

# Structured Reporting of Lymph Node Cytopathology using the 2020 Sydney System Guidelines-A Retrospective Study

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## ABSTRACT

**Introduction:** Fine Needle Aspiration Cytology (FNAC) is a valuable diagnostic aid for evaluation of lymph node pathology. The new Sydney System (2020) for classification and reporting of lymph node FNAC has put forth guidelines for a categorical classification using uniform terminology and morphologic criteria, a major step towards standardisation.

**Aim:** The study was aimed to evaluate cytopathology of lymph node lesions during 2 year period by applying the proposed Sydney system and to assess the category wise Risk Of Malignancy (ROM) by comparing with histopathology diagnosis in available cases.

**Materials and Methods:** A retrospective observational study was conducted in 2021 December, on lymph node aspirates obtained during two-year period from January 2018 till January 2020 in the department of Pathology of a tertiary care centre. FNAC of 250 lymph node aspirates were evaluated. Smears were reviewed and categorised as per the Sydney System of reporting as, L1: non diagnostic/inadequate, L2: benign, L3: atypical cells/atypical lymphoid cells of undetermined significance, L4: suspicious for malignancy, L5: malignant. The diagnostic accuracy of cytology and ROM in each category was

assessed comparing with the gold standard histopathology diagnosis where available.

**Results:** Category wise distribution of 250 cytological diagnosis of lymphadenopathy reclassified in Sydney system were L1-14 (5.60%); L2-159 (63.60%); L3-04 (1.60%); L4-05 (2%); and L5-68 (27.20%) cases. Using histopathology as gold standard available in 53 cases, the ROM in each category was found to be 0%, 3%, 66.66%, 100% and 100%, respectively. The sensitivity, specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV) and diagnostic accuracy of cytological diagnosis was found to be 95.65%, 96.29%, 95.65%, 96.29% and 96%, respectively. Reactive lymphadenitis in 86 (34.40%) and metastatic carcinoma in 61 (24.40%) cases were the most common benign and malignant lesions respectively.

**Conclusion:** The Sydney system of structured reporting in lymph node cytology provides a clear-cut terminology, uniformity, and reproducibility of reports. It enhances the role of FNAC by alerting the clinician for follow-up and ancillary studies in atypical and equivocal cases. In the non diagnostic L1 category, repeat procedure or biopsy should be recommended to avoid False Negative (FN) diagnosis.

**Keywords:** Cytopathology, Fine Needle Aspiration Cytology, Lymph node, Malignancy risk, Sydney system

## INTRODUCTION

Lymphadenopathy may be a sign of a self-limited infection in children while in adults it may be a sign of metastatic malignancy. The aetiology of infectious pathology varies based on geographical areas [1]. Tuberculosis is reported to be the most common infectious cause of cervical lymphadenopathy in endemic areas of developing countries [2]. Most lymph node lesions are non neoplastic, the smaller subset of neoplastic lesions need to be identified for optimal management [3].

FNAC is a quick diagnostic tool which is an integral part of the initial diagnosis and management of patients with lymphadenopathy [4]. The aspirated material can be used for ancillary studies of flow cytometry, immunocytochemistry or immunohistochemistry on cell block preparations. The diagnosis of metastatic malignancy in lymph node cytological smear is highly reliable [5]. Aspiration cytopathology reporting of thyroid, salivary gland, breast, pancreaticobiliary is now based on category wise reporting formats, which include the diagnostic categories, adequacy criteria, prediction of the ROM. These are easy to interpret and have better acceptance among clinicians [6].

In May 2019, a categorical system for performance, classification, and reporting of lymph node cytopathology was proposed at the 20<sup>th</sup> International Congress of Cytology held in Sydney. According to this system, the cytologic aspirates from lymph nodes should be categorised into 5 categories based on the specific cytologic

features. The cytology report should provide one of the five first-level diagnostic categories followed by a clear description of cytomorphology. Further recommendations can be made for management options. The essential features of the five basic categories are as follows: [7].

**I/L1-Inadequate/Insufficient:** Non diagnostic due to scant cellularity, necrosis, or technical limitations; repeat FNAC or biopsy should be requested based on the specific clinical context.

**II/L2-Benign:** Includes suppurative, granulomatous or specific infections in cases with a heterogeneous lymphoid population with small lymphocytes predominating.

