e-ISSN: 0975-1556, p-ISSN:2820-2643
Available online on www.ijpcr.com
International Journal of Pharmaceutical and Clinical Research 2024; 16(4); 861-865
Original Research Article

Clinicopathological Study of Lymphadenopathy: A Hospital-Based Retrospective Study.

K Mohini Rao[1], Pratibha Samant Roy[2], Deepika Sahu[3], Swagatika Agrawal[1]*, Saswat Acharya[4]

[1]Professor, Department of Pathology, IMS SUM II, Bhubaneswar, Odisha, India.
[2]Senior consultant Microbiology, Jagannath Hospital, Bhubaneswar, Odisha, India.
[3]Assistant Professor, Department of Pathology, Hi-Tech Medical College, Bhubaneswar, Odisha, India.
[4]Post-graduate Student, Department of Pathology, Hi-Tech Medical College, Odisha, Bhubaneswar, India.

Received: 07-02-2024 / Revised: 01-03-2024 / Accepted: 18-03-2024
Corresponding Author: Dr. Swagatika Agrawal
Conflict of interest: Nil

Abstract

Introduction: Knowledge of the typical lymphadenopathy patterns in a specific region is crucial for accurate diagnosis and suspicion of specific diseases. However, in many clinical settings, differentiating between reactive (non-cancerous) and neoplastic lymphadenopathy remains a challenge.

Aims & Objectives: To describe the clinicopathological features of patients who admitted to our wards with a primary presenting feature of lymphadenopathy.

Materials and Methods: This hospital based retrospective study comprises 168 patients of all ages presenting with enlarged lymph nodes who were referred to our Department of Pathology by the clinicians in outpatient department (OPD) of a tertiary care hospital, Bhubaneswar over a period of 1 year.

Results: Localized lymphadenopathy was more prevalent than generalized lymphadenopathy. In generalized lymphadenopathy cases, granulomatous and malignant diagnosis was higher in while in localized lymphadenopathy, reactive lymphadenitis was higher followed by granulomatous lesion. Localized lymphadenopathy cases were most common in below 20 years age while generalized lymphadenopathy were most commonly presented above >20 years age. The sensitivity, positive predictive value and accuracy of lymph node FNAC was 94.49%, 96.26%, and 91.15% respectively.

Conclusion: FNAC as a simple, inexpensive, relatively painless, rapid, repeatable, and reliable method of investigation for lymphadenopathy, especially in OPDs, peripheral hospitals, and dispensaries, thus reducing the incidence of surgery and therefore, bed occupancy. However, it is not a substitute for conventional surgical pathology but is complimentary to it.

Keywords: Fine-Needle Aspiration Cytology, Lymphadenitis, Lymphadenopathy, Granulomatous Lymphadenitis.

Introduction

Lymph nodes, a vital part of the body's defense system, are small, rounded or kidney-shaped structures of lymphoid tissue. They filter particulate matter and microorganisms from lymph fluid.[1] Lymph node enlargement, termed lymphadenopathy (LAP), can stem from various causes, including infectious diseases, neoplastic (cancerous) disorders, lipid storage diseases, endocrine disorders, and conditions like sarcoidosis and histiocytosis. [2] Due to this wide variety of etiologies, diagnosing LAP can be challenging and often requires extensive investigations. [3] Fine-needle aspiration cytology (FNAC) is a safe, reliable, rapid, and cost-effective method for diagnosing superficial lymph node enlargement and guiding further investigation. Knowledge of the typical LAP patterns in a specific region is crucial for accurate diagnosis and suspicion of specific diseases. However, in many clinical settings, differentiating between reactive (non-cancerous) and neoplastic lymphadenopathy remains a challenge. [4] There is a significant gap in literature regarding the prevalence and underlying causes of LAP in India. [5]

The present study aims to retrace the current patterns in the etiology of lymph node enlargement among urban population, and to examine the distribution of lesions among various age and sex groups. Here, knowledge about the pattern of lymphadenopathy is helpful to the clinician for solving the dilemma.

Materials and Methods

This hospital based retrospective study comprises 168 patients of all ages presenting with enlarged lymph nodes who were referred to our Department of Pathology by the

clinicians in outpatient department (OPD) of a tertiary care hospital, Bhubaneswar over a period of 1 year. In each instance, a brief clinical history and physical examination along with an evaluation of relevant investigations, if available, was carried out. The FNAC procedure was performed using23/24-gauge needles attached to a 20 ml syringe. Deep-seated lesions were aspirated under image guidance (both computed tomography and ultrasonography).

