

## Factors Associated with Pediatric Acute Leukemia. Medellín, Colombia. 2008-2011

Carlos A Gómez<sup>1\*</sup>, Duleza Mena<sup>2</sup> and Francisco Ochoa-Jaramillo<sup>3</sup><sup>1</sup>Graduate School, CES University, Medellín, Colombia<sup>2</sup>Faculty of Nursing, University of Córdoba, Montería, Colombia<sup>3</sup>Faculty of Medicine, CES University, Medellín, Colombia**\*Corresponding author**

Carlos Alberto Gómez Mercado, Graduate School, CES University, Calle 10 # 22 - 04, Medellín, Colombia, Tel: (574) 444 0555; Ext: 1156; E-mail: klargomez@gmail.com

**Submitted:** 17 Feb 2018; **Accepted:** 27 Mar 2018; **Published:** 06 Apr 2018**Abstract****Introduction:** Acute leukemias have generated great interest in the world to be within the ten most common cancers, and children ranks first in malignancies.**Objective:** Analyze the demographic, genetic, environmental, pre and perinatal factors associated with acute lymphoblastic leukemia in pediatric acute leukemia group in Medellin during 2008 - 2011.**Methods:** Cross-sectional study in children under 15 years with leukemia acute in Medellin and the metropolitan area during 2008 -2011. Se implemented a logistic regression model to identify factors associated with acute lymphoblastic leukemia. Results: 80 patients were studied. Factors associated with multivariate analysis were acute**lymphoid leukemia:** Daily consumption of alcohol by the father (OR: 3.95; 95% CI 1.26 to 7.55) and that the child had been breastfed (OR: 0.036, 95% CI 0.002 to 0.83).**Conclusions:** The identification of risk and protective factors associated with acute lymphoid leukemia (ALL) in Medellin and its metropolitan area; they are a useful tool for health planning input.**Keywords:** Leukemia, acute, pediatric, factors, lymphoblastic, environmental.**Introduction**

Acute leukemias have generated great interest in the world because they are among the ten most frequent types of cancers, and in children it occupies the first place in malignant neoplasms [1]. The World Health Organization (WHO) in 2012 declared that of 56 million deaths in the world about 6.2 million (12%) were due to malignancies. It is estimated that until 2020 these figures will increase to 75%, especially in developing countries such as South America, Africa, the Caribbean and Southeast Asia [1].

The causes of most pediatric leukemias are unknown, however, three possible associations have been related to the increase in the incidence that occurred in some countries: it is an artificial finding because there are better diagnostic tools and registration procedures; it is a real secondary finding to a wider range of environmental exposures such as chemicals and very low frequency electromagnetic fields; it is real and secondary to changes in endogenous factors such as increased birth weight and the later development of acquired immunity [2,3].

Cancer is uncommon in children and adolescents, with an annual incidence of 15.4 cases per 100,000 people under 20 years of age in the United States, with acute lymphoid leukemia (ALL) being the most frequent cancer in the population under 15 years, representing 23% of cancers diagnosed in this age group. It is estimated that more than 160,000 children worldwide are diagnosed with cancer each year and this figure could be considerably higher. The data on the incidence of childhood cancer in developed countries are; mostly, imprecise [4].

The main risk factors that have been associated with the development of leukemias in children are ionizing radiation, exposure to pesticides and hydrocarbons at different times of conception, the use of alcohol and the use of psychoactive substances in the pregnant mother. From the observations of elders the probability of developing leukemias in twins the interactions between genetic and environmental factors have become even more evident as a risk factor [5-10].

The annual incidence rates in Colombian girls and boys are 5.6 and 6 new cases per 100,000, respectively [3,5]. Therefore, this country is part of the group with the highest incidence among developed countries, although, contrary to these, it is also part of the group with the highest mortality. In the National Institute of Cancerology of Colombia it was found that ALL was the most frequent institutional

diagnosis among pediatric patients during 2002 (84.5% of leukemias and 27.7% of total malignant diseases). Cases in children under one year constituted 7.6%; retinoblastomas and leukemias were the most frequent tumors. Solid tumors accounted for 53.2% (191 cases) and hematological malignancies (leukemias and lymphomas) 46% (165 cases). The most frequent diagnoses of hematological malignancies were leukemias (30.4%), and in solid tumors, neoplasms of the central nervous system (11.1%) [6] and the cause of death (58.8% of cases). leukemia and 27.0% of the total of basic causes of death. The three most common basic causes of death were solid tumors.

In the Municipality of Medellin, there are no known registries or previous studies that talk about the factors associated with the development of acute leukemia, because the surveillance system for Leukemia is very recent, considering the disease rare and even rare. The importance of this study lies in characterizing and analyzing the factors associated with pediatric acute lymphoid leukemia and having a basis for further studies.

## Materials and Methods

### Study area

The study was conducted in the metropolitan area of Medellin, capital of the department of Antioquia in Colombia. The year 2011 had, according to a population of 2'393.011 inhabitants and its metropolitan area (10 municipalities), with 3'592,100 inhabitants which makes it the second urban agglomeration of the country.

