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To study the age-wise spectrum of neoplastic and non-neoplastic lesions of lymph node based on histopathological and cytomorphological study in 100 cases in a tertiary care hospital

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Abstract
Lymphadenopathy is one of the commonest presentations in OPD with varied etiology ranging from inflammatory condition to malignant. The various modalities available for this are clinical evaluation, FNAC, open biopsy. Fine needle aspiration cytology (FNAC) was introduced to reduce the number of excisional biopsies of lymph nodes. Although histopathological examination is considered to be gold standard in diagnosis especially in lymphomas, FNAC maybe the only tool for diagnosis and further management of the patients in some cases of metastatic malignancy. The aim is to study the histopathological and cytomorphological spectrum of lymph node lesions in 100 cases and to know the incidence of various lesions of the lymph node in different age groups. All the specimens of lymph node submitted for histopathological and cytomorphological examination will be included in the material to study. The relevant data of patient will be recorded in pre designed performa. Total of 100 cases would be included in the study.

Keywords: Lymphadenopathy, presentations, OPD, FNAC

Introduction
Lymphadenopathy is a common presenting symptom in various disorders. The lymph nodes react to various known and unknown stimuli and undergo reactive changes leading on to vast array of non-neoplastic lymphoid proliferations or hyperplasias. FNAC is performed, because of their wide distribution and easy accessibility. Lymph node aspiration is of great value for diagnosis of lymphadenitis, lymphomas and metastatic carcinoma [1]. Lymphadenopathy is defined as an abnormality in the size or character of the lymph nodes. It is caused by invasion or propagation of either inflammatory or neoplastic cells into the nodes [2]. FNAC is an out-patient procedure with a higher acceptance when compared to open biopsy. Superficial lymph nodes are easily approached and deep seated lymph nodes can be aspirated with the aid of USG, CT or MRI [3]. FNAC is an easy, speedy, cheap and reliable tool for investigating the cause of lymphadenopathy [4]. Thus, FNAC provides a simple and cost-effective test for the diagnosis of reactive lesions, hyperplasia, infections etc. In cases of reactive lymphadenopathy, FNAC can significantly decrease the number of open biopsies and aid in diagnosing a specific infectious etiology and planning the treatment. FNAC is a well-established tool for diagnosis of metastatic malignancies of lymph nodes. It confirms the presence of metastasis while also giving clues to the nature of primary site [5]. The diagnostic accuracy of FNA cytology for Hodgkin's Lymphoma has also been invariably high (>85%). Yet, the role of cytology in primary diagnosis, sub-classification and management of patients with lymphoma remains controversial [6].

Aim and Objectives
1. To study the histopathological and cytomorphological patterns of lymph node lesions.
2. To compare the results of the current study with the findings of similar studies conducted by various other authors.
3. To arrange the age wise distribution of the lesions.

Materials and Methods
All the specimens of lymph node submitted for histopathological and cytomorphological examination were included in the material to study. The relevant data of patient was recorded in pre designed proforma. A total of 100 cases were included in the study. The patients who presented with lymphadenopathy were subjected to fine needle aspiration and the fixed slides were stained with MGG, ZN stains. The corresponding specimens of lymphadenopathy received from surgery department were fixed in 10% buffered formalin. After fixation, the specimen was subjected to gross examination for size external appearance. After processing, the specimens were subjected to histo-pathological examination and the results were correlated with those of cytological findings.

Observations
The present study was based on cytological examination of lymph node aspiration smears in 100 patients, who presented with lymphadenopathy in the department of Pathology and their correlation with histopathological specimens, wherever possible. This was a prospective study, conducted at Government Medical College, Patiala and

Amritsar. The age of the patients included in the study ranged from 2 years to 78 years. The maximum number of patients was in the first decade of life, followed by the second decade. Out of a total of 100 patients, maximum number of patients were male constituting about 56% while females constituted the remaining 44% (Male:Female-1.2:1).

In this study, the most common site of involvement was the cervical group of lymph nodes constituting 48%, followed by the submandibular group of lymph nodes constituting 14% of total cases. The most frequent cause of lymph node enlargement was due to benign etiology (87%) cases, followed by malignant (13%).

