ORIGINAL ARTICLE

Frequency of Bone Marrow Involvement in Hodgkin's Lymphoma in Patients Presented at Shoukat Khanum Memorial Cancer Hospital Lahore

REHAN ANWAR[1], USMAN JAVED IQBAL[2], NASIR AHMAD[3]

ABSTRACT

Aim: To find out the frequency of bone marrow involvement in Hodgkin's lymphoma and to see the pattern of its various clinical stages with bone marrow involvement.
Study design: Cross sectional study.
Setting: Oncology department Shoukat Khanum Memorial Cancer Hospital Lahore.
Duration: Six months.
Methods: Using non probability purposive sampling 200 newly diagnosed Hodgkin's lymphoma patients were enrolled. After taking informed consent bone marrow biopsy of each patient was done and slides were reviewed to identify its various subtypes and bone marrow involvement. Depending upon CT scan findings and clinical examination clinical stages were identified. Including basic demographic details all information were recorded on predefined questionnaire. Frequency and percentage were used for qualitative analysis while mean and standard deviation was used for quantitative analysis.
Results: Mean age of our patients was 17±4.3 years. There was an overall male predominance (70%). The most common subtypes of Hodgkin lymphoma that was detected in our patients included mixed cellularity HL (MCHL) in 103 patients (51.5%) and nodular sclerosis HL (NSHL) in 88 patients (44%). With respect to pattern of various clinical stage at presentation there were 19 (9.5%) patients with stage-I, 48 (24%) with stage-II, 55(27.5%) with stage-III and 78(39%) patients were presented with stage IV. Bone marrow involvement was found in 20 patients (10%).
Conclusion: Early stage Hodgkin lymphoma (stage I and II) is unlikely to present with bone marrow involvement hence bone marrow biopsy can be avoided in these cases while reserving bone marrow biopsy for more clinically advance stages.
Keywords: Malignancy, Lymphoma, Trephine needle biopsy, Reed-Sternberg cell.

INTRODUCTION

First described by Thomas Hodgkin in 1832 Hodgkin lymphoma (HL) is a lymphoproliferative disease involving lymph nodes and spleen primarily[1]. Subtypes of HL are Nodular sclerosis (NS), Mixed cellularity (MC), Lymphocyte rich classical HL (LRCHL), Lymphocyte depleted HL and nodular lymphocyte predominant HL (NLPHL)[2]. Hallmark of the disease is Reed-Sternberg cell, described by Sternberg (1898) and Dorothy Reed (1902)[3]. In U.S 2010, 8,490 new case were registered and total numbers of death were 1320[4]. In 2008 incidence of new cases in India and Pakistan were 7371, 1513 and mortality cases were 3587, 1248 respectively[5]. The extent of disease determined at the time of diagnosis in the light of staging investigations according to Ann Arbor staging system with Cotswold's modification[6]. According to this staging system patient is staged from stage I to stage IV. Patient is labeled as stage IV disease if it has visceral involvement like liver, lung or bone marrow involvement. Since treatment is dependent on stage at the time of presentation and bone marrow involvement is considered as stage IV disease so it has a prognostic importance. In literature variable proportions of bone marrow involvement in Hodgkin lymphoma has been reported with respect to its stages[7,8].

The purpose of this study is to determine the frequency of bone marrow involvement by Hodgkin lymphoma according to the clinical stage. As being the largest cancer institute in country a large number of patients with Hodgkin lymphoma are treated and referred in the facility so our study will be able to give generalized results in order to find at what clinical stage bone marrow biopsy should be done.

MATERIALS AND METHODS

It was a cross sectional study conducted at Shoukat Khanum Memorial Cancer Hospital and Research Centre, Lahore. Using non probability purposive

[1]*Assistant Professor Sialkot Medical College.*
[2]*Demonstrator Gulab Devi PGMI, M.Phil Public Health.*
[3]*Consultant Physician DHQ Sheikhupura.*
Correspondence to Usman Javed Iqbal
Email: sh.usmanjavediqbal@gmail.com

sampling 200 newly diagnosed Hodgkin's lymphoma patients were enrolled. Patients with platelets counts less than 20 thousands and those with advance chronic liver disease were excluded. After taking informed consent bone marrow biopsy of each patient was done and slides were reviewed to identify its various subtypes and bone marrow involvement. Bone marrow involvement was labeled as positive if large binucleated or multinucleated cell (Reed Sternberg cell) were found in bone marrow sample. Depending upon CT scan findings and clinical examination clinical stages were identified according to Ann Arbor staging system[6] with Cotswold's modification. Including basic demographic details all information were recorded on predefined questionnaire.

