CLINICAL SPECTRUM AND FREQUENCY OF BONE MARROW INFILTRATION IN HODGKIN LYMPHOMA PATIENTS PRESENTING TO A TERTIARY CARE

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Abstract

Background and Objectives: Hodgkin lymphoma (HL) is a lymphoid malignancy that affects peripheral lymph nodes as well as organs like lungs, liver and bone marrow. It has 05 types. The clinical features of HL include lymphadenopathy and constitutional 'B' symptoms (fever, night sweats & weight loss). This study was conducted to describe the clinical spectrum and frequency of bone marrow infiltration in Hodgkin lymphoma patients presenting to Hematology department of AIMC Lahore.

Methods: This descriptive study has utilized data of known cases of HL, referred by Oncology department for bone marrow biopsy from January 2019 to December 2022, retrieved from medical records. Information was noted regarding demographic profile of the patient along with the clinical features, type of HL and infiltration of bone marrow. Data were analyzed using SPSS version 24.0.

Results: The study consisted of 24 HL patients between 10 to 60 years of age. The median age was 41 years. There were 21 male (87.5%) and 03 female (12.5%) patients (male-to-female ratio: 7:1). Lympha-denopathy was the predominant clinical feature present in all 24(100%) patients followed by 'B" symptoms in 09(37.5%) cases while bone marrow infiltration was present in 7 (29.1%) patients.

Conclusion: Lymphadenopathy serves as a distinctive clinical feature of Hodgkin lymphoma and presence of bone marrow infiltration may be reasonable factor for accurate disease staging.

Keywords: Hodgkin lymphoma, lymphoid malignancy, bone marrow infiltration, staging

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Hodgkin lymphoma (HL) is a lymphoid malignancy that affects peripheral lymph nodes as well as the organs like lungs, liver and bone marrow. It is divided into 05 types based on the histological features. These include nodular sclerosis, mixed cellularity, lymphocyte-rich, lymphocyte-depleted and nodular lymphocyte-predominant types. The first four types are collectively termed as Classic HL.[1] The median age of onset of classic HL is around 33 years. Although it is extremely uncommon before the age of 12 but it is the most frequently occurring lymphoma in young adults and can also affect individuals of age 80 years and above, thus, having a bimodal distribution. Lymph node biopsy and immunohistochemistry are required for diagnosis of HL and staging is done according to Ann-Arbor system (Stage I-IV). The characteristic histological feature of classic HL is Reed-Sternberg (RS) cell that has abundant basophilic cytoplasm and a bilobed nucleus. It is derived from germinal centre B-cells.[2]

Among the different types of classic HL, the most common is mixed cellularity followed by nodular sclerosis, lymphocyte-depleted and lymphocyte-predominant type. In a study conducted by Nawaz et al. on

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36 and Siddiqui et al. on 650 HL patients it was concluded that mixed cellularity was the most common type and had a male predominance.[3,4]

Bone marrow infiltration is crucial in staging of HL and indicates an advanced stage of the disease that has an impact on the treatment and prognosis of the disease. For staging of Hodgkin lymphoma, bone marrow biopsy is a recommended and commonly performed procedure and bone marrow involvement represents Stage IV for the disease. Bone marrow infiltration pattern can be focal or diffuse the latter being more common.[5]

In recent years, there has been an increasing use of positron emission tomography scan (PET) for evaluation and staging of malignancies including HL. However studies have shown that it cannot replace bone marrow biopsy for staging purposes and only has a complementary role.[6]

According to SKMCH&RC annual cancer registry report, the incidence of HL in Pakistan has increased from 3.4% in 2019 to 5.9% in 20217. Due to this increasing burden of HL in our population, it is important to determine its stage since it has a direct impact on the treatment and prognosis. The existing literature on this topic shows variable results and utilization of advanced radiologic modalities for detecting bone marrow infiltration. Although the radiologic modalities have a higher sensitivity, but because of their cost and limited availability, bone marrow biopsy remains superior and a cornerstone especially in our setup.

METHODS

This descriptive cross-sectional study was conducted at Haematology Department of Allama Iqbal Medical College (AIMC), Lahore. The study protocol was approved by the Ethical Review Board of AIMC/JHL in its 139th meeting (Ref No. ERB139/6/20-02-2023/S1 ERB). Data of known cases of HL, diagnosed on lymph node biopsy, referred from Oncology department for bone marrow examination from January 2019 to December 2022 was retrieved from the medical record using convenient sampling technique. Data was extracted from medical record, stratified for age and gender and analyzed using SPSS version 21.0. Medical record with incomplete patient history or no evidence of HL on lymph node biopsy was excluded. Quantitative variables like age were presented as mean and standard deviation while qualitative variables like clinical features and bone marrow infiltration were presented as frequency and percentage.

RESULTS

The study population consisted of 24 HL patients between 10 to 60 years of age. The patients were divided into five age groups. The median age was 41 years and incidence of HL was highest in the age group of 41 to 50 years (29.17%) (Figure 1).

Out of 24, there were 21 male (87.5%) and 03 female (12.5%) patients with a male-to-female ratio of 7:1.