**III/L3-Atypical Lymphoid (Cells) of Undetermined Significance/ Atypical (Cells) of Uncertain Significance (ALUS/AUS):** Cases with a heterogeneous lymphoid population suggest a reactive process, but a follicular lymphoma cannot be excluded/or excess of large cells/or immature small lymphoid cells/or atypical non lymphoid cells present. For these last cases, AUS should be used [7].

**IV/L4-Suspicious category:** Small or medium-sized, monomorphic atypicallymphoidcellssuspiciousoflymphoma,butthecytomorphology alone is not sufficient/or cases in which Reed-Sternberg-like cells seen or/atypical cells suspicious for metastasis are detected, but too scant to be diagnostic [7].

**V/L5-Malignant:** Includes small to medium-sized cells of NHL supported by flow cytometry or molecular studies, Hodgkin's

Lymphoma if diagnostic Reed-Sternberg cells seen as well as metastatic neoplasms [7].

The present study was aimed to describe the cytological evaluation of lymph node pathology in our setting by applying the proposed Sydney system and to assess the ROM in each category by comparing with histopathology where available.

## MATERIALS AND METHODS

The present study was a retrospective observational analysis of lymph node aspirates obtained during two-year period from January 2018 till January 2020, done in the department of pathology of a tertiary care centre in December 2021. The study was approved by the Institutional Ethical Committee (IEC No. IEC/42/17).

**Eligibility criteria:** FNAC of 250 patients of all ages presented with lymphadenopathy were included. Non lymph node aspirates were excluded. Lymph node biopsy diagnosis of corresponding cases was evaluated for final diagnosis in available cases. Cases referred to other centres for biopsy and immunohistochemistry were followed-up.

**Sample size calculation:** Sample size was calculated using the formula:  $n=3.84pq/d^2$ . Taking the average prevalence of non neoplastic and neoplastic lymphoid lesions of 13% in the study by Duraiswamy R et al., the values applied in the formula were, prevalence  $p=13%$ ,  $q=87%$  and absolute precision  $d=6$ . Sample size  $(n)=3.84 \times 0.13 \times 0.87 \div 0.06 \times 0.06=120$  [8].

**Procedure:** FNAC procedures were performed after obtaining informed consent from patients. Rapid Onsite Evaluation (ROSE) using toluidine blue stain was done for assessing specimen adequacy. Ultrasound/CT guided FNAC were taken for smaller and deep-seated lymph nodes. Smears were fixed in 85% isopropyl alcohol for Papanicolaou stain and air-dried smears used for May Grunwald Giemsa stain. Special stains, such as Ziehl-Neelsen staining for acid fast bacilli was done for suspected tuberculosis cases. Cell block preparations were processed for bloody samples. Diagnosis of lesions was made based on specific morphological patterns and as per standard cytological guidelines [9].

Cytology diagnosis was further categorised into 5 categories using the Sydney system guidelines. Slides were reviewed by two pathologists to maintain objectivity. Corresponding Lymph node biopsy in available cases was processed by paraffin embedding, stained with haematoxylin and eosin. The cytology results were compared with the gold standard histopathological diagnosis in these cases. Specific diagnosis of malignancies was made based on WHO guidelines for Haemato-lymphoid tumours [10].

The ROM was calculated by dividing the number of cases confirmed malignant on histopathology by the total number of cases with available histopathology diagnosis in that category [11]. Cases with concordant and discordant results of benign or malignant diagnosis on histopathology were noted. Cases which were diagnosed malignant on cytology and histopathology were considered True Positive (TP). Cases diagnosed benign on cytology and histopathology was considered True Negative (TN). Cases which were malignant on cytology but were found benign on histopathology were False Positive (FP). Cases which were benign on cytology but found malignant on histopathology were considered FN cases. The sensitivity, specificity, PPV, NPV and diagnostic accuracy were also calculated. Using the formula  $\text{diagnostic accuracy} = (TP) + (TN) / (TP + TN + FP + FN)$ , the accuracy of FNAC was found.

## STATISTICAL ANALYSIS

Statistical analysis was done using MS Excel spread sheet and the Statistical Package for the Social Sciences (SPSS) version 21 software. Qualitative variables expressed using frequency and percentage. Association with qualitative variables was using chi-square test. The level of statistical significance is a p-value of  $<0.05$ .

The sensitivity, specificity, PPV, NPV, and overall diagnostic accuracy of lymph node FNAC were assessed.

