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A Histomorphological and Immunohistochemical Study of Malignant Nodal Lymphomas

Burji Rutuja, A[1], B. R. Vani[2]*, V. Srinivas Murthy[1]

[1]ESI Post Graduate Institute of Medical Science and Research, ESI Hospital, 41st cross road, Rajajinagar, Bengaluru, Karnataka 560010,India
[2]Professor ESIC Medical College and Hospital Sedam Road Gulbarga-585106 Karnataka

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***Corresponding Author**
B. R. Vani

Professor ESIC Medical College and Hospital Sedam Road Gulbarga-585106 Karnataka

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A B S T R A C T

Background: Lymphomas are malignant clonal neoplasms of lymphocytes and their precursor forms. They are mainly of two types – non-Hodgkin lymphoma (NHL) and Hodgkin lymphoma (HL). Incidence of lymphomas, especially NHL is increasing worldwide and also in India, therefore morbidity due to the disease is also increasing. Thus, knowledge of its pathogenesis, histomorphology and immunophenotype will lead to possible early diagnosis and treatment of this potentially curable disease. In this background, a study has been conducted. ***Objective:*** 1) To study the histomorphological features of malignant nodallymphomas. 2) To evaluate the expression of a panel of immunohistochemical markers for categorisation of nodal malignant lymphomas and theirsubtypes. ***Methods:***A study was conducted for a period of 6 and a half years from January 2012 to June 2018 at the Department of Pathology, ESIC Medical College and PGIMSR with a sample size of 75 cases. All the cases diagnosed as nodal lymphomas during that period, were included in the study. Immunohistochemistry (IHC) was performed. Data was compiled onto a masterchart and descriptive statistics performed. ***Results***: Majority patients presented with cervical lymphadenopathy. NHL was morecommon than HL among nodal lymphomas. Among NHL, diffuse large B cell lymphoma was the most common.AmongHL,nodularsclerosiswasthemostcommonsubtype.BothHLandNHLhad a male predominance. The mean age in HL was lower than that inNHL. ***Interpretation and Conclusion*:** Clinicopathological correlation and a goodhistomorphological diagnosis,supplementedbyimmunohistochemistrywillenableefficientdiagnosisofmalignant nodal lymphomas, and enable application of targeted therapyoptions

Keywords: Lymphoma; Subtypes; Immunohistochemistry; Histomorphology.

INTRODUCTION

Lymphomas are malignant clonal neoplasms of lymphocytes and their precursor cells, arising from a single transformed cell of T, B or null phenotypes. (Goldblum *et al*., 2011) In adults, lymphoma constitutes 3.4% of all cancers, while in children they are the second most common cancers, second only to leukaemia (Arora *et al*., 2009).

With the understanding that lymphoma cells are those which are arrested at a particular stage of maturation, it became evident that their diagnosis and classification depends on immunohistochemistry (IHC) or flow cytometry to detect the lineage specific antigens and markers of maturity. (Kumar *et al*., 2014). The WHO adopted REAL classification, along with immunologic and genetic features to publish the WHO 2001, 2008 classifications and an update in 2017. Better understanding of immunologic and molecular processes has enabled detection of subtypes having diverse aetiologies, different prognosis, with targeted treatment options and outcomes.

There is an increasing incidence of lymphomas worldwide and in India, especially Non Hodgkin lymphoma (NHL). Nair *et al*.,'s (2016) study found the mortality rate of NHL in India to be 1.5/100000.

In this background, a study has been attempted to examine the clinicopathological features, histomorphology and immunohistochemical profiles of nodal lymphomas.

Etiopathogenesis

Though extremely varied, a few common factors which can be considered in the etiopathogenesis are as follows:

- Chromosomal Translocations and Other Acquired Mutations. Ex: t(8;14 in Burkitt lymphoma and t(14;18) in follicular lymphoma). Also causal are chromosomal region gains and losses and genomic aberrations producingoncoproteins.
- Proto oncogene activation, especially during antigen receptor gene rearrangement and diversification, in the germinal centre Bcells.
- Class switching and somatichypermutation.
- Upregulation of AID (activation-induced cytosinedeaminase).
- Inherited Genetic Factors: Examples - Fanconi's anaemia and Bloom syndrome,rarely Down's syndrome and type Ineurofibromatosis
- Viruses: Three lymphotropic viruses. the human T cell leukaemia virus -1 (HTLV-1), Ebstein – Barr virus (EBV) and Kaposi sarcoma- Herpes virus/human herpesvirus-8 (KSHV/HHV-8). HCV (Hepatitis C virus) and SV40 (Simian virus 40) have also been implicated. (Ekström-Smedby *et al.*,2006).
- Chronic Immune Stimulation: by agents like Helicobacter pylori and gluten in gastric B cell lymphomas and intestinal T cell lymphomasrespectively.
- Other bacteria like Borrelia burgdorferi and chlamydia have been associated in cutaneousMALTlymphomaandocularMALTlymphomasrespectively(Swerdlow*et al*., 2008).
- Iatrogenic Factors like chemotherapy and ionisingradiation.
- Smoking
- A study conducted by Zhang *et al*., (2014) also found inverse association of lymphoma occurrence with higher intake of fruits and vegetables suggesting a role of dietary factorsalso.

Methodology

A study on all cases of nodal lymphoma was conducted (from January 2012 to June 2018) for a period of 6 and a half years.

SAMPLE SIZE OF ESTIMATION: The proportion of non-Hodgkin lymphoma was presumed to be 65% (based on previous studies). The sample size for the present study was calculated with 80% power, 95% confidence interval, relative precision of 11% and design effect of 1.
The sample size was estimated to be 73 and was calculated using www.OpenEpi.com.

Sample size: 75 cases

ExclusionCriteria:

1. Extranodallymphomas
2. Recurrent cases and patients started ontreatment.
3. Leukemias
4. Plasma celldisorders.

Both lymph node biopsies and specimens were considered. Clinical data was collected. Gross examination was done. Specimens were fixed in 10% neutral buffered formalin and representative bits taken. Tissue bits were subjected to routine processing in automatic tissue processor STP-120 and embedded in paraffin wax. 3-4µm sections were taken with Thermoscientific Rotary microtome HM355S and stained with haematoxylin and eosin using autostainer.

Immunohistochemistry was performed using the peroxidase-antiperoxidase method with secondary antibodies from BioGenex manufacturer. A panel of markers such as CD20, CD15, CD30, CD3, CD5, CD45, BCL2, and BCL6 were used as per case requirement.

Basedontheimmunostain,subtypingofmalignantnodallymphomaswasdoneasperthecases classified into sub types as per WHO classification(2008).

Statistical Analysis:

ThedatawascompiledintoamasterchartusingMicrosoftExcelsoftware.Descriptivestatistics were performed for age distribution, sex distribution, clinical features, distribution of various subtypes of NHL and HL. Numeric variables were expressed as mean and non-numeric as frequencies and percentages. The results were analysed using SPSS software version20.

RESULTS

In the present study, a total of 75 cases of nodal lymphomas were evaluated, out of which, majority 49 (65.33%) were non-Hodgkin lymphomas. Rest 26 cases were of Hodgkin lymphomas constituting 34.67%cases.

Table 1: Number and Age distribution of NHL and HL in nodal lymphomas

	NHL Number (%) 49 (65.33)	**HL Number (%) 26 (34.67)**	**Total 75**	**% (100)**
0-9	1(1.3)	1 (1.3)	2	2.6
10-19	0(0)	2(2.6)	2	2.6
20-29 (2^{nd} decade – Maximum HL cases)	1(1.3)	8 (10.7)	9	12
30-39	7 (9.3)	1 (1.3)	8	10.6
40-49	11 (14.7)	4 (5.3)	15	20
50-59 (5^{th} decade – Maximum NHL cases)	18 (24)	4 (5.3)	22	29.3
60-69	10 (13.3)	3(4)	13	17.3
70-79	2(2.6)	2(2.6)	4	5.3
Total	49 (65.3)	26 (34.7)	75	100

Theagedistributionofnodallymphomasrangedfrom6to79yearswithameanageof 45.7 years. The age range of NHL was 6 to 79 years with a mean of 49.5 years.

InHodgkinlymphoma,agerangedfrom6to72yearswithameanagebeing38.5years.There wasastatisticallysignificantdifferencebetweentheHodgkinandnon-Hodgkincasesinterms f mean age with equal variances assumed (t = 3.2; p = 0.002).

