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The diagnostic value of FNAC in cervical lymphadenopathy

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ABSTRACT

Background. Fine-needle aspiration cytology (FNAC) is the basic investigation that can be performed even in small centers, with low costs, without major complications and with good patient compliance. The broad spectrum of diseases can be classified into inflammatory conditions, malignancies or lymphoma, which allows the planning of the treatment strategy or further investigation that is necessary for diagnosis. *Materials and Methods*. A prospective study was performed on 100 individuals with enlarged cervical lymph nodes who underwent FNAC and surgery, from 2017 to 2019. The histopathological reports of the patients were correlated with the preoperative cytological reports. *Results*. Of the studied cases, reactive lymphadenopathy was the most common - 43%, followed by tuberculous lymphadenopathy - 21%, granulomatous lymphadenopathy - 16%, and malignancy - 16%. Among malignancy, the most common is the secondary from squamous cell carcinoma – 11 cases (68.75%) followed by metastasis from thyroid carcinoma – 4 cases (25%) and metastasis from adenocarcinoma – 1 case (6.25%). By the age of 40, the most common malignancy is metastasis from thyroid carcinoma, while over 40, the secondary tumor from squamous cell carcinoma is the most common. Sensitivity, specificity and accuracy of FNAC are high in carcinomatous (93.75%, 100%, 99%), lymphomatous (75%, 98.96%, 98%) and tuberculous lymphadenopathy (95.24%, 96.20%, 96%). *Conclusion*s. FNAC is a simple and safe test, with a good accuracy of diagnosis and low complications, being therefore an effective diagnostic tool.

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Introduction

One of