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Impact of ABO and Rh Blood Groups Combined with Family History on Pediatric Leukemia Risk

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Abstract

Pediatric Leukemia is the most common childhood cancer, yet its exact causes remain unclear. Both genetic predisposition and host biological factors may influence susceptibility. ABO and Rhesus (Rh) blood group systems, beyond their role in transfusion compatibility, have been linked to the risk of various cancers through mechanisms involving immune response, cell adhesion, and inflammation. Family history of malignancy is another established risk marker, reflecting shared genetic and environmental influences. Objectives of the study is to investigate the combined influence of ABO and Rh blood group types and family history of malignancy on the risk of developing pediatric leukemia. The current study was conducted on 50 patients with leukemia of all kinds in the Central Teaching Hospital of Pediatrics in Baghdad, Iraq. The diagnosis was confirmed based on bone marrow aspiration and blood film. ABO and Rh blood group was tested manually for all patients, and Family history was determined through the medical records. The blood groups were predominantly O+ (20; 40%), followed by B+ (12; 24%), A+ (10; 20%), AB+ (7; 1%), and O- (1; 2%), respectively. The analysis of family history regarding cancer in the patient samples revealed that a majority of children with leukemia had a negative family history, compared to those with a positive family history (80% vs. 20%). Furthermore, the majority of the case group's leukemic children were evaluated and classified as being at standard (low) risk (42%), with high and intermediate risks coming in second and third, respectively, at 36% and 22%. This study highlights that pediatric leukemia risk patterns differ by subtype, with predominance of low-risk classifications in B-ALL, ALL, and AML, while T-ALL cases were uniformly high-risk. The findings suggest that ABO blood group and family history may influence leukemia susceptibility and prognosis in a subtype-specific manner, blood group O and Rh D positive are risk factors for the incidence of ALL in children underscoring the need for larger studies to clarify these associations

Keywords: Blood groups, Family history, Pediatric leukemia.

Introduction

One of the most dangerous diseases affecting children, pediatric leukemia destroys healthy cells, causes uncontrolled white blood cell proliferation, and spreads throughout the body (1). Leukemia, which is also known as "White Blood Cancer," is the most common type of blood cancer and kills a lot of people (2). Although committed stem cells with a limited capacity for self-renewal may occasionally be involved, malignant transformation typically takes place at the pluripotent stem cell level. Due to abnormal proliferation, clonal expansion, aberrant differentiation, and decreased apoptosis (programmed cell death), normal blood components are replaced by malignant cells (3). Currently, risk stratification is determined by laboratory parameters (number of white blood cells (WBCs) at diagnosis, karyotype, and cytogenetic findings), clinical factors (presence of extramedullary disease), and demographic factors (age and sex) (4).

The exact cause of leukemia is unknown. Ionizing radiation, petrochemicals (including benzene), previous chemotherapy, and Down syndrome are risk factors. It is thought that a combination of environmental (non-inherited) and genetic factors is involved. Additionally, people who have a history of leukemia in their family are more at risk (5). They are categorized according to their rate of progression (acute or chronic) and the cell of origin (myeloid or lymphoid). The four main subtypes are acute myeloid leukemia (AML), chronic myeloid leukemia (CML), acute lymphoblastic leukemia (ALL), and chronic lymphocytic leukemia (CLL). Acute lymphoblastic leukemia (ALL) accounts for ~85% of leukemia cases in childhood (6).

The ABO blood group system plays a pivotal role in blood transfusion and has long been of interest in disease epidemiology. ABO antigens are carbohydrate-based molecular structures located on the surface of red blood cells (RBCs) and, importantly, also present on leukocytes, platelets, plasma proteins, certain organ tissues, and in soluble form in body fluids such as saliva, breast milk, urine, and gastric secretions (7). These antigens are genetically determined glycoconjugates, with their synthesis directed by specific glycosyltransferase enzymes. While the antigens themselves are considered secondary gene products, they significantly influence cell physiology, immune recognition, and interactions with pathogens (8).

Since the 1953 discovery of an association between blood type A and gastric cancer, numerous studies have explored potential links between ABO blood types and various infectious and non-infectious diseases, including autoimmune disorders and malignancies (9). The presence or absence of specific ABO antigens can alter RBC membrane form and function, potentially impacting disease susceptibility. Mechanistically, ABO antigens may influence carcinogenesis and tumor progression by modulating cell adhesion, immune evasion, and inflammatory responses, although the precise pathways remain unclear (10).

