Original Article

Standardizing Cytological Reporting: The WHO Reporting System of Lymph Node Cytology and its Impact on Clinical Practice

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Abstract

Background: Lymphadenopathy commonly results from benign conditions such as reactive hyperplasia or lymphadenitis. Fine needle aspiration cytology (FNAC) is widely used for initial evaluation due to its speed, affordability, and diagnostic utility. To improve consistency, the World Health Organization (WHO) and International Academy of Cytology developed a standardized reporting system for lymph node cytology. In this study, we aim to classify the findings of lymph node cytopathology as per the WHO system and assess the Risk of Malignancy through histopathological correlation.
Methods: A retrospective study of 240 cases was conducted at SMCH over one year (July 2023–July 2024). Cases with available histopathology or follow-up data were included. ROM was calculated by correlating cytological diagnoses with final outcomes.
Results: Cervical lymphadenopathy was most frequent (82%), with a slight male predominance. Benign lesions comprised 71.25% of cases, mostly reactive lymphadenitis (76%). Malignant cases (17.91%) were predominantly metastatic squamous cell carcinoma (77%). ROM was highest in the suspicious and malignant categories (100%) and lowest in the benign group (2.34%).
Conclusion: The WHO Reporting System for Lymph node Cytopathology provided a clear, reproducible framework that improved diagnostic accuracy in our study. High Risk of Malignancy in atypical, suspicious, and malignant categories aligns with previous research, confirming the system's reliability. Low Risk in benign and inadequate categories emphasizes cautious interpretation and follow-up. This standardized approach enhances communication between cytopathologists and clinicians, improving patient management.

Keywords: lymphadenopathy; FNAC; WHO; reactive lymphadenitis; metastatic squamous cell carcinoma; Risk of Malignancy

Introduction

Lymphadenopathy refers to the abnormal enlargement, consistency, or number of lymph nodes, and it is a common clinical finding across various age groups and clinical settings [1]. Lymph nodes, as integral components of the immune system, respond to a wide range of stimuli, including infections, autoimmune diseases, malignancies, and drug reactions. Therefore, lymphadenopathy can be either a localized or generalized response to a variety of underlying conditions [2].

In clinical practice, the most frequently encountered cause of lymphadenopathy is reactive hyperplasia secondary to infections, particularly of the upper respiratory tract [3]. However, persistent or unexplained lymphadenopathy raises concerns about more serious etiologies such as lymphomas, leukemias, or metastatic malignancies [4]. The location, duration, and associated symptoms—such as fever, weight loss, or night sweats—are important parameters in narrowing the differential diagnosis.

A study by Ferrer et al. emphasized that cervical lymphadenopathy is the most common form encountered in primary care, and while it is usually benign, persistent or hard nodes warrant further evaluation [5]. In children, most lymphadenopathy is self-limiting and benign, whereas in adults, especially when generalized, it may reflect a systemic disease process such as HIV, tuberculosis, or malignancy [6].

Fine Needle Aspiration Cytology (FNAC) is a well-established, minimally invasive diagnostic technique for evaluating lymphadenopathy. It is particularly useful in distinguishing between reactive, infectious, and neoplastic causes of lymph node enlargement, making it an indispensable tool in clinical practice [7]. Numerous studies have confirmed FNAC's high diagnostic accuracy. Haque et al. reported a sensitivity of 88% and specificity of 96% for diagnosing malignant lymphadenopathy through FNAC [8]. It has proven particularly effective in detecting metastatic deposits and granulomatous inflammation, while being more limited in the subtyping of lymphomas, which may require histopathology and ancillary techniques, such as flow cytometry or immunohistochemistry [9].

The World Health Organization (WHO) introduced a standardized reporting system for lymph node cytopathology to improve diagnostic clarity, reproducibility, and communication among clinicians and pathologists. This system was published in The WHO System for Reporting Lymph Node Cytopathology, released in 2022, and provides a tiered framework for categorizing cytological findings based on risk stratification and clinical correlation [10].

