

Relationship between Breast Feeding and Acute Lymphoblastic Leukemia

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Abstract: Leukemia is the most common cancer in children, representing approximately one-third of pediatric cancers. Breastfeeding is common but not universal in very early infancy in Egypt. Among infants under two months of age, 71 percent are receiving only breast milk. However, the proportion exclusively breastfed drops off rapidly among older infants. By age 4-5 months, only around 1 in 8 children were being exclusively breastfed. This study aimed to explore the relation between breast feeding and acute lymphoblastic leukemia. A descriptive correlational design was utilized on a purposive sample with a total of 200 mothers with previous breast feeding and their children were younger than 18 years. This study was conducted at the National Cancer Institute (NCI), Cairo, Egypt. A structured interview questionnaire sheet was constructed by the researchers. Results revealed that no statistically significant correlation between breast feeding duration and onset of acute lymphoblastic leukemia. It was concluded that breast feeding was not associated with risk of childhood leukemia. Other risk factors related to mother such as; mother's age, exposure to smoking and drugs used during pregnancy, mothers' knowledge about concept of complementary feeding were detected. Exclusive breastfeeding for 6 months for its health benefits for children and mothers was recommended.

Keywords: breast feeding, acute lymphoblastic leukemia, children, risk factors.

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I. Introduction

Leukemia is the most common cancer in children, representing approximately one-third of pediatric cancers. Approximately 3800 children are diagnosed annually with acute lymphoblastic leukemia (ALL) or acute myeloblastic leukemia (AML) in the United States of America (U.S.A) [1]. Acute lymphoblastic leukemia defined as a type of cancer of blood and bone marrow, the spongy tissue inside bones where blood cells are produced. It is an aggressive cancer affecting the white blood cells called lymphocytes [2]. Moreover, mentioned that ALL occurs in both children and adults but its incidence peaks between 2 and 5 years of age. Caution is multifactorial and exogenous or endogenous exposures, genetic susceptibility, and chance have roles [3]. Emphasized that there is a growing body of literature has implicated several environmental, infectious, and dietary risk factors in the etiology of childhood leukemia, mainly for acute lymphoblastic leukemia, the most common subtype. For example, exposures to pesticides, tobacco smoke, solvents, and traffic emissions have consistently demonstrated positive associations with the risk of developing childhood leukemia. However, intake of vitamins and folate supplementation during the preconception period or pregnancy, breastfeeding, and exposure to routine childhood infections have been shown to reduce the risk of childhood leukemia [4]. Furthermore, [2] indicated that many previous studies about ALL have found a link between feeding practices and its development, they found that children's risk for this type of leukemia seemed to increase the longer they were fed formula and not solid foods. [5] stated that type of feeding in the first months of life appears as one of the most important determinants of the child well-being, and its protective action seems to rely mainly on its ability to modulate intestinal microflora composition at early stages of life. The World Health Organization (WHO) and United Nations Children's Fund (UNICEF) recommend early initiation of breastfeeding, exclusive breastfeeding during the first 6 months of life and continued breastfeeding until 24 months of age. Although breastfeeding rates globally generally remain low [6]. Only 43% of the world's newborns are put to the breast within 1 h of birth and 40% of infants aged 6 months or less are exclusively breastfed [7]. In Egypt, the Egypt Demographic and Health Survey 2014 showed that exclusive breastfeeding is common but not universal in very early infancy in Egypt. Among infants under two months of age, 71 percent are receiving only breast milk. However, the proportion exclusively breastfed drops off rapidly among older infants. By age 4-5 months, only around 1 in 8 children were being exclusively breastfed [8]. [9] Emphasized that exclusive breastfeeding is a cornerstone of child survival and child health because it provides essential, irreplaceable nutrition for a child's growth and development. It serves as a child's first immunization—providing protection from respiratory

infections, diarrhoeal disease, and other potentially life-threatening ailments. Exclusive breastfeeding also has a protective effect against obesity and certain non-communicable diseases later in life.[10]; [11] found that breastfeeding has also been linked to various other health impacts from protecting the baby against chronic disorders later in life, to improving their cognitive ability and even Intelligence Quotient (IQ). It's also important for proper digestive development (balancing out the baby's gut bacteria). Breastfeeding also has beneficial aspects for the mother herself, by lowering her risk of recurring breast cancer, keeping her connected with her baby, and possibly even preventing her from relapsing back into smoking after she quits.

