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ORIGINAL ARTICLE

Can Breastfeeding Lower the Risk of Childhood Leukemia? Insights From a Duhok, Iraq. Case Control Study

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Abstract

Introduction: **To study the association between breastfeeding practices and the risk reduction of childhood leukemia and identify the ideal duration for breastfeeding duration for infants' health, a case−control study was conducted involving children aged 0−16 years with leukemia and a control group.**

Methods: **The study examined breastfeeding duration, type of feeding in the first six months, maternal characteristics (age, education, smoking during pregnancy, history of abortion, birth control pill use), and child-related variables (sex, age at diagnosis, and birth order). Data analysis was conducted using SPSS Version 27 and employing odds ratio and 95 % confidence intervals (CIs) were calculated. p-value of <0.05 was considered statistically Significant.**

Results: **A study analyzed 100 leukemia cases and 100 controls, having similar mean ages (5.05 ± 3.433 vs. 5.84 ± 3.404) and male participants (63 % vs. 57 %), to assess breastfeeding's impact on leukemia risk in children. The study found no significant associations between leukemia and factors like smoking during pregnancy (5 % of cases vs. 3 % of controls), abortion history (45 % in both groups), birth control pill use (22 % vs. 34 %), and age group of 2−5 years (68 % vs. 54 %). However, A significant association was found with maternal education ($p = 0.001$); 39 % of case mothers had primary education, while 52 % of control mothers had intermediate or higher education. Exclusive breastfeeding was higher in controls (53 %) than cases (28 %) ($p < 0.001$), while formula feeding was more common in cases (57 %) than controls (33 %). Shorter breastfeeding (<6 months) was more common in cases (56 %) than controls (31 %) ($p = 0.001$), while >12 months was higher in controls (32 %) than cases (16 %). Maternal education and longer breastfeeding inversely correlated with leukemia risk. Logistic regression supported the protective effect of exclusive breastfeeding (OR = 0.501, $p < 0.001$) and >12 months duration (OR = 0.721, $p = 0.001$).**

Conclusion: **This study highlights that exclusive and prolonged breastfeeding protects against childhood leukemia. Maternal education plays a role in reducing the frequency of leukemia, thus emphasizing the importance of maternal awareness and health education. However, smoking during pregnancy, history of abortion, and birth control use showed no significant associations.**

Keywords: Breastfeeding, Childhood leukemia, Maternal education, Exclusive breastfeeding, Prolonged breastfeeding, Risk factors, Protective effect

Introduction

Leukemia accounts for 30 % of all pediatric malignancies, making it the most common malignancy in children (Karimi et al., 2016). Two main types of childhood leukemia are: acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML). AML is less frequent and accounts for approximately 17 % of leukemia cases in children (Health Service Executive (HSE); Metayer

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et al., 2013). Childhood leukemia's exact etiology is unclear, however research indicates links to several risk factors, like environmental exposures (chemicals, infections, and radiation) and genetic disorders such as Down syndrome, ataxia telangiectasia, Fanconi anemia, and Bloom syndrome (Karimi et al., 2016).

Human milk contains numerous antimicrobial and anti-inflammatory agents. Many studies showed that breast-feeding protects against acute infections of gastrointestinal tract through transmitting maternal antibodies, lymphocytes and macrophages (Kakaje et al., 2020; Li et al., 2014). Breast milk can also protect against various diseases including cardiovascular diseases, obesity, diabetes, and some forms of cancer (Brahm and Valdes, 2017).

Agency for Healthcare Research and Quality (AHRQ), notes that any breastfeeding is associated with a 64 % reduction in nonspecific gastrointestinal infections, and this effect lasts for two months beyond cessation of breastfeeding (Health Service Executive (HSE)). There is an inverse relationship between lactation duration and risk of being overweight; each month of breastfeeding reduces the risk by 4 % (Breastfeeding et al., 2012). Those not breastfed at discharge had 33 % higher risk of diabetes in the first 20 years (Health Service Executive (HSE)).