The WHO Reporting System for Cytology of Lymph Nodes has created five categories using ancillary studies including clinical, radiological, and important cytopathological aspects: Inadequate/Insufficient, Benign, Atypical, Suspicious for Malignancy, and Malignant.

Each category carries an estimated risk of malignancy (ROM), which guides further diagnostic or therapeutic interventions. For instance, benign categories (e.g., reactive lymphoid hyperplasia) typically have a low ROM (<10%), while malignant categories (e.g., metastatic carcinoma, lymphoma) approach nearly 100% ROM [10, 11].

The WHO reporting system for lymph node cytology is a significant advancement aimed at standardizing cytopathological diagnoses, facilitating clinical decision-making, and improving patient outcomes in the evaluation of lymphadenopathy.

Materials and Methods

Aims and objective: To classify the findings of lymph node cytopathology as per the WHO system and assess the Risk of Malignancy through histopathological correlation.

Study design: The study was cross-sectional and retrospective in design, and information regarding pathological records and demographic and clinical details were retrieved from the electronic databases in the Department of Pathology at SMCH. A prior ethical clearance was taken from the Institutional Ethical Committee.

Study Period: Patients who underwent lymph node FNAC in the period from July 2023 to July 2024 were studied.

Inclusion criteria: All cases of lymphadenopathy undergoing FNAC during the study period for which subsequent histopathological reports or clinical follow up data were available.

Exclusion criteria: Cases without corresponding histopathological correlation or loss to follow up cases for subsequent clinical data were excluded from the study.

Cytological samples: A total of 240 samples were collected for the study which has either histopathological correlation or clinical follow up data. In all lymphadenopathy cases FNAC was performed by cytopathologist and under ultrasound guidance as and when needed. A 23G needle was used to conduct the procedure and direct smear was prepared from the first pass. In case of scant material yielding, a 2nd pass was performed. The smear was stained using May Grunwald and Giemsa stain. The cytopatholgical data of each lymphadenopathy case were collected. To assess the risk of malignancy of each category histopathological diagnosis data were retrieved and correlated, and in cases where biopsy was not performed, clinical follow up data was correlated.

Statistical analysis: All datas were collected, integrated and analyzed statistically utilizing chi-square testing. P-values were deemed statistically significant if they were less than 0.05. Graphs, tables, and other data were generated using Microsoft Office Word and Excel.

Diagnostic criteria

With the application of adequate blinding, the cytological slides were re-evaluated and classified into one of the following categories: Insufficient/Inadequate/Nondiagnostic; benign; atypical; suspicious for malignancy; malignant [10]. The diagnostic feature of each category is given in Table 1.

Results

Among the 240 lymphadenopathy cases analyzed, cervical lymphadenopathy was the most common, observed in 82% of patients. Axillary and inguinal lymphadenopathy were significantly less frequent, accounting for 11% and 7% of cases, respectively. This distribution was found to be statistically significant (Chi-square ≈ 92.82, $p < 0.0001$), emphasizing a

strong predominance of cervical node involvement, which may reflect the higher frequency of infectious, inflammatory, or neoplastic conditions affecting the head and neck region. The age-wise distribution revealed the highest number of cases in the 11–20 year age group (22.1%), followed closely by the 0–10 year group (20%), indicating that children and adolescents are the most commonly affected populations. Adult cases gradually declined with increasing age, although a secondary rise was noted in individuals above 60 years (13.8%). Gender distribution showed a slight male predominance, with 54.6% of cases being male and 45.4% female, yielding a male-to-female ratio of 1.2:1.

Cytological examination based on WHO classification, demonstrated that the majority of cases (71.25%) were benign, with non-specific reactive lymphadenitis comprising 76% of those, suggesting that most lymph node enlargements were reactive in nature. Granulomatous lymphadenitis accounted for 22% of benign cases, indicative of conditions such as tuberculosis or sarcoidosis. Malignant lesions were diagnosed in 17.91% of total cases, with metastatic squamous cell carcinoma (SCC) being the predominant subtype, found in 77% of all malignant cases. Less common malignancies included adenocarcinomas, lymphomas, and other undifferentiated tumors (23%). The distribution of diagnostic categories showed a statistically significant pattern (Chi-square ≈ 303.62, $p < 0.0001$), reinforcing the accuracy of cytological evaluation.