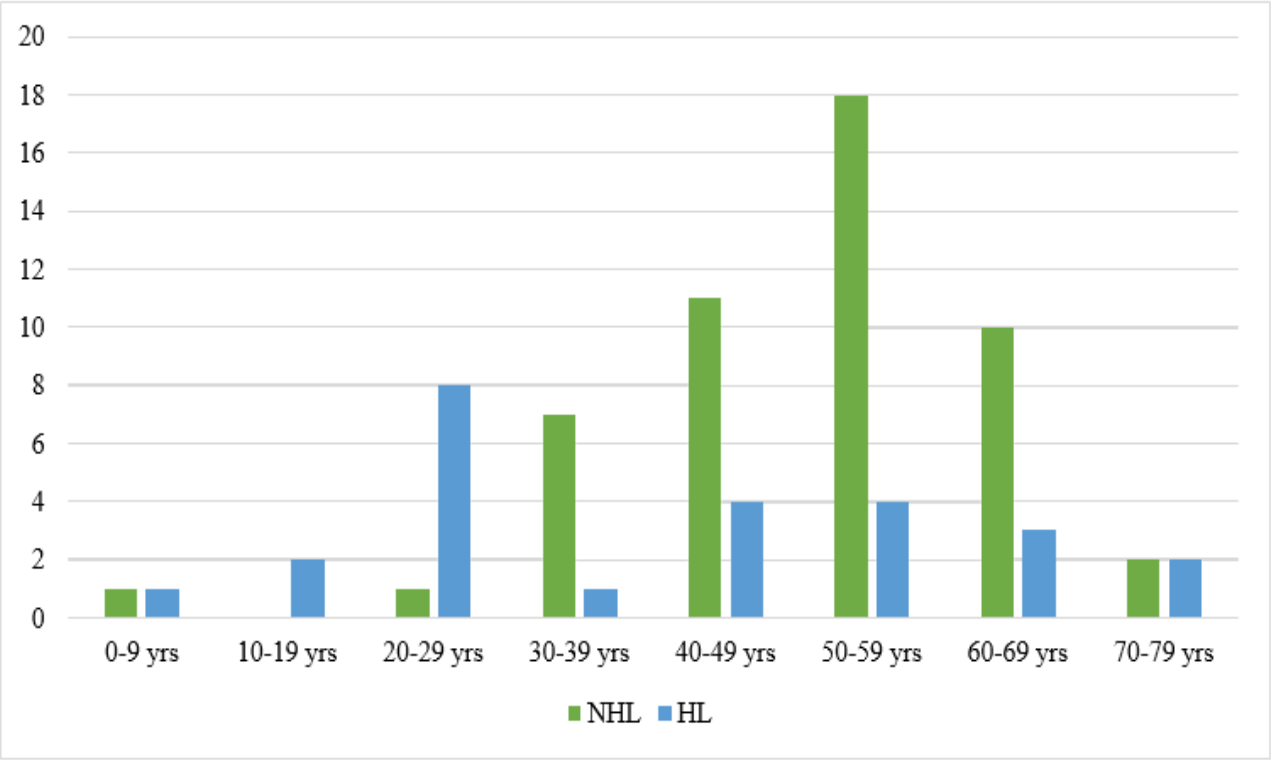

Figure 1: Age distribution of NHL and HL in nodal lymphomas

Sex Distribution in nodallymphomas

Both non-Hodgkin and Hodgkin lymphomas exhibited a male predominance. A total of 50 (66.6%) cases were male and 25 (33.4%) were female with an overall M:F ratio of 2:1. The M:F ratio in NHL and HL was 1.7:1 and 2.7:1 respectively.

There was no statistically significant difference between the sex distribution in either Hodgkin or non-Hodgkin lymphoma. (χ^2 = 0.736; p = 0.391). In both NHL and HL, females presented at earlier age.

Table 2: Sex distribution of NHL and HL in nodal lymphomas

Sex	NHL n= 49 (%)	HL n=26					Total	Percentage (%)
		NS	MC	LR	LD	NLPHL		
Male	31 (41.3)	7 (9.3)	8 (10.7)	2 (2.7)	1 (1.3)	1 (1.3)	50	66.6
Female	18 (24)	5 (6.7)	2 (2.7)	-	-	-	25	33.4
Total	49	12	10	2	1	1	75	100
		26						

Table 3: Mean age in males and females

Mean age in male		Mean age in female	Overall mean age
NHL	51	46.5	49.5
HL	39.3	36.5	38.5

ClinicalPresentation

Mostcommonclinicalpresentationwasonlylymphadenopathy in both NHL and HL (81.3%). B symptoms like fever, drenching night sweats, unexplained weight loss (>10% of total body weight) were seen in a total of 18.7% of cases. One case was incidentally detected in the axillary lymph nodes of a patient who underwent modified radical mastectomy specimen for infiltrating ductal carcinoma breast.TwocaseswerepreviouslydiagnosedasKoch'sandhadtakentreatmentforthe same.

Table 4: Groups of lymph nodes affected by NHL and HL in nodal lymphomas

Group of LN affected	NHL Number (%)	HL Number (%)	Total	%
Cervical	30 (40)	18	48	64
Inguinal	11 (14.7)	2 (2.6)	13	17.3
Axillary	3 (4)	5 (6.7)	8	10.7
Submandibular	3(4)	0(0)	3	4
Supraclavicular	1(1.3)	1(1.3)	2	2.7
Submental	1(1.3)	0(0)	1	1.3
Total	49(64.3)	26 (34.7)	75	100

Table 5: Size of largest lymph node in NHL and HL

Size of largest lymph node	NHL (%)	HL (%)	Total	%
2cm to 5cm	23 (30.7)	12 (16)	35	46.7
Less than 2cm	22 (29.3)	12(16)	24	45.3
More than 5cm	4 (5.3)	2 (2.7)	6	8

Eighteen cases (32%) had a fleshy consistency and five had a nodular appearance, 3 of which were follicular lymphomas.

Among NHL, majority was formed by B cell neoplasms constituting 79.6% whereas T cell neoplasms constituted 20.4%.

Subtypes of B cell NHL are denoted in Figure 2.

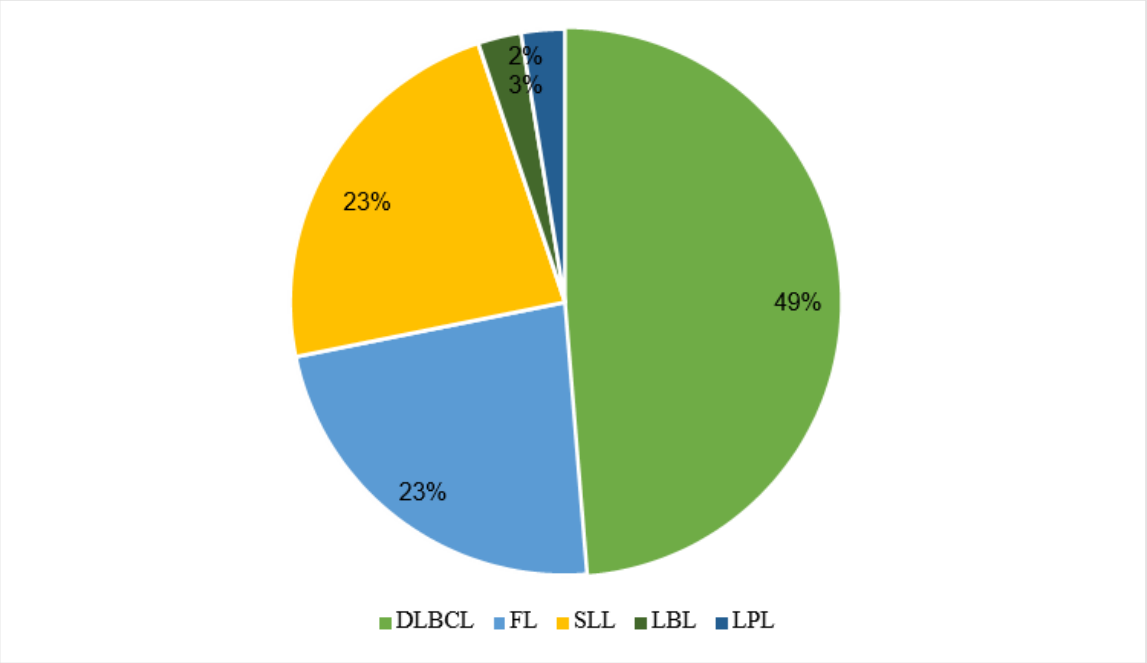

Figure 2: Histological subtypes of B cell NHL

Oftheninecases(23%)offollicularlymphoma,twoweregrade1,fourweregrade2andthree belonged to grade 3. IHC in SLL cases showed CD 20 positivity in 8 (88.9%) cases. CD5 positivityandCD10negativitywasseeninall(100%)cases.LPLwascharacterisedbymixed population of which, CD 20 was immunoexpressed in the lymphocytes. LBL cells were found to express CD99 positivity.

