Breastfeeding and acute lymphoblastic leukaemia: potential leukemogenesis in children in developing countries

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Abstract

Background: Breastfeeding (BF) is known to decrease acute lymphoblastic leukaemia (ALL) incidence. However, most of these studies were conducted in developed countries and mothers in developing countries may be exposed to different substances which could be transferred via breastmilk which emphasise on the importance of conducting studies in developing countries to assess the effect of these different factors.

Methods: Our case-control study was conducted in the major paediatric cancer centre in Syria. Information was obtained from the hospital's records of patients who did not have a hereditary or chromosomal syndrome and aged 4 years and less. The cases were ALL patients and controls were hospital inpatients. The patients were divided into 3 groups depending on their feeding habits before the age of 6 months.

Results: Our sample had 70 cases of ALL with 42 males (60%) and 60 controls with 36 males (60%) aging four years and younger. Sixty cases and 41 controls were exclusively breastfed, 8 cases and 6 controls used extra infant formula with BF and two cases and 13 controls relied on only infant formula. We found statistical significant difference when comparing cases and controls and BF ($P < 0.05$) with cases being exclusively breastfed more. In case group, being born with no complication, and having low educational parents educational level were correlated with BF ($P < 0.05$). However, gender, consanguinity, CD10, FAB classification, ALL-subtypes, risk and family history were not significant.

Conclusion: There are certain practices among the Syrian people, especially among low educational level parents that makes their children more vulnerable to ALL when BF. We speculate certain substances and behaviours being responsible. Even in the higher educational level parents, the protection factor that BF had was insignificant as they also practice these harmful behaviours but less often. BF had minor effects on the prognosis and subtype of ALL.

1. Background:

Breastfeeding (BF) provides the best source of nutrition for infants and the ideal source is exclusive breastfeeding (EBF) in the first six months of life [1]. However, in some cases BF is not attainable and therefore infant formula is a rational substitution to meet the infant's nutritional needs. The World Health Organization (WHO) has warned that cow's milk should never be used in infants without modifications. As it is not feasible to produce infant formula that mimics breast milk, infant formula is mostly cow's milk or soymilk with supplemented ingredients, with certain modifications on proteins and fatty acids, and iron and vitamins added to approximate human breastmilk. Quantities of such supplement ingredients are advised to be carefully monitored for the safety and wellbeing of infants, and as such their manufacturing is strictly regulated to meet designated quality criteria [2, 3].

The most common cancer in children younger than 15 years old is leukaemia, with a prevalence that can reach up to 30% of malignancies. There are two main types of childhood leukaemia with 78% being acute

lymphoblastic leukaemia (ALL), with a peak onset age between three and four years [4–6]. While childhood leukaemia has been widely researched in the past half century, its aetiology and risk factors are still uncertain. Specific genetic syndromes such as Down syndrome in addition to infections, and other environmental factors may be linked to a small percentage of cases [6, 7]. BF has been proven to have an important effect on the newborn's immune system, and in protecting them from early infections, such as gastrointestinal infections, with the effect continuing beyond infancy in some cases [8, 9]. Greaves et al. suggested a relationship between early infections and subtypes of ALL [10], and meta-analyses have showed that short or long term BF reduced risks of childhood leukaemia [11, 12]. However, most studies were not conducted in developing countries which have a wide variety of different environmental exposure and different habits that can lead to different outcome. Although BF has a complex relationship with ALL and protective, and beneficial immune factors from many conditions, BF can also be a means of transferring harmful or oncogenic substances from the mother to the infant. In this study, we are going to discuss the relationship between BF with its characteristics and ALL in developing countries and discussing different factors that could have led to these findings.

2. Methods:

Our case-control study was conducted in the Children's University Hospital of Damascus University between 21st August 2017, and 21st August 2018. This hospital is one of two major paediatric centres in Syria, and it is the major centre across the country which provides free healthcare and chemotherapy to its patients.

We performed a case-control study of childhood ALL to determine the relationship between BF, incidence of childhood ALL and its relationship to ALL variables. Information from the sample groups for case and control groups were obtained from the hospital's records and all information were provided by the child's caregiver.

1) Ethical commute approval and consents:

The study was approved by the ethics committee of Damascus University. Informed consent from the caregiver was taken after their examination and diagnosis at the Children's University Hospital. Consent was also obtained to use the data and publish it without any indication for the identity of the child.