## RESULTS

A total of 250 aspirates of lymphadenopathy were analysed. The corresponding lymph node histopathology diagnosis was available in 53 (21.20%) cases. The age of patients varied from 8 months to 90 years with a mean age of 45.9 (SD 23.27) years in the study. There were 26 (10.40%) cytology aspirates in paediatric group and 65 (26%) in the age group above 60 years. Out of the 250 aspirates obtained, there were 139 (55.60%) males and 111 (44.40%) females, with an overall male to female ratio of 1.25:1. Number of females outnumbered males in the age group of 21 to 30 years and in 31-40 years [Table/Fig-1].

	Age group	Male	Female	Total frequency (%)	p-value=0.179
1	<13 years	14 (5.60%)	12 (4.80%)	26 (10.40%)	
2	14-20	13 (5.20%)	5 (2%)	18 (7.25%)	
3	21-30	16 (6.40%)	17 (6.80%)	33 (13.20%)	
4	31-40	12 (4.80%)	19 (7.60%)	31 (12.40%)	
5	41-50	18 (7.20%)	17 (6.80%)	35 (14%)	
6	51-60	27 (10.80%)	15 (6%)	42 (16.80%)	
7	>60 years	39 (15.60%)	26 (10.40%)	65 (26%)	
	Total	139 (55.60%)	111 (44.40%)	250	
Overall male female ratio-1.25:1					

**[Table/Fig-1]:** Percentage of lymph node FNAC according to age groups and gender. (n=250)

There were 159 (63.60%) non neoplastic lesions and 68 (27.20%) neoplastic lesions. Non diagnostic aspirates were 14 (5.60%), atypical cells and suspicious cases were 9 (3.60%). Malignancies showed a male preponderance with 52 (76.47%) males and 16 (23.53%) females, with a M:F ratio of 3.25:1. The group of commonest lymph nodes aspirated were cervical nodes in 144 (57.60%) cases. Out of 38 supraclavicular lymph nodes, 17 (44.73%) were of neoplastic aetiology. Diagnostic categories in each lymph node groups are shown in [Table/Fig-2].

Lymph node group %	Non diagnostic category I	Benign category II	AUS category III	Suspicious category IV	Malignant category V	Total frequency (%)
Cervical (57.60%)	08 (5.50%)	91 (63.20%)	02 (1.40%)	01 (0.70%)	42 (29.20%)	144 (100%)
Supraclavicular (15.20%)	-	18 (47.36%)	01 (2.63%)	02 (5.26%)	17 (44.73%)	38 (100%)
Axillary (11.60%)	03 (10.34%)	23 (79.31%)	-	-	03 (10.34%)	29 (100%)
Inguinal (8%)	03 (15%)	12 (60%)	-	01 (5%)	04 (20%)	20 (100%)
Sub-mandibular (3.20%)	-	06 (75%)	01 (12.50%)	-	01 (12.50%)	08 (100%)
Postauricular (2.40%)	-	06 (100%)	-	-	-	06 (100%)
Sub-mental (2%)	-	03 (60%)	-	01 (20%)	01 (20%)	05 (100%)
	14	159	04	05	68	250

**[Table/Fig-2]:** Category wise distribution of cytological lesions across lymph node groups. (n=250).

Size of lymphadenopathy varied from 0.5 cm to 4 cm, average size of 1 to 2 cm was seen in 137 (54.80%) cases. In paediatric population, there were 26 (10.40%) cases and majority, 25 (96.15%) cases were non neoplastic. Diagnostic categories per the Sydney system are shown in [Table/Fig-3].

Category I/L1-There were 14 (5.60%) non diagnostic aspirates, 8 (3.20%) were blood only and 6 (2.40%) were scanty material. Repeat aspiration/biopsy was recommended.

	Diagnostic category	Total frequency (%) 250	Cytology diagnosis (n-250)	Frequency (%)
1	Category I/(L1) inadequate/non diagnostic	14 (5.60%)	Blood only	8 (3.20%)
			Scanty material	6 (2.40%)
2	Category II/(L2) benign	159(63.60%)	Reactive lymphoid hyperplasia-	86(34.40%)
			Acute/suppurative lymphadenitis	16 (6.40%)
			Granulomatous lymphadenitis	53(21.20%)
			Miscellaneous-reactive lymphadenitis with Histiocytes	4 (1.60%)
3	Category III/(L3) ALUS/AUS	4 (1.60%)	Atypical lymphoid cells	4 (1.60%)
4	Category IV/(L4): suspicious	5 (2%)	Suspicious of lymphoma	3 (1.20%)
			Suspicious of metastasis	2 (0.80%)
5	Category V/(L5): malignant	68 (27.20%)	Lymphoma	7 (2.80%)
			Metastasis	61(24.40%)