The most common site for involvement of lymph node lesions was cervical group (52%) of lymph nodes followed by submandibular (13%), submental (11%), supraclavicular (9%), axillary (7%), inguinal (4%), occipital (4%) for lesions with benign etiology while cervical (30%) and supraclavicular (30%) followed by abdominal (15%), submandibular (15%), inguinal (10%) for lesions with malignant etiology.

The most common cause of lymph node enlargement diagnosed cytologically was non-specific reactive lymphadenitis which constituted 55% cases followed by granulomatous lymphadenitis (30%), secondary malignancies (9%), non-Hodgkin's lymphoma (3%), suppurative lymphadenitis (2%), Hodgkin's lymphoma (1%) as shown in table 8. Amongst the various benign causes of lymphadenopathy, the most common cause was found to be non-specific reactive lymphadenitis in 55% with male preponderance of cases followed by granulomatous lymphadenitis (34%), suppurative lymphadenitis (03%) as shown in table 1.

1. Benign lesions of the lymph node

a. Non Specific Reactive Lymphadenitis

NSRL was diagnosed in 55 patients (55%). The age of the patients ranged from 2 years to 55 years with majority of the patients being in 1st decade of life. The majority of the cases with reactive hyperplasia were due to infection in the area drained by regional lymph nodes. Among these, the cervical lymph nodes were enlarged in 57%, submandibular in 14%, supraclavicular and submental in 9% each, axillary and occipital in 04% each, inguinal in 2%. The cytological smears derived from the reactive node showed a polymorphous population of lymphoid series of cells comprising of centroblasts, centrocytes, immunoblasts and plasma cells in various proportions (Fig. 1).

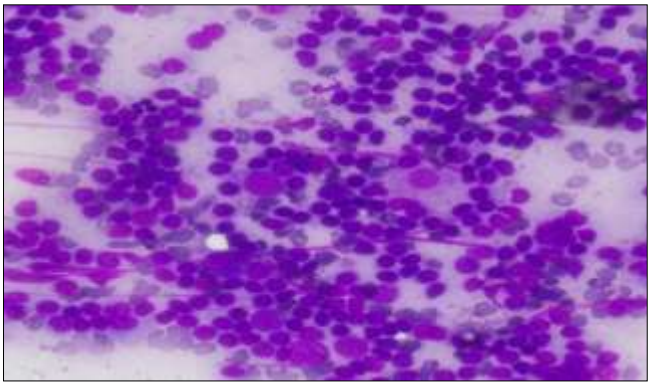

Fig 1: FNAC smear of Non specific reactive lymphadenitis of lymph node (MGG X1000)

Out of the 55 patients with cytological diagnosis of non-specific reactive hyperplasia, lymph node biopsy specimens were available from 19 patients. The histopathological examination was consistent with cytological examination in 17 cases (Fig. 2) while one came out to be granulomatous lymphadenitis and one case is diagnosed as Hodgkin's lymphoma. On statistical analysis, in cases of non-specific reactive lymphadenitis FNAC has a sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of 100%, 88.89%, 89.47%, 100% and 94.29% respectively.

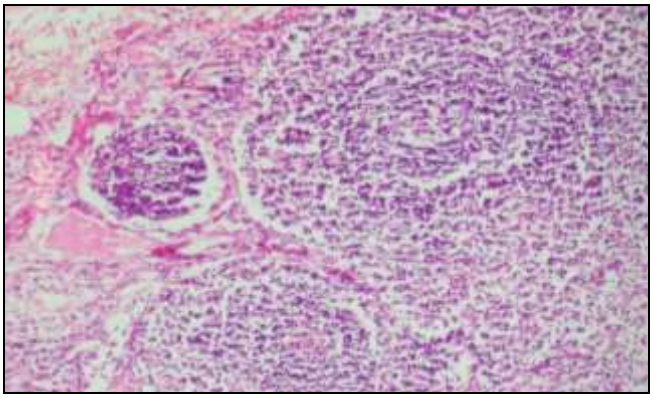

Fig 2: Histopathological section exhibiting reactive lymphoid follicular hyperplasia (H&E X400)

b. Granulomatous Lymphadenitis

A diagnosis of granulomatous lymphadenitis was made in 30 patients (30%). The age group varied from 3 years to 55 years. The maximum number of patients were in the second decade of life. The most common site of involvement was the cervical lymph nodes in 46%, submandibular in 13%, submental in 16%, supraclavicular in 10%, axillary in 6%, occipital and inguinal in 3% each. The cytological smears derived from the granulomatous lesion showed epithelioid cell granulomas with or without necrosis along with various cells of chronic inflammation like lymphocytes, histiocytes. (Fig. 3)

