Unveiling the Hidden Burden: A 5-Year Retrospective Analysis of Double-Hit Lymphoma in Lebanese Patients

M. HACHEM[1], Z. ZALAQUETT[1], C. KESEROUANI[2], A. CHEBLY[3], V. NAJJAR[2,4,5], R EL FERKH[6,7], A. SAROUFIM[1], J. WAKIM[1], C. HANNA[1], F. EL KARAK[1], M. GHOSN[1], J. KATTAN[1], F. NASR[1], G. CHAHINE[1], H. KOURIE[1]
[1] Hematology-Oncology Department, Faculty of Medicine, Saint Joseph University of Beirut, Beirut, Lebanon. [2] Pathology Department, Hôtel-Dieu de France University Hospital, Saint Joseph University of Beirut, Beirut, Lebanon. [3] Center Jacques Loiselet for Medical Genetics and Genomics, Faculty of Medicine, Saint Joseph University, Beirut, Lebanon. [4] Pathology Department, LAU Medical Center-Rizk Hospital, Beirut, Lebanon. [5] Pathology and Laboratory Medicine, Clemenceau Medical Center, Beirut, Lebanon. [6] Hematology-Oncology Department, Lebanese University Hospital Geitaoui, Beirut, Lebanon. [7] Saint-Joseph University of Beirut, Beirut, Lebanon.

INTRODUCTION

Double-hit lymphoma (DHL) is a highly aggressive hematological malignancy characterized by genetic abnormalities involving the *MYC* oncogene and either the *BCL2* or *BCL6* genes. Despite the current standard of chemoimmunotherapy, DHL has a poor clinical prognosis with a high risk of relapse and short overall survival. More input on DHL is therefore needed to further characterize this malignancy and improve patient management and outcome.

OBJECTIVE

This study aimed to determine the prevalence of DHL among Lebanese patients diagnosed with Diffuse Large B-Cell Lymphoma (DLBCL) and explore their epidemiological and demographic characteristics, which is so far scarcely described in the medical literature.

METHODS

We conducted a retrospective analysis of 116 patients diagnosed with DLBCL, who were evaluated by fluorescence *in situ* hybridization (FISH) for *MYC*, *BCL2*, and *BCL6* rearrangements between January 2018 and December 2022, at the Center Jacques Loiselet for Medical Genetics and Genomics, a tertiary referral center in Beirut, Lebanon.

DIAGNOSTIC APPROACH

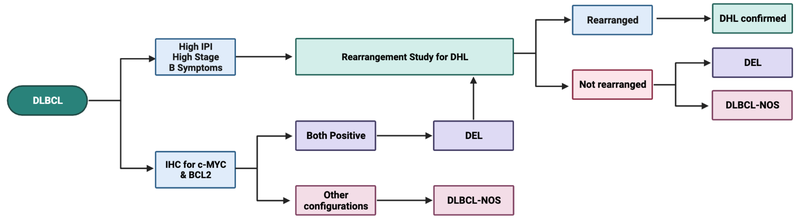


Figure 1. Differential Diagnostic Approach for DHL, DEL, and DLBCL-NOS
This flowchart outlines a diagnostic pathway to identify Double-Expressor DLBCL (DEL), a subtype characterized by co-expression of c-MYC and BCL-2 through immunohistochemical (IHC) analysis. DEL exhibits a less favorable prognosis compared to the non-double expressor DLBCL phenotype. Nevertheless, its prognostic outlook is better than that of double-hit and triple-hit B-cell lymphomas. This flowchart gives a systematic approach to differentiate among these DLBCL subtypes, for a better prognostic assessment and therapeutic stratifications. Taken from Mehta et al, Indian J Hematol Blood Transfus 36, 627–634 (2020)