**[Table/Fig-3]:** Category wise cytology diagnosis as per the proposed Sydney System in the present study (n-250).

Category II/L2-Out of 159 (63.60%) cases in L2, there were reactive hyperplasia in 86 (34.40%), granulomatous lymphadenitis in 53 (21.20%) and suppurative lymphadenitis in 16 (6.40%) cases. Diagnosis of reactive background with histocytes, to rule out toxoplasmosis by serology was given in 4 (1.60%) cases. Epithelioid granulomas were seen in all 53 (100%) cases of granulomatous lymphadenitis. Necrosis was seen in 31 (58.49%) cases (58.50%). Acid-Fast Bacilli (AFB) positivity was seen in 9 (29.03%) cases. AFB positivity was graded according to the original grading of AFB for the sputum smears [12].

Category III/L3-There were 4 (1.60%) cytology diagnosis. Atypical cells in a reactive background, large cells and immunoblasts were found. Biopsy and IHC were recommended.

Category IV/L3-There were 5 (2.00%) cases. Two were suspicious of metastasis, where granuloma, necrosis and atypical cells found. Cases suspicious of lympho proliferative lesions in 3 cases were advised biopsy with recommendation for ancillary studies.

Category V-Included 68 (27.20%) malignant lesions, 61 (89.71%) were metastatic malignancy and 7 (10.29%) cases were lymphomas. Out of 7 (2.80%) cytology diagnosis of lymphomas, one case was Hodgkin's lymphoma and 6 cases were Non Hodgkin's lymphomas. Hodgkin's lymphoma was confirmed on histopathological examination. Among the 6 cases of NHL, two cases were further confirmed as NHL on histopathology in our centre. Four cases were followed up and diagnosis was confirmed by immunohistochemistry

Cytologic category Sydney system	Total no of cases with HP diagnosis %	Cytology diagnosis	Histopathology diagnosis concordant	Histopathology diagnosis discordant
L1- Non diagnostic	3/14 (2.14%)	Blood only and inadequate material (n=3)	*Reactive lymphoid hyperplasia (n=3)	NA*
L2 Benign	27/159 (16.98%)	Reactive lymphoid hyperplasia (n=11)	Reactive lymphoid hyperplasia (n=11)	nil
		Acute suppurative lymphadenitis (n=4)	Acute suppurative lymphadenitis (n=3)	Granulomatous lymphadenitis (1)
		Granulomatous lymphadenitis (n=12)	Granulomatous lymphadenitis (n=9)	Reactive lymphoid hyperplasia (2) Hodgkin's Lymphoma (1)
L3-Atypical ALUS/AUS	3/4 (75%)	Atypical cells (n=3)	Non Hodgkin's Lymphoma(n=2)	Reactive lymphoid hyperplasia (1)
L4 Suspicious	2/5 (40%)	Suspicious of metastatic carcinoma (n=2)	Metastatic carcinoma (n=2)	nil
L5 Malignant	18/68 (26.47%)	Lymphoma (n=3)	Non Hodgkin's Lymphoma (n=2) Hodgkin's Lymphoma (n=1)	nil
		Metastasis (n=15)	Metastasis (n=15)	nil
Total	53/250 (21.20%)			

**[Table/Fig-5]:** List of cytologic diagnosis and the corresponding HP diagnosis with the category wise concordant and discordant cases.

\*NA: Not applicable in non diagnostic L1 category.

elsewhere. Metastatic malignancy in 61 (24.40%) was the second most common cause of lymphadenopathy, second to reactive lymphadenitis in the present study. The breakup of metastatic lymphadenopathy in 61 cases showed highest incidence for squamous cell carcinoma, 26 (42.60%) cases, out of which 24/26 were males. The other metastatic tumours were poorly differentiated carcinoma, adenocarcinoma, small cell lung carcinoma, melanoma,

Metastatic carcinoma	Males	Females	Total frequency (%)
Squamous cell carcinoma	24	2	26 (42.60%)
Poorly differentiated carcinoma	13	3	16 (26.22 %)
Adenocarcinoma	6	6	12 (19.67%)
Small cell carcinoma	4	0	04 (6.50%)
Small round cell neoplasm	1	0	1 (1.63%)
Melanoma	2	1	3 (4.91%)
Papillary thyroid Carcinoma	-	1	1 (1.63%)
Total	48	13	61 (100%)

**[Table/Fig-4]:** Distribution metastatic carcinoma (category V) in males and females (n=61).

small round cell neoplasm and papillary thyroid carcinoma. Distribution of metastatic malignancies given in [Table/Fig-4].

