Comparison of Fine Needle Aspiration Cytology and Histopathology in the diagnosis of lymph node pathologies at health facilities located in Hawassa: A 5-year retrospective study

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Abstract

Objective: The aim of this study was to evaluate the performance of Fine Needle Aspiration Cytology in the diagnosis of lymph node pathologies in comparison with Histopathologic examination.

Methods: A retrospective health facility-based cross-sectional study was carried out at health facilities located in Hawassa city among 101 patients who had both Fine Needle Aspiration Cytology and Histopathologic examination on the same site from 13 September 2016 to 30 August 2021. Background data were collected using a structured questionnaire and analyzed by SPSS version 20.

Results: A total of 3892 patients had Fine Needle Aspiration Cytology for lymphadenopathies within a specified 5-year span, out of which 101 cases had both Fine Needle Aspiration Cytology and Histopathologic examination. The overall sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of fine needle aspiration cytology for the diagnosis of lymphoma were 88.2%, 92%, 91.8%, 88.5%, and 90.1%, respectively.

Conclusions: Fine Needle Aspiration Cytology can be recommended for clinically significant lymphadenopathy as a first-line diagnostic test since it is fast, safe, cost-effective, reasonably sensitive, and specific with significant positive and negative predictive values and diagnostic accuracy.

Introduction

Lymphadenopathy is a common clinical condition encountered in the outpatient clinic. The etiology of lymphadenopathy varies from an inflammatory process to a malignant condition.[1] Lymphadenopathy is an enlargement of the normal lymph nodes. Reactive lymph nodes are usually enlarged due to some degree of stimulation. Normally, they do not exceed a diameter of 1 cm; however, during immune reactions, they become considerably larger. A lymph node with a diameter of greater than 3 cm during immune stimulation is uncommon and may lead to the suspicion of malignancy.[2]

There are various ways of diagnosing lymphadenopathies: histopathologic examination, molecular techniques, immuno-histochemical techniques, and Fine Needle Aspiration Cytology (FNAC). Molecular techniques and immunohistochemical techniques are important to further characterize cytomorphologically difficult cases diagnosed as lymphoproliferative disorders.[3,4]

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FNAC technique was initially introduced in the early 1900's.[5] FNAC involves collecting cells by aspirating the affected organ or tissue using a thin needle to study them under a microscope after appropriate staining. It is easy to collect specimens from superficial organs such as skin, breast, thyroid, lymph nodes, soft tissue, and lymph node; however, collecting a specimen from a deep organ is difficult as it needs aspiration under the guidance of fluoroscopy, computed tomography (CT) scan, or ultrasound.[6]

FNAC can be used to distinguish tumors from infective or reactive pathology; as a result the application of FNAC in the diagnosis of lymphadenopathy was accepted and it is being practiced widely. Moreover, FNAC is cost-effective, less invasive, accurate, and is a simple method to perform. With the recent advances in ultrasound and CT scan technologies, focal lesions can be aspirated easily.[1]

FNAC has gained considerable importance in the management of patients with lymphadenopathy.[7] During the histopathologic examination, the pathologist looks for abnormal structures in the tissue. Tissues for histopathologic examination are obtained by biopsy; tissue samples are collected from a living person to diagnose pathologic conditions. A biopsy can be either incisional or excisional.[6] Histopathology is the gold standard for the diagnosis of lymph node pathologies.[8] Even though FNAC is recommended for clinically significant lymphadenopathy as a first-line diagnostic test, there is no published data that shows the performance of FNAC in the Hawassa area. The aim of the present study was to evaluate the performance of FNAC for the diagnosis of lymphadenopathies.

