SOHO ANNUAL MEETING 2024

MOLECULAR PROFILING OF HIGH-GRADE B-CELL LYMPHOMAS IN PAKISTAN

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INTRODUCTION

- In the current World Health Organization (WHO) classification, the designation high-grade B-cell lymphoma (HGBL) is applied to a specific group of neoplasms.
- Most cases fit within the subgroups of *MYC/BCL2* double-hit lymphoma (DHL), *MYC/BCL6* DHL, and *MYC/BCL2/BCL6* triple-hit lymphoma (THL).
- Cytogenetically defined DHL/THL can show variable morphologies including diffuse large B-cell lymphoma (DLBCL), B-cell lymphoma-unclassified (BCL-U) or with blastoid features.
- Patients with DHL and THL often have advanced-stage disease and a poor prognosis.
- As a distinct clinical phenotype or pathologic morphology cannot be identified to accurately predict for underlying HGBL-DH/TH, the molecular features of the underlying lymphoma are a more objective means to screen for HGBL-DH/TH.

AIM

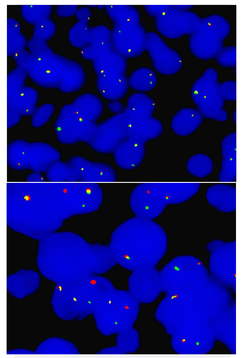
- **The aim of this study is to determine the frequency of high-grade B-cell lymphomas with double-hit (DH) and triple-hit (TH) genetic rearrangements in Pakistan and to evaluate the discrepancies between immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH) in detecting these lymphomas.**
- **This study emphasizes the importance of molecular diagnostics for accurate detection and improved prognostication of patients with high-grade B-cell lymphomas.**

METHOD

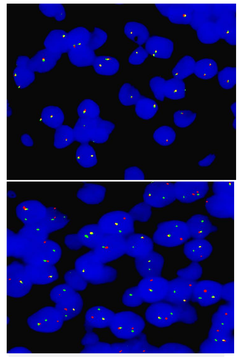
- The study was conducted at the Department of Pathology & Laboratory Medicine, Aga Khan University Hospital, Pakistan.
- All cases of biopsy-proven HGBL were included.
- Fluorescence *in situ* hybridization (FISH) was performed in all cases for *MYC, BCL2,* and *BCL6*.
- Appropriate statistics were applied using SPSS software to analyze the data.

RESULTS

- A total of 76 patients including 31 females and 45 males were diagnosed as HGBL during the study period.
- Forty-five (59%) and 23 (30%) were interpreted as triple- and double-expressors, respectively, on immunohistochemistry (IHC).
- No hit was identified in 4 (5%) patients, whereas isolated *MYC, BCL2,* and *BCL6* were detected in 4 (5%).
- FISH identified triple-hit in 1 (1.3%) and double-hit in 4 (5%) patients only.



Fluorescence in situ hybridization showing a negative (upper) and a positive (lower) *MYC* signal, indicated by distinct red signals in the nuclei of the cells, consistent with *MYC* gene rearrangement.



Fluorescence in situ hybridization showing a negative (upper) and a positive (lower) *BCL6* signal, indicated by distinct red signals in the nuclei of the cells, consistent with *BCL6* gene rearrangement.

Category	Total (n = 76)	Percentage (%)
Gender:		
- Female	31	40.8
- Male	45	59.2
IHC Findings:		
- Triple-expressors	45	59.2
- Double-expressors	23	30.3
- No hit identified	4	5.3
-Isolated *MYC, BCL2,* and *BCL6* detected	4	5.3
FISH Findings:		
- Triple-hit	1	1.3
- Double-hit	4	55.3

CONCLUSIONS

- Frequency of THT and DHT and hence FISH-based prognosis in Pakistan is comparable to previously reported literature.

- The discrepancy between IHC and FISH results underscores the need for molecular diagnostics, as reliance on immunohistochemistry alone is insufficient.

- Integrating molecular diagnostics is essential for accurate detection and improved prognostication of HGBL patients.

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ACKNOWLEDGEMENTS

We are thankful to laboratory staff who helped us in retrieval of the data.

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