Section: Pathology

Original Research Article

EVALUATING THE UTILITY OF THE SYDNEY SYSTEM FOR LYMPH NODE CYTOLOGY REPORTING AT A RURAL TERTIARY CARE CENTER IN MAHARASHTRA

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ABSTRACT

Background: Lymphadenopathy has varied causes, from reactive to malignant. Fine-Needle Aspiration Cytology (FNAC) is a rapid, minimally invasive, cost-effective diagnostic tool. The Sydney System (2019) standardises lymph node cytology, enhancing consistency. This study assesses its applicability, accuracy, and diagnostic performance in a tertiary center.

Materials and Methods: A prospective observational study was carried out in the Pathology Department at a tertiary care rural hospital in Maharashtra from May 2024 to April 2025. All lymph node FNAC cases received during this period were included. Clinical details were systematically recorded, and smears were categorized using the Sydney System for Lymph Node Cytology. Based on available follow-up, histopathological correlation and Risk of Malignancy (ROM) were determined. Data were compiled in Microsoft Excel and analyzed descriptively.

Results: Patient ages ranged from 6-months to 94-years (mean 32.6-years), with a slight female predominance (M:F = 0.98). Among 208 cases, 53% involved cervical nodes, and 85.1% were classified as L2 (Benign). L5 (Malignant) and L4 (Suspicious) accounted for 5.3% and 4.8%, respectively, while L1 and L3 each comprised 2.4%. Histopathological follow-up (24 cases) showed ROM values of L2 7.7%, L3 50%, L4 100%, and L5 100%. Using expanded criteria, FNAC sensitivity, specificity, PPV, NPV, and accuracy were 91%, 92%, 91%, 92%, and 91.7%. With strict criteria, sensitivity was 83%, specificity 100%, PPV 100%, NPV 92%, and accuracy 94.4%.

Conclusion: The study validates Sydney System's utility for lymph node cytology, showing predominantly benign cases, common cervical involvement, and high diagnostic accuracy with sensitivity (>80%) and specificity (>90%).

Keywords: Fine Needle Aspiration Cytology (FNAC), Lymphadenopathy, Sydney System, Lymph Node Cytology, Risk of Malignancy (ROM).

INTRODUCTION

Lymph nodes are clusters of lymphoreticular tissue distributed throughout the body, constituting a crucial part of the lymphatic system and contributing to the body's immune response. Lymphadenopathy (LAP), a condition characterized by enlarged lymph nodes, is one of the most common clinical presentations of patients attending the outpatient department. It can arise due to infectious or neoplastic diseases.[1]

Many researchers have documented the history of fine-needle aspiration cytology (FNAC). At the beginning of the 20th century, lymph node needle aspiration was attempted by a number of investigators to diagnose various diseases, including trypanosomiasis, lymphoblastoma, and Hodgkin's disease. The technique of FNAC gained quick acceptance in clinical services and became the first line of investigation for most of the patients who presented with swellings in various sites.[2] Today, FNAC has become a simple, safe, reliable, and inexpensive method for diagnosing lesions and masses in a variety of sites and organs, making it the most convenient diagnostic aid. FNAC serves as a

valuable diagnostic tool for the initial assessment of lymphadenopathy with an unknown cause. Beyond its recognized benefits, such as being minimally invasive, rapid, and cost-effective, FNC's ability to yield material suitable for various ancillary techniques has enhanced the accuracy of lymph node evaluations.[3,4]

Although the definitive diagnosis of malignant lymphadenopathies typically necessitates excisional biopsy and histological examination, benign cases can often be confidently diagnosed by integrating FNAC microscopic findings with data from flow cytometry (FC), immunocytochemistry (ICC), microbiological analysis, and molecular testing. Nevertheless, the traditional method of presenting lymph node smears lacks a standardized diagnostic classification, a shared terminology among cytopathologists, and clear communication to clinicians regarding the risk of malignancy and subsequent management.[5,6]

The current World Health Organisation (WHO) classification of lymphoproliferative disorders incorporates data like clinical, morphological, and ancillary data necessary for specific diagnoses. Fine-Needle Aspiration Cytology (LN-FNAC) of lymph nodes provides valuable cytomorphological details along with material for ancillary investigations, making it an important diagnostic tool in the assessment of lymphadenopathy. Although considerable progress has been made in the technique, interpretation, and integration of LN-FNAC with ancillary studies, its acceptance among clinicians and pathologists remains variable. The main limitation lies in the lack of universally established guidelines and a standardized cytopathological classification system that directly impacts clinical management.[7-9]