Breastfeeding can support the immune system and help against many infections and health problems but may also transfer oncogenic substances, the mother was exposed to (Kakaje et al., 2020).

Breastfeeding is not only beneficial for children but also for mothers (Masi and Stewart, 2024). It reduces the risk of ovarian cancer, breast cancer, and osteoporosis in mothers. However, there is no clear correlation between breastfeeding and childhood leukemia. Several studies demonstrated that breastfeeding was not associated with ALL (Health Service Executive (HSE)). A meta-analysis concluded that breastfeeding for 6 months or more can decrease the incidence of childhood leukemia and other health benefits for children and mothers (MacArthur et al., 2008).

Recent case–control studies demonstrated that breastfeeding for more than 6 months may be effective against childhood ALL (Amitay and Keinan-Boker, 2015; Kakaje et al., 2020; Kwan et al., 2004).

Multiple meta-analyses established that both short- and long-term breastfeeding decreased the risk of leukemia in childhood (Amitay and Keinan-Boker, 2015). But most of these studies were not done in developing countries where there may be different risk factors such as daily practices and environmental exposure that can lead to different outcomes. Although breastfeeding is beneficial for the immune system against infections and other medical conditions, breastfeeding may transfer some oncogenic substances to which the mother was exposed (Kakaje et al., 2020).

Despite the global consensus on the benefits of breastfeeding, there is limited local evidence regarding its potential protective role against childhood leukemia in Middle Eastern populations, especially in Iraq. Cultural practices, environmental exposures, and socioeconomic conditions vary significantly across regions, which may influence disease risk and the impact of early-life interventions. Therefore, findings from other settings may not be directly applicable. This study fills a critical regional knowledge gap by investigating the association between breastfeeding and childhood leukemia in Duhok, Kurdistan province, Iraq—a region with distinct sociodemographic and cultural characteristics.

Materials and methods

A case–control study was conducted in Duhok, Kurdistan province, north of Iraq, from June 1, 2021, to June 1, 2023. The study included all children aged 0–16 years with childhood leukemia and chemotherapy at Jin Oncology Hospital and whose mothers could accurately recall the timing of breastfeeding. Controls were healthy children aged 0–16 years, frequency matched to cases by age and sex, to reduce confounding.

The researcher filled out a questionnaire through direct interviews with the mothers, focusing on the following: duration of breastfeeding, type of feeding in the first six months, maternal age, mother's education, smoking during pregnancy, abortion history, history of using birth control pills before pregnancy, sex, age at diagnosis, and birth order of the child.

All statistical analyses were carried out using the Statistical Package for Social Sciences (SPSS) Version 27. The data are expressed as mean and standard deviation or frequency and percentage. The similarities between two independent groups were compared using the Student's t-test for continuous variables. The chi-squared (χ^2) test was employed for categorical variables. Multivariable logistic regression analysis was utilized to assess the risk factors for childhood leukemia. Multivariable logistic regression was performed to adjust for confounding. Results are summarized in a separate paragraph highlighting which variables remained significant after adjustment. Odds ratios (ORs) and 95 % confidence intervals (CIs) were discussed. A

two-sided p-value <0.05 was considered statistically significant for all analyses.

Results

Demographic characteristics

The study included 100 cases of leukemia and 100 controls, as provided in Table 1. The mean age of the patients was 5.05 ± 3.433 years, and the average age of the controls was 5.84 ± 3.404. The percentage of males was 63 % in the case group and 57 % in the control group (Table 1). Smoking by mothers during pregnancy was observed in 5 % of cases and 3 % of controls, with no significant difference ($p = 0.470$, Tables 1 and 3, OR = 0.546). The history of abortion was present in 45% of mothers in both cases and controls ($p = 1.0$, Table 1, Table 3, OR = 0.998). The use of birth control pills before pregnancy was reported in 22 % of the mothers of cases and 34 % of the mothers of controls, with no significant difference ($p = 0.059$, Tables 1 and 3, OR = 1.851). Although not statistically significant (p = 0.056), a trend toward association was observed, suggesting a potential link that warrants further investigation. The predominant age group was 2–5 years (68 %), and in the controls, it was 2–5 years (54 %), with no significant difference ($p = 0.119$, Table 1). The most frequent birth orders for both cases and controls were the fourth and above, at 39 % and 38 %, respectively ($p = 0.126$, Table 1). Maternal age at the time of delivery was most commonly 25–30 years (60 %) in both groups, with no major difference ($p = 1.0$, Table 1).