Subtypes of T cell NHL

Peripheral T cell lymphoma (PTCL) was most common among T cell lymphomas and constituted 60%. Two cases (20%) each of angioimmunoblastic T cell lymphoma (AILT) and anaplastic large cell lymphoma (ALCL) were found. CD3 and CD5 positivity in all cases characterised T cell NHL.

Both cases of ALCL showed characteristic CD30 positivity in IHC. Also, a differential of metastatic deposits was ruled out in one case by proving CK negativity.

Table 6: Subtypes of Hodgkin lymphoma

Subtype	Number	% of all HL	% of all nodal lymphomas (Total =75)
Nodular sclerosis	12	46.1	16
Mixed cellularity	10	38.6	13.3
Lymphocyte rich	2	7.7	2.7
Lymphocyte depleted	1	3.8	1.3
NLPHL	1	3.8	1.3
Total	26	100	34.6

Immunophenotype of HL

TheHLcasesweresubdividedintofivecategories(A-E)basedonKonkay*etal*.,'s(2016)study. This was based on positivity or negativity of the RS cells for CD15, CD30 andCD20.

Table 7: Immunophenotype of RS cells in HL

Groups	CD15	CD30	CD20	NS	MC	LR	LD	NLPHL	Total
Group A	+	+	-	**6**	**4**	**1**	**1**	-	**12**
Group B	-	+	-	**3**	**4**	-	-	-	**7**
Group C	+	+	+	**1**	-	-	-	-	**1**
Group D	-	+	+	**2**	**2**	**1**	-	-	**5**
Group E	-	-	+	-	-	-	-	**1**	**1**
	Total			**12**	**10**	**2**	**1**	**1**	

Bone marrow involvement of nodal lymphomas

Bonemarrowinvolvementwasseenin5casesofNHLand2casesofHL,amountingto10.2% and 7.7% respectively and all these belonged to stage IV. Findings in the uninvolved bone marrow cases included erythroid hyperplasia and mild megakaryocytichyperplasia.

Hepatosplenomegalywasseenin6cases(12.2%)ofNHLand2cases(7.7%)casesofHLand these cases were classified as stage IV. Only splenomegaly was found in 5 cases (10.2%) of NHL and 1 case (3.8%) of HL and were classified under stageIII.

Staging of nodal lymphomas

(The Ann- Arbor staging system (Kumar *et al*., 2014), Carbone *et al*., 1971).

Table 8: Stage at presentation of NHL and HL

Stage	NHL (%)	HL (%)	Total	Percentage
I	22 (29.4)	15 (20)	37	49.4
II	7 (9.3)	5 (6.7)	12	16
III	10 (13.3)	3 (4)	13	17.3
IV	10 (13.3)	3 (4)	13	17.3
Total	49 (65.3)	26 (34.7)	75	100

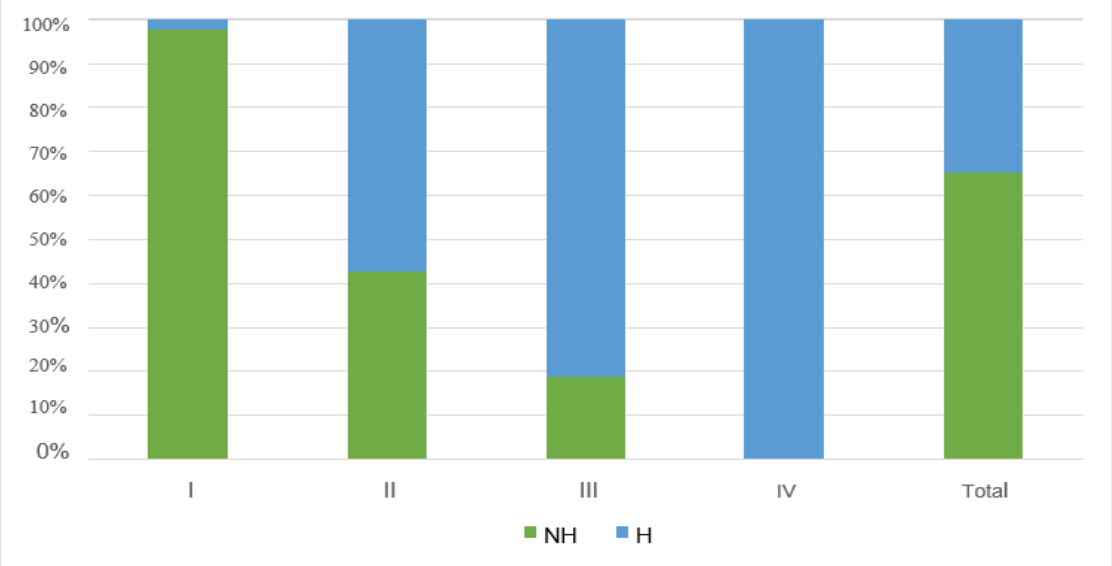

Figure 3: Stage of lymphomas at presentation

Figure 4: Gross picture of enlarged lymph node with grey white fleshy cut surface

Figure 5: Gross picture of enlarged lymph node with capsule and grey white solid cut surface, Vague nodularity seen

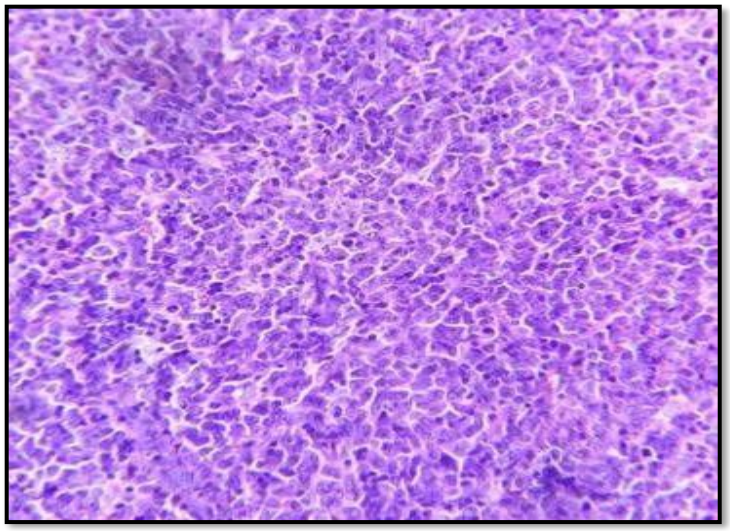

Figure 7: Microphotograph showing diffuse pattern of sheets of neoplastic cells in DLBCL. The cells are large (2-3 times the size of a lymphocyte) (H&E, 40x)

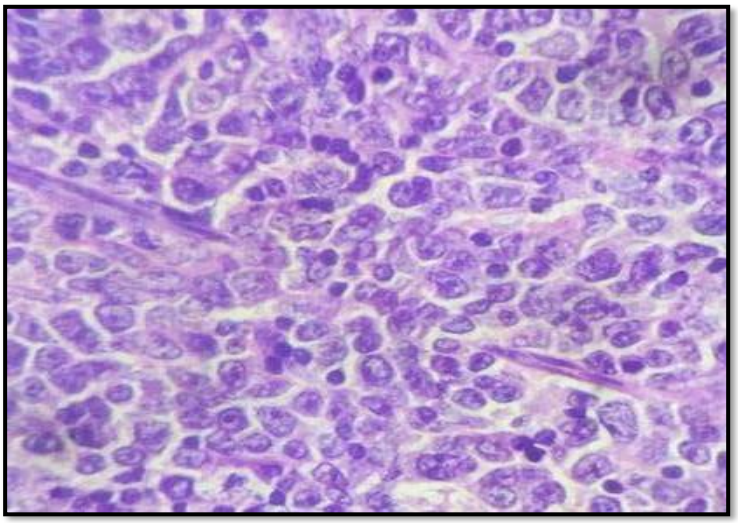

Figure 8: Microphotograph of DLBCL showing large cells with prominent nucleoli (H&E, 100x)