Several epidemiological studies have examined the role of ABO blood group in leukemia risk, with mixed findings. Some reports indicate a higher prevalence of certain blood groups, such as type O in acute lymphoblastic leukemia (ALL) or type A in acute myeloid leukemia

(AML), whereas others found no significant associations. Despite these inconsistencies, ABO blood group antigens remain of interest as potential epidemiological markers that could help identify high-risk populations (11).

In addition to blood group, family history is a recognized factor in leukemia susceptibility. Familial aggregation of hematological malignancies suggests that inherited genetic variations, shared environmental exposures, or both may contribute to disease risk. Studies have shown that children with a first-degree relative affected by leukemia or other hematologic cancers may have an elevated lifetime risk, highlighting the importance of considering both genetic and immunopharmacological factors. While not all cases are hereditary, individuals with a family history of blood cancers may benefit from genetic counseling and testing to assess their risk and guide preventive measures and screening protocols. Advances in genetic research continue to enhance our understanding of familial patterns in blood cancers, leading to improved strategies for early detection, personalized treatment, and cancer prevention (12).

Given these observations, the present study aims to investigate the combined influence of ABO and Rh blood group types and family history of malignancy on the risk of developing pediatric leukemia.

Subjects and methods:

Study Design and Study sampling

A cross-sectional study was approved by the College of Medicine, Al-Iraqia University, the sample was collected from each child after obtaining consent from their parents. Between November 2024 and January 2025, 50 blood samples were collected at the Central Teaching Hospital of Paediatrics in Baghdad. The age distribution of the patients ranged from 1 to 13 years. The type of sample is non-probability sampling.

Blood types were determined through manual ABO and Rh analysis performed on all patients at the Central Teaching Hospital of Pediatrics in Baghdad. Family history was determined through the medical records of the patients participating in the study. Risk stratification of leukemia patients into standard categories (low, intermediate, and high risk) was performed according to the treatment protocol determined by hematologists and oncologists based on several criteria, including patient age, initial white blood cell count, central nervous system involvement, and initial response to chemotherapy.

Ethical Approval

Initial ethical approval for this study was obtained from the Ethics Committee at the College of Medicine, Al-Iraqia University. A second ethical approval was secured from the Research Committee of the Ministry of Health, along with permissions from the AL- Karkh Health Directorate. Additionally, written consent was obtained from participants, who were informed that their participation was voluntary, with an emphasis on the confidentiality of information, which would be used solely for research purposes.

Statistical Analysis

Data were entered and analyzed using the software of the computer program of Statistical Package of Social Science (SPSS) version 26, as well as STATISTICA version 12.

Results

The study included fifty pediatric leukemia patients of various types. There were 21 females and 29 males, aged 1-13 years. Regarding the types of leukemia in children,

acute lymphoblastic leukemia (ALL) was the most prevalent type of leukemia (42 cases; 84%), and B-precursor acute lymphoblastic leukemia (B-ALL) was more prevalent than T-precursor acute lymphoblastic leukemia (T-ALL) (30 cases; 60% versus 12 cases; 24%), respectively. The other types were mainly acute and chronic myeloid leukemia (AML) and chronic myeloid leukemia (CML) (7 cases; 14% and 1 case; 2%), respectively (Figure 1).

The blood groups were predominantly O+ (20; 40%), followed by B+ (12; 24%), A+ (10; 20%), AB+ (7; 1%), and O- (1; 2%), respectively (Figure 2).AS for the family history of cancer for the patient samples, it was found that the family history was predominantly negative among children with leukemia compared to those with positive family history (40 cases; 80% vs. 10 cases; 20%), respectively (Figure 3).

Additionally, most of the leukemic children in the case group were assessed and categorized as at standard (low) risk (21 cases; 42%), followed by high and intermediate risks (18 cases; 36% and 11 cases; 22%), respectively (Figure 4)

