

# EVALUATION OF THE RELATIONSHIP BETWEEN LYMPHOMA AND ABO BLOOD GROUP: A TEN-YEAR RETROSPECTIVE STUDY

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#### **Abstract**

**Background:** The role of ABO blood group in cancer biology has been extensively documented in the literature. However, studies on the association between lymphoma and ABO blood types have been largely contentious.

Aims: To determine the frequency and distribution of ABO blood groups among a cohort of patients with lymphoma as well as to examine the association, if any, between the lymphoma and the ABO blood groups.

**Methods:** This was a retrospective descriptive cross-sectional study involving the review of records of patients with lymphoma over a 10-year period.

**Results:** The records of 111 patients with lymphoma over a 10-year period were reviewed. The mean age of the patients was  $41.70 \pm 14.7$  years. The peak age incidence of the subjects was within the fourth to the firth decades of life. The male to female ratio was 1.4:1. Non-Hodgkin lymphoma (NHL) was commoner than Hodgkin lymphoma (HL) (62.2%), and diffuse large B-Cell lymphoma was the most common NHL histologic subtype (43.5%) while nodular sclerosis

was the most common histologic subtype of HL seen (59.5%). Majority of the patients were of the O blood group, followed by B, A and AB blood groups. There was no statistically significant association between lymphoma and ABO blood types of the patients.

**Conclusion:** The association of ABO blood groups and risk of occurrence of lymphoma is not statistically significant. However, we recommend that a large multicenter prospective study on the influence of ABO blood group on the risk of occurrence of lymphoma be done in Nigeria and other countries in Sub-Saharan Africa for the purpose of validating our findings.

**Keywords:** Non-Hodgkin lymphoma, Hodgkin lymphoma, blood group, ABO, Nigeria.

#### INTRODUCTION

Lymphomas are a heterogeneous group of clonal malignant neoplastic disorders of the immune system. These disorders are broadly classified into Hodgkin Lymphoma (HL) and Non-Hodgkin Lymphoma (NHL) each characterized by distinct natural histories, varying histologic subtypes and require intricate diagnostic evaluation and management [1].

The aetiology of lymphomas is not fully elucidated. However, growing epidemiological and biological data have revealed some risk factors that are associated with the development of these malignancies [2, 3]. Lymphomas are increasingly prevalent and have become the tenth most common cancer globally [4]. HL accounts for 0.5% of all cancers and 0.5% of cancer deaths, while NHL accounts for 2.8% of cancer diagnosis and 2.6% of cancer mortality worldwide [5 – 7]. However, the burden of lymphoma varies considerably across different geographical regions over time [5,6]. In the United States, HL comprises about 0.5% of newly diagnosed cases of cancer and about 0.2% of all oncological mortality. On the other hand, NHL accounts for 4% of all cancer cases and represents 3.3% of all cancer deaths in the country [8,9]. The prevalence and mortality rates are much less in the Orient. In Korea for instance, HL and NHL account for 0.12% and 2.3% of all cancer diagnoses and 0.08% and 2.4% of cancer mortality, respectively [10]. In

Africa, a study conducted in Egypt showed a HL prevalence of 1.7% and NHL prevalence of 5.4%, whereas prevalence of 1.2% and 2.4% were observed for HL and NHL in Kano, Northcentral region of Nigeria [11,12] when compared to other cancers. The lymphomas are associated with unsettling mortality figures in African cohorts, owing to the menace of human immunodeficiency virus (HIV) infection as well as poorly equipped health systems to deal with the challenge [13].

The ABO blood group is the most important and most immunogenic of the human blood group systems [14]. The antigens of this blood group system are defined by carbohydrate moieties expressed on the surface of a large number of normal cells and tissues, including erythrocyte membrane, endothelium, neurons, platelets and body fluids as well as some tumours [15, 16]. Due to the presence of carbohydrate moieties on the red blood cell membrane, four blood groups notably A, B, AB and O have been identified [17]. The ABO blood group system can be classified as the O and the non- O blood groups, the latter comprising blood groups A, B and AB. Furthermore, the A and AB blood groups have been further sub-classified. About 80% of persons with A antigen or B antigen in their blood are classified as A<sub>1</sub> or A<sub>1</sub>B, while the remaining 20% are either A<sub>2</sub> or A<sub>2</sub>B [18].

