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# Evaluation of Lymphoproliferative Disorders in Core Needle Biopsy (CNB) Samples and its Diagnostic Pitfalls: An Observational Study at A Tertiary Level Hospital in Bangladesh

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***Abstract***

***Introduction:*** *Lymphoproliferative disorders (LPDs) are a diverse group of conditions that arise from the abnormal proliferation of lymphoid cells. Core Needle Biopsy (CNB) is a minimally invasive procedure that has been widely used for the diagnosis of LPDs due to its accuracy and reliability. However, the histological interpretation of CNB samples can be challenging and may result in diagnostic pitfalls, which can have serious clinical consequences. To evaluate the usefulness of CNB in the diagnosis of LPDs and to identify potential diagnostic pitfalls, the present study was conducted at a tertiary-level hospital in Bangladesh.*

***Methods:*** *This observational prospective study was conducted at the Department of Histopathology, Armed Forces Institute of Pathology, Dhaka, Bangladesh during a 1-year period, with a total of 180 core biopsy specimens collected from both male and female populations following the inclusion and exclusion criteria.*

***Result:*** *Non-Hodgkin Lymphoma (NHL) accounted for 61.11% of cases, followed by Hodgkin lymphoma at 14.44%, granulomatous inflammation at 12.22%, metastatic carcinoma at 5.56%, and reactive hyperplasia at 6.67%. Lymph nodes were the most commonly affected site (53.85%), followed by the palatine tonsils (11.54%) and mediastinum (19.23%). DLBCL was the most common type of NHL (32.73%), followed by Peripheral T Cell Lymphoma (10.91%). Other types of NHL observed included Follicular Lymphoma, Mantle Cell Lymphoma, Burkitt Lymphoma, and several others. Frequencies ranged from 1 to 10 cases.*

***Conclusion:*** *The results show that CNB is a useful tool for the diagnosis of lymphoproliferative disorders, with non-Hodgkin lymphoma being the most commonly diagnosed entity. The study's identification of potential diagnostic pitfalls highlights the importance of careful evaluation of clinical and histopathological features to avoid misdiagnosis. The study's findings can be used to improve the accuracy of lymphoma diagnosis and ultimately improve patient care.*

***Keywords:*** *Biopsy, Lymphoproliferative, Pitfall, Core Needle Biopsy (CNB)*

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## I. INTRODUCTION

Lymphoma is a malignant neoplastic disorder that arises from the clonal expansion of lymphoid cells, including B cells, T cells, and natural killer cells.(1,2) The evaluation of primary lymphoid disorders has been revolutionized by the increasing use of core needle biopsies (CNB).(3–5) However, this approach puts significant pressure on pathologists to render a diagnosis based on limited tissue samples. The exact categorization and diagnosis of lymphoma pose a significant challenge for pathologists, with excisional biopsy being considered the gold standard procedure for diagnosis and classification of lymphoma.(6,7) The role of core needle biopsy in the diagnosis of lymphoma has been controversial, but it has become a popular intervention method for diagnosing lymphoma.(8,9) Core biopsies are typically performed by interventional radiologists or pathologists. Several studies have demonstrated a high diagnostic accuracy of core needle biopsies (CNB); however, it was still not

comparable to that of excisional biopsies.(10,11) Moreover, core biopsies from both superficial and deep-seated lesions are less traumatic, more cost-effective, and well-tolerated by patients. Lymphomas are a diverse group of cancers that require careful evaluation and accurate diagnosis. This typically involves examining the lymph node architecture, including the pattern of lymphocyte proliferation and the presence of abnormal cells, such as Reed Sternberg cells.(12,13) The neoplastic proliferation may be located within follicles, interfollicular areas, mantle, or marginal zones. As core biopsy samples are thin cores of tissue, about 0.1-1.5 cm in length, it is difficult to ascertain a diagnosis based solely on morphology of lymphoid tissue under light microscopy by conventional H&E or Pap stain.(14) To aid in the diagnosis and subtyping of lymphomas, immunohistochemistry plays a crucial role.(15) It has therapeutic and prognostic implications, and its use in clinical practice is well-established. The panel of immunological markers used for the subtyping of lymphomas includes CD45, B cell markers (CD19, CD20, CD79a, MUM1), T cell markers (CD3, CD5, CD7), follicular dendritic cell markers CD23, follicular lymphoma BCL2, anaplastic lymphoma kinase (ALK), proliferative index ki67, R-S cell markers (CD15, CD30, Pax5, LMP1) and others (15). The most important aspect is the type of positivity (membranous, cytoplasmic or nuclear) and the percentage of positive cells required in accurate categorization and distinguishing from reactive processes. The objectives of this study were to determine the common categorization of lymphoma using immunohistochemistry in small core biopsies from different age groups of the population and to identify the diagnostic difficulties and pitfalls of using core biopsy samples for lymphoma diagnosis (16). The study's findings may have important implications for improving the accuracy and reliability of lymphoma diagnosis and classification, particularly in settings where excisional biopsy is not feasible.