Method

Study design and area

This is a 5-year (13 September 2016 to 30 August 2021) health facility-based retrospective cross-sectional study that was conducted at Hawassa University Comprehensive Specialized Hospital (HUCSH), pathology department, and Yanet Medical center (YMC). Hawassa is the capital city of Sidama Regional State located 275 km to the South of Addis Ababa. The city has two governmental and four private primary hospitals and several public and private clinics and pharmacies. HUCSH is one of the referral hospitals in the region serving as a teaching hospital with a catchment population of 18 million. It provides health care services for about 53,384 patients per year. The department of pathology is one of the specialized departments in HUCSH and examines blood, biopsy, and cytology specimens. YMC is a private clinic located in Hawassa city that provides various diagnostic services such as imaging, histological examination, and laboratory services.

Source and study population

The source population includes all patients who had lymph node biopsy examinations at HUCSH and YMC department of pathology during the specified period. The study population includes all patients who had both lymph node biopsy and FNAC at HUCSH and YMC department of pathology during the specified period.

Inclusion and exclusion criteria

Patients who had both lymph node biopsy and FNAC of the same site during the study period were included. Patients with known primary malignancy having a lymph node metastasis were excluded.

Operational definition

FNAC. A cytologic diagnostic method based on morphologic findings of individual and small group of cells aspirated using a fine needle by creating a negative pressure.

Histopathology/biopsy. A procedure by which a tissue sample is taken by a surgical extraction and subsequently processing of sections or whole of the tissue is done to produce thin tissue sections with preserved architecture which can be examined under the microscope after staining.

Data collection and management

For data collection, a questionnaire tested among population representing 5% of study population was used. All records with histopathology diagnoses of lymph node tissue during the study period were identified and their biopsy request form and biopsy reports were reviewed. Previous FNAC report of cases with biopsy report was searched and analyzed. Data were collected using a structured data collecting format. The data were checked for completeness, cleaned, and coded for entry and analysis. For data analysis Statistical Package of Social Sciences (SPSS) version 20 was used. All data collected were cross-checked by retrieving patients' medical record charts using their medical registration numbers.

Statistical analysis

The cytological and histopathologic analysis was reported in terms of frequencies and percentages. Furthermore, diagnostic accuracy of FNAC for lymphadenopathy was measured using histopathology as the gold standard. Sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) were calculated using their respective standard formulas.

Results

Demographic and clinical characteristics

Between 13 September 2016 and 30 August 2021, 3892 patients had FNAC of lymphadenopathies. Of these, 101 cases had both FNAC and biopsy and are considered for the current study. The age of participants ranged from 5 to

Table 1. Demographic and clinical characteristics of study participants at Hawassa University Comprehensive Specialized Hospital and Yanet Medical Center (N = 101).

Variables		Frequency (%)
Age in years	<10	6 (5.9)
	11–20	19 (18.8)
	21–30	15 (14.9)
	31–40	22 (21.8)
	41–50	15 (14.9)
	51–60	11 (10.9)
	>61	13 (12.9)
Duration of the LAPs in month	<1/2	2 (2)
	½–1	13 (12.9)
	2–6	57 (56.4)
	>6	29 (28.7)
Site of the LAPs	Cervical area	43 (42.6)
	Sub mandibular	7 (6.9)
	Axillary	13 (12.9)
	Inguinal	16 (15.8)
	Mesenteric	3 (3)
	Generalized	19 (18.8)
Size of the LAPs in centimeters	<1	2 (2)
	1.1–3	69 (68.3)
	3.1–6	24 (23.8)
	>6	6 (5.9)

LAPs: lymphadenopathies.

Table 2. Cytomorphologic and Histomorphologic patterns of LAPs among study participants at Hawassa University Comprehensive Specialized Hospital and Yanet Medical Center (N = 101).

Condition	Diagnosis method, n (%)	
	FNAC	Histomorphology
Reactive lymphoid hyperplasia (RLH)	8 (7.9)	6 (5.9)
Tuberculous lymphadenitis (TL)	19 (18.8)	20 (19.8)
Hodgkin's lymphoma (HL)	15 (14.9)	18 (17.8)
Non-Hodgkin's lymphoma (NHL)	34 (33.7)	33 (32.7)
Metastasis	20 (19.8)	23 (22.8)
Others	5 (5)	1 (1)
Total	101 (100)	101 (100)

FNAC: Fine Needle Aspiration Cytology.