Right from the pioneer work in 1953 that demonstrated an association between stomach cancer and blood group A [19], there have been increasing evidence from recent literature of a plausible association or relationship of blood types to some disease conditions [20,21]. For instance, Chen et al [22], in their study found that blood group A significantly increases the risk of esophageal and gastric cancers. The probable explanation may be that tumor cells expressing "A – like antigens" in individuals with blood group A are not easily recognized by the host's immune cells

for rejection [23,24]. Another study also showed that blood group AB is associated with an increased risk of liver cancer [25]. However, the mechanism by which blood type AB contributes to the heightened risk of hepatic cancer is not very clear. Similar findings though with subtle differences in the distribution of ABO blood types among other solid tumours have been reported [26-28].

Similarly, several studies have demonstrated associations between haematological malignances and blood groups though these studies have been largely inconsistent [29 – 31]. A study that examines the risk and prognosis of multiple myeloma and lymphoma with respect to ABO blood types, found that patients with blood group O have an increased risk and poor prognosis for multiple myeloma while those with blood group A have a lower risk and better prognosis for lymphoma [30]. Also, in a study to assess the frequency and distribution of ABO blood groups among patients with lymphoma and acute leukaemia, the authors reported that there was an increased proportion of B blood group among HL patients and also more patients with blood group O with acute lymphoblastic leukaemia (ALL) when compared to other blood groups [31].

To the best of our knowledge, studies that have assessed the frequency and distribution of ABO blood groups among patients with lymphoma as well as the association between these malignancy and ABO blood groups in our environment are few and far between. In addition, if the risk of occurrence of different diseases and/or malignancies are established for different ABO blood groups, it could serve as a prospective epidemiological marker to identify at risk individuals in the population. Therefore, the objectives of this study were to determine the frequency and distribution of the ABO blood groups among patients diagnosed with lymphoma and to determine the association, if any, between the lymphoma and ABO blood groups as seen in our locality.

#### **MATERIALS AND METHODS**

## 2.1 Study Location

This study was conducted in the Department of Haematology, University of Uyo Teaching Hospital, Uyo, Nigeria. The hospital is a referral health facility that provides specialized healthcare services to residents of Uyo and its environs. The Department of Haematology attends to adult patients with various haematological conditions including haematological malignancies.

## 2.2 Study Population

This consisted of male and female adult patients diagnosed with lymphoma in the last ten years from January 2014 to December 2024. A total of 111 patients with lymphoma were reviewed during the study period.

## 2.3 Study Design

This was a retrospective descriptive cross-sectional study of all lymphomas seen in the Department over a ten-year period (Jan. 2014 – Dec. 2024). Information on the type of lymphoma, the age and sex of the subjects, and their ABO blood types were extracted from patients' case files and recorded in a proforma designed for the study.

#### 2.4 Inclusion and Exclusion Criteria

The case notes of patients who had confirmed diagnoses of lymphoma and with complete clinical and laboratory records were used in the study. Case notes with incomplete data or presumptive

diagnoses were excluded from the study. Also, records from pediatric patients were excluded from the study.

#### 2.5 Ethical Consideration

Ethical approval was obtained from the University of Uyo Teaching Hospital Institutional Health Research Ethics Committee before the commencement of the study.

## 2.6 Data Analysis

Data obtained were analyzed using STATA software for windows version 10.0. The results were recorded using simple descriptive statistics (frequencies and percentages) and presented in simple proportion tables.

### **Results**

A total of 111 adult patients with lymphoma were reviewed during the study period. The mean age of the subjects was  $41.7 \pm 14.7$  years. There were more male than female patients (58.6% and 41.4% respectively) Table 1.