### Type of study

A cross-sectional study in a population of 80 pediatric patients diagnosed with acute myeloid leukemia and acute lymphoid leukemia registered in the oncology units databases in the city of Medellin and its metropolitan area.

### Data collection

Information was obtained from the databases of the epidemiological surveillance system (SIVIGILA) in the individual service delivery records (RIPS) from 2008 to 2011 and from the clinical records of the oncology units where the patients received their treatment.

The inclusion criteria were considered for patients from 0 to 15 with a diagnosis confirmed by bone marrow aspirate and / or histopathological report of ALL and LMA registered in the SIVIGILA and IPS databases (Oncology Units) that are being treated. Children in Medellin and the Metropolitan Area at the time of data collection and patients who did not live in the Metropolitan Area of Medellin were excluded. The variables were grouped according to sociodemographic, environmental, genetic and prenatal and perinatal exposures. The instruments for the collection of information were designed taking into account the variables and adjusted by means of a pilot test, carried out on a sample of 20 children under 15 years of age in Medellin. It is highlighted that the project and the instrument was approved by the ethics committee of the CES University of the City of Medellin - Colombia.

For the process of obtaining the information, the institutions that provide health services that have oncological units were identified in the databases; the project was presented to them and the respective permits of their ethics and research committees were requested. Once the permits were available, we proceeded to review the medical records and extract information from them. On the other hand, children diagnosed with myeloid or lymphoid leukemia were visited

in their homes in Medellin and the Metropolitan Area, after telephone contact and authorization. Once the address was located; the informed consent was taken and a survey was applied that sought to complement information that was not in the clinical history; for that end.

### Analysis of the data

For the registration and organization of the data, a database was designed in the SPSS 20® software. An explanatory logistic regression model was applied where the factors associated with leukemia were adjusted and prevalence ratios of the independent variables and their confidence intervals were calculated.

The ethical considerations established in Resolution 8430 of 1993 were taken into account, which allowed the viability of the investigation and the respect of the rights of the people who participated in it. Among the considerations were: privacy, anonymity and confidentiality. Each participant of the research was made aware of the objectives of the research and the instrument that was applied. In addition, written informed consent was taken.

## Results

The study was performed on a total of 80 patients diagnosed with acute pediatric leukemia. When analyzing the results of the study population, 77.5% of the children were confirmed with acute lymphoblastic leukemia and 22.5% with acute myeloblastic leukemia, with a higher proportion of women 53.8% than of men 46.3%. The median age was 8.5 years and the average birth weight was 3.155 grams. The median age between mother and father at the time of conception of the patient was 25 and 28 years respectively, and the average age of the mother in pregnancy is 25 years.

Regarding the level of studies of the mother, it was found that 28.8% of the mothers had high school studies, followed in 26.3% with incomplete secondary and 20.0% complete primary. Some differences were observed with respect to the level of studies of the father, where 24% presented complete primary studies, followed by complete secondary and incomplete primary with 22.7% and 20.0%, respectively.

Regarding the occupation of the father before the birth of the patient or during his early childhood, it was observed that some tasks as messenger, zootechnician and worker of a factory are equivalent to 32.9%, the occupation of farmer responds to a 19, 0%, the construction provides 12.9% and the work of the driver 8.9%.

When inquiring about the child's exposure to high-voltage electromagnetic fields, it was found that 65% had exposure to this factor. On the other hand, 75% reported a history of cancer in their family; while 17.5% reported a family history of leukemia.

Regarding the mother's alcohol consumption during pregnancy, it was found that 6.3% consumed the substance during pregnancy and 2.5% was exposed to household pesticides.

In the bivariate analysis, it was observed that children living in the urban area have 1.36 times the probability of having acute lymphoid leukemia, compared with the probability of children living in the rural area. (OR: 1.36, CI: 1.18 - 1.58) this association is statistically significant. (p: 0.0034). In the study, it is observed that having cousins with a history of cancer, behaves as the factor that increases the probability of having acute lymphoid leukemia. OR (1.35, CI: 1.17-1.55) (p: 0.05). (table 1).

**Table 1: Factors related to pediatric acute lymphoid leukemia, Medellín, 2008 - 2012**

Variable	ALL		AML		OR [IC]	X2 (p value)
	N°	%	N°	%		
<b>Origin of the patient</b>						
Rural	13	21,0	0	0,0	1	0,034
Urban	49	79,0	18	100,0	1,36 [1,18 - 1,58]	
<b>Cousins with Cancer</b>						
Yes	11	17,7	0	0,0	1,35 [1,17- 1,55]	0,05
No	51	82,3	18		1	

On the other hand, multivariate analysis was performed, where it was found that the probability that a child has acute lymphoid leukemia, when the father consumes alcohol daily until he is drunk is 3.95 (1.26 - 7.56) times the probability they have children with parents who do not consume alcohol. This association could be explained by the teratogenic risk caused by alcohol.