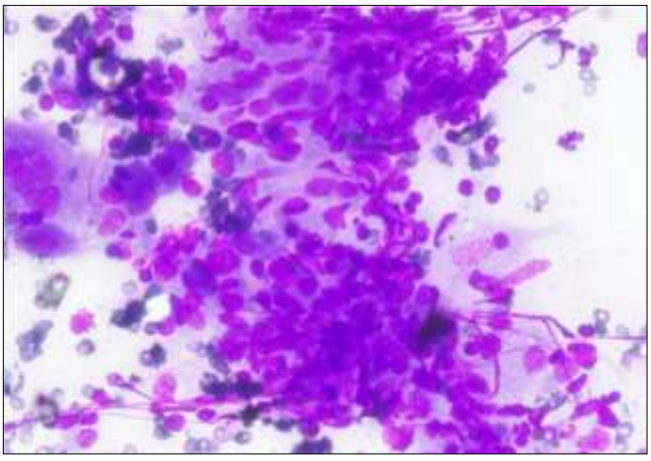

Fig 3: FNAC smear of a granulomatous lymphadenitis showing granuloma comprising of epithelioid cells, histiocytes and lymphocytes. (MGG X400)

Out of 30 cases of granulomatous lymphadenitis, lymph node biopsy (Fig. 4) was available for 9 patients and all

were consistent with cytological findings. On statistical analysis, in cases of granulomatous lymphadenitis FNAC has a sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of 100%, 96.15%, 90%, 100% and 97.14% respectively.

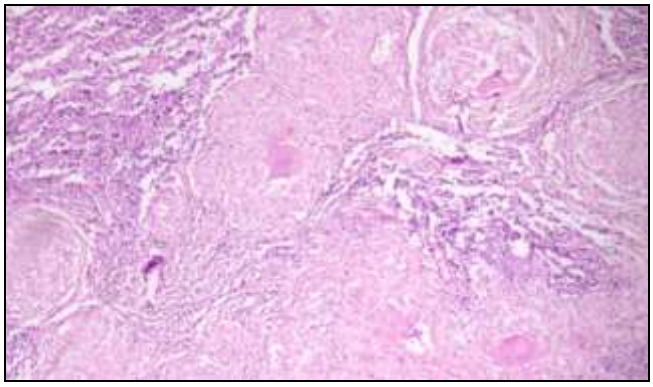

Fig 4: Histopathological section of granulomatous lymphadenitis with presence of multinucleated giant cells with foci of caseous necrosis. (H&E X400)

c. Suppurative lymphadenitis

It was diagnosed in 2 patients with the ages of 3 years and 24 years. The male to female ratio was 1:1. On Cytological examination of suppurative lymphadenitis infiltration by neutrophils was seen (Fig. 5)

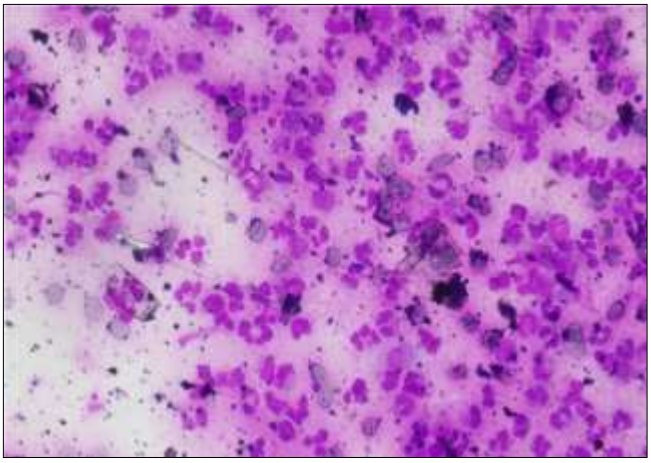

Fig 5: FNAC smear of suppurative lymphadenitis showing infilteration by neutrophils (MGG X400)