80 years. The average duration of the lesions was 7 months. The most common site of lymphadenopathies was the cervical area (42.6%) followed by generalized lymphadenopathy (18.8%) (Table 1). The average size of the lymph nodes was 3.2 cm.

Morphologic patterns of lymph node pathologies

Out of 101 cases who had FNAC, non-Hodgkin's lymphoma (NHL) was the most frequently observed diagnosis (n=34; 33.7%), followed by metastasis (n=20; 19.8%) and tuberculous lymphadenitis (TL; n=19; 18.8%). The most common histopathologic diagnosis was NHL 33(32.7%), followed by metastasis 23(22.8%) and TL (Table 2).

Morphologic diagnosis according to different conditions

Reactive lymphoid hyperplasia (RLH) was common among those aged >60 years (n=2; 15.4%) and among patients with an inguinal site of the lymph node. TL was common among those within the age group of 11–20 years (n=7; 38.9) and at inguinal site. Hodgkin's lymphoma (HL) was common among participants ≤10 years old (n=4; 66.7%) (Table 3).

Table 3. Distribution of Histomorphologic diagnosis according to age groups, size of lymph nodes, duration of LAP, and sites of lymph nodes.

Variables		Reactive lymphoid hyperplasia, n (%)	Tuberculous lymphadenitis, n (%)	Hodgkin's lymphoma, n (%)	Non-Hodgkin's lymphoma, n (%)	Metastasis, n (%)	Total n
Age in year	<10	–	2 (33.3)	4 (66.7)	–	–	6
	11–20	1 (5.6)	7 (38.9)	2 (11.1)	5 (27.8)	3 (6.7)	18
	21–30	–	4 (26.7)	4 (26.7)	3 (20)	4 (26.7)	15
	31–40	1 (4.6)	3 (13.6)	4 (18.2)	9 (40.9)	5 (22.7)	22
	41–50	1 (6.7)	2 (13.3)	1 (1.67)	6 (40)	5 (33.3)	15
	51–60	1 (9)	1 (9)	1 (9)	5 (45.5)	3 (27.3)	11
	>60	2 (15.4)	1 (7.7)	2 (15.4)	5 (38.5)	3 (23.1)	13
	Total	6 (5.9)	20 (19.8)	18 (17.8)	33 (32.7)	23 (22.8)	100
Size of the lymph nodes in cm	<1	2 (100)	–	–	–	–	2
	1.1–3 cm	4 (5.8)	20 (29)	12 (17.4)	19 (27.5)	14 (20.3)	69
	3.1–6 cm	–	–	4 (16.7)	14 (58.3)	5 (20.8)	23
	>6	–	–	2 (33.3)	–	4 (66.7)	6
	Total	6 (5.9)	20 (19.8)	18 (17.8)	33 (32.7)	23 (22.8)	100
Duration of LAs in months	<1/2	–	–	–	2 (100)	–	2
	½–1	3 (23.1)	6 (46.2)	–	2 (15.4)	3 (23.1)	14
	2–6	2 (3.5)	7 (12.3)	12 (21.1)	20 (35.1)	15 (26.3)	56
	>6	1 (3.5)	7 (24.1)	6 (20.7)	10 (34.5)	5 (17.2)	29
	Total	6 (5.9)	20 (19.8)	18 (17.8)	33 (32.7)	23 (22.8)	100
Site of the lymph nodes	Cervical	1 (2.3)	9 (20.9)	14 (32.6)	9 (20.9)	10 (23.3)	43
	Submandibular	1 (14.3)	3 (42.9)	–	–	3 (42.9)	7
	Axillary	2 (5.4)	3 (23.1)	1 (7.7)	4 (30.7)	3 (23.1)	13
	Inguinal	2 (12.5)	4 (25)	–	4 (25)	5 (31.25)	15
	Mesenteric	–	–	1 (33.3)	1 (33.3)	1 (33.3)	3
	Generalized	–	1 (5.3)	2 (10.5)	15 (79)	1 (5.3)	19
	Total	6 (5.9)	20 (19.8)	18 (17.8)	33 (32.7)	23 (22.8)	100

LAP: lymphadenopathy.

