Ministry of Higher Education and Scientific Research
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Blood Groups Relationship with Incidence of Malignancy in Children

A project submitted to the council of University of Diyala College of Medicine in Partial fulfillment of the Requirements for the Degree of Bachelor in medicine and general surgery.

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2021 1442

Abstract

Background: Despite their obvious clinical importance, the physiological functions of ABO blood group antigens remain a mystery.

Objective: To investigate the association of ABO and Rh blood groups with various types of malignant diseases in children, regarding incidence.

Patients and Methods: Cross-sectional comparative study was conducted in Oncology Center of Baquba Teaching Hospital in Diyala, Iraq. All registered patients in the center, with different malignant diseases, were included in the study from 1st of October to 1st of December 2020, ABO and Rh blood group was tested manually for all patients. Statistical Package for Social Sciences soft ware (SPSS), version 20 was used to analyze data, p value was consider significant at level of <0.05.

Results: The study enrolled 226 patients of different malignant diseases, Male: Female ratio was 1.5:1 and most of enrolled patients were between 1yr- 12yr old. Regarding the type of malignant disease, Acute lymphoblastic leukemia was the commonest (n= 91, 40.5%), followed, in order, by Retinoblastoma (n= 26, 11.5%), Non-Hodgkin lymphoma (n=25, 11%) and Neuroblastoma (n=22, 9.7%). Regarding ABO blood groups, O was the commonest (n=103, 45.6%) with significantly associated (p value .011) with all malignant diseases, in general, when individualizing the results to the type of malignancy, this association will fade away. Rh D positive was commonest in all types of malignancy like that of general population (n=215, 95.1%) with significant association (p value .011) with acute lymphoblastic leukemia.

Conclusion: A blood group O and Rh D positive are risk factors for incidence of ALL in children and group AB and Rh D negative children seemed to be less susceptible.

Key words: ABO/ Rh blood groups, Malignancy.

Introduction

ABO blood group are a set of antigens [agglutinogens] that are genetically determined molecules of carbohydrate carried on the red blood cell surface membranes, Anti-A and Anti-B are mostly IgM antibodies formed in the infancy by sensitization to environmental antigens, such as bacteria, viruses, and foods, they are not red blood cell antibodies but usually bacterial antibodies cross-reacting with red blood cells and the studies also suggested that ABO blood groups could be served as an epidemiological marker or a primary screening aid to identify populations at high risk for certain hematological malignancies [1,2].

There are many types of malignancies that associated with ABO blood group in children mostly are Leukemia and Lymphoma, the first most common neoplasm in childhood is Leukemia and represents about 41% of all malignancies < 15 yrs of age, genetic and environmental factors predispose to childhood malignancies and one most common type of it is acute lymphoblastic leukemia (ALL) is a malignant (clonal) disease of the bone marrow in which early lymphoid precursors proliferate and replace the normal hematopoietic cells of the marrow, ALL accounts for 77% of pediatric leukemia cases and there is a three types of ALL, ALL-A is the first most common type followed by ALL-B and ALL-C [3,4,5].

Second type of leukemia is acute myelogenous leukemia (AML) account about 11% of total cases of childhood leukemia, there are several chromosomal abnormalities associated with AML, but there are no predisposing genetic or environmental factors and the most common classification of the subtypes of AML is the FAB system which divides AML into 7 types (M1, M2.....M7), and third type of leukemia is chronic mylogenous leukemia (CML) account about 2-3% of total, about 99% of cases are characterized by Philadelphia chromosome and it may be associated with the exposure to the ionizing radiation [6,7].

The second most common neoplasm in children is Lymphoma and divided into two types, one type of lymphoma is Non-hodgkin lymphoma (NHL), is more

common and more serious than Hodgkin disease, it can occur at any age generally, most cases of lymphoma below 10 yr of age are NHL and has 3 sites of origin which wide range of presentations, one most common site is extra nodal lymphatic tissues as lung and git, second next common is nodal disease and third least common is extra lymphatic tissue, second type of lymphoma is hodgkin disease (HD), it is rare below 5 years of age. The peak age incidence is from 15-30 yr and >50 yr [8,9,10].

