

Investigation of Leukemia Frequency in Children of Qazvin Province and its Correlation with Gender, Age, and Blood Groups between 2006-2016

Tahere Dargahi¹, Mehdi Goudarzi², Naser Mobarra³, Hoda Poorkarim⁴, Sajjad Rahmani⁵, Mojtaba Khalili⁵, Mehran Amini⁵, Javad Hamedani⁵, Mehdi Azad^{5*}

¹ High Institute for Research and Education in Transfusion Medicine, Hematology Department, Tehran, Iran

² Department of Microbiology, School of Medicine, Shahid Beheshti University of Medical Science, Tehran, Iran

³ Stem Cell Research Center, Department of Biochemistry, School of Medicine, Golestan University of Medical Sciences, Gorgan, Iran

⁴ Department of Hematology, Allied Medical School, Tehran University of Medical Sciences, Tehran, Iran

⁵ Department of Medical Laboratory Sciences, Faculty of Allied Medicine, Qazvin University of Medical Sciences, Qazvin, Iran

Received: 15 March, 2016; Accepted: 18 September, 2016

Abstract

Background: About 8 percent of all cancers in human population are related to leukemia and it is one of the most common malignancies in children. The aim of this study was to compare the prevalence of age, gender and blood group types with the frequency of leukemia among the children with leukemia in Qazvin province during the 2006 to 2016.

Materials and Methods: This was a cross-sectional analysis. Investigated population was 110 children and adolescents under 18 years in the hospitals of Qazvin province. The data collecting method was through review of medical records of the patients and their analysis performed by using SPSS version 16.

Results: According to data from this study, leukemia ALL-L1 is more frequent in Qazvin than other types of leukemia, and children with ages 0-5 years was more than other age groups. This disorder is more common in boys than girls, and among the patients, the people who has A and O blood groups, and Rh + are the most abundant.

Conclusion: such factors like age, gender and blood groups can use as prognostic factors in children leukemia. So that leukemia in children less than 5 years old is more than any other age. In addition to that; the incidence of leukemia ALL-L1 reduced with increasing age in the general population in Qazvin and number of boys with leukemia is more than girls.

Keywords: leukemia, children, frequency, blood group

***Corresponding Author:** Mehdi Azad, Department of Medical Laboratory Sciences, Faculty of Allied Medicine, Qazvin University of Medical Sciences, Qazvin, Iran. Email: Haematologicca@gmail.com

Please cite this article as: Dargahi T, Goudarzi M, Mobarra N, Poorkarim H, Rahmani S, Khalili M, et al. Investigation of Leukemia Frequency in Children of Qazvin Province and its Correlation with Gender, Age, and Blood Groups between 2006-2016. *Novel Biomed.* 2016;4(4):135-41.

Introduction

Neoplastic diseases are the second or third cause of mortality in the most developed and uncivilized

country. About 2 thousand new cases of cancer were reported in children in Iran annually and because of its importance and threatens the nation's health, so, it's necessary to have special consideration to this issue.

Leukemia is the most common neoplasm in childhood and it is about 41% of all malignancies in children under 15 years¹⁻⁴.

Neoplastic changes of white blood cell leads to hematopoietic cancers in body tissues (bone marrow and lymphatic system). White blood cells are usually proliferating regularly and under control, according to body needs, but in the leukemia, this process faces with disorder and cells proliferate out of control⁵⁻⁷. Term acute leukemia, refers to hematological malignancies of myeloid or lymphoid cell by increasing the number of blasts that lymphocytic type have significant incidence.

From the point of clinical and epidemiological view, only 10% of leukemia cases in children can justify and no specific etiology in the 90% of cases. It seems that children's hematological cancer is a multifactorial disease, like other cancers, where genetic and environmental factors are interact with each other in its development⁸⁻¹⁰.

Ionizing radiation and chemical mutagens can involve in initiation of leukemia. Moreover, exposure to X-rays in utero can also increase the predisposition to ALL, to some extent. Lack or decrease of infection in early years of life can predispose the immune system to aberrant response to external factors that can accelerate the ALL through apoptotic stress differentiation. In addition to the above mentioned, recent studies has shown that living near high-voltage power lines increases the risk of ALL in children, so that each 600 meters away from high voltage power lines, reduces 6/0 times the risk of ALL and exposure to high-voltage transmission line over the likelihood of further increases. The magnetic field also affects the risk of ALL^{8,11}.

