Original Article

Assessment of Interobserver Variability and Cytomorphological Analysis in Lymph Node FNAC: A Comparative Study of Conventional and Sydney Systems

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Abstract

Background: Fine Needle Aspiration Cytology (FNAC) plays a vital role in the initial evaluation of lymphadenopathy. However, the absence of a standardized reporting system has led to variability in diagnosis. The Sydney system was recently proposed to address this issue by providing structured criteria for lymph node cytology reporting. The objective is to assess and compare interobserver variability and cytomorphological interpretation of lymph node FNAC using the conventional system and the Sydney system of reporting. **Material and Methods:** An observational study was conducted on 150 cases of lymph node FNACs with available histopathological correlation. Each case was evaluated and categorized independently by three primary investigators and two blinded pathologists using both the conventional and Sydney systems. Cytomorphological parameters were documented, and interobserver agreement was statistically analyzed using kappa values. **Results:** The Sydney system demonstrated improved reproducibility among pathologists compared to the conventional system. Kappa values for interobserver agreement were significantly higher with the Sydney system, particularly in borderline and indeterminate categories. The structured format and defined criteria of the Sydney system contributed to reduced ambiguity in reporting. **Conclusion:** The Sydney system improves interobserver consistency and offers a more standardized approach to lymph node cytology reporting. Its adoption in routine pathology practice can enhance diagnostic communication and potentially reduce diagnostic errors.

Keywords: FNAC, lymph node, interobserver variability, Sydney system, diagnostic consistency, cytopathology.

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Introduction

Lymphadenopathy, defined as an abnormality in the size, number, or consistency of lymph nodes, is a common clinical finding in both paediatric and adult populations. Its underlying etiology are diverse, ranging from benign reactive conditions and infections to primary lymphoid neoplasms and metastatic malignancies.[1] Among the various diagnostic tools used for evaluating lymphadenopathy, Fine Needle Aspiration Cytology (FNAC) has emerged as an essential first-line, minimally invasive diagnostic procedure. FNAC is particularly favoured due to its rapid turnaround time, cost-effectiveness, low complication rates, and ability to provide both cytomorphological information and samples for ancillary testing.

In the context of lymph node pathology, FNAC aids in distinguishing between neoplastic and non-neoplastic lesions and helps in the early detection of both lymphoid and non-lymphoid malignancies. However, despite its widespread utility, FNAC of lymph nodes lacks a universally accepted, standardized reporting system. This deficiency has resulted in substantial interobserver variability, especially in cases that present with borderline cytological features or require nuanced interpretation.[2]

Traditionally, lymph node FNAC reports have been generated using conventional descriptive formats, which vary from institution to institution and even between pathologists within the same department. These conventional reporting systems are often narrative, subjective, and lack defined diagnostic categories. Consequently, there is a wide variability in interpretation and diagnostic categorization, particularly in indeterminate or suspicious lesions. This variation not only hampers reproducibility but also complicates clinical decision-making and communication between pathologists and treating physicians.[3]

To address these limitations, the Sydney System of Lymph Node Cytopathology was proposed. Introduced and endorsed by the International Academy of Cytology and the European Federation of Cytology Societies in 2019, the Sydney System aims to bring

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a structured, tiered diagnostic framework to lymph node FNAC, similar to other organ-specific reporting systems such as the Bethesda System for thyroid cytopathology or the Milan System for salivary gland lesions. The Sydney System proposes five main diagnostic categories: (1) Inadequate/Non-diagnostic, (2) Benign, (3) Atypical Cells of Undetermined Significance (AUS)/Atypical Lymphoid Cells of Uncertain Significance (ALUS), (4) Suspicious, and (5) Malignant. Each category is defined with clear cytomorphological criteria and associated clinical management guidelines.[4]

One of the key advantages of the Sydney System is its potential to reduce interobserver variability by providing clear, objective definitions for each diagnostic category. It encourages a more systematic approach to cytomorphological evaluation and offers guidance for ancillary testing where appropriate. This systematization can enhance diagnostic clarity, improve reproducibility, and foster better communication with clinicians.