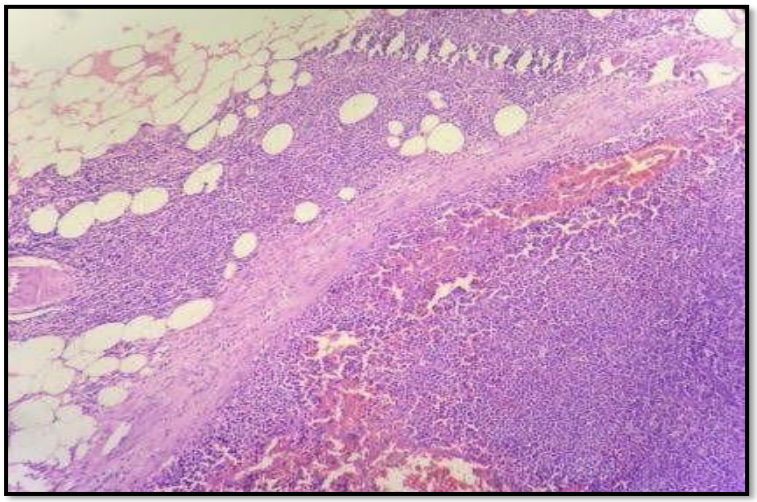

Figure 9: Microphotograph showing subcapsular filling and extracapsular extension into perinodal fat in DLBCL (H&E, 10x)

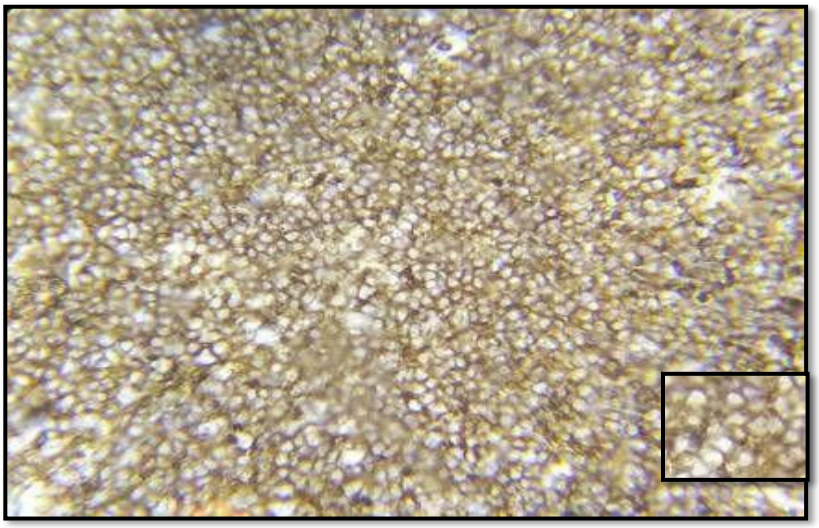

Figure 10: CD 45 membranous positivity in tumour cells of DLBCL (IHC - 10x) [Inset: High power (40x) of the same]

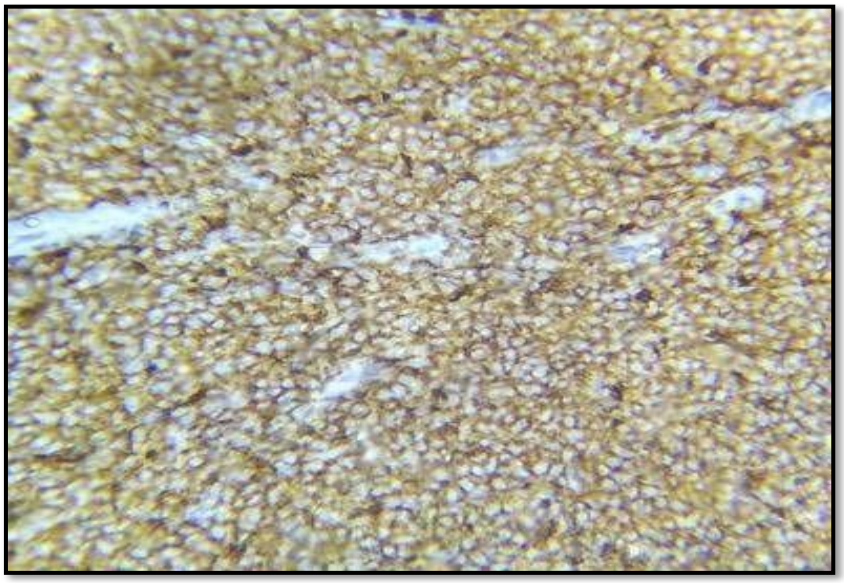

Figure 11: CD 20 membranous positivity in tumour cells of DLBCL (IHC - 10x)

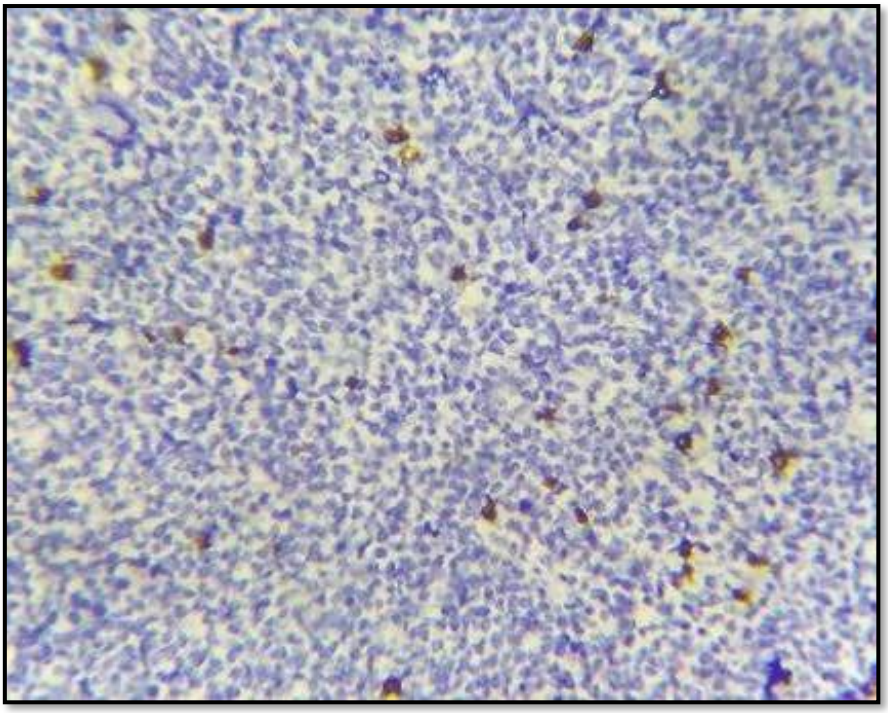

Figure 12: CD 3 positivity in scattered native T cells in DLBCL (IHC - 10x)

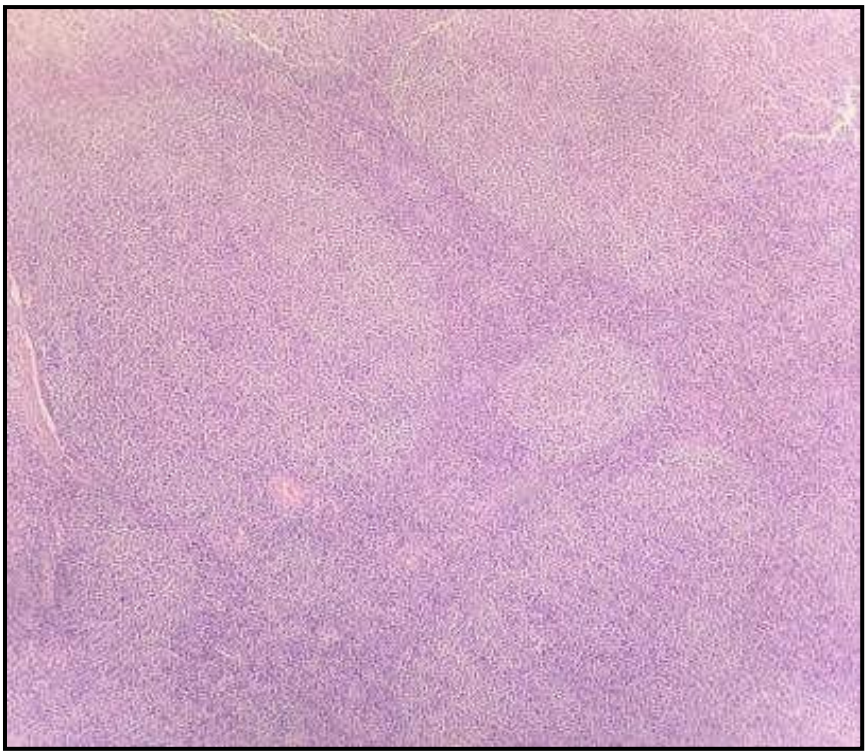

Figure 13: Microphotograph showing expanded homogenous looking nodules lacking mantle zone in follicular lymphoma (H&E, 10x)

