Section: Pathology

Original Research Article

BONE MARROW INVOLVEMENT IN NON HODGKIN LYMPHOMA AT TERTIARY CARE HOSPITAL

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ABSTRACT

Background: Non-Hodgkin's lymphomas (NHLs) represent a heterogeneous group of disorders that arise from the lymphoid system. NHL occurs in individuals at virtually all ages, but it's uncommon in children. Low-grade NHL (Follicular lymphoma, and Chronic lymphocytic leukemia) are more common in the USA, whereas Diffuse Large B cell Lymphoma (DLBCL) is most common in India. Bone marrow aspiration and biopsy are an important component of staging workup in NHL.

Materials and Methods: This is a Prospective study, done for a period of 24 months. Total number of cases studied are 50 cases of NHL, with bone marrow correlation. CD3 and CD 20 IHC was done to differentiate between B and T cell Lymphoma.

Results: In the present study out of 50 cases, 22 cases had both Bone marrow aspiration and Bone marrow biopsy. Of these 22 cases, BMB showed positive infiltrations in 16 (72.7%) of cases, while the remaining 6 (27.3%) cases were negative for infiltration and showed normal bone marrow study.Of the 50 cases of NHL, there were 49 cases of B cell – NHL constituting to 98%, and only 1 case of T- NHL. CD3 and CD 20 IHC was done to differentiate between B and T cell Lymphoma. Out of these 49 cases of B-cell NHL, the major subtype was Chronic lymphocytic lymphoma.

Conclusion: Bone marrow aspiration is a simple and rapid procedure and it is alternative to biopsy, and it is supported by its easier and earlier diagnostic availability in the study of NHL. B cell lymphoma were more frequent than T cell lymphoma with predominance of Chronic Lymphocytic Lymphoma and Para trabecular infiltrations in the present study.

Keywords: Non Hodgkin lymphoma, Bone marrow aspiration and Bone marrow biopsy.

INTRODUCTION

Non-Hodgkin's lymphomas (NHLs) represent a heterogeneous group of disorders that arise from the lymphoid system[1] .NHL tends to be a disease of older age in North America and Europe.[1,2] NHL are characterized by neoplastic transformation of lymphoid lineage with the high potential for spread to various tissues throughout the body, liver, and spleen especially bone marrow.[3,4] Follicular lymphoma and Diffuse Large B-cell Lymphoma (DLBCL) are the two commonest types and together account for about 53 percent of cases.

Bone marrow biopsy is an important component of staging workup in NHL and the patients presenting with bone marrow infiltration have shown poor prognosis.[3] It has been regularly reported that patients in developing countries often present at a relatively advanced stage in comparison with patients from the Western site.[5-8] Currently, non invasive clinical staging by computed tomography (CT), magnetic resonance imaging (MRI), or positron emission tomography (PET)-CT cannot fully assess

Bone marrow (BM) involvement, which is possible only by pathological staging (bone marrow aspiration and bone marrow trephine biopsy). Thus, although clinical stage can suggest localized diseases (stage I or II), it's not uncommon for the final stage to change to stage IV due to positive Bone marrow (BM) involvement.[9-11]

Incidence: The incidence of NonHodgkin's lymphoma (NHL) is rising worldwide. Non-Hodgkin lymphoma occurs in individuals at virtually all ages, but it's uncommon in children. Lowgrade NHL (Follicular lymphoma, and Chronic lymphocytic leukemia) are more common in the USA, Whereas Diffuse Large B cell Lymphoma (DLBCL) is most common in India.[12] Within India, the incidence is several fold higher in urban cancer registries compared to rural areas; the incidence being higher in metropolitan cities and Indian immigrants than rural areas suggesting that urban lifestyles and economic progress may increase the cancer incidence.[13]

MATERIALS AND METHODS

This is a Prospective study done for a period of 24 months. Total number of cases studied are 50 cases of NHL, with bone marrow correlation. The morphology and histologic pattern of bone marrow infiltration were categorized as diffuse, interstitial, nodular and paratrabecular. Patient details concluded with the age, clinical details,blood counts and peripheral blood smears were also studied.