In May 2019, during the 20th International Congress of Cytology in Sydney, a systematic approach for assessing performance, classification, and reporting of lymph node cytopathology was introduced. This proposed system suggests classifying cytological aspirates from lymph nodes into five categories based on distinct cytological features. The essential features of the categories are as follows: Category I/L1: Inadequate / Non-Diagnostic; Category II/L2: Benign; Category III/L3: Atypical Cells of Undetermined Significance or Atypical Lymphoid Cells of Uncertain Significance; Category IV/L4: Suspicious for Malignancy; Category V/L5: Malignant.[10]

The primary objective of this system was to establish consensus guidelines and a framework for enhancing communication among various health care professionals (HCPs), like pathologists, clinicians, and surgeons. Additionally, it offers essential diagnostic cytopathological characteristics and management recommendations associated with reporting categories.[10]

Only a small number of studies have been conducted on the Sydney system for reporting lymph node cytology, and only 4 of these are from India.[11] It appears to be one of the promising and robust classification and reporting systems. However, large sample size studies are needed to assess the reliability and validity of this system. The underutilization of the Sydney system for classification and reporting of lymph node pathologies, combined with limited literature, contributes to the knowledge gap regarding its applicability.[12] Therefore, the current study aims to evaluate the applicability and accuracy of this system in diagnosing lymph node cytology.

MATERIALS AND METHODS

The present study was conducted in a tertiary care centre / the Department of Pathology at Rural Hospital, Maharashtra, after taking approval from the Institutional Ethics Committee. The study includes data collection from May 2024 to April 2025.

Prior to the procedure, written informed consent was obtained from each patient (or parent/guardian in the case of minors). The following key elements were explained to the patient: The nature of the FNAC procedure, the purpose of the test, Potential risks and complications, Expected benefits, and possible alternatives. Respect for patient privacy and confidentiality was maintained throughout. Ethical standards were strictly followed, and any patient concerns were addressed in advance.

Patients were often apprehensive about the level of pain, usually anticipating more discomfort than what was actually experienced. Therefore, it was important to establish good doctor–patient communication, clearly explaining the procedure beforehand. This enhanced the patient's confidence and cooperation. FNAC is often performed by the pathologist themselves, offering a near-patient clinical experience. While this role involves direct interaction and aspects not traditionally emphasized in pathology training, it is essential to provide clear information, build rapport, and support the patient throughout the process. All procedures were performed in accordance with institutional ethical guidelines.

Study Criteria

Inclusion criteria

- All the patient cases of Fine Needle Aspiration of Lymph node lesions received in Pathology department, at Tertiary Care Centre between May 2024 and April 2025 (12 months)
- All the patient who give consent for the study

Exclusion criteria

- Patients with bleeding disorders
- Patients who did not give consent for the study

In the current study, the term "utility" refers to the system's practical applicability in routine pathology practice—specifically its feasibility in categorizing aspirates, its ease of use across a wide range of lymph node lesions, and its potential to improve communication between pathologists and clinicians through structured reporting. By enabling reproducible categorization into diagnostic tiers such as benign, malignant, or inadequate, the system helps

streamline diagnostic workflows and guides further clinical management. This study primarily focuses on describing the cytological spectrum using the Sydney classification and offers preliminary insights into the distribution of diagnostic categories observed.

Patient details, including age, sex, clinical history, provisional clinical diagnosis, radiological findings, and peripheral smear results (if relevant) were documented in a structured format. FNAC was performed on both palpable and impalpable lymph nodes. Slide were prepared based on two staining technique - Alcohol-fixed smears stained with Papanicolaou (Pap) stain and Ziehl-Neelsen stain was performed when tuberculous lymphadenitis was suspected.

All smears were examined by experienced cytopathologists and classified according to the Sydney System of Lymph Node Cytology into five classes, which includes:

1. L1 – Inadequate / Non-diagnostic
2. L2 – Benign
3. L3 – Atypia of Undetermined Significance (AUS)
4. L4 – Suspicious for Malignancy
5. L5 – Malignant

Smears were evaluated for cellularity, cytomorphological features, background elements, and architectural patterns.

