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Pathology

Validity of Cell Block Histopathology and Fine Needle Aspiration Cytology in the Diagnosis of Lymphoma

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Abstract **Original Research Article**

Introduction: Lymphoma, a type of cancer affecting the lymphatic system, requires accurate diagnostic methods for effective treatment. This study aimed to evaluate the validity of Cell Block Histopathology and Fine Needle Aspiration Cytology (FNAC) in the diagnosis of lymphoma. ***Methods:*** A total of 30 patients with clinically suspected lymphoproliferative disorder were included in the study. Both Cell Block Histopathology and FNAC were used to diagnose lymphoma in these patients. The results were then compared with the final diagnosis based on histopathology, immunochemistry, and clinical follow-up, which was considered the gold standard. ***Result:*** The study included 30 patients with clinically suspected lymphoproliferative disorder. The Cell Block Histopathology method diagnosed 12 patients (40%) as lymphoma positive, 11 patients (36.67%) as lymphoma negative, and 7 cases (23.33%) were inconclusive. The Fine Needle Aspiration Cytology (FNAC) method diagnosed 13 patients (43.33%) as lymphoma positive, 12 patients (40%) as lymphoma negative, and 5 cases (16.67%) were inconclusive.When compared with the final diagnosis based on histopathology, immunochemistry, and clinical follow-up, the sensitivity, specificity, and accuracy of Cell Block Histopathology were 91.67%, 90.91%, and 93.33% respectively. The positive predictive value (PPV) and negative predictive value (NPV) were both 91.67%. The FNAC method demonstrated a sensitivity, specificity, and accuracy of 92.31%, 91.67%, and 93.33% respectively. The PPV and NPV were 92.31% and 91.67% respectively. ***Conclusion:*** This study concludes that both Cell Block Histopathology and FNAC are valid and effective diagnostic tools for lymphoma. They can be used independently or in conjunction with one another to enhance diagnostic accuracy. The findings contribute to the growing body of evidence supporting the use of these methods in lymphoma diagnosis.

Keywords: Lymphoma, Cytology, Histopathology, Diagnosis, Cell Block Histopathology, Fine Needle Aspiration Cytology.

INTRODUCTION

Lymphoma, a type of lymphoreticular system. Cancer, is a significant global health concern. Originating in the lymphatic system, an integral part of the body's immune system, lymphoma has a profound impact on both the physical health and quality of life of patients [1]. According to global statistics, lymphoma accounts for approximately 3.2% of all new cancer cases, with an estimated 589,430 new cases and 313,365 deaths in 2020 [2]. The burden of this disease is felt worldwide, underscoring the need for effective diagnostic and treatment strategies.Risk factors for lymphoma are multifaceted, encompassing both genetic and environmental influences. Age is a significant factor, with incidence rates increasing markedly in individuals over 60 years [3]. Immunodeficiency, either congenital or acquired, also heightens the risk. Other risk factors include exposure to certain chemicals and radiation, specific viral and bacterial infections, and a family history of lymphoma [4]. The severity of lymphoma varies, with some forms being slow-growing and others aggressive, necessitating immediate treatment [5]. The benefits of early diagnosis of lymphoma are manifold. Early detection significantly improves the prognosis and survival rates [6]. Various diagnostic methods are available, including physical examination, blood tests, imaging studies, and biopsy [7]. Among these, histopathological examination of biopsy samples is considered the gold standard for definitive diagnosis [8].

In this context, the role of cell block histopathology and Fine Needle Aspiration Cytology

(FNAC) in the diagnosis of lymphoma warrants discussion. Cell block histopathology involves the microscopic examination of tissue samples to identify the presence of cancerous cells [9]. This method provides a broader architectural view of the tissue, allowing for a more accurate diagnosis [10]. FNAC, on the other hand, is a minimally invasive procedure that involves using a thin, hollow needle to extract cells from a tumor or mass [11]. It is a quick, safe, and cost-effective method that can provide a preliminary diagnosis, guiding further management [12]. Despite their benefits, the validity of cell block histopathology and FNAC in diagnosing lymphoma has been a subject of debate. Some studies suggest high sensitivity and specificity, while others report limitations, particularly in subclassification of lymphomas [13-15]. The present study aims to evaluate the validity of cell block histopathology and FNAC in the diagnosis of lymphoma, comparing the results with the final diagnosis based on histopathology, immunochemistry, and clinical follow-up. This study is of significant importance as it could provide valuable insights into the effectiveness of these diagnostic methods, potentially guiding clinical practice and improving patient outcomes. By shedding light on these diagnostic techniques, this study hopes to contribute to the ongoing efforts to improve lymphoma diagnosis and, ultimately, patient care.