Analysis of the risk of malignancy (ROM) across categories revealed 100% ROM in both malignant and suspicious-for-malignancy cases. Atypical cases carried a high ROM of 66.67%, necessitating further diagnostic intervention. Interestingly, even inadequate (non-diagnostic) samples showed an 18% ROM, underscoring the importance of repeat sampling in such cases. Benign cases had a ROM of 2.34%, pointing to the occasional possibility of false-negative cytology.

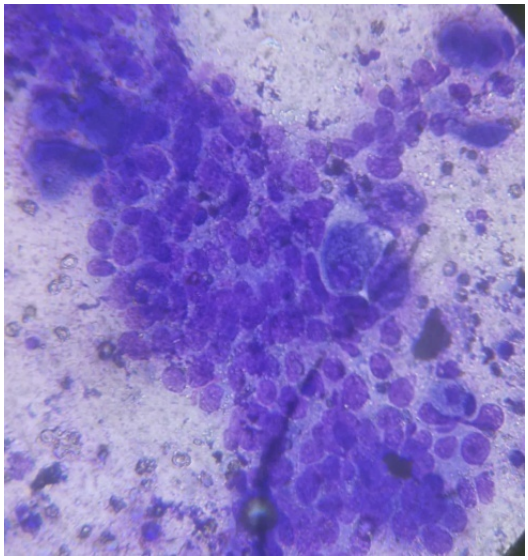

Figure 1: Photomicrograph of benign category lymphadenopathy. Non specific reactive lymphadenitis showing a polymorphic lymphoid population(left, MGG stained) and granulomatous lymphadenitis(right, MGG stained) at 40x.

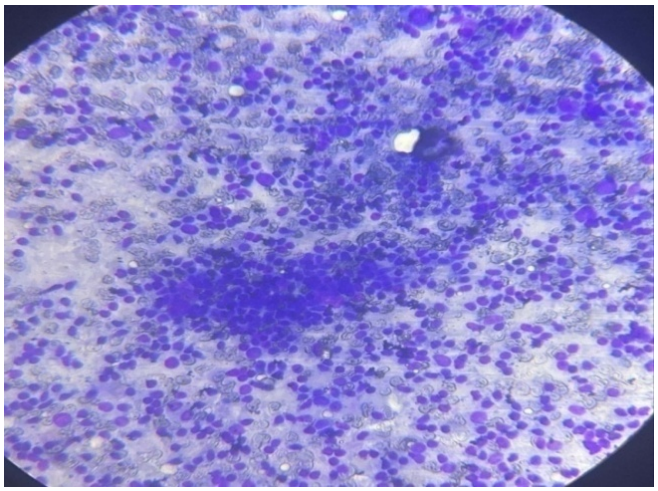

Figure 2: Photomicrograph of MGG stained smear of Metastatic SCC at 10x and 40x showing malignant squamous cells in clusters and scattered singly.

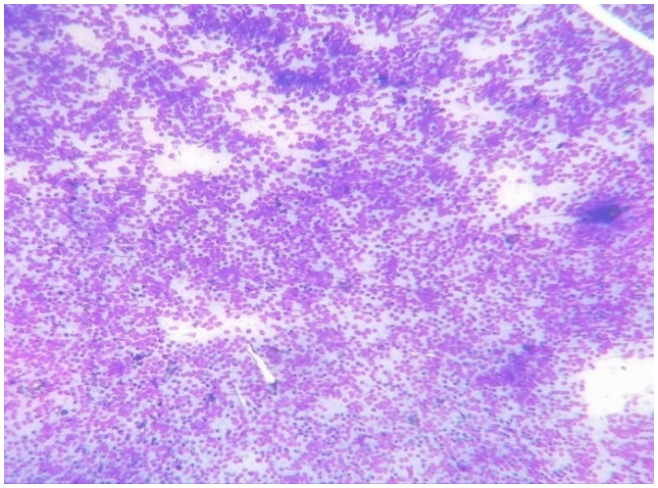

Figure 3: Photomicrograph of Hodgkins lymphoma (on the right, MGG stained at 40x) showing Reed Sternberg cells.