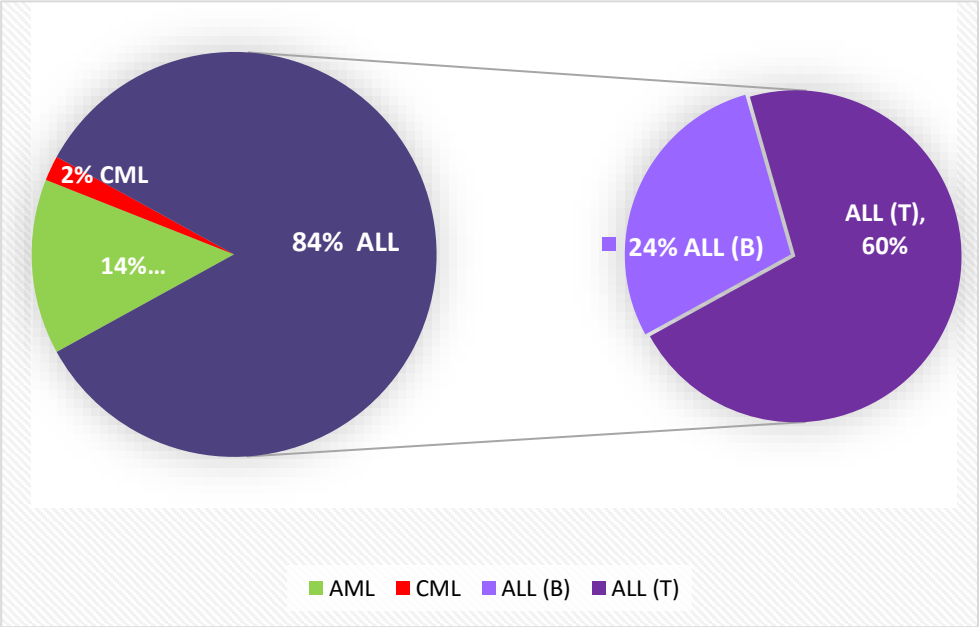

Figure 1 Distribution of cases study sample according to their leukemia type (n=50)

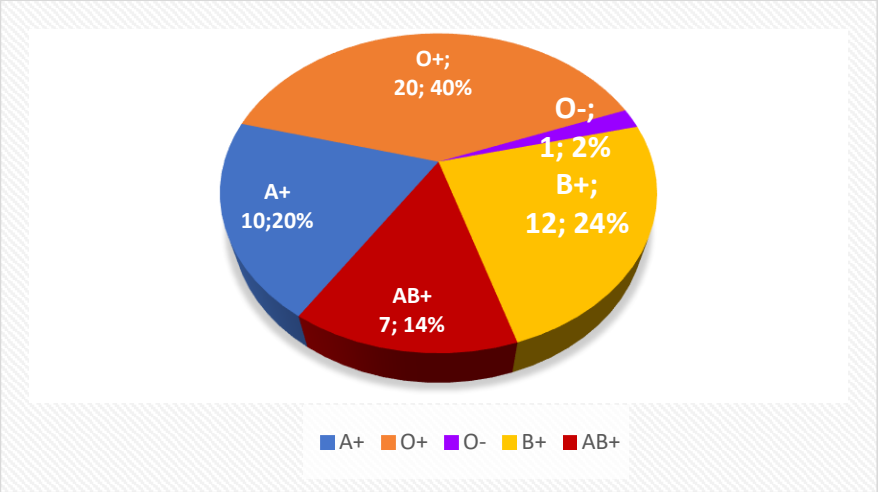

Figure 2 Distribution of cases study sample according to their blood groups (n=50)

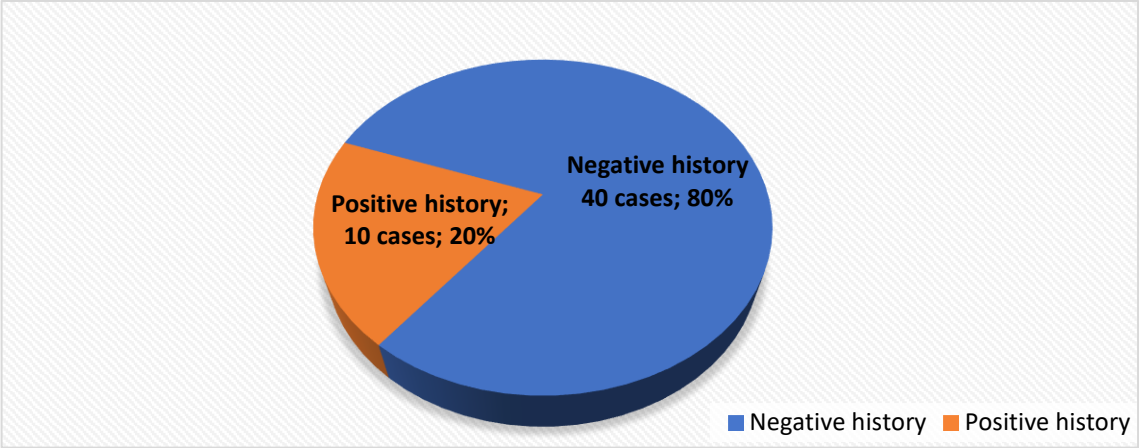

Figure *3 Distribution* of cases study sample according to family history of Leukemia (n=50)

