Histomorphological Features of Neoplastic and Non-Neoplastic Lymph Node Lesions in a Tertiary Care Hospital in South India

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ABSTRACT

BACKGROUND

Lymphadenopathy is a common clinical condition and biopsies are usually undertaken to determine the cause of nodal enlargement, which may be neoplastic or non-neoplastic. The neoplastic disorders are categorized into haematolymphoid malignancies and metastasis, while the causes of non-neoplastic lymphadenopathy are diverse. This study was undertaken to determine the histopathological spectrum in lymph node biopsies.

METHODS

This was a descriptive study of 357 cases of histologically diagnosed peripheral lymph node biopsies in the Department of Pathology, Govt. Medical College, Thiruvananthapuram, Kerala, S. India conducted from January 2019 to December 2019. Treated cases of malignancies were excluded.

RESULTS

The non-neoplastic lesions were more common accounting for 67.2 % (240 cases) which included 40.3 % (144 cases) of non-specific reactive lymphoid hyperplasia, 3.9 % (14 cases) of other specific lymphoid hyperplasia, 16.2 % (58 cases) of tuberculous lymphadenitis, 6.7 % (24 cases) of other granulomatous lesions. Neoplastic lesions accounted for 32.8 % (117 cases) and included 16.2 % (58 cases) of non-Hodgkin's lymphoma, 3.9 % (14 cases) of Hodgkin's lymphoma and 12.6 % (45 cases) of metastatic lesions.

CONCLUSIONS

Lymph node biopsy plays an important role in establishing the cause of lymphadenopathy. Among the biopsied nodes, reactive follicular hyperplasia was the most common (40.3 %) followed by Non-Hodgkin's lymphoma and tuberculous lymphadenitis (16.2 % each) and metastasis (12.6 %).

KEYWORDS

Lymphadenopathy, Lymph Node, Metastasis, Non-Hodgkin's Lymphoma, Reactive Lymphoid Hyperplasia, Tuberculosis

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BACKGROUND

Lymphadenopathy is a common clinical condition and biopsies are usually taken to determine the cause of nodal enlargement, which may be neoplastic or non-neoplastic, and can affect any age group. The neoplastic disorders are categorized into haematolymphoid malignancies which includes Hodgkin's lymphoma and Non-Hodgkin's lymphoma and metastasis. Lymph nodes are the most common site of metastatic malignancy, and it may be the first clinical manifestation of the disease.[1,2,3]

The non-neoplastic lymphadenopathy may be due to a variety of causes like infections (bacterial, viral, fungal), drug reactions and a wide range of specific lymphoproliferative disorders such as Kikuchi Fujimoto disease, systemic lupus erythematosus, Castleman disease, Rosai Dorfman disease etc. The age of the patient is one of the most important factor in determining the cause of lymph node enlargement. In children, most lymphadenopathies are benign, whereas in adults, the probability of malignancy increases with age.[4] Lymph nodes smaller than 1 cm in size are rarely malignant.[5]

Clinically lymphadenopathy may be peripheral or visceral. Peripheral lymphadenopathies are easily detectable by physical examination and are often biopsied. Visceral lymphadenopathy on the other hand requires imaging modalities for detection. Among the peripheral nodes, those in the upper part of the body (cervical, supraclavicular, axillary) are preferentially biopsied than nodes in the lower part of the body (popliteal, inguinal or femoral) as the former are more likely to yield definitive diagnosis, whereas the latter usually reveal nonspecific reactive or chronic inflammatory and fibrotic changes.[6]

When node biopsy is indicated, selection of the most abnormal node will best enable the pathologist to determine a diagnosis. Excision biopsy and histopathological examination of the lymph node remains the "Gold standard" for diagnosis.[7,8] However, there is a dearth of information on the spectrum of diseases affecting lymph nodes from this region

Objectives

- To evaluate the spectrum of histopathological diagnosis in lymph node biopsies.
- To study the histomorphological features of neoplastic and non- neoplastic lymph node lesions.
- To evaluate the frequency of occurrence and age distribution of various lymph node lesions.
- To categorise lymph node neoplasms into lymphoid and non- lymphoid malignancies.
- To categorise lymphomas according to the WHO 2017 classification.