Biopsy diagnosis of FNACs in categories I, II, III, IV and V were available in 03, 27, 03, 02, and 18 cases respectively. Category wise concordant and discordant diagnosis on cytology and histopathology are tabulated in [Table/Fig-5].

Category I /L1(03cases) Category IV/L4 (02 cases) -3/14 cases of inadequate cytology were biopsied, histopathology diagnosis in all 3 cases was reactive follicular hyperplasia.

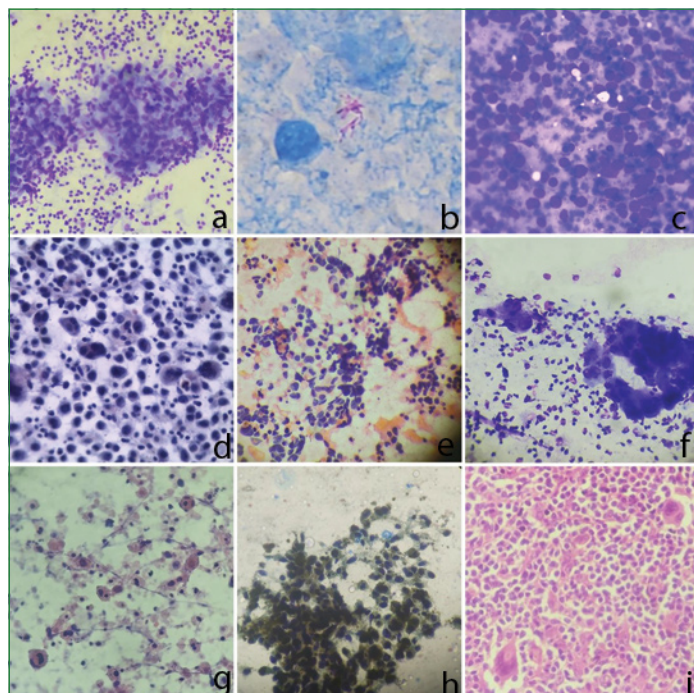
Category II/L2 (27 cases)-Out of the 11 cytological smears of reactive lymphadenitis, 11 were diagnosed as reactive follicular hyperplasia on histopathology. Out of the 4 smears of suppurative lymphadenitis, 3 were confirmed histologically, one case turned out to be granulomatous lymphadenitis on biopsy. Out of the 12-cytology diagnosis of granulomatous lymphadenitis, 9/12 was confirmed to be granulomatous lymphadenitis consistent with tuberculosis on histopathology, 2/12 cases were diagnosed as reactive hyperplasia. One case (1/12) in category II turned out to be Hodgkin's lymphoma on histopathology, was a discordant diagnosis of malignancy.

Category III/L3 (03 cases), there were 3 diagnoses of atypical lymphoid cells, out of which, 2 were diagnosed as NHL, one case diagnosed as benign reactive hyperplasia, was another discordant diagnosis on histological correlation.

Category IV/L4 (2)-On biopsy, 2 cases suspicious of metastatic carcinoma were confirmed as metastatic carcinoma.

Category V/L5 (18 cases)-Cytological diagnosis of metastasis were confirmed on biopsy in all 15 cases. In 3 cases of Lymphoma, 2 cases were confirmed as NHL and one case as Hodgkin's Lymphoma, which also was concordant.

Photomicrographs of lymph node aspirates and biopsy are depicted in [Table/Fig-6].



**[Table/Fig-6]:** Photomicrographs of Lymph node aspiration cytology (A-H) & Biopsy (I) (a) L2-Granulomatous lymphadenitis (Pap stain 40X); (b) AFB bacilli (ZN stain 100X); (c) L3-Atypical lymphoid cells (MGG 40X); (d) L4-Suspicious of NHL-ALCL (Pap-40X); (e) L5-Small cell carcinoma (Pap-40X); (f) L5-Adenocarcinoma metastasis (MGG stain 40X); (g) L5-Squamous cell carcinoma Metastasis (Pap-40X); (h) L5-Malignant melanoma metastasis with pigment in lymph node (Pap stain 40X); (i) Hodgkin's Lymphoma histopathology (H&E 40X).