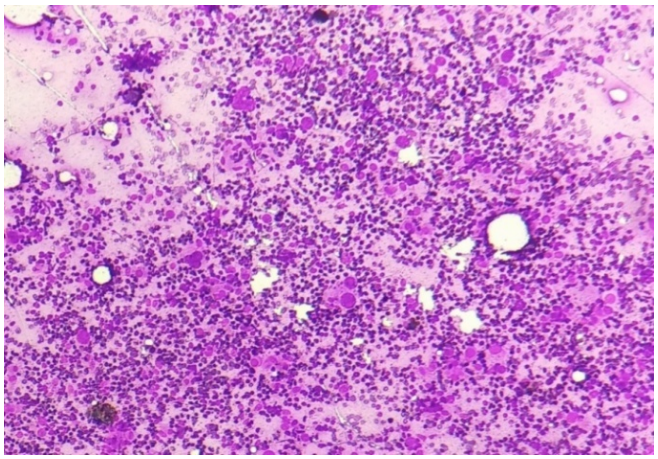

Figure 4: Photomicrograph of Non-Hodgins lymphoma (MGG stained,10x) showing high cellularity and monomorphic population of atypical lymphoid cells.

Table 1: Diagnostic criteria of each category of the WHO reporting system for lymph node cytology [10]

Category	Criteria for Diagnosis
Insufficient/Inadequate/Nondiagnostic	”No material for assessment. Technical problems, which prevent assessment and diagnosis of the material on the slides”
Benign	Inflammatory/Infectious processes:-Acute inflammation; Granulomatous inflammation; Benign reactive lymphadenopathy.
Atypical	”Scant or poorly prepared cellular material demonstrates predominantly benign cytological features, while a few cells may show minimal features of atypia, raising the possibility of a malignant lesion”
Suspicious for Malignancy	Some cytopathological features suggestive of malignancy but with insufficient features either in quantity or quality to make an unequivocal diagnosis of malignancy
Malignancy	Unequivocal cytopathological features of malignancy

Discussion

The implementation of the WHO Reporting System for Lymph node Cytopathology has introduced a standardized, tiered framework aimed at improving diagnostic precision, interobserver consistency, and communication between pathologists and clinicians. Our study demonstrates the practical utility and diagnostic accuracy of this system when applied to lymph node FNAC cases in a tertiary care setting.

In this study, the majority of lymphadenopathy cases were found in the cervical region (82%), which aligns with the findings

Table 2: Distribution of cases in each category as per WHO reporting system for lymph node cytology

Category	
Insufficient/Inadequate/Nondiagnostic	11 (4.58%)
Benign	171 (71.25%)
Atypical	12 (5%)
Suspicious for Malignancy	03 (1.25%)
Malignant	43 (17.91%)

Table 3: Distribution of benign and malignant cases

Category	**Diagnosis**	**Percentage Distribution**
Benign (171 Cases)	Non specific reactive lympadenitis	76% (130)
	Granulomatous lymphadenitis	22% (38)
	Others	2% (3)
Malignant (43 Cases)	Metastatic SCC	77% (33)
	Others	23% (10)

Table 4: Risk of Malignancy

Category (Total cases)	**Malignant Cases/ Total Cases**	**Risk of Malignancy (ROM)**
Inadequate	02/11	18%
Benign	04/171	2.34%
Atypical	08/12	66.67%
Suspicious for Malignancy	03/03	100%
Malignant	43/43	100%

by Ferrer et al., who observed cervical lymphadenopathy as the most frequent clinical presentation, often associated with benign and self limiting etiologies in both pediatric and adult populations [12]. The male predominance (M:F ratio 1.2:1) observed in our cohort is also consistent with previous literature, reporting a slight male preponderance in lymphadenopathy presentations due to occuapational exposures and behavioural risk factor [13].

