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Prevalence of diffuse large B cell lymphoma subgroups by immune-histochemical markers

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Abstract

Background: One of the non-Hodgkin's lymphomas (NHL) with the highest incidence rate and making up the vast majority of aggressive lymphoid neoplasms is diffuse large B cell lymphoma. The most prevalent form of NHL in Pakistan is DLBCL

Objective: To determine the prevalence of diffuse large b cell lymphoma subgroups by immune-histochemical markers.

Methodology: This cross sectional study was carried out at the department of histopathology Fatima memorial hospital, Lahore. The duration was from January 2024 to June 2024. DLBCL was diagnosed using a panel of lymphoid antibodies that comprised CD20, CD79a, CD3, Ki-67, and Pax5 . On silane-coated slides, slices were mounted for immunohistochemical staining. In order to analyze the data, IBM SPSS version 24 was used.

Results: In the current study, a total of 80 patients were enrolled. The male patients were 45 (56.25%) and female were 35 (43.75%). The mean age (SD) in our study was 42 (4.43) years. Out of 80 cases, 37 (46.25%) cases were observed as germinal center while 43 (53.75%) cases were observed as were non-germinal center like subgroup. In our study, 45 (56.25%) cases observed as extranodal while 35(43.75%) cases were observed as nodal lymphoma.

Conclusion: Our study concludes that the prevalence of non germinal sub- group of diffuse large B-cell lymphoma is higher than the germinal centre like sub- group.

Key words: Subgroups; Diffuse large B cell lymphoma; Immune-histochemical markers

Introduction

Hodgkin's (HL) and Non-Hodgkin's lymphomas (NHL) are the two types of lymphoid neoplasms according to the world health organization. NHL may also be divided into "mature B, mature T, and mature NK cell neoplasms" (1). B-cell NHL is more prevalent than T-cell NHL, making up 80–85% of all instances of NHL, with T-cell NHL making up the rest of the 10% (2). In adults, diffuse large B-cell lymphoma (DLBCL) accounts for 30–50% of all NHL and is the most prevalent lymphoid neoplasm (3). A lymphoid malignancy with a diffuse or nodular development pattern, DLBCL is characterized by medium- to large-sized B lymphoid cells. The tumor cell size is determined by comparing it to the typical macrophage nucleus or the size of a normal lymphocyte, which should be greater. Site and molecular subtype determine clinical signs and symptoms, behavior, and prognosis in DLBCL (4). By using gene expression profiling (GEP), DLBCL may be divided into two unique molecular forms. One is germinal center B-cell (GCB) and the other is activated B-cell (ABC). Both have varying predictions and treatment outcomes. To predict the molecular forms, immunohistochemistry (IHC) methods have been proposed. Hans' method, which primarily relies on three immunohistochemical stains—CD10 (which emphasizes the GCB subtype), Bcl6 (which links to both the GCB and the ABC subtype), and MUM1 (which highlights the ABC subtype)—is used routinely. Three immunohistochemical stains (for GCB, ABC subtype, and CD20) allow the Hans algorithm to classify DLBCL, NOS cases into two categories (5-7). The ABC subtype of DLBCL reacts more effectively to recently suggested therapeutic drugs such as "bortezomib, lenalidomide, or ibrutinib", whereas the GCB type is more chemosensitive and has superior median survival rates (5-7). According to the many research done, ABC is more common than GCB. For ABC Lu TX et al. found an incidence of 61.3% in China (5). U Hassan et al. (8) and U Bukhari et al. (9), who both recorded prevalence rates of 56% in Pakistan, found a slightly comparable prevalence. A

recently published research (10) found that the 5-year overall survival rate for 49% germinal center lymphoma was 70.2% while the 5-year overall survival rate for 51% non-germinal center lymphoma was 18.4%. P was less than 0.001. The current study was doneto assess the occurrence of diffuse large b cell lymphoma subgroups by immune-histochemical markers.