Among the 27 cytologically benign cases, 26 cases were proved to be histopathologically benign, TNs. One case was diagnosed histopathologically as malignant, FN. Among the 23 cytologically malignant/suspicious cases, 22 cases were proved to be malignant histopathologically were TP, and one case was diagnosed as benign, FP on cytology. The true and FPs and negatives in comparison to gold standard shown in [Table/Fig-7].

		Histopathology Diagnosis		
		Malignant	Benign	Total
Cytology Diagnosis	Malignant	22 (TP)	1 (FN)	23
	Benign	1 (FP)	26 (TN)	27
Total*		23	27	50

**[Table/Fig-7]:** The true and False Positives (FP) and negatives in comparison to gold standard.

\*L1-non diagnostic category (3 cases) excluded;

TP: True positive; TN: True negative; FP: False positive; FN: False negative

The sensitivity, specificity, PPV, NPV, and overall diagnostic accuracy of lymph node FNAC were assessed by comparing with the histopathological diagnosis in 50 cases (non diagnostic category excluded). Using the formula, Diagnostic accuracy was found to be  $(TP)+(TN)/(TP+TN+FP+FN)=(22+26/50)=96\%$ .

The statistical values of FNAC diagnosis compared to gold standard are represented in [Tables/Fig-8].

ROM in each category was calculated by dividing the number of cases with a confirmed malignant diagnosis by the total number of cases in each diagnostic category [Table/Fig-9].

	Statistical analysis	Percentage
1	Sensitivity	95.65%
2	Specificity	96.29%
3	PPV	95.65%
4	NPV	96.29%
5	Diagnostic accuracy	96%
6	Positive likelihood ratio	25.826%
7	Negative likelihood ratio	0.0451%

**[Table/Fig-8]:** Statistical analysis of FNAC in comparison to histopathology diagnosis.

Diagnostic category Sydney system	Number of cases biopsied in each category (%)	Confirmed malignancy by histopathology	Risk of malignancy
L1	3 (2.14%)	nil	0%
L2	27 (16.98%)	1	3%
L3	3 (75%)	2	66.6%
L4	2 (40%)	2	100%
L5	18 (26.47%)	18	100%

**[Table/Fig-9]:** Risk Of Malignancy (ROM) for each Sydney system category in the present study (n=53)

## DISCUSSION

A standardised reporting system assures uniformity in use of terminology and better communication to the clinician in a reproducible manner. The proposed Sydney system for performance, diagnosis and classification of lymph node cytopathology has addressed the issue favourably. Recommendations to perform ROSE, comments on use of additional investigations at a second diagnostic level, management recommendations for each category and the calculation of ROM related to each category of cytological diagnosis are the highlights of the proposed classification system [7].

Evaluation of 250 Lymph node FNACs in all ages and 53 Lymph node biopsies in corresponding cases were done. Mean age was 45.9 years. In paediatric age, there were 26 cases (10.24%). Male to female ratio of 1.25:1. In 3<sup>rd</sup> and 4<sup>th</sup> decades, females outnumbered males with a male-to female ratio of 1:1.3. Similar observations of ratio as 1.5:1 were noted by Qadri SK et al., [13]. Mohanty R described Male female ratio of 1.05:1 in their study of 355 cases [14].

Cervical lymphadenopathy in 144 (57.60%) cases was the commonest group of nodes seen in the present study. Non neoplastic disorders seen in 159 (63.60%) outnumbered neoplastic disorders in 68 cases (27.20%). A total of 53 (22.80%) of granulomatous lymphadenitis were seen in the present study, AFB positivity was seen in 9 (29.03%) cases. Qadri SK et al., in their study of 1579 lymphadenopathy reported reactive lymphadenitis as the commonest finding in 36.90%, Granulomatous lymphadenitis in 9.10% and metastatic malignancy in 38.20% cases of lymphadenopathy [13]. Khajuria R et al., in their study of 656 cases found that granulomatous lymphadenitis seen in 52.3%, was the most prevalent lesion, reactive lymphadenitis in 37.20% and metastatic malignancy only in 3.80% in their experience [15].

Comparison of ROM for Sydney system categories in other studies shown in [Table/Fig-10] [11,16,17].

Category I, three out of 14 lesions were examined on histopathology and were benign reactive hyperplasia, hence ROM was found to be zero for category I. Though repeat FNAC or excision biopsy was advised, the cases were not available for follow-up. Gupta P et al., described that ROM was high for category I lesion (27.50%) [11]. The discrepancy seen in the present study, was due to the smaller number of nodes biopsied, smaller nodes and paediatric FNACs.