Among all types of leukemia, acute leukemia is the most common malignancies in children and includes about 20% of children malignancies. 80% of children leukemia is acute lymphoblastic type (ALL) and 11% myelocytic type (AML). Acute lymphoblastic leukemia prevalence age is 2-5 years and more common in boys than girls. The prevalence of acute myelocytic leukemia (AML) increases with age¹².

Acute lymphoblastic leukemia (ALL) in children is primarily a disease that is associated with an increased incidence between the ages of 2-3 years, then the prevalence reduced. So that, in the age

between 25-50 years, is a rare disorder and then again its prevalence increases up to the second peak (but with a lower incidence) reaches the age of 80¹³⁻¹⁵.

A small population of patients with ALL in children has background genetic diseases. Children with Down syndrome have a 10-30 times greater chance for ALL. Other genetic disorders like ataxia telangiectasia and Bloom syndrome, which associated with various types of leukemia. Twins more than non-twin children are susceptible to leukemia about 2-4 times during the first decade of their life. In identical twins, when one has ALL, the risk of leukemia in the other is 20%, however, it is likely that ALL transmission in utero can happen through common placenta blood circulation. If leukemia is diagnosed at the age under one year old, it may also be seen in his twin brother or sister in a few months later¹².

Leukemia is including about 8% of all cancers in the human population and is known as the fifth most common cancer in the world^{1-4,16}. The risk of ALL in Iran estimated about 6.1 per 100,000 men and 5.2 per 100,000 women. Average diagnosis age is 13 years and almost 60% of cases are diagnosed in children less than 20 years. ALL is the most common malignancy in people under 15 years, 23% of cancers and 76% of all types of leukemia are in this age group. The risk of ALL, particularly those with the origins of T, is more in boys than in girls. In the first year of life the risk of ALL, is about 1.5 times the ratio of girls to boys^{3,13,17}. Risk of ALL in European and industrial countries is more than African¹⁸ and the age of 2-5 years have the highest incidence in developed countries.

This study was done due to the importance of leukemia in children. The main aim of this study was to compare the prevalence of age, gender and blood group types with the frequency of leukemia among the leukemic children in Qazvin province during the 2006 to 2016 and report these results to the officials of hospital, university and province in order to better manage and providing medical facilities that these patient's need them.

Methods

This study is a cross-sectional study that relates to the period between the years 2006 to 2016. The study population was 110 children and adolescent that has different types of hematological cancers that are in a

range under 18 years old.

Most of the information was collected from the patient’s record with leukemia at Children's Hospital of Qazvin (Quds hospital). All patients’ history and information were gathered with complete satisfaction and awareness of hospital staff and patients' families. In this study, factors, such as age, sex, blood group and type of hematological cancer, obtained from patient records and analyzed with statistical studies. The collected data divided into two categories: quantitative and qualitative. Quantitative data include various types of cancer, including age, blood group ABO, Rh, and gender. Quantitative and qualitative data of this study was analyzed by using SPSS version 16. To facilitate reporting in this study, the most common types of leukemia in the age studied group classified in three groups: AML, ALL-L1 and ALL-L2.

Results

The data showed that among children with leukemia, ALL-L1 is more frequent than other types of leukemia and AML and ALL-L3 are respectively the most frequent. The occurrence of this leukemia was different according to gender, age, blood group and Rh between boys and girls, it is explained in

Table 1: The relation between gender and leukemia type.

		Leukemia				
		ALL-L1	ALL-L3	AML	Total	
Sex	Male	Count	44	5	14	63
		%	69.8	7.9	22.2	100.0
		within sex				
	Female	Count	32	7	8	47
		%	68.1	14.9	17.0	100.0
		within sex				
Total	Count	76	12	22	110	
	%	69.1	10.9	20.0	100.0	
	within sex					

following in more detail.

In the data that obtained from this study, the frequency of boys population with leukemia were more than girls (53.3% to 42.7%) and among the types of leukemia, ALL-L1 has a greater incidence than AML and ALL (Table 1).

ALL-L1, the frequency is higher in patients with blood types A and O than other blood groups, and the lowest incidence of leukemia, related to people with blood group AB (Table 2).

Among patients with leukemia, people with Rh + blood group had a higher frequency than those with Rh- blood (Table 3).