2) Subject identification:

Information was taken in the out-patient clinics by direct interview with the care givers, as self-reported family history was found to be a reliable means to determine the individuals at risk of being predisposed to cancer [13]. Caregiver was the person responsible for the care of the child. Most information was sought to be obtained from the mother or father unless they were diseased, then information would be taken from the next family member responsible for the care. The relationship of caregiver was written in the records and physicians do not write down any information they found unreliable. Moreover, any invalid or unclear response would be rejected for the study. All information obtained was from patients records; they were recorded either during time of diagnosis of the child or when the child stayed at

hospital, returned to the hospital clinic, or when procedures done such as bone marrow aspiration and flow cytometry. Records were later retrieved for the study after obtaining approval from the care giver.

The case group comprised of children with ALL aged four years and younger. ALL was diagnosed by bone marrow aspiration and immune-phenotyping. Approximately, for each case, one non-cancer patient was selected and matched for age when diagnosed for both groups and gender. We excluded any patient with hereditary haematological, metabolic disorders, constitutional hereditary diseases, aneuploidy syndromes, or single gene traits. We also excluded any patient who had a medical indication for formula feeding before having the disease. We also excluded Burkitt leukaemia (L3) as it has a viral etiology that might be a confounding factor. The children who were selected as controls were hospital inpatients, randomly selected for the study and matched before enrolling. Controls were randomly selected from other departments than haematology while excluding patients older than 4 years old and any patient who had a medical indication for infant formula. We also excluded from either case or control groups any patient who had missing or invalid data concerning feeding status in the first six months, or substantial data such as gender and age.

Children who required special infant formula other than cow's milk such as soymilk were excluded. Formula feeding was based on cow milk that was modified to meet the quality criteria [2, 3]. As this is the only fully-working centre for children in Syria, response rates was excellent provided that it is full anonymous. Patients data were recorded for the study without using names, but only data records. Cases data was also divided by the ALL subtype (T-ALL and B-ALL) and by L1 and L2.

3) Exposure measurements and groupings:

The patients' caregivers provided the information to the supervising hospital physicians about method of feeding for the first 6 months and were written down in the hospital's records. We divided children into 3 Groups depending on their feeding habits before the age of 6 months:

- Group A: It contains children who were exclusively breastfed even if rarely but irregularly used infant formula. Any child who required using formula in regular basis with the breastfeeding, for instance not just for once or twice in special occasions, are not considered in Group A
- Group B: It contains children who regularly took infant formula with breastmilk, for instance who required additional formula with their feeding as the child required this or the mother's milk was not enough.
- Group C: It contained children who ceased breastfeeding altogether before the age of 6 months and were only dependent on infant formula even if they were breastfed in their first months of their life.

Records did not trace milk-feeding habits after 6 months. All enrolled patients did not start taking solid food beside milk before the age of 6 months. No more detailed records were available. Any missing or invalid data was excluded. Physicians do not write down any information if the source was unreliable.

4) Covariate measurement:

Demographic data was obtained from the medical records including date of birth, gender, province of origin, number of siblings and whether the child's delivery was complicated or not. The patients' caregivers provided the on the biological relationship between both the father and the mother (whether it was consanguineous or not). The study authors considered them to be consanguineous if the father and mother were first cousins, second cousins, or second cousins once removed. History of cancer in the family such as leukaemia was also recorded. We considered a parent who was illiterate or only finished his/her primary school as a parent with low educational level, who finished high-school as a parent with medium-educational level, and who entered a university or any higher educational institute as a parent with high educational level.

The study authors also checked for method of delivery and divided them into two Groups: uncomplicated delivery Group which included normal delivery and C-section without any complications, and complicated delivery Group when children had delivery complications such as hypoxia. We also recorded data from the flow cytometry for each patient to determine the type of ALL (B or T cell leukaemia) and to identify if CD10 was positive. An experienced Professor in haematology was involved in determining FAB classification [14] for each ALL patient whether it was L1 or L2. FAB classification is based on morphology and cytochemical staining, and it remains effective despite cytogenetics and potentially adds diagnostic accuracy in some cases [15].

Patient's prognostic risk was defined as low, intermediate or high and was assessed based on age, white blood cell count at time of diagnosis, biologic and cytogenetic changes such as having Philadelphia chromosome, medical comorbidities, cerebrospinal fluid (CSF) analysis, testicular involvement, inability to tolerate standard chemotherapy, response to initial therapy, predicted outcome, organomegaly and lymphadenopathy on examination or chest x-ray; these were all considered in the determination of each patient's prognosis to conduct a correct chemotherapy protocol [16].