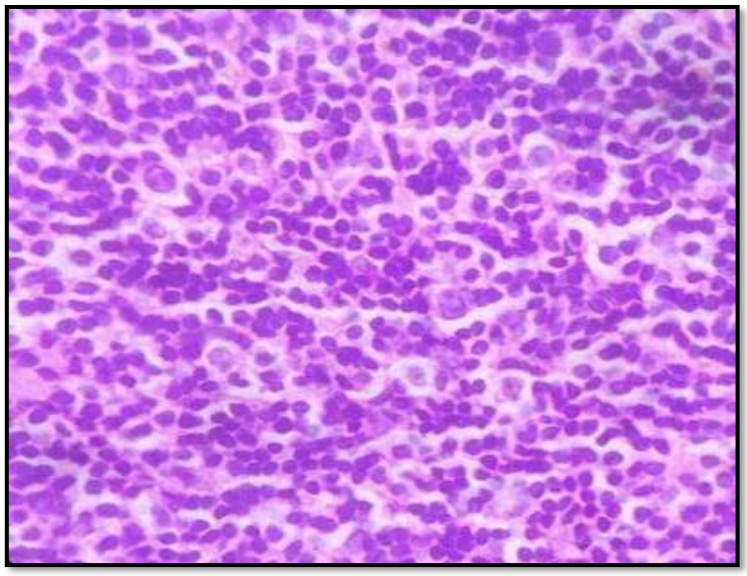

Figure 14: Microphotograph showing grade 2 follicular lymphoma with 6-15 centroblasts/HPF (H&E, 40x)

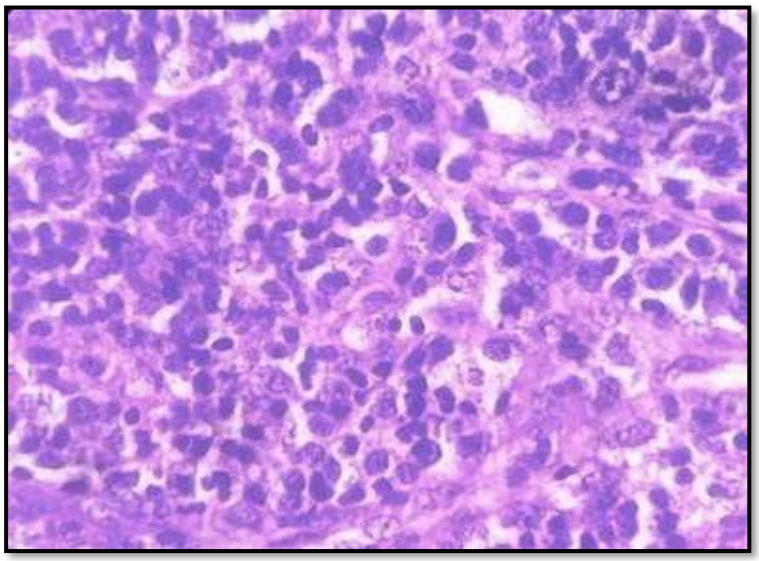

Figure 15: Microphotograph showing grade 3 follicular lymphoma with more than 15 centroblasts/HPF (H&E, 40x)

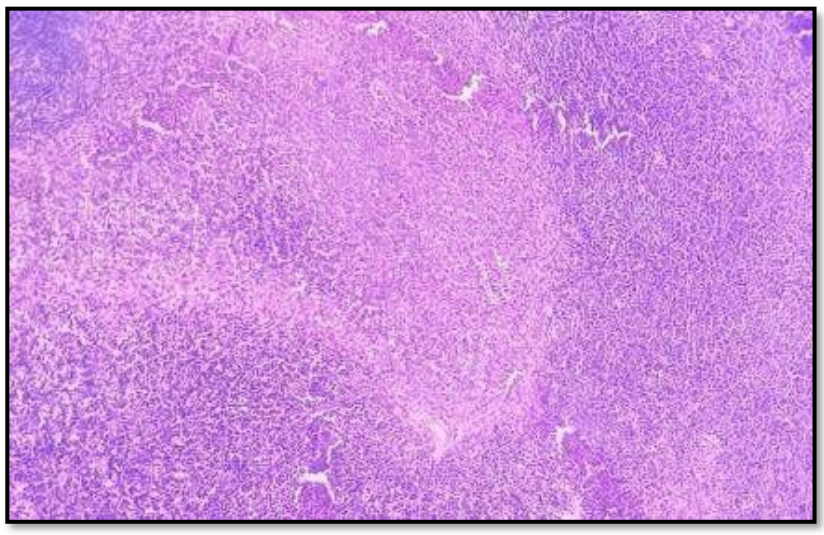

Figure 16: Microphotograph showing pale proliferation centres in Small lymphocytic lymphoma (H&E, 10x)

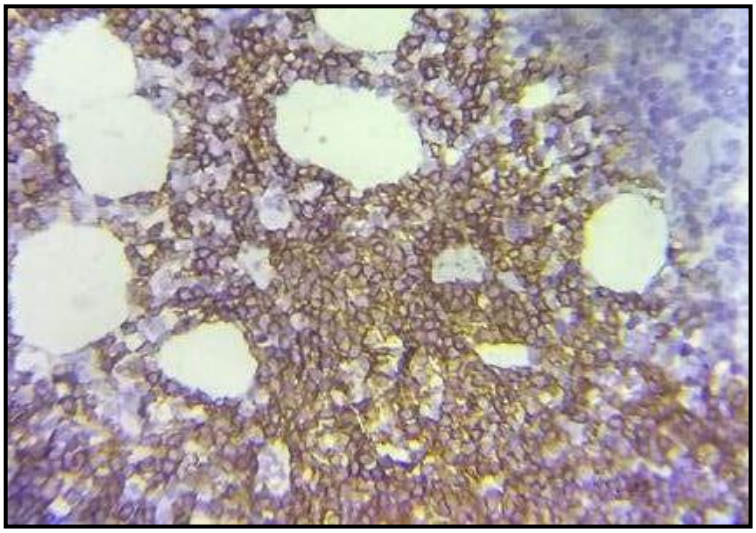

Figure 17: Microphotograph of CD20 positivity in lymphoma cell infiltrate in the bone marrow of patient having SLL of cervical lymph node(IHC-40x)

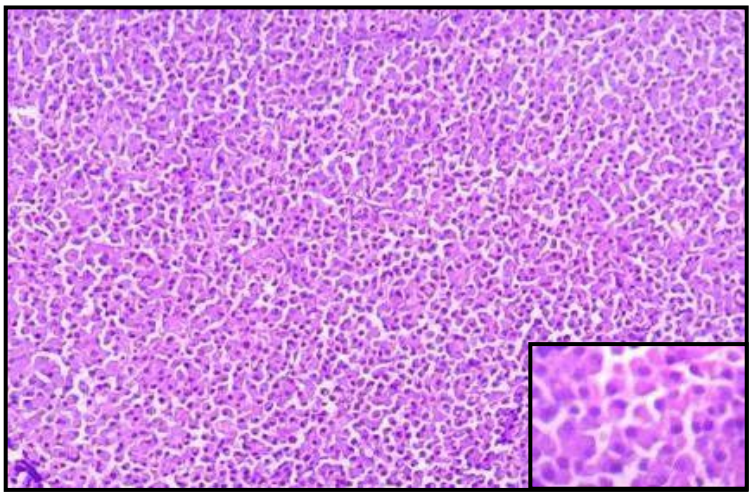

Figure 18: Microphotograph showing lymphoplasmacytoid cells in LPL. (H&E, 10x). [Inset: High power (40x) of the same]