The relationship between age and type of leukemia is such that the frequency of leukemia ALL-L1 decreases with age, which means that ALL-L1 in ages 0-5 years had the highest frequency and by increasing age, the incidence of this type of leukemia has significantly decreased. The P value of less than 2%, showed a significant relationship between age and the type of leukemia (Table 4).

Discussion

This study aimed to evaluate the frequency of leukemia in children in Qazvin province and trying to find a correlation between leukemia and age, gender, blood groups.

Table 2: The relation between blood groups and type of leukemia.

			Leukemia			
			ALL-L1	ALL-L3	AML	Total
BG	A	Count	28	4	10	42
		% within BG	66.7	9.5	23.8	100.0
	B	Count	18	4	4	26
		% within BG	69.2	15.4	15.4	100.0
	O	Count	27	4	6	37
		% within BG	73.0	10.8	16.2	100.0
	AB	Count	3	0	2	5
		% within BG	60.0	.0	40.0	100.0
Total		Count	76	12	22	110
		% within BG	69.1	10.9	20.0	100.0

Table 3: The relation between RH and leukemia.

			Leukemia			
			ALL-L1	ALL-L3	AML	Total
RH	+	Count	70	12	21	103
		% within RH	68.0	11.7	20.4	100.0
	-	Count	6	0	1	7
		% within RH	85.7	.0	14.3	100.0
Total		Count	76	12	22	110
		% within RH	69.1	10.9	20.0	100.0

Leukemia is the most common cancer of childhood (1-4). 100,000 children between 0-15 years and 3-5 people infected with the disease each year (3).

Prevalence of cancer include the following: ALL 30.3%, AML 9.4%, non-Hodgkin lymphoma 9%, Extra cranial germ cell tumor 8.3%, neuroblastoma

Table 4: The relation between age and leukemia type.

			Leukemia			
			ALL-L1	ALL-L3	AML	Total
Age	0-5	Count	52	6	10	68
		% within Age	76.5	8.8	14.7	100.0
	5.1-10	Count	18	5	4	27
		% within Age	66.7	18.5	14.8	100.0
	10.1-15	Count	4	1	8	13
		% within Age	30.8	7.7	61.5	100.0
	15.1+	Count	2	0	0	2

7.8% (18).

Leukemia include the 31% of malignancies in children aged below 15 years and 25% of cancers in children under 20 years (1, 2), as well as, it considered as the biggest cause of mortality in children due to the cancer^{4,13}. Virchow and Benet introduced it for the first time in 1945 and according to their clinical behavior (acute or chronic) or tissue involved (myeloid, lymphocytic vs. lymphoblastic) classified⁴.

Although the etiology of more leukemia in children is unknown, but some factors like socioeconomic status, ionizing radiation, benzene, infectious agents and genetic risk factors associated with this disease¹³. Even some studies have shown a lower risk of childhood cancer among Asian children¹⁸.

The rate of Leukemia in children under 15 years estimated about, 4 of every 100,000 people a year in advanced countries and 2.5 per 100,000 people in developing countries¹³.

In America and Oceania its prevalence is high, but it's lower in Asia and East Europe. The incidence of ALL in children is 4 times higher than adults while the recovery rate is nearly about 90%. Peak incidence age of ALL is 1-4 years for children and 50 years old for adults¹⁴.

Age distribution percentage of leukemia for children is 0-5 years in Qazvin that this percentage decreases with age. Among all types of leukemia, ALL-L1 in age among 0-5 years had the highest frequency. ALL is a groups of heterogeneous lymphoid neoplasms that derived from B and T lymphocytes¹⁵ that, according to other studies, including, 25% of cancers and 80% of leukemia in childhood^{1,13} and more likely in children between 2-5 years^{13,15}.

AML and CML, constitute 20% and 5% of leukemia respectively¹. ALL and CML highest percentage age prevalence is 2-5 years and 6-14 years for AML¹³. The most common type of leukemia in this study, are ALL-L1, AML, and then followed by ALL-L3 which been confirmed by earlier studies.

The data obtained from this study, showed that the frequency of boys population with leukemia was more than girls (53.3% to 42.7%). In most countries, leukemia in men with 1.3 to 1.4: 1 male to female

ratio is more common than women^{3,13,17}. However, in a study conducted by Pahloosye no gender difference was observed but age differences in patient is expressed and in children under 5 years old prevalence of all types of leukemia is high¹.