Comparison of FNAC and Histopathologic examination

The true-positive, false-positive, false-negative, and true-negative values of FNAC for the diagnosis of TB lymphadenitis were 15, 4, 5, and 77, respectively (Table 4). The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of FNAC for the diagnosis of metastasis were 82.6%, 98.7%, 95%, 95%, and 95%, respectively. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of FNAC for the diagnosis of HL were 66.7%, 96.4%, 35.3%, 96.4%, and 91%, respectively (Table 5). The overall sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of FNAC for lymphoma diagnosis (HL and NHL) were 88.2%, 92%, 91.8%, 88.5%, and 90.1%, respectively.

Discussion

The overall performance of FNAC found in this study is comparable with a study conducted in India by Gupta M. and Singh K.[8] According to Gupta M and Singh K, the sensitivity, specificity, positive predictive value, and negative

predictive value of FNAC in diagnosing TL were 100%, 96.7%, 90.0%, and 100.0%, respectively.[8] Except for the higher sensitivity and negative predictive value, these findings are in line with the current study. The higher sensitivity according to Gupta M. and Singh K. as compared to the current study could be because they performed AFB on FNAC material for suspicious cases of TL on FNAC, which in turn increased the true positivity rate and decreased the false positivity rate. Moreover, they recommended a biopsy for cases of granulomatous lymphadenitis on FNAC.[8]

In the current study, we did not find a single case that is diagnosed as granulomatous lymphadenitis on FNAC and had subsequently biopsy. This could be because such cases probably had typical clinical manifestations and were diagnosed and treated without undergoing biopsy, which decreases the number of true positive values. However, our findings were comparable with a study conducted in Bangladesh[9] in which the sensitivity, specificity, positive predictive value, and negative predictive value of FNAC in diagnosing TL were 84.62%, 94.12%, 91.67%, and 88.89%, respectively.

The commonest site of metastatic lesions of lymph nodes observed was the cervical area. This result is in accordance

Table 4. Summary of frequencies of true-positive, true-negative, false-positive, and false-negative results of FNAC in comparison with Histopathologic examination (gold standard) of the LAPs (N = 101).

FNAC diagnosis of LAPs		Histopathologic examination of LAPs								Total
		TB lymphadenitis		Hodgkin's lymphoma		Non-Hodgkin's lymphoma		Metastasis		
		Yes	No	Yes	No	Yes	No	Yes	No	
TB lymphadenitis	Yes	15 (TP)	4 (FP)							19
	No	5 (FN)	77 (TN)							82
Hodgkin's lymphoma	Yes			12 (TP)	3 (FP)					15
	No			6 (FN)	80 (TN)					86
Non-Hodgkin's lymphoma	Yes					27 (TP)	7 (FP)			34
	No					6 (FN)	61 (TN)			67
Metastasis	Yes							19 (TP)	1 (FP)	20
	No							4 (FN)	77 (TN)	81
Total		20	81	18	83	33	68	23	78	

FNAC: Fine Needle Aspiration Cytology; LAPs: Lymphadenopathies; TB: Tuberculosis; TP: true positive; FN: false negative; FP: false positive; TN: true negative.

Table 5. Summary of statistical measures of FNAC examination in diagnosing of lymph node pathologies (N = 101).

