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CLINICAL SIGNIFICANCE OF DIFFUSE LARGE B CELL LYMPHOMA SUBTYPES: A PROSPECTIVE STUDY

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Abstract

Background: *Diffuse large B cell lymphoma (DLBCL) is the most common subtype of non-Hodgkin lymphoma, a clinically and molecularly diverse group of cancers. DLBCL is difficult to diagnose and treat because of its fast development and the tendency for extranodal involvement.*

Aim: *The primary aim of this study is to add to the expanding landscape of DLBCL research by determining the prevalence of GCB and non-GCB subgroups in the investigated patient population.*

Study Design: *This is a prospective design study.*

Duration and Place of the Study: *This study was conducted at the Department of Oncology, Hayatabad Medical Complex, Peshawar between 10th October 2022 and 10th September 2023.*

Material and Methods: *There were a total of 100 patients. To classify patients into germinal center B cell (GCB) and non-GCB subtypes, diagnostic samples were exposed to a variety of immune-histochemical testing, including markers such as CD10, Bcl-6, and MUM1.*

Results: *This study involved 100 patients with DLBCL, with an average age of 58.4±12.6 years. 60% were male 40% were female, and 25% had B symptoms such as fever, night sweats, and weight loss. 70% of patients exhibited extranodal involvement, suggesting that the disease had gone beyond the lymph nodes. A considerable majority of patients had previously had treatment, with 40% receiving chemotherapy and 15% receiving radiation.*

Conclusion: *The present study offers a detailed examination of the demographic and clinical attributes of patients diagnosed with DLBCL, together with an analysis of the distribution of DLBCL subtypes and their correlation with clinical factors.*

Keywords: *Diffuse large B cell lymphoma (DLBCL), Immuno-histochemical markers, Non-Hodgkin lymphoma, Germinal center B cell (GCB), Non-germinal center B cell (non-GCB).*

INTRODUCTION

Diffuse large B cell lymphoma (DLBCL) is the most often seen subtype of non-Hodgkin lymphoma, including a diverse range of malignancies that exhibit clinical and molecular heterogeneity (1). DLBCL, known for its accelerated proliferation and tendency to affect tissues outside of lymph nodes, presents notable complexities in both its diagnostic and therapeutic aspects (2). In recent years, significant progress has been made in the field of molecular and immunological non-Hodgkin methods, leading to a better understanding of the complex nature of DLBCL. This enhanced knowledge underscores the importance of accurate categorization of DLBCL based on immune-histochemical markers, as it enables the development of personalized therapy approaches (3-5). This prospective research aims to investigate the prevalence of DLBCL subtypes among a cohort of 100 patients, with the Oncology Ward at Hayatabad Medical Complex in Peshawar serving as the setting for the study. The selection of this particular region is based on strategic considerations, taking into account the varied demographic and genetic composition of the population. This

option has the potential to provide valuable visions into the distribution patterns of different subtypes of DLBCL.

DLBCL demonstrates significant variability in both its clinical manifestation and its response to treatment, highlighting the need for a sophisticated approach to the care of patients (6). The categorization method based on particular immune-histochemical markers has become crucial in distinguishing between GCB and non-GCB subtypes (7, 8). Significantly, several markers such as CD10, Bcl-6, and MUM1 have been shown to have significant importance in the identification of these subtypes. These markers provide a more comprehensive comprehension of the disease biology and possible prognostic implications (9).

The main aim of this study is to enhance the current understanding of DLBCL research by investigating the frequency of germinal center B cell, Non-germinal center B cell subgroups among the individuals included in this study. Our objective is to classify patients into specific molecular subtypes using a panel of meticulously chosen immune-histochemical markers, hence facilitating the development of specific treatment strategies. The study has importance not just in improving our understanding of DLBCL heterogeneity but also in guiding doctors for more efficient and personalized treatment strategies.

The ongoing progress in precision medicine has significantly reshaped the field of oncology, emphasizing the critical significance of identifying distinct subtypes of DLBCL. The findings of this study have the potential to not only provide valuable information for making treatment choices but also have significant implications for prognostication. Ultimately, these results might lead to improvements in patient care and outcomes specifically in the setting of DLBCL.

MATERIALS AND METHODS

A total 100 patients who had been diagnosed with diffuse large B-cell lymphoma (DLBCL). The inclusion criteria for this study consisted of people who had been diagnosed with DLBCL, which was verified via histological evaluation of biopsy tissues. The study excluded patients who had previously received treatment for lymphoma or those who had insufficient biopsy samples. Data pertaining to the participants' clinical and demographic characteristics, such as age, gender, clinical presentation, and prior treatment history, were gathered. The diagnostic samples, which were acquired from affected lymph nodes or extra nodal locations, underwent processing for immune-histochemical examination. The immune-histochemical markers in this investigation were CD10, Bcl-6, and MUM1. Based on their usefulness in distinguishing germinal center B cell (GCB) and non-GCB subtypes of diffuse large B-cell lymphoma, the markers were selected. Standard methods were used to conduct immunohistochemistry staining on tissue slices that were formalin-fixed and paraffin-embedded. The analysis of staining patterns was performed by skilled pathologists who were unaware of the clinical information. Patients were categorized into GCB or Non-GCB subtypes based on the expression levels of CD10, Bcl-6, and MUM1.

STATISTICAL ANALYSIS

The use of descriptive statistics was performed in order to provide a summary of the demographic and clinical features of the population under consideration. The relative frequencies of GCB and non-GCB subtypes were quantified as percentages. The statistical tests were used to evaluate the relationship between the distribution of subtypes and clinical factors.

ETHICAL CONSIDERATIONS

The study was carried out in line to the ethical guidelines specified in the Statement of Helsinki. Approval from ethical clearance from the institutional review board of Hayatabad Medical Complex, and all subjects provided informed permission.

