

## Lymph node FNA cytology reporting using new proposed IAC sydney system for reporting lymph node cytology- A single institution retrospective study

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### Abstract

**Introduction:** Lymph node enlargement is a common clinical finding in a wide spectrum of diseases and its evaluation is essential for proper patient care. Fine needle aspiration cytology has been used as an initial diagnostic method in such conditions especially for infective conditions and also to differentiate between benign and malignant lesions. A standardized category based cytology reporting system was proposed by IAC in 2019 which gives 5 categories of cytological diagnosis and also provides management category for each class. **Aim and Objectives:** The present study aims to analyze and classify lymph node samples as per new proposed Sydney system and also to assess the risk of malignancy of each category. **Material and Methods:** This single institution retrospective study included lymph node FNAC cases over 5 year duration. Clinical details of all included cases were recorded. Cytology aspirate slides were reevaluated as per new reporting system. Histopathology correlation was done in cases where possible. Statistical analysis was done. **Results:** 1409 lymph node aspirates were evaluated with cases having slight male predominance and average age of 31.24 years. Benign category diagnosis was most common. Overall the most common diagnosis was reactive hyperplasia of lymph node. Metastatic squamous cell carcinoma was most common malignant diagnosis. Risk of malignancy calculated after histopathological correlation was highest in malignant category where it was 96.7%. Diagnostic accuracy of the new system in current study was 94.16%. **Conclusion:** Using standard categorical cytology reporting system will allow improved reports and clinical communication for better patient care.

**Keywords:** Lymph node, FNAC, risk of malignancy, category, metastatic.

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### Introduction

Lymph nodes are collection of lymphoreticular tissue at many sites in the human body. They are a part of the lymphatic system and have a role in the immune mechanism of the body. Lymph node enlargement is termed as lymphadenopathy. This can occur in various diseases, either infectious or neoplastic. Thus, lymphadenopathy is a common presenting symptom in clinical practice which requires proper evaluation.

Biopsy has been considered gold standard for diagnosing lymph node masses as it gives good amount of tissue for examination in which disease pattern and extent can be seen. But fine needle aspiration cytology (FNAC) is also a useful diagnostic technique as it has the advantages of being a minimally invasive procedure with generally fast results. Its application helps to screen infectious diseases, especially granulomatous diseases and also help to differentiate between benign and malignant conditions. Apart from material for cytomorphological examination the aspirated material is also useful for additional tests like Ziehl-Neelsen stain (ZN) for finding acid fast bacilli[1].

However, due to occurrence of lymphadenopathy in various diseases the cytological features can be wide and variable, and many times features may overlap thus preventing a definite diagnosis using FNAC[2,3].

Diagnosis of primary malignant lymphadenopathy requires biopsy of lesion and histopathological examination[3].

Previously no standardized reporting system or common terminology was available for lymph node cytology like those for cervical cytology[4] and thyroid cytology[5].

For better patient care future aim would be use of standardized and

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integrated reporting with more involvement of cytopathologists with treating clinicians[6].

In the 20<sup>th</sup> International Congress of Cytology held at Sydney in 2019 a panel of experienced cytopathologists from all over the world proposed a standardized category based lymph node cytology reporting system. This was endorsed both by IAC and EFCS. It provided a categorical classification of aspirates into five different categories based on specific cytological features. It also provides a management category for each class. The categories are as follows- category I/L1: inadequate/non-diagnostic, Category II/L2: benign, category III/L3: atypical cells of undetermined significance/atypical lymphoid cells of uncertain significance, category IV/L4: suspicious for malignancy and category V/L5: malignant[7, 8].

The present study aims to analyze and classify lymph node samples as per new proposed Sydney system and also to assess the risk of malignancy of each category by correlating with histopathology report wherever possible.

### Materials and methods

In the present retrospective study, cases of lymph node FNAC conducted from January 2016 to December 2020 were included. The cytopathology records of this duration were included in the study. Cases of both genders and all ages were included. The relevant clinical and demographic details of the cases were recorded from the received test requisition forms.

All FNA procedure were performed under aseptic precautions after explaining the procedure and taking written consent. For superficial swellings a 22G needle was used to do the process.