Significance of the Study

Childhood cancer is a leading cause of mortality among children and adolescents in the developed world and the incidence increases by 0.9% each year. Leukemia accounts for about 30% of all childhood cancer but its etiology is still mostly unknown [10]. The crude incidence rate of cancer in Egypt is estimated at 117.3/100.000 people [12]. Each year 8500 Egyptian children are diagnosed with cancer compared to 300 in Sweden and 12,060 in the United States. Cancer mortality in Egypt was the highest among the three at 70% according to the WHO in 2001 compared to 25% in Sweden and 11% in the States [13]. [14]; WHO and UNICEF reported that the distinction between exclusive breastfeeding and partial breastfeeding in the analyses of the association between breastfeeding and the risk for childhood leukemia is essential given that the addition of infant formula, together with breast milk or instead of it, changes the infant's gut microbiota, affecting the immunology of the infant. [2]Reported that researchers found that each additional month a infant was kept on formula was associated with a 16 % increase in the relative risk for ALL; and every additional month of delay in the introduction of solid foods increased the risk for this type of cancer by 14 % [6].[10]. Analyzed 8 studies and found a statistically significant inverse association between breastfeeding for longer than 6 months and AML risk (Odd Ratio, 0.85; 95% Coefficients Interval, 0.73-0.98), although there was no significant association for breastfeeding for less than 6 months. Although study done by [15] showed that duration of breastfeeding was not associated with risk of childhood leukemia in Oman and there may be some other environmental and genetic factors that might be responsible for the occurrence of this disease and must be explored further. However, there is a dearth of researches regarding relation between breast feeding and childhood leukemia in Egypt. So it was important to assess breast feeding and its duration as risk factors for childhood leukemia with other risk factor could be responsible for the occurrence of this disease. Hopefully, the results of the current study will add significant evidence in the field of childhood leukemia and breast feeding.

1.2 Aim of the study

This study aimed to explore the relationship between breast feeding and acute lymphoblastic leukemia.

1.3 Research Question

The study results will answer the following research question:

What is the relationship between the breast feeding and the risk of acute lymphoblastic leukemia?

II. Subjects And Methods

2.1 Research design:

A descriptive correlational design was utilized to achieve the aim of the study. In correlational studies, the investigator examine the strength of the relationships between dependent and independent variables by determining how change in one variable is correlated with change in other variable [16].

2.2 Subjects:

Purposive sample with a total of 200 mothers with previous breast feeding and their children were selected according to the following inclusion criteria: children younger than 18 years, suffering from acute lymphoblastic leukemia (ALL).

2.3 Setting:

This study was carried out in the pediatric outpatient clinics and Oncology Department at the National Cancer Institute (NCI), Cairo University (CU) that provides care for all children with all types of cancer from all over Egypt.

2.4 Tool for data collection:

A structured interview questionnaire sheet was constructed by the researchers after reviewing the relevant literature. It consisted of three parts with 23 items:

Part I: personal characteristics of children included 7 items as age, gender, and rank within the family, number of siblings, child health problems after birth, diagnosis and type of medications.

Part II: personal characteristics of mothers included 10 items as age, level of education, occupation, passive smoking, exposure to radiation (frequency, types), mother's health problems, and medications used during pregnancy.

Part III: breast feeding and complementary feeding practices included 6 items as breast feeding duration, artificial milk combined with breast feeding, reason for using artificial milk, concept of complementary feeding, complementary feeding time and types.

2.5 Validity and reliability:

Validation of the tool was done through submission to the 5 experts in the field of pediatric oncology, pediatric oncology nursing and breast feeding consultant. Modifications were carried out according to the experts' judgments on the clarity of sentences, the appropriateness of content and adding question about breast feeding. Reliability test was done using Cronbach's alpha for tool was 8.5.

2.6 Pilot study:

A pilot study was carried out on 20 mothers with previous breastfeeding and their children with ALL to test study tools in terms of their clarity, applicability, time required to fill in them and accordingly no modifications were done. Subjects who shared in the pilot study were included in the sample.