Materials and methods

This cross sectional study was carried out at the department of histopathology Fatima memorial hospital, Lahore. The duration was from January 2024 to June 2024. The study approval was properly taken from the ethical and research committee of the hospital. The sample size of our study was 80 patients based on WHO sample size calculator. The inclusion criteria of our study was all the patients of both the gender having age 18-80 years, assessment of all nodal and extra nodal disease and patients of all incisional, core and excisional biopsies while the criteria for exclusion were all the patients with HIV positivity and patients DLBCL as secondary disease. Sections were obtained after grossing all specimens. Following that, hematoxylin and eosin was used to evaluate the morphology of the tissue sections that had been formalin-fixed and paraffin-embedded. On silane-coated slides, slices were mounted for immunohistochemical staining. For quality assurance, appropriate positive controls were used on the same slides. All large biopsy patients received negative controls in accordance with appropriate antigen retrieval. DLBCL was diagnosed using a “panel of lymphoid antibodies that comprised CD20, CD79a, CD3, Ki-67, and Pax5". Then, three antibodies were employed for the subgroups of DLBCL, including the "monoclonal antibodies CD 10 (Clone 56C6 Cell Marque), BCL-6 (Clone BL6-02 Neo Mark), and IRF-4 (MUMIp) (Clone MUMIp Santacruz)". Patients that are negative for CD10, positive for Bcl-6 and negative for MUM1 are considered to be members of the germinal center-like subgroup by employing the Hans algorithm. Instances with CD10 expression by more than 30%

of cells are also considered to be members of this subgroup. All the additional instances are classified as belonging to the non-germinal centre subgroup. In order to analyze the data, IBM SPSS version 23 was used. Mean and standard deviation were determined for continuous variables like age, whereas percentages and frequencies were calculated for categorical parameters like sex and subgroups. To examine the influence of effect modifiers, the data were stratified by age and sex.

Results

In the current study, a total of 80 patients were enrolled. The male patients were 45 (56.25%) and female were 35 (43.75%). (Figure 1) The mean age (SD) in our study was 42 (4.43) years with maximum age of 78 and minimum age of 18 years. Out of 80 cases, 37 (46.25%) cases were observed as germinal center while 43 (53.75%) cases were observed as were non-germinal center like subgroup (Figure 2). On the basis of gender stratification, the germinal center subgroup was observed in 21(56.76%) male participants while it was observed in 16(43.24%) female participants. In case of non germinal center subgroup, males were 22 (51.16%) while females were 21 (48.84%). On the basis of age stratification, germinal center subgroup was observed in 20 (54.05%) cases having age <50 years while 17 (45.95%) cases were observed with age >50 years. In case of non germinal center subgroup, 23 (53.49%) patients were observed with age <50 years whereas 20 (46.51%) patients were observed with age <50 years. (Table 1) In 33 (89.19%) cases of germinal center like subgroup, CD-10 was observed as positive. In germinal center like subgroup, Bcl-6 was observed positive in 35 (94.59%) cases while in case of non germinal subgroup it was observed as positive in 34 (79.07%) cases. MUM-1 was observed positive in 19 (51.35%) cases of germinal and 41 (95.35%) cases of non germinal center subgroups. In our study, 45 (56.25%) cases observed as extranodal while nodal lymphoma was

observed in 35(43.75%) cases. Non germinal center subgroup was predominant both in nodal (n=21, 60%) and "extranodal lymphoma" (n=25, 55.56%). (Figure 3)

