

## RESEARCH COMMUNICATION

# Hodgkin's and Non-Hodgkin's Lymphomas in an Indian Rural Medical Institution: Comparative Clinicopathologic Analysis

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### Abstract

In this prospective, hospital-based two year study, we comparatively evaluated clinicopathologic features of Hodgkin's lymphoma (HL, n = 48) and Non-Hodgkin's lymphoma (NHL, n = 76) in an Indian rural medical institution. A lower median age of onset (28.1 versus 39.9 years) and higher male to female ratio (3.8:1 versus 3.2:1) were noted for HL compared to NHL. The commonest symptom was neck swelling (58.3% versus 65.8%) while peripheral lymphadenopathy was the commonest sign (83.3% versus 94.7%). The commonest lymph-node group involved was cervical (79.2% versus 79.0%). Bone marrow involvement was lower in HL (8.33% versus 18.4%). The commonest histological subtype was mixed cellularity (45.8% in HL and diffuse mixed variant (31.6%) in NHL. Most cases presented at advanced stage (54.2% in HL, 71.1% in NHL). Hence a distinct clinicopathologic profile was noted in HL and NHL that are comparable to other Indian studies but different from Western studies. Recognition of such characteristic features should assist in providing appropriate diagnosis and suitable management in rural communities having limited access to sophisticated medical services.

**Keywords:** Hodgkin's lymphoma - non-Hodgkin's lymphoma - clinicopathology - rural India

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### Introduction

Lymphoid-hemopoietic malignancies are a significant category of neoplasm in India representing 9.5% of all cancers in men and 5.5% in women (Indian Council of Medical Research, 2001). Among this category of neoplasia the distribution of different subtypes of lymphomas varies across different geographic region of the country (Naresh et al., 2000). Conventionally, Hodgkin's lymphoma (HL) has been classified separately because of the specific identifying cell and limited morphological range together with its distinctive clinical features. In contrast, features of non-Hodgkin's lymphomas (NHL) are much less distinct and more wide-ranging for any given subtype (Isaacson, 2005). Wide range of geographic variation of HL in respect of histologic subtypes, extent of disease at the time of diagnosis, and consequent variations in the treatment responses are well-documented (Dawar and Mangalik, 1978; Talvalkar et al., 1982). Only a few studies have been undertaken in India which describes the clinico-pathologic picture of lymphomas among the rural population (Ramani et al., 1991).

A prospective study was undertaken at North Bengal Medical College and Hospital (NBMCH) which caters six northern districts of the province West Bengal of India

comprising mostly of rural and hilly areas. In this study, clinical presentation, hematologic features classification and staging of patients of lymphomas were analyzed. The aim of the present study was to compare the clinicopathological profile of HL and NHL and to find their geographic pattern in this rural health care center of West Bengal, India. Recognition of different clinical and hematological features in such population will accelerate the process of proper diagnosis and commencement of management.

### Materials and Methods

The study group consists of all cases of lymphomas detected over a period of two years in NBMCH, Darjeeling, West Bengal. Detailed clinical history and thorough clinical examination was done in all cases. All patients were subjected to routine hematological (estimation of hemoglobin, total and differential leukocyte count, platelet count, peripheral smear study for abnormal cells etc.) and biochemical (liver function tests, urea, creatinine, uric acid) investigations. The diagnosis of lymphoma was established by biopsy from lymph nodes or involved tissues, and they were grouped as HL or NHL. The radiological studies included chest radiogram

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**Table 1. Age and Sex Distribution in Hodgkin's (HL) and Non- Hodgkin's Lymphoma (NHL)**

| Lymphoma      | Age range in years |       |       |       |       |       |      | Sex distribution |           |
|---------------|--------------------|-------|-------|-------|-------|-------|------|------------------|-----------|
|               | 1-10               | 11-20 | 21-30 | 31-40 | 41-50 | 51-60 | > 60 | M/F              | Sex Ratio |
| HL (n=48)     | 12                 | 08    | 04    | 12    | 10    | 02    | 0    | 38/10            | 3.8:1     |
| NHL (n=76)    | 08                 | 08    | 04    | 26    | 06    | 12    | 12   | 58/18            | 3.23:1    |
| Total (n=124) | 20                 | 16    | 08    | 38    | 16    | 14    | 12   | 96/28            | 3.43: 1   |