All aspirate smears were stained with Giemsa stain (MGG) and ZN staining was performed in cases where required.

The cytology smears were reexamined by two pathologists using defined cytological criteria before the histopathological correlation was done.

Histopathology records for all included cases were looked up for in the department archives and the diagnosis was correlated wherever available.

Risk of malignancy (ROM) for a category was calculated by dividing the number of cases confirmed malignant on histopathology by number of total cases with available histopathology in the category. Histopathology was considered standard of diagnosis in the study. All cases which were malignant both on cytology and histopathology were considered true positive (TP). True negative (TN) were cases diagnosed benign on both cytology and histopathology. False positive (FP) were cases given malignant on cytology but were found benign on histopathology. The cases marked as benign lesion on cytology but found malignant on histopathology were considered false negative cases (FN). The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy were also calculated.

**Results**

In the duration of the study a total of 6203 FNA were performed. 1409 (22.7%) aspirations were from the lymph nodes. Mean age of cases in the study was 31.24 years and age range was from 1 year to 90 years. The most common age group undergoing lymph node FNA in the study was age 21 to 30 years group. The gender ratio in the study cases was 1.09:1 for male to female. Cervical nodes were the most commonly aspirated lymph nodes in the study. 148 cases were included in the category L1 of non-diagnostic /inadequate for interpretation. 49 cases showed necrotic material without presence of any lymphoid cells. 99 cases showed only blood or acellular fluid. The category of benign cytological diagnoses category L2 was given

in 934 cases (66.28%). This formed the most common category in the study. The most common benign cytological diagnosis was reactive hyperplasia seen in 548 cases (38.89%). Other benign diagnoses were granulomatous lymphadenitis, necrotizing granulomatous lymphadenitis and acute lymphadenitis.

Granulomatous lymphadenitis and necrotizing granulomatous lymphadenitis was diagnosed in a combined total of 379 cases (26.89%). ZN stain for AFB was positive in 47.5% of these cases. One case also showed presence of microfilaria.

The L3 category called as atypical cells of undetermined significance/atypical lymphoid cells of uncertain significance (ALUS) category included 32 cases by cytology. The suspicious for malignancy category L4 was given in 73 cases and more than half of these cases were diagnosed as suspicious for metastasis (49 out of 73). Remaining cases were termed as suspicious for lymphoid malignancy. The malignant category L5 was diagnosed in 222 cases (15.75%) out of which 183 cases were diagnosed as metastatic deposit in lymph node while 39 cases were diagnosed as lymphoid malignancy. The most common type of metastatic deposits was from squamous cell carcinoma which was seen in 98 cases out of 222. Other cases showed metastatic deposits from adenocarcinoma, breast carcinoma, small cell carcinoma and melanoma. 37 cases were also termed as just metastatic without defining type. The most common malignant cytological diagnosis of the study was metastatic squamous cell carcinoma seen in 98 cases. 31 cases of NHL were diagnosed by cytology in the study making it the most common lymphoid malignancy.

The category wise cytological diagnoses in the study are shown in table 1.

**Table 1: Category wise cytological diagnosis in number**

S. No	Category	Cytological diagnosis	Number
1	L1- Inadequate/non-diagnostic	Blood only	99
		Necrosis	49
2	L2-Benign	Acute lymphadenitis	7
		Reactive hyperplasia	548
		Granulomatous lymphadenitis	224
		Necrotising granulomatous lymphadenitis	155
3	L3- Atypical cells of undetermined significance/atypical lymphoid cells of uncertain significance	Atypical non-lymphoid cell	10
		Atypical lymphoid cell	22
4	L4- suspicious for malignancy	Suspicious for metastasis	49
		Suspicious for lymphoid malignancy	24
5	L5-Malignant	Metastases	37
		Metastatic squamous cell carcinoma	98
		Metastatic adenocarcinoma	24
		Metastatic breast carcinoma	10
		Metastatic small cell carcinoma	3
		Metastatic melanoma	1
		Metastatic poorly differentiated carcinoma	4
		Metastatic thyroid carcinoma	4
		Non-Hodgkin's lymphoma	31
		Hodgkin's lymphoma	3
		Leukemia infiltration	3
Burkitt lymphoma	2		

Histopathological slides were available for 264 cases (18.7%) out of the 1409 cases whose cytology was considered in this study. Of these 88 were benign diagnoses while 176 were malignant diagnoses. The most common histopathological diagnosis was metastatic squamous cell carcinoma. The most common benign diagnosis was reactive hyperplasia of lymph node.

