

## Pattern of T-cell Non-Hodgkin's Lymphoma in a Tertiary Care Center in North East India

### Abstract

**Context:** The non-Hodgkin's lymphomas (NHLs) are lymphoid neoplasms that arise primarily in the lymph nodes. They are classified into B-cell, T-cell, and natural killer cell types and are subtyped on the basis of morphologic and immunohistochemical studies. T-cell neoplasms are clonal tumors of mature and immature T-cells at various stages of differentiation. T-cell lymphoma is common in Asia compared to Europe and America. The pattern and prevalence of T-cell lymphoma in India are, however, different from that of other Asian countries. **Aims:** The main aim of this study is to analyze the prevalence and pattern of T-cell NHL in North East India, as less number of studies have been carried out in this part of the country. **Settings and Design:** A 5-year retrospective study (2012–2016) was carried out in our institute, which is a regional cancer center located in North East India. **Materials and Methods:** Five-year records of previously diagnosed cases were obtained, and then the hematoxylin- and eosin-stained sections and the immunohistochemistry slides were reviewed and studied. **Results:** A total number of 294 cases of NHL were reviewed in the study period. Seventy-one cases were found to be of T-cell NHL type which comprised 24% of the total NHL. Peripheral T-cell lymphoma not-otherwise specified (PTCL-NOS) (62%) was the most common followed by anaplastic large cell lymphoma (27%). T-lymphoblastic lymphoma (7%) was common in children and young adults. **Conclusion:** PTCL-(NOS) was found to be the most common T-cell lymphoma. Treatment of most of the cases was by chemotherapy using the cyclophosphamide, doxorubicin, vincristine, and prednisone regimen.

**Keywords:** Immunohistochemistry, North East India, peripheral T-cell lymphoma, T-cell non-Hodgkin lymphoma

### Introduction

T-cell lymphomas are a heterogeneous group of neoplastic disorders of T-cells.

Its classification depends on morphologic, immunophenotypic, and genetic studies. A number of newer entities have been added, and the nomenclature of few others has been changed in the new revised 2016 WHO Classification of T and natural killer (NK) cell neoplasms.<sup>[1]</sup> According to 2014 World Cancer Report, there were 566,000 new lymphoma cases of which T-cell neoplasms comprised only 10%–15% of all non-Hodgkin's lymphomas (NHLs).<sup>[1,2]</sup>

T-cell lymphomas are common in Asia primarily due to a lesser proportion of certain B-cell lymphomas.<sup>[3]</sup> T-cell NHL also shows a racial predisposition toward Asians.<sup>[4]</sup> In India, the pattern is different from the rest of Asia. The most

common T-cell lymphomas in India are peripheral T-cell lymphoma not-otherwise specified (PTCL-NOS), anaplastic large cell lymphoma (ALCL), and pre-T-lymphoblastic lymphomas (T-LBL).<sup>[2]</sup>

T-cell lymphoma has an aggressive course compared to most B-cell lymphomas.<sup>[3]</sup> PTCL and T-LBL had a 5-year overall survival of <30% compared to most high Grade B-cell lymphomas. ALCL was an exception with a 5-year overall survival of more than 70%.<sup>[5]</sup>

Compared to the rest of India, a lesser number of studies on T-cell NHL have been carried out in the North Eastern region of the country, and therefore, this study was carried out to analyze the prevalence and pattern of T-cell lymphomas.

### Materials and Methods

Patients coming to our institute between January 2012 and December 2016, who

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were diagnosed as T-cell lymphoma were included in the study. The hematoxylin- and eosin (H and E)-stained sections and the immunohistochemistry slides, as well as the patient particulars, clinical, radiological, and biochemical findings, wherever available, were reviewed. In cases where the H- and E-stained slides were not found, sections were obtained from the paraffin blocks. The IHC panel used for T-cell lymphoma comprised of CD45, CD3, CD20, CD30, EMA, ALK, and TdT. Cases, for which proper history and investigation details were unavailable, were excluded from the study. Cases of suspected lymphoma on morphology, and without IHC findings were excluded from the study.

**Results**

**Prevalence**

Over a period of 5 years, from 2012 to 2016, 294 cases of NHL were diagnosed after complete morphological and immunohistochemical workup, and of these, 71 (24%) cases were classified as T-cell lymphomas [Figure 1].

**Age pattern**

The middle-aged population was the commonly affected age group. PTCL-NOS was the most common T-cell lymphoma in the middle-aged and the elderly population. It presented at a median age of 46.5 years. ALCL presented at a median age of 36 years. T-LBL was common in

children and young adults and presented at a median age of 19 years [Table 1 and Figure 2].