(CXR), ultrasonography (USG) of abdomen, computer axial tomography (CT) of chest. Bone marrow aspiration smears were stained by Leishman's stain. Cell blocks were prepared from the remaining marrow particles, and histological sections were stained by Hematoxylin and Eosin (H&E). Trepine biopsy was also done, stained by H&E and reticulin stain to assess the marrow involvement by the neoplastic cells and reactive fibrosis.

Patients of HL group were classified on the basis of histopathologic diagnosis according to WHO classification (Yung and Linch, 2005) and staging was done by Ann Arbor staging system Cotswolds modifications (Yung and Linch, 2005). Similarly patients of NHL group were classified according to Working Formulation (Non-Hodgkin's Lymphoma Pathologic Classification Project,1982) and staging was done by Ann Arbor staging system (Avivi and Goldstone, 2005). After collecting all data, two groups of lymphomas were classified and compared in respect of clinical features, presentations, groups of lymph nodes involved, different organ involvement, grading and staging.

**Results**

A total of 124 cases of lymphoma were diagnosed during the study period, of them 96 were male and 28 were female; and male female ratio was 3.43: 1. In the study population, 48 cases were diagnosed as HL and 76 cases were as NHL, and the ratio between HL and NHL was 1:1.58. In the HL group, there were 38 male and 10 female cases and the male to female ratio was 3.8: 1. Whereas in NHL group, there were 58 male and 18 female cases and the male female ratio was 3.23:1. A bimodal pattern of age of onset of disease was noted in HL group (Table 1) with 20 cases (41.7%) occurred in the age group 1 to 20 years and 22 cases (45.8%) noted in the age group 31 to 50 years. Bimodal onset of disease was also demonstrated in NHL with 26 (34.21%) cases occurred in the age group of 31 to 40 years, followed by 24 (31.58%) cases occurred above the age of 50 years. The mean age was 28.1 year in

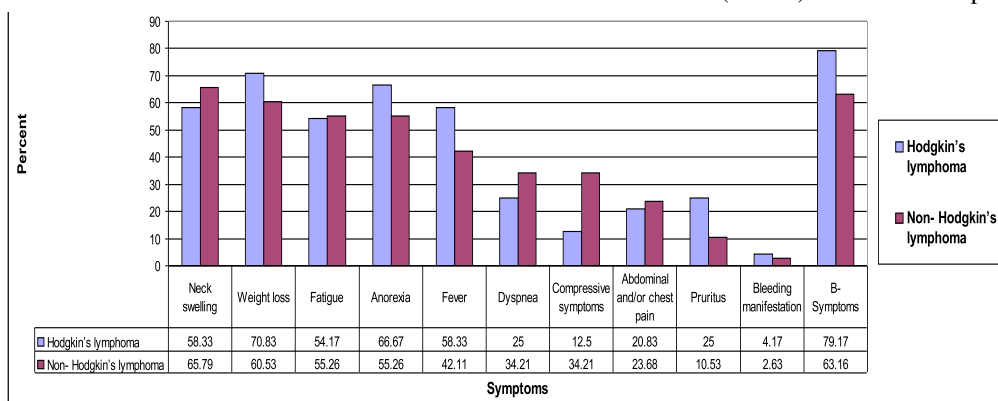
**Table 2. Histopathological Classification of Hodgkin's Lymphomas (n=48)**

| Histopathological classification | No. | Percent |
|----------------------------------|-----|---------|
| Nodular Lymphocyte predominance  | 7   | 14.6%   |
| Lymphocyte rich                  | 1   | 2.1%    |
| Mixed cellularity                | 22  | 45.8%   |
| Nodular sclerosis                | 16  | 33.3%   |
| Lymphocyte depleted              | 2   | 4.2%    |