## II. METHODS

This observational prospective study was conducted at the Department of Histopathology, Armed Forces Institute of Pathology, Dhaka, Bangladesh. The study duration was one year, from March 2021 to March 2022. During this period, a total of 180 core biopsy specimen were received, after obtaining clinical information like age, sex, site of biopsy etc., which were subjected to tissue processing according to the standard tissue processing protocol. All cases of clinically suspicious lymphoma and through cytological screening were included into the study. However, all known cases which were undergoing treatment and badly preserved specimens were excluded from the study. Informed consent was obtained from the participants or their legal guardians prior to data collection, and ethical approval for this study was also obtained from the ethical review committee of the study hospital. Concordance rate was 100% between light microscopy and IHC studies. The panel of immunological markers that was used for subtyping the lymphomas included CD45, B cell markers (CD19, CD20, CD79a, MUM1), T cell markers (CD3, CD5, CD7), Follicular dendritic cell markers CD23, Follicular lymphoma BCL2, anaplastic lymphoma kinase (ALK), proliferative index ki67, R-S cell markers (CD15, CD30, Pax5, LMP1), among others. Inaccurate categorization and distinguishing from reactive processes were prevented by considering the type of positivity (membranous, cytoplasmic or nuclear) and the percentage of positive cells. All data were analyzed in Microsoft excel sheets and statistical analysis was done by SPSS V.25.

## III. RESULTS

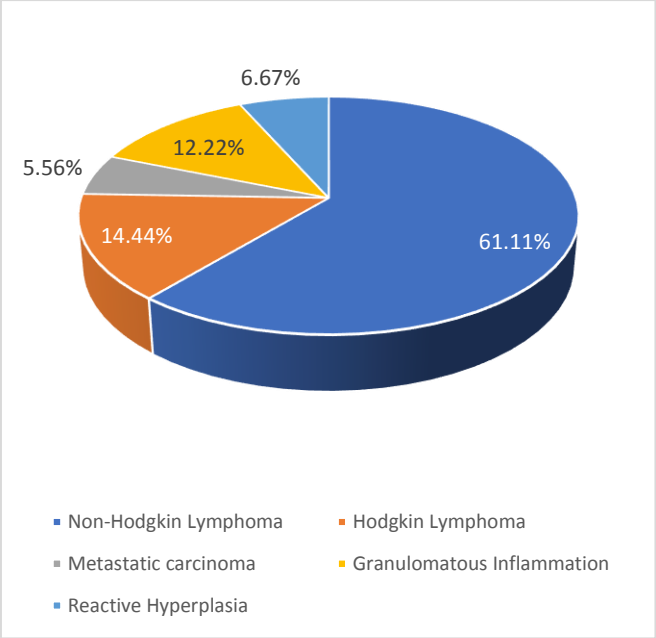


**Figure 1:** Distribution of participants by diagnosis of core biopsy sample

Non-Hodgkin lymphoma was the most common diagnosis, accounting for 61.11% of all cases, followed by Hodgkin lymphoma at 14.44%, granulomatous inflammation at 12.22%, metastatic carcinoma at 5.56%, and reactive hyperplasia at 6.67%.

**Table 1:** Distribution of Hodgkin Lymphoma patients by Site (n=26)

| Site | Frequency | Percentage |
|---|---|---|
| Lymph node | 14 | 53.85% |
| Palatine tonsils | 3 | 11.54% |
| Mediastinum | 5 | 19.23% |
| Lung | 2 | 7.69% |
| Soft tissue | 2 | 7.69% |

The most common site of involvement was lymph nodes, with a frequency of 14 patients (53.85%). The palatine tonsils were affected in 3 patients (11.54%), and the mediastinum was involved in 5 patients (19.23%). Two patients (7.69%) had HL involving both soft tissue and lung.