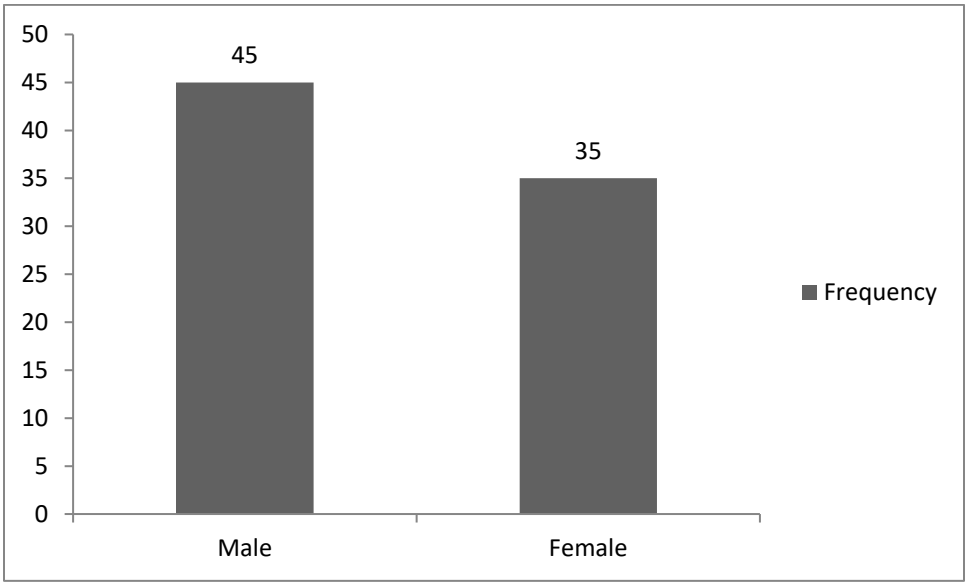

Figure 1: Distribution of patients based on gender

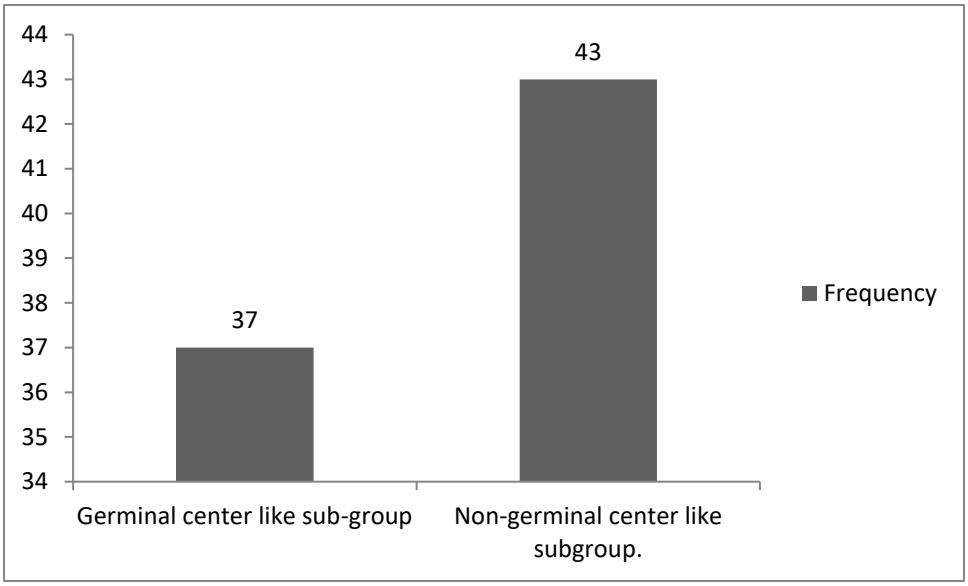

Figure 2: Frequency of germinal center and non-germinal subgroup

Table 1: Stratification of gender and age with respect to germinal and non germinal subgroup