Histopathological Correlation: Histopathological follow-up was available in selected cases where biopsy or excision was clinically indicated. Correlated histology reports were used to assess concordance with the cytological diagnosis whenever it was available.

Risk of Malignancy Calculation: Where histopathological correlation was available, Risk of Malignancy Calculation (ROM) was calculated for each category using:

ROM (%) = (Number of histologically confirmed malignant cases) / (Number of histopathological follow-ups in that category) × 100

Sample size justification and statistical analysis:

The sample size was not determined through prior statistical calculations because this study is time-bound in nature, meaning it includes all eligible cases encountered during the defined study period. A total of 200 patients are expected based on last year data for the similar duration. All eligible cases reported during the study period were included to ensure adequate representation and enhance the validity of the observations. The inclusion of all cases within this period helps minimize selection bias and ensures a real-world representation of the spectrum of lesions encountered in routine diagnostic practice. All the patients with clinically suspected lymphadenopathy fulfilling the study criteria were included in the study. Patient demographics, clinical data, FNAC findings, and histopathological outcomes were recorded in a structured format. Data were entered in Microsoft Excel and analyzed using descriptive statistics. Due to the limited number of histopathological correlations, only ROM was calculated without application of inferential statistics.

RESULTS

A total of N=208 patients who underwent fine needle aspiration cytology (FNAC) of lymph nodes were included in the study. The age of patients ranged from 6 months to 94 years. The mean (± SD) age of the study patients was 32.61 (± 12.02) years, with a median age of 29 years. Overall, there was a slight female predominance with 103 males and 105 females, yielding a male-to-female ratio of 0.98.

Lymph Node Site Distribution

The most common site of lymph node involvement was the cervical region (53%), followed by axillary (15%), Submandibular Lymph Node (12%), and Supraclavicular Lymph Node (6%). The remaining lymph nodes (Submental Lymph Node, Inguinal Lymph Node, Post Auricular Lymph Node, Pre Auricular Lymph Node) contribute < 5% each. The details are mentioned below in [Figure 1].

Cytological Diagnosis

Cytological evaluation was performed, and cases were classified according to both the conventional reporting method and the Sydney System. The most common Cyto diagnosis was Chronic Granulomatous Lymphadenitis (21%), followed by Chronic Nonspecific Lymphadenitis (19%) and Reactive Lymphoid Hyperplasia (18%). The least common Cyto diagnosis was Spindle Cell Neoplasm (0.5%). The cyto diagnosis of Lymphoproliferative Disorder, Necrotising Lymphadenitis, and Suspicious of Malignancy was less than 5% each. The category "No Opinion Possible" was observed 2.4% cases. The details are mentioned below in [Tables 1].

The majority of cases fall under L2 – Benign, as per the Sydney system of classification, followed by L5 – Malignancy. The remaining three categories contribute to less than 5% of the total cases each. The details are mentioned below [Table 2 and Figure 2].

Histopathological Correlation

Histopathological follow-up was available in only 24 cases. Out of 24 confirmation, 15 cases confirmed over histopathological diagnosis in present study institute whereas remaining 9 cases confirmed their diagnosis over telephonic follow up. This results in 11.5% follow-up rate, i.e., 24/208. Out of the total 24 cases included in the study, a majority—13 cases—were categorized under the L2 classification. Additionally, 2 cases were identified as belonging to the L3 category, while 4 cases were classified under L4. The remaining 5 cases fell within the L5 category. The details are mentioned in the [Table 3].

The Risk of Malignancy (ROM) was calculated for the 24 cases for which histopathological correlation was available, in accordance with the Sydney System for reporting lymph node cytopathology. Among these, 13 cases belonged to the L2 category (Benign). Out of these, 1 case was subsequently diagnosed as malignant on histopathology, resulting in a calculated ROM of 7.7% for L2. There were 2 cases in the L3 category (Atypical), of which 1 case turned out to be malignant, giving a ROM of 50% for this category.