**Table 2:** Distribution of Non-Hodgkin Lymphoma patients by Site (n=110)

| Site | Frequency | Percentage |
|---|---|---|
| Lymph node | 70 | 63.64% |
| Colon | 6 | 5.45% |
| Soft tissue mass | 4 | 3.64% |
| Tonsil | 3 | 2.73% |
| Sino nasal | 4 | 3.64% |
| Mediastinum | 4 | 3.64% |
| Oral cavity | 2 | 1.82% |
| Duodenum | 1 | 0.91% |

| | | |
|---|---|---|
| Jejunum | 1 | 0.91% |
| Brain | 3 | 2.73% |
| Tounge | 2 | 1.82% |
| Ovary | 1 | 0.91% |
| Testis | 2 | 1.82% |
| Eye | 1 | 0.91% |
| Skin | 2 | 1.82% |
| Lung | 2 | 1.82% |
| Soft tissue | 2 | 1.82% |

The majority of patients (63.64%) had lymph node involvement, followed by colon (5.45%), soft tissue mass (3.64%), tonsil (2.73%), and sinonasal (3.64%) involvement. Other less commonly involved sites included the mediastinum (3.64%), oral cavity (1.82%), duodenum (0.91%), jejunum (0.91%), brain (2.73%), tongue (1.82%), ovary (0.91%), testis (1.82%), eye (0.91%), skin (1.82%), lung (1.82%), and soft tissue (1.82%).

**Table 3:** Distribution of Non-Hodgkin Lymphoma patients by Pattern (n=110)

| Type of NHL | Frequency | Percentage |
|---|---|---|
| DLBCL | 36 | 32.73% |
| Follicular lymphoma | 10 | 9.09% |
| Mantle cell lymphoma | 8 | 7.27% |
| Burkitt Lymphoma | 6 | 5.45% |
| Extra nodal marginal zone lymphoma | 5 | 4.55% |
| Peripheral T cell lymphoma | 12 | 10.91% |
| Angioimmunoblastic lymphoma | 6 | 5.45% |
| Small cell lymphoma | 6 | 5.45% |
| Enteropathy associated T cell lymphoma | 2 | 1.82% |
| Primary Mediastinal B cell lymphoma | 2 | 1.82% |
| Anaplastic T cell lymphoma-ALK positive | 3 | 2.73% |
| Anaplastic T cell lymphoma-ALK Negative | 2 | 1.82% |
| Extra nodal NK/T cell lymphoma | 2 | 1.82% |
| Primary cutaneous T cell lymphoma | 2 | 1.82% |
| Lymphoblastic lymphoma | 5 | 4.55% |
| Lymphoplasmacytic lymphoma | 2 | 1.82% |
| T cell rich B cell lymphoma | 1 | 0.91% |

The most common type of NHL observed was Diffuse Large B-Cell Lymphoma (DLBCL) with a frequency of 36, accounting for 32.73% of the cases. The second most common type of NHL observed was Peripheral T Cell Lymphoma with a frequency of 12, accounting for 10.91% of the cases. Other types of NHL observed in the study were Follicular Lymphoma, Mantle Cell Lymphoma, Burkitt Lymphoma, Extra Nodal Marginal Zone Lymphoma, Angioimmunoblastic Lymphoma, Small Cell Lymphoma, Enteropathy Associated T Cell Lymphoma, Primary Mediastinal B Cell Lymphoma, Anaplastic T Cell Lymphoma-ALK Positive, Anaplastic T Cell Lymphoma-ALK Negative, Extra Nodal NK/T Cell Lymphoma, Primary Cutaneous T Cell Lymphoma, Lymphoblastic Lymphoma, Lymphoplasmacytic Lymphoma, and T Cell Rich B Cell Lymphoma, with frequencies ranging from 1 to 10 cases.

**Table 4:** Immunohistochemical profile of non-Hodgkin lymphoma

| Subtype of NHL | Positive markers | Negative markers |
|---|---|---|
| DLBCL | CD20, CD79a, CD10, BCL-6, MUM-1, High Ki67 | CD3, CD5, CyclinD1 |
| Follicular lymphoma | CD20, CD79a, CD10, Bcl-2 &Bcl6 | CD3, CD5, CD43, CyclinD1 |

| | | |
|---|---|---|
| Burkitt lymphoma | CD19, CD20, PAX5, CMYC, high KI67 | CD3, CD5, BCL2, Tdt |
| Mantle cell lymphoma | CD19, CD20, CYCLIN D1, CD5, SOX11 | CD10, BCL2, BCL6 |
| Marginal zone lymphoma | CD19, CD20, CD79a, CD43 | CD5, CD10, CyclinD1, Sox11 |
| Small cell lymphoma | CD5, CD79a, CD23, CD43 | CD10, BCL6, SOX11, Cyclin D1 |
| T cell rich B cell lymphoma | CD20, CD79a, PAX5, CD10, CD3, CD5 | CD15, CD30, CD23 |
| Peripheral T Cell lymphoma | CD2, CD3, CD5, CD4/CD8 | CD20, CD79a, PAX5 |
| Angioimmunoblastic T cell lymphoma | CD3, CD4, CD7, CXCL13, CD10 | CD7/CD8, CD20, PAX5, CD79a |
| Anaplastic T cell lymphoma | CD30, EMA, ALK, CD2, CD4, CD5, GranzymeB, CD25 | CD15, CD20, PAX5, CD79a |
| Mycosis fungoides | CD2, CD3, CD5, CD7 | CD7/CD8 loss |

The table represents the various subtypes of NHL in the first column of the table, and the positive and negative markers are listed in the second and third columns, respectively.