The interobserver variability, or discrepancy in diagnostic judgments achieved by two or more observers, is also an important problem in cytopathology. It is also especially troublesome in lymph node FNAC where it seems frequently necessary to observe the difference between reactive hyperplasia and low-grade lymphoma or to distinguish between suspicious and definitely malignant lesions using judgement and consistency. A high level of interobserver variability not only has an impact on diagnostic accuracy but in addition, affects the credibility of reports on cytology, which results in possible over-treatment or under-treatment of patients.[5]

Considering these concerns, it is essential to determine the extent to which the Sydney System has a comparative advantage over traditional reporting formats in the measure of reproducibility and agreement in observation. The agreement between the impression of various pathologists with the Sydney System, as to the state of the art, must be measured quantitatively, particularly under a real-life scenario with a range of diagnostic complexity.

This gap is the objective of this study because the interobserver discrepancy between pathologists using the conventional and Sydney systems of reporting LN FNAC is to be evaluated systematically. It also aims at examining the cytomorphological parameters underscored in every system and how it can yield diagnostic consensus. The findings will present information as to whether the Sydney System provides a more consistent and predictable way of FNAC lymph node and whether it ought to be used more frequently in daily practice of diagnostic pathology.

The proposed research will help in the changing environment of cytological standardization and could help popularize the use of the Sydney System as a diagnosis and reporting tool of lymph node pathology overall.

Materials and Methods

Study Design and Setting: This was a prospective observational study that had taken place in the Depth the Department of Pathology in Mahatma Gandhi Medical College and Research Institute, Puducherry. It was conducted during a specific period of time, between December 2020 and May 2022, and institutional ethical approval was obtained before the study started.

Study Population: The cases that were used in the study comprised of 150 FNAC of lymph nodes which had both cytological and historical pathological diagnosis. These were subject cases that were chosen considering certain inclusion criteria. Palpable and deep-seated lymph nodes were either sampled manually or by use of image guidance to obtain the FNAC samples. The cases that had sufficient cytological smears, and the presence of the histopathological tissue against which the gold standard would be compared were only considered. To have a comprehensive analysis, the sample of cases included a range of lesions (benign, atypical, suspicious, and malignant cases) to include in the study, cases were excluded, and sample cases were determined by the rule: only FNAC was carried out without histopathological follow-up, or the quality of staining or destruction of smears was poor, or some required clinical or imaging data were absent. These exclusion criteria guaranteed that the dataset that was included was both diagnostically complete as well as making it analytically reliable.

Cytological Assessment procedure: The standard procedures of FNAC were performed using the usual methods of working with 23G or 25G needles connected to 10 mL syringes. The smears made of the aspirated material were air-dried and stained either using May-Grunwald Giemsa (MGG) or using alcohol-fixed smears stained using Pap (Papanicolaou) procedure. Special stains were reserved or were left to be prepared as cell blocks where considered to be necessary.

Primary investigator who was a postgraduate student undertook the initial assessment and categorization of all cases in collaboration with two supervising pathologists. The analysis was conducted in terms of the traditional reporting system and Sydney system of classification. After this preliminary analysis of all identifiable data, information and earlier interpretations were cleared, and the smears anonymized. Two more pathologists not a part of the initial examination or the study design were then inspected to examine the anonymised slides independently hence making it possible to make an unbiased judgement.

Diagnostic Systems Compared: Diagnostic comparison was done using two classification systems. The traditional system was comprised of four types, such as non-diagnostic, benign, suspicious, and malignant. Sydney system, in its turn, employed a 5-level system with L1 (Inadequate/Insufficient) at the bottom and L5 (Malignant), L4 (Suspicious), and L3 (Atypical—ALUS/AUS) in the middle. Both observers categorized the smears, using a set of uniform cytomorphological characteristics, which comprised cellularity, whether the lymphoid population was normal or atypical and malignant, whether or not they contained background inflammatory cells, necrosis, and the presence of granulomatous features.