Other rare types of neoplasm in children associated with ABO blood group are neuroblastoma is the most common extracranial solid tumor of infancy, it is an embryonal malignancy of the sympathetic nervous system arising from neuroblasts, Wilms tumor (nephroblastoma), is the most common childhood abdominal malignancy and the median age at diagnosis of this kidney tumor is approximately 3.5 years[11,12,13].

Hepatoblastoma account about 2%, osteosarcoma 2% and ewing sarcoma related to bone 1% [14,15].

Aim of the study

To investigate the association of ABO and Rh blood groups with various types of malignancy in children, regarding incidence and other characters.

Patients and Methods

A cross-sectional comparative study was conducted in Oncology Center of Baquba Teaching Hospital in Diyala, Iraq.

The study started with collection of data from 1st of October to 1st of December 2020, and the study continued for writing till the 1st of May 2021. The study enrolled children diagnosed previously with different malignant diseases and continued for treatment in the center.

ABO and Rh blood group was tested manually for all patients. Matching of ABO blood group distribution in the sample of the study was carried out with that of general population, unfortunately, in Diyala province we have no data of ABO/ Rh blood groups, so it was depended on data of neighboring province, Babylon , those province having the same ethnic Arabic population background as that of the study area.

Statistical Analysis

Statistical Package for Social Sciences soft ware (SPSS), version 20 was used to analyze data. Chi square test was used to look for the association between variables, p value was taken significant at level of <0.05.

Results

The study enrolled 226 patients of different malignant diseases, Male:Female ratio was 1.5:1, most of enrolled patients were between 1yr- 12yr old, table(1).

Table (1): Demographic criteria of the study group patients.

Age/Gender	Male number (%)	Female number (%)	Total number (%)
Birth - 1yr	10 (53%)	9 (47%)	19 (100%)
> 1- 3 yrs	35 (59.3%)	24 (40.7%)	59 (100%)
> 3 - 6 yrs	56 (70.8%)	23 (29.2%)	79 (100%)
> 6 - 12 yrs	30 (51.7%)	28 (48.3%)	58 (100%)
> 12 yrs - 15 yrs	4 (36.4%)	7 (63.6%)	11 (100%)
Total	135 (59.7%)	91 (40.3%)	226 (100%)

Regarding the type of malignant diseases, Acute lymphoblastic leukemia was the commonest followed, in order, by Retinoblastoma, Non-Hodgkin lymphoma and Neuroblastoma, table (2).

Table (2): Malignant diseases in data of study.

Diseases	number (%)
Acute Lymphoblastic Leukemia (ALL)	91 (40.5%)
Acute Myelogenous Leukemia (AML)	16 (7.1%)
Non Hodgkin lymphoma NHL	25 (11%)
Hodgkin disease HD	12 (5.3%)
Retinoblastoma	26 (11.5%)
Neuroblastoma	22 (9.7%)
Wilms tumor	18 (7.9%)
Ewing sarcoma	8 (3.5%)
Hepatoblastoma	7 (3%)
Immature Teratoma	1 (0.4%)
Total	226 (100%)

In general, blood group (O) was commonest in most of patients with malignant diseases, in addition to the general population, followed by blood groups A, B, and lastly AB. There was a clears significant association of the blood group (O) with total numbers of patients (p value = .011), this association was fade away when individualized to each type of malignancy.

Table (3): Distribution of ABO blood groups in the study group versus general population of Babylon.