The aspirated material was smeared onto four slides in each case. Two slides were immediately immersed in 95% ethanol and remaining air-dried. The air-dried smears were routinely stained by May-Grunwald-Giemsa stain and alcohol fixed smears stained by hematoxylin and eosin stain and Papanicolaou stain. Special stains like Ziehl-Neelsen stain (ZN) stain for acid-fast bacilli (AFB) and periodic acid–Schiff for mucin were done whenever required. The diagnosis was classified according to various morphological patterns and correlated clinically.

In 132 cases (65.02%) cytology and histopathology correlation were available. Standard guidelines for cytological diagnosis were followed as far as practicable.

Data were analyzed using a computer software Epi Info version 6.2 (Atlanta, Georgia, USA) and Microsoft Excel for Windows.

Results

A total of 212 cases underwent FNAC. Of these, 203 cases (95.75%) yielded adequate material for interpretation; while nine cases (4.25%) yielded inadequate material. Aspiration was performed on palpable superficial lymph nodes in 164 patients (80.78%), while 39 patients (19.21%) had deep-seated lymph node aspirations.

The age of the patients ranged from 11 months to 72 years. The mean age for all patients with lymphadenopathy (LAP) was 23.7 years. A total of 92 cases (45.3%) were in patients under 20 years old. Cytopathological examination revealed benign features in 150 cases (73.89%) and malignant features in 53 cases (26.1%). Overall, reactive lymphadenitis was the most common diagnosis, identified in 103 cases (47%) (Figure 1A, B). Granulomatous lymphadenitis was the next most frequent diagnosis, seen in 47 cases (23.2%) (Figure 1C, D).

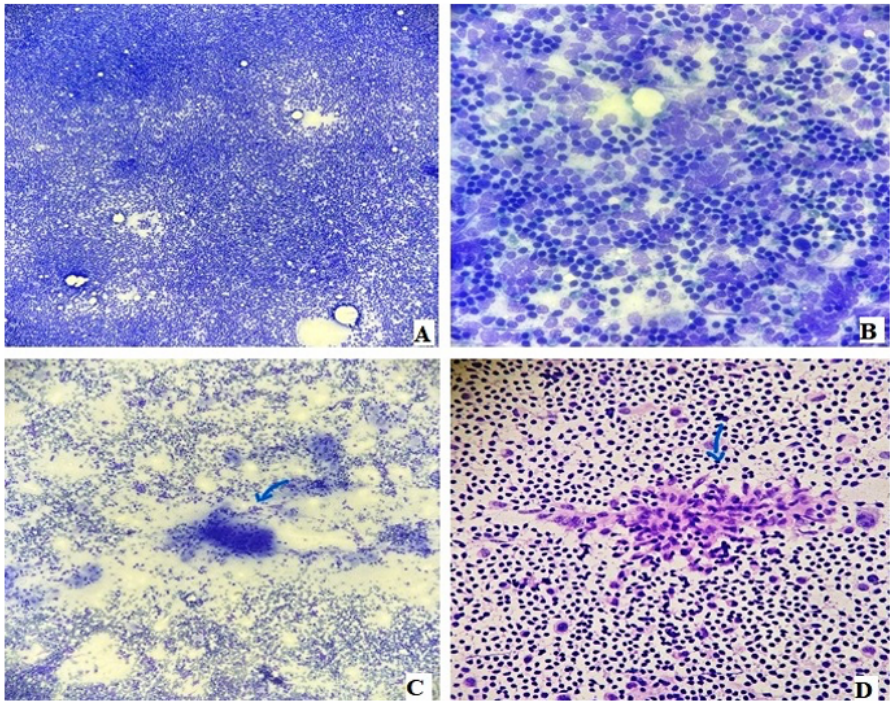

Figure 1: A) Reactive lymphadenitis (10x, Diff quick); B) Reactive lymphadenitis (40x,Diff quick);C) Epithelioid cells, necrosis in GML (PAP 10X) D) Epithelioid cells in granulomatous lesion (40x-giemsa)

Localized lymphadenopathy was more prevalent than generalized lymphadenopathy **[Table 1]**.

Table 1: Pattern of lymphadenopathy and diagnosis in a tertiary care hospital.

