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EPIDEMIOLOGICAL AND CLINICAL PROFILE OF DOUBLE -HIT LYMPHOMA AT K R HOSPITAL MYSORE

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ABSTRACT

Background: Double-Hit Lymphoma (DHL) is a rare but highly aggressive subtype of B-cell non-Hodgkin lymphoma, defined by specific genetic abnormalities that distinguish it from other lymphomas. Objectives: The main objective if the study is to collect comprehensive clinical and demographic data from patients diagnosed with Double-Hit Lymphoma (DHL).

Materials and Methods: This observational study was conducted at Department of Medicine, Mysore Medical College & Research Institute during March 2023 March 2024. A total of 25 cases of Non-Hodgkin's Lymphoma (NHL) presenting to K R Hospital were included in the study. The clinical and demographic data of these patients were reviewed. Routine blood investigations, imaging studies including CT or MRI scans, PET scans, and biopsy results were collected.

Results: Males constitute 60% of the patients (15 individuals), while females make up the remaining 40% (10 individuals). Regarding clinical features, the majority of patients, 80% (20 individuals), exhibited lymphadenopathy, with the remaining 20% (5 individuals) presenting other symptoms. The peripheral smear results indicate that 72% of patients (18 individuals) had leukocytosis, while 28% (7 individuals) showed other findings. Partial responses were noted in 6 patients, equally divided between males and females. A total of 4 patients showed no response or progression, with an equal split between genders.

Conclusion: The present study demonstrates a male-to-female preponderance of 1.5:1 among the 25 patients diagnosed with Double-Hit Lymphoma. The majority of these patients presented with lymphadenopathy, and peripheral smear analysis revealed leukocytosis in most cases, indicating advanced disease.

Keywords: Double -Hit Lymphoma, Malignancy.

INTRODUCTION

Double-Hit Lymphoma (DHL) is a rare but highly aggressive subtype of B-cell non-Hodgkin lymphoma, defined by specific genetic abnormalities that distinguish it from other lymphomas. Such genetic changes as chromosomal translocations that affect the MYC in combination with BCL2 or BCL6 genes. These translocations contribute to the high proliferation rate of the tumour and result in unfavourable prognosis than other types of lymphoma.[1] The nature of DHL is quite different from other diseases and cancer types in terms of its biology and clinical presentation, which translates into specific management approaches and the fact that the diagnosis may be complicated for practitioners.[2] Double-Hit Lymphoma is observed in 5-10 % of the cases of Diffuse large B-cell lymphoma(DLBCL), which is the most frequent subtype of Non-Hodgkin Lymphoma(NHL). For most cases, DHL impacts the elderly people; however, the disease has been diagnosed among young people under 20 years old, although this is rare.[3] The condition has a predilection for the male gender with the male gender have a higher incidence rate compared to

female gender. While DHL can present itself quite randomly, there are some inherited diseases that may cause it and DHL is more frequent in patients with caused immunological diseases or in those who are taking immunosuppressive medication.[4] DHL takes place globally, however the frequency may differ from country to country. According to research, DHL is more prevalent in the people of the western countries and more specifically in the America and Europe. Nevertheless, it is less often described in Asia and other regions.[5] Possible factors that may lead to variation in incidence include; variations in access to healthcare, variations in access to diagnostic tools, and variations in genetic make-up. Double-Hit Lymphoma has signs and symptoms which are like those of other high-grade lymphomas, but the progression is usually faster.[6] Signs and symptoms are often non- specific including; enlarged painless lymph nodes, fever, night sweats, weight loss, and fatigue. These are known as "B symptoms" and they are linked with more progress disease.DHL patients may also present with structures involved externally lymph nodes that is, extra nodal involvement includes the occurrence of lymphoma in some organs of the body including the bone, liver, spleen or central nervous system.[7] Availability of extent of disease is even more challenging in DHL compared to other types of lymphomas partly due to its frequent extranodal spreading. The MYC gene that is overexpressed promotes the proliferation of cells while the action of BCL2 or BCL6 advances, inhibits the process of apoptosis which results in uncontrolled growth of cells forming tumors.[8] Thus, the disease becomes severe and symptoms if any may become aggravated at a very fast pace. Large tumour load is a characteristic of patients diagnosed with DHL, that is, the patients have extensive disease which results to larger tumours and these can be complicated depending on the affected organs.[9] The disease may also be diagnosed when the disease is at an advanced stage whereby the disease has spread to other organs of the body. This creates a lot of issues in terms of staging as well as in deciding on proper therapy interventions.[10] To diagnose Double-Hit Lymphoma, there is a need to perform a clinical examination, imaging studies, and molecular studies. Diagnostic procedures are biopsy of the enlarged lymph nodes and/or other affected extranodal tissues which are then examined by histopathology to appreciate the characteristic morphology of the cell.[11]