Diseases	ABO blood group Number (%)				p value+
	O	A	B	AB	
Acute lymphoblastic leukemia ALL	33 (32%)	26 (44%)	26 (50%)	6 (50%)	.949
Acute myelogenous leukemia AML	4 (3.9%)	8 (13.6%)	3 (5.8%)	1 (8.3%)	.263
Non hodgkin lymphoma NHL	13 (12.6%)	5 (8.5%)	6 (11.5%)	1 (8.3%)	.374
Hodgkin disease HD	5 (4.9%)	2 (3.4%)	4 (7.7%)	1 (8.3%)	.860
Retinoblastoma	17 (16.5%)	4 (6.8%)	5 (9.6%)	-	-
Neuroblastoma	13 (12.6%)	5 (8.5%)	4 (7.7%)	-	-
Wilms tumor	9 (8.7%)	4 (6.8%)	3 (5.8%)	2 (16.7%)	.521
Ewing sarcoma	4 (3.9%)	4 (6.8%)	-	-	-
Hepatoblastoma	5 (4.9%)	1 (1.6%)	1 (1.9%)	-	-
Immature teratoma	-	-	-	1 (8.3%)	-
Total	103 (45.6%)*	59 (26.1%)	52 (23%)	12 (5.3%)	.011
General population in Babylon (%)	35.7	27.7	28.3	8.3	

+ p value was calculated by comparison of data of each row (each type of malignancy) with percents of the general population in Babylon which are mentioned in end of the table.
* significant association.

In general, blood group (Rh D positive) was commonest in all patients with malignant diseases, in addition to the general population. There was a clears significant association of the blood group (Rh D positive) with ALL.

Table (4): Distribution of Rh blood groups in the study group versus general population of Babylon.

Diseases	Rh D positive	Rh D negative	P value[+]
Acute lymphoblastic leukemia ALL	89 (97.8%)*	2 (2.2%)	.014
Acute myelogenous leukemia AML	15 (93.8%)	1 (6.2%)	.625
Non hodgkin lymphoma NHL	24 (96%)	1 (4%)	.323
Hodgkin disease HD	12 (100%)	-	-
Retinoblastoma	23 (88.5%)	3 (11.5%)	.780
Neuroblastoma	21 (95.5%)	1 (4.5%)	.400
Wilms tumor	16 (88.9%)	2 (11.1%)	.863
Ewing sarcoma	7 (87.5%)	1 (12.5%)	.806
Hepatoblastoma	7 (100%)	-	-
Immature teratoma	1 (100%)	-	-
Total	215 (95.1%)*	11 (4.9%)	.011
General population in Babylon %	90.1	9.9	

[+]p value was calculated by comparison of data of each row (each type of malignancy) with percents of the general population in Babylon which are mentioned in end of the table.

* significant association.

Discussion

The purpose of this study was to show any association between ABO blood groups and type of malignancy in children treated in Baquba Teaching Hospital. Male to Female ratio was 1.5:1 especially in age groups between 1yr to 12yrs old. Regarding in type of malignant diseases, Acute lymphoblastic leukemia was the commonest (n= 91, 40.5%). Regarding in ABO blood groups, O was the commonest (n=103, 45.6%) with (p value .011) and Rh D positive was (n=215, 95.1%) with significant association (p value .011). This study showed that Rh D positive more exposed to acute lymphoblastic leukemia than Rh D negative, whereas the other malignant diseases with Rh D positive also there was a difference but statistically not significant.

This study showed in total general, that O blood group was significant in malignancy but which type of malignancy is not specified this may be due to our data was collected in a single hospital, further research in a large population based is need. A previous study carried out in Iraq for the distribution of ABO blood groups in Iraqi samples of leukemia patients where O type of blood group was the main blood group followed by A, B and AB, this study goes in agreement with the current study [16]. In North India they observed a definite bias towards males with a ratio of 3.2:1. Literatures mentioned that the peak incidence of ALL occurs between 2yrs to 5yrs old [17,18]and this goes in agreement with the current study. Another study was done by Melihasakic to indicate the distribution of ABO groups in children with leukemia in Federation of Bosnia and Herzegovina. The result however, showed an equal percentage of distribution of both A and O blood groups among the children with ALL [19]. One study was conducted in Iran, showed although there was not any association between ABO/Rh blood groups and acute lymphoblastic leukemia but probably females with B blood group are more susceptible toward ALL and this study goes in disagreement with the current study[20].