**Sex pattern**

Overall males were affected more (76%) than females (24%) [Table 1 and Figure 3].

**Subtype**

PTCL-(NOS) was the most common subtype of T-cell lymphoma with 44 cases (62%), followed by ALCL with 19 cases (27%). Five cases (7%), all males, were diagnosed as TLBL. Remaining three cases (4%) could not be subtyped and were placed under T-cell NHL (others) [Tables 2, 3 and Figure 4].

**Nodal and extranodal disease**

Of the 71 cases studied, 65 (91.5%) cases had definite involvement of lymph nodes without any primary extranodal disease. Extranodal lymphoma was seen in six cases (8.45%). Of the nodal lymphomas, most of the cases presented with cervical lymphadenopathy. Generalized lymphadenopathy was present in few patients. Five patients presented with inguinal adenopathy. Axillary and abdominal lymphadenopathy was noted in few other cases. Mediastinal mass was detected in few cases [Table 4]. Of the extranodal lymphomas, three cases arose from the nasopharynx, one from the oropharynx, one from nasal cavity, and one was a thigh mass.

**Discussion**

T-cell and NK-cell neoplasms are uncommon neoplasms. According to International T-cell Lymphoma study

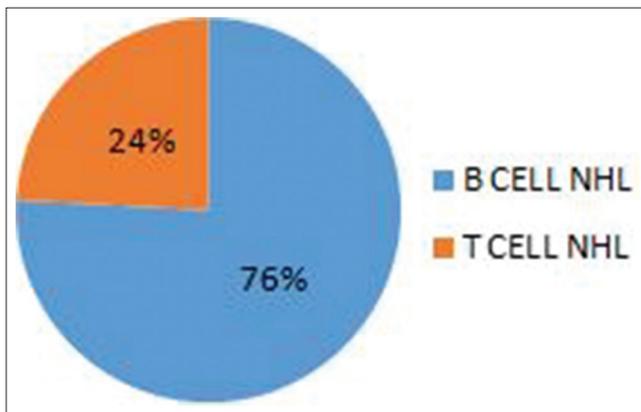


Figure 1: Prevalence of T-cell non-Hodgkin's lymphoma

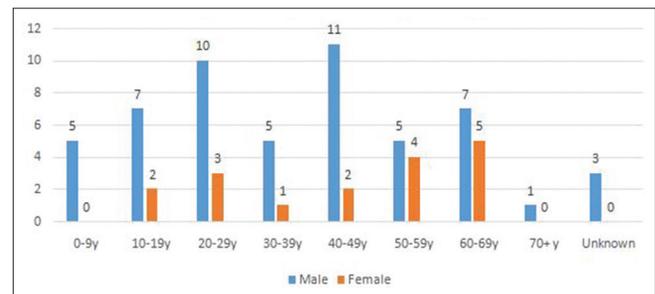


Figure 2: Age and sex pattern of T-cell non-Hodgkin's lymphoma

**Table 1: Age and sex distribution of T-cell non-Hodgkin's lymphoma**

Age (years)	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70+	Unknown age	Total
Male	5 (3 ALCL, 2 TLBL)	7 (2 TLBL, 5 PTCL)	10 (1 TLBL, PTCL-4, ALCL-4, TNHL-1)	5 (3 PTCL, 1 ALCL, 1 TNHL)	11 (8-PTCL, 3-ALCL)	5 (5 PTCL)	7 (6 PTCL, 1 ALCL)	1 PTCL	3 PTCL	54 (76%)
Female		2 (1 ALCL, 1 PTCL)	3 (ALCL-1, PTCL-2)	1 (PTCL)	2 (1 PTCL, 1 ALCL)	4 (3-ALCL, 1-TNHL)	5 (4 PTCL, 1 ALCL)			17 (24%)
Total	5	9	13	6	13	9	12	1	3	71

ALCL – Anaplastic large cell lymphoma; PTCL – Peripheral T-cell lymphoma; TNHL –T-cell non-Hodgkin's lymphoma; TLBL – T-lymphoblastic lymphoma