Maternal factors

Regarding mothers' education, a significant difference was observed ($p < 0.001$, Tables 1 and 2, OR for illiteracy = 0.759). Most mothers were primary school graduates (39 %) and illiterate (28 %), while in the control group, most mothers were university graduates (26 %) and intermediate school graduates (26%).

Breastfeeding patterns

The feeding practices of the cases and controls in this study are outlined in Table 2. Majority were breastfed for 0–6 months (56 %), whereas most controls were breastfed for 7–12 months (37 %),

Table 1. Demographic and clinical characteristics of cases and controls.

Variables		Case	Control	Total	P value
		Frequency (%)	Frequency (%)	Frequency (%)	
Gender	Male	63 (63 %)	57 (57 %)	120 (60 %)	0.386
	Female	37 (37 %)	43 (43 %)	80 (40 %)	
Age group (case/control)	Less than 2 years	2 (2 %)	2 (2 %)	4 (2 %)	0.119
	2_5 years	68 (68 %)	54 (54 %)	122 (61 %)	
	Above 5 years	30 (30 %)	44 (44 %)	74 (37 %)	
Categorization of maternal age at delivery	<25	28 (28 %)	28 (28 %)	56 (28 %)	1
	25_35	60 (60 %)	60 (60 %)	120 (60 %)	
	>35	12 (12 %)	12 (12 %)	24 (12 %)	
Mother's education level	Illiterate	28 (28 %)	20 (20 %)	48 (24 %)	<0.001
	Primary	39 (39 %)	16 (16 %)	55 (28 %)	
	Intermediate	8 (8 %)	26 (26 %)	34 (17 %)	
	Preparatory	10 (10 %)	12 (12 %)	22 (11 %)	
	Graduate	15 (15 %)	26 (26 %)	41 (21 %)	
Type of feeding during the first 6 months	Exclusive breastfeeding	28 (28 %)	53 (53 %)	81 (40.5 %)	<0.001
	Predominantly breastfeeding	15 (15 %)	14 (14 %)	29 (14.5 %)	
	Predominantly formula feeding	57 (57 %)	33 (33 %)	90 (45 %)	
Duration of breastfeeding	0–6 Months	56 (56 %)	31 (31 %)	87 (43.5 %)	0.001
	7–12 Months	28 (28.0 %)	37 (37 %)	65 (32.5 %)	
	>12 Months	16 (16.0 %)	32 (32 %)	48 (24.0 %)	
Birth order category	First	18 (18 %)	29 (29 %)	47 (24 %)	0.126
	Second	25 (25 %)	14 (14 %)	39 (20 %)	
	Third	18 (18 %)	19 (19 %)	37 (19 %)	
	Fourth and above	39 (39 %)	38 (38 %)	77 (39 %)	
Smoking during pregnancy	Yes	5 (5 %)	3 (3 %)	8 (4 %)	0.470
	No	95 (95 %)	97 (97 %)	192 (96 %)	
History of using birth control pills before pregnancy	Yes	22 (22 %)	34 (34 %)	56 (28 %)	0.059
	No	78 (78 %)	66 (66 %)	144 (72 %)	
Abortion history	Yes	45 (45 %)	45 (45 %)	90 (45 %)	1
	No	55 (55 %)	55 (55 %)	110 (55 %)	

Table 2. Logistic Regression Analysis of Maternal Education, Breastfeeding Duration, and Feeding Type in cases and controls.

