

Original Research Article

SYDNEY SYSTEM-BASED REPORTING OF LYMPH NODE CYTOPATHOLOGY: AN INSTITUTIONAL STUDY

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ABSTRACT

Background: Lymphadenopathy is a common clinical presentation with causes ranging from reactive and infectious conditions to lymphoid neoplasms and metastatic malignancies. Fine-needle aspiration cytology (FNAC) is a rapid, minimally invasive, and cost-effective investigation for superficial lymphadenopathy. The Sydney System for Reporting Lymph Node Cytopathology provides standardized diagnostic categories and incorporates the Risk of Malignancy (ROM), facilitating uniform reporting and clinical management. **Aim:** To evaluate the applicability of the Sydney System in categorizing lymph node lesions into L1–L5 categories and determine the Risk of Malignancy by correlating cytological findings with histopathological diagnosis.

Materials and Methods: This retrospective observational study included 270 lymph node FNAC cases received at the Department of Pathology, ESIC Medical College and Hospital, Kalaburagi, from August 2023 to July 2025. Archived FNAC smears were reviewed for adequacy, cellularity, cytomorphological features, architectural patterns, and background elements. Cases were categorized according to the Sydney System as L1 (Inadequate/Non-diagnostic), L2 (Benign), L3 (Atypical Cells/Atypical Lymphoid Cells of Undetermined Significance), L4 (Suspicious for Malignancy), and L5 (Malignant). Histopathological correlation was available in 27 cases, and ROM was calculated.

Results: Patients ranged from 1–79 years, with 31–40-year age group being most commonly affected (18.5%). A slight male predominance was observed (1.6:1). Cervical lymph nodes were the commonest site (56.3%). L2 was the predominant category (202 cases, 74.8%), followed by L5 (54 cases, 20%). Reactive lymphadenitis was the commonest benign lesion, while metastatic carcinoma, particularly squamous cell carcinoma, predominated among malignant lesions. ROM was 8.33% for L2, 25% for L3, and 100% for both L4 and L5. FNAC demonstrated sensitivity of 84.6%, specificity of 100%, PPV of 100%, NPV of 86.7%, and diagnostic accuracy of 88.9%.

Conclusion: The Sydney System provides a simple and standardized approach to lymph node cytology. Progressive increase in ROM across categories supports its utility in risk stratification and clinical decision-making. FNAC demonstrated good diagnostic performance, particularly for malignant lesions.

Keywords: Lymphadenopathy; Fine-needle aspiration cytology; Sydney System; Lymph node cytology; Risk of Malignancy; Histopathology; Metastatic carcinoma.

INTRODUCTION

Lymph nodes are specialized lymphoreticular organs distributed throughout the body and constitute an essential component of the immune system.^[1] Lymphadenopathy is one of the most common clinical presentations accounting for 0.6–1.0% of primary care consultations and up to 5% of general medical evaluations,^[2] and represents a wide spectrum of pathological conditions ranging from reactive hyperplasia and infectious diseases to primary lymphoid neoplasms and metastatic malignancies. The aetiology of lymphadenopathy varies with age and geographical region. Cervical lymphadenopathy associated with self-limiting infection is most common in children (80-90%) and young adults, while in adults over 40 years, the risk of malignancy increases (about 4% of unexplained cases). In developing countries such as India, tuberculosis remains one of the leading causes of cervical lymphadenopathy. Accurate pathological evaluation is essential for appropriate diagnosis, prognostication and patient management.^[3]

Fine Needle Aspiration Cytology (FNAC) has become the first-line investigation for patients with superficial lymphadenopathy because it is a simple, rapid, minimally invasive, safe and cost-effective diagnostic technique.^[4] Aspirated material can also be utilized for ancillary investigations like flow cytometry, immunocytochemistry, immunohistochemistry on cell blocks, microbiological studies, molecular testing and cytogenetic analysis, which significantly improves diagnostic accuracy. FNAC is particularly reliable in the diagnosis of metastatic malignancies, while lymphoid lesions often require correlation with histopathological examination and ancillary studies.^[5]

Lymph node cytology lacked a universally accepted reporting system, which resulted in variations in diagnosis. While standardized reporting systems were available for thyroid, salivary gland, breast, and serous fluid cytology, a similar system for lymph node cytology was absent.