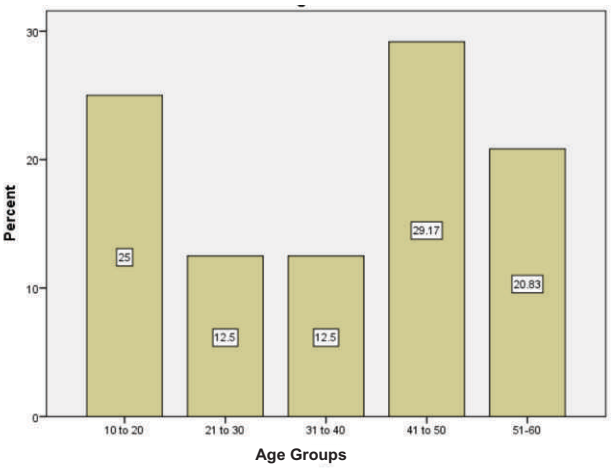

Figure 1: *Age statistics in Hodgkin Lymphoma patients*

The most common type of HL in our study population was mixed cellularity (n=13; 54.1%) followed by nodular sclerosis (n=09; 37.5%). The predominant clinical feature was lymphadenopathy that was present in all 24 patients while B symptoms were present in 09 patients (37.5%). The most commonly involved lymph nodes were of cervical and inguinal region followed by abdominal and axillary group (Table 1).

Out of the 24 cases of HL that presented for bone marrow biopsy, 07 exhibited bone marrow infiltration (Stage IV disease) with an overall infiltration frequency of 29.1%. Bone marrow involvement was most common in mixed cellularity type (n=05; 38.4%) (Table 2).

Table 1: Spectrum of clinical features (n=24)

CLINICAL FEATURES	NO. OF CASES
LYMPHADENOPATHY	24 (100%)
Cervical Lymph nodes	07 (29.1%)
Inguinal Lymph nodes	07 (29.1%)
Axillary Lymph nodes	02 (8.3%)
Abdominal Lymph nodes	03 (12.5%)
Multiple Lymph node groups	05 (20.8%)
B SYMPTOMS (fever, night sweats, weight loss)	09 (37.5%)
NON-SPECIFIC SYMPTOMS (abdominal pain)	02 (8.3%)

Table 2: Hodgkin Lymphoma Types & Bone Marrow infiltration (n= 24)

Type Of Hodgkin Lymphoma	No. of cases	Bone Marrow Infiltration		Percentage (%)
		Present	Absent	
Mixed cellularity	13	05	08	38.4
Nodular sclerosis	09	02	07	22.2
Lymphocyte rich	0	0	0	-
Lymphocyte depleted	0	0	0	-
Nodular lymphocyte predominant	02	0	02	-
Total No of Cases	**24**	**07**	**17**	**29.1**

DISCUSSION

Hodgkin lymphoma (HL) is globally ranked as the second most common malignancy in developed and third most common in the developing countries. It has a male predominance. The frequency of HL in Pakistan is 4.9% and it is rising because of several factors that promote disease progression.[8] In the United States, HL accounts for about 10% of all the lymphoma cases.[9] In the last few decades many studies have been conducted in Pakistan to determine the incidence and prevalence of lymphoma in general, but no recent study has been done focusing specifically on the increasing burden of advanced stage HL.

A total of 24 diagnosed cases of HL were referred to us by Oncology department for bone marrow biopsy. There was male predominance (87.5%) with mixed cellularity (54.1%) being the most common histological type and overall frequency of bone marrow infiltration by HL in present study was 29.1%. These findings were quite similar to the results of the study conducted in Lahore in 2011, which reported frequency of bone marrow infiltration by HL as 38% with mixed cellularity being the most common type.[10] Similar observations were made in the study done by Anwar et al. in 2015 that reported male predominance (70%) and mixed cellularity (51.5%) as the most common type.[11] In a study conducted at Oncology department of CMH Rawalpindi in 2009, bone marrow infiltration frequency by HL was reported as 17.14% which is slightly less than that observed in current study.[12] However, in 2022 a similar study done at NORI Islamabad reported bone marrow infiltration frequency by HL as 27.6% thus reflecting an increase in frequency of Stage IV disease as observed in present study.[13]

Hodgkin lymphoma has a bimodal age distribution with the first peak between 6-10 years and second peak between 26-30 years as reported by Konkay et al. in 2016.[14] In contrast, the present study has reported first peak in 10-20 years age group and second peak in 41-50 years age group with median age of presentation as 41 ± 16.21 SD years.

The clinical presentation of HL varies. There may be painless lymphadenopathy alone or in combination with other symptoms like fever, night sweats and weight loss, collectively termed as B symptoms which are present in about 30% of cases and are more common in advanced stage (Stage III&IV) and mixed cellularity type of HL. 15 These findings are consistent with the observations made in present study in which lymphadenopathy was present in all 24 patients while B symptoms were present in only 09 patients (37.5%).

There are a number of important limitations in our study. As our study population is limited to one centre only so it does not represent a clear picture. A larger sample size would be a better predictor of the disease burden. Secondly, due to the absence of a central cancer registry, the study does not accurately reflect the total number of HL cases throughout Pakistan. More extensive research is required to determine the precise number of HL cases in Pakistan and to timely determine its stage and thus treat patients accordingly to lessen the burden of this treatable disease.

CONCLUSION

The most common clinical feature of Hodgkin lymphoma in all age groups is painless lymphadenopathy. Approximately one-third of the patients had stage IV disease at the time of presentation which indicates that majority of the patients seek medical attention at an advanced stage of the disease reflecting a lack of awareness and limited diagnostic facilities in our part of the world.

Ethical Approval:

The ethical Approval was obtained from Allama Iqbal Medical College. (Reference No. ERB 139/6/20-02-2023/SL ERB)

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