Variables		Case	Control	Total	OR	P value
		Frequency (%)	Frequency (%)	Frequency (%)		
Mother's education level	Illiterate	28 (28 %)	20 (20 %)	48 (24 %)	0.759	0.007
	Primary	39 (39 %)	16 (16 %)	55 (28 %)		
	Intermediate	8 (8 %)	26 (26 %)	34 (17 %)		
	Preparatory	10 (10 %)	12 (12 %)	22 (11 %)		
	Graduate	15 (15 %)	26 (26 %)	41 (21 %)		
Breastfeeding duration	0–6 Months	56 (56 %)	31 (31 %)	87 (44 %)	0.721	0.001
	7–12 Months	28 (28 %)	37 (37 %)	65 (33 %)		
	>12 Months	16 (16 %)	32 (32 %)	48 (24 %)		
Type of feeding during the first 6 months	Exclusive breastfeeding	28 (28 %)	53 (53 %)	81 (40.5 %)	0.501	<0.001
	Predominantly breastfeeding	15 (15 %)	14 (14 %)	29 (14.5 %)		
	Predominantly formula feeding	57 (57 %)	33 (33 %)	90 (45 %)		

with a significant inverse relationship between the duration of breastfeeding and the risk of leukemia ($p = 0.001$, OR for 0–6 months = 0.721, Table 2, Fig. 2). Exclusive breastfeeding was registered in 28 % of the cases and 53 % of the controls, with a significant association ($p < 0.001$, OR = 0.501, Table 2). Predominant breastfeeding was observed in 15 % of the cases and 14 % of the controls, with no significant difference ($p = 0.721$, Table 2). Predominantly, formula feeding was reported in 57 % of cases and 33 % of controls, showing a significant association ($p < 0.001$, Table 2, Fig. 1).

Multivariable analysis

The maternal factors associated with childhood leukemia are categorized in Table 3. Smoking during pregnancy was not significantly associated with a higher risk of leukemia (OR = 0.546, p = 0.422, Table 3). In contrast, the use of birth control pills before pregnancy (OR = 1.851, p = 0.056) and a history of abortion (OR = 0.998, p = 0.988) were not significantly associated with childhood leukemia.

Multivariable logistic regression findings

After multivariable adjustment, exclusive breastfeeding (OR = 0.501, p < 0.001) and breastfeeding >12 months (OR = 0.721, p = 0.001) remained significant. Maternal education also remained a significant predictor. Smoking, abortion, and contraceptive use were not significant after adjustment.

Discussion

This case–control study in Duhok, Iraq, found that exclusive breastfeeding for the first six months and extended breastfeeding beyond 12 months as significant protective factors against childhood leukemia. These findings align with global trends but also