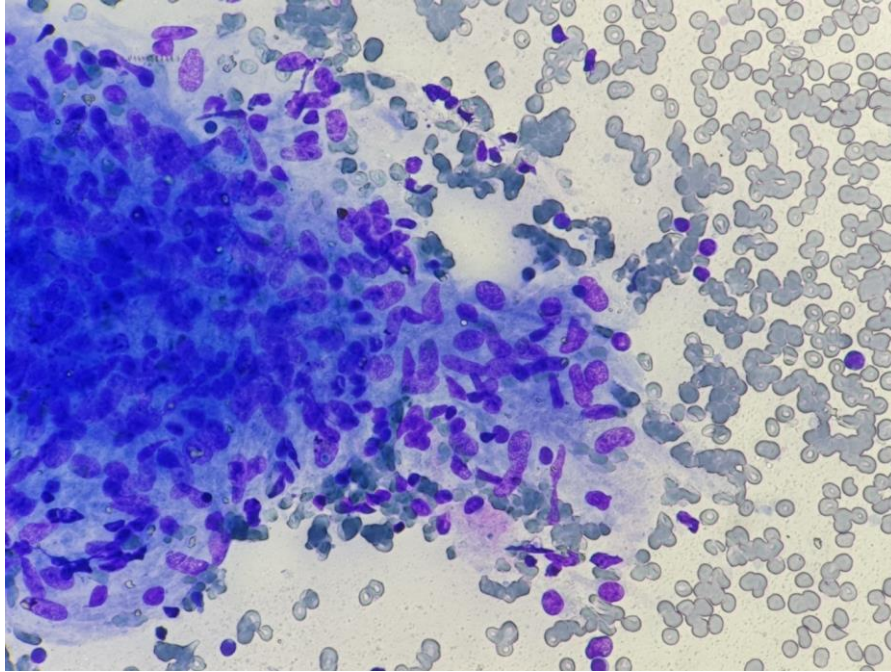
In the L1 non-diagnostic category, histopathology correlation was available for 46 cases of which 16 turned out to be malignant. The ROM for this category was 34.7%. In the L2 category of benign

cytology, histopathology was available for 35 cases out of which 7 showed features of malignancy. The ROM for this category was 20%. The L3 category of ALUS had histopathology of 20 cases and 3 were found malignant. One case also showed features of Rosai Dorfman disease on histopathology. The ROM of L3 category came out as 15%. There were 42 cases of histopathology available for correlation in category L4 of suspicious for malignancy out of which 33 were positive for malignancy on histopathology. The ROM in this category was 78.5%.

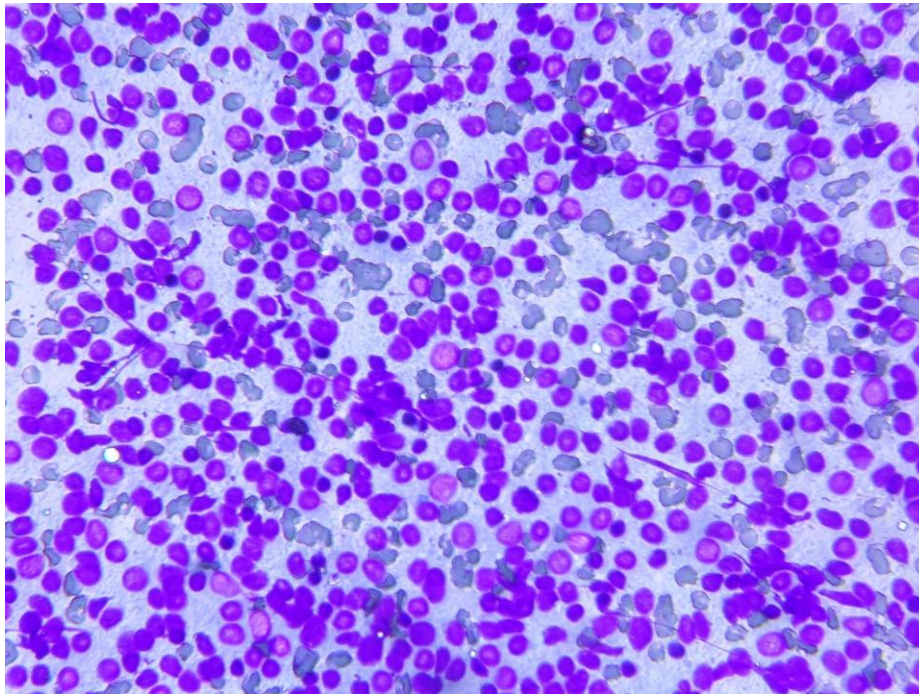
In the L5 category of malignant diagnosis by cytology histopathological correlation was available in 121 out of the 222 cases. Malignancy was diagnosed in 117 cases. The most common primary lymphoid malignancy in the study on histopathology in the study was NHL. The L5 category ROM was 96.7%.