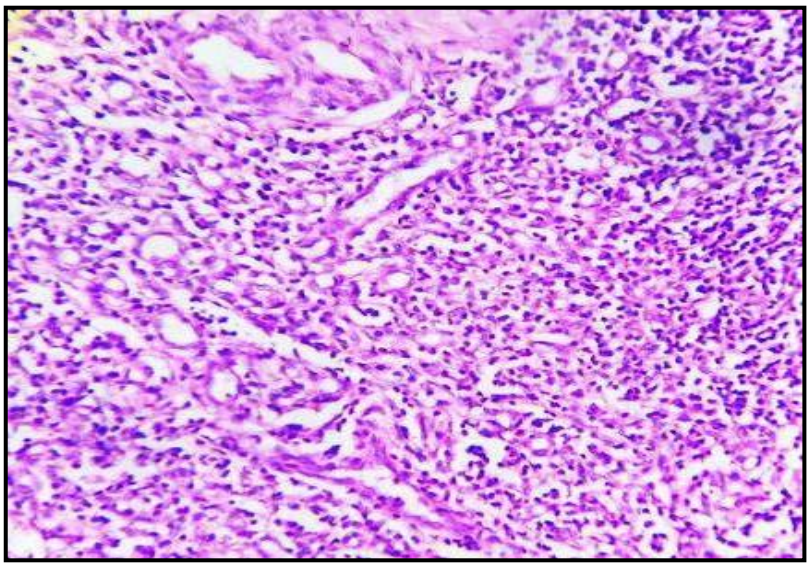

Figure 19: Microphotograph showing mixed cell population with few plasma cells with prominent and arborizing pattern of blood vessels in AILT (H&E, 40x)

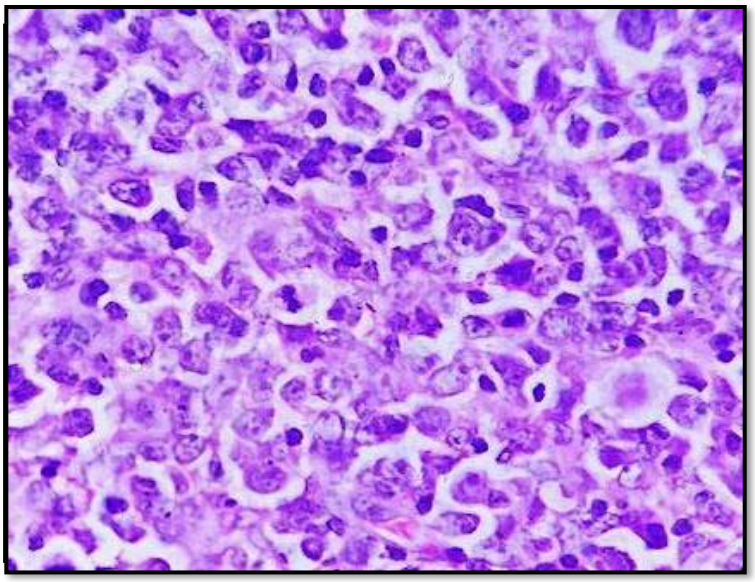

Figure 20: Microphotograph showing cells exhibiting marked pleomorphism, indented nuclei and conspicuous nucleoli in ALCL. (H&E, 100x)

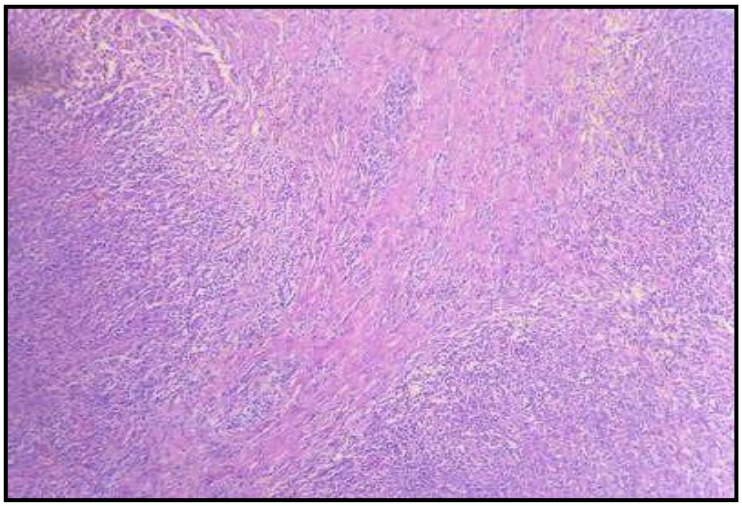

Figure 21: Microphotograph showing broad bands of fibrosis dividing nodules in HL- nodular sceloris (H and E, 10x)

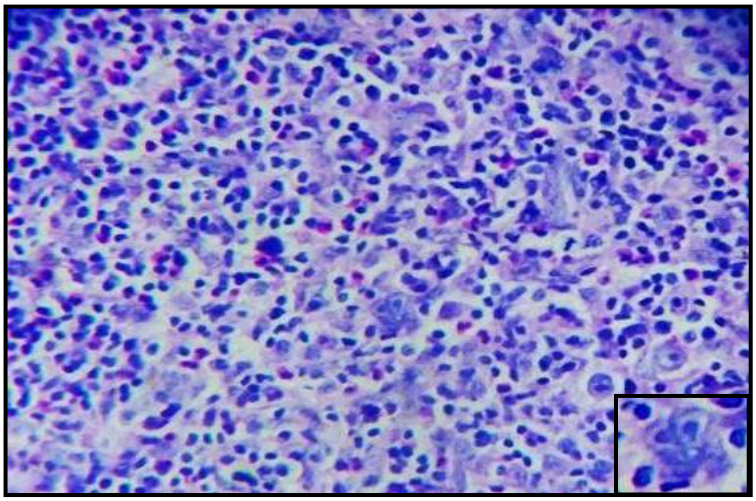

Figure 22: Microphotograph showing an RS cell in polymorphous background of inflammatory cells including numerous eosinophils. (H and E, 40x). [Inset: High power (100x) of the RS cell]

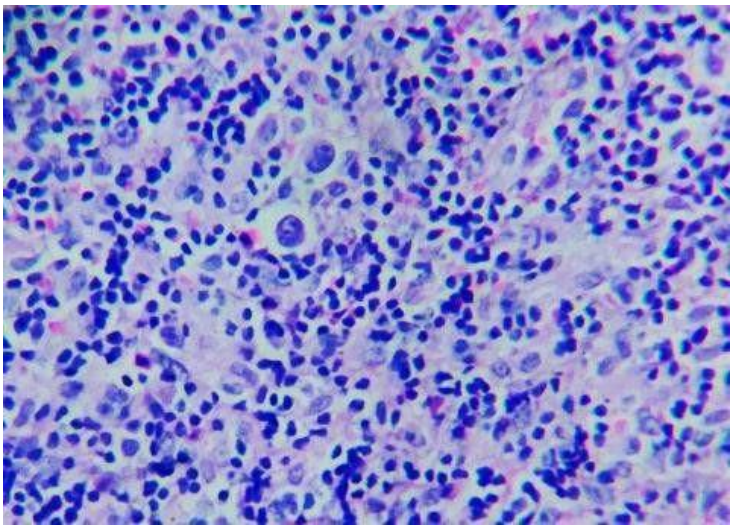

Figure 23: Microphotograph showing an RS cell in polymorphous background of inflammatory cells including numerous eosinophils (H and E, 40x)

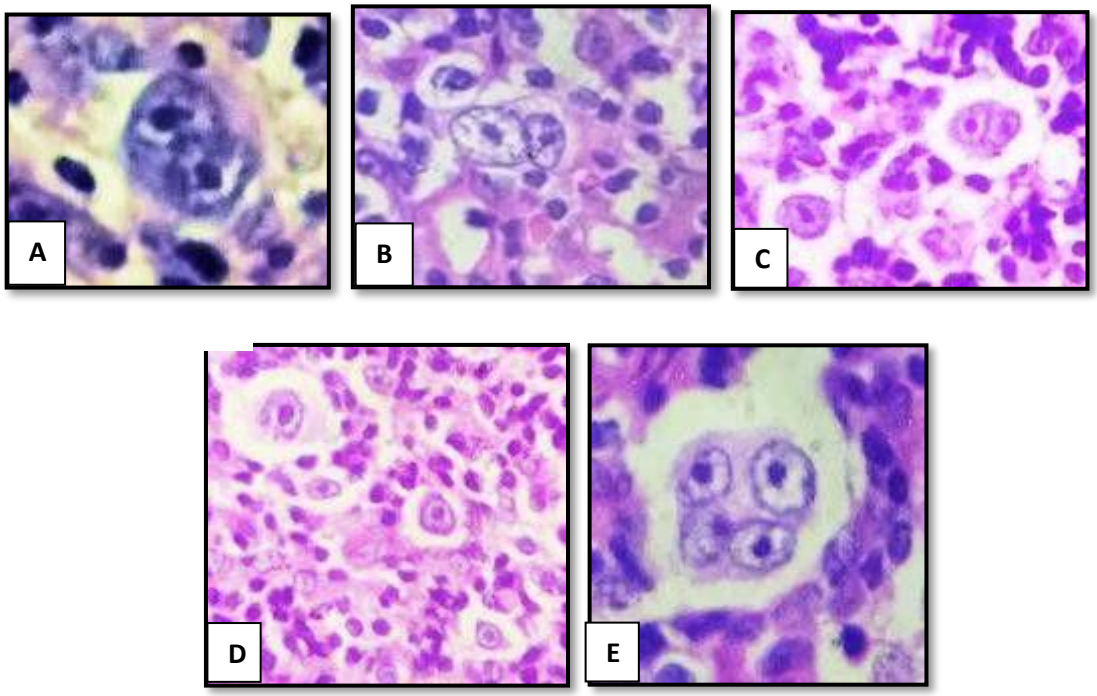

Figure 24: Microphotograph showing different types of RS cell: A, B-classic RS cells. C- classic lacunar, D-Mononuclear, E- quadrinucleate RS cell (H and E, 100x)