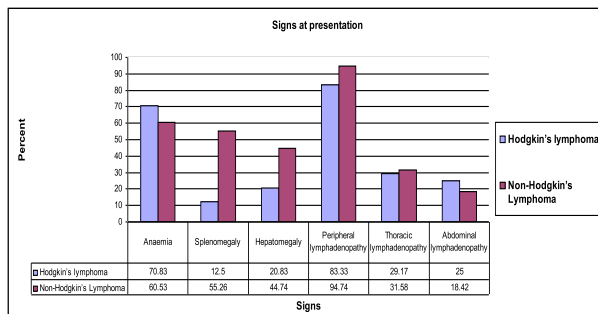
the HL group and 39.9 years in the NHL group.

In the HL group, nodular swelling of neck was the dominant complaint (28 cases, 58.3%), followed by weight loss (in 34 cases, 70.8%), fever (in 28 cases, 58.3%), anorexia (in 32 cases, 66.7%), compressive symptoms due to lymph nodal enlargement (in 6 cases, 12.5%), dyspnoea (in 12 cases, 25.0%), abdominal and /or chest pain (in 10 cases, 20.8%), pruritus (in 12 cases, 25.0%) and bleeding in one case. In the NHL group (Figure 1), neck swelling was also the commonest complain (50 cases, 65.8%) followed by weight loss (46 cases, 60.5%), fever (in 32 cases, 42.1%), anorexia and fatigue (in 42 cases, 55.3% each), compressive symptoms (in 26 cases, 34.2%), dyspnoea (in 26 cases 34.2%), abdominal and /or chest pain (in 18 cases, 23.7%), pruritus (in 8 cases, 10.53%) and bleeding (in 2 case, 2.63%). Occurrence of "B" symptoms (fever >38°C, night sweats, or weight loss >10% of body weight in the last 6 months, or a combination of these) was noted in 38 (79.17%) cases of HL and in 48 (63.16%) cases of NHL. History of addiction was noted in 10 cases, 20.83% (tobacco in 8, alcohol in 2 patients) of HL and 28 cases, 36.84% (tobacco in 26, alcohol in 2 patients) of NHL.

Peripheral lymphadenopathy was the commonest sign, detected in 40 (83.3%) cases of HL and in 72 (94.7%) cases of NHL (Figure 2). Anemia was found in 34 (70.8%) cases of HL and 46 (60.5%) cases of NHL. Hepatomegaly and splenomegaly were found to be more common in NHL in 34 (44.7%) cases and 42 (55.3%) cases respectively, whereas they were found in 10 (20.8%) cases and in 6 (12.5%) cases of HL respectively. Thoracic



**Figure 1. Comparison of Occurrence of Symptoms between Hodgkin's and Non-Hodgkin's Lymphomas**



**Figure 2. Chart Showing Comparative Occurrence of Different Physical Signs in Cases of Hodgkin's and Non-Hodgkin's Lymphoma at Presentation**

lymphadenopathy was found in 14 (29.2%) cases and abdominal lymphadenopathy in 12 (25.0%) cases of HL, whereas they were found in 24 (31.6%) cases and in 14 (18.4%) cases of NHL respectively. In HL group, major lymph node groups involved were cervical in 38 (79.2%) cases, inguinal in 22 (45.83%) cases, axillary in 14 (29.17%) cases and epi-trochlear in 4 (8.33%) cases, and the diameter of lymph nodes were between 2 and 8 cm. In NHL major lymph node groups involved were cervical in 60 cases (78.95%), axillary in 42 (55.3%) cases and inguinal in 30 cases (39.47%), and the average diameter of lymph node ranged from 1 cm to 8 cm. Stomach was involved in one case of HL, whereas gastro-intestinal tract was involved in 5 (6.58%) cases and skin was involved in 4 (5.26%) case of NHL.