Four cases were classified under L4 (Suspicious for malignancy) and five cases were under L5 (Malignant). All cases in these two categories were histopathologically confirmed as malignant, yielding a ROM of 100% for both L4 and L5. For L1 category where no histopathological follow-up was available, the ROM could not be determined due to lack of confirmatory data. The details are mentioned in the [Table 4 and Figure 3].

The diagnostic performance of Fine Needle Aspiration Cytology (FNAC), interpreted using the Sydney System of Classification, was assessed by comparing cytological diagnoses with the available histopathological follow-up data. To evaluate this performance, two distinct analytical approaches were employed:

The sensitivity of FNAC was calculated to be 91%, while the specificity was 92%. The positive predictive value (PPV) was found to be 91%, and the negative predictive value (NPV) was 92%, reflecting the overall diagnostic utility of the method when L3 to L5 categories are considered as indicative of malignancy. [Accuracy – 91.7%]

The sensitivity of FNAC was calculated to be 83%, while the specificity was 100%. The positive predictive value (PPV) was found to be 100%, and the negative predictive value (NPV) was 92%, reflecting the overall diagnostic utility of the method when only L5 categories are considered as indicative of malignancy. [Accuracy – 94.4%].

Table 1: Cyto Diagnosis of Patients Undergoing FNAC for Lymph Node Evaluation

Sr No	Cyto Diagnosis	No of patient	% of patients
1	Chronic Granulomatous Lesion with Abscess	14	6.73%
2	Chronic Granulomatous Lymphadenitis	44	21.15%
3	Chronic Nonspecific Lymphadenitis	39	18.75%
4	Inflammatory Lesion	15	7.21%
5	Lymphoproliferative Disorder	5	2.40%
6	Necrotising Lymphadenitis	6	2.88%
7	Positive for Malignancy	11	5.29%
8	Reactive Lymphadenitis	22	10.58%
9	Reactive Lymphoid Hyperplasia	37	17.79%
10	Spindle Cell Neoplasm	1	0.48%
11	Suspicious of Malignancy	9	4.33%
12	No Opinion Possible	5	2.40%
	Total	208	100%

Table 2: Sydney System classification of Patients Undergoing FNAC for Lymph Node Evaluation

Sr No	Sydney System Classification	No of patient	% of patients
1	L1 - Non-Diagnostic/Inadequate	5	2.40%
2	L2 - Benign	177	85.10%
3	L3 - Atypia of Undetermined Significance	5	2.40%
4	L4 - Suspicious for Malignancy	10	4.81%
5	L5 - Malignancy	11	5.29%
	Total	208	100%

Table 3: Histopathological diagnosed cases from study

Sr. No	Sydney System Classification Category	No. of cases	% of cases
1	L1 - Non-Diagnostic/Inadequate	0	0%
2	L2 – Benign	13	54.17%
3	L3 - Atypia of Undetermined Significance	2	8.33%
4	L4 - Suspicious for Malignancy	4	16.67%
5	L5 – Malignancy	5	20.83%
Total		24	100%

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

Sr. No	Sydney System Classification	Total no. of cases with histopathologic diagnosis in each diagnostic category	Total cases reported as malignant on histopathology	Overall risk of malignancy (%)
1	L1 - Non-Diagnostic/Inadequate (n=5)	0	-	-
2	L2 – Benign (n=177)	13	1	7.7%
3	L3 - Atypia of Undetermined Significance (n=5)	2	1	50%
4	L4 - Suspicious for Malignancy (n=10)	4	4	100%
5	L5 – Malignancy (n=11)	5	5	100%

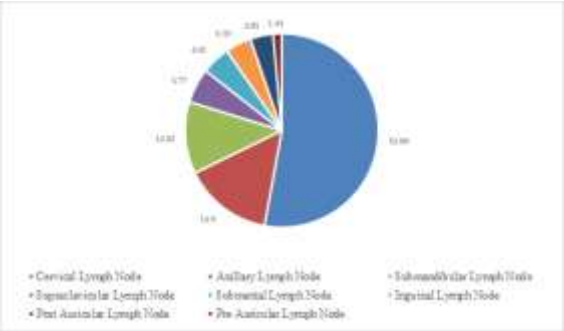

Figure 1: Lymph Node Distribution in Patients Undergoing Lymph Node FNAC

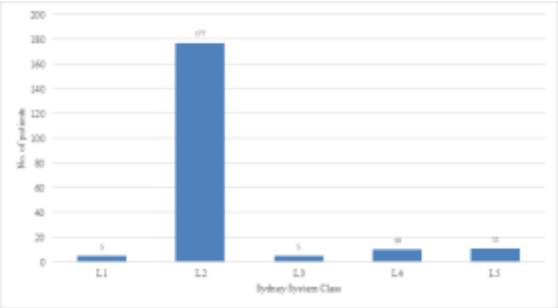

Figure 2: Sydney System Classification of Patients Undergoing FNAC for Lymph Node Evaluation