Interobserver Variability Analysis: The degree of consensus among the various observers was determined by Cohens, kappa (κ), statistical test, which takes into consideration agreement, which can have been done by chance. Kappa values have been interpreted relative to given thresholds: values below 0.20 were taken to indicate poor agreement, 0.21 to 0.40 fair, 0.41 to 0.60

moderate, 0.61 to 0.80 good and 0.81 to 1.00 very good agreement. The kappa values in each of the two diagnostic systems, conventional and Sydney, were individually calculated and allowed to draw a direct comparison on reproducibility.

Statistical Analysis: The data were inserted into Microsoft Excel and processed with the help of the SPSS software (version 20.0). Categorical variables were computed by frequency and percentages. The main outcome of interest was interobserver agreement.

Results

The study involved a sample of 150 cases of lymph node fine needle aspiration cytology (FNAC). Counts of cases were rated under the conventional system and under the Sydney system of reporting and the interobserver agreement as well was compared between the two system. The cases were a range of diagnostic potentials that included an example of benign, atypical, suspicious, and evidence of malignant lesions, all of which have histopathological validations that could be compared.

Table 1: Comparison of FNAC Categorization – Conventional vs Sydney System

Category	Conventional System	No. of Cases (%)	Biopsy-Confirmed Malignant	Sydney System	No. of Cases (%)	Biopsy-Confirmed Malignant
Inadequate / Non-diagnostic	Non-diagnostic	12 (8%)	5	L1: Inadequate / Insufficient	12 (8%)	1
Benign	Benign	85 (56.7%)	5	L2: Benign	78 (52%)	1
Atypical / Indeterminate	–	–	–	L3: Atypical (ALUS/AUS)	15 (10%)	2
Suspicious	Suspicious	23 (15.3%)	4	L4: Suspicious	17 (11.3%)	1
Malignant	Malignant	30 (20%)	20	L5: Malignant	28 (18.7%)	25
Total		150 (100%)	34		150 (100%)	30

When categorized according to the conventional system [Table 1], 12 cases (8%) were reported as non-diagnostic due to inadequate cellularity or obscuring artifacts. Benign lesions formed the largest group with 85 cases (56.7%). A total of 23 cases (15.3%) were considered suspicious, often due to cellular atypia or low cellularity that precluded a definitive diagnosis. Malignant lesions, including both lymphomas and metastatic carcinomas, accounted for 30 cases (20%).

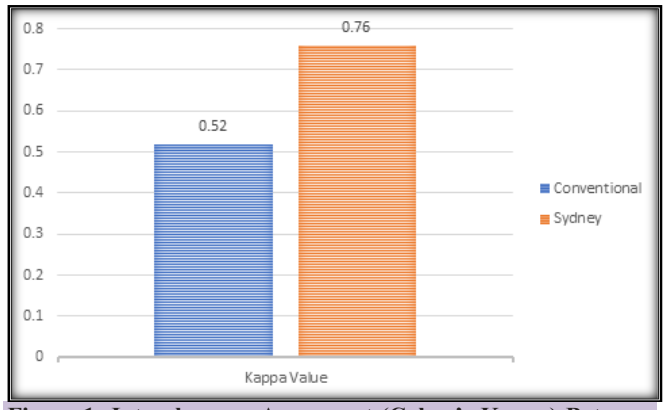

Figure 1: Interobserver Agreement (Cohen's Kappa) Between Reporting Systems

In contrast, when the same cases were evaluated using the Sydney system [Table 1], a more refined distribution was observed. The inadequate category (L1) still included 12 cases (8%), mirroring the conventional system. Benign cases under the Sydney system (L2) totalled 78 cases (52%), a slight reduction compared to the conventional benign category. The atypical category (L3), which is specific to the Sydney system and refers to atypical lymphoid or undetermined significance (ALUS/AUS), accounted for 15 cases (10%). This category helped separate equivocal cases that might have otherwise been grouped under benign or suspicious in conventional reporting. The suspicious category (L4) included 17 cases (11.3%), and the malignant category (L5) included 28 cases (18.7%). When confirmed with histopathology [Table 1], in the Conventional system, 34 of the 150 cases were confirmed as malignant by histopathology, including false negatives from the benign and non-diagnostic categories and in the Sydney system, a total of 30 cases were biopsy-confirmed malignancies. The improved classification helped reduce false positives and false negatives by isolating atypical and suspicious cases into distinct categories.

