)	1.333 (0.928–1.916)
	BPD	40	0.52	2.760 (1.978–3.852)	2.211 (1.423–3.434)
	NEC	10	0.45	2.220 (1.181–4.175)	1.576 (0.819–3.030)
	Sepsis	62	0.33	1.793 (1.356–2.371)	1.556 (1.162–2.084)
	ROP	7	0.46	2.266 (1.069–4.802)	1.353 (0.616–2.972)
Exposure	Oxygen	160	0.31	2.124 (1.696–2.660)	1.324 (1.006–1.742)
	IMV	102	0.42	2.557 (2.015–3.245)	1.097 (0.777–1.547)
	RBC transfusion	102	0.63	4.136 (3.259–5.250)	4.027 (2.817–5.759)
	Radiography examinations	249	0.28	1.655 (1.321–2.073)	1.215 (0.358–4.118)
	Phototherapy	164	0.25	1.582 (1.259–1.988)	0.392 (0.140–1.093)

OR Odds ratio, *CI* Confidence interval, *RDS* Respiratory distress syndrome, *BPD* Bronchopulmonary dysplasia, *NEC* Necrotizing enterocolitis, *ROP* Retinopathy of prematurity, *Ref.* Reference, *IMV* Invasive mechanical ventilation, *RBC* Red blood cell

The analysis for oxygen exposure, IMV support, X-ray, RBC transfusion, and phototherapy was expressed as quartiles

*Adjusted for sex and income level; additional models included days of IMV support, oxygen exposure, or number of RBC transfusions where indicated