RESULTS

Out of 116 patients, 9 patients (7.75%) were found to have DHL. Among the DHL cases, 5 patients (55.6%) had rearrangements in the *BCL6* and *MYC* genes, while 4 patients (44.4%) had rearrangements in the *BCL2* and *MYC* genes. The median age of the DHL patients was 58 years, ranging from 44 to 69 years. The sex ratio of DHL patients was 1.25 (male to female). Notably, 1 patient (0.86%) was found to have triple-hit lymphoma with rearrangements in the *BCL2*, *BCL6* and *MYC* genes. In addition, 17 patients (14.6%) had isolated rearrangements involving the *BCL6* gene, 9 patients (7.75%) had isolated rearrangements involving the *BCL2* gene, and 5 patients (4.3%) had rearrangements involving the *MYC* gene solely. Moreover, a single case presented rearrangements in both *BCL2* and *BCL6* genes; however, due to the absence of *MYC* rearrangement, it did not meet the criteria for DHL classification.

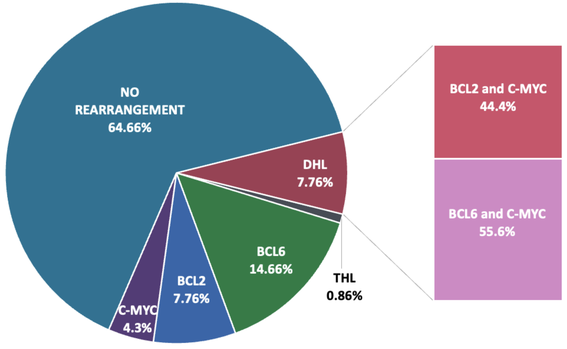


Figure 2. Prevalence Breakdown of Genetic Rearrangements in Lebanese DLBCL Patients
This pie chart displays the prevalence of different genetic rearrangements: Double-Hit Lymphoma (DHL) cases at 7.75% (9 patients), isolated BCL6 rearrangements at 14.66% (17 patients), isolated BCL2 rearrangements at 7.75% (9 patients), isolated MYC rearrangements at 4.31% (5 patients), Triple-Hit Lymphoma (THL) cases at 0.86% (1 patient), and cases without detected rearrangements (64.66%). The chart underscores the impact of DHL, a highly aggressive malignancy resulting from rearrangements involving MYC and either BCL2 or BCL6 genes, within the patient cohort.

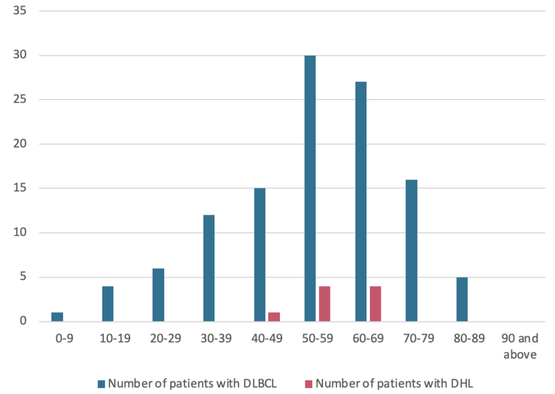


Figure 3. Age Distribution of DLBCL Patients and Double-Hit Lymphoma (DHL) Patients
This bar chart represents the age distribution of Diffuse Large B-Cell Lymphoma (DLBCL) patients. The blue bar represents all DLBCL patients, while the second bar in pink overlays Double-Hit Lymphoma (DHL) cases within the same distribution.

CONCLUSION

This study on Lebanese patients with DLBCL reveals a DHL prevalence of 7.75%, consistent with existing literature. The median age of 58 years and male predominance align with known patterns. Improved treatment strategies and targeted therapies are urgently needed to address DHL's aggressive nature and poor prognosis.

ACKNOWLEDGEMENTS

This research was made possible through the essential support of the Hematology-Oncology Department and the Center Jacques Loiselet for Medical Genetics and Genomics at Saint Joseph University of Beirut.

Created with BioRender Poster Builder