In the logistic regression model obtained through the enter method, it was found that the probability of ALL is reduced by 64% when the child receives breastfeeding, in contrast to the probability of children not breastfeeding (OR Adjusted : 0.036 IC: 0.002 - 0.83). On the other hand, it was found that children from parents who drink alcohol on a daily basis have 3.95 times the probability of ALL compared to the probability that children whose parents consume alcohol have a lower frequency. The variables that explain the ALL, were adjusted by the other variables, to control the confusion that could exist with them (table 2).

**Table 2: Factors that explain the probability of pediatric acute lymphoid leukemia, Medellín, 2008 - 2012**

Variable	ORc* [IC]	ORA* [IC]
<b>Did the child receive breastfeeding?</b>		
Yes	0,30[0,07 - 1,29]	0,036[0,002 -0,83]
No	1	1
<b>How often does the father consume alcohol?</b>		
Daily until and without getting drunk	2,66[0,63 - 11,1]	3,95 [1,26 -7,55]
Weekly, monthly and sporadically until getting drunk	1	1

\* OR crude, OR adjusted

## Discussion

The literature review shows that in more than 70% of the leukemias diagnosed before the first year of life translocations that affect the MLL gene (mixed lineage leukemia) are observed, the finding of identical MLL rearrangements in monozygotic twins suggested that they are acquired in utero and that there is presence of transplacental metastasis of cells affected with translocation [11,12], this does not agree with the results of the study where twinning is observed as a possible protective factor for pediatric ALL, in the bivariate analysis with a statistically significant relationship.

In the bivariate analysis of the study, another of the variables of interest that behaves as a possible associated factor is the antecedent

of viral pathologies in the patient, including varicella; that although its OR behaved as a possible factor that increases the likelihood of ALL, it is not statistically significant, this relationship is in agreement with that presented by J. Alonso López in his study of risk factors for childhood acute leukemia and other researchers who support the etiological role of infections in pediatric leukemias including ALL, since they suggest that infectious agents play an important role in human leukemogenesis [13-19]. This association was not resolved in this study and it would be worth clarifying this question in future research, increasing the size of the population since the scientific evidence shows an association with ALL and the proportion of cases with varicella in the population studied within the results of this study draws attention [20,21].

With respect to family factors, some researchers have described numerous cases of families with two or more members with first and second degree kinship with leukemia or other types of cancer [22], this finding is in agreement with those of the study where it was observed in the analysis of association that having cousins, uncles and relatives greater than the third degree of consanguinity with cancer is associated with pediatric ALL, compared with the group of children diagnosed with AML; the types of cancers in the family that showed statistical significance were breast cancer and colon cancer in the bivariate analysis of this study; and to a lesser degree, the history of leukemia, although in the study it did not show statistical significance.

Many studies developed in children, which have focused mainly on the relationship between active parental smoking or environmental tobacco smoke and childhood brain tumors, leukemia and lymphoma, have been less constant. Some studies have significantly linked the consumption of cigarettes by parents before conception with childhood cancers, including neuroblastoma and lymphoma [23]; Although there is evidence that active maternal smoking especially in the first weeks of pregnancy, there is no clear epidemiological evidence that parental smoking before conception or prenatal exposure to tobacco smoke will increase the likelihood of childhood leukemia, in this study a percentage of 17% in mothers and 28% in fathers have smoked or smoked before conception, in the bivariate analysis to look for possible association with pediatric ALL and when adjusting it with other variables in the multivariate it agrees with what the evidence shows since there is an increase in the RPA with no significant CI.

Within the exposure to substances it is important to note that the frequency with which the father consumes alcohol daily, weekly and sporadically until getting drunk by adjusting it with the other variables in the logistic regression model is the variable that Highest RPA was observed with a CI statistically This is consistent with the statements made by Hernandez-Morales, Zonana-Nacach and Zaragoza-Sandoval in a case-control study conducted in 2008 in Mexico with the aim of analyzing the factors associated with acute leukemia in children, where it was found that the consumption of alcohol or any type of alcoholic beverage ingested three months before or during pregnancy and the birth of the patient is an associated factor for the disease, but it was not statistically significant in his study. RP: 1.9; CI [0.76 - 5.1] [24].

The association between breastfeeding and LLA has been evaluated as a study hypothesis in several investigations. Shu [25,26] reported that the history of breastfeeding was associated with a



lower probability of ALL (OR = 0.8, 95% CI: [0.6-0.9]). Infante-Rivard [27] also found a lower probability of ALL in those who received breastfeeding (OR = 0.6, 95% CI: [0.4-0.9]). Gibson RW [28] showed that the protective effect due to breastfeeding was more evident between 6 and 11 months (OR = 0.5, 95% CI: [0.2-1.1]). These results agree with those of the study where the RPA of the multivariate analysis shows within the substances breastfeeding as a protective factor [29-32].

Finally, it is important to note that the main limitation of the study was to establish contact with the relatives of some children who were registered in the database; since, their addresses or telephone numbers were out of date or some relatives in their grief did not accept to answer the questions.

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