2.7 Data collection procedure:

An official permission was obtained from NCI administrators where a clear explanation was given to children and their mothers about the nature, importance and expected outcomes of the study. The researchers met the mothers at the Out and inpatient Pediatric oncology departments at the NCI, where they came for the first time or for follow-up of their conditions, The researchers introduced themselves to the mothers and informed them that the study posed no risks or hazards on their health and they asked for verbal consent from the mothers. The researchers faced the mothers individually, asked them the questions and recorded their answers in a structured interview questionnaire sheet. The interview lasted for about 20-30 minutes for each mother. The field work was carried out from the first of December 2016 to the end of May 2017 (6-months).

2.8 Statistical analysis :

Data was analyzed using SPSS advanced statistics version 20 (SPSS Inc., Chicago, IL). Numerical data were expressed as mean and standard deviation as appropriate. Qualitative data were expressed as frequency and percentage. Partial Correlation was used to assess the relationship between dependent and independent variables. Statistical significance was considered at p -value <0.05 and <0.001 .

2.9 Ethical consideration:

An official permission was granted from the administrative personnel in the selected setting. The researchers explained the aim of the study to the mothers and informed them information obtained will be confidential and their participation was in a voluntary base. A verbal consent was taken from mothers and their children to obtain their acceptance to participate in the research. The mothers and their children informed that they have a right to withdraw from the study at any time.

III. Results

Findings of this descriptive study were presented in three main parts; part I. Personal characteristics of the study participants. Part II. Breast feeding and complementary feeding practices. Part III. Relation among variables. Part I. Personal characteristics of the study participants (mothers and children). As regards personal characteristics of the children with ALL table (1) revealed that the mean age was 8.2 ± 4.4 years, with more than half of them were females (60%). Concerning children rank in the family, it was found that more than one third of children (36.5%) were third child and less than half of children had two siblings (47%). As regards mothers mean age table (2) proved that the mean was 36.6 ± 5.88 years, with more than two fifth of them had secondary school education (46%) while minority of mothers (15.5%) didn't read and write and more than half of them were house wife's (57%). In relation to history of pregnancy among mothers as shown in table (3) all mothers didn't smoke or used alcohol and more than half of them exposed to passive smoking (62%). Concerning mother exposure to radiation, it was found that more than half of them 62.5% exposed to radiation; most of mother (99.2%) exposed to ultrasound and the mean frequency of exposure was 2.5 ± 2.27 time.

As regard mother's health problems during pregnancy as illustrated in table (4) more than two thirds of mothers (62%) had health problems and more than one third of them (40%) diagnosed as hypertensive followed by 33% were diabetic while, minority 0.8% were had breast cancer and hepatitis C. Concerning types of

medications used during pregnancy, more than one third of them were took antihypertensive drugs ,oral hypo glyceic agents and antipyretic (32.2%, 33.0% & 33.0% respectively).Regarding to children health problems after birth as revealed in table (5) onset of ALL occurred at children mean age 7.07 ± 245 years. More than one third of children (39.5%) had health problems and less than half of them (49%) diagnosed as repeated upper respiratory tract infections. As regard type of medications used after birth, more than one third of them were used upper respiratory tract infections and antibiotics medications (49% & 37.9% respectively).Part II. Breast feeding and complementary foodspractices. The data was as shown in table (6), the results indicated that the mean duration of breast feeding was 13.1 ± 5.5 months, half of children (50%) were breastfed for 12- 24 months followed by 41.5% their duration of breast feeding was between 6- 12months , while, minority 8.5% their duration of breast feeding was less than six months. More than half of children (56.5%) administered artificial milk with breast feeding. Most of mothers (94.6%) stated that the not enough breast milk was the reason for using artificial milk. Table (7), indicated that the majority of mothers (82.5%) unable to define the concept of complementary feeding and their complementary feeding time was less than six months their started it from less than six months. While the minority (23.5%) of mothers followed the correct technique of complementary foodsconcerning types of complementary foods given to children, more than two fifth 41.5% of mother gave milky products followed by 24% gave cereals while minority of them gave vegetables and fruits (11.5%). Part III. Correlation among variables. Table (8) indicated a significant relation between onset of acute lymphoblastic leukemiaand personal and health problems of mothers during pregnancy as mothers age, exposure to passive smoking , health problems anduse of medications during pregnancy ($p < .001$, $p = .031$, $r = .022$, $p = 0.001$, $r = .862$ $p = 0.001$, $r = .857$ & $p = 0.023$, $r = -.025$ respectively). Also, results indicated that statisticallysignificant positive correlation between onset of ALL and child health problemsandused of medications after birth($p = .013$, $r = -.046$, $p = .003$, $r = .658$ respectively).