To overcome these limitations, the Sydney System for Reporting Lymph Node Cytopathology was proposed at the 20th International Congress of Cytology held in Sydney in 2019. The system classifies lymph node aspirates into five diagnostic categories: L1 – Inadequate/Non-diagnostic, L2 – Benign, L3 – Atypical Cells/Lymphoid Cells of Undetermined Significance (AUS/ALUS), L4 – Suspicious for Malignancy and L5 – Malignant. Each category has defined adequacy criteria, characteristic cytomorphological features, an estimated Risk of Malignancy (ROM) and management guidelines.^[6] Incorporation of ROM enables better risk stratification and facilitates clinical decision-making.

The present study was undertaken to evaluate the applicability of the Sydney System in the Indian

population along with validation at an institutional setting. The aim is to categorise lymph node into L1 to L5 Sydney system category and to determine risk of malignancy by correlating cytological findings with available histopathological cases.

MATERIALS AND METHODS

This retrospective observational study was conducted in the Department of Pathology, ESIC Medical College and Hospital, Kalaburagi, after obtaining approval from the Institutional Ethics Committee. The study included archived FNAC cases of lymph node lesions received from August 2023 to July 2025. The Data was retrieved from cytology registers, laboratory requisition forms, departmental records and archived cytology smears. Relevant clinical information including age, sex, site of lymphadenopathy and patient clinical history was noted.

The minimum sample size obtained with Cochran's formula and finite population correction was 160 cases. However, as the study employed a universal sampling method, all eligible lymph node FNAC cases available during the study period were included. As a result, 270 cases will constitute the final study population.

Patients of all age groups and genders who presented with lymphadenopathy and underwent FNAC at the Department of Pathology, ESIC Medical College and Hospital, Kalaburagi, during the study period were included in the study.

The study excluded lymph nodes that are not accessible to FNAC, aspirates obtained from non-lymph node swellings, lymph nodes that have undergone prior treatment, and aspirates that are inadequate for reporting.

Previously prepared FNAC smears stained with H & E and Leishman stain were retrieved and studied microscopically to look for smear adequacy, cellularity, cytomorphological features, architectural patterns, and background elements

Based on the cytological findings, each case was classified according to the Sydney System for Reporting Lymph Node Cytopathology into one of five diagnostic categories: L1 (Inadequate/Non-diagnostic), L2 (Benign), L3 (Atypical Cells of Undetermined Significance/Atypical Lymphoid Cells of Uncertain Significance), L4 (Suspicious for Malignancy) and L5 (Malignant).

Histopathological correlation was performed wherever biopsy or excision specimens were available. The cytological diagnosis was compared with the corresponding histopathological findings to assess diagnostic concordance. The Risk of Malignancy (ROM) for each Sydney System category was calculated using the formula:

ROM (%) = (Number of histologically confirmed malignant cases in a category ÷ Total number of cases with histopathological follow-up in that category) × 100.

Only those cases with available histopathological follow-up were included for ROM estimation. The collected data was entered into Microsoft Excel and analysed. Continuous variables such as age were expressed as mean $\pm$ standard deviation, while categorical variables including sex, site of lymphadenopathy, Sydney System category, and final diagnosis were presented as frequencies and percentages. The association between categorical variables were analysed using the Chi-square test. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 270 FNAC cases were included in the present study. Histopathological correlation was available in 27 cases.

The age of the patients ranged from 1 to 79 years. The most commonly affected age group was 31–40 years, accounting for 50 cases (18.5%), followed by 21–30 years with 47 cases (17.4%) and 11–20 years with 43 cases (15.9%). Children aged 1–10 years constituted 39 cases (14.4%). The age groups of 51–60 years and above 60 years each accounted for 28 cases (10.4%). [Table 1]

Table 1: Age Distribution of lymph node lesions (N = 270)

Sl No	Age	Male	Female	Total Frequency (%) (n=270)
1	1-10	22	17	39(14.4%)
2	11-20	30	13	43(15.9%)
3	21-30	27	20	47(17.4%)
4	31-40	26	24	50(18.5%)
5	41-50	23	12	35(13.0%)
6	51-60	18	10	28(10.4%)
7	>60	21	7	28(10.4%)

Among 270 patients, 167 (61.8%) were males and 103(38.2%) were females, with male-to-female ratio of 1.6:1, indicating a slight male predominance.