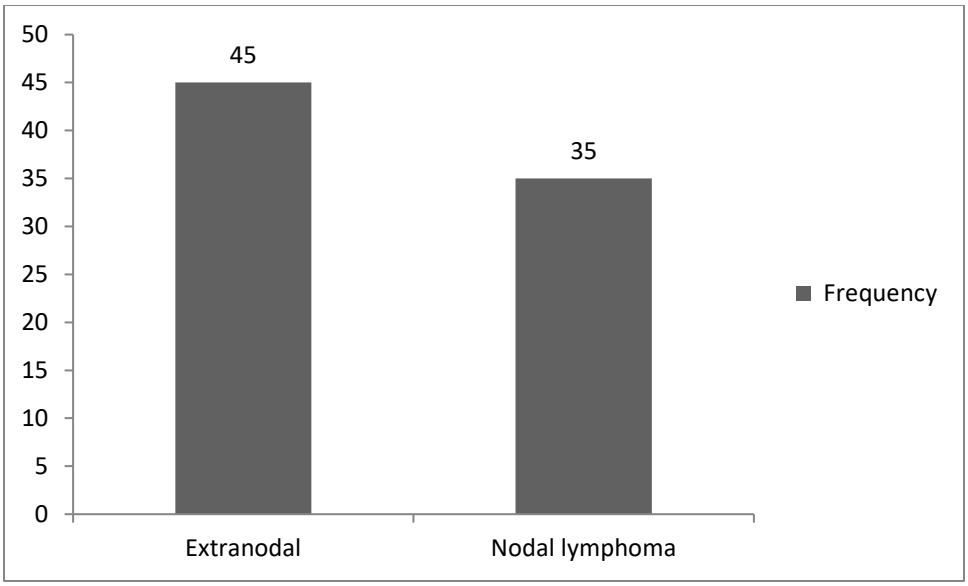

Figure 3: Frequency of Extranodal and Nodal lymphoma

Discussion

One of the non-Hodgkin's lymphomas (NHL) with the highest incidence rate and making up the vast majority of aggressive lymphoid neoplasms is diffuse large B cell lymphoma (11). The most prevalent form of NHL in Pakistan is DLBCL (12, 13). Although the exact cause of DLBCL's "emerging epidemic" status is still unknown, at least a few key factors and how they interact are believed to be responsible (14). In the current study, a total of 80 patients were enrolled. The male patients were 45 (56.25%) and female were 35 (43.75%). These findings are consistent with a local research (12) that found that diffuse large B cell lymphoma is more common in men than women. The mean age (SD) in our study was 42 (4.43) years with maximum age of 78 and minimum age of 18 years. Out of 80 cases, 37 (46.25%) cases were observed as germinal center while 43 (53.75%) cases were observed as were non-germinal center like subgroup. Our results are consistent with a local investigation that found 42 instances of DLBCL in 34 (55%) non-GCB subgroups and 27 (45%) GCB subgroups (12). Our findings are close to those of a research from Spain (15), which reported 53% non-GCB subgroups in comparison to 47% GCB

subgroups. The findings of other Asian investigations (16-19) were likewise comparable. Contrary to this, the prevalence of the germinal center-like subgroup was 52% and 58%, accordingly, in Western nations like Sweden (20) and the USA (21). The prevalence of the GCB subtype was often somewhat greater than that of the non-GCB subtype in western research. It is unknown why GCB frequency varies from non-GCB frequency. In our study, 45 (56.25%) cases observed as extranodal while 35(43.75%) cases were observed as nodal lymphoma. Non germinal center subgroup was predominant both in nodal (n=21, 60%) and extranodal lymphoma (n=25, 55.56%). Our results are consistent with previous research from Pakistan (12, 14) and Korea (22), which likewise found that extranodal DLBCL predominated. Our results, yet, are in conflict with investigations from the USA (23)and Europe (24-26) which showed lower frequencies of extranodal lymphoma. Correct recognition of extranodal lymphoma as a potential condition should result in an early diagnosis. Physicians who are neither hematologists nor oncologists should be aware of this fact. On the basis of gender stratification, the germinal center subgroup was observed in 21(56.76%) male participants while it was observed in 16(43.24%) female participants. In case of non germinal center subgroup, males were 22 (51.16%) while females were 21 (48.84%). On the basis of age stratification, germinal center subgroup was observed in 20 (54.05%) cases having age <50 years while 17 (45.95%) cases were observed with age >50 years. In case of non germinal center subgroup, 23 (53.49%) patients were observed with age <50 years whereas 20 (46.51%) patients were observed with age <50 years. (Table 1) In 33 (89.19%) cases of germinal center like subgroup, CD-10 (>30%) was observed as positive. In cases of germinal center like subgroup, Bcl-6 was observed as positive in 35 (94.59%) cases while in case of non germinal center subgroup it was observed as positive in 34 (79.07%) cases. MUM-1 was observed positive in 19 (51.35%) cases of germinal and 41

(95.35%) cases of non germinal center subgroups.These findings differ considerably with a local research by Naz et al. (12), who found that men had a greater frequency of the non-germinal center subgroup (74%) while females had a little higher frequency of the germinal center subgroup (53%) in that study. Their low sample size of 42 cases may be the cause of this difference. Our findings concur with those of a Malaysian research (17). By comparing our findings to those of a local study (12) , we discovered that there was a larger frequency of the germinal center like subgroup in patients who were younger than 60 years old, while the non germinal center like subgroup was more often seen in patients who were either equal to or older than 60 years old. This discrepancy in age group may be the result of a lower sample size (42 instances). According to a Spanish research (15), the age range for germinal center-like subgroup lymphomas is 22–93 years, whereas the age range for non-germinal center lymphomas is 24-85 years.

Conclusion

Our study concludes that the frequency of non germinal centre like sub- group of diffuse large B cell lymphoma is higher than the germinal centre like sub- group. Additional population-based investigations that can identify any etiological factors relating to sub-grouping of diffuse large B cell lymphoma are required in order to confirm our findings and provide further evidence for our conclusions.

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