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ASSOCIATION BETWEEN LOW BIRTH WEIGHT (LBW) INFANTS AND TH INCIDENCE OF ACUTE LEUKEMIA IN CHILDREN

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ABSTRACT

Background: Acute leukemia is a blood cells malignancy disease originating from the bone marrow, characterized by the proliferation of white blood cells, with manifestations of abnormal cells in peripheral blood. Perinatal conditions such as low birth weight can increase the risk of leukemia in children. Low birth weight infants cause resistance towards GH and IGF-1 which triggers leukemia. The purpose of this study is to determine the correlation between low birth weight infants and the incidence of acute leukemia in children. **Methods:** A case-control analytic observational study, carried out at RSUP Dr. Kariadi. The study was conducted in July-October 2019. Subjects were patients with acute leukemia as the case group and non-leukemia patients as the control group aged 0-18 years old. Data was collected by interview using a questionnaire and then data analysis was conducted using the chi square test. **Results:** Research subjects 82 people, aged 0-18 years old consisting of 46 males (56.1%) and 36 females (43.9%). No significant relationship was found between low birth weight infants with the incidence of acute leukemia in children. Different results were obtained for the duration of breastfeeding with the incidence of acute leukemia in children with *P = 0.002*. **Conclusion:** There was no association between low birth weight (LBW) infants and the incidence of acute leukemia in children.
Keywords: acute leukemia in children, LBW

INTRODUCTION

Leukemia is a blood cells malignancy disease originating from the bone marrow, characterized by the proliferation of white blood cells, with manifestations of abnormal cells in the peripheral blood. Acute leukemia in children reaches 97% of all leukemia in children, and consists of 2 types, namely acute lymphoblastic leukemia (ALL) 82% and acute myeloblastic leukemia (AML) 18%. In developing countries, acute lymphoblastic leukemia (ALL) reaches 83% while acute myeloblastic leukemia (AML) 17%.[1, 2]

The cause of leukemia is still unknown, but children with low birth weight are at higher risk for leukemia.[3] The risk of acute myeloblastic leukemia (AML) is increased in low birth weight infants. This is related to the presence of a chromosomal abnormality during development in the uterus.[4] Leukemia in children starts from the uterus when lymphoid and myeloid cells are not fully differentiated and are very susceptible to malignant transformation.[3]

Another study mentioned that the risk of leukemia in children increased in infants with birth weights >4500 grams.[1] Due to the different results of previous studies, the authors were encouraged to examine the correlation between low birth weight infants and the incidence of acute leukemia in children. The purpose of this study was to determine the correlation between low birth weight infants and the incidence of acute leukemia in children.

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METHODS

This study was an observational analytic study with a case control design. The design was chosen because the dependent variable in this study consisted of two groups: pediatric patients with a diagnosis of acute leukemia as the case group and non-leukemia children as the control group where each group consisted of 41 subjects with criteria as follows:

a. Inclusion criteria: (1) Patients aged 0-18 years old, (2) Patients with a diagnosis of acute leukemia, (3) Willing to be involved in this study after receiving infromed consent from the researcher.
b. Exclusion criteria: (1) Patients of acute leukemia with other malignancies.

The data collected was then edited, coded and entered in computer files. The history of the infants' birth weight was obtained using a questionnaire given to the parents or guardians of children with acute leukemia and non leukemia. The data obtained was then analyzed using a computer program. Hypothesis testing was conducted in the form of cross tabs using the chi-square hypothesis test and then the odds ratio was searched. P values less than 0.05 were considered significant.

Research ethics

This study has passed the research ethics by the Health Research Ethics Commission RSUP Dr. Kariadi Semarang numbered No. 294/EC/KEPK-RSDK/2019.

RESULTS

This research was conducted in July-October 2019 at Dr. Kariadi Semarang with 82 subjects aged 0-18 years old consisting of 41 case subjects (leukemia sufferers) and 41 control subjects (non leukemia sufferers) who met the inclusion criteria. Among these subjects, there were 46 males (56.1%), 36 females (43.9%), with the most dominant age category which was age 0-5 years as many as 36 people (43.9%).