RESULTS

There were total 50 Cases of Non Hodgkin lymphoma, with of 29 males and 21 females with ratio of 1.3:1. Age of the patients ranged from 20 to 85 years and Overall the mean age was 54.02 and median was 43years.

Table 1: Showing sex distribution, mean and median age in patients of NHL.

	Males	Females
No. of cases	29	21
Mean age (yrs)	54.3	53.6
Median age (yrs)	70	50

Table 2: Age and percentage Distribution of patients in NHL

Age	Males %	Females %	Total %	
20-30Years	2 (4%)	1 (2%)	3 (6%)	
31-40Years	3 (6%)	2 (4%)	5 (10%)	
41-50Years	7 (14%)	6 (12%)	13 (26%)	
51-60Years	6 (12%)	7 (14%)	13 (26%)	
61-70Years	8 (16%)	4 (8%)	12 (24%)	
71-85Years	3 (6%)	1 (2%)	4 (8%)	
			50 (100%)	

Table 3: Bone marrow results as regard the bone marrow aspiration (BMA)among studied

BMA infiltration by NHL	Number	Percentage
Positive	45	90%
Negative	5	10%

In the present study bone marrow aspiration is done for all cases (50 cases). Out of 50 cases of BMA 45 (90%) cases show positive infiltrations by lymphoma and 5 (10%) are negative for infiltrations.

Table 4: Percentage of peripheral blood involvement in NHL

CBP involvement	No of patients	Percentage
Involved	21	42%
Normal	29	58%
Total	50	100%

Table 5: Bone marrow results as regard the bone marrow biopsy (BMB) among studied cases.

BMB infiltration by NHL	Number (22 Cases)	Percentage
Positive	16/22	72.7%
Negative	6/22	27.3%

Bone marrow aspiration and biopsy are done for same patients. Out of 50 cases of NHL. Bone marrow biopsy was done for 22 cases, Out of these 22 cases, 16 (72.1%) cases show positive infiltrations and 6 (27.3%) cases are negative for infiltrations.

Table 6: Comparision of bone marrow aspiration to the bone marrow biopsy among studied cases

Group	Total (50)	Postive	Negtive
BMA	50/50	45(90%)	5(10%)
BMB	22/50	16(72.7%)	6(27.3%)

In the present study of bone marrow aspiration was done in all 50 cases and bone marrow biopsy was done for 22 (22/50) cases. Out of the 50 cases, 45 (90%) cases show infiltrations on bone marrow aspiration by lymphoma and 5 (10%) cases are negative for infiltrations. Out of the 22 cases of BMB, 16 (16/22) cases show positive infiltrations and 6 (6/22) cases do not show infiltrations by lymphoma and are negative.

Table 7: Bone marrow biopsy compared to the bone marrow aspiration among studied cases

Group	Number (22)	Percent
+ve BMB, +ve BMA	14/22	63.6%
+ve BMB, -ve BMA	2/22	9.09%
-ve BMB, +ve BMA	3/22	13.6%
-ve BMB, -ve BMA	3/22	13.6%

Table 8: Patterns of BM infiltration among positive BMB studied cases (16 cases)

Pattern	Number (16/22)	Percentage
Paratrabecular	8	50%
Interstitial	4	25%
Diffuse	2	12.5%
Nodular	2	12.5%