NHL was commoner than HL (62.2%), and Diffuse Large B-Cell Lymphoma (DLBCL) was the most common NHL histologic subtype (43.5%) while Nodular Sclerosis (NS) was the most common histologic variant of HL seen (59.5%) Table 2.

The peak age incidence of the disorders was within the fourth to the fifth decades of life. HL was observed to be predominant in patients between the age bracket of 30-39 years with a few cases

recorded in other age groups. However, a good number of NHL cases were seen in all age groups

Table 3. Table 1: Age and Sex distribution of Subjects

Characteristics	Frequency	Percentage %
Sex		
Male	65	58.6
Female	46	41.4
Age group		
18-29	24	21.6
30-39	30	27.1
40-49	25	22.5
50-59	14	12.6
≥ 60	18	16.2

Age in years (mean  $\pm$  SD) 41.7  $\pm$  14.7 years



 $\begin{tabular}{ll} Table~2~Distribution~and~Histologic~Subtypes~of~Hodgkin~Lymphoma~and~Non-Hodgkin~Lymphoma \\ \end{tabular}$ 

Types	of	Histologic Subtypes	Frequency	Percentage (%)
lymphoma				
HL		Nodular Lymphocyte Predominant	11	26.2
		(NLPL)		
		Nodular Sclerosis (NS)	25	59.5
		Lymphocyte Rich (LR)	1	2.4
		Lymphocyte Depleted (LD)	3	7.1
		Mixed Cellularity (MC)	2	4.8
NHL		Diffuse large B-cell lymphoma	30	43.5
		(DLBCL)		
		Small Lymphocytic Lymphoma (SLL)	18	26.1
		Follicular Lymphoma (FL)	3	4.3
		Mantle Cell Lymphoma (MCL)	1	1.4
		Mucosa-Associated Lymphoid Tissue	3	4.3
		Lymphoma (MALTOMA)		
		Lymphoblastic Lymphoma (LL)	1	1.4
		Splenic Marginal Cell Lymphoma	2	2.9
		(SMCL)		
		Burkitt Lymphoma (BL)	8	11.6
		Adult T-Cell Lymphoma (ATCL)	rearc	1.4
		Angioimmunoblastic Lymphoma (AIL)	1	1.4
		Mycosis Fungoides (MF)	1	1.4

Table 3: Age Distribution of HL and NHL

AGE		HO	DGK	IN				_	NON-HODGKIN LYMPHOMA										
GROUP																			
	HISTO	)LO	GIC S	SUBT	YPES	1			H	ISTOLOGIC	SUB'	TYPES							
	NLPL	NS	LR	LD	MC	DLBCL	SLL	FL	MCL	MALTOMA	LL	SMCL	BL	ATCL	AIL	MF			
18 – 29	3	8	0	1	0	2	1	0	0	0	0	0	5	0	0	0			
30-39	5	12	0	2	1	5	2	0	0	0	0	0	3	0	0	0			
40 - 49	2	3	1	0	1	11	3	0	0	0	0	1	0	0	1	0			
50 – 59	1	1	0	0	0	5	7	2	0	1	1	0	0	1	0	1			
≥ 60	0	1	0	0	0	70	5	1	<b>e</b> 1 <b>e</b>		0		0	0	0	0			

Subjects with O RhD positive blood group were the majority (61.3%) while subjects with AB RhD positive (0.9%) and ARhD negative (0.9%) were the least common. Collectively, subjects with the O blood group were more than non-O blood group Table 4.

Table 4: Distribution of types of Lymphoma among the ABO and Rh(D)

Blood groups of Subjects

Blood group	Lymphoma	
	Hodgkin Lymphoma	Non-Hodgkin Lymphoma
O RhD positive	25	43
O RhD negative	1	2
A RhD positive	5	9
A RhD negative	0	1
B RhD positive	9	13
B RhD negative	2	0
AB RhD positive	0	aren Journal
AB Rh <mark>D n</mark> egative	0	0
O blood group	25	43
Non-O blood group	17	26

The histologic subtypes of HL and NHL were commoner among subjects with O blood group than the non-O blood group in the following order: O > B > A > AB Table 5. Table 6 shows the associations between the different histologic subtypes of HL and NHL and selected characteristics which include blood group, gender

and age. There were no statistically significant differences between the histologic subtypes and the selected variables P > 0.05.