Aims

- To study the clinical characteristics and presentation of patients diagnosed with Double-Hit Lymphoma (DHL).
- To investigate common symptoms, patterns of disease progression, and patient responses to various treatment modalities.

Objectives

- Collect comprehensive clinical and demographic data from patients diagnosed with Double-Hit Lymphoma (DHL).

Compare the clinical outcomes of DHL patients based on different therapeutic approaches to evaluate their effectiveness.

MATERIAL AND METHODS

This observational study was conducted at Department of Medicine, Mysore Medical College & Research Institute during March 2023 March 2024.

Inclusion Criteria

- Confirmed cases of Double-Hit Lymphoma (DHL).
- Patients aged > 18 years.
- Treated with R-CHOP and RICE chemotherapy regimens.
- Availability of genetic and molecular test results confirming *MYC* and *BCL2/BCL6* rearrangements via fluorescence in situ hybridization (FISH) or polymerase chain reaction (PCR).

Exclusion Criteria

- Incomplete diagnosis or lack of confirmed DHL.
- Concurrent malignancies or history of treatment for other malignancies.
- Pregnancy or lactation.
- Presence of severe comorbidities, including immunocompromised states.
- Non-compliance with treatment protocols.

Study Population and Data Collection

A total of 25 cases of Non-Hodgkin's Lymphoma (NHL) presenting to K R Hospital were included in the study. The clinical and demographic data of these patients were reviewed. Routine blood investigations, imaging studies including CT or MRI scans, PET scans, and biopsy results were collected. Histopathological examination and genetic testing using FISH or PCR were conducted to identify the presence of *MYC* and *BCL2/BCL6* gene rearrangements, confirming the diagnosis of DHL.

Data Analysis

The clinical presentation, disease progression, and treatment responses of patients diagnosed with DHL were analysed using SPSS v29. The outcomes of patients treated with R-CHOP and RICE chemotherapy regimens were compared. The effectiveness of the treatment was assessed by tracking patient remission rates, relapse rates, and overall survival.

RESULTS

Table 01 shows a gender distribution where males constitute 60% of the patients (15 individuals), while females make up the remaining 40% (10 individuals). Regarding clinical features, the

majority of patients, 80% (20 individuals), exhibited lymphadenopathy, with the remaining 20% (5 individuals) presenting other symptoms. The peripheral smear results indicate that 72% of patients (18 individuals) had leukocytosis, while 28% (7 individuals) showed other findings.

Table 02 summarizes survival and outcome metrics for the patients, broken down by gender. The event-free survival rate stands at 10, evenly split between males and females. Overall survival is higher at 13, with males having a higher survival rate of 8 compared to 5 females. Both genders experienced 2 deaths each, and remission was achieved in 18 cases, with males leading at 11 and females at 7. There were 5 relapses in total, with a higher incidence among females (3) compared to males (2). [Table 2]

Table 03 details the treatment responses of patients categorized by gender. A complete response was observed in 12 patients, with males accounting for 7 and females 5. Partial responses were noted in 6 patients, equally divided between males and females. A total of 4 patients showed no response or progression, with an equal split between genders. Treatment-related toxicity was reported in 3 cases, with males experiencing more frequent toxicity (2 cases) compared to females (1 case). [Table 3]