2. Malignant lesions of lymph node

a. Lymphomas

Lymphomas formed 4% of the total cases. Out of these 4 four cases, three were diagnosed cytologically as non-Hodgkin's lymphoma and one was diagnosed as Hodgkin's lymphoma. The age varied from 4 years to 62 years. Male to female ratio was 1:3.

On cytological examination of lymph node the smears revealed large anaplastic cells which were diagnosed as non-Hodgkin's lymphoma. (Fig. 6).

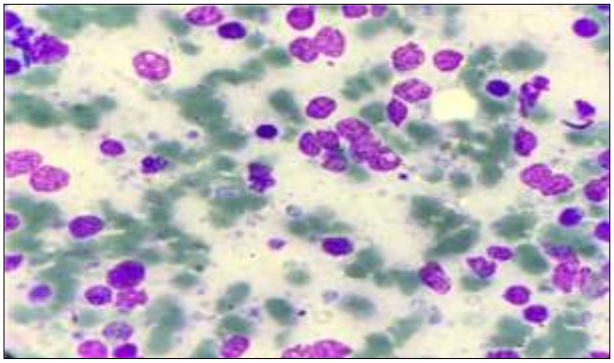

Fig 6: FNAC of lymph node with non-Hodgkin's lymphoma showing monomorphic population of tumor cells. (MGG X1000)

On cytological examination the smears revealed binucleated Reed Sternberg cells and a mixed inflammatory infiltrate in the background, diagnosed as Hodgkin's lymphoma (Fig. 7).

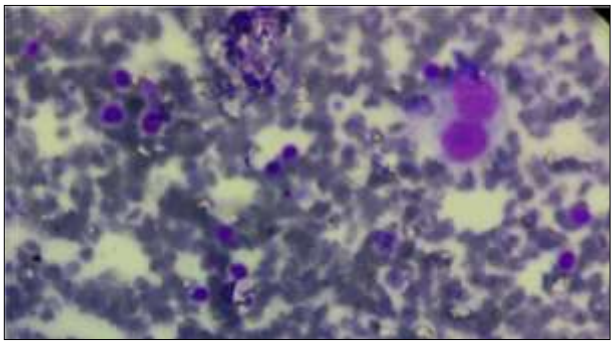

Fig 7: FNAC smear of lymph node of Hodgkin's Lymphoma showing classical Reed-Sternberg cell. (MGG X1000)

Majority of the smears showed monotonous population of tumor cells on cytology and a diagnosis of NHL was made in 3 cases and 1 was diagnosed as a case of Hodgkin's lymphoma. Lymph node biopsy was available for 2 patients of non-Hodgkin's lymphoma and 1 patient of Hodgkin lymphoma. On histopathological examination, all were in concordance with the cytological findings.

On histopathological examination of the case diagnosed as non-Hodgkin's lymphoma on cytology the sections showed replacement of normal architecture of lymph node by large anaplastic cells (Fig. 8). On statistical analysis, FNAC for non-Hodgkin's Lymphoma has a sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of 100% each.

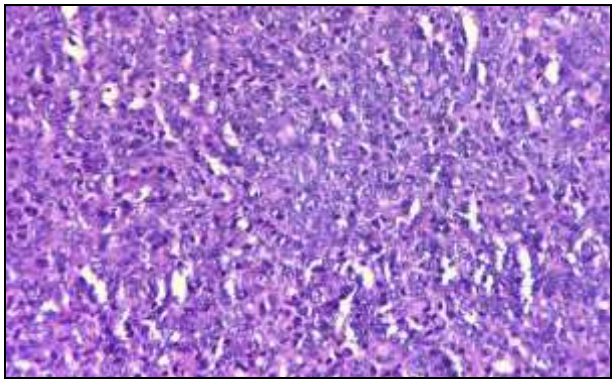

Fig 8: Histopathological section of lymph node with Non-Hodgkin's Lymphoma showing replacement of normal architecture by large anaplastic cells. (H&E X1000)

On histopathological examination of the case diagnosed as Hodgkin's lymphoma on cytology the sections showed, replacement of normal architecture of lymph node by monomorphic tumor cells and presence of classical Reed-Sternberg cells (Fig. 9).