Data Analysis: Data will be analyzed in SPSS version 17. Frequency and percentage were used for qualitative variables i.e. Bone marrow involvement, clinical stage, subtypes of HL etc. Mean and standard deviation was used for quantitative variables.

RESULTS

Mean age of our patients was 17±4.3 years. Out of 200 patients, 70% were males and 30% were females with a male to female ratio of 2.4:1.

Table 1: Socio-demographic Profile

Age (Mean±S.D	17 ± 4.3 years
Range	05 - 60 years
Gender	
Male	140 (70%)
Female	60 (30%)

Hodgkin's lymphoma subtypes that were diagnosed in our patients included mixed cellularity HL (MCHL) in 103 patients (51%), nodular sclerosis HL (NSHL) in 88 patients (44%), lymphocyte rich HL (LRHL) in 06 patients (03%), nodular lymphocyte predominant HL (NLPHL) in 02 patients (1%) while only 01 patient was diagnosed of having lymphocyte depleted HL (LDHL). Most common histology subtype involving the bone marrow was mixed cellularity i.e., 14 patients out of 103, while nodular sclerosis was the second most common histology subtype involving the bone marrow i.e. 07 patients out of 48 patients.

Table 2: Subtypes of Hodgkin's Lymphoma

	Frequency (n=200)
Nodular Sclerosis	48 (44%)
Mixed Cellularity	103 (51%)
Lymphocyte Rich	06 (3%)
Lymphocyte Depleted	01 (0.5%)
Nodular lymphocyte predominant (NLPHL)	02 (1%)

The overall frequency of bone marrow involvement in Hodgkin's Lymphoma was 11% i.e. out of 200 patients only 22 patients had bone marrow involvement as detected on bone marrow biopsy.

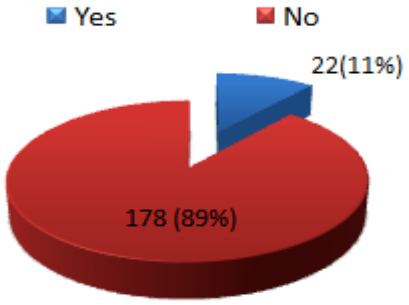

Fig-01: Frequency of Bone Marrow Involvement

With respect to clinical stage at presentation 19 (9%) patients were presented at Stage-I, 48 (24%) at Stage-II, 55 at Stage-III while 78 (39%) at Stage-IV. Bone marrow involvement was detected only in 03 cases (5%) of stage-III and 19 cases (24%) of stage-IV as shown in Fig-02

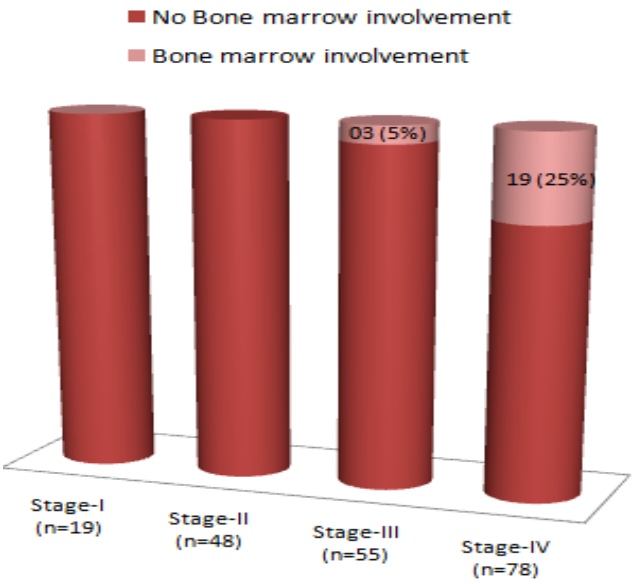

Fig-02: Different stages of Hogdkin's lymphoma & Bone marrow involvement

DISCUSSION

Hodgkin lymphoma is a lymphoproliferative disorder and is one of the treatable hematological malignancies with good outcome.[9] Treatment depends on stage at presentation which is determined by bone marrow examination an invasive and painful procedure and many patients are reluctant to undergo this procedure.

In Hodgkin lymphoma age at presentation has bimodal presentation with two peaks, one in twenties

and second in sixty years.[10] In our study median age of presentation was 17 years. Similarly there were 70% males and 30 females as reported in our study these findings are in consistent with the findings of Nadeem et al[8] which also demonstrated an overall male predominance

Histological subtype has geographic as well as economic advancement. In developed countries, commonest histology is Nodular sclerosis while MC is the commonest subtype in less well developed countries.[11] In our study the commonest subtype was MC i.e. 51.5%.