5) Statistical analysis:

Data was processed using IBM SPSS software version 25 for Windows (SPSS Inc, IL, USA). Chi-square and Fisher's exact tests were performed to determine the statistical significance between the Groups of cases and controls. We calculated odds ratios (ORs) and the 95% confidence intervals for the Groups using Mantel–Haenszel test by using the same software. Values of less than 0.05 for the two-tailed P values were considered statistically significant.

3. Results

1. General characteristics

Our sample had 70 cases of ALL and 60 controls and aged (0–4) years. The case group had 42 males and 28 females and the control group had 36 males and 24 females (Table 1). Control groups were hospital inpatients that were randomly selected. This results were patients from departments of gastroenterology (12 patients), urology (9 patients), metabolic and neonatology (4 patients), ENT for tonsillectomy and middle-ear tube insertion (7 patients), minor surgeries such as foreign body ingestion

(6 patients), neurology (4 patients), infection (8 patients), asthma (9 patients), and endocrinology (1 patient).

There was no statistical significant difference in feeding habits when comparing patients who had infections and other presentations and when comparing all presentations $P = 0.663$ and $P = 0.605$ respectively. Sixty-nine cases and 60 controls were validated for complications of delivery with 68 cases and 57 controls born with no complications. Sixty-seven cases and 59 controls were validated for place of living. Twenty-three cases and 26 controls were from major cities and their suburbs in Syria (Damascus, Rif-Dimashq, and Aleppo), 17 cases and nine controls from Homs and Hama, 13 cases and 15 controls from Al-Jazira region in Syria (Deir ez-Zur, Ar Raqqa and Al Hasakah), eight cases and six controls from southern Syria (Daraa, As Suwayda and Quneitra), three cases and one control from the Syrian coast (Latakia and Tartus), and three cases and two controls were from Idlib (Table 1).

Sixty cases were exclusively breastfed until 6 months of age (Group A), 8 needed additional infant formula (Group B) and 2 relied only on infant formula (Group C). In comparison, 41 controls were exclusively breastfed (Group A), 6 required additional formula feeding (Group B) and 13 relied only on infant formula (Group C).

2. Breastfeeding exposure

A. Case-control groups:

There was a statistically significant difference between Group A and Group B + C when comparing cases and controls (OR, 2.78; 95% CI, 1.174–6.588). It was also statistically significant between Group A + B and Group C when comparing cases and controls (OR, 1.10; 95% CI, 0.35–3.40). However, the authors did not find a statistically significant difference when comparing Group A and Group B in cases and controls ($P > 0.05$).

In contrast, there was a statistically significant difference when we compared children of Group B and Group C among cases and controls (OR, 8.67; 95% CI, 1.40-53.85). Overall, ALL incidence was increased in children who were breastfed in comparison with infant formula (**Table 2**). When excluding patients with any parent of low educational level, we had 24 cases and 22 controls.

We found no statistical significant difference when comparing cases and controls with all any of BF groups $P > 0.05$. No significant difference found when comparing case and control groups with educational levels $P > 0.05$.

Comparison of Characteristics between Breastfed children and relying on Infant formula is demonstrated in (**Table 3**). In case-control population, a statistically significant difference was found between having a father with low and medium educational level with Group A and Group B + C, with Group A being associated with a lower educational level of the father (OR, 2.83; 95% CI, 1.11–7.17). This was also the case for the mother when compared with the same groups, but the result was insignificant ($P = 0.0569$). Statistically significant differences were found between having a father or a mother with low educational level and medium educational level with Group A and Group B, with Group A having a higher incidence for

a father with low educational level (OR, 5.65; 95% CI, 1.41–22.71), and for a mother with low educational level (OR, 6.44; 95% CI, 1.34–31.05).

Moreover, when comparing Group A with B, we found no statistically significant difference when compared with mothers with medium educational level and high educational level $P = 0.1$, and when comparing Group B and C, there was not a statistically significant difference ($P = 0.0737$), with Group C having higher incidence for low educational level mothers.

Moreover, we found a higher incidence of positive family history in subjects with low educational level mothers when compared to medium educational level mothers ($P = 0.0290$). However, we found no statistically significant difference when comparing having a positive family history with being breastfed overall.