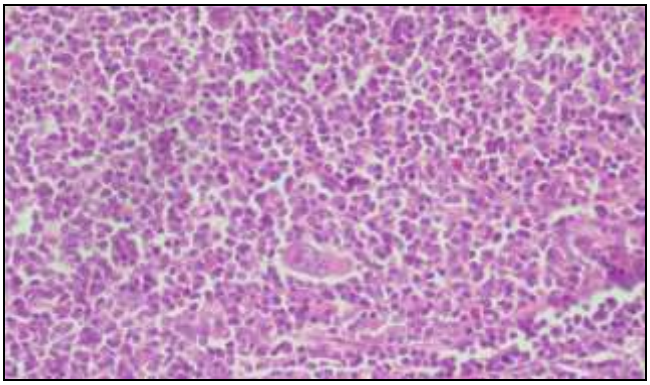

Fig 9: Histopathological section of lymph node of Hodgkin's lymphoma showing monomorphic tumor cells, infiltration with eosinophils and classical Reed-sterberg cell. (H&E X1000)

b. Secondary malignant lymph node lesions

A total of 9 cases were diagnosed of metastatic malignancy by FNAC in the age ranging from 25 years to 70 years. Male to female ratio was 2:1. On cytological examination the smears were highly cellular and showed atypical cells along with lymphoid cells (Fig. 10).

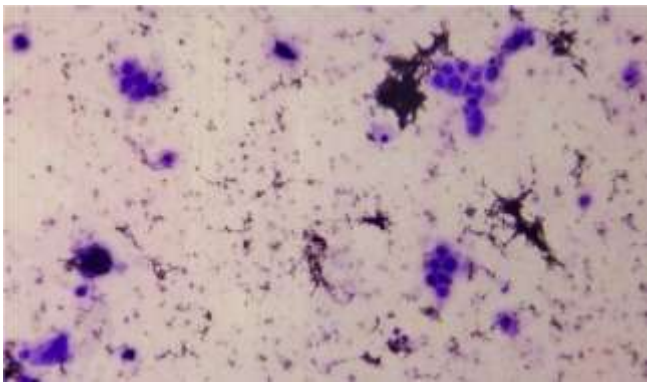

Fig 10: FNAC smear of a secondary malignancy of lymph node showing atypical cells. (MGG X400)

On histopathological examination the sections showed presence of atypical (metastatic) cells along with lymphoid tissue. Out of the 9 cases, 67% were of squamous cell carcinoma, 22% were of adenocarcinoma and 11% of undifferentiated carcinoma as shown in table 16 and figure 12. Histopathological sections were available in 4 cases and all were consistent with the cytological diagnosis. On statistical analysis, FNAC for Hodgkin's Lymphoma and Metastasis has a sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of 100%, 97.06%, 50%, 100% and 97.14% respectively (table 2). Therefore, on statistical analysis, the sensitivity, specificity and diagnostic accuracy of FNAC for diagnosing lymph node lesions came out to be 100%, 87.5% and 97.14% respectively.

Discussion

FNAC is an easy, quick, and cheap procedure that is used to sample superficial masses.

Age distribution

In the present study, the age of the patients ranged from 2 to 78 years. Other studies have also shown a similar wide range of age range in patients presenting with lymphadenopathy like Vimal *et al*., 2015 [7], Singh *et al* (2013) [8]. Majority of the patients were in the 1st decade of life in concordance with the study of Mainali *et al* **(**2015**)** [9]**.**

Sex distribution

In this study there is a slight male preponderance with a male to female ratio of 1.2:1. A similar sex distribution was also reported by Bhatta *et al* (2018) [10] and Singh *et al* (2013) [8]. However, an increase in incidence of lymphadenopathy in female patients was seen by Ahmed *et al* (2008) [11].