The key parameter of the study was interobserver agreement among pathologists for both reporting systems, calculated using Cohen's kappa (κ) statistics [Figure-1]. The analysis revealed a kappa value of 0.52 for the conventional system, which is interpreted as moderate agreement. Comparatively, the kappa of the system in Sydney was 0.76, which shows that there was a good level of agreement between observers. Such a high level of reproducibility indicates that the Sydney system with its specific criteria and systematic categories makes it easier to achieve the similarity of diagnosis across various pathologists.

The interobserver agreement difference was marked in the borderline cases i.e. those that were classified as suspicious or atypical. With the traditional system, the diagnostic doubt in such instances usually resulted in inconsistency in reporting. The Sydney system however offered this category a more suitable label L3 category and thus relieving the burden of wanting to label the indeterminate cases benign or malign. On the same note, disagreement was low within L2 and L4 of Sydney system compared to the conventional ones.

All in all, it was not only that the Sydney system offered increased clarity in diagnosis, but also assisted in more reproducible reporting practices with difficult cases. These findings support the use of the Sydney system as a more reliable

alternative to conventional lymph node FNAC reporting, especially in settings where multiple pathologists are involved in diagnostic interpretation.

Discussion

Fine Needle Aspiration Cytology (FNAC) remains a cornerstone technique in the initial evaluation of lymphadenopathy. It is widely appreciated for being minimally invasive, inexpensive, and capable of providing rapid diagnostic information. However, despite its widespread use, FNAC has traditionally lacked a standardised and universally accepted reporting framework, which has been a significant limitation. The absence of such standardisation has contributed to variable interpretations, particularly in borderline or indeterminate cases, thus reducing the reproducibility of reports across observers. This variability in cytological interpretation is not only academically concerning but also has real-world clinical consequences, potentially leading to inconsistent management of patients.[6,7]

This study compared the interobserver variability between the conventional system and the recently proposed Sydney System for lymph node cytology reporting. The findings are very much favorable to the Sydney System that is more dependable, systematic, and replicable. The increase in the interobserver agreement, which was measured by Cohen kappa statistic, was significant. Whereas the traditional system gave a kappa value of 0.52 (moderate agreement) the Sydney System gave a kappa value of 0.76 and this is an indication that there is good agreement among the observers. This goes a long way to indicate that structured reporting leads to minimization of subjectivity and improves consistency among pathologists.

The Sydney System presents five categories of defined diagnostics: L1 (Inefficient), L2 (Benign), L3 (Atypical Cells of Undetermined Significance), L4 (Suspicious), and L5(Malignant). All categories have certain cytomorphological criteria and guidelines of management. Among the additions, the addition of the so-called Atypical category (L3) that enables the borderline cytological features to be viewed with caution without being positioned with certainty either in the benign or malignant domain is one of the main additions. In the traditional order, such incidences would have muddily been termed as suspicious resulting in broad diagnostic gap.[3,4]

The Sydney System in the present research served to minimize misunderstandings in the cases of ambiguity. As an example, when considering the cases which are classified as being atypical (L3), the agreement when compared to similar cases that are suspicious in the traditional system was higher. It can be explained by the fact that there are rather descriptive criteria of each category of Sydney that improves the level of diagnostic accuracy and minimizes the interpretation biases of individuals. But cases with low cellularity, mixed lymphoid populations or minor amounts of atypia that tend to produce discordance in conventional reporting were better managed in the framework of the structured Sydney System. Results are in agreement with the research in the worldwide literature. Vigliar et al. documented an interobserver kappa agreement which was found to be improved after 0.42 in traditional systems to 0.74 in structured systems such as Sydney5. Equally, the Caputo and Gupta et al. studies, demonstrated increased diagnostic confidence and decipherability when the Sydney framework was used particularly in atypical and suspicious categories. These results are in line with the findings of the current study, emphasizing the possibility of the global suitability of the Sydney System.[8]