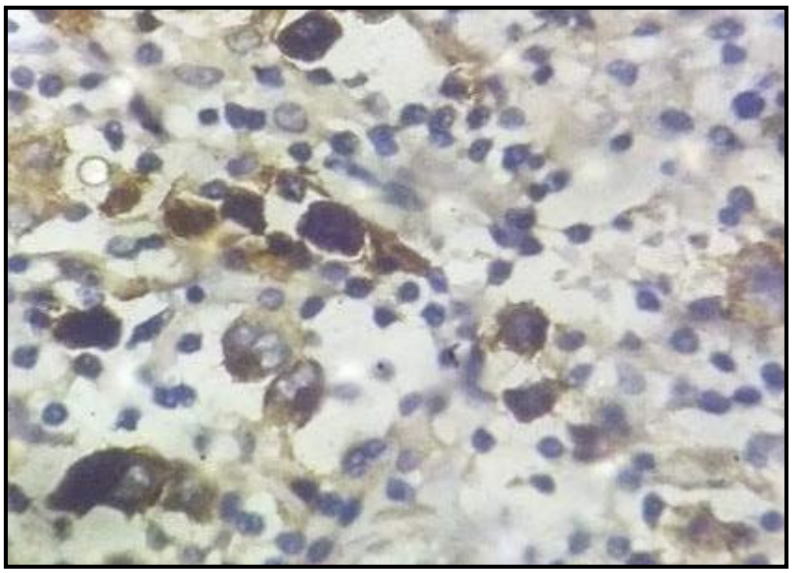

Figure 25: CD 15 membranous positivity with Golgi zone accentuation in RS cells (IHC -40x)

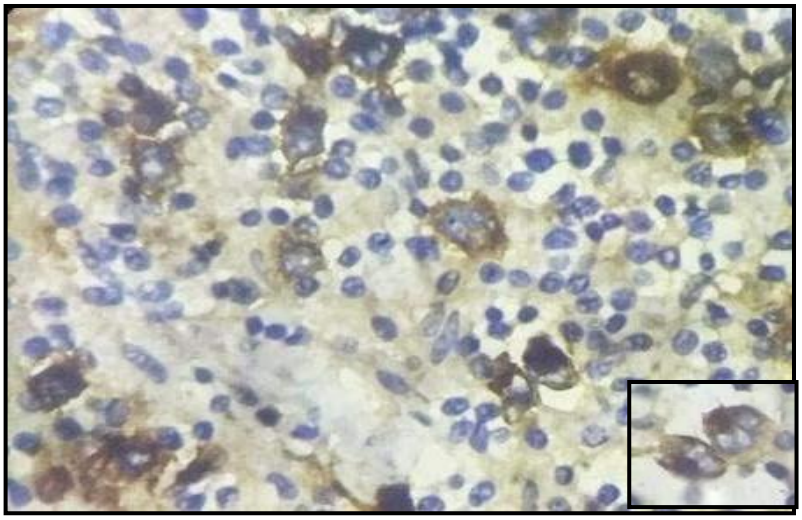

Figure 26: CD 30 membrane and Golgi positivity in RS cells. (IHC -40x) [Inset: High power (100x) of the RS cell]

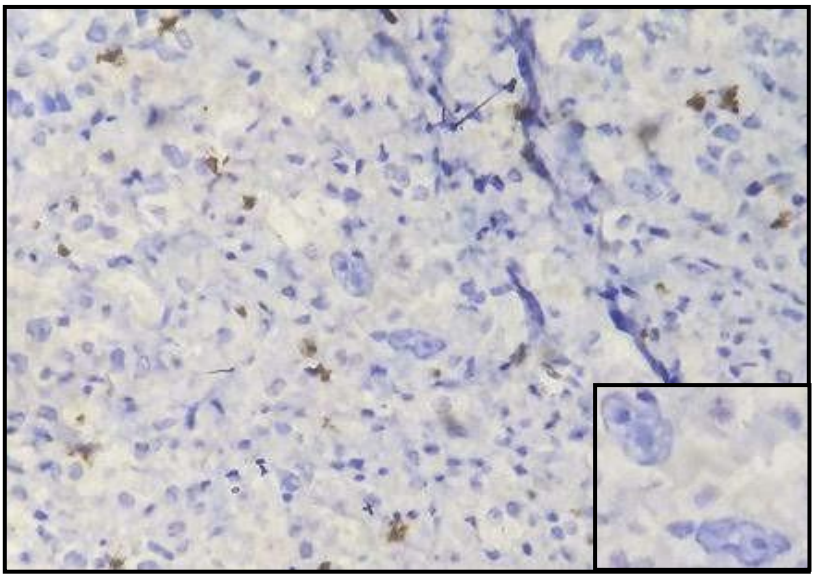

Figure 27: CD 15 negativity in RS cells. (IHC -40x) [Inset: High power (100x) of the RS cell]

DISCUSSION

In the present study, majority of cases were NHL (49 in number), constituting 65.33% and 26 cases(34.67%)wereofHL.Thepresentstudyisconcordantwithstudiesconductedby Zubair *etal*.,(2015),Sharma*etal*.,(2014)andOtrock*etal*.,(2013).Whereas,Mushtaq*etal*.,(2008),Sader-Ghorra*etal*.,(2014)andImpana*etal*.,(2016)reportedahigherpercentageofNHLascompared to these above studies. This is due to the inclusion of extranodal lymphomas in theirstudies.

Table 9: Comparison of proportion of NHL and HL with other studies

Study	NHL (%)	HL (%)
Zubair *et al*., (2015)	61	39
Sharma *et al*., (2014)	61	39
Otrock*et al*., (2013)	67	33
Mushtaq *et al*., (2008)	73	27
Sader-Ghorra*et al*., (2014)	76	24
Impana *et al*., (2016)	84	16
Present study	65.3	34.7

Comparison of Age distribution in various studies

In the present study, the mean age in Hodgkin lymphoma was much lower than the mean age for non-Hodgkin lymphoma. These observations were similar to those of Yang *et al*., (2011), Yoon *et al*., (2010), Waravita*et al*., (2015) and Miura *et al*., (2011).

Table 10: Comparison of age distribution with other studies

Study	Mean age in NHL	Mean age in HL	Overall mean age
Yang *et al*., (2011)	44.1	35.8	39.9
Yoon *et al*., (2010)	47.8	38.8	47.5
Waravita*et al*., (2015)	49.8	43.2	48.8
Miura *et al*., (2011)	67	44	66
Present study	49.5	38.5	45.7

Comparison of Gender distribution

Present study is concordant with Roy *et al*., (2013) and Mushtaq *et al*., (2008).

Also,ofnoteisthehigherM:FratioinHodgkinlymphoma(2.7:1)thaninNHL(1.7:1).Similar observationsweremadeinstudiesconductedbyYoon*etal*.,(2010),Mushtaq*etal*., (2008),Sader- Ghorra*et al*., (2014), Roy *et al*., (2013) and Chakrabarti *et al*.,(2015).