Diagnostic category Sydney system	Gupta P et al., (2021) [11]	Vigliar E et al., (2021) [16]	Joshee A and Joshee R (2021) [17]	Present Study (2023)
L1	27.5	50%	34.7	0%
L2	11.5	1.92%	20	3%
L3	66.7	58.3%	15	66.6%
L4	88	100%	78.5	100%
L5	99.6	100%	96.7	100%

**[Table/Fig-10]:** comparison of Risk Of Malignancy (ROM) stratification with other study results [11,16,17].

In category II, one diagnosis of suppurative lymphadenitis and 2 cases of granulomatous lymphadenitis turned out to be reactive lymphadenitis on histopathology. On reviewing the slides, pauci cellular nature of aspirate was one reason attributed to this disparity. A discordant diagnosis in this category was a FN case of Hodgkin's Lymphoma, reported as granulomatous lymphadenitis on cytology. Gupta P et al., has described the problems encountered with pauci cellular nature of sclerotic pattern in nodular sclerosis causing diagnostic difficulty on cytological aspirates [11]. Interpretation of AFB staining on second diagnostic level has enabled confirmatory diagnosis of tuberculosis in 9 cases of granulomatous lymphadenitis. The ROM was 3% in the present study, similar observation by Vigliar E et al., have reported ROM of 1.92% for category II lesions [16].

In category III-In this group, 2/3 cases were lymphoma NHL, on biopsy. One cytology among this category was reactive hyperplasia on biopsy. Advice on excision and recommendation for ancillary testing is warranted in cases in this category as the ROM can be high, 66.6 % in our study and high in other studies [11,16]. Joshee A and Joshee R have reported ROM was 15% for category III lesions [17].

In category IV-5/5 cytology among this category turned out to be malignant on histopathology. Two metastatic nodes were biopsied in our centre, 3 lymphomas were diagnosed in other centres which were followed up, ROM in this category is 100%. Vigliar E et al., reported similar findings [16].

In category V-There were 68 lesions in cytology and 18 biopsy proven cases. Primary malignancy of oropharynx, lung, were the commonest known primary in these cases. ROM was 100%. Findings of Vigliar E et al., Joshee A and Joshee R have reported similar findings [16,17]. Bhagwan I et al., in their evaluation of cervical lymphadenopathy observed that the most common tumours metastasising to the lymph nodes originated in the head and neck region followed by the respiratory system and then tumours of unknown origin [18].

Comparison of statistical evaluation applying Sydney system in cytology in other studies given in [Table/Fig-11] [11,16,17].

	Gupta P et al., (2021) (n=6983) [11]	Vigliar E et al., (2021) (n=300) [16]	Joshee A and Joshee R (2021) (n=1409)[17]	Present (2023) (n=250)
Sensitivity%	79.9	98.47	95.12	95.65
Specificity%	98.7	95.33	90.32	96.29
PPV%	98.4	96.27	97.5	95.65
NPV%	83.1	98.08	82.35	96.29
Diagnostic accuracy%	89.3	97.06	94.16	96

**[Table/Fig-11]:** Comparison of statistical evaluation of Lymph node cytology using Sydney System with the gold standard in studies [11,16,17].

Gupta P et al., on evaluation of 6983 cases has found that FNAC has high diagnostic accuracy, application of the Sydney system can help in achieving uniformity and reproducibility in cytologic diagnoses and help in risk-stratification [11]. Similar conclusions were drawn by Vigliar E et al., and Joshee A and Joshee R

concluding that FNAC coupled with use of ancillary studies and implementation of Sydney system will be effective in evaluation of lymph node pathology [16,17].

### Limitation(s)

The present study has the limitation that the ancillary tests for the final diagnosis of lymphoid malignancy such as flow cytometry, immunohistochemistry or molecular studies were not available.

### CONCLUSION(S)

The diagnostic accuracy of FNAC was found to be 96%. The FNAC is a minimally invasive, reliable, and accurate investigation in the evaluation of lymphadenopathy. The Sydney system is useful in creating uniformity and reproducibility of cytology reports, category wise risk stratification can provide information for further management. It enhances the role of FNAC by confirming benignity in benign lesions and by alerting the clinician for follow-up and ancillary studies in atypical and equivocal cases. ROM in L1 is variable and cannot be generalised, recommendation for repeat procedure or biopsy in such cases is required depending on the context to avoid FN diagnosis.