Table 9: Percentage of B cell and T cell lymphoma in the present study

Group	Number (50)	Percentage
B cell lymphoma	49/50	98%
T cell lymphoma	1/50	2%

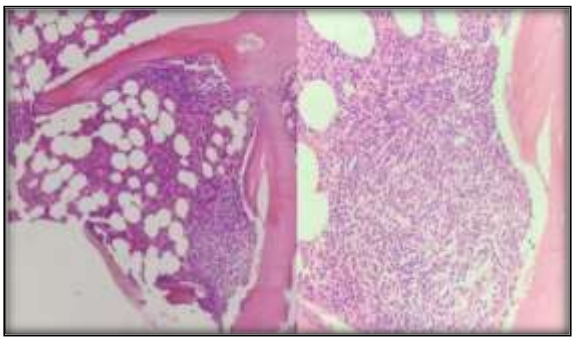


Figure 1: Paratrabecular infiltrations

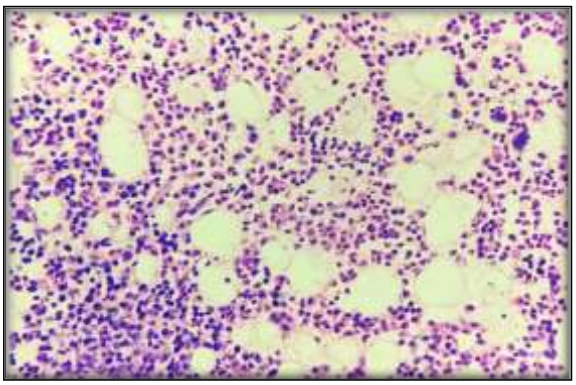
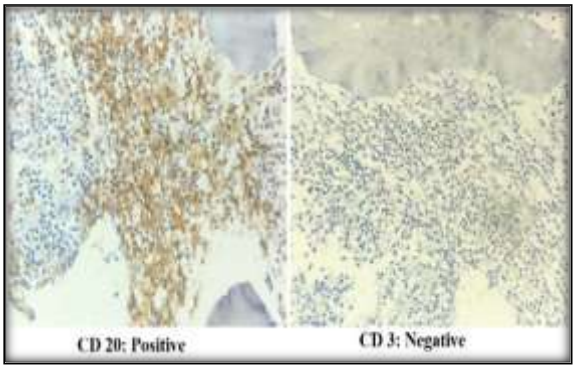
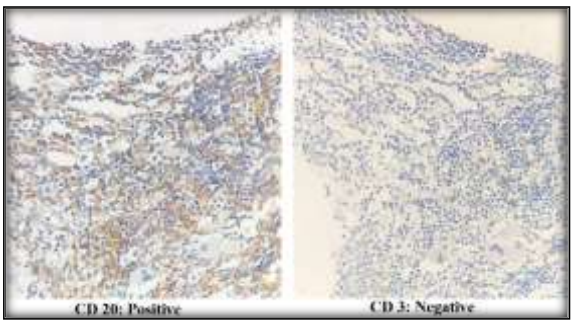