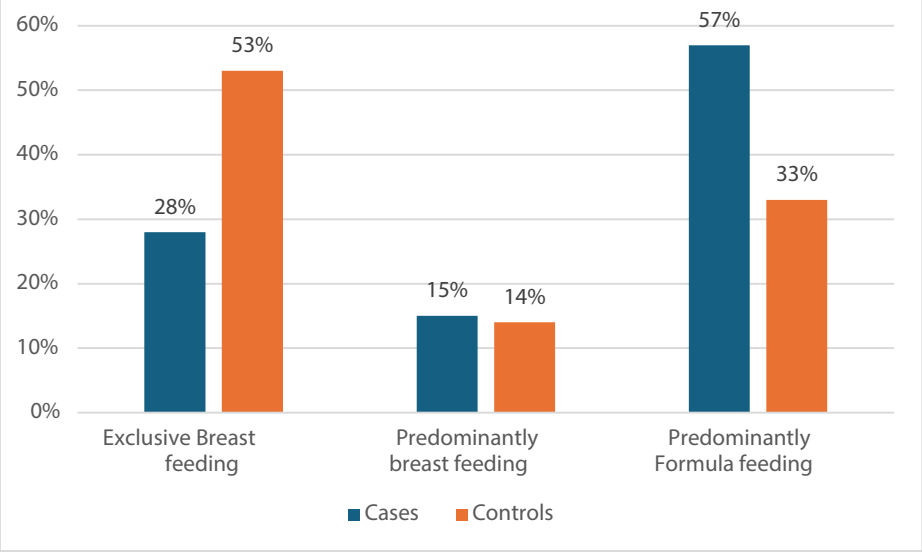

Fig. 1. Distribution of feeding types during the first 6 months among cases and controls.

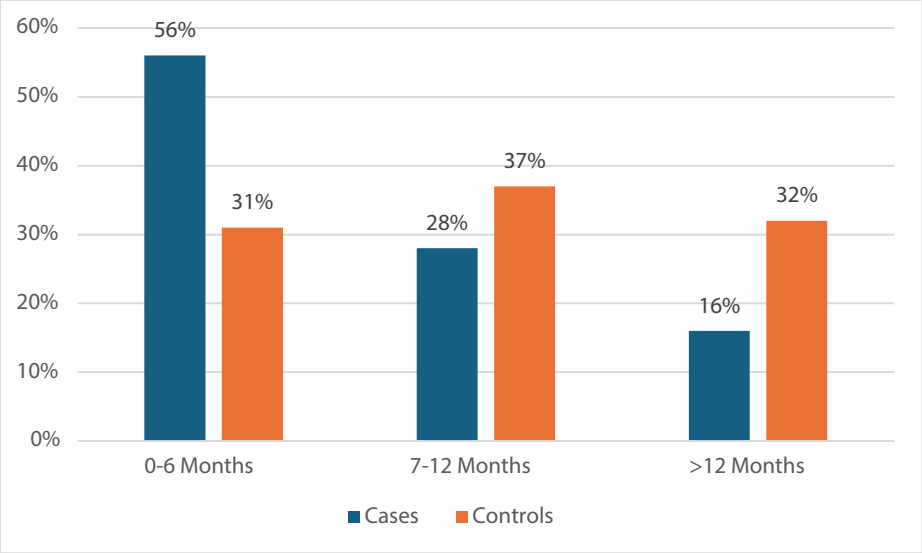

Fig. 2. Distribution of breastfeeding duration among cases and controls in Duhok.

highlight regional nuances, particularly regarding sociodemographic and age-related patterns.

Breastfeeding duration and leukemia risk

The inverse association between exclusive breastfeeding and leukemia risk (OR = 0.50, p < 0.01) corroborates Pooled analyses indicated a 15 % reduction for acute lymphoblastic leukemia (ALL) among children breastfed for 7–12 months (OR 0.85), highlighting breastfeeding's protective effect (Schraw et al., 2022a). A dose–response relationship was evident, with breastfeeding >12 months further lowering odds (OR = 0.72, p = 0.01). These findings mirror population-based studies meta-analysis (Schraw et al., 2022b; Søegaard, 2024). Mechanistically, breast milk's immunomodulatory components, such as secretory IgA and oligosaccharides, may suppress inflammation and infection-driven leukemogenesis (Waly et al., 2011). Conversely, formula feeding, prevalent in cases (57 % vs. 33 %), may heighten leukemia risk by depriving infants of these protective factors, as observed in studies linking artificial feeding to immune dysregulation (Steliarova-Foucher et al., 2017). While many studies support the protective role of prolonged breastfeeding against ALL, some research has shown no significant association. For instance, a study conducted in Oman found that the breastfeeding duration did not exhibit any shielding effect against childhood leukemia, suggesting that environmental and genetic factors might also contribute significantly to the disease's occurrence (Waly et al., 2011). The discrepancies may reflect population-specific exposures, differences in data collection, or genetic susceptibility. For example, lower statistical power or differences in breastfeeding practices may explain why the Omani study found no association.