METHODS

The present study was a retrospective study of 357 lymph node biopsies diagnosed in the Department of Pathology in a large tertiary care teaching hospital in South Kerala, from January 2019 to December 2019. The study was approved by the Research & Ethical committee. All histopathological proven cases of lymph node lesions were included in the study which were analysed according to the histomorphology. Clinical details of the patient were obtained from the biopsy requisition forms. Specimens were fixed in 10 % neutral buffered formalin. The standard tissue processing protocols were followed. Sections were cut at 4 - 5 micron thickness and were stained with Haematoxylin and Eosin. Special stains and immunohistochemistry were carried out in relevant cases. All lymph node lesions were analysed according to age & sex distribution and histopathology. Treated cases of malignancies were excluded. Lymph node lesions were broadly categorized into non neoplastic and neoplastic lesions. Neoplasms were again classified into haematolymphoid and metastatic malignancies. The lymphomas were classified according to WHO classification 2017. The data was analysed using Microsoft Excel, Version 15.21.1 (Mac)

RESULTS

A total of 357 lymph node biopsies were received during the period under review, accounting for 1.27 % of all surgical biopsy specimens. Out of these, 56.6 % (202 cases) were males and 43.4 % (155 cases) females with a male to female ratio of 1.3:1. The age range was from 9 months to 81 years in case of males and 7 months to 82 years in case of females. Most cases were seen in the age group of 50 - 59 years (63 cases, 17.6 %) and the least cases were seen in the age group of 80 - 82 years (4 cases, 1.1 %). (Table 1). Out of 357 lymph node biopsies analysed, non-neoplastic lesions were more common comprising 67.2 % (240 cases), which included 40.3 % (144 cases) of non-specific reactive lymphoid hyperplasia, 3.9 % (14 cases) of other reactive or specific lymphoid hyperplasia, 16.2 % (58 cases) of tuberculous lymphadenitis and 6.7 % (24 cases) of other granulomatous lesions.

Neoplastic lesions were comprising 32.8 % (117 cases), which included 16.2 % (58 cases) of non-Hodgkin's lymphoma (NHL), 3.9 % (14 cases) of Hodgkin's lymphoma (HL) and 12.6 % (45 cases) of metastatic lesions. (Table - 2)

Among the non-neoplastic lesions, reactive lesions were by far most common accounting for 65.8 % (158 cases) of which reactive lymphoid hyperplasia constituted 60 % (144 cases). There was male preponderance and male to female ratio was 1.9:1. Common age group affected was 31 – 39 years.

The rest 5.8 % (14 cases) had other specific patterns of lymphoid hyperplasia or lymphadenopathy in 11 cases and included 8 (3.3 %), 2 (0.8 %), 1 (0.4 %), Kikuchi Fujimoto disease, Systemic lupus erythematosus (SLE) lymphadenopathy, Rosai Dorfman disease respectively and 3 (1.3 %) were not otherwise specified or categorized.

Tuberculous lymphadenitis comprising 24.2 % (58 cases) of non-neoplastic lesions and the second most common histologic pattern encountered occurred predominantly in young adult females and 46.5 % (27 cases)

occurred before the age of 40 years with a peak between 20 and 38 years with slight female preponderance (M:F = 1:1.3). Other granulomatous lesions included six cases of sarcoidosis, six cases of necrotising granuloma, three cases of BCG adenitis, one case of cat scratch disease, one case of fungus, one case of toxoplasmosis and six cases could not be further categorised.