Figure 2: Interstitial infiltrations





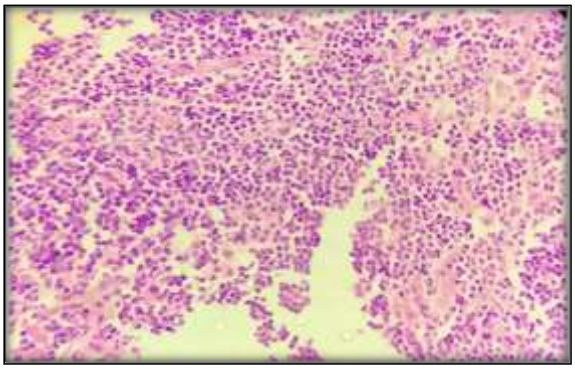


Figure 3: Diffuse infiltrations

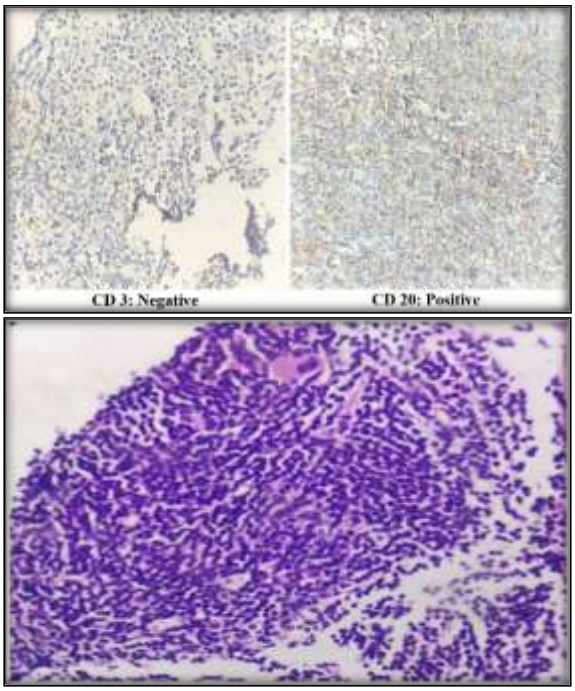
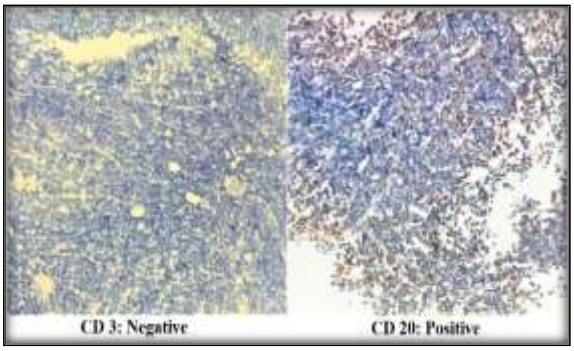


Figure 4: Nodular infiltrations



DISCUSSION

The present study is done in the Upgraded Department of Pathology, MNJ IO-RCC and Osmania General Hospital, Hyderabad. In this study Bone marrow aspiration and biopsy were done in cases of NHL.

Non-Hodgkins lymphoma (NHL) includes heterogenous group of neoplasms each with distinct clinical, morphological, immunophenotypic, genetic features and different response to therapy. Peripheral blood film (PBF), Bone marrow aspiration (BMA) and Bone marrow biopsy (BMB) is routinely performed to diagnose haematological diseases.

The aim of this study was to analyze the incidence and histological pattern of bone marrow involvement in diagnosed cases of NHL.

Bone marrow examination is useful in the diagnosis of both hematological and non hematological disorders. Indications have included the diagnosis, staging, and therapeutic monitoring for lymphoproliferative disorders. In the present study, the majority of cases are B-cell Non Hodgkin's lymphoma 49/50 (98%) while only 1/50 (2%) case was of T-NHL.

Table 10: Comparison of the Present study by gender wise distribution with other studies

Studies	Males	Females
Present study (50 cases)	58% (29 cases)	42% (21 cases)
Nidhi Goel et al [14]	56.6%	43.4%
Hassan et al [15]	65%	35%
Durosinmi et al [16]	66.6%	33.3%
Kumar et al [17]	66.6%	33.3%

Gender wise distribution of patients with NHL were compared with other studies in TABLE 19. Out of 50 cases of NHL, 29 (58%) were male and 21(42%) were females. In all other studies there was a male preponderance was observed. In our study we have observed male to female ratio of 1.3:1 with slight male predominance. Our study results were comparable with above all studies.

Table 11: Comparision of the bone marrow involvement in the present study of Non-Hodgkin Lymphoma cases with other studies

Studies	Bone marrow involvement % - Positive	Bone marrow involvement % - Negative
Present study (22 cases)	72.7% (16/22 cases)	27.3% (6/22 cases)
Suneet Kumar,[18]	55.1%	44.9%
Ahmad Mokhtar Ahmad,[19]	40%	60%
Nidhi Goel et al,[14]	32%	68%
Baroni et al,[20]	21.8%	78.2%
Haddy et al,[21]	18.9%	81.1%
Lai et al,[22]	30%	70%
Conlan et al,[23]	32%	68%
Juneja et al,[24]	38%	62%
Campbell et al,[25]	27%	73%
Mondal et al,[26]	30.3%	69.7%