Table 5: Blood Groups and the Histologic Subtypes of HL and NHL

Blood	HOD	YKI	N LY	MPH	OMA				NON	N-HODGKIN	LYN	<b>ИРНОМ</b>	A			
GROUP																
	HISTO	OLO	GIC	SUBT	TYPES				H	ISTOLOGIC	SUB	TYPES				
	NLPL	NS	LR	LD	MC	DLBCL	SLL	FL	MCL	MATOMA	LL	SMCL	BL	ATCL	AIL	MF
$O_{+}$	7	15	1	0	2	19	14	2	1	2	1	1	1	1	1	0
O-	0	1	0	0	0	1	1	0	0	0	0	0	0	0	0	0
$A^+$	1	3	0	1	0	4	3	0	0	0	0	0	2	0	0	0
A-	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0
$\mathbf{B}^{+}$	3	5	0	1	0	9	3	0	0	0	0	0	1	0	0	0
B-	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0
		IINR	D2506	165	Inte	rnational Jour	nal of No	vel Res	earch and	Development (www	vw.ijnr	d.org)	b531			

$AB^+$	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
AB-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Table 6: Association between Selected Characteristics and Histologic Subtypes of HL and NHL

FACTORS							HISTO	LOGIC	SUB	TYPES									
			HL									NI							
	NLP	NS	LR	LD	MC	STATISTICAL	DLBCL	SLL	FL	MCL	MALTOMA	LL	SMC	BL	ATCL	AIL	M	STATIST	ICAL
	L					TESTS ANI	)						L				F	TESTS	AND
						VALUES												VALUES	
Blood group								-											
ORh+	7	15	1	0	2	0.72	19	14	2	1	2	1	1	1	1	1	0	0.45	
Non ORh+	4	8	0	2	0		13	6	0	0	0	0	0	1	0	0	1		
ORh-	0	1	0	0	0		1	1	0	0	0	0	0	0	0	0	0		
Non ORh-	0	1	0	0	1		0	0	1	0	0	0	0	0	0	0	0		
			II	NRD2	50616	5 Interna	tional Iourna	l of Novel	Resear	rch and D	Development (w	ww iin	rd org)	1	1532				

Gender																		
Male	7	10	1	2	1	0.09	18	11	1	1	3	1	1	4	1	0	0	1.00
Female	4	15	0	1	1		12	7	2	0	0	0	0	4	0	1	1	
Age																		
18-29	3	8	0	1	0	0.78	2	1	0	0	0	0	0	5	0	0	0	0.45
30-39	5	12	0	2	1		5	2	0	0	0	0	0	3	0	0	0	
40-49	2	3	1	0	1		11	3	0	0	0	0	1	0	0	1	0	
50-59	1	1	0	0	0		5	7	2	0	1	1	0	0	1	0	1	
≥ 50	0	1	0	0	0		7	5	1	1	2	0	1	0	0	0	0	



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#### Discussion

Several studies have described the relationship between ABO blood group and cancer risk. A number of proximate mechanisms have been portrayed to relate to these associations, however, data generated from studies evaluating the aetiological role and prognostic relevance of ABO antigens in various haematological cancers including lymphomas have been largely inconsistent [3,21,22].