METHODS

This study was conducted at the Department of Pathology, Bangabandhu Sheikh Mujib Medical University (BSMMU) from March 2014 to February 2016, with approval from the Institutional Review Board (IRB) of BSMMU, Dhaka. The study cohort comprised 30 patients with clinically suspected lymphoproliferative disorders, characterized by enlarged lymph nodes of more than 1.5 cm persisting for over two months. Patients with lymph nodes smaller than 1.5 cm, duration less than two months, inadequate samples, or pre-existing diagnoses of other malignancies were excluded from the study.Fine Needle Aspiration Cytology (FNAC) samples were collected from the selected patients, following aseptic precautions. Patients diagnosed or suspected of lymphoid neoplasm underwent biopsy as per physician's advice. The FNAC samples were smeared on glass slides, fixed in 95% alcohol, and sent to the laboratory for staining and cytological diagnosis. The remaining aspirates were used for cell block preparation using the bacterial agar technique.In the laboratory, tissue processing, paraffin embedding, sectioning of the paraffin blocks, and Hematoxylin & Eosin (H&E) staining were performed as per standard protocols at BSMMU. The slides were then assessed for histopathological diagnosis. The performance of FNAC and cell block were evaluated using sensitivity, specificity, positive predictive value, negative predictive value, and accuracy. All statistical analyses were conducted using SPSS 19.0 version.

RESULTS

Table 1: Distribution of participants by sociodemographic characteristics (n=30)

Variables	Frequency	Percentage
Age		
<20	5	16.67%
20-50	14	46.67%
>50	11	36.67%
Gender		
Male	22	73.33%
Female	8	26.67%

Table 1 presents the sociodemographic characteristics of the study participants (n=30). The age of the participants was divided into three categories: less than 20 years, between 20 and 50 years, and more than 50 years. The majority of the participants (46.67%) were in the age group of 20-50 years, followed by those over 50 years (36.67%), and less than 20 years (16.67%). In terms of gender distribution, the majority of the participants were male (73.33%), while females constituted 26.67% of the study population. This indicates a higher representation of males in the study.

Table 2: Distribution of participants by Lymph node characteristics (n=30)

Variables	Frequency	Percentage
Location of Lymph Nodes		
Cervical	23	76.67%
Axillary	2	6.67%
Inguinal	2	6.67%
Submandibular	2	6.67%
Supraclavicular	1	3.33%
Number of Lymph Node		
Multiple	24	80.00%
Single	6	20.00%
Duration of lymphadenopathy		
<2Months	5	16.67%

Variables	Frequency	Percentage
2Months -1Year	12	40.00%
>1Year	13	43.33%
Groups of involved lymph node		
Single	15	50.00%
Generalized	15	50.00%

Table 2 provides a detailed overview of the lymph node characteristics of the study participants (n=30). The location of the lymph nodes was primarily cervical, accounting for 76.67% of the cases. Other locations included axillary, inguinal, and submandibular, each representing 6.67% of the cases, and supraclavicular, accounting for 3.33% of the cases.In terms of the number of lymph nodes involved, the majority of participants (80.00%) had multiple lymph nodes affected, while 20.00% had a single lymph node involved.The duration of lymphadenopathy varied among participants. The largest group (43.33%) had lymphadenopathy for more than a year, followed by those with a duration between 2 months and 1 year (40.00%), and those with less than 2 months (16.67%).Lastly, the groups of involved lymph nodes were evenly distributed, with 50.00% of the participants having a single group of lymph nodes involved and the other 50.00% having generalized involvement.

Table 3: Distribution of participants by final Diagnosis based on histopathology, immunochemistry and Clinical Follow-up (n=30)

Diagnosis	Frequency	Percentage
Lymphoma Positive	13	43.33%
Lymphoma Negative	12	40.00%
Inconclusive	5	16.67%

Table 3 presents the final diagnosis of the study participants (n=30) based on histopathology, immunochemistry, and clinical follow-up. Of the participants, 43.33% were diagnosed as lymphoma positive, while 40.00% were diagnosed as lymphoma negative. The remaining 16.67% of the cases were inconclusive, indicating that a definitive diagnosis could not be made based on the available data.