In the present study out of 50 cases of NHL, for 22 (22/50) cases we have done bone marrow biopsy and for the rest of cases we have used other ancillary techinques for accurate diagnosis. Out of these 22 cases,16 (72.7%) cases showed bone marrow involvement and 6 (27.3%) did not show bone marrow involvement. The results of this study were compared with other studies. Present study shows more cases of bone marrow involvement compared with other studies. Our study results are closely related to the study of Suneet Kumar.[18]

Table 12: Comparison of peripheral blood involvement in the present study of NHL cases with other studies

Studies	Present	Absent
Present study	42% (21 Cases)	58% (29 Cases)
So youn jeong et al,[27]	35.6%	64.4%
Nidhi Goel et al,[14]	31.7%	68.3%
Arber and George,[28]	29%	71%
Sovani et al,[29]	31.7%	68.%

In the present study of 50 cases of NHL, 21 (42%) cases showed peripheral blood involvement and 29 (58%) did not show peripheral blood involvement. Where as in all other studies peripheral blood involvement was <50%. Our study shows more cases of peripheral blood involvement and our study is compared with all above studies.

Table 13: Comparison of frequency of pattern of involvement in cases of NHL with other studies (BMB of 16/22)

Studies	Paratrabecular	Interstitial	Diffuse	Nodular
Present study	50% (8 Cases)	25% (4 Cases)	12.5% (2 Cases)	12.5% (2 Cases)
Sadia sultan et al,[30]	6.5%	6.5%	14.6%	4.8%
Suneet kumar et al,[18]	11.11%	7.4%	7.4%	22.22%
Jeong et al,[27]	34.5%	20%	40%	5.5%
Ahmad Mokhtar Ahmad et al,[19]	20%	50%	25%	5%
Nidhi Goel et al,[14]	35.3%	5.9%	41.2%	0%
Li et al,[31]	29.3%	11.6%	44.9%	6.1%

In the present study of 50 cases, 22 cases had bone marrow biopsy, of which 16 (16/22) cases showed bone marrow involvement. Out of these 16 cases, paratrabecular pattern of involvement was observed in 8 cases (50%), followed by 4 cases (25%) of interstitial pattern, 2 cases (12.5%) of diffuse pattern and 2 case (12.5%) of nodular pattern. The results of this study were compared with other studies. Its found that in the present study the maximum number of (50%) cases showed Paratrabecular pattern of involvement, followed by Intestitial pattern (25%). Diffuse and Nodular pattern were (12.5%) of cases. However in all the studies there was variation in the pattern of involvement, with a predominace of the diffuse pattern of involvement followed by paratratrabecular pattern.

Table 14: Comparision of spectrum of NHL with other studies

Studies	B cell lymphoma	T cell lymphoma
Present study (50 cases)	98% (49 Cases)	2% (1 Case)
Sadia sultan et al,[30]	91.3%	8.6%
Suneet kumar et al,[18]	77.5%	22.4%
So young jeong et al,[27]	79.7%	20.3%
Ahmad Mokhtar Ahmad et al,[19]	96%	4%

In the present study of 50 cases of lymphoma, 49 (98%) were B lymphoma and only 1 (2%) case was T cell lymphomas. In all other these studies too B cell lymphomas was most common. Our study results were most comparable to that of Ahmad Mokhtar Ahmad et al.[19]

Table 15: Comparision of spectrum of percentage(%) of B cell and T cell NHL with other studies