Table 1. Characteristics of the participants

Characteristics	n (%)
Gender	
Male	46 (56.1%)
Female	36 (43.9%)
Age	
0-5	36 (43.9%)
6-11	29 (35.4%)
12-18	17 (20.7%)

Table 2. Association between independent variables and confounding variables and the incidence of acute leukemia in children

Variable	Acute Leukemia (n=41)	Non Leukemia (n=41)	Total	P
History of birth weight				
≤2500 gram	2	3	5	1,000[£]
>2500 gram	39	38	77	
History of breastfeeding				
>12 bulan	36	22	58	
≤12 bulan	5	19	24	0,002[*]

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History of Exposure towards High-Voltage Overhead Power Lines				
Exposed (<200m)	0	1	1	
Not exposed (>200m)	41	40	8	1,000[£]
Family history of cancer				
Present	4	5	9	
Not present	37	36	73	1,000[£]
History of exposure towards pesticides				
Exposed	27	20	47	0,180[¥]
Not Exposed	14	21	35	
Parents' smoking behaviour				
Yes	25	25	50	
No	16	16	32	1,000[¥]

n= number of subjects; *significant P<0.05; [£]fisher test; [¥]chi square test

DISCUSSION

In this study, it was obtained that the number of acute leukemia male patients were more than those who were female. These data are in accordance with some previous studies which stated that the incidence of acute leukemia was more dominant in male patients.[5, 6] This is due to the presence of genes on chromosome 9 which are protective factors for acute leukemia in women, thus the incidence acute leukemia is more common in men.[7]

No significant correlation was found between low birth weight infants and the incidence of acute leukemia in children. This is in line with previous research which states that a history of low birth weight is not associated with the incidence of leukemia in children. The cause of leukemia is not due to the history of low birth weight, but is caused by medical treatments carried out during handling low birth weight infants.[8] One of the treatments for low birth weight infants is the usage of phototherapy. However, the usage of phototherapy has a carcinogenic effect on hematopoietic cells and is associated with DNA damage and apoptosis of lymphocyte cells.[9] Research showed that after phototherapy was conducted in infants there was DNA damage, changes in cytokine levels and oxidative stress. All of these changes are related to the mechanism by which cancer occurs.[10, 11]

In this study, the results showed that the duration of breastfeeding showed an association to the incidence of acute leukemia in children. The results of this study are supported by previous research which stated that the best delivery duration for infants is 7-9 months. Breastfeeding too long did not reduce the risk of leukemia, which might be related to differences in nutrient components with lactation time. Protein, lactose, mineral content, and breast milk density decreased with the increase of lactation time. The fat content of mature milk is relatively high, which is not a benefit for infants.[12]

Hypothesis test results indicated that there is no statistically significant relationship between the history of exposure towards high-voltage overhead power lines

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and the incidence of acute leukemia in children. The results of the study are in line with previous research which showed no significant relationship between children living near high-voltage overhead power lines with a distance of <500 m and the incidence of acute leukemia in children.[13] High-voltage overhead power lines are often located near with other potential risk factors such as highways and railroads that can produce higher exposure to air pollutants. Several previous studies reported a correlation between traffic density, distance of houses close to main roads, and exposure to air pollution caused by traffic density to the incidence of leukemia, especially AML and ALL types.[14, 15]

No significant relationship was found between environmental exposure to pesticides and the incidence of acute leukemia in children. These results contradict previous studies.[16] This might happen due to the unknown clear distance between the house and the plantation area or rice fields, and also the unknown exact level of pesticides produced by the fertilizers used in the houses of the research subjects.

The results of this study indicated that a family history of cancer is not related to the incidence of acute leukemia in children. Types of cancers obtained from research data are breast cancer and cervical cancer. The results of this study are supported by previous studies which stated that family history of cancer is not related to the incidence of acute leukemia in children, but is associated with Hodgkin's and non-Hodgkin's lymphoma. This can be caused by environmental influences and the presence of infection.[17]

In this study, confounding variables such as the effect of exposure to cigarette smoke at home to the incidence of acute leukemia in children was also examined (P = 1.000). The results of the study were in line with previous studies. There was no significant relationship found, and it can be caused by not knowing exactly the number of cigarettes consumed in a day and not knowing accurately the process of exposure towards cigarette smoke pollutants to children, thus it can confound the results of the analysis obtained.[18]

CONSLUSION

No significant association was found between low birth weight infants and the incidence of acute leukemia in children. Duration of breastfeeding showed an association to the incidence of acute leukemia in children.

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