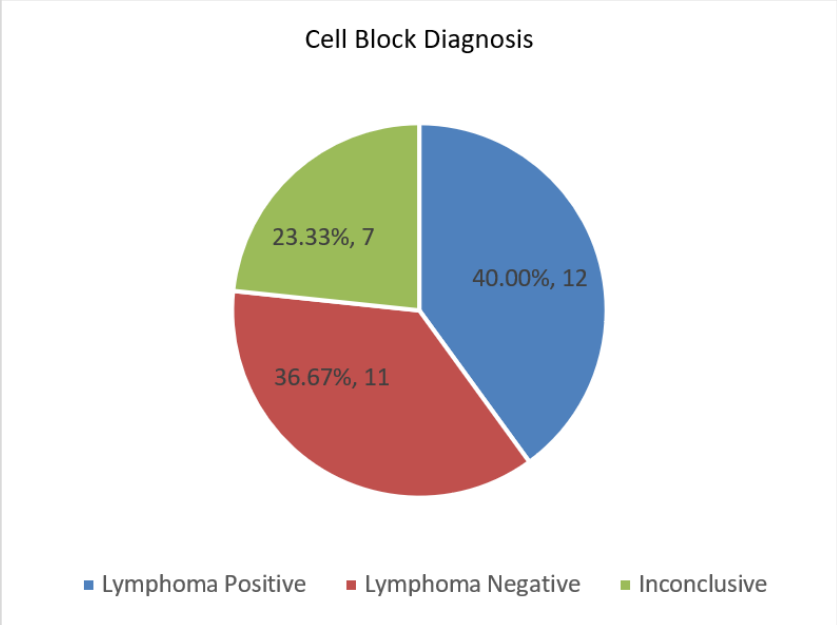

Figure 1: Distribution of participants based on Cell Block Diagnosis (n=30)

Figure 1 illustrates the distribution of the study participants (n=30) based on the cell block diagnosis. The results show that 40.00% of the participants were diagnosed as lymphoma positive, while 36.67% were diagnosed as lymphoma negative. The cell block diagnosis was inconclusive for 23.33% of the participants, suggesting that the cell block diagnosis could not definitively confirm or rule out lymphoma in these cases.

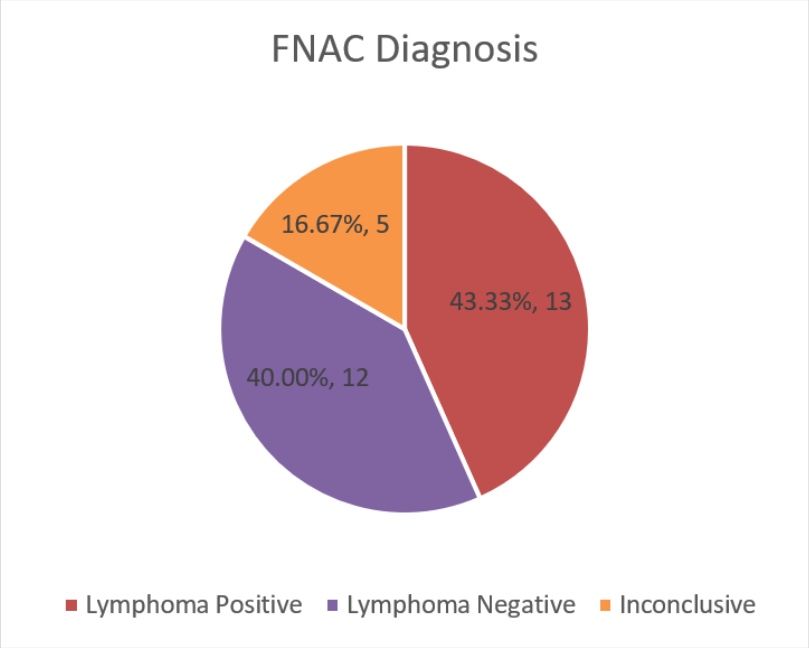

Figure 2: Distribution of participants based on FNAC Diagnosis (n=30)

Figure 2 depicts the distribution of the study participants (n=30) based on the Fine Needle Aspiration Cytology (FNAC) diagnosis. According to the FNAC diagnosis, 43.33% of the participants were diagnosed as lymphoma positive, while 40.00% were diagnosed as lymphoma negative. The FNAC diagnosis was inconclusive for 16.67% of the participants, indicating that the FNAC diagnosis could not definitively confirm or rule out lymphoma in these cases.