Of the neoplastic lesions, NHL constituted 58 cases, which accounted for 16.2 % of lymph node biopsies and constituted 80.5 % of all lymphomas. Out of these 70.6 % (41 cases) occurred after the age of 50 years with a peak between 70 and 78 Years and a male (37 cases) preponderance (M:F ratio = 1.7:1). Among 58 cases of NHL, T cell lymphoma comprised 5.2 % (3 cases) and B cell lymphoma 94.8 % (55 cases) with diffuse large B cell lymphoma being the most common subtype comprising 43.1 % (25 cases). Other subtypes of B cell lymphoma were 24.1 % (14 cases) of follicular lymphoma, 3.4 % (2 cases) of CLL / SLL, 1.7 % (1case) of T cell rich B cell lymphoma.

T cell lymphoma were 5.1 % (3 cases), of which 3.4 % (2 cases) were peripheral T - cell lymphoma NOS. 1.7 % (1 case) of angioimmunoblastic T cell lymphoma.

Hodgkin's lymphoma accounted for 14 cases, constituting 3.9 % of lymph node biopsies and 19.4 % of all lymphoma. All the 14 cases were classical Hodgkin's lymphoma and the predominant subtype was mixed cellularity. Out of these 64.2 % (9 cases) occurred after the age of 30 years with a peak between 32 and 38 Years and a male (9 cases) preponderance.

Thirteen (22.4 %) cases could not be further sub classified due to the outside slides having been submitted for review with non-availability of blocks or due to non-contributory Immunohistochemistry (IHC), possibly due to poor antigenic preservation.

Metastasis contributed the remaining malignancies representing 12.6 % of total lymph node biopsies. The majority of cases were found within the age group of 60 – 68 years (17 cases, 37.7 %). The male female ratio was 1.5:1, Out of 45 cases of metastatic lymphadenopathy 51.1 % (23 cases) were adenocarcinoma, 17.8 % (8 cases) were squamous cell carcinoma, 11.1 % (5 cases) were poorly differentiated carcinoma, 6.7 % (3 cases each) were melanoma and neuroendocrine carcinoma, 2.2 % (1 case each) of papillary thyroid carcinoma, alveolar rhabdomyosarcoma and malignant peripheral nerve sheath tumour. (Figure 1)

Age	Total No.	Male		Female	
		No.	(%)	No.	(%)
0 - 10	19	12	3.4 %	7	2 %
10 - 20	54	34	9.5 %	20	5.6 %
20 - 30	48	28	7.8 %	20	5.6 %
30 - 40	46	21	5.9 %	25	7.0 %
40 - 50	47	20	5.6 %	27	7.5 %
50 - 60	63	34	9.5 %	29	8.1 %
60 - 70	45	31	8.7 %	14	3.9 %
70 - 80	31	20	5.6 %	11	3.1 %
80 - 90	4	2	0.6 %	2	0.6 %
	357	202	56.6 %	155	43.4 %

Table 1. Age- and Sex-Wise Distribution of 357 Cases

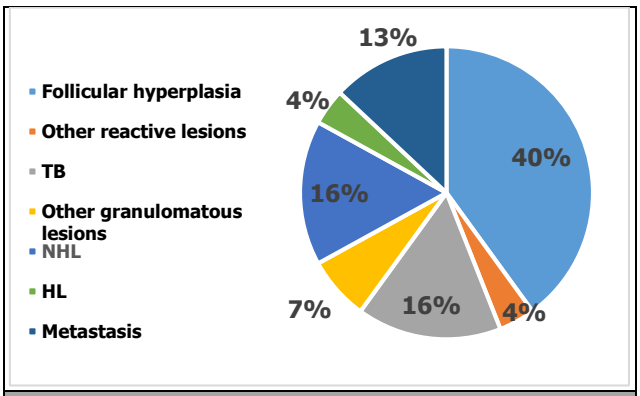

Figure 1. Different Types of Lesions on Lymph Node Biopsies

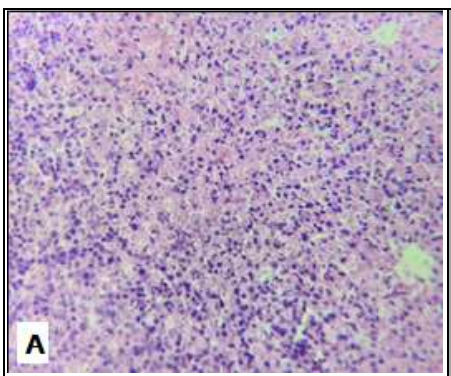

Figure 2A. Kikuchi's Disease (H&E, 40x)