In other studies showed that male to female ratio in AML, ALL, CLL, aplastic anemia, and PNH significantly increased, although this ratio has decreased in ITP¹⁹. Male patient with high WBC count, has poor prognosis, however, early chemotherapy can alter the result¹.

Numerous studies been conducted on the relationship between blood group system with various type of diseases and the first study was done on, patients with gastric cancer (19). ABO antigen is among the first known human being markers. Serological studies classified blood groups to four group, that include: A, B, AB, and O¹⁵.

If the correlation between blood group system and risk of various diseases known, so it can used as an initial epidemiological biomarker or screening tool to identify at-risk populations¹⁵.

Various studies have reported conflicting results about the different blood groups distribution among acute leukemia. The present study results showed that the frequency of A and O blood group in ALL-L1 patients is the highest and the lowest frequency rate of leukemia is for AB group. In previous studies both similar and different results have seen, for instance in study that conducted by Farhad and et al, the highest prevalence is for O blood group in CML and then A and B has the higher prevalence and AB group also has the lowest¹⁹.

A study on children with ALL was reported that the percentage of patient with A and O blood group are the same but in AML the incidence of O blood group is high and then B is more³.

In some studies was reported the higher percentage of the O blood group in acute leukemia patient¹⁵. In ALL the frequency of O blood group and then A blood group is high^{20,21} but in AML the A blood group is higher²¹. In 2011 Tavassoli and et al, was shown a significant correlation between ALL and ABO blood group and expressed that the AB blood group is associated with a high risk of ALL¹⁵.

Some previous studies on acute leukemia did not show a significant difference in the distribution of ABO

blood group among leukemic and normal subjects²². Stein berg study was one of them, that find no difference in the distribution of ABO blood group among patients with acute leukemia comparing to the normal population in the society²³.

In a study the incidence of O blood group among female patients with acute leukemia in the years 1974-1980 was proved. the O blood group in women with acute leukemia significantly more than men and the A blood group in men with acute leukemia is more than women²⁴. ABO distribution analysis by gender showed that a significant differences in the distribution of ABO blood groups among girls with AML and ALL^{3,24}.

Alavi et al. in a multi-center study of patients with AML and ALL above 12 years concluded that general distribution of blood groups in both ALL and AML patients was significantly different from the control group²¹. Significant reduction in RH negative patient's with AML (7.15%) was identified¹⁹.

The studies that investigated the relationship between survival time and blood group showed different results. that some reported that survival rates in patients with B blood group is higher, and in another study there were no link between the two issues found¹⁵. Studies show that the relationship between ABO blood groups and hematologic malignancies, needs further population based prospective study²¹.

The present study shows a correlation between ABO blood group and leukemia, but our data were collected from a hospital and there was no available control group, therefore, further studies are needed with higher populations.

This study shows that there is a significant difference between the distributions of ABO blood group in leukemia patients. These findings may be used blood groups as an epidemiological marker for the introduction of risk population for that specific disease.

Conclusion

Such prognostic factor like age, gender, blood group and Rh can be used in leukemia planning for prevention and treatment. In general this epidemiological study showed that the highest incidence of leukemia related to the age of 0-5 years old children in Qazvin province, which decreases

with age and among the types of leukemia, ALL-L1 had the highest frequency and then AML and aLL-L3. Leukemia incidence in Qazvin province, as well as, the most countries statistic, is more common in men. And among ALL-L1 patient, the frequency of blood groups A and O is higher than others and the lowest incidence of leukemia is related to people with blood group AB.

Acknowledgment

We especially appreciate Ms. Manouchehri and the Mr. Khoeini due to their special collaboration with the authors. We also thankful to Mr. Sajjad Rahmani, Mehran Amini and Ali Hamedani and Ms. Sajedah Rahmani for a concerted effort in successful implementation of the project and collecting more detailed information.

Conflict of Interest

The authors have no financial interest in the products discussed in this article.