Table 1: Demographic data of patients

Category	Subcategory	Number of Patients	Percentage
Gender Distribution	Total	25	100%
	Males	15	60%
	Females	10	40%
Clinical Features	Lymphadenopathy	20	80%
	Others	5	20%
Peripheral Smear	Leukocytosis	18	72%
	Others	7	28%

Table 2: Survival and outcomes

Category	Total	Males	Females
Event-Free Survival	10	5	5
Overall Survival	13	8	5
Deaths	2	1	1
Remission	18	11	7
Relapse	5	2	3
Deaths	2	1	1

Table 3: Treatment response

Category	Total	Males	Females
Complete Response	12	7	5
Partial Response	6	3	3
No Response/Progression	4	2	2
Treatment-Related Toxicity	3	2	1

DISCUSSION

The results of this study highlight several important aspects of Double-Hit Lymphoma (DHL), including its clinical presentation, survival outcomes, and treatment responses. DHL remains a highly aggressive and challenging form of lymphoma, requiring timely diagnosis and effective therapeutic interventions.[12] Gender distribution revealed slightly higher proportion of males in this cohort with 60 percent. This is in line with other investigations that found that we observed that DHL more common among male patients. Analyzing clinical characteristics, one could conclude the fact that the majority of the patients had lymphadenopathy – 80% of cases, which is quite characteristic of the aggressive types of lymphomas.[13] Also, 72% of patients presented leukocytosis, a factor, which tends to be linked to higher stage and increased tumor mass. Results by survival analysis in this study indicates a problem in the management of DHL – Survival outcomes. According to EFS, only 10 patients were alive without any event and OS were available in 13 patients. Even these numbers can be considered rather low given the fact that DHL is an aggressive cancer and has a very high rate of relapses. Similarly, the comparison in the survival rate proportions of EFS and OS between male and female patients imply that gender may not be a factor in the prognosis of DHL and this observation needs to be further investigated with large samples sizes.[14] Outcomes touching on remission, relapse, death stress the challenges towards lower disease control in DHL. A major portion of the patients (72%) were in remission, but the rest (20%) had recurrence. Patients with DHL are said to have poor prognosis if they relapse and as such, the high relapse rate identified in this study should alert clinicians to formulate better treatment regimens and frequently monitor patients who completed their treatment.[15] Another piece of evidence presented from the treatment response data is the need for variability in patients' response. Out of them, 12 patients had a complete response to the treatment while 6 patients had a partial response, 4 had no

response or had progressive disease. Treatment-related toxicity in 3 patients demonstrated another major feature of DHL management – very intensive treatment compared with the potential toxicity of various therapeutic options.[16] All together, these results underscore the necessity of ongoing investigation for optimized DHL treatment methods that are less hazardous to the patient.[17] Novel targets, including BCL2 and MYC, have shown some recent progress; however, the safety and efficacy of these agents in large clinical trials remain unknown.[18] Moreover, diagnosis of DHL at the preliminary stages, and the accurate molecular test preferred for diagnosis, enhances patient's chances due to the fact that delays in identification of DHL worsen patient's prognoses.

CONCLUSION

The present study demonstrates a male-to-female preponderance of 1.5:1 among the 25 patients diagnosed with Double-Hit Lymphoma. The majority of these patients presented with lymphadenopathy, and peripheral smear analysis revealed leukocytosis in most cases, indicating advanced disease. Survival outcomes showed that 40% of the patients achieved event-free survival, while 50% had overall survival, with a mortality rate of 10%. In terms of treatment response, 72% of patients achieved remission, while 18% experienced relapse, and 10% succumbed to the disease despite undergoing treatment with the R-CHOP and RICE chemotherapy regimens. These findings highlight the aggressive nature of DHL and the challenges associated with its management.

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