Table 11: Comparison of sex distribution with other studies

Study	M: F in NHL	M: F in HL	Overall M: F
Yoon *et al*., (2010)	1.3:1	1.5:1	1.3:1
Mushtaq *et al*., (2008)	1.9:1	2.8:1	2.5:1
Sader-Ghorra*et al*., (2014)	1:1	1.3:1	1.1:1
Roy *et al*., (2013)	2.2:1	2.5:1	1.7:1
Chakrabarti *et al*., (2015)	3.2:1	3.8:1	3.4:1
Present study	1.7:1	2.7:1	2:1

Comparison of Clinical features in nodal lymphomas

In the present study, a greater percentage of HL patients (26.9%) had B symptoms compared to those of NHL (12.2%), similar to studies conducted by Hingorjo*et al*., (2008) and Chakrabarti *et al*., (2015).

The postulated reason for the above is the abnormal immune response seen in Hodgkin lymphoma,whichisduetotheeffectsofvariouscytokinesandchemokinesproducedprimarily by the neoplastic RS cells. These also bring in the polymorphous background inflammatory cells which are classically seen in Hodgkin lymphoma. This reactive inflammatory infiltrate secondarily produces furthermore cytokines, thus resulting in more marked B symptoms overall (Skinnider& Mak,2002).

Table 12: Comparison of proportion of B cell and T cell NHLs with other studies

Studies	B cell type	T cell type	Unclassified
Yoon *et al.,* (2010)	81.6	17.1	1.2
Naresh *et al*., (2000)	79.1	15.2	5.6
Waravita*et al*., (2015)	77.1	22.9	0
Present study	79.6	20.4	0

Table 13: Comparison of subtypes of B cell NHL with other studies (as a percentage of all B cell NHLs cases)

Subtype	DLBCL	FL	B-LBL	LPL	SLL	Mantle cell	Burkitt	Others
Zubair *et al*., (2015)	42.8	38.1	9.5	2.3	4.7	2.3	0	0.3
Yang *et al*., (2011)	50	1.7	12.3	1.6	11.1	6.1	2.3	14.9
Roy *et al*., (2013)	54.3	12.6	4.6	0.5	6.9	7.4	3.4	10.3
Present study (n=39)	48.8	23.1	2.5	2.5	23.1	0	0	0

Table 14: Comparison of subtypes of T cell NHL with other studies (as a percentage of all T cell NHLs cases)

Subtype	PTCL (%)	ALCL (%)	AILT (%)	T-LBL (%)	Others
Shahid *et al*., (2016)	20.8	41.6	4.2	33.3	0
Zubair *et al*., (2015)	31.25	31.25	18.75	18.75	0
Roy *et al*., (2013)	45.2	27.4	4.8	19.4	3.2
Present study	60	20	20	0	0

Comparison of subtypes of Hodgkin's lymphoma

Nodular sclerosis was the most common subtype of HL found in studies conducted by Roy *et al*., (2013), Lee *et al*., (2006), Zubair *et al*., (2015), Kim *et al*., (2011) and present study.

However, mixed cellularity was found to be the most common subtype found in Waravita*et al*.,'s (2015)study.

Mixed cellularity subtype is often more associated with EBV and lower socioeconomic status (Konkay*et al*., 2016). Since present study was done in a tertiary care centre, it could point to a higher socio-economic status group and hence the higher incidence of the nodular sclerosissubtype.

Table 15: Comparison of subtypes of Hodgkin lymphoma

Subtype	Nodular Sclerosis	Mixed cellularity	Lymphocyte rich	Lymphocyte depleted	NLPHL	Unclassified
Waravita*et al*., (2015)	37.1	57.1	2.9	0	0	2.9
Roy *et al*., (2013)	39.2	32.8	11.2	4.8	3.2	8.8
Kim *et al*., (2011)	47.4	30.6	9.2	0.6	12.1	0
Zubair *et al*., (2015)	67.6	16.2	2.7	2.7	5.4	5.4
Lee *et al*., (2006)	69.5	4.7	4.7	0	7.1	14.2
Present study	46.1	38.6	7.7	3.8	3.8	0

Immunohistochemistry (IHC)

- In a study conducted by Miura *et al.,* (2011), CD20 was positive in 92.4% of B cell neoplasms. Present study was concordant with the study conducted by Miura *et al.,* (2011) with 97.4% CD20 positivity.
- DLBCL was characterised by CD 20 expression in all (100%) cases. Aberrant expression of CD5 was seen in 2 cases (10.5%). Studies conducted by Tsuyama*et al*., (2017) and Suzuki *et al*., (2013) reported similar findings of 13.9% and 9.1% respectively. CD5 positive DLBCL are found to have a poorer prognosis as compared to CD5 negative DLBCL (Alinari *et al*.,2014).
- All 9 cases of follicular lymphoma (100%) showed CD20 and BCL2 expression in the presentstudy.
    - Varied range of BCL6 positivity in follicular lymphoma is reported in literature (Goteri*et al*., 2011), (Dogan *et al*., 2000), (Mahmoud *et al*., 2011). Goteri*etal*., (2011)hasreported92.7%positivityofBCL6andDogan*etal*., (2000)reported94.4%.Presentstudyshowed77.8%andwascomparablewith the abovestudies.
    - CD10 positivity is variable ranging from 60% – 90% (Ioachim, 2009), (Swerdlow, 2017). In the present study CD10 was positive in 8 (88.9%) of cases.
    - Literature search revealed that follicular lymphoma is negative for CD5 (Ioachim, 2009). However,

occasional cases are positive and these are postulated to have a poorer prognosis and higher rate of transformation, according to a study done by Li *et al*.,(2015).

- In our study two cases of DLBCL showed aberrant CD5 expression and these could possibly represent the FL which have transformed intoDLBCL.
- Both the cases in the present study (100%) of ALCL were CD 30positive.

➢ Hodgkin lymphoma:

Table 16: Comparison of immunophenotype of Hodgkin lymphoma with other studies

	CD 15	**CD 30**	**CD 20**	**Patkar *et al.*, (2008)**	**Konkay*et al.*, (2016)**	**Von Wasielewski *et al.*, (1997)**	**Present study**
Group A	+	+	-	44.6	60.6	83	46.3
Group B	-	+	-	40.1	35.8	12	26.9
Group C	+	+	+	5.5	2.75	5	3.8
Group D	-	+	+	9.6	1.37	0	19.2
Group E	-	-	+	0.2	0	0	3.8

Comparison of bone marrow involvement

Table 17: Comparison of bone marrow involvement with other studies

Studies	**BM involved in NHL**	**BM involved in HL**
Impana *et al*., (2016)	10 (23.8%)	1 (12.5%)
Chakrabarti *et al*., (2015)	14 (18.42%)	4 (8.33%)
Mondal *et al*., (2014)	70 (30.3%)	4 (9.3%)
Present study	5 (10.2%)	2 (7.7%)

Comparison of stage of lymphoma

Table 18: Comparison of stage of NHL with other studies

Studies	**NHL as a percentage**			
Stage	I	II	III	IV
Lee *et al*., (2006)	28.8	23.1	20.9	27.2
Chakrabarti *et al*., (2015)	7.9	21.1	44.7	26.3
Present study	81.6	12.2	6.2	0

Majority of cases (50%) of HL presented at Stage III in our study, similar to observations by Konkay*et al*., (2016) and Chakrabarti *et al*., (2015), Eddo *et al*., (2011) also observed that majority (66.1%) presented in the advanced stage (Stage III and IV).

The late presentation could be due to lack of awareness and the rather slowly appearing clinical manifestations of the disease (Impana *et al*., 2016).

Table 19: Comparison of stage of HL with other studies

Studies	**HL as a percentage**			
Stage	I	II	III	IV
Eddo *et al*., (2011)	33.9		66.1	
Konkay*et al*., (2016)	11.25	21.25	42.5	25
Lee *et al*., (2006)	2.4	54.8	19	23.8
krabarti *et al*., (2015)	29.2	16.7	45.8	8.3
Present study	3.8	30.8	50	15.4

CONCLUSION

Lymphoma diagnosis starts primarily at the histomorphological level and is greatly indebted to

immunohistochemistry and molecular studies.

Among nodal lymphomas, NHL is more common than HL. Both NHL and HL have male predominance, however females present at an earlier age. NHL occurs in elderly age groups compared to HL. Cervical group of lymph nodes is most commonly affected in both NHLand HL. B symptoms are seen more in HL. Among NHL, B cell neoplasm is more common, amongst which, DLBCL is the predominant subtype. Among T cell NHL, PTCL is the most common subtype. Nodular sclerosis is the most common subtype of HLfound.

Clinicopathological correlation with knowledge of histomorphology supplemented by IHC leads to early diagnosis, treatment and exploitation of potential targeted therapies, thus reducing overall morbidity and mortality due to lymphomas.

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