Applying the WHO classification, most cytology cases (71.25%) were categorized as benign. Among these, nonspecific reactive lymphadenitis was the predominant subtype (76%), followed by granulomatous inflammation (22%). This distribution is comparable to previous studies by Haque et al. and others, which have shown reactive processes as the leading cause of lymphadenopathy in low to middle income settings [14, 15].

The malignant category comprised 17.91% of the total cases, with metastatic squamous cell carcinoma (SCC) accounting for the majority (77%) of these cases. These findings support the results of studies such as those by Sharma et al., who reported SCC as the most common metastatic malignancy found in lymph node aspirates, especially in regions with high prevalence of head and neck cancers [16]. The high proportions of metastatic SCC highlights the diagnostic value of FNAC in detecting secondary malignancies, particularly in patients with known or suspected primary epithelial cancers.

The Risk of Malignancy (ROM) observed in our study, showed a clear stepwise increase across WHO categories, with benign cases showing a ROM of 2.34%, atypical cases 66.67%, and suspicious and malignant categories 100% each. The inadequate category, though not diagnostic, still had an 18% ROM. 2 cases out of 11 cases in the inadequate category, were found malignant in the final histopathological diagnosis. Both were cases of metastasis, and the result was due to inadequate targeting of representative site and lack of cellular material in the cytological smears, owing to the presence of cystic components in these cases, reinforcing further clinical work-up in such cases. When compared to prior studies Caputo et al. reported a ROM of 9.38% in benign cases, which is higher than the 2.34% seen in our study [17]. Gupta et al. reported a ROM of 11.5% in benign cases and 27.5% for inadequate samples, slightly higher than our findings, reflecting possible differences in case selection and cytological thresholds [18]. Vigliar et al. observed a benign ROM of 1.92% and inadequate ROM of 50%, indicating variability in sample quality and interpretation across settings [19]. For the atypical category, our ROM of 66.67% was closely consistent with findings by Gupta et al. (66.7%) and slightly higher than Caputo et al. (28.6%) and Vigliar et al. (58.3%) [17, 18, 19]. These results validate the role of the atypical category as a high risk group requiring further diagnostic evaluation, including histopathology or advanced immunophenotyping. The suspicious for malignancy and malignant categories showed a ROM of 100% in our study, fully aligning with Caputo et al., Vigliar et al., and closely with Gupta et al. (88% ROM in suspicious category and 99.6% in malignant category), confirming the high predictive value of these cytological diagnoses [17, 18, 19].

Limitations: Limitations of this study include its potential referral bias and the absence of ancillary tests such as immunohistochemistry of flow cytometry, which are particularly useful in subtyping lymphomas.

Conclusion

The application of the WHO Reporting System for Lymph Node Cytopathology in our study demonstrated its effectiveness in providing a structured, reproducible, and clinically meaningful framework for diagnosing lymphadenopathy. The clear stratification of categories based on risk of malignancy (ROM), enhances diagnostic accuracy and aids in clinical decision making. Our findings, particularly the high ROM in the atypical, suspicious, and malignant categories, are in strong agreement with the previously published studies, reinforcing the validity and reliability of the WHO system.

The low ROM in benign and inadequate categories, underscores the need for cautious interpretation and clinical follow-up, especially in non-diagnostic cases. Integration of this standardized reporting approach can significantly improve diagnostic communication between cytopathologists and clinicians, ultimately leading to better patient management and outcomes.

Future directives: Future directions for the WHO system of lymph node cytopathology, include doing more prospective multicentric studies across different regions and health care settings, with more focus on the Atypical and Suspicious for malignancy categories, to establish uniform risk of malignancy (ROM) for each WHO category. Ancillary techniques, training modules can improve accuracy and consistency, whereas outcome-based studies, and regular evidence based updates will keep the system relevant for clinical practice.

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