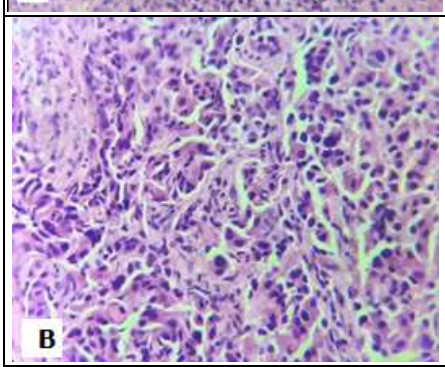

Figure 2B. Metastasis from Adenocarcinoma (Lung) (H&E, 40x)

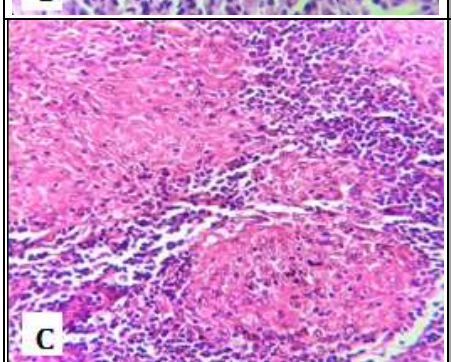

Figure 2C. Sarcoidosis (H&E, 40x)

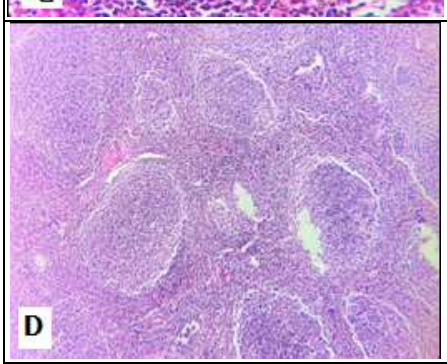

Figure 2D. Follicular Lymphoma (H&E, 10x)

		Lesions Lymph nodes	Total No. 357		%
I		**Non neoplastic**		240	67.2 %
	a.	Reactive lesions	158		
	(i)	Reactive follicular hyperplasia	144		
	(ii)	Kikuchi	8		
	(iii)	Autoimmune	2		
	(iv)	Rosai Dorfman disease	1		
	(v)	unclassified	3		
	b.	Granulomatous	82		
	(i)	Tuberculosis	58		
	(ii)	Necrotising granuloma	6		
	(iii)	Sarcoidosis	6		
	(iv)	BCG adenitis	3		
	(v)	Toxoplasmosis	1		
	(vi)	Fungus	1		
	(vii)	Cat scratch	1		
	(viii)	unclassified	6		
II.		**Neoplastic**		117	32.8 %
	a.	**NHL**	58		
		B cell			
	(i)	DLBCL	25		
	(ii)	Follicular	14		
	(iii)	CLL / SLL	2		
	(iv)	T cell rich B cell	1		
	(v)	unclassified	13		
		T cell			
	(i)	PTCL	2		
	(ii)	AITC	1		
	b.	**HL**	14		
		Classical Hodgkin's	14		
	c.	**Metastasis**	45		
	(i)	Adeno ca	23		
	(ii)	Squamous cell ca	8		
	(iii)	Poorly differentiated ca	5		
	(iv)	Melanoma	3		
	(v)	Neuroendocrine ca	3		
	(vi)	MPNST	1		
	(vii)	Alveolar RMS	1		
	(viii)	Papillary ca	1		
		Total		**357**	