Variables		Total (203)		Localized (129)		Generalized (74)	
		N	%	N	%	N	%
Age	<10	40	19.7	29	22.0	11	14.9
	11-20	52	25.6	36	28.0	16	21.6
	21-30	38	18.7	21	16.0	17	23.0
	31-40	30	14.8	19	15.0	11	14.9
	41-50	18	8.9	11	9.0	7	9.5
	51-60	14	6.9	8	6.0	6	8.1
	61-70	7	3.2	3	2.0	4	5.4
	>71	5	2.3	3	2.0	2	2.7
Sex	Male	107	52.7	66	51.2	41	55.4
	Female	96	47.3	63	48.8	33	44.6
Pathology	RLA	103	50.7	89	69.0	14	18.9
	GML	47	23.2	24	18.6	23	31.1
	HL	7	3.4	3	2.3	4	5.4
	NHL	39	19.2	11	8.5	28	37.8
	Metastasis	7	3.4	2	1.6	5	6.8

RLA: reactive lymphadenitis; GML: granulomatous lymphadenitis; HL: Hodgkins lymphomal; NHL: Non-Hodgkins lymphoma.

In generalized lymphadenopathy cases, granulomatous and malignant diagnosiswas higher in comparison to localized lymphadenopathy.The maximum number of cases was found in the age group >20 years (64%). Forty-one cases (55.40%) were found in men, and 35 cases (44.6%) were found in women **[Table 2]**

Table 2: Age and gender-wise distribution of various lymphadenopathy cases.

Age & Sex	Localized (N=129)					Generalized (N=74)				
	RLA (N=89) %	GML (N=24) %	HL (N=3) %	NHL (N=11) %	Met (N=2) %	RLA (N=14) %	GML (N=23) %	HL (N=4) %	NHL (N=28) %	Met (N=5) %
<10	29.2	8.3	-	9.1	-	28.6	13.0	25.0	10.7	-
11-20	27.0	37.5	-	27.3	-	14.3	21.7	25.0	28.6	-
21-30	13.5	25.0	33.3	18.2	-	35.7	26.1	-	21.4	-
31-40	18.0	16.7	0.0	9.1	-	7.1	13.0	25.0	21.4	-
41-50	4.5	16.7	-	27.3	-	7.1	13.0	-	7.1	-
51-60	5.6	4.2	-	9.1	50.0	7.1	4.3	-	7.1	40.0
61-70	1.1	4.2	33.3	-	-	0.0	8.7	25.0	3.6	20.0
>71	1.1	-	33.3	-	50.0	0.0	-	-	-	40.0
Male	47.2	66.7	33.3	54.5	50.0	35.7	56.5	25.0	67.9	60.0
Female	52.8	33.3	66.7	45.5	50.0	64.3	43.5	75.0	32.1	40.0

In cases with tubercular lymphadenitis, epithelioid cells were present in 29 cases (61.7%) and Langhans giant cells were detected in 18 cases (38.2%). Cytological features were described under three major categories: Epithelioid granuloma without necrosis, epithelioid granuloma with necrosis and necrosis without epithelioid granuloma. ZN staining for AFB was performed and forty cases (40.4%) were positive.

In 113 cases of lymphadenopathy, the results obtained on FNAC were compared with the histopathological diagnosis of the corresponding excised lymph node(Figure 2). One hundred and three cases (91.15%) were true positives, six cases (6.78%) were false negatives and only four cases (4.52%) were false positives. Thus, a sensitivity of 94.49%, positive predictive value of 96.26%, and accuracy of 91.15% was observed.

Discussion

Lymphadenopathy as a clinical manifestation of the regional or systemic disease serves as an excellent clue to the underlying disease. It can arise either from benign ormalignant causes depending on the geographical condition and socioeconomic setup.