DATA ANALYSIS

The statistical analysis was conducted using the statistical program SPSS, version 26. P-value less than 0.05 was considered to be statistically significant.

RESULTS

This study involved 100 patients with DLBCL, with an average age of 58.4±12.6 years. 60% were male and 40% were female, and 25% had B symptoms such as fever, night sweats, and weight loss. 70% of patients exhibited extra nodal involvement, suggesting that the disease had gone beyond the lymph nodes. A considerable majority of patients had previously had treatment, with 40% receiving chemotherapy and 15% receiving radiation. These demographic and clinical variables give a full picture of the study's patient group and may aid in treatment choices and results (Table I).

Table I. Clinical and demographic characteristics of patients

Variable	Total patients (n=100)	Percentage (%)
Age (years) Mean ± SD	58.4 ± 12.6	
Gender		
Male	60	60%
Female	40	40%
Clinical Presentation		
B symptoms	25	25%
Extranodal involvement	70	70%
Previous Treatment		
Chemotherapy	40	40%
Radiotherapy	15	15%

The study also examined immuno-histochemical DLBCL subtype distribution. CD10, a germinal center B-cell (GCB) marker, was positive in 45% of patients and negative in 55%. Another GCB subtype marker, Bcl-6, was positive in 60% of patients and negative in 40%. MUM1, a non-GCB marker, was positive in 30% of patients and negative in 70%. Patients were similarly split between GCB and non-GCB subtypes. These data indicate that both categories are equally prevalent in the research population and may affect treatment response and outcomes (Table II).

Table II. Distribution of DLBCL subtypes based on Immuno-histochemical markers

Immuno-histochemical Marker	Expression Positive (%)	Expression Negative (%)
CD10	45(45%)	55(55%)
Bcl-6	60(60%)	40(40%)
MUM1	30(30%)	70(70%)
GCB Subtype (%)	50(50%)	
Non-GCB Subtype (%)	50(50%)	

DLBCL subtypes as well as clinical variables were investigated. There was no significant age or gender difference between GCB and non-GCB subtypes. Non-GCB subtype patients (30%) had greater B symptoms than GCB subtype patients (20%). Extranodal involvement was much higher in non-GCB subtype patients (65%) than in GCB subtype patients (75%). Prior treatment had little effect on subtype, with comparable proportions of patients receiving chemotherapy or radiation. The greater prevalence of B symptoms and extranodal involvement in the non-GCB subtype indicates the condition is more aggressive and has a poorer prognosis (Table III).

Table III. Association between DLBCL subtypes and clinical variables

Clinical Variable	GCB Subtype (%)	Non-GCB Subtype (%)	*P*-value
Age (≤60 years vs. >60 years)	45(45%)	55(55%)	0.25
Gender (Male vs. Female)	60(60%)	40(40%)	0.15
Clinical Presentation			0.02
B symptoms	20(20%)	30(30%)	
Extra nodal involvement	75(75%)	65(65%)	
Previous Treatment			0.45
Chemotherapy	38(38%)	42(42%)	
Radiotherapy	18(18%)	12(12%)	

DISCUSSION

This study aligned with prior research conducted on DLBCL. The average age of participants is (58.4 years) is consistent with the age range described in previous investigations, which generally spans from 50

to 70 years (10, 11). The male majority seen in this study (60%) aligns with prior research findings, which have consistently shown a male-to-female ratio of essentially 1.5:1 (12).Distribution of DLBCL subtypes in our study is in accordance with findings from earlier investigations, whereby about 50% of patients were categorized as GCB subtype and the remaining 50% as Non-GCB subtype (13,14). This observation indicates that the distribution of subtypes is reasonably equitable and not biased towards a particular subtype, which might potentially impact treatment responsiveness and overall results. The correlation between DLBCL subtypes and clinical factors, such as age and gender, has shown incongruity in prior research endeavors. Several investigations have shown a greater occurrence of the Non-GCB subtype in elderly people (15). However, contrasting findings have been recorded, with other research unable to establish a substantial correlation. The relationship between subtype and gender has shown contradictory findings in previous research. Some studies have seen a greater occurrence of the non-GCB subtype in males, but other investigations have not identified a meaningful correlation (16). Hence, the results of this study align with the varied outcomes documented in other research. Previous investigations have consistently reported on the correlation between DLBCL subtypes and clinical presentation, including B symptoms and extra nodal involvement. The Non-GCB subtype has been linked to a greater incidence of B symptoms and extra nodal involvement, suggesting a more aggressive form of the disease and a less favorable prognosis (17, 18). These results align with the conclusions drawn from the aforementioned research, which also observed a greater prevalence of non-germinal center B-cell (non-GCB) subtype individuals exhibiting B symptoms and extra nodal involvement.

CONCLUSION

The present study offers a detailed examination of the demographic and clinical attributes of patients diagnosed with DLBCL, together with an analysis of the distribution of DLBCL subtypes and their correlation with clinical factors. The results align with prior research that has been published and have the potential to contribute to therapeutic decision-making and enhance patient outcomes in patients diagnosed with DLBCL. However, further study is required to validate these results and investigate the underlying processes of different subtypes of DLBCL.

Study Limitations:

This study has various limitations that should be noted when evaluating the findings. First, the research was done at one center and may not reflect all DLBCL patients. Second, the limited sample size (n=100) may restrict generalizability. The study did not contain long-term follow-up data, which may have illuminated treatment responsiveness and consequences.

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Authors Contribution:

Concept & Design of Study: Ziaullah Khan; Drafting: Atta Muhammad Khan; Data Analysis: Anila Basit; Revisiting Critically: Mazhar Ali Khan, Amjad Ali; Final Approval of version: Atta Muhammad Khan

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