Hemoglobin value was below normal level (according to age and sex) in 34 (70.83%) cases of HL and in 54 cases (71.1%) of NHL. We noticed eosinophilia in 14 (29.2%) cases of HL and in 18 cases (23.7%) of NHL. We found lymphocytosis in 4 (8.33%) cases, leukopenia in 3 cases (6.25%) and thrombocytopenia in 1 case of HL at the time of diagnosis. Blast cells were noted in peripheral smear in 4 (5.26%) cases of NHL at the time of diagnosis. Bone marrow involvement by the neoplastic process was detected in 4 (8.33%) cases of HL and in 14 cases (18.42%) of NHL. Reactive changes observed in HL were myelofibrosis in 4 cases (8.33%), myeloid hyperplasia in 2 (4.17%) cases, increased plasma cells in 1 case and marrow hypocellularity in 1 case. Whereas reactive changes detected in NHL were, erythroid hyperplasia in 16 case (21.05%), myeloid hyperplasia in 2 (2.63%) cases and lymphoid hyperplasia in 5 (6.58%) cases. Minor abnormalities of liver function tests (mainly raised alkaline phosphatase level) were noted in 22 cases (45.83%) of HL and in 16 cases (21.1%) of NHL. Abnormality of renal function was noted in none of the HL group but in 1 (2.63%) case of NHL. CXR and CT thorax showed mediastinal lymphadenopathy along with unilateral hilar lymphadenopathy in 8 cases (16.67%), bilateral hilar lymphadenopathy in 4 (8.33%) cases and pleural effusion in 4 cases (8.33%) of HL. On the other hand, we found unilateral hilar lymphadenopathy in 16 cases (21.1%), bilateral hilar lymphadenopathy in 6 (7.89%) cases, paratracheal lymph node enlargement in 10 (13.2%) cases, peripheral parenchymal infiltration in 8 cases (10.53%) and pleural effusion in 8 cases (10.5%) of NHL.

In HL group, mixed cellularity was the commonest (22

cases, 45.8%) histological subtype followed by nodular sclerosis (16 cases, 33.3%); lymphocyte predominant (7 case, 14.6%); lymphocyte depleted (2 cases, 4.17%) and lymphocyte rich (1 case, 2.08%). Where as in NHL group, diffuse mixed variant was the commonest (24 case, 31.58%) followed by diffuse large cell (14 cases, 18.42%). Low grade lymphoma was found in 18.4%, intermediate grade lymphoma in 55.3% and high grade lymphoma in 26.3% patients.

At presentation, 29.2% cases of HL and 7.89% of NHL were in stage I; 16.7% cases of HL and 21.1% cases of NHL were in stage II; 45.83% cases of HL and 44.7% cases of NHL were in stage III; and 8.33% cases of HL and 26.32% cases of NHL were in stage IV.

## Discussion

NBMCH is the sole tertiary care center for six northern districts of the province of West Bengal, India which include mostly rural and hilly areas. Cases described in this study represent all lymphomas that occurred in this region and referred to this institution. Therefore these patients will provide an insight into the clinico-pathological profiles of lymphomas in this area of Eastern India.

We found that the mean age of onset of HL was 28.1 year, and 41.7% cases occurred in the age group between 1 to 20. Worldwide, HL occurs commonly in the age group 15 -34 (Yung and Linch, 2005). In India, the mean age of presentation is 34 years (Ramani et al., 1991). The male to female ratio of HL in the present study was 3.8:1 whereas the ratio was 6.75:1 in the study of Ramani et al., (1991) and higher than in the West. This might be the result of the higher preponderance of mixed cellularity HL in Indian population (Bhutani et al., 2002).