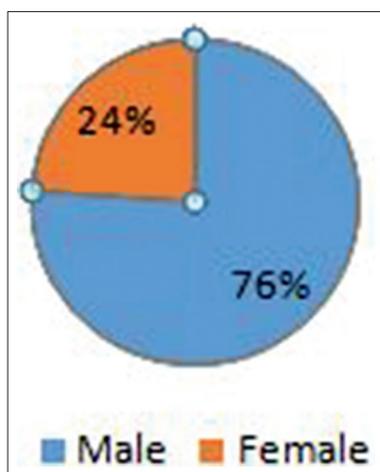


Figure 3: Male-to-female ratio

group series, all types of T-cell lymphomas and NK cell disorders made up only 12% of NHL cases.<sup>[6]</sup> PTCL (unclassified) (25.9%) and angioimmunoblastic T-cell lymphoma (AITL) (18.5%) are the most common T-cell lymphomas worldwide.<sup>[4]</sup>

In India, the incidence rate of NHL in 2012 was 2.2/100,000, and the mortality rate was 1.5/100,000.<sup>[2]</sup> T-cell lymphoma comprises 10%–15% of cases. PTCL-NOS, lymphoblastic lymphoma, and ALCL are the three common subtypes of T-cell NHL seen in the Indian subcontinent according to Nair *et al.*<sup>[2]</sup> The frequency of extranodal NK/T-cell lymphoma (NKTCL) in India is higher than that in Western countries but lower than that in other Asian countries such as China, Hong Kong, and Taiwan.<sup>[2]</sup> Adult T-cell leukemia/lymphoma (ATLL) is rare in India.<sup>[2]</sup>

In India, a study by Naresh *et al.* found T-cell lymphomas to comprise 15.2% of all cases of NHL.<sup>[7]</sup> In our study, T-cell NHL comprised 24% of all cases of NHL.

Men are affected more than women.<sup>[4]</sup> The male-to-female ratio is 1.6 in Asia compared to 1.2 and 1.1 in North America and Europe, respectively.<sup>[2]</sup> In our case, 76% of the affected were males and rest 24% were females. The male-to-female ratio was found to be 3.2:1.

The median age in India is lower than in other countries.<sup>[2]</sup> PTCL-(NOS) is common in the middle-aged population; ALCL has a wider age range whereas T-LBL is found to be more common in adolescent males.

ALK-positive ALCL accounts for about 3% of adult NHL and 10%–20% of childhood lymphomas.<sup>[4,6]</sup> Its occurrence is more common in the first three decades of life and shows a male predominance. The peak incidence of ALK (negative) ALCL is in adults (aged 40–65 years).<sup>[4]</sup>

In our study, the median age of presentation of PTCL was found to be 46.5 years, median age for ALCL was 36 years, and 19 years for LBL.



Figure 4: Subtypes of T-cell lymphoma

Table 2: Subtypes of T-cell lymphoma

Subtype	n (%)
TLBL	5 (7)
PTCL (NOS)	44 (62)
ALCL	19 (27)
Others (TNHL)	3 (4)

ALCL – Anaplastic large cell lymphoma; PTCL – Peripheral T-cell lymphoma; TNHL – T-cell non-Hodgkin’s lymphoma

Table 3: Male and female distribution of various subtypes

	Male	Female
PTCL	35	9
ALCL	12	7
TLBL	5	0
Other TNHL	2	1

ALCL – Anaplastic large cell lymphoma; PTCL – Peripheral T-cell lymphoma; TNHL – T-cell non-Hodgkin lymphoma; NOS – Not otherwise specified; TLBL – T lymphoblastic lymphoma

Table 4: Nodal/extranodal disease

Nodal	Extranodal
65 (91.5%)	6 (8.45%)
	Nasopharynx-3 (PTCL)
	Oropharynx-1 (PTCL)
	Nasal cavity-1 (PTCL)
	Thigh-1 (ALCL)

ALCL – Anaplastic large cell lymphoma; PTCL – Peripheral T-cell lymphoma

Morphology is essential for the initial diagnosis as certain architectural patterns and cell types are characteristic of specific lymphomas, and immunohistochemistry is essential for confirmation of the diagnosis and to exclude reactive changes. A panel of markers is used to confirm the diagnosis of lymphoma, to classify into B- and T-cell types, and to further subtype these lymphomas.