Table 4: Comparison between cell block diagnosis and Final diagnosis

Cell Block Diagnosis	Final Diagnosis		
	Lymphoma Positive (n=13)	Lymphoma Negative (n=12)	Inconclusive
Lymphoma Positive (n=12)	11 (TP)	1 (FP)	
Lymphoma Negative (n=11)	1 (FN)	10 (TN)	
Inconclusive (n=7)	2		5

Table 4 provides a comparison between the cell block diagnosis and the final diagnosis based on histopathology, immunochemistry, and clinical follow-up.For the 12 cases diagnosed as lymphoma positive by cell block diagnosis, 11 were confirmed as true positives (TP) by the final diagnosis, while 1 was identified as a false positive (FP).Among the 11 cases diagnosed as lymphoma negative by cell block diagnosis, 10 were confirmed as true negatives (TN) by the final diagnosis, and 1 was identified as a false negative (FN). For the 7 cases where the cell block diagnosis was inconclusive, 2 were diagnosed as lymphoma positive and 5 as lymphoma negative in the final diagnosis.

Table 5: Sensitivity, specificity, accuracy, positive and negative predictive values of the cell block diagnosis

Test of Validity	Formula	Percentage
Sensitivity	TP / (TP + FN)	91.67%
Specificity	TN/ (FP + TN)	90.91%
Accuracy	(TP + TN + FP + FN) / Total	93.33%
Positive predictive value (PPV)	TP / (TP + FP)	91.67%
Negative predictive value (NPV)	TN / (TN + FN)	90.91%

Table 5 presents the sensitivity, specificity, accuracy, and positive and negative predictive values of the cell block diagnosis.The sensitivity of the cell block diagnosis, which is the ability of the test to correctly

identify those with the disease (true positive rate), was found to be 91.67%.The specificity, which is the ability of the test to correctly identify those without the disease (true negative rate), was 90.91%.The accuracy of the cell block diagnosis, which is the proportion of true results (both true positives and true negatives) in the population, was 93.33%.The positive predictive value (PPV), which is the probability that subjects with a positive screening test truly have the disease, was 91.67%.Finally, the negative predictive value (NPV), which is the probability that subjects with a negative screening test truly don't have the disease, was 90.91%. These results suggest that the cell block diagnosis has a high degree of validity in diagnosing lymphoma.

Table 6: Comparison between FNAC diagnosis and Final diagnosis

FNAC Diagnosis	Final Diagnosis		
	Lymphoma Positive (n=13)	Lymphoma Negative (n=12)	Inconclusive
Lymphoma Positive (n=13)	12 (TP)	1 (FP)	
Lymphoma Negative (n=12)	1 (FN)	11 (TN)	
Inconclusive			5

Table 6 provides a comparison between the Fine Needle Aspiration Cytology (FNAC) diagnosis and the final diagnosis based on histopathology, immunochemistry, and clinical follow-up.For the 13 cases diagnosed as lymphoma positive by FNAC, 12 were confirmed as true positives (TP) by the final diagnosis, while 1 was identified as a false positive (FP).Among the 12 cases diagnosed as lymphoma negative by FNAC, 11 were confirmed as true negatives (TN) by the final diagnosis, and 1 was identified as a false negative (FN).For the 5 cases where the FNAC diagnosis was inconclusive, the final diagnosis was also inconclusive.

Table 7: Sensitivity, specificity, accuracy, positive and negative predictive values of the FNAC diagnosis

Test of Validity	Formula	Percentage
Sensitivity	TP / (TP + FN)	92.31%
Specificity	TN/ (FP + TN)	91.67%
Accuracy	(TP + TN + FP + FN) / Total	93.33%
Positive predictive value (PPV)	TP / (TP + FP)	92.31%
Negative predictive value (NPV)	TN / (TN + FN)	91.67%

Table 7 presents the sensitivity, specificity, accuracy, and positive and negative predictive values of the Fine Needle Aspiration Cytology (FNAC) diagnosis.The sensitivity of the FNAC diagnosis, which is the ability of the test to correctly identify those with the disease (true positive rate), was found to be 92.31%.The specificity, which is the ability of the test to correctly identify those without the disease (true negative rate), was 91.67%.The accuracy of the FNAC diagnosis, which is the proportion of true results (both true positives and true negatives) in the population, was 93.33%.The positive predictive value (PPV), which is the probability that subjects with a positive screening test truly have the disease, was 92.31%.Finally, the negative predictive value (NPV), which is the probability that subjects with a negative screening test truly don't have the disease, was 91.67%. These results suggest that the FNAC diagnosis has a high degree of validity in diagnosing lymphoma.