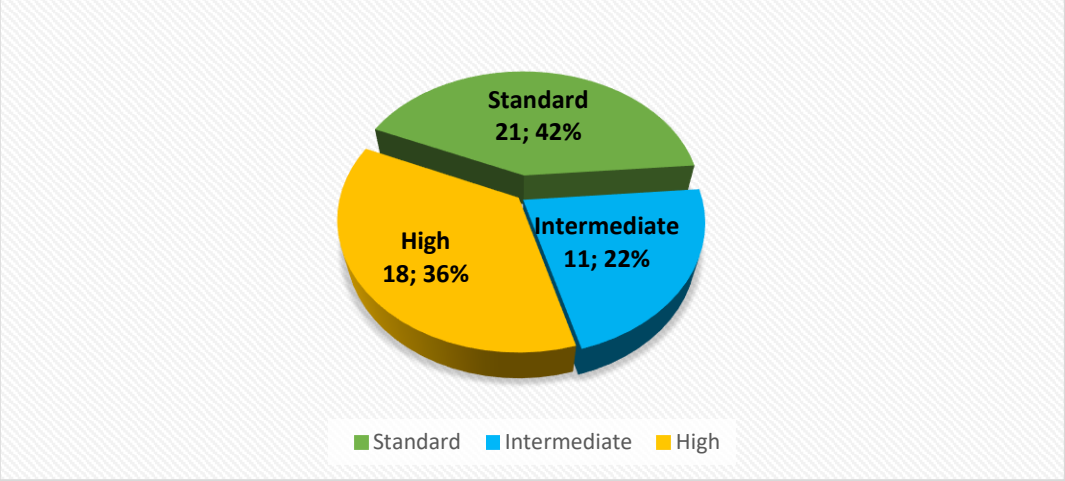

Figure 4 Distribution of cases study sample according to their risk assessment (n=50)

The table (1) allows rapid comparison of ABO group patterns, family history prevalence, and clinical risk trends across leukemia types, while also identifying which associations are statistically significant. It combines descriptive statistics with inferential analysis to highlight both observed distributions and their potential epidemiological relevance.

Table 1 Statistical Overview of ABO Blood Group Distribution, Family History, Risk Category, and Chi Square Significance by Leukemia Type.

Leukemia Type	Total Cases	Most Common ABO	ABO % Distribution				Positive Family History %	Most Frequent Risk Category	Chi square p value
			O%	A%	B%	AB%			
B-ALL	28	O	46.4 %	19.6 %	28.6 %	10.7 %	21.4%	Low (36%)	0.002
ALL	6	O	83.3 %	16.7 %	0%	0%	33.3%	Low (66.7%)	0.045
T-ALL	8	AB	12.5 %	12.5 %	25.0 %	50.0 %	25.0%	High (100%)	0.038
AML	7	O & B (tie)	28.6 %	28.6 %	42.9 %	0%	28.6%	Low (57.1%)	0.210
CML	1	A	0%	100%	0%	0%	0%	High (100%)	N/A

Discussion

The association between ABO and Rh blood groups and the risk of childhood leukemia remains a subject of debate after decades of research; some studies have found no connection, while others have reported strong correlations. Likewise, although family history has long been known to increase the risk of developing cancer in general, its precise role in pediatric leukemia is less clear (13).

Understanding the interplay between blood group phenotype and family cancer history could enhance risk assessment models and help identify children who may benefit from early genetic counseling or targeted screening. In the present study of fifty pediatric leukemia patients, acute lymphoblastic leukemia (ALL) was the predominant subtype, consistent with global epidemiological patterns in which ALL is

the most common childhood leukemia. A slight predominance was also observed, in line with previous reports (14,15).