The most common site of lymphadenopathy was cervical group comprising of 152 cases (56.3%) followed by axillary group seen in 40 cases (14.81%). Supraclavicular lymph node was least commonly involved seen in only 7 cases (2.59%). [Table 2]

On cytological examination, L2 (Benign) category was the most common cytological diagnosis according to the Sydney System, accounting for 202

cases (74.8%). Among these, reactive lymphadenitis was the most frequent diagnosis, seen in 102 cases (50.5%) showing microscopically polymorphous lymphoid population, followed by granulomatous lymphadenitis in 54 cases (26.73%) showing epithelioid cells, small lymphocytes in periphery. Remaining cases were suppurative lymphadenitis showing dense neutrophilic aggregates, necrotizing lymphadenitis showing inflammatory cells against a necrotic background and chronic nonspecific lymphadenitis. [Figure 1]

Table 2: Location of lymph nodes

Location	Number of cases	Frequency (Percentage)
Cervical	152	56.30%
Axillary	40	14.81%
Submandibular	22	8.15%
Inguinal	12	4.44%
Supraclavicular	7	2.59%
Other	37	13.7%

The L1 (Inadequate/Non-diagnostic) category included 6 cases (2.2%), primarily due to scant cellularity and haemorrhagic aspirate. [Figure 1]

Only 6 cases (2.2%) were categorized as L3 (Atypical Cells of Undetermined Significance/Atypical Lymphoid Cells of Uncertain Significance), while 2 cases (0.6%) were reported as L4 (Suspicious for Malignancy). The L5 (Malignant) category comprised 54 cases (20%), including 48 cases of metastatic deposits and 6 cases of lymphoma. Among the metastatic deposits, squamous cell carcinoma was the most common, accounting for 34 cases showing squamoid tumor cells exhibiting pleomorphism with abundant eosinophilic cytoplasm., followed by adenocarcinoma with 9 cases showing focal

glandular and pseudopapillary pattern. [Table 3] [Figure 1]

Histopathological follow-up was available for 27 cases, and the Risk of Malignancy (ROM) was calculated for each Sydney System category. No histopathological follow-up was available for the L1 (Inadequate/Nondiagnostic) category. Of the 202 cases categorized as L2 (Benign), histopathological correlation was available in 12 cases. Eleven cases showed concordance between cytological and histopathological diagnoses, while one case diagnosed as reactive lymphadenitis on FNAC was confirmed as squamous cell carcinoma on histopathology, resulting in a ROM of 8.33%.

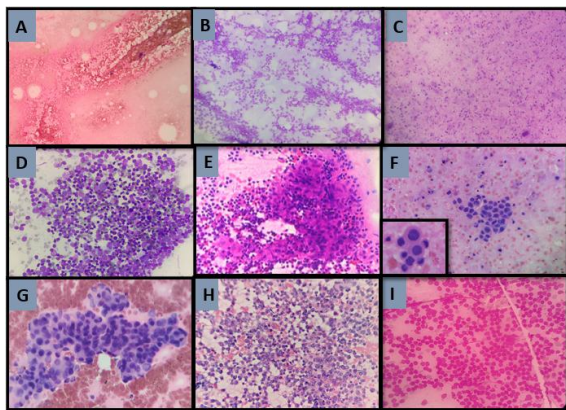


Figure 1: Fine Needle Aspiration Cytology (A-I): A. Inadequate smear (H&E) B. Suppurative lymphadenitis(H&E) C. Necrotizing Lymphadenitis (H&E) D. Reactive lymphadenitis (Giemsa stain) E. Granulomatous lymphadenitis (H&E) F. Metastatic deposits from Squamous cell carcinoma (H&E), G. Metastatic deposits from adenocarcinoma (H&E) H. Non-Hodgkins lymphoma (H&E) I. Small lymphocytic lymphoma(H&E).

Among the four cases with histopathological follow-up in the L3 (Atypical Cells of Undetermined Significance/Atypical Lymphoid Cells of Uncertain Significance) category, one case was discordant, with FNAC suggesting reactive lymphadenitis and histopathology revealing squamous cell carcinoma, yielding a ROM of 25%. [Figure 2]

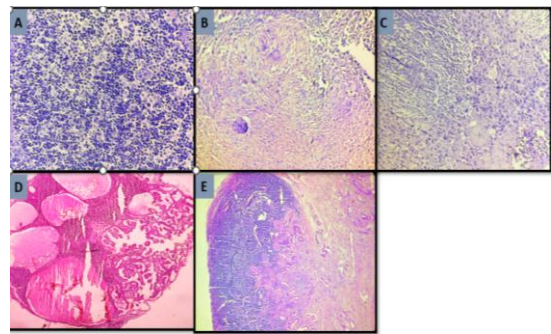


Figure 2: Lymph Node Biopsy (A-E): A. Reactive lymphadenitis B. Granulomatous lymphadenitis C. Metastatic deposit from Squamous cell carcinoma D. Metastatic deposit from Papillary thyroid carcinoma E. Metastatic deposit from Adenocarcinoma colon

The ROM was 100% for both the L4 (Suspicious for Malignancy) and L5 (Malignant) categories, with all cases showing complete concordance between cytological and histopathological diagnoses. The malignant lesions predominantly comprised squamous cell carcinoma and adenocarcinoma, followed by papillary thyroid carcinoma and lymphomas [Figure 2]. Overall, the ROM showed a progressive increase across the Sydney System diagnostic categories.