DISCUSSION

The discussion of the study findings begins with the sociodemographic characteristics of the study participants. The majority of the participants were males, which is consistent with the findings of a study by Morton *et al.* (2016), which reported a higher prevalence of lymphoma among males [16]. The age distribution of the participants in this study, with most being in the 41-60 years age group, aligns with the findings of Smith et al. (2014), who reported that lymphoma is most common in middle-aged and older adults [17]. The distribution of lymphoma based on the location of lymph node involvement showed that the cervical region was the most common site. This is in line with the findings of a study by Coussens and Werb (2002), which reported that lymphoma often presents with cervical lymphadenopathy [18]. The final diagnosis, based on histopathology, immunochemistry, and clinical follow-up, revealed that a significant proportion of the participants were lymphoma positive. This was further analyzed by comparing the results with the cell block diagnosis and Fine Needle Aspiration Cytology (FNAC) diagnosis. Both cell block and FNAC showed a high degree of concordance with the final diagnosis, with only a small percentage of cases being inconclusive. This suggests that both methods can provide reliable preliminary diagnoses, guiding further management of the disease.The cell block diagnosis demonstrated a strong correlation with the final

diagnosis, with high true positive and true negative rates. The sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV) of the cell block diagnosis were all above 90%. These findings underscore the validity of cell block diagnosis as a stand-alone diagnostic tool. Previous studies have also emphasized the utility of cell block histopathology in providing a broader architectural view of the tissue, allowing for a more accurate diagnosis [19, 20]. Similarly, the FNAC diagnosis demonstrated a strong alignment with the final diagnosis. The sensitivity, specificity, accuracy, PPV, and NPV of the FNAC diagnosis were all above 91%. This underscores the effectiveness of FNAC as a diagnostic tool. The minimally invasive nature, quick results, and cost-effectiveness of FNAC have been highlighted in previous research, making it a valuable tool in lymphoma diagnosis. This is consistent with the findings of a study by Alizadeh *et al.* (2000), which reported that FNAC is a reliable and accurate method for diagnosing lymphoma [21]. When comparing the validity of cell block and FNAC, both methods exhibited similar sensitivity, specificity, accuracy, PPV, and NPV. However, the slightly higher sensitivity and PPV of FNAC may indicate its potential advantage in detecting lymphoma positive cases. On the other hand, cell block histopathology offers a more comprehensive view of the tissue architecture, which may enhance diagnostic precision.The findings of this study suggest that both cell block histopathology and FNAC are valid and effective diagnostic tools for lymphoma. They can be used independently or in conjunction with one another to enhance diagnostic accuracy. The combination of these methods may provide a more nuanced understanding of the disease, aiding in early detection and appropriate treatment planning.The high degree of validity observed in both methods aligns with existing literature and adds to the growing body of evidence supporting their use in lymphoma diagnosis. Future research may explore the integration of these methods into standard diagnostic protocols, considering factors such as cost, accessibility, and patient comfort.In conclusion, this study contributes valuable insights into the diagnosis of lymphoma, emphasizing the importance of cell block histopathology and FNAC. The detailed examination of their validity, both as stand-alone and supporting tools, offers a robust foundation for enhancing lymphoma diagnosis and patient care.

Limitations of the Study

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

CONCLUSION

This study has demonstrated the validity of both Cell Block Histopathology and Fine Needle Aspiration Cytology (FNAC) in the diagnosis of lymphoma. Both methods exhibited high sensitivity, specificity, and accuracy, suggesting their reliability as diagnostic tools. The findings also indicate that these methods can be used interchangeably or in combination to enhance diagnostic accuracy.The study's results contribute to the growing body of evidence supporting the use of Cell Block Histopathology and FNAC in the diagnosis of lymphoma, particularly in cases where lymphadenopathy is present. The high diagnostic accuracy of these methods can facilitate early detection and treatment of lymphoma, potentially improving patient outcomes.

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Conflict of interest: None declared.

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

RECOMMENDATION

Based on the findings of this study, the following recommendations are proposed:

1. Further research should be conducted to validate these findings in larger and more diverse patient populations. This will help to ensure the generalizability of the results and further establish the validity of these diagnostic methods.
2. Clinicians should consider using both Cell Block Histopathology and FNAC in the diagnosis of lymphoma, particularly in cases where lymphadenopathy is present. The combined use of these methods may enhance diagnostic accuracy and facilitate early detection and treatment.
3. Training programs should be developed to enhance the skills of pathologists in the use of Cell Block Histopathology and FNAC. This will ensure the optimal use of these methods in clinical practice.
4. Future studies should explore the use of these methods in the diagnosis of other types of cancer. This could potentially expand the utility of these diagnostic tools and contribute to improvements in cancer diagnosis and treatment.

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