As per cytology and histopathology correlation, sensitivity and specificity in this study was 95.12 % and 90.32 % respectively. The positive predictive value and negative predictive value was found as 97.5% and 82.35%.

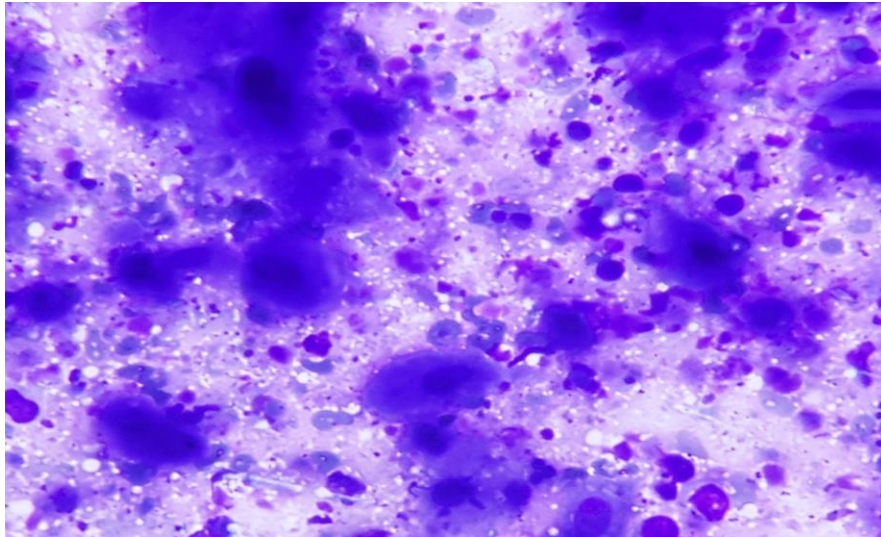
The diagnostic accuracy of the proposed lymph node cytology reporting system in our study was found to be 94.16 %.



**Fig. 1: Granulomatous lymphadenitis- Epithelioid cell cluster with interspersed lymphoid cells (40x, Giemsa stain)**



**Fig. 2: Cellular smear showing enlarged slightly pleomorphic cells with high nucleocytoplasmic ratio on a background showing few lymphoid cells. Diagnosed as Non-Hodgkins lymphoma (Category Malignant). 40x, Giemsa stain**



**Fig. 3: Smear shows many scattered atypical keratinized cells with variable appearance, pleomorphic nuclei and high nucleocytoplasmic ratio. Background is dirty with necrosis. Diagnosed as metastatic squamous cell carcinoma. 40x, Giemsa stained**

### Discussion

Lymph node enlargement is a common presenting symptom in the general outpatient department. It is one of the first and very common presenting features in variety of diseases, either infective or benign or malignant. The application of FNA to evaluate the lymph node swellings is advantageous as it is a rapid and relatively faster method. The cytology results can help in early distinction of benign and malignant lesions. Also it is helpful in diagnosis of early diagnosis of granulomatous lesions which are common in India[1]. The IAC has proposed a standardized categorical lymph node cytology reporting system which has defined criteria for diagnosis and it also provides management guidelines for each category. Its aim is improved clinical integration and overall better disease management[7,8].