Conclusion

In the light of the present results, this study showed that a blood group O and Rh D positive are a risk factors for incidence of ALL and group AB and Rh D negative children seemed to be less susceptible, whereas for other types of malignancies, a large population study is needed for each type to obscure the relationship with blood groups.

References

1. Garratty G. Relationship of blood groups to disease: Do blood groups antigens have a biological role. J. 2005; 43:113-121.

2. Liumbruno GM, Franchini M. Hemostasis, cancer, and ABO blood group: the most recent evidence of association. J. Thromb Thrombolysis. 2014;38:160–6.

3. Vadivelu, M.K., Damodaran, S., Solomon, J. and Rajaseharan, A. Distribution of ABO blood groups in acute leukaemias and lymphomas. Hematol 2004; 83: 584-587.

4. Karen Seiter, MD. Acute lymphoblastic leukemia in children. J. Oct 26, 2020;10(2):16078.

5. Zwerdling,T. Pediatric Acute Lymphoblastic Leukemia. Hematology and Transfusion International Journal 2020;5(3)450-455.

6. Hartmut Döhner, Daniel J Weisdorf, Clara D Bloomfield. Acute myeloid leukemia. New England Journal of Medicine 2015;373(12)1136-1152.

7. Nelson R. 'Too Clean' Could Be a Trigger for Childhood Acute Leukemia. Essential Nelson Textbook In Pediatrics. May 25, 2018;22(6):1090-1104.

8. Swerdlow SH, Campo E, Pileri SA, Harris NL, Stein H, Siebert R, et al. The revision of the World Health Organization classification of lymphoid neoplasms. Blood. May 19,2016;127 (20):2375-90.

9. Zhang QY, Foucar K. Bone marrow involvement by Hodgkin and non-Hodgkin lymphomas. Hematol Oncol Clin North Am. 2009;23(4):873-902.

10. Bradley W Lash, MD. Hodgkin lymphoma in pediatric. Journal of the National Cancer Institute. Aug 3, 2020;185(1):25-41.

11. Norman J Lacayo. Pediatric neuroblastoma. Schwartz's Clinical Handbook of Pediatrics. Jul 18, 2019;21(8):1093-1103.

12. Brecht IB, Kaatsch P. Epidemiology. In: Schneider DT, Brecht IB, Olson TA, Ferrari A, Rare tumors in children and adolescents. Berlin Heidelberg Springer. 2012;71(8):340-348.

13. Arnold C Paulino, MD. Wilms Tumor in pediatrics neoplasm. J. Jun 5, 2020;84(6):437-445.

14. Mary Elizabeth Mc Carville, MD. Pediatric Hepatoblastoma. Conference presentation. Jun 10, 2016;31(2):84-91.

15. Gorlick R, Janeway K, Lessnick S, Randall RL, Marina N, COG Bone Tumor Committee. Children's Oncology Group's blueprint for research: bone tumors. Pediatr Blood Cancer. 2013;60 (6):1009-15.

16. Shirley R, Desai R. Association of leukaemia and blood groups. Journal of Medical Genetics. 2012;2(3):189.

17. Wolpin BM, Chan AT, Hartge P, Chanock SJ, Kraft P, Hunter DJ, et al. ABO blood group and the risk of pancreatic cancer. Journal of the National Cancer Institute. 2009;101(6):424-31.

18. Zuppa AA, Cardiello V, Lai M, Cataldi L, D'Andrea V, Romagnoli C. ABO hemolytic disease of the fetus and newborn: an iatrogenic complication of heterologous technology-induced 2010;50(10):2102-4.

19. MacMahon B, Forman D. Variation in the duration of survival of patients with acute leukemia. Blood.2012;12(8):683-93.

20. Iodice S, Maisonneuve P, Botteri E, Sandri MT, Lowenfels AB. ABO blood group and cancer. European journal of cancer. 2010;46(18):3345-50.