The diagnostic performance of FNAC, when compared with histopathological diagnosis showed a sensitivity of 84.6%, specificity and positive predictive value (PPV) of 100%, negative predictive value (NPV) of 86.7%, and an overall diagnostic accuracy of 88.9%. p value was <0.05 and was found to be statistically significant.

Table 3: Sydney System classification of Patients Undergoing FNAC for Lymph Node Evaluation

Diagnostic Criteria	No of cases ((n=270)	Frequency (%)
L1- Inadequate /nondiagnostic	6	2.22%
Only haemorrhage	4	1.5%
scant cellularity	2	0.7%
L2- Benign	202	74.81%
Reactive lymphadenitis	102	50.5%
Granulomatous lymphadenitis	54	26.73%
Suppurative lymphadenitis	7	3.47%
Necrotising lymphadenitis	8	3.96%
Chronic nonspecific lymphadenitis	10	4.95%
Inflammatory lesion	7	3.47%
Others	14	6.93%
L3-AUS	6	2.22%
L4-Suspicious for malignancy	2	0.74%
L5-Malignancy	54	20%
Primary	6	2.2%
Metastatic	48	17.8%

Table 4: Risk of Malignancy for each Diagnostic category of the Sydney system classification for Reporting Lymph node cytopathology

Sl No	Criteria	Total no. of cases with histopathologic diagnosis in each diagnostic category	Total cases reported as malignant on histopathology	Overall risk of malignancy (%)
L1	Inadequate /nondiagnostic	0	0	0
L2	benign	12	1	8.33
L3	AUS	4	1	25
L4	Suspicious for malignancy	2	2	100
L5	Malignancy	9	9	100

Table 5: Distribution of Malignant Cases (category L5)

Malignant category	Total number of cases(n=54)	Total frequency (%)
Squamous cell carcinoma	34	62.96 %
Adeno carcinoma	9	16.67%
Papillary thyroid carcinoma	2	3.70%
Small cell carcinoma	1	1.85%
Poorly differentiated carcinoma	2	3.70%
Non-Hodgkin's lymphoma	4	7.41%
Hodgkins's lymphoma	2	3.70%
Total	54	100%

DISCUSSION

Fine Needle Aspiration Cytology (FNAC) has become the primary diagnostic modality for the evaluation of superficial lymphadenopathy because of its simplicity, rapidity, cost-effectiveness and high diagnostic accuracy. However, until recently, the absence of a standardized reporting terminology resulted in considerable interobserver variability and inconsistent communication between pathologists and clinicians. The introduction of the Sydney System for Reporting Lymph Node Cytopathology has addressed this limitation by providing uniform diagnostic categories with corresponding Risk of Malignancy (ROM) and management recommendations. The present study evaluated the applicability of the Sydney System in a tertiary care centre and assessed the distribution of lymph node lesions according to the five diagnostic categories.

A total of 270 lymph node FNAC cases were included in the study. The mean age was 35 years with majority of them belonged to the third (17.4%) and fourth decades of life (18.5%). The mean age distribution observed in our study is comparable with Sreelekshmi et al. study, who have reported that lymphadenopathy affects a broad age range but is more frequently encountered among young and middle-aged adults.^[7] Similar observations were reported by Qadri et al. and Mohanty et al., who also found the majority of patients in the reproductive age group.^[8,9]

A slight male predominance was observed in our study, with a male-to-female ratio of 1.6:1. This is comparable to the studies done by Mohanty et al (1.05:1) and Qadri et al (1.5:1).^[8,9] The slight male predominance could be due to increased exposure to infectious diseases, tobacco-related malignancies, and occupational risk factors among males in the study population.