Table (9), indicated that statistically significant positive correlation between onset of ALL and mothers concept of complementary feeding as ($p = .002$, $r = .096$).While breast feeding duration, combination artificial feeding with breast feeding ,complementary feeding start time , type of complementary foods were not significant ($p = .662$, $r = .031$, $p = .742$, $r = -.023$, $p = .654$, $r = -.421$, $p = .561$, $r = .014$).

Table 1: Personal characteristics of children with ALL in percentage distribution (n =200)

Personal characteristics	NO	%
Age (years):		
<8	150	75.5
8+	50	24.5
Mean±SD	8.2±4.4	
Gender:		
Male	80	40.0
Female	120	60.0
Rank:		
First	44	22.0
Second	71	35.5
Third	73	36.5
Fourth and more	12	6.0
Numbers of siblings:		
Non	14	7.0
One	32	16.0
Two	94	47.0
Three and more	60	30

Table 2: Personal characteristics of mothers in percentage distribution (n= 200)

Mothers personal characteristics	NO	%
Age (years):		
20 -30	25	12.5
31- 41	142	71
42 - 54	33	16.5
Mean±SD	36.6±5.88	
Level of education:		
Not read and write	31	15.5
Read and write	32	16.0
Secondary school education	92	46.0
University graduate	45	22.5
Occupation:		
Working mothers	86	43.0
Housewife's	114	57.0

Table 3:History of pregnancy among mothers in children with ALL in percentage distribution (n = 200)

Mothers history	NO	%
Smoking :		

Yes	0	00.0
No	200	100.0
Passive smoking:		
Yes	124	62.0
No	76	38.0
Radiation exposure:		
Yes	125	62.5
No	75	37.5
Frequency of exposure (n=125) :		
<4	5	4.0
4+	120	96.0
Mean±SD	2.5±2.27	
Types of radiation (n= 125):		
Ultrasound	124	99.2
Laser	1	0.8

Table 4:Mothers exposure to health problems during pr

Health problems	NO	%
Health problems during pregnancy		
Yes	124	62.0
No	76	38.0
Types of health problems (n=124):		
Hypertension	40	32.2
Repeated upper respiratory tract infections	41	33.0
Breast cancer	1	0.8
Diabetes	41	33.0
Hepatitis C	1	0.8
Medications during pregnancy:		
Yes	124	62.5
No	76	38.0
Type of medications (n=124):		
Antihypertensive	40	32.2
Antipyretic	41	33.0
Cancer medications	1	0.8
Oral hypoglycemic agents	41	33.0
Hepatitis C medications	1	0.8

Pregnancy in children with ALL in percentage distribution (n = 200)

Table 5:Health problems among children with ALL after birth in percentage distribution(n= 200)

Health problems	NO	%
Onset of ALL (years)		
4 -6	111	55.5
7 - 11	99	49.5
Mean±SD	7.07± 245	
Health problems:		
Yes	79	39.5
No	121	60.0
Types of health problems (n=79):		
Anemia	19	24.5
Repeated upper respiratory tract infections	39	49.0
Neonataljaundice	21	26.5
Use of medications after birth:		
Yes	79	39.5
No	121	06.0
Types of medications (n=79):		
Antibiotic	30	37.9
Antipyretic	10	12.6
upper respiratory tract infection medications	39	49.0

Table 6:Breast feeding practices for children with ALL in percentage distribution (n = 200)

Breast feeding practices	NO	%
Breast feeding duration (months):		
< 6	17	8.5
6-<12	83	41.5
12-24	100	50.0
Mean±SD	13.1±5.5	
Artificial milk combined with breast feeding:		
Yes	113	56.5

No	87	43.5
Reason for using artificial milk :(no=113)		
Not enough milk	107	94.6
New pregnancy	6	5.4

Table 7:Complementary feeding practices by mothers for children with ALL in percentage distribution (n 200).