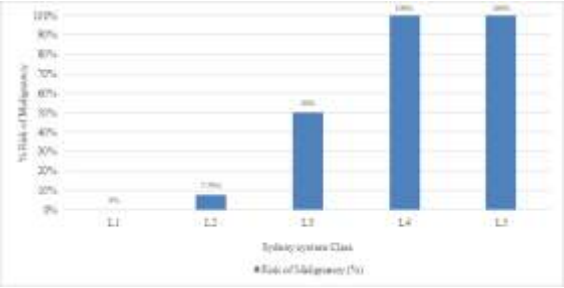

Figure 3: Risk of Malignancy Associated with each Diagnostic category of the Sydney system classification for Reporting Lymph node cytopathology

DISCUSSION

Lymphadenopathy, or the abnormal enlargement of lymph nodes, is a common clinical finding encountered in routine practice, arising from a wide spectrum of etiologies ranging from infectious and reactive processes to autoimmune disorders, primary lymphoid neoplasms, and metastatic disease. The distribution and underlying causes of lymphadenopathy vary considerably across populations, influenced by age, geographic region, and the availability of healthcare resources. Reactive and infectious causes predominate globally; tuberculosis leads in India, while malignant causes are common in adults at tertiary centers.[13,14]

Accurate tissue diagnosis is vital for identifying underlying pathology. Though hematological tests and imaging aid evaluation, they cannot replace direct tissue analysis. FNAC serves as the first-line diagnostic tool for lymphadenopathy due to its safety, speed, and cost-effectiveness. It differentiates reactive, granulomatous, malignant, and lymphomatous lesions, with enhanced accuracy using immunohistochemistry, flow cytometry, and ultrasound guidance despite occasional sampling limitations.[15]

The WHO classification of lymphoid neoplasms emphasizes integrating clinical, morphological, and ancillary data. To standardize FNAC reporting, the Sydney System was proposed in 2019, providing structured diagnostic categories, technical guidelines, and management recommendations. It enhances communication, reproducibility, and confidence, proving adaptable across diverse healthcare settings, including India, where both infectious and neoplastic lymphadenopathies are prevalent.[10]

In this study, 208 patients (aged 6 months–94 years) who underwent lymph node FNAC were analyzed. Most cases (53.4%) occurred in individuals under 30 years, consistent with the higher prevalence of reactive and infectious lymphadenopathy in younger populations due to greater immune activity. Elderly patients formed a smaller proportion but showed a higher incidence of neoplastic causes such as metastatic malignancy and lymphoma. A gradual decline in lymphadenopathy prevalence was observed with increasing age, reflecting reduced lymphoid activity and immune responsiveness. However, lymphadenopathy in older patients often indicates malignant etiology. The observed age distribution parallels findings from previous studies and highlights the importance of demographic analysis in understanding etiological patterns, refining differential diagnoses, and optimizing investigation strategies across different age groups.[13,14]

In this study, females constituted 50.48% of cases (male-to-female ratio 0.98), showing near-equal gender distribution. Lymphadenopathy prevalence was consistent across ages, with minor variations: males under 18 years showed slightly higher rates, possibly due to infection exposure, while females aged 18–30 years had higher prevalence, likely from healthcare-seeking behavior, hormonal influences, or tubercular lymphadenitis. Overall, gender differences were minimal but age-specific trends offered etiological insights.[16]

In this study, about two-thirds of lymphadenopathy cases involved cervical and axillary regions, aligning with literature. Cervical lymphadenopathy, common in patients under 18, was mainly reactive or tubercular. Axillary nodes in women often related to breast pathology, benign or malignant. Elderly patients showed more inguinal and submandibular involvement, often metastatic. Reactive, granulomatous, and nonspecific lymphadenitis comprised over half of cases, while malignant findings accounted for around 10%, highlighting age- and site-specific diagnostic patterns.[17,18]