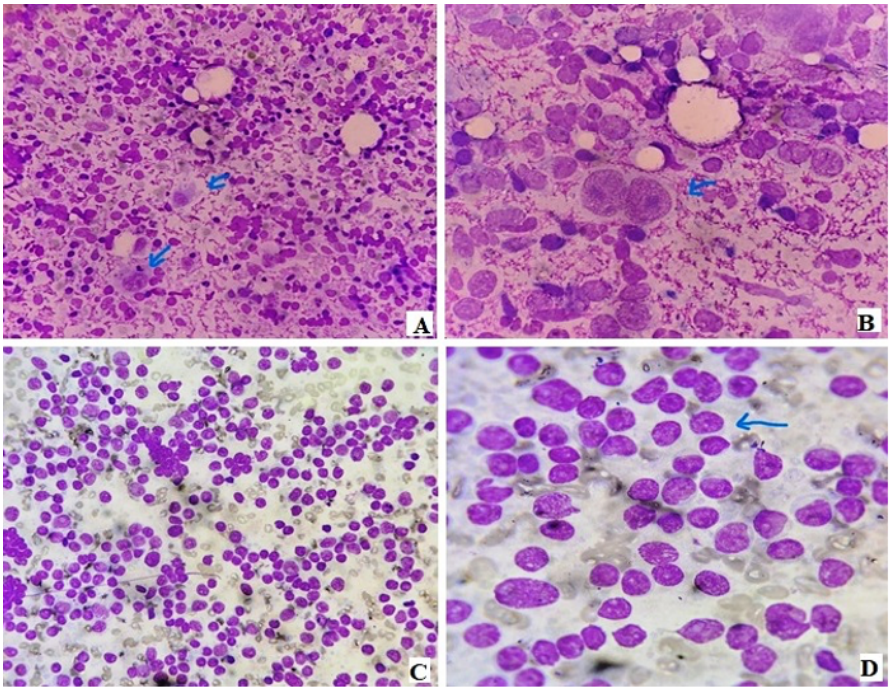

Figure 2: A) Hodgkin's lymphoma, mononuclear cells (10x, Giemsa); B) Hodgkin's lymphoma, RS cells (40x, Giemsa); C) Non-Hodgkin's lymphoma (10x, Giemsa); D) Non-Hodgkin's lymphoma (40x, Giemsa)

The peripheral groups are those readily palpable by clinical examination, and routinely looked for, but only those in the submandibular, axillary or inguinal regions may normally be palpable in healthy individuals.

Lymphadenopathy is considered to be localized if only one group of LN is involved, limited if 2-3 groups of LN are involved and generalized if more than three non-contiguous groups are involved.[1,2] Localized LAP is more common and it has been reported to affect nearly 75 percent of patients presenting with LAP, whereas 25 percent of those patients had generalized LAP. In our study of 203 adults who presented with LAP as a presenting feature, localized LAP occurred in 63.6%, and generalized in 36.5%.Distinguishing between the extensions of LAP is important in formulating a differential diagnosis. Generalized LAP is almost always due to a significant systemic illness.[6]

Lymph node lesions can be seen in patients ranging from very early to advanced age. In our study, the youngest patient with lymphadenopathy was a 11 months male infant and the oldest one was 78-year-old, with a mean age of 23.7 years. In our study, a male preponderance was noted with a male-to-female ratio of 1.1:1 which correlated with others.[7,8,9] In contrast, some other studies found a slight female predominance with a male to female ratio of 1:1.2.[10,11]

In our study, non-neoplastic lesions constituted 73.89%, and neoplastic lesions constituted 25.11% of all aspirates. Of the non-neoplastic lesions, 50.7% were reactive lymphadenitis, and 23.2% were granulomatous lymphadenitis. In contrast, in a study by Sibanda et al. [12] the prevalence of reactive hyperplasia was 33%, and that of granulomatous lymphadenitis was 26.7%. The higher incidence of granulomatous lymphadenitis in the present study is probably due to the high prevalence of tuberculosis in this part of India. [6]

In our study, the most common cause of generalized lymphadenopathy was Non-Hodgkin's lymphoma and granulomatous lymphadenitis. In other study, the most common cause of generalized lymphadenopathy was granulomatous lymphadenitis, followed by reactive lymphadenitis. [4]Although this study relates to the histopathological study of lymphadenopathy in India, a similar incidence of reactive lymphadenitis, granulomatous lymphadenitis and neoplastic lesions has been found in studies conducted in other developing countries.[10,11]

In the present study, lymphoma accounted for 22% of all cases, while metastatic disease accounted for 3.4% of all cases. In a study by Sibanda et al. [12] 7% of cases were lymphomas and 12.4% of cases were metastatic disease. In a study by Oluwale et al. [13] lymphoma constituted 23.8% of cases, while metastasis was seen in 24.5% of cases.5 In a study by Sinclair et al.[14] 63.29% of cases were lymphoma, while 17.72% of cases were metastatic deposits.

In the present study, there were eight cases of non-Hodgkin's lymphoma, out of which anaplastic large-cell lymphomas accounted for four cases (50%), follicular lymphomas accounted for three cases

(37.5%), and small lymphocytic lymphoma accounted for a single case (12.5%). In a study by Strauss et al. [15] 77% of cases were diffuse non-Hodgkin's lymphoma, 21% were nodular non-Hodgkin's lymphoma,2% were nodular and diffuse non-Hodgkin's lymphoma, and 1% was unclassifiable.