Age, sex distribution

Most cases (68 %) and controls (54 %) were aged 2–5 years (p = 0.019), consistent with global ALL incidence peaks in early childhood (Steliarova-Foucher et al., 2017). Male predominance in cases (63 % vs. 57 % controls; p = 0.386) aligns with epidemiological trends, though the lack of statistical significance here contrasts with meta-analyses reporting a 10–20 % higher leukemia risk in males

Table 3. Logistic regression analysis of maternal factors associated with childhood leukemia in cases and controls.

Variables		Case	Control	Total	OR	P value
		Frequency (%)	Frequency (%)	Frequency (%)		
Smoking during pregnancy	Yes	5 (5 %)	3 (3 %)	8 (4 %)	0.546	0.422
	No	95 (95 %)	97 (97 %)	192 (96 %)		
History of using birth control pills before pregnancy	Yes	22 (22 %)	34 (34 %)	56 (28 %)	1.851	0.056
	No	78 (78 %)	66 (66 %)	144 (72 %)		
Abortion history	Yes	45 (45 %)	45 (45 %)	90 (45 %)	0.998	0.988
	No	55 (55 %)	55 (55 %)	110 (55 %)		

(Dorak and Karpuzoglu, 2012). This discrepancy may reflect regional genetic or environmental modifiers, warranting further investigation.

Maternal education and sociodemographic factors

Maternal illiteracy trended toward higher leukemia risk (OR = 0.76, p = 0.07), consistent with studies shown that children of mothers with higher educational attainment tend to have a lower risk of developing childhood leukemia (Ezzat et al., 2016; Metayer et al., 2014). However, a study in Denmark found that high maternal education was linked to a threefold increase in the risk of AML in children aged 0–4 years (OR = 3.07), which is supported by Nematollahi et al. (2023) (Erdmann et al., 2021; Nematollahi et al., 2023).

Emerging risk factors: birth control pills

Pre-pregnancy oral contraceptive use showed a marginal risk association (OR = 1.85, p = 0.056), Maternal use of hormonal contraceptives within 3 months before or during pregnancy is linked with a 22 % higher risk of childhood leukemia, particularly non-lymphoid leukemia (HR = 1.69) (Hemmingsen et al., 2025).

Non-significant factors

Smoking during pregnancy and abortion history lacked significant associations, this is consist with Italian study (SETIL) who found no evidence linking maternal smoking during pregnancy to childhood ALL (Farioli et al., 2014). However, a large cohort study of 1,440,542 Swedish children found that maternal smoking during pregnancy was associated with an increase in the risk of childhood leukemia and lymphoma. The study emphasized that maternal smoking adversely affects pregnancy outcomes and may contribute to leukemogenesis in offspring (Mucci et al., 2004).

Limitations

Although our findings support a protective role of breastfeeding, limitations such as recall bias, small sample size, and unmeasured confounders must be acknowledged. Larger prospective studies are needed to confirm these findings.

Conclusion

Exclusive and long-term breastfeeding emerged as significant protective factors for childhood leukemia, so it's public health importance. Maternal education and oral contraceptive use showed possible association, further research is needed to clarify these associations and to explore regional differences. Breastfeeding may be a key preventive strategy to reduce childhood leukemia incidence.

Ethics

Ethical approval was obtained from Ethical committee at General directorate of Health in Duhok province, Kurdistan region, Iraq.

Author Contributions

- Bashar I. Mohammed: Conceptualization, methodology, data analysis, manuscript drafting, corresponding author.
- Akrem M. Atrushi: Study design, clinical oversight, manuscript review.
- Ibrahim A. Naqid, Eman H. Ali, Raad E. Omar, Kavi M. Sadoun, Daveen A. Muhammad, Baderkhan I. Abdullah,
- Huda H. Mohammed, Elaf F. Salim: Data collection, patient recruitment, literature review, manuscript editing.

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Conflicts of interest

The authors have no conflict of interest.

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