In Sydney system the majority of lymph node aspirates were categorised into benign (L2 category), accounting for 74.8% of all cases. Among this category, reactive lymphoid hyperplasia (50.5%) was the most frequent diagnosed followed by granulomatous lymphadenitis (26.73%). Similar findings have been reported by Qadri et al, studies, where reactive lymphadenitis was most common lesion.^[8] Khajuria et al. reported granulomatous lymphadenitis as the predominant lesion in regions with a high prevalence of tuberculosis. Such geographical variation reflects differences in disease burden and endemic infections.^[10]

Granulomatous lymphadenitis was seen in 27% cases in our study. Sreelekshmi et al., also showed 21% of granulomatous lymphadenitis cases.⁷ FNAC serves as an effective first-line investigation in these patients because it permits not only cytomorphological evaluation but also ancillary investigations such as Ziehl–Neelsen staining, GeneXpert, microbiological culture and molecular testing whenever required. The ability to establish an early diagnosis facilitates prompt initiation of anti-tubercular therapy and reduces the need for invasive biopsy in many patients.

Only six cases (2.2%) were categorized as L1 (Inadequate/Non-diagnostic). Inadequate aspirates from our study are due to poor cellularity, cystic degeneration, extensive necrosis, fibrosis or technical difficulties during aspiration. The Sydney System recommends repeat FNAC under image guidance or excision biopsy in such cases to minimize false-negative diagnoses and improve diagnostic accuracy.

The L3 category (Atypical Cells/Atypical Lymphoid Cells of Undetermined Significance) comprised only six cases (2.2%), while two (0.7%) were categorized as L4 (Suspicious for Malignancy). The low frequency of these indeterminate categories demonstrates that most lymph node aspirates could be confidently classified as either benign or malignant based on cytomorphological features. Nevertheless, these categories remain clinically important because they identify patients requiring repeat aspiration, ancillary investigations, flow cytometry, immunocytochemistry, or excisional biopsy for definitive diagnosis. Sreelekshmi et al have similarly reported relatively few cases in the L3 and L4 categories but consistently demonstrated a high Risk of Malignancy associated with these groups.

The malignant (L5) category accounted for 20% (54 cases) of all cases, comprising metastatic malignancies (88%) and lymphomas (12%). Histopathological follow-up available for nine malignant cases demonstrated complete concordance with the cytological diagnosis, indicating excellent diagnostic accuracy for clearly malignant lesions with sensitivity of 87% and specificity of 100%. Sreelekshmi et al., have similarly demonstrated sensitivity of 95% and specificity of 96% for metastatic malignancies on lymph node cytology.^[7] In many cases, FNAC also provides sufficient material for immunocytochemistry and cell block preparation,

thereby facilitating identification of the primary tumour and guiding further clinical management. Among the benign(L2) cases, ROM is 8.33%. One case was diagnosed as benign on cytology was found to be metastatic deposit of squamous cell carcinoma on histopathology. This was due to sampling error as metastatic deposit was confined to the subcapsular lesion which was not sampled during FNAC.

ROM in L3 category was 25%. Cytology–histopathology discrepancies in the L3 is most likely due to scant atypical cells, focal metastatic involvement of the lymph node, or sampling error resulting in an indeterminate cytological diagnosis. Discrepancy can also be due to morphological overlap between reactive atypia and metastatic squamous cell carcinoma may have also contributed to the discordance.

Although histopathological follow-up was limited in the present study, the available cases showed complete agreement with the cytological diagnosis in the malignant category. Study done by Gupta et al, Vigliar et al., and Joshee et al. have demonstrated increasing ROM from L1 to L5, with the 100% ROM observed in the suspicious and malignant categories.^[11,12,13] Such risk stratification represents one of the major strengths of the Sydney System because it allows clinicians to adopt evidence-based management strategies according to the estimated probability of malignancy.^[14,15]

The limitations of our study include its retrospective, single-centre design. Histopathological correlation was available only in a limited number of cases, particularly in the benign categories, and ancillary investigations were lacking. Consequently, the category-wise Risk of Malignancy (ROM) could not be accurately estimated for all diagnostic groups. Large multicentric studies are required to further validate the Sydney System in the Indian population.

CONCLUSION

The **Sydney System** for lymph node cytopathology is a simple, practical, and easy-to-use classification system for routine cytology reporting. It provides standardized diagnostic categories, which help reduce ambiguity and improve communication between pathologists and clinicians. The inclusion of **Risk of Malignancy (ROM)** and management recommendations helps guide patient care by indicating the need for repeat FNAC, additional investigations, biopsy, or treatment. The system is especially valuable in **resource-limited settings**,

where FNAC is often the primary diagnostic tool for evaluating lymphadenopathy.

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