In this study, most lymph node aspirates (85.1%) were classified as L2 – Benign per the Sydney System, consistent with literature reporting 20.1%–85.1%. The L1 – Inadequate/Nondiagnostic category formed only 2.4%, within the reported 0.6%–9.8%

range, indicating good sampling and smear quality. Confirmed malignancy (L5) accounted for 5.3% of cases, aligning with lower-end values (5.3%–57.2%) from published studies. Variations in L5 rates across studies likely reflect differences in population profiles, healthcare access, and study settings (primary vs tertiary centers). Our L5 proportion parallels Kanhe et al.'s findings but is lower than reports from tertiary cancer institutes like Juanita et al. and Gupta et al. (over 40%). Similarly, L3 (Atypical) and L4 (Suspicious) cases were fewer, suggesting benign and reactive lesions predominated in our population, consistent with the demographic trend of infectious and reactive lymphadenopathy being more common in community-based healthcare settings.[19-21]

In this study, histopathological correlation was available in only 24 of 208 cases (11.54%), reflecting limited follow-up and patient compliance. Similar variation is reported in literature, ranging from 8.85% to 98.74%, depending on study design and healthcare access. Despite few malignant cases, available histopathology confirmed FNAC's diagnostic accuracy. The low follow-up rate highlights the need for improved patient counseling, referral systems, and awareness to ensure definitive management and maximize FNAC's clinical utility.[19-21]

In this study, the calculated Risk of Malignancy (ROM) for Sydney System categories showed a clear stepwise rise from benign to malignant categories: L5 and L4 (100% each), L3 (50%), and L2 (7.7%), with no L1 cases. These findings align with global reports—L5 (98.2–100%), L4 (82.4–100%), L3 (28.6–100%), and L2 (0.2–15.6%)—confirming the Sydney System's diagnostic reliability. Variation in ROM, particularly in L1 and L3, reflects differences in case selection, cytological thresholds, and histopathological correlation across studies. The high concordance of our L4 and L5 ROM values with published data reinforces FNAC's accuracy in detecting malignancy, while intermediate categories warrant careful clinicoradiological assessment.[11,22]

Diagnostic performance analysis using expanded criteria showed FNAC sensitivity of 91%, specificity 92%, PPV 91%, NPV 92%, and overall accuracy 91.7%. With strict criteria (excluding borderline cases), sensitivity decreased to 83%, but specificity and PPV reached 100%, with accuracy 94.4%. These results align with literature values (sensitivity 45.8–100%, specificity 91.9–100%), comparable to Gupta (2021), Uzun (2022), and Kanhe (2023). The high PPV (100%) confirms FNAC's reliability for positive diagnoses, and our NPV (92%) exceeded several prior reports, indicating effective exclusion of malignancy. Variations in reported accuracy likely reflect differences in study design, disease prevalence, and operator expertise.[19,20,23] Overall, FNAC remains a highly specific, accurate, and minimally invasive diagnostic tool for lymphadenopathy, with cautious interpretation of equivocal categories enhancing clinical confidence.[22]

This study has limitations, including its one-year duration and relatively small sample size, which may restrict statistical strength and generalizability. Limited histopathological correlation further constrained diagnostic validation. Conducted in a rural setting, follow-up was affected by limited access, financial barriers, and low awareness. Nonetheless, the findings offer valuable insights into FNAC's diagnostic performance, emphasizing the need for larger, multicentric studies with extended follow-up to enhance reliability and evidence strength.

CONCLUSION

The present study highlights the applicability of the Sydney system as a structured framework for lymph node cytology reporting. The majority of cases were benign, with cervical lymph nodes most commonly involved. Histopathological follow-up in 24 cases demonstrated clinically relevant risk of malignancy (ROM) stratification, with acceptable diagnostic accuracy: sensitivity 83% - 91% and specificity 92% - 100%. Despite limitations of small sample size, short duration, and limited follow-up inherent to a rural setting, the study reinforces FNAC's diagnostic utility and underscores the need for larger, multicentric validation studies.

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