B. Case Groups:

In summary, in the case group we found that gender, having consanguineous parents, being born with complications, having positive CD10, ALL type, FAB classification, prognostic risk, or having a family history for malignancies do not have a statistically significant difference when compared with Group A, Group B, or Group C ($P > 0.05$). However, having a mother with a low educational level was significantly correlated with a higher incidence of EBF in comparison to a higher educational level when comparing Group A with Group B (OR = 8.8; 1.01–76.71).

3. Sub-analysis:

The mean number of siblings for all patients was 3.77 (SD $\pm$ 2.222), with 3.81 (SD $\pm$ 0.278) for cases and 3.72 (SD $\pm$ 0.286) for controls. There was no statistical significant difference between case and control groups in the method of delivery when comparing C-section and normal delivery $P = 0.410$. There was also no statistical significant difference between Group A and Group B + C or Group A + B and Group C when compared with normal delivery and C-section $P = 0.471$ and $P = 0.118$ respectively. No statistical difference was found when comparing cases and controls by gender, complications of delivery, educational level of parents, city of origin, and number of siblings ($P > 0.05$).

4. Discussion

Overall, this study found that EBF or even BF with infant formula in the first 6 months is positively correlated with higher incidence of ALL in the first four years of life, and relying on only formula can lower the incidence. This study also found that relying on only formula is associated with a decreased percentage of high risk patients of ALL from 40–30% but with this result was not significant ($P > 0.05$). However, having a mother or father with lower educational background was associated with EBF and when excluding low educational parents, we found no statistical significant difference between cases and controls with BF which suggests that this positive correlation between BF and ALL is among low educational parents only and it had no affect with medium educational level or higher.

Our cases differed from other studies which found that mothers with high socio-economic status (SES) breastfed their children more frequently in contrast to low SES mothers who relied more on infant formula [17–19]. Our findings also contradicted many studies that found an association between BF and a decreased risk of ALL [11, 12]. In one meta-analysis that included multiple meta-analyses, studies and trials found that children who were fed with infant formula had a greater risk for ALL than BF for more than 6 months in developed countries [20]. The potential risk of leukaemia, especially ALL, may have a negative correlation with BF in more than one study mainly in developed countries, suggesting that there might be additional factors that could have contributed to our findings. This could lead to several hypotheses which could explain additional underlying factors in developing countries which positively correlate BF with a higher incidence of ALL, especially that many factors in developing countries might worsen the prognosis and they have different factors from developed countries [21].

Potential factors

Tobacco and diet:

Several factors affect childhood cancer and especially ALL. Many studies over the years, such as the study of the effect of tobacco and cigarettes in both mothers and fathers during stages of pregnancy had varied results; they were inconclusive for mothers. However, paternal smoking was associated with significantly raising the risk for childhood ALL [22, 23]. Hookah (which is also known as shisha or water pipe) exposure, by either smoking or attending hookah social events, is also linked to benzene exposure which is a risk factor for leukaemia [24].

Dietary options such as high consumption of coffee, and any quantity of cola were also associated with causing ALL, but tea was found to be inversely associated with ALL [25]. Furthermore, mothers with a healthy diet were found to have lower risk of having a child with ALL [26], but a higher risk was found with the increased intake of dietary options that contained compounds from N-nitroso precursors such as hotdogs [27]. Mate, a traditional South American caffeine-rich infused drink which is traditionally consumed in South America and is very commonly consumed in Syria, was also found to contain N-nitroso and it contains polycyclic aromatic hydrocarbons (PAH) and other substances which are also carcinogenic [28]. PAH was found as a cause for childhood leukaemia from parental occupational exposure from vehicle exhaust [29], in paternal smoking [22, 23] and hookah which was found to have 16 components of PAH [30]. Furthermore, nitrosamine compounds, which feature a nitroso Group, were found in cigarettes, in the urine of hookah smokers, in children who were exposed to its smoke [31] and in fertilisers that are commonly used in Syria [32]. Moreover, hookah was found to have many carcinogens and risks that were discussed in literature reviews and meta-analyses [33, 34], which can even affect children and pregnant women.

Other potential causes

PAH and other polluting substances can also be found in drinking water as has been documented in Iran, a neighbouring country [35]. Mothers with lower education, who worked in agriculture, or were exposed to

pesticide, were more frequently found to have a child with childhood leukaemia [19]. BF might have a protective role against asthma and eczema especially in developing countries [36]. Higher rates of asthma, atopic and allergic medical conditions were also found in cow's milk allergy [37]. Although pre-labour caesarean delivery may be associated with childhood leukaemia [38], we found no such an association between case and control groups or between different feeding groups.