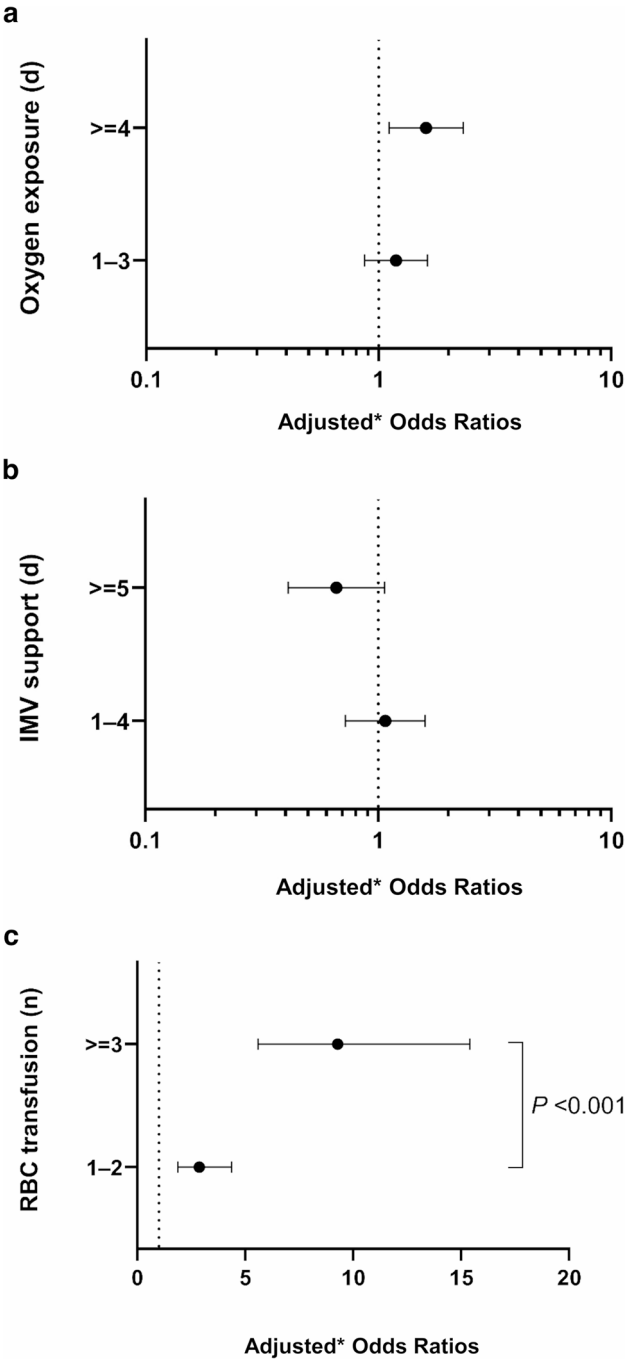

Fig. 2 Adjusted odds ratios (aOR) for the development of childhood cancer in low birth weight infants according to neonatal exposures during the first year of life. **a** Association between oxygen exposure duration and childhood cancer risk, adjusted for sex, income level, duration of invasive mechanical ventilation (IMV), and number of red blood cell (RBC) transfusions. **b** Association between IMV duration and childhood cancer risk, adjusted for sex, income level, oxygen exposure, and number of RBC transfusions. **c** Association between the number of RBC transfusions and childhood cancer risk, adjusted for sex, income level, duration of oxygen exposure, and IMV All models included sex and income as basic covariates, with mutual adjustment for the other relevant exposures as indicated Oxygen exposure and IMV duration (d) indicate the number of exposure days, and RBC transfusions (*n*) indicate the number of transfusion events within the first year of life. Error bars indicate 95% confidence intervals (CIs)

the neonatal period was associated with cancer in childhood [25, 26], which is supported by the present study's demonstration of a similar association in LBW infants for the first time.

Sepsis, another common neonatal condition associated with systemic inflammation, has also been implicated in cancer risk. A Swedish case-control study reported a potential association between neonatal infection and childhood brain tumors [27]. Furthermore, a possible link between systemic inflammation and cancer has been observed in adults with autoimmune diseases [28]. Various molecular and cellular signaling pathways link inflammation with cancer pathogenesis, and factors related to sepsis, such as infection, inflammation, and antibiotic use, may contribute to this relationship [28–30].

Among neonatal interventions in LBW infants, RBC transfusion was also associated with subsequent cancer development. Past studies have highlighted associations between blood transfusions and adult liver cancer and lymphoma, often attributed to transfusion-transmitted viruses such as hepatitis B and Epstein-Barr [31]. Transfusions may also contribute to cancer risk through the delivery of biologically active substances or modulation of immune function [32]. However, causality remains unclear. Alternatively, the number of RBC transfusions may reflect illness severity or underlying neonatal complications—such as extreme prematurity—that independently increase cancer risk [33].

The overall incidence of childhood cancer observed in our cohort (0.16%) was comparable to national estimates, supporting the completeness of case ascertainment in the NHIS dataset. According to the Korea Central Cancer Registry, the age-standardized incidence rate of childhood cancer (ages 0–14 years) was 134.9 per million between 1999 and 2011, with the highest incidence among children younger than five years (277.3 per million in < 1 year and 164.9 per million in 1–4 years) [1]. Although our study covered a slightly later period (2008–2018) and primarily included children followed up to age five, the comparable incidence levels suggest that under- or over-capture of cancer cases is unlikely.

Additionally, as the follow-up period extended only up to approximately five years of age, our findings primarily represent cancers that develop during early childhood, such as hepatoblastoma, central nervous system tumors, and leukemia. Pediatric malignancies that typically occur after age five, including lymphomas, bone tumors, and germ cell tumors, were beyond the scope of this study. Therefore, the present results should be interpreted as reflecting early-onset childhood cancers.