As the proposed reporting system is a recent development in cytopathology field, only few publications are available for comparison. The present retrospective study included cases of FNA of superficial lymphadenopathy over a period of 5 year duration and included 1409 cases. All of these were non guided FNA procedures. In comparison to the retrospective study by Gupta P et al[9] which included 6983 cases, ours is a smaller study as per number of cases. The retrospective study by Rivas HE et al[10] and Vigliar E et al[11] also published in 2021 evaluated 363 and 300 cases respectively but included only ultrasound guided FNA of lymphadenopathy.

In the current study the age range of patient undergoing FNA was from 1 year to 95 years with mean age of all being  $31.24 \pm 20.22$  years. Mean age was lower compared to study by Gupta P et al[9] ( $38.9 \pm 19.1$  years) and Vigliar E et al[11] (54.6 years).

The current study had more number of male patients undergoing lymph node FNA. The cervical lymph nodes were the most common site to be evaluated and this was similar in study by Vigliar E et al[11] and Gupta P et al[9]. Rivas HE et al [10] included all palpable and non-palpable lymphadenopathy cases visualized using ultrasonography (USG).

In the current study category L1 of insufficient aspirates was seen in 148 cases (10.5%) while Gupta P et al[9] had 289 cases (4.1%) as they used rapid on-site evaluation (ROSE)[12] technique. The study by Rivas HE et al[10] had 13 aspirates (3.58%) in this category which could be because of FNA being done using USG guidance.

The L2 benign cytology category included most number of cases (66.29%) in our study that was similar to the studies by Gupta P et al[9] and Rivas HE et al[10].

The L3 category of ALUS was given in 30 cases (2.13%) of our study. This was at bit more than study results of Gupta P et al[9] and Rivas HE et al[10] who had 0.5% and 1.93 % cases in this category respectively.

The suspicious for malignancy category L4 had 5.18% cases in the current study which was comparable to the study result of Rivas HE et al[10] (5.79%) but a bit higher than Gupta P et al[9] (1.4%).

The last category of malignant cytology L5 was diagnosed in 222 cases (15.76%) in the current study. This is a much smaller number than studies by Gupta P et al[9] and Vigliar E et al[11] who had 41.76% and 46% malignant cytological lesions respectively. This could be due to larger number of cases included in study by Gupta P et al[9]. Also Vigliar E et al[11] used USG guided FNA in all lymphadenopathy cases that was additional help.

The most common cytological diagnosis in our study was reactive hyperplasia of lymph node. The most common malignant lesion diagnosed on cytology was metastatic squamous cell carcinoma. In the study by Gupta P et al[9] the most common cytological diagnosis was metastatic squamous cell carcinoma.

In the present study histopathological correlation was available in 264 (18.7%) cytologically evaluated cases. 8.8% cases available with histopathological correlation in the study done by Gupta P et al[9] while this number was 80.6% in Study by Vigliar E et al[11].

ROM was calculated in each category using available data.

In our study, out of 148 non diagnostic category cases, histopathological correlation as available in 46 cases. 16 were found to be malignant on histopathology. The ROM was for this category 34.7% which was a bit higher than ROM for category L1 by Gupta P et al [9] where it was 27.5% and lower than the 50% in study by Vigliar E et al[11].

In category L2 of benign cytology, histopathological correlation showed malignancy in 7 out of the 35 evaluated cases. The ROM was 20% in our study which was higher than study results of both Gupta P et al[9] (11.5%), Rivas HE et al [10] (3%).

The L3 category termed as ALUS/AUS had a ROM of 15% as 3 out of the 20 histopathologically correlated cases showed malignant features. The ROM was significantly lower than results of Gupta P et al[9] where ROM was 66.7% and Rivas HE et al[10] with 50%.

The L4 category termed as suspicious for malignancy had histopathology available in 42 cases. 33 were found malignant. A high ROM of 78.5% was obtained in the current study which is comparable to results of 88% and 100% seen in the studies by Gupta P et al[9] and Rivas HE et al[10] respectively.