Speculations

Tobacco and diet:

The study authors speculate that common factors could be causing these findings, all of which are found more frequently in low educational level of parents which we found to be correlated with a higher frequency of BF, such as hookah smoking or just attending hookah social events as they are quite common in Syria. Moreover, we hypothesize that diet in Syria could provide additional risk factors from consuming large quantities of tea, coffee and especially mate which is also very common in low educational level populations which made this differences among cases and controls.

Pesticide:

Another theory is that using pesticide without adequate protection and working in agriculture are common practice among such populations in Syria. Although developed countries use high quantities of pesticide as well, but in developing countries particularly Syria, old types of pesticides are used which are cheaper and they tend not to use adequate protection equipment as it can be very expensive for them, for instance many only use hand-made masks when spraying pesticide as 82.5% is below poverty line in Syria and 75.8% of land is used for agriculture [39]. This is very common, especially in less educated population.

As a result, BF in these populations could impose a risk as harmful elements could be transferred to the infant with BF through these practices. All these theories could all together contribute to our findings.

In conclusion, more studies are required in developing countries and the Levant in specific to determine whether the underlying factors are being carried by BF from the local diet, tea, coffee, mate, or from Hookah, imposing a risk for leukaemia in children and potentially other malignancies. This raises a concern as similar findings can be found in other populations, so we need to widely investigate if cow's milk can reduce the risk for leukaemia in cases of the mother being exposed to leukemogens, and if BF imposes a risk for ALL as it could have a role in transferring carcinogens and facilitating malignant transformation.

5. Limitations

- This study included only patients older than five years as doctors tend not to ask about feeding in the first six months if the child presenting older than five years.

- This study could not adjust for multiple confounding and could not determine the factors mentioned in the article, especially related to war and environment. However, we tried to minimise such effects as they were all randomly taken from the same hospital at the exact time using the same sources.
- This was only one-centre study as Syria did not have any working hospital at that time for children as the one centre in Aleppo was closed due to war.
- This is a hospital-based study which does not represent the general population.
- Children who are not breast-fed tend to be early hospitalised and thus the control group may be biased.
- We did not anticipate these findings and thus we could not eliminate potential confoundings especially that no similar studies were found to compare with.
- Information was not always taken from the mother who can give the most reliable information for breastfeeding. However, any unreliable or invalid information about breastfeeding was rejected for the study and this confounding is equal for the cases and control and the caregiver relationship to the child was written down in the records, but they were not collected for this study.
- As most Syrian prefer breastfeeding as it is a reliable and cheaper source, more mothers from high socioeconomic status background would tend to use formula feeding which could bias the results. However, this hospital is a public hospital and deals with many children and thus those with high SES would prefer to go to private hospitals or to a nearby country for cure for leukaemia.
- For caesarean delivery, we were could obtain the information if it was pre-labour or not.

Abbreviations

ALL	Acute lymphoblastic leukaemia
BF	breastfeeding
CI	Confidence interval
EBF	Exclusive breastfeeding
Group A	children who were exclusively breastfed
Group B	children who regularly took infant formula with breastmilk
Group C	children who ceased breastfeeding altogether
OR	Odds ratio
PAH	polycyclic aromatic hydrocarbons
SES	Socioeconomic status
SPSS Inc	Statistical Package for the Social Sciences incorporated

Declarations

Ethics approval and consent to participate:

This study was approved by faculty of medicine, Damascus University. Written consent from participants was taken before admitting and commencing treatment.

Consent for publication:

Written consent was taken when admitting to the hospital for using and publishing their data with full anonymity and that their data will be freely available and be published for research purposes.

Availability of data and materials:

Data and materials can be made available upon request.

Competing interests:

There is no conflict of interest to declare.

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Authors' contribution:

All Authors read and approved the manuscript.

AK: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Supervision; Validation; original draft; Writing - review & editing.

MMA: Data curation; Formal analysis; Software; original draft; Writing - review & editing.

AG: Software; Methodology; Conceptualization; Validation; Writing editing; investigation.

BK: Software; Methodology; Conceptualization; investigation.