Several limitations should be noted. First, as a retrospective cohort study, we were able to determine associations but not causality. Our analysis did not include

information on genetic susceptibility or parental environmental exposures such as smoking, alcohol use, or radiation, which are known to influence childhood cancer risk [34–36]. Although these unmeasured confounders could have affected the observed associations, their impact is likely to be limited given the population-based design and the consistency of the findings across multiple neonatal conditions and interventions. To minimize residual confounding from socioeconomic and environmental disparities, we included parental income as a proxy measure of socioeconomic status in all multivariable models. Further studies integrating genetic and environmental data are warranted to clarify potential causal pathways. While conditions like BPD, sepsis, and RBC transfusion (predominantly performed in LBW infants) were linked to cancer, they may act as proxies for prematurity. Thus, while these factors are associated with cancer risk, their role as indicators of underlying prematurity warrants careful consideration in the interpretation of the results. Second, the study period may not have been long enough to detect all cancer cases, especially those that develop later in childhood. However, in the Korean childhood cancer study, most cases were diagnosed before age five, with the highest incidence in infants under one year, followed by those aged 1–4 years [1]. Finally, our analysis was limited by the absence of gestational age data in the NHIS, which safeguards patient privacy. Although birth weight often correlates with gestational age, this is not always the case—particularly in infants with intrauterine growth retardation— highlighting the need to assess multicollinearity between these two variables in future studies.

Despite these limitations, our study has a number of strengths. Several prior investigations—including small case-control studies and cohort studies—have reported that LBW is a risk factor for childhood cancer. A key strength of our analysis is its use of a large, population-based dataset, in contrast to earlier research with smaller or nonrepresentative samples. Furthermore, this is the first study to examine the role of neonatal morbidity and treatment in the relationship between LBW and childhood cancer.

Conclusion

This study demonstrates that LBW infants are at a heightened risk of developing childhood cancer. Among this population, common neonatal conditions such as BPD and sepsis were also associated with increased cancer risk. Additionally, exposure to oxygen therapy and RBC transfusions was linked to childhood cancer in LBW infants. However, these associations are not conclusive, and further research—including prospective longitudinal studies and biological investigations—is needed to explore causality. These findings may inform the development of long-term follow-up systems for LBW infants.

Abbreviations

LBW	Low birth weight
NHIS	National Health Insurance Service
NHSPIC	National Health Screening Program for Infants and Children
NBW	Normal birth weight
CNS	Central nervous system
RDS	Respiratory distress syndrome
BPD	Bronchopulmonary dysplasia
NEC	Necrotizing enterocolitis
ROP	Retinopathy of prematurity
OR	Odds ratio
CI	Confidence interval
aOR	Adjusted odds ratio
IMV	Invasive mechanical ventilation
RBC	Red blood cell

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12887-025-06382-1.

Supplementary Material 1.

Acknowledgements

Not applicable.

Authors' contributions

E.J. and I.G.S. conceptualized and designed the study, had full access to all data, took responsibility for the integrity and accuracy of the data analysis, and drafted the original manuscript. Y.L. and Y.M.C. led data acquisition, extracted and linked variables from different sources, and contributed to the study design. S.H.S. and H.S.K. conceptualized and designed the study, supervised and coordinated data collection, provided direction across all phases, had full data access, took responsibility for the integrity and accuracy of the data analysis, and contributed to writing and editing the manuscript.

Funding

This research was funded by the SNUH Lee Kun-hee Child Cancer & Rare Disease Project, Republic of Korea (24 C-014-0000). The funders had no role in the study design, data collection, analysis, interpretation, manuscript writing, or decision to publish.

Data availability

The data that support the findings of this study are available from NHIS, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. However, data may be obtained from the corresponding author (SHS, revival421@snu.ac.kr) upon reasonable request and with permission from NHIS.

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of Korea University Guro Hospital (K2021-2127-001) and the Korea NHIS Medical Information Disclosure Committee (NHIS-2021-2-227). All methods were conducted in accordance with the IRB-approved protocol and in compliance with relevant guidelines and regulations. Informed consent was waived due to the retrospective nature of the study and use of anonymized administrative data.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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Received: 23 July 2025 / Accepted: 10 November 2025
Published online: 01 December 2025

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