In our study the overall frequency of bone marrow involvement in Hodgkin's Lymphoma was 11% i.e., out of 200 patients only 22 patients had bone marrow involvement as detected on bone marrow biopsy. Our findings are in coalescence with findings of studies conducted in Italy[12], Mexico[13] and India[14] in which bone marrow involvement has been reported as 8%, 3.3% and 20% respectively.

With respect to clinical stage at presentation 19 (9%) patients were presented at Stage-I, 48 (24%) at Stage-II, 55 at Stage-III while 78(39%) at Stage-IV. Bone marrow involvement was detected only in 03 cases (5%) of stage-III and 19 cases (24%) of stage-IV. The reason for a higher frequency may be the late presentation of patients as the maximum number of patients with bone marrow infiltration had CS IV disease. Among the patients with early stage disease in our study not even a single patient was having bone marrow involvement. Our results are quite comparable with the results of Nadeem et al[8]. Similarly Vassilakopoulos et al[15] found that 24.1% of patient with advance stage disease has bone marrow involvement with Hodgkin lymphoma. Ultimately it can be demonstrated that advance stage i.e., stage III-IV has more frequency of bone marrow involvement as compared to early stage disease

CONCLUSION

The overall frequency of bone marrow involvement in Hodgkin's Lymphoma was 11%. Early stage Hodgkin lymphoma (stage I and II) is unlikely to present with bone marrow involvement hence bone marrow biopsy can be avoided in these cases while reserving bone marrow biopsy for more clinically advance stages.

REFERENCES

1. Bonadonna G. Historical review of Hodgkin's disease. British journal of haematology. 2000;110(3):504-11.
2. Hoster HA, Dratman MB. Hodgkin's Disease-(Part I) 1832–1947. Cancer Research. 1948;8(1):1-48.
3. Eberle FC, Mani H, Jaffe ES. Histopathology of Hodgkin's lymphoma. The Cancer Journal. 2009;15(2):129-37.
4. Shenoy P, Maggioncalda A, Malik N, Flowers CR. Incidence patterns and outcomes for Hodgkin lymphoma patients in the United States. Advances in hematology. 2010;2011.
5. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. International journal of cancer. 2010;127(12):2893-917.
6. Olweny C. Cotswolds modification of the Ann Arbor staging system for Hodgkin's disease. Journal of Clinical Oncology. 1990;8(9):1598-.
7. Kini JR, Suresh PK, Sinha R, Sahu KK, Kumar S, Prasad K. Value of bone marrow examination in Hodgkin lymphoma: Report of three cases with review of literature. Journal of cancer research and therapeutics. 2012;8(3):457.
8. Nadeem M, Naqi N, Hussain I, Khattak J, Ahmed R, Khan B. Frequency of bone marrow involvement in Hodgkin's Lymphoma on first presentation. J Coll Physicians Surg Pak. 2009;19(12):768-71.
9. Thomas R, Re D, Zander T, Wolf J, Diehl V. Epidemiology and etiology of Hodgkin's lymphoma. Annals of oncology. 2002;13(suppl 4):147-52.
10. Ries L. EM, Kosary CL, Hankey BF, Miller MBA, Clegg L, al. e. SEER cancer statistics review. 1997:197-2000.
11. Correa P, O'Conor G. Geographic pathology of lymphoreticular tumors: summary of survey from the geographic pathology committee of the international union against cancer. Journal of the National Cancer Institute. 1973;50(6):1609-17.
12. Levis A, Pietrasanta D, Godio L, Vitolo U, Ciravegna G, Di Vito F, et al. A large-scale study of bone marrow involvement in patients with Hodgkin's lymphoma. Clinical lymphoma. 2004;5(1):50-5.
13. Gómez-Almaguer D, Ruiz-Argüelles G, López-MartÍnez B, Estrada E, Jaime-Pérez J. Role of bone marrow examination in staging Hodgkin's disease: experience in Mexico. Clinical & Laboratory Haematology. 2002;24(4):221-3.
14. Ananthamurthy A, Kurien A, Ramnarayan K. The bone marrow in Hodgkin's disease--a two year study. Indian journal of cancer. 2000;37(4):173-83.
15. Vassilakopoulos TP, Angelopoulou MK, Constantinou N, Karmiris T, Repoussis P, Roussou P, et al. Development and validation of a clinical prediction rule for bone marrow involvement in patients with Hodgkin lymphoma. Blood. 2005;105(5):1875-80