References

1. Pahloosye A, Hashemi AS, Mirmohammadi SJ, Atefi A. Presenting Clinical and Laboratory Data of Childhood Acute Lymphoblastic Leukemia. Iranian journal of Pediatric Hematology Oncology. 2011;1(3):71-7.
2. Linet M, Devesa S. Descriptive epidemiology of childhood leukaemia. British journal of cancer. 1991;63(3):424.
3. Sakic M. Distribution of ABO blood group in children with acute leukemias. Journal of Health Sciences. 2012;2(3).
4. Babu KLG, Doddamani GM, Mathew J, Jagadeesh KN, Naik LRK. Pediatric leukemia. Journal of Pediatric Dentistry. 2015;3(1):8.
5. Group UCSW. Incidence and mortality web-based report. Atlanta: Department of Health and Human Services; 2009.
6. Jemal A, Thun MJ, Ries LA, Howe HL, Weir HK, Center MM, et al. Annual report to the nation on the status of cancer, 1975-2005, featuring trends in lung cancer, tobacco use, and tobacco control. Journal of the National Cancer Institute. 2008;100(23):1672-94.
7. Mossoomy Z, Mesgari M. Detection of leukemia epidemiology in Iran using GIS and statistical analyses. Pediatric Hematology and Oncology. 2008;32:441-8.
8. Belson M, Kingsley B, Holmes A. Risk factors for acute leukemia in children: a review. Environmental health perspectives. 2007:138-45.
9. Fauci AS. Harrison's principles of internal medicine: McGraw-Hill Medical New York; 2008.
10. Elliot P, Wakefield JC, Best NG, Briggs D. Spatial epidemiology: methods and applications: Oxford University Press; 2000.
11. Health UDo, Services H. Agency for toxic substances and disease registry. Toxicological Profile for Asbestos Update Agency for Toxic Substances and Disease Registry. 1999.
12. Malphettes M, Gérard L, Carmagnat M, Mouillot G, Vince N, Boutboul D, et al. Late-onset combined immune deficiency: a subset

of common variable immunodeficiency with severe T cell defect. *Clinical Infectious Diseases*. 2009;49(9):1329-38.

13. Alrudainy L, Mahmood Salih H, Mohammed A. Incidence and pattern of childhood leukaemia in Basrah, Iraq during 2003– 2007. *Iran J Blood Cancer*. 2009;2:11-7.

14. Katz AJ, Chia VM, Schoonen WM, Kelsh MA. Acute lymphoblastic leukemia: an assessment of international incidence, survival, and disease burden. *Cancer Causes & Control*. 2015;26(11):1627-42.

15. Tavasolian F, Abdollahi E, Vakili M, Amini A. Relationship between ABO blood group and Acute Lymphoblastic Leukemia. *Iranian journal of pediatric hematology and oncology*. 2014;4(1):1.

16. Deschler B, Lübbert M. Acute myeloid leukemia: epidemiology and etiology. *Cancer*. 2006;107(9):2099-107.

17. Gurney JG, Davis S, Severson RK, Fang J-Y, Ross JA, Robison LL. Trends in cancer incidence among children in the U. S. *Cancer*. 1996;78(3):532-41.

18. Liu Y-L, Lo W-C, Chiang C-J, Yang Y-W, Lu M-Y, Hsu W-M, et al. Incidence of cancer in children aged 0–14 years in Taiwan,

1996–2010. *Cancer epidemiology*. 2015;39(1):21-8.

19. Farhud D, Sadighi H, Andonian L, Saffari M, Poursadegh Fard M, et al. Study of Sex Ratio, Abo and Rh Blood Groups Distribution In Some Haematological And Lymphatic Diseases In Iran. *Iranian Journal of Public Health*. 1995;24:1-2.

20. Vadivelu MK, Damodaran S, Solomon J, Rajaseharan A. Distribution of ABO blood groups in acute leukaemias and lymphomas. *Annals of hematology*. 2004;83(9):584-7.

21. Alavi S, Ashraf H, Rashidi A, Hosseini N, Abouzari M, Naderifar M. Distribution of ABO blood groups in childhood acute leukemia. *Pediatric hematology and oncology*. 2006;23(8):611-7.

22. Shirley R, Desai R. Association of leukaemia and blood groups. *Journal of medical genetics*. 1965;2(3):189.

23. Steinberg AG, Steinfeld JL. The genetics of acute leukemia in children. *Cancer*. 1960;13(5):985-99.

24. Nagy P, Jako J, Kiss A, Tamas E, Telek B, Rak K. Sex-Linked Difference in Blood-Group Distribution among Patients Suffering from Acute Leukaemias. *British journal of haematology*. 1981;48(3):507-12.