**DIAGNOSTIC PITFALLS OF CORE NEEDLE BIOPSY**

Core needle biopsy is a minimally invasive diagnostic procedure used to obtain tissue samples from suspicious areas in the body for further examination.(16) However, despite its high diagnostic accuracy, there are potential pitfalls associated with this procedure that can affect its reliability.

- One potential pitfall is the sampling error, which occurs when the biopsy needle misses the target tissue or fails to obtain enough tissue for an accurate diagnosis.(17,18) Sampling error can be minimized by performing multiple biopsies from different angles or using imaging guidance to ensure precise needle placement.(19)
- Another pitfall is the interpretation error, which can occur due to a variety of factors such as inadequate sampling, poor tissue preservation, or inexperienced pathologists.(17) It is essential to have experienced pathologists to interpret the biopsy results accurately.
- In some cases, the biopsy results may be inconclusive, leading to a diagnostic dilemma for the clinician. This may be due to the nature of the lesion, inadequate sampling, or technical issues during the biopsy procedure.(20,21) In such situations, repeat biopsy or alternative diagnostic tests may be necessary.
- Lastly, there is a risk of complications associated with the biopsy procedure, such as bleeding, infection, or damage to adjacent organs or structures.(22,23) Although these complications are rare, it is essential to consider them when deciding on the best diagnostic approach.

Overall, while core needle biopsy is a valuable diagnostic tool with high accuracy, potential pitfalls should be considered to ensure reliable results. Close communication between the clinician and pathologist is also crucial to address any diagnostic dilemmas and ensure accurate interpretation of the biopsy results.

## IV. DISCUSSION

The present study aimed to evaluate lymphoproliferative disorders in core needle biopsy (CNB) samples and identify potential diagnostic pitfalls. The results of the study showed that non-Hodgkin lymphoma was the most common diagnosis, accounting for 61.11% of all cases, followed by Hodgkin lymphoma at 14.44%, granulomatous inflammation at 12.22%, metastatic carcinoma at 5.56%, and reactive hyperplasia at 6.67%. This was similar to other global findings which observed a higher incidence of NHL's compared to other disorders of lymphoproliferative nature.(24,25) NHL is globally recognized as the most common hematological disorder, and is responsible for approximately 3% of global cancer mortality rate. The study also observed that the majority of patients with non-Hodgkin lymphoma had lymph node involvement (63.64%), followed by colon, soft tissue mass, tonsil, and sino-nasal involvement. Diffuse Large B-Cell Lymphoma (DLBCL) was found to be the most common type of NHL observed, accounting for 32.73% of the cases. Peripheral T Cell Lymphoma was the second most common type of NHL, accounting for 10.91% of cases. The high prevalence of DLBCL w2as similar to the finding of another previous study.(26) The study's findings have brought to light the significance of Core Needle Biopsy (CNB) in diagnosing lymphoproliferative disorders, where NHL is the most commonly diagnosed type. Nevertheless, the study has also shown that other types of NHL are not frequently observed, indicating the importance of considering a broader range of lymphoma subtypes when making a diagnosis. Furthermore, the study has identified potential diagnostic pitfalls such as granulomatous inflammation, metastatic carcinoma, and reactive hyperplasia, which can mimic lymphoma histologically, and can lead to inappropriate management if misdiagnosed.(27,28) Therefore, clinicians should exercise caution and carry out a thorough evaluation of clinical

and histopathological features to avoid misdiagnosis. The study's findings can provide valuable insights for clinicians and help them avoid diagnostic pitfalls while diagnosing lymphoproliferative disorders.

*Limitations of The Study*

One limitation of the study was its small sample size. A larger sample size would increase the study's power and generalizability of the results. Another limitation was the lack of long-term follow-up data, which would provide valuable information on the clinical course and treatment response of the diagnosed patients.

## V. CONCLUSION

In conclusion, this study provides valuable insights into the utility of Core Needle Biopsy in the diagnosis of lymphoproliferative disorders, with non-Hodgkin lymphoma being the most commonly diagnosed entity. The study's findings also emphasize the importance of considering a broad range of lymphoma subtypes when making a diagnosis, as well as the potential diagnostic pitfalls that can occur. Clinicians should carefully evaluate all clinical and histopathological features to ensure an accurate diagnosis and appropriate management. The study's findings can be used to improve the accuracy of lymphoma diagnosis and ultimately improve patient care.

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***Conflict of interest:*** None declared

***Ethical approval:*** The study was approved by the Institutional Ethics Committee

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