Complementary feeding	NO	%
Concept of complementary feeding:		
Didn't know	165	82.5
Incomplete	35	17.5
Complementary feeding time (months):		
< 6	154	82.5
6 +	46	17.5
Mean±SD		
Follow Correct technique of complementary feeding:		
Yes	47	23.5
No	153	76.5
Types of complimentary foods:		
Cereals	48	24.0
Milky products	83	41.5
Vegetables & Fruits	23	11.5
Juices	43	21.5
All of them	3	1.5

Table 8:Correlation between mothers and childrenpersonalcharacteristics,health problems and onset of ALL.

Variables	r	P value
Mothers age	.022	.031
Passive smoking	.862	.001
Health problems during pregnancy	.857	.001
Mothers use of medications during pregnancy	-.025	.023
Mother exposure to ultrasound during pregnancy	.783	.991
Children health problems after birth	-.046	.013
Use of medication after birth children	.658	.003

Significant at P<0.05, p <0.001

Table 9:correlation between breast feeding, complementary feeding practices and onset of ALL.

Variables	r	P
Breast feeding duration	.031	.662
Artificial milk combined with breast feeding	-.023	.742
Concept of complementary feeding	.096	.002
Complementary feeding time	-.421	.654
Types of complimentary feeding	.014	.561

Significant at P<0.05, p <0.001

IV. Discussion

The specific etiology of childhood leukemia and other cancers and the protective effect of breastfeeding against cancer are still unclear [16] . Breastfeeding has been associated with many benefits as well as protective effects against many diseases. There is limited evidence for the relationship between breastfeeding and the incidence of leukemia. This study found that no relation between breast feeding practice and the onset of acute lymphoblastic childhood leukemia. Regarding to the onset of ALL the current study show that the mean peak occurrence of leukemia was in 7.07 ± 245 years. The same explanation was mentioned by [18] who study breastfeeding as a protective effect against childhood leukemia and lymphomaThe mean peak age of the experimental and control groups were $6.6 + 4$ years and $6.8 + 4.2$ years, respectively. The present study shown that all mothers hadn't smoke or used alcohol and more than half of them exposed to passive smoking. The current study results were in accordance with[19] who evaluatedenvironmental, maternal, and reproductive risk factors for childhood acute lymphoblastic leukemia in Egypt. Found that, tobacco smoking was rarely reported by the mothers (1.3 % and1.7 % among cases and controls, respectively). Maternal exposure to passive smoking at work or at home from sources other than the husband was strongly associated with ALL risk.

The results of the current study indicated that, more than half of them exposed to ultrasound and the mean frequency of exposure was 2.5 ± 2.27 .A recent study by [20]suggest that ALL is not linked with exposure to ultrasound tests during pregnancy, regardless of the number of such tests. Our current study found that more than half of children had health problems and less than half of them diagnosed as repeated upper respiratory tract infections after birth .In contrast, studies based on medical records

or health claims databases reported null or positive associations [21] ,[22] , suggesting that children who develop leukemia are more likely to have had clinically diagnosed infections in infancy. Breastfeeding appeared to be a very common practice in Egypt. The results of the present study indicated that all of children had breast fed, 50% of children were breastfed for 12- 24months; 41.5% between 6- 12months and, 8.5% for less than six months On the same line, [15] who investigate the relationship between duration of breastfeeding and risk of childhood leukemia in Oman reported that 75% of the cases and 81% of controls were breastfed for 12 to 24 months and only 8% and 3% of cases and controls were breastfed for less than six months mentioned in the current study, more than half of children administer artificial milk with breast feeding and most of mothers stated that the not enough milk was the reason for using artificial milk, may be due to mothers' lack of knowledge about the anatomy and physiology of breast. Our result showed that 82.5% mothers introduced complementary foods to infants early from less than six months .Overall, majority of the mothers in the study introduced complementary food to their infant before the recommended age of 6 months. This high frequency is similar with studies in Nasarawa, Nigeria, by [23] where 69.0–82% mothers are reported to have introduced complementary foods before 6 months A burgeoning literature has also demonstrated that breast milk is a total food meant to exclusively supply nutritional needs of infants. Current recommendations of leading health organizations, including the American Academy of Pediatrics (AAP)[24] and the World Health Organization, stated that “infants should be exclusively breastfed for the first six months of life to achieve optimal growth, development and health. Thereafter, to meet their evolving nutritional requirements, should receive nutritionally adequate and safe complementary foods while breastfeeding continues for up to two years of age or beyond.” Regarding types of complementary feeding given to children, more than two fifths of mother gave milky products followed by about one quarter gave cereals while minority of them gave vegetables and fruits. The study results were contradicted with and Manuel [20] who reported that the frequency of consumption of carbohydrate rich foods from the cereals and grains group was the highest (60%) mainly the bread and different types of cooked rice. In the current study, we observed statistically significant positive correlation with the mother's age, exposure to passive smoking, health problems, and use of medications during pregnancy and onset of ALL. Our finding about the onset of ALL with increasing maternal age is consistent with [19] who evaluate environmental, maternal, and reproductive risk factors for childhood acute lymphoblastic leukemia in Egypt. However, our results contradict the findings from an Iranian study, which reported no statistically significant difference of the mother's age at time of childbirth between the case and control groups [25]. This could be partly explained by younger age of marriage and pregnancy especially in rural areas and the effect of genetics and other environmental factors.