Studies	B Cell						T cell (1)
	CLL (27)	DLBCL (4)	FL (4)	MCL (2)	MZL (1)	Burkitts (1)	
Present study	54%	8%	8%	4%	4%	2%	2%
Sadiasultan et al,[30]	1.6%	67.9%	7.6%	3.2%	3.8%	2.7%	8.6%
Suneet kumar et al,[18]	6.1%	39%	18.3%	2%	0%	4%	0%
Surbhi Goyal et al,[32]	15%	13%	11.3%	11.3%	0%	0%	0%
Ahmad Mokhtar Ahmad et al,[19]	0%	80%	2%	6%	2%	4%	4%

In the present study out of 50 cases of NHL, major subtype was CLL 27 (54%), followed by 4 (8%) cases of each Diffuse Large B cell Lymphoma and Follicular lymphoma, 2 (4%) cases of Mantle cell lymphoma,1 (2%) case of each Burkitt's and Marginal zone lymphoma, Low grade B cell lymphoma are 10 (20%) cases and 1(2%) case was T cell lymphoma. Our study results different from other

studies.In Sadia sultan et al,[30] Suneet Kumar et al,[18] and Ahmad Mokhtar Ahmad et al,[19] Studies diffuse large B cell lymphomas were most common. Our study results were however comparable to Surbhi Goyal et al,[32] where it has more predominance of CLL.

Summary

This is a Prospective study, done for a period of 24 months. Total number of cases studied are 50 cases of NHL, with bone marrow correlation. Age range was from 20 to 85 years. Majority of cases were in 4th to 6th decade. There were 29 males and 21 females with a slight male predominace.

Of the 50 cases of NHL, there were 49 cases of B cell – NHL constituting to 98%, and only 1 case of T-NHL. Out of these 49 cases of B-cell NHL, the major subtype was Chronic lymphocytic lymphoma 27 (54%), followed by 4 (8%) cases each of Diffuse Large B cell Lymphoma and Follicular lymphoma. There were 2 (4%) cases of Mantle cell lymphoma and 1 (2%) case each of Burkitt's and Marginal zone lymphoma. In addition there were 10 cases (20%) of Low grade B cell lymphoma and only 1(2%) case was T cell lymphoma.

In the present study, out of 50 cases, 22 cases had both BMA and BMB. Of these 22 cases, BMB showed positive infiltrations in 16 (72.7%) of cases, while the remaining 6 (27.3%) cases, were negative for infiltration and showed normal bone marrow study.

In this study, of the 16 positive cases in BMB, maximum number 8 cases (50%) show paratrabecular pattern of involvement, 25% (4 cases) showed interstitial pattern and 2 cases each (12.5%) showed Diffuse and nodular involvement.

The Peripheral blood analysis of these 50 cases show positivity in 21 cases (42%) and 29 cases (58%) did not show peripheral blood involvement.

It has been found that there is a discrepancy in the evaluation and features between BMA and BMB in this study as depicted in [Table 7]. Of the 22 BMB – 14 cases had positive in both BMA and BMB. 3 cases were negative in BMB but positive on BMA. Whereas 2 cases were positive on BMB but negative on BMA. And 3 cases were negative on both BMA and BMB. Hence, in all cases of NHL, complete bone marrow evaluation is very essential to get a complete analytical data of NHL.

CONCLUSION

The incidence of Non-Hodgkin's lymphoma (NHL) is rising worldwide and within India the incidence is higher in metropolitan cities. Peripheral blood film and bone marrow examination are two most important diagnostic pillars in haematological disorders. Bone marrow aspiration is a simple and rapid procedure and it is alternative to biopsy, whereas biopsy provides additional information like marrow fibrosis, pattern of marrow involvement, post chemotherapy changes which are prognostically useful. The data from the present study shows that bone marrow aspiration is a useful procedure with which we can detect marrow infiltration by lymphoma. Although it cannot be a substitute for examination of the bone marrow core biopsy, the utility of the bone marrow aspiration is supported by its easier and earlier diagnostic availability in the study of NHL. To conclude B-cell lymphoma were more frequent than T-cell lymphoma with predominance of Chronic Lymphocytic Lymphoma and Paratrabecular infiltrations in the present study.

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