The age distribution of NHL in the present cohort was different from that noted in the Western literature but similar to elsewhere in India (Garg et al., 1985; Ramani et al., 1991). However, this was considerably low compared to the average age of onset around 50 to 55 years in Western countries (Elias, 1979; Anderson et al., 1982; Straus et al., 1983). We observed that in NHL the male to female ratio was 3.23:1, whereas the same was 1.5:1 in Western studies (Elias, 1979; Anderson et al., 1982; Straus et al., 1983). On the other hand, in north India the ratio was found to be 4.5:1 (Garg et al., 1985). Male predominance was observed in all histological subtypes in the present series which was similar to that of Elias (1979). We observed a higher occurrence of "B" symptoms (79.17%) in HL. Similar high frequency of B symptoms (73%) was reported by Chandi et al., (1998). The frequency of "B" symptoms (63.2%) in NHL in our study was similar (65.2%) to the findings of Ramani et al. (1991) but higher (49.6%) compared to the observation of Garg et al. (1985). In a large Indian study (Chandi et al., 1998), the unfavorable factors in HL that decreased overall survival were age more than 40 years, presence of 'B' symptoms, lymphocyte depletion histological subtype and stage IV disease.

Our findings for lymphadenopathy contrasted with the observations of Ramani et al. (1991) 6 where mediastinal lymph node involvement was found to be more common

in HL (38.7%). Among the organ showing extranodal involvement liver was the commonest site followed by spleen. Bone marrow was involved in 8.33% cases of HL which was comparable to 9.68% as reported by one Indian study (Ramani et al., 1991), 9.4% by another such study (Chandi et al., 1998) and even similar (10%) to one Western study (Medeiros and Greiner, 1995). Bone marrow involvement was lower than in a similar study conducted in India (Ramani et al., 1991). Western studies noted that bone marrow examination could detect disease in 20 to 40% of all NHL cases (Moormeier et al., 1990).

The most common subtype of HL noted in our study was mixed cellularity followed by nodular sclerosis. Similar observation was noted by other studies done in India (Talvalkar et al., 1982; Ramani et al., 1991; Chandi et al., 1998). In contrast nodular sclerosis variant was the most common subtype (51%) followed by mixed cellularity (23.8%) in a large Western registry (Medeiros and Greiner, 1995).

The Working Formulation (Non-Hodgkin's Lymphoma Pathologic Classification Project, 1982) used for classification of NHL in this study is based on histomorphological study that is easily reproducible and does not require expensive and sophisticated immunophenotyping or genetic studies. The most common subtype of NHL noted in our study was diffuse mixed cell subtype (intermediate grade). As a group, the diffuse lymphomas (includes all intermediate grade as well as large cell immunoblastic type of working classification) accounted for 54 (71.1%) cases. In contrast nodular (follicular) lymphomas accounted for only 6 (7.89%) cases. Our ratio between diffuse and nodular lymphomas was 9.0:1, similar to that (9.8:1) observed by Garg et al., (1985). Comparison of histological subtypes of NHL with earlier Indian studies was difficult, as most studies were based on older classification of NHL. In HL cohorts 45.84% were in limited stage (stage I & II) and 54.16% were in advanced stage (stage III & IV). In contrast 71.06% of NHL cases were in advanced stage of disease at the time of presentation.

The higher incidence of diffuse NHL might be related to advance clinical staging, associated with decreasing degree of nodularity (Tokunaga et al., 1980). Histological progression from nodularity to diffuse pattern was reported in many studies (Hubbard et al., 1982; Garvin et al., 1983). We could not compare histological types between two types of lymphoma as their classifications are different.

We observed a distinct geographic pattern of both HL and NHL in Northern region of West Bengal, India. We found lower age of onset, higher male female ratio, higher occurrence of B symptoms, and advance stages of diseases at presentation in both. We noted predominance of mixed cellularity histological pattern in HL and diffuse histological patterns in NHL, comparable with findings of other Indian studies but e significantly different from the pattern observed in Western countries. Identification of this distinct pattern of clinical and hematological profile in rural population of this region having limited access to advanced medical facilities will hasten the diagnosis and provide a chance for suitable management.

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