AH: Conceptualization; original draft; Writing - review

BM: Software; Project administration; Conceptualization; Writing editing; investigation

BZ: Software; Project administration; investigation

OH: Project administration; Resources; Validation;

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Tables

Characteristics of Children in Case and Control Groups

Characteristic	Cases (percentage %)	Controls (percentage %)
Age	42 (60%)	36 (60%)
Gender	28 (40%)	24 (40%)
Residence		
Latakia, Rif-Dimashq, and Aleppo	23 (34.3%)	26 (44.1%)
Latakia and Hama	17 (25.4%)	9 (15.3%)
Latakia region	13 (19.4%)	15 (25.4%)
Latakia and Syria	8 (11.9%)	6 (10.2%)
Latakia coast	3 (4.5%)	1 (1.7%)
Latakia inland	3 (4.5%)	2 (3.4%)
Education level		
Primary	23 (40.4%)	26 (43.3%)
Secondary	28 (49.1%)	24 (40.0%)
Tertiary	6 (10.5%)	10 (16.7%)
Marital status		
Married	27 (48.2%)	32 (54.2%)
Single	22 (39.3%)	19 (32.2%)
Divorced	7 (12.5%)	8 (13.6%)
Occupation		
Unemployed	38 (55.1%)	36 (60.0%)
Employed	30 (43.5%)	21 (35.0%)
Retired	1 (1.5%)	3 (5.0%)
Cancer History		
Yes	5 (7.8%)	6 (10.2%)
No	59 (92.2%)	53 (89.8%)

total subjects between groups occur as some data is missing.

TABLE 2

Breastfeeding between Case and Control Groups in ALL children in first 6 months

	Cases (Percentage%)	Controls (Percentage %)	OR (CI=95%)
EBF (Group A)	60 (85.7%)	41 (68.3%)	2.78 (1.17-6.59)
BF with IF and only IF (Group B+C)	10 (14.3%)	19 (31.7%)	
EBF and BF with IF (Group A+B)	68 (97.1%)	47 (78.3%)	9.40 (2.03-43.62)
Only IF (Group C)	2 (2.9%)	13 (21.7%)	
EBF (Group A)	60 (88.2%)	41 (87.2%)	1.10 (0.35-3.40)
BF with IF (Group B)	8 (11.8%)	6 (12.8%)	
BF with IF (Group B)	8 (80.0%)	6 (31.6%)	8.667 (1.40-53.85)
Only IF (Group C)	2 (20.0%)	13 (68.4%)	

ALL: acute lymphoblastic leukemia; EBF: exclusively breastfed; BF: Breastfed; IF: infant formula; OR: odds ratio; CI: confidence interval; Group A: being EBF; Group B; being BF with requiring additional IF; Group C; being dependent on only IF.

Chi square and Fischer exact tests were used.

TABLE 3

Comparison of Characteristics between Breastfed children and relying on Infant formula

	EBF (Group A)	BF with IF (Group B)	P value ^a	Only IF (Group C)	P value ^a	BF with IF + Only IF (Group B+C)	P value ^a
Delivery					-		
No complication	60	6	0.104	2		8	0.130
Complicated	0	1		0		1	
Mother education level					0.488		
Low	22	1	0.103	0	1.0	1	0.031
Medium	20	6	0.564	2		8	0.297
High	6	0		0		0	
Father education level					1.0		
Low	25	1	0.071	1	1.0	2	
Medium	16	5	1.0	1		6	0.117
High	6	1		0		1	0.646
CD 10					0.778		
Negative	7	1		0		1	
1-20%	1	0	0.568	0		0	0.430
20% - 80%	11	0		2		2	
80% and above	34	6		0		6	
FAB classification					1.0		
L1	29	3	0.218	2		5	0.461
L2	16	4		0		4	
Types					1.0		
B ALL	54	7	1.0	2		9	1.0
T ALL	6	1		0		1	
Risk					0.518		
intermediate	33	5	1.0	2		7	0.729
High	22	3		0		3	

ALL: acute lymphoblastic leukemia; EBF: exclusively breastfed; BF: Breastfed; IF: infant formula; NS: not significant; FAB: French-American-British classification. Group A: being EBF; Group B; being BF with requiring additional IF; Group C; being dependent on only IF.

Different total subjects between groups occur as some data is missing.

Chi square and Fischer exact tests were used.

^a All p values are when compared the previous group with EBF group.

Figures

Figure 1

showing feeding in infancy habits among the 130 patients, males and females, according to case and control groups provided that Group A is exclusively breastfed, Group B is breastfed with requiring additional formula feeding and Group C is being dependent on only formula feeding.

Figure 2

showing feeding in infancy habits among the 70 cases, males and females, according to FAB classification of L1 and L2 provided that Group A is exclusively breastfed, Group B is breastfed with requiring additional formula feeding and Group C is being dependent on only formula feeding.