Table 2. Histopathology of Lymph Node Biopsies

DISCUSSION

Palpable lymph nodes offer an important diagnostic clue to the aetiology of the underlying condition. Though fine needle aspiration cytology is commonly used to establish the etiological diagnosis, excision biopsy of the lymph node remains the "gold standard" for diagnosis.[8-10]

In our study, total number of cases were 357, of which 202 cases were male (56.6 %) and 155 were females (43.4 %) male to female ratio 1.3: 1. Most cases were seen in the age group of 50 – 59 years (17.6 %) and least cases were seen in the age group 80 – 82 years (1.1 %). Our study shows that males were more commonly affected. Patients with benign aetiology were younger when compared with those patients with malignant aetiology.

The present study showed non-neoplastic lesions 67.2 % predominate over neoplastic lesions 32.8 % and these results were consistent with Kamat GC et al. (88.92 %),[11] Rahman Md A (70.2 %) Saraswat A et al. (90.9 %),[12] Vacchani A et al. (75 %)[13] and Rao MN et al. (56 %).[14] In contrast, study done by Olu-Eddo AN et al. (2006)[15] revealed malignancy being the predominant lesion constituting 55 % of cases.

Reactive lymphadenitis (65.8 %) comprised of the predominant pattern in non-neoplastic lesions. This was consistent with study of Moore SW et al. found 47.8 % of reactive lesions.[16] Among the non-neoplastic lesions, reactive lymphoid hyperplasia was the most common cause of lymphadenopathy (60 %) trailed by granulomatous lesions (82 cases, 34.2 %).

Among the granulomatous lesions, tuberculosis was the predominant cause of lymph node enlargement, (58 cases, 70.7 %) and constitute 24.2 % of non-neoplastic lesions and is the second most common histologic pattern encountered.

Similar results were obtained by Dalmle R et al. (2016),[17] 53.8 % patients were diagnosed with reactive lymphadenitis. Also in a study by Vachhani AB et al.[18] reactive lymphadenitis predominated with 51 % cases, followed by granulomatous pathology in 24 % cases.

However, in a study by Shrestha et al. (2009),[19] the most common cause of lymphadenopathy was tubercular lymphadenitis (42 percent), followed by reactive lymphadenitis (23 percent).

Tuberculosis is followed by other granulomatous lesion which include necrotizing granuloma 7.3 % (6 cases), sarcoidosis 7.3 % (6 cases), BCG adenitis 3.7 % (3 cases) and1 case each of cat scratch disease, fungal infection and toxoplasma (1.2 %)and six cases could not be further categorized.

Among the neoplastic lesions, lymphomas predominate 61.5 % over metastatic lesions 38.5 %. Of the neoplastic lesions, NHL constituted 58 cases, which accounted for 16.2 % of lymph node biopsies and constituted 80.5 % of all lymphomas.

In study conducted in Zimbabwe by Sibanda et al.[20] the total number of patients were 2194, 7 % of cases were lymphomas. In study conducted in Nigeria by Akinde E et al.[21] the total number of patients were 733, lymphoma cases constituted 16.85 % of cases. In study conducted by Nigeria Anunobi C et al.[22] the total number of patients were 720, lymphoma cases constituted 14.20 % of cases.

Among 58 cases of NHL, T cell lymphoma comprised 5.2 % (3 cases) and B cell lymphoma 94.8 % (55 cases) with diffuse large B cell lymphoma being the most common subtype comprising 43.1 % (25 cases). Other subtypes of B cell lymphoma were 24.1 % (14 cases) of follicular lymphoma, 3.4 % (2 cases) of CLL / SLL, 7 % (1 case) of T cell rich B cell lymphoma.