On the same line, [26] reported that more than 50.0% of the 16 studies that assessed maternal exposure to infection observed increased risk of leukemia associated with episodes of influenza, pneumonia, chickenpox, herpes zoster, lower genital tract infection, skin disease, sexually transmitted diseases, Epstein-Barr virus, and *Helicobacter pylori*. Our finding about the onset of ALL with mothers exposure to passive smoking is consistent with [27], who found that maternal environmental tobacco smoke exposure during pregnancy at work or at home from sources other than the husband was the strongest association with childhood ALL status, neither paternal smoking nor the child's exposure to cigarette smoke showed statistically significant associations. These differences may suggest the possibility of a critical window of environmental exposure in the prenatal exposure period, consistent with some models of the pathogenesis of ALL. Also, results indicated that a significant positive correlation between children health problems and using drug after birth and onset of acute lymphoblastic leukemia and. Moreover, previously cited research literatures commented by [28] that, the exact etiology of childhood leukemia and lymphoma has not been determined. However, several reports have shown that many risk factors including genetic abnormalities such as Down's syndrome, Fanconi's anemia, ataxia telangiectasia and Bloom's syndrome, infections have been associated with these malignancies. It is apparent from the current study no significant correlation between the breast feeding duration and the onset of ALL, Similarly the study about breastfeeding and the risk of developing childhood leukemia in the sultanate Oman by [15] found that duration of breast feeding did not have any significant effect on the risk of childhood leukemia in Oman. In respect of, combination of artificial feeding with breast feeding , complementary feeding start time , type of complementary foods were not significant with ALL. In the same context, a study conducted by [29] who assess the benefits and harms of additional food or fluid for full-term healthy breastfeeding infants and to examine the timing and type of additional food or fluid mentioned that in children who were breastfed, none of the complimentary feeding characteristics such as type of milk/formula used at or before age 6 months, age started eating solid foods, and type of solid food/baby food was associated with ALL risk. The findings indicated that a significant positive correlation between onset of lymphoblastic leukemia and mothers knowledge about concept of complementary feeding. Poor practice of early introduction of complementary foods may be due to the wrong perception mothers have about breast milk alone for the recommended duration of 6 months. In fact we observed that majority of mothers in the study area (94.6%) believed that the child was not satisfied with breast

milk as such they felt complementary feeding should commence. There is evidence that adequate mothers' knowledge on child feeding is pertinent to better health and development of the children.

V. Conclusion And Recommendation

In conclusion, the findings of the current study presented that breast feeding was not associated with risk of acute lymphoblastic leukemia. Other risk factors related to mother such as; mother's age, exposure to smoking and drugs used during pregnancy, mothers' knowledge about concept of complementary feeding. Also some risk factors related to child such as child health problems after birth and using medications after birth were detected from the results of the study. The study recommends the encourage exclusive breastfeeding for 6 months for its health benefits for children and a mother is essential, and risk factors of childhood leukemia should be communicated openly to health team and general public to increase their awareness. Further studies on larger sample size are needed to generalize the results and also to clarify the relation between exclusive breast feeding and childhood leukemia.

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