Non-Hodgkin lymphoma was commoner than Hodgkin lymphoma in this study. The higher prevalence of NHL observed in this study was comparable to those reported by many authors [1,11,12]. Studies from several parts of the world have reported similar findings with NHL being the most common haematological cancer and among the top ten cancers [1, 4]. Diffuse large B-Cell lymphoma formed the vast majority of the NHL cases encountered in our study. It constituted 43.5% of the cases. This finding is in keeping with those of other studies conducted in other parts of Africa [18, 19], South America [20], Asia [21] and Europe [22], but contrasts with a much earlier study in your centre which reported that small lymphocytic lymphoma was the commonest histologic subtype [1]. Small lymphocytic lymphoma was the second most common subtype in the present review, accounting for 26.1% of cases seen. This figure closely approximates with the general global prevalence [2, 20-22]. It is important to note that we encountered a good number of cases of Burkitt lymphoma. All the patients were within the age brackets of 18-29 years and 30-39 years. This is not on unusual occurrence given that Burkitt lymphoma is common in areas where malaria is endemic like ours [23]. The endemic form of the disease is found majorly in African children with some cases occurring in young adults [24].

Nodular sclerosis was the most dominant histologic subtype of the HL cases reported in our review. This finding is consistent with the general observation in most studies [20 - 22], but at variance with that of a study conducted in Maiduguri, North-East Nigeria, where nodular lymphocyte predominant was

catalogued as the most prevalent histologic variant [25]. Nodular lymphocyte predominant accounted for 26.2% of the HL cases seen in this study. This was closely followed by lymphocyte depleted (7.1%) mixed cellularity (4.8%) and lymphocyte rich (2.4%), these figures are comparable with rates reported in other studies [25-26]. While environmental factors have been identified for their deleterious role in lymphomagenesis, certain pathogens especially those of viral origin have been equally incriminated [27.28].

In this study, males were slightly more affected than females with a male to female ratio of 1.4:1. This finding agrees with findings from studies by some researchers in United kingdom and less developed nations in Central and South America, Africa and Asia [34,35]. The gender of an individual has been recognized as a major determinant of the risk for contracting lymphoma [36]. Hasenclever et al [37] in their study reported that male sex factor was an adverse prognostic index for advanced lymphoma.

Furthermore, majority of the cases of NHL were observed among patients in the fourth and fifth decades of life while the HL cases were more prevalent in late adolescence and early adulthood. These findings were in consonance with those of studies conducted in the country and other parts of Africa [38,39]. However, in western economies, the lymphomas particularly NHL affect the elderly usually in the seventh decade of life [40,41]. The differences observed in the age incidence in our clime and the developed nations could be attributed largely to our relatively younger population and shorter life expectancy among the populace owing to precarious socio-economic condition and environmental factors.

Most of the subjects were of the O blood group while the non-O blood group was less than 50%. Of the non-O blood group, the AB blood group was the least common. The observed pattern is in tandem with the ABO blood group distribution in our locality [42], except for the greater frequency of B blood group observed in the patients when compared to A blood group. Similar findings were reported by Abouzari et al [43] and Qin et al [14], in Asian subjects. The increased

proportion of O and B blood groups was also observed among the different histologic subtypes of HL and NHL, however these differences were not statistically significant. Our observation is consistent with the study by Ekanem et al [44] who reported that the blood group distribution in a cohort of 132 haematological cancer patients including 49 lymphoma patients was not statistically different from that of the general population. Moreover, our findings contrast with an earlier study by Ula et al [45] who observed a correlation between the incidence of lymphoma and blood group A. It also contrasts study by Tizro et al [46] who demonstrated that AB blood group was associated an increased risk of lymphoma. The obvious inconsistencies in the various studies including ours could generally be ascribed to environmental and ethnic differences in the study populations. Studies evaluating the involvement of ABO blood group in the development of various disease conditions in different populations have shown substantial variation in different geographic regions hence, reflecting the underlying genetic, ethnic and racial heterogeneity of human populations [46].

#### **CONCLUSION**

The age, sex and ABO blood group distribution among patients with lymphoma in our study are comparable to those reported by other authors with NHL being the commoner type of lymphoma and diffuse large B-Cell lymphoma and nodular sclerosis being the commonest histologic variants of NHL and HL, respectively, in our environment. Majority of the patients were of the O blood group, followed by B, A and AB blood groups. There was no association between the lymphoma and ABO blood groups of the patients. However, to better understand the role of ABO blood groups in lymphoma and the mechanisms of their associations, future large multicenter experimental studies are recommended.

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