The last category of cytologically malignant lesions showed ROM of 96.7%. 117 out of 121 histopathologically evaluated cases confirmed malignancy. This high ROM is comparable to the results of Rivas HE et al[10] (100%) and Gupta P et al[9] (99.6%).

On basis of all calculated data the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy in

the current study were 95.12%, 90.32%, 97.5%, 82.35% and 94.16% respectively. These values are compared with other study results in table 2.

	Current study	Gupta P et al[9]	Vigliar E et al[11]
Sensitivity	95.12	79.9	98.47
Specificity	90.32	98.7	95.33
Positive predictive value	97.5	98.4	96.27
Negative predictive value	82.35	83.1	98.08
Diagnostic accuracy	94.16	89.3	97.06

The aspirates of non-diagnostic category showed either only blood or necrosis. This could be due to improper aspiration techniques and also due to not using of ROSE[12]. This category cases were lost in follow up when repeat aspiration was not possible. In the 99 cases showing only blood, there were 13 which showed features of metastasis on histopathology. Also in 49 cases showing only necrosis, 3 cases showed metastatic deposits on histopathology. Such cases were considered as false negative (FN).The categorical ROM was higher when compared to study result of Gupta P et al[9] and Rivas HE et al[10].

In the benign cytological category L2 there were 7 cases showing discordant results out of the 35 cases evaluated on histopathology. 6 of these showed metastatic deposits and one showed features of Non-Hodgkin lymphoma (NHL).These were added to false negative cases. A lesser amount of material is available in FNA smears as compared to histopathology sections. When a strong clinical suspicion is present in cases revealing negative for malignancy by cytology then multiple needle passes should be done to get more amount of cells to examine. Also in cases of metastatic deposits, lymph node involvement may be partial and may be missed by FNA needle. Thus radiological assistance is helpful. One case of NHL was missed because of less number of atypical cells in cytology smear. In cases of lymphoid malignancy techniques of flow cytometry, immunocytochemistry and molecular based test are more conclusive towards final diagnosis. These were not available at our institute.

Category of ALUS showed 3 false negative cases on histopathology which showed metastatic deposits. These were designated as showing 'Atypical non-lymphoid cells' on cytology. ROM of this category was 15% and was lower than study results of Gupta P et al[9] and Vigliar E et al[11]. Due to possible risk of both over and under reporting of malignancy by the untrained eye in such aspirates, the cases of this category should be interpreted using help of additional diagnostic methods with clinical correlation. Directions for proper follow up and repeat aspiration should be given.

Category of suspicious lesions in our study had a ROM of 78.5%, which was similar to the results of Gupta P et al[9] and Vigliar E et al[11] where guided FNA was the used method. This category included 9 cases showing differing histopathological diagnosis. 3 cases where metastasis was suspected on cytology showed only inflammatory material on histopathology. 24 cases were marked as suspicious for lymphoid malignancy but 6 cases showed differing histopathology. 2 showed only inflammation while 4 were showing reactive hyperplasia of the lymph node. Such differing diagnoses warranted use of ancillary diagnostic techniques.

The last category of malignant lesions L5 had a high number of cases with histopathology correlation (121 out of 222). Calculated category ROM was 96.7% which is similar to study results of Gupta P et al[9], Rivas HE et al [10] and Vigliar E et al[11]. By histopathology 4 divergent diagnoses were obtained where histopathology showed only inflammation and reactive hyperplasia of lymph node.

In the current study a relatively higher ROM in category L1 points towards lack of use of ancillary techniques like ROSE that would have reduced inconclusive aspiration. Rapid staining to check adequacy is essential to prevent delayed reporting. Also radiological assessment is helpful.

Another important fact in L1 category was that a higher number of cases underwent biopsy. 46 out of 148 cases had histopathology correlation (31%). Only 13% cases underwent histopathological examination in study by Gupta P et al[9].

#### Conclusion

FNAC has important application and diagnostic significance in lymph node swellings. The new proposed Sydney reporting system provides defined diagnostic categories and helps in evaluating risk of malignancy. Its use will be beneficial both in improving cytology practice with uniform reporting and also allow better understanding of cytology report by the treating physician ultimately leading to improved patient management.

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