Sites of lymphadenopathy

The cervical group of lymph nodes was most commonly involved in this study (55%). Our findings are consistent with many other studies on lymph node aspiration like Bhatta *et al* (2018) [10], Vimal *et al* (2015) [7]. Biradar *et al* (2017) [12] reported cervical lymphadenopathy in 69% of patients in their study.

Benign vs malignant lymphadenopathy

In our study, benign lymphadenopathy was the most common presentation of lymphadenopathy amounting to 87% of all cases. Our findings were correlating well with the studies done by Bhatta *et al* (2018) [10], Sarda *et al* (1990) [13]. However Al-Alwan *et al* (1996) [14] observed only 53% cases of non-neoplastic lesions in his study.

In our study, benign lesions were more common than malignant ones. Non-specific reactive lymphadenitis was the most common finding of enlarged lymph nodes amounting to 55%, followed by granulomatous lymphadenitis amounting to 30%. This is correlating well with the study of Mainali *et al* **(**2015**)** [9], Bhatta *et al* (2018) [10]. However Rani *et al* (2014) [15] observed that granulomatous lymphadenitis constituted the majority of lesions which was not similar to our study.

Metastasis to lymph nodes was seen in 09 (09%) patients in this study. Chawla *et al* [16] found 10.7% incidence of metastatic malignancy. Also Singh *et al* (2013) [8] found 8.9% of metastatic malignancy in his study. The age of the patients of lymph node metastasis was from 25 years to 70 years. Most of the patients were in the seventh decade. Singh *et al* (2013) [8] found maximum cases of metastasis in seventh decade. In this study, out of all the metastatic

diseases, squamous cell carcinoma formed the majority of cases (67%) followed by adenocarcinoma (22%) and undifferentiated carcinoma (11%). Rani *et al* (2014) [15] found 55% cases of Squamous cell carcinoma, 07% cases of adenocarcinoma and 13% cases of undifferentiated carcinoma. Vimal *et al* (2015) [7] found 51% cases of squamous cell carcinoma, 07% cases of adenocarcinoma and 04%% cases of undifferentiated carcinoma. Table 3:

Comparison of sensitivity and accuracy of FNAC in lymphadenopathies with various other studies.

Table 1

Studies	Sensitivity	Accuracy
Singh *et al* [8] (2013)	97.5%	99.4%
Malhotra *et al* [17] (2017)	94.49%	91.15%
Present Study	100%	97.15%

Table 2: Cytopathological diagnosis of lymph node lesions

Cytological Diagnosis		No. of Cases	% Age	Gender		Age Range (in years)
				Male	Female	
Benign Lesions	Non-specific reactive lymphadenitis	55	55%	31	24	2-58
	Granulomatous lymphadenitis	30	30%	17	13	5.5-60
	Suppurative lymphadenitis	2	2%	1	1	6-24
Malignant Lesions	Hodgkin's lymphoma	1	1%	0	1	18
	Non-Hodgkin's lymphoma	3	3%	1	2	48-61
	Secondary malignancies	9	9%	6	3	30-78
Total Cases		100	100%	56	44	2-78

Table 3: Correlation between histopathological and cytopathological diagnosis of lymph node lesions

Cytological Diagnosis	No. of cases	% Age	Histopathological Diagnosis			
			Benign		Malignant	
			No. of Cases	% age	No. of Cases	% age
Benign	28	80%	27	96%	1	4%
Malignant	7	20%	0	0%	7	100%
Total	35	100%	27	77%	8	23%

Conclusion

The present study comprised of 100 patients who underwent fine needle aspiration of enlarged lymph nodes. The eminent aim was to evaluate the cytomorphological and histopathological spectrum of lymph node lesions and arrange them according to age. FNAC is a safe, affordable, effective, non-invasive technique with high patient acceptance. In this study, it was found that FNAC is a very effective diagnostic tool having a high sensitivity and specificity in the diagnosis of various lymph node lesions ranging from benign to malignant. It has a high diagnostic accuracy of 97% and is therefore a good preliminary investigation for diagnosing various lymph node lesions.

Conflict of interest: None
Source of funding: None

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