### REFERENCES

- [1] Darnal HK, Karim N, Kamini K, Angela K. The profile of lymphadenopathy in adults and children. *Med J Malaysia*. 2005;60(5):590-98.
- [2] Ochicha O, Edino ST, Mohammed AZ, Umar AB, Atanda AT. Pathology of peripheral lymph node biopsies in Kane, Northern Nigeria. *Ann Afr Med*. 2007;6(3):104-08.
- [3] Mohseni S, Shojaiepard A, Khorgami Z, Alinejad S, Ghorbani A, Ghafouri A. Peripheral lymphadenopathy: approach and diagnostic tools. *Iran J Med Sci*. 2014;39(2 Suppl):158-70.
- [4] Prasad RR, Narasimhan R, Sankaran V, Veliath AJ. Fine-needle aspiration cytology in the diagnosis of superficial lymphadenopathy: an analysis of 2,418 cases. *Diagn Cytopathol*. 1996;15(5):382-86.
- [5] Ton Eryilmaz O, Ucak R, Ozagari AA, Kabukcuoglu F. Diagnostic value of lymph node fine-needle aspiration cytology. *Cytojournal*. 2021;18:8.
- [6] Sundling KE, Kurtycz DFI. Standardised terminology systems in cytopathology. *Diagn Cytopathol*. 2019;47(1):53-63.
- [7] Al-Abbad MA, Barroca H, Bode-Lesniewska B, Calaminici M, Caraway NP, Chhieng DF, et al. A proposal for the performance, classification, and reporting of lymph node fine-needle aspiration cytopathology: The Sydney system. *Acta Cytologica*. 2020;64(4):306-22.
- [8] Duraiswami R, Margam S, Chandran P, Prakash A. Spectrum of pathologies on FNAC evaluation of peripheral lymph nodes at a tertiary care center in Hyderabad: a retrospective study. *International Journal of Advances in Medicine*. 2017;4(1):27-33.
- [9] Orell SR, Sterrett GF. *Orell and Sterrett's fine needle aspiration cytology*. 5<sup>th</sup> ed. Edinburgh: Churchill Livingstone; 2012.
- [10] World Health Organization. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues [internet]. Geneva: WHO; 2017. Available from <https://www.iarc.who.int/news-events/who-classification-of-tumours-of-haematopoietic-and-lymphoid-tissues-2/>
- [11] Gupta P, Gupta N, Kumar P, Bhardwaj S, Srinivasan R, Dey P, et al. Assessment of risk of malignancy by application of the proposed Sydney system for classification and reporting lymph node cytopathology. *Cancer Cytopathology*. 2021;129(9):701-18.
- [12] Central TB Division, Directorate General of Health Services, Ministry of Health & Family Welfare, Government of India. Technical and operational guidelines for tuberculosis control. New Delhi, India: Ministry of Health & Family Welfare; 2005. <http://health.bih.nic.in/Docs/Guidelines-TB-Control.pdf> Accessed November 2019.
- [13] Qadri SK, Hamdani NH, Shah P, Lone MI, Baba KM. Profile of lymphadenopathy in Kashmir valley: a cytological study. *Asian Pac J Cancer Prev*. 2012;13(8):3621-25.
- [14] Mohanty R. Utility of fine needle aspiration cytology of lymph nodes. *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*. 2013;8(5):13-18. e-ISSN: 2279-0853, p-ISSN: 2279-0861.
- [15] Khajuria R, Goswami KC, Singh K, Dubey VK. Pattern of lymphadenopathy on fine needle aspiration cytology in Jammu. *JK Science Journal of Medical Education and Research*. 2006;8(3):157-59.
- [16] Vigliar E, Acanfora G, Iaccarino A, Mascolo M, Russo D, Scalia G, et al. A novel approach to classification and reporting of lymph node fine-needle cytology: Application of the proposed Sydney System. *Diagnostics*. 2021;11(8):1314.

- [17] Joshee A, Joshee R. Lymph node FNA cytology reporting using new proposed IAC sydney system for reporting lymph node cytology-A single institution retrospective study. *Int J Heal Clin Res.* [Internet]. 2022Jan.18 [cited 2022Oct.23];5(3):95-99. Available from: <https://www.ijhcr.com/index.php/ijhcr/article/view/4304>.
- [18] Bhagwan I, Kane SV, Chinoy RF. Cytologic evaluation of the enlarged neck node: FNAC utility in metastatic neck disease. *The Internet Journal of Pathology.* 2007;6. Available from: [http://www.ispub.com/journal/the\\_internet\\_journal\\_of\\_pathology](http://www.ispub.com/journal/the_internet_journal_of_pathology).

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