Statistical measure	Values			
	TB (%)	HL (%)	NHL (%)	Metastasis (%)
Sensitivity	75	66.7	81.8	82.6
Specificity	95.1	96.4	89.7	98.7
Positive predictive value	79	35.3	79.4	95
Negative predictive value	93.9	96.4	91	95
Accuracy	91	91	87.1	95

TB: Tuberculosis; HL: Hodgkin's lymphoma; NHL: Non-Hodgkin's lymphoma.

with a study conducted in Pakistan, Islamabad[10] which observed the most frequent site of metastatic lesions to lymphnodes to be the cervical group.

In our study, the sensitivity of FNAC in diagnosing metastasis is relatively lower than in the study conducted in Pakistan.[10] According to a study conducted in Pakistan, the sensitivity and positive predictive value of FNAC in diagnosing lymph node metastasis were 97.37%, while the specificity and negative predictive value were 93.75%. The overall diagnostic accuracy of FNAC was 96.29%.[10] This discrepancy might be due to high numbers of false-negative results which could affect the sensitivity. In the current study, four cases were incorrectly diagnosed as metastasis by FNAC; out of which two were diagnosed as high-grade NHL. Moreover, the study in Pakistan[10] was conducted only among those cases suspected of metastasis by FNAC and the findings were correlated with the biopsy test results. In the current study, the most frequently observed metastatic lesions to the lymph nodes were squamous cell carcinoma and melanoma.

According to our study, the commonest site, size, and age at diagnosis of Hodgkin's lymphoma were cervical area (77.8%), 1.1–3 cm, and ≤10 years, respectively. These findings are in line with a study conducted in Bangladesh in which the most common anatomical site involved was the cervical lymph nodes (86.67%).[9]

The performance of FNAC in diagnosing Hodgkin's lymphoma in this study is in line with a study conducted in Bangladesh in which the sensitivity, specificity, positive predictive value, and negative predictive value of FNAC in diagnosing Hodgkin's lymphoma were 66.67%, 92.59%, 50%, and 96.15%, respectively.[9] In both the Bangladesh[9] and our studies, the sensitivity of FNAC in diagnosing Hodgkin's lymphoma was low (66.7%), which may be due to the fact that Hodgkin's lymphoma is diagnosed in a reactive lymphoid background and the scattered malignant Hodgkin's cells may be scanty on FNAC as has been observed in our study where two of the cases diagnosed as reactive hyperplasia on FNAC are confirmed to be Hodgkin's lymphoma on biopsy.

In this study, the commonest site affected by NHL was a cervical area with the highest number occurring in the age range of 31–40 years. The performance of FNAC in diagnosing NHL in our study was in agreement with a report from Turkey, in which the overall diagnostic sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of FNAC in diagnosing NHL were 95.4%, 94.1%, 95.4%, 94.1%, and 94.9%, respectively.[11] The slight difference observed could be due to the relatively larger sample size used in the current study as compared to relatively smaller sample size in the Turkey study.[11]

The overall sensitivity, specificity, positive predictive value, negative predictive value and, accuracy of FNAC in diagnosing lymphoma (HL and NHL) were comparable with reports from Sweden.[12] A study conducted in Bangladesh[9] reported the sensitivity and specificity of FNAC in diagnosing lymphomas as 81% and 75%, respectively, which is slightly lower than the findings of the current study. In contrast, a study conducted at the University of Arizona, USA reported very low sensitivity (12%) of FNAC in diagnosing lymphoma.[13] This discrepancy between the USA and the current study might be due to the fact that the US study aimed to diagnose specific types of lymphomas on FNAC as opposed to the current study which categorized lymphomas as NHL and HL.