ABO and Rh Blood Group Distribution

Blood group O+ was the most frequent among leukemia patients (40%), followed by B+ (24%), A+ (20%), AB+ (14%), and O− (2%). Subtype analysis showed that blood group O predominated in B-ALL (46.4%) and ALL (83.3%), while T-ALL displayed an unusual predominance of AB (50%). In AML, groups O and B were equally common (28.6% each), and the single CML case was A.

The predominance of blood group O+ suggests a possible link between ABO/Rh phenotypes and leukemia susceptibility, particularly for acute lymphoid subtypes. This finding is consistent with a previous Iraqi study conducted in 2020, which reported O as the most common blood group among leukemia patients, followed by A, B, and AB (16).

On the contrary, a comprehensive study on the distribution of ABO blood types in leukemia patients reported that blood type O is more common in chronic leukemia, whereas blood type A is more common in acute leukemia. The association between leukemia and variations in ABO blood types was also validated by this study (17).

Although some literature shows variability depending on region and study population, the overall trend suggests a potential link between blood group O and increased susceptibility to ALL and B-ALL as a major subtype (18).

Family History of Cancer

In our study, 80% of children had no family history of cancer, while 20% reported affected relatives, supporting the notion that pediatric leukemia is largely sporadic and multifactorial. Positive family history was most common in ALL (33.3%), followed by AML (28.6%), T-ALL (25%), and B-ALL (21.4%), and was absent in the CML case. The positive family History occurred across multiple ABO groups—most frequently O in B-ALL and AB in T-ALL—and was more common in high- and intermediate-risk categories, particularly in B-ALL and T-ALL. This pattern supports existing epidemiological evidence that genetic predisposition or shared environmental exposures may influence not only leukemia susceptibility but also the likelihood of more aggressive disease (19).

The literature shows mixed findings regarding family history. Wong et al. reported only a modest and non-significant effect of family history of cancer on leukemia, which is consistent with the results of the current study (20). In contrast, another Iraqi study showed that having a family history of cancer increases the likelihood of developing leukemia and other neoplasms, which is at odds with our findings (21). This variation may indicate the potential influence of confounding factors such as genetic or geographic background, or differences in data collection methods.

Similar to Wong et al., several Iranian studies have reported a limited or inconsistent impact of family history on childhood leukemia risk. For example, a case series from Mahak Hospital (Tehran) found an association between family history and relapse risk in pediatric AML in certain subgroups, whereas a national survival analysis suggested that family history might be linked to poorer outcomes in childhood cancers (22).These mixed findings support our conclusion that the effect of family history may

be modest and context-dependent, influenced by leukemia subtype and local genetic–environmental interactions .

Risk Category Distribution

Most patients were classified as standard risk, but a notable proportion fell into the high-risk group. Risk distribution varied by subtype: low-risk classification predominated in B-ALL, ALL, and AML, whereas T-ALL and the single CML case were exclusively high-risk.

The clustering of high-risk status in T-ALL suggests inherent biological aggressiveness. Genetic alterations such as NOTCH1 mutations are common in T-ALL and can influence prognosis (23).

These findings align with a previous study by the National Institutes of Health (NIH) reporting similar subtype-specific risk distributions in childhood leukemia, finding that low-risk B-cell acute lymphoblastic leukemia (B-ALL) was more common, while T-cell ALL (T-ALL) exclusively comprised high-risk cases. reporting similar subtype-specific risk distributions in childhood leukemia (24).

Overall, our findings reinforce the predominance of blood group O+, particularly in acute lymphoid subtypes, and suggest a potential association with leukemia risk in children. Family history of cancer appears to play a modest and variable role, more evident in certain subtypes and higher-risk cases. Subtype-specific differences in risk category further emphasize the importance of individualized prognostic assessment. Larger, multi-center studies with genetic and environmental profiling are needed to clarify these associations and improve risk prediction models.

Conclusion:

Risk factors for childhood leukemia differed by subtype, ABO blood type, and family history. While AB was remarkably prevalent in high-risk T-ALL, blood group O predominated in ALL and B-ALL. Although it only occurred in 20% of cases, a positive family history was more common in high- and intermediate-risk groups, particularly in B-ALL and T-ALL, indicating a possible association with more aggressive disease. Overall, the results show that risk status is highly subtype-specific and that family history and ABO type may influence leukemia prognosis and susceptibility.

Recommendation:

Larger, multi-center investigations are necessary to explore the underlying mechanisms and confirm the relationships between ABO blood group, family history, and the risk of pediatric leukemia.

Conflict of Interest: There are no conflicts to declare

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