In the present study, there were 7 cases of metastatic malignancy, of which three cases were metastatic squamous cell carcinoma, and four cases were metastatic adenocarcinoma. In a study by Rao et al. [16] of 14 metastatic tumors, metastatic bronchogenic carcinoma was found in eight cases (57.15%), and metastasis from an unknown primary was found in three cases (21.43%), while metastases from carcinoma of the stomach, pancreas and testes contributed to one case each (7.14%). [3] In the present study, out of 7 patients with lymph nodes with metastatic tumors, all were older than 50 years. In a study by Sriwatanawongsa et al. [17] the incidence of secondaries after the age of 55 years was 75.8%, which is consistent with the present study.

Conclusion

In this study we found that, lymphoma and tuberculosis are the leading cause of generalized lymphadenopathy. It is important for physicians to be aware of these findings. This study highlights the usefulness of FNAC as a simple, inexpensive, relatively painless, rapid, repeatable, and reliable method of investigation for lymphadenopathy, especially in OPDs, peripheral hospitals, and dispensaries, thus reducing the incidence of surgery and therefore, bed occupancy. However, it is not a substitute for conventional surgical pathology but is complimentary to it.

References

1. Afzal W, Arab T, Ullah T, Teller K, Doshi KJ. Generalized Lymphadenopathy as Presenting Feature of Systemic Lupus Erythematosus: Case Report and Review of the Literature. J Clin Med Res. 2016 Nov;8(11):819-823.
2. GC Kamat. A ten-year histopathological study of generalized lymphadenopathy in India, South African Family Practice, 2011;53:3, 267-270,
3. Ali M, Elhatw A, Hegazy M, et al. The Evaluation of Lymphadenopathy in a Resource-Limited Setting. Cureus. October 24, 2022; 14(10): e30623.
4. Malhotra AS, Lahori M, Nigam A, Khajuria A. Profile of lymphadenopathy: An institutional based cytomorphological study. Int J App Basic Med Res 2017; 7:100-3.
5. Sharadamani GS. Prevalence of various causes of lymphadenopathy in a rural setting in India. Indian Journal of Pathology and Oncology, July-September 2017;4(3):462-464.
6. Ozkan EA, Goret CC, Ozdemir ZT, Yanik S, Goret NE, Dogan M, Cihan FG. et al. Evaluation of peripheral lymphadenopathy with excisional biopsy: six-year experience. Int J ClinExpPathol. 2015;8(11):15234–15239.
7. Dhingra V, Misra V, Mishra R, Bhatia R, Singhal M. Fine needle aspiration cytology (FNAC) as a diagnostic tool in paediatric lymphadenopathy. J ClinDiagn Res 2010; 4: 2452-7.
8. Patra AK, Nanda BK, Mohapatra BK, Panda AK. Diagnosis of lymphadenopathy by fine needle aspiration cytology. Indian J Pathol-Microbiol. 1983; 26:273-8.
9. Hirachand S, Lakhey M, Akhter J, Thapa B. Evaluation of fine needle aspiration cytology of lymph nodes in Kathmandu Medical College, Teaching hospital. Kathmandu Univ Med J (KUMJ) 2009; 7:139-42.
10. Nidhi P, Sapna T, Shalini M, Kumud G. FNAC in tuberculous lymphadenitis: Experience from a tertiary level referral centre.Indian J Tuberc 2011;58:102-7.
11. Ageep AK. Assessment of adult peripheral lymphadenopathy in Red Sea State, Sudan. Internet J Trop Dis Health 2011; 2:24-32.
12. Sibanda EN, Stanczuk G. Lymph node pathology in Zimbabwe: a review of 2 194 specimens. Q J Med. 1993;86(12):811-817.
13. Oluwale SF, Odesanmi WO, Kalidasa AM. Peripheral lymphadenopathy in Nigeria. Acta Trop. 1985;42(1):87-96.
14. Sinclair S, Beckman E, Ellman L. Biopsy of enlarged superficial lymph nodes. JAMA. 1974;22 8(5):602-604.
15. Strauss DJ, Filippa DA, Libermann P, et al The non-Hodgkin's lymphoma: a retrospective clinical and pathologic analysis of 499 cases diagnosed between 1958 and 1969. Cancer. 1983;51(1):101-109.
16. Rao MN, Raju YS, Prasad AK, et al. Evaluation of lymphadenopathy at a referral centre. JAPI. 2002; 50:1488-1489.
17. Sriwatanawongsa V, Cardoso R, Chang P. Incidence of malignancy in peripheral lymph node biopsy. Am Surg. 1985;51(10):587-590