According to the International PTCL study, PTCL-NOS was the most common subtype in both North America and Europe, whereas NK/T-cell lymphoma and ATLL were common in Asia. ATLL was frequent in Japan but was rare in the other Asian countries. NK/T-cell lymphoma made up 44% of the cases in Asia excluding Japan.<sup>[6]</sup>

In another study, by Ko *et al.* in Korea, 17.2% of cases were diagnosed as T-cell NHL. The most common subtype was extranodal NKTCL, nasal type (33.6%), followed by PTCL (U) (29.8%) and ALCL (10%).<sup>[8]</sup> In contrast, the three most frequent subtypes in the West were PTCL-U (60.8%), ALCL (13.4%), and Nasal type (7.8%).<sup>[8]</sup>

In India, in one of the first studies carried out by Naresh *et al.*, it was found that T-LBL and ALCL were more prevalent in India compared to PTCL and NK/T-cell lymphoma, nasal type, seen in other Asian countries.<sup>[7]</sup>

In a study carried out by Arora *et al.*, PTCL-(NOS) (5.91%) was the most common T-cell lymphoma followed by ALCL (5.04%).<sup>[2,9]</sup>

In a study carried out by Burad *et al.* in the Southern part of India, mature T-cell NHL comprised 17.4% of all cases of NHL. PTCL-(NOS) (26.1%) was the most common T-cell lymphoma followed by ALCL (22.8%).<sup>[10]</sup>

In a hospital-based study carried out by Hazarika *et al.* in this institute, T-cell lymphoma comprised only 18.9% of the total lymphoma cases. ALCL was the most common T-cell lymphoma followed by PTCL.<sup>[11]</sup>

Our study showed results similar to most of the Western and few Indian studies (Arora *et al.*, Burad *et al.*).<sup>[9,10]</sup> T-cell NHL comprised 24% of all cases of NHL, and the most common was PCTL-(NOS) (62%), followed by ALCL (27%) and T-LBL (7%). The pan T-cell marker CD3 was used to subclassify the lymphomas as T-cell lymphomas. This combined with the characteristic morphology and additional markers such as TdT, CD30, EMA, and ALK were helpful in subtyping the T-cell lymphomas. Few cases (4%) were found to be CD3 positive but immunohistochemical and morphologic correlation could not be done, and they have been categorized as T-cell NHL (others).

Most patients presented with generalized lymphadenopathy. Bone marrow involvement was seen in two cases of PTCL. Extranodal disease was present in five cases of PTCL and one case of ALCL.

ALCL was diagnosed in 27% of cases (19 cases). The characteristic morphology along with the specific markers – CD30, EMA, and ALK were used to diagnose the ALCL cases. ALK-positive ALCL is common in young children and has a better prognosis compared to ALK-negative ALCL.<sup>[3]</sup>

T-LBL presents mostly as a mediastinal mass and is common in adolescent males. In our study, 7% cases were reported as T-LBL, and the median age was 19 years. All the cases were males. Mediastinal involvement was present in all the cases and bone marrow was uninvolved in three of the cases. The cases were immunoreactive for CD3 and TdT.

Extranodal presentation was seen in 8.45% cases (6 cases), and nodal lymphoma in 91.5% cases. All the extranodal

lymphomas were PTCL-(NOS), except for one case of ALCL in the thigh. Extranodal presentation is usually very common in T-cell lymphoma. No case of ATLL was found in this study. None of the other T-cell lymphomas could be detected in this study.

Laboratory investigations such as complete blood count, lactate dehydrogenase, uric acid, and viral markers, along with computed tomography and positron emission tomography (PET) reports are used for staging lymphoma cases. Males have a bad prognosis and Epstein-Barr virus-positive cases have a poor outcome. The International Prognostic Index (IPI) is used to prognosticate subtypes of PTCL and NK/T-cell lymphomas.<sup>[6]</sup> Most T-cell lymphomas including those in the low-risk IPI category have a poor outcome, compared with aggressive B-cell lymphomas such as diffuse large B-cell Lymphoma. IPI is not helpful in subtypes such as ATLL, Enteropathy type, hepatosplenic PTCL, and extranasal NKTCL.<sup>[6]</sup>

ATLL, AITL, and PTCL-(NOS) have a worse prognosis than ALCL. The ALK-positive ALCL cases have a 5-year overall survival of 70% compared to a 5-year overall survival of 49% for ALK-negative ALCL.<sup>[6]</sup>

## Conclusion

T-cell NHL comprised only 24% of all cases of NHL, and PTCL was found to be the most common subtype, followed by ALCL and T-LBL. Morphology combined with immunohistochemistry helps in the accurate diagnosis and subclassification of T-cell lymphomas. FDG-PET has emerged as a useful tool for delineation of disease extent and thereby aiding in disease staging. Treatment is by chemotherapy – six cycles of cyclophosphamide, doxorubicin, vincristine, and prednisone with or without Rituximab. Radiotherapy is indicated in few selected cases. T-cell lymphoma has an overall worse prognosis than B cell lymphoma. Newer treatment modalities and advanced diagnostic tools aim at improving the disease outcome in the near future.

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## Conflicts of interest

There are no conflicts of interest.

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