The other strength of the Sydney System lies in it being consistent with the histopathological results. A correlation coefficient between Sydney System categorisation and histopathology diagnosis in this study took a value of 0.7722, which is normal to imply that the two are strongly related. This supports clinical relevance and predictive accuracy of the Sydney-based FNAC reports, more to the point, it supports its usefulness in the diagnostic workflows of the real world.

Besides, the stratification of Risk of Malignancy (ROM) within the Sydney categories in the present study is well correlated with the previous published records. The L2 (Benign) and L3 (Atypical), L4 (Suspicious), and L5 (Malignant) ROM were 0.9 and 22, 50, and 92.5 respectively. The values are quite similar to results of the studies of Makarenko et al,[9] and Ahuja et al,[10] who determined equally stratified malignancy risks in categories. What is critical to traditional approaches to managing clinical issues is the capability to reliably map FNAC categorisation to the actual potential of a lesion to be malignant, and this research paper confirms that the Sydney System fulfills that imperative.

Although these positive findings were made, one must note that the study has some drawbacks. To begin with, it was a single-centre study that had a fairly small sample size of 150 cases. These findings should be proven by larger, multi-institutional studies to address the issue of the generalizability of the findings. Second, not all atypical or suspicious cases were subject to comparative analysis with confirmation of histopathology, immunohistochemistry and flow cytometry because of resources and this could have possibly affected the ultimate classification of some cases. Nevertheless, the interobserver consistency and the correlation with histopathological findings still give the study results a considerable power.

Also, the successful implementation of the Sydney System is dependent on the presence of sufficient training and familiarity of the pathologists whereas the Sydney System enhances categorisation and reproducibility. The systematic criteria seem at first glance to be prescriptive, yet after experience, they are more permissive than restrictive to subtle interpretation. Thus, the new system, the Sydney System, should be introduced because of specific training sessions and discussions within the departments because it is necessary to guarantee its efficient implementation.[11]

The Sydney System also enhances communication between the cytopathologist and the referral clinician regarding clinical communication. Both categories are associated with the particular recommendations of further management such as clinical follow-up, repeat FNAC, or biopsy which increases the transparency and minimizes the chances of mismanagement. The result of the present study provides strong arguments to implement the use of the Sydney System in lymph node FNAC reporting, therefore, leading to an improved coordination of

care.[12] To conclude, the findings of the current study give a strong argument to employ the use of the Sydney System in the context of lymph node FNAC reporting. It increases interobserver agreement, diagnostic accuracy, is in close agreement with the histopathological results, and leads to more meaningful communication with clinicians.

Conclusion

The paper has shown that Sydney System of lymph node FNAC reporting has substantial benefits compared with the traditional descriptive system, especially in regards to both interobserver agreement and diagnostic consistency. The category based, structure of the Sydney System minimises subjectivity and offers definite interpretation standards, particularly indeterminate or borderline cases. We found that the interobserver concordance was significantly better with the Sydney framework and the values of kappa were increased between moderate and good levels.

Furthermore, introduction of the intermediate atypical classification in the Sydney System offers a much needed diagnostic buffer of the cases, which neither as benign nor overtly malignant, can be interpreted with much caution and closer accuracy. This reduces over-diagnosis and supports better clinical decision-making.

The improved reproducibility, strong correlation with histopathological outcomes, and clearer communication pathways between cytopathologists and clinicians highlight the Sydney System as a valuable advancement in lymph node cytology. While further multicentric studies with larger cohorts are recommended to validate these findings, our results strongly support the integration of the Sydney System into routine cytopathological practice for lymph node aspirates. Its implementation can enhance diagnostic reliability and optimize patient management across varied clinical settings.

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Conflicts of interest

There are no conflicts of interest.

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