In the present study, 3892 FNACs of lymph nodes were performed during the study period; however, only 101 histopathology reports of respective cases were found. The reason why there was low follow-up (FNAC-histopathology) is the great majority of the cases in our study which are subjected to FNAC were reactive lymphoid hyperplasias that did not require a histopathology test subsequently in the follow-up. In addition, those cases that are suspicious and/or suggestive of TL on FNAC in our setup are treated for TB without subsequent biopsy confirmation because clinicians strongly consider TB in such cases as TB is epidemiologically common in our setup.[14]

Limitations of the study

Even though we tried to assess the efficacy of FNAC in diagnosing lymph node pathologies by comparing it with histopathology, a few of the limitations of our study include thus: (1) as this is a retrospective cross-sectional study, it was not possible to retrieve important slides (because of poor handling) for reevaluation and further explanation of discrepant cases; (2) small sample size which could affect statistical measurements of specific lymph node pathologies; (3) shortage of published African-based similar studies to compare with the current study; (4) lack of molecular and immunohistochemical techniques in the facility to further characterize the lymphomas and cases diagnosed as lymphoproliferative disorders on FNAC; and (5) the other limitation of the study was we did not determine the sample size.

Conclusion

The sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of FNAC in diagnosing lymph node pathologies are fairly comparable with other studies. The sensitivity of FNAC in diagnosing TL and Hodgkin's lymphoma was slightly low. The highest diagnosing efficacy of FNAC was observed for metastatic disease of the lymph nodes.

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Supplemental material

Supplemental material for this article is available online.

References

1. Hafez NH and Tahoun NS. Reliability of fine needle aspiration cytology (FNAC) as a diagnostic tool in cases of cervical lymphadenopathy. *J Egypt Natl Canc Inst* 2011; 23(3): 105–114.
2. Lee SC. Histology for pathologists. *Pathology* 2007; 39(5): 536.
3. Marino FZ, Aquino G, Brunelli M, et al. High performance of multiplex fluorescence in situ hybridization to simultaneous detection of BCL2 and BCL6 rearrangements: useful application in the characterization of DLBCLs. *Virchows Arch* 2021; 479(3): 565–573.
4. Caputo A, Ciliberti V, Zeppa P, et al. Cytological diagnosis of aggressive small-cell lymphomas. *Acta Cytol* 2022; 66(4): 269–278.
5. Bezabih M and Mariam DW. Determination of aetiology of superficial enlarged lymph nodes using fine needle aspiration cytology. *East Afr Med J* 2003; 80(11): 559–563.
6. Barkan H. General pathology. *Am J Ophthalmol* 1918; 1(11): 217–221.
7. Hirachand S, Lakhey M, Akhter J, et al. Evaluation of fine needle aspiration cytology of lymph nodes in Kathmandu Medical College, Teaching hospital. *Kathmandu Univ Med J* 2009; 7(26): 139–142.
8. Gupta M and Singh K. Correlation of fine needle aspiration cytology lymph node with histopathological diagnosis. *Int J Res Med Sci* 2016; 4(11): 4719–4723.
9. Islam MR, Hoque MA and Ekram AS. A study of peripheral lymphadenopathy with correlation between fine needle aspiration cytology (FNAC) and biopsy in a tertiary care hospital. *Bangladesh J Med* 2015; 26(2): 49–54.
10. Mustafa Z, Baloch FA and Khalid A. Diagnostic accuracy of fine needle aspiration cytology (FNAC) in metastatic lymphadenopathy. *Int J Pathol* 2015; 13(1): 7–13.
11. Altınboğa AA and Yüce G. Fine-needle aspiration cytology in the diagnosis of lymph nodes: correlation with histopathological diagnosis. *South Clin Ist Eurasia* 2019; 30(1): 52–59.
12. Landgren O, Porwit MacDonald A, Tani E, et al. A prospective comparison of fine-needle aspiration cytology and histopathology in the diagnosis and classification of lymphomas. *Hematol J* 2004; 5(1): 69–76.
13. Hehn ST, Grogan TM and Miller TP. Utility of fine-needle aspiration as a diagnostic technique in lymphoma. *J Clin Oncol* 2004; 22(15): 3046–3052.
14. Biadglegne F, Tesfaye W, Anagaw B, et al. Tuberculosis lymphadenitis in Ethiopia. *Jpn J Infect Dis* 2013; 66(4): 263–268.