Diffuse large B-cell lymphoma (DLBCL) accounting for 45.4 % of all B cell lymphomas, 43.1 % of all NHL and is the single largest subset of NHLs seen in India. In a study by Naresh et al.[23] DLBCL comprised 34 % of all NHL. Follicular lymphoma (FL) accounted for 25.5 % of all B-cell lymphomas. This reiterates the reported low frequency of FL in developing countries and Asia.[24] CLL / SLL formed 3.6 % of all B-cell lymphomas, a proportion that is similar to or lower than those seen in most developed countries and some Asian countries. However, it is higher than in Hong Kong and Korea.[25]

T cell lymphoma were 5.2 % of all NHL (3 cases), of which 3.4 % (2 cases) were peripheral T cell lymphoma NOS. 1.7 % (1 case) of angioimmunoblastic T cell lymphoma. Reports from Hong Kong and Shanghai quote T-cell lymphomas constitute 25 % of all NHLs.

Hodgkin's lymphoma (14 cases) constituted 3.9 % of lymph node biopsies and 19.4 % of all lymphomas. All the 14 cases were classical Hodgkin's lymphoma and the predominant subtype was mixed cellularity.

In a study by Roy A, Kar R, Basu D, Badhe BA et al. HL, which accounted for 12.4 % of all lymph node biopsies and

constituted 27.8 % of all lymphomas and the predominant subtype was nodular sclerosis.

Thirteen (22.4 %) cases could not be further sub classified due to the outside slides having been submitted for review with non-availability of blocks or due to non-contributory IHC, possibly due to poor antigenic preservation.

Metastasis contributed the remaining malignancies representing 12.6 % of total lymph node biopsies. Out of 45 cases of metastatic lymphadenopathy, 51.1 % (23 cases) were adenocarcinoma, 17.8 % (8 cases) were squamous cell carcinoma, 11.1 % (5 cases) were poorly differentiated carcinoma, 6.7 % (3 cases each) were melanoma and neuroendocrine carcinoma and 2.2 % (1 case each) of papillary thyroid carcinoma, alveolar rhabdomyosarcoma and malignant peripheral nerve sheath tumour.

In a study by Roy A, Kar R et al. metastases constituting 8.5 % of all lymph nodes biopsies. Among them, metastatic adenocarcinoma was the most common. In the United States metastases comprising 29 % of peripheral lymph nodal enlargement, second only to reactive hyperplasia.[26]

CONCLUSIONS

Lymph node biopsy plays an important role in establishing the cause of lymphadenopathy. In our study, reactive hyperplasia was the most common cause of lymphadenopathy followed by tuberculous lymphadenitis. Among malignancies, lymphomas predominate over metastatic lesions with NHL comprising 49.6 % and HL comprising 12 %. T cell lymphomas show a lesser prevalence compared with other studies. Among the NHL, DLBCL was the most common and among the HL, mixed cellularity was the most common subtype. Adenocarcinoma was the predominant subtype among the metastatic malignancies.

The study highlights the importance of lymph node biopsy for establishing the cause and early diagnosis of lymphadenopathy. So, more attention should be given to lymph node swelling for the appropriate clinical management of patients.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
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REFERENCES

[1] Delves PJ, Roitt IM. The immune system. First of two parts. N Engl J Med 2000;343(1):37-49.
[2] Van Der Valk P, Meijer CJLM. Lymph nodes. In: Mills SE, edr. Histology for pathologists. 3rd edn. Philadelphia: Lippincott Williams and Wilkins 2007: p. 763-782.
[3] Cottier H, Turk J, Sobin L. A proposal for a standardized system of reporting human lymph node morphology in relation to immunological function. Bull World Health Organ 1972;47(3):375-417.
[4] Habermann TM, Steensma DP. Lymphadenopathy. Mayo Clin Proc 2000;75(7):723-732.
[5] Pangalis GA, Vassilakopoulos TP, Boussiotis VA, et al. Clinical approach to lymphadenopathy. Semin Oncol 1993;20(6):570-582.
[6] Ferrer R. Lymphadenopathy: differential diagnosis and evaluation. Am Fam Physician 1998;58(6):1313-1320.
[7] Sibanda EN, Stanczuk G. Lymph node pathology in Zimbabwe: a review of 2194 specimens. Q J Med 1993;86(12):811-817.
[8] Moore SW, Schneider JW, Schaaf HS. Diagnostic aspects of cervical lymphadenopathy in children in the developing world: a study of 1877 surgical specimens. Pediatr Surg Int 2003;19(4):240-4.
[9] Rahman MA, Biswas MMA, Siddika ST, et al. Histopathological evaluation of lymph node biopsies: a hospital based study. J Enam Med Coll 2012;2(1):8-14.
[10] Adeniji KA, Anjorin AS. Peripheral lymphadenopathy in Nigeria. Afr J Med Med Sci 2000;29(3-4):233-237.
[11] Kamat GC. A ten-year histopathological study of generalized lymphadenopathy in India. S Afr Fam Pract 2011;53(3):267-270.
[12] Saraswat A, Rajender A, Purohit K. Lymph node biopsy: spectrum and clinical significance as diagnostic tool at tertiary care centre. J of Evolution Med and Dent Sci 2015;4(6):1008-1014.
[13] Vachhani A, Bhuva K, Jasani JH, et al. Histopathological study of lymph node biopsy. International Journal of Biomedical and Advance Research 2013;4(11):790-795.
[14] Rao MN, Raju YS, Prasad AK, et al. Evaluation of lymphadenopathy at a referral centre. JAPI 2002;50:1488-1489.
[15] Olu-Eddo AN, Ohanaka CE. Peripheral lymphadenopathy in Nigerian adults. J Pak Med Assoc 2006;56(9):405-408.
[16] Moore SW, Schneider JW, Schaaf HS. Diagnostic aspects of cervical lymphadenopathy in children in the developing world: a study of 1877 surgical specimens. Pediatr Surg Int 2003;19(4):2040-2044.
[17] Damle RP, Suryawanshi K, Dravid NV, et al. Descriptive study of histological patterns of lymph node biopsies in a tertiary care hospital. Annals of Pathology and Laboratory Medicine 2017;4(02):131-136.
[18] Vachhani A, Bhuva K, Jasani J, et al. Histopathological study of lymph node biopsy. International Journal of Biomedical and Advance Research 2013;4(11):790-795.
[19] Shrestha A, Chalise PR, Shrestha ML. Lymph node biopsies: a hospital based retrospective study. J Nepal Med Assoc 2009;48(176):306-309.
[20] Sibanda EN, Stanczuk G. Lymph node pathology in Zimbabwe: a review of 2194 specimens. Q J Med 1993;86(12):811-817.
[21] Akinde OR, Anunobi CC, Abudu EK, et al. Pattern of lymph node pathology in Lagos. Nig Q J Hosp Med 2011;21(2):154-158.
[22] Anunobi CC, Banjo AA, Abdulkareem FB, et al. Review of the histopathologic patterns of superficial lymph node diseases, in Lagos (1991-2004). Niger Postgrad Med J 2008;15(4):243-246.

[23] Naresh KN, Srinivas V, Soman CS. Distribution of various subtypes of non-Hodgkin's lymphoma in India: a study of 2773 lymphomas using R.E.A.L. and WHO classifications. Ann Oncol 2000;11(Suppl 1):63-67.
[24] Sukpanichnant S, Sonakul D, Piankijagum A, et al. Malignant lymphoma in Thailand: changes in the frequency of malignant lymphoma determined from a histopathologic and immunophenotypic analysis of 425 cases at Siriraj Hospital. Cancer 1998;83(6):1197-1204.
[25] Lee YT, Terry R, Lukes RJ. Biopsy of peripheral lymph nodes. Am Surg 1982;48(10):536-539.
[26] Henry PH, Longo DL. Enlargement of lymph nodes and spleen. In: Braunwald E, Hayser SL, Fauci AS, eds. Harrison's Principles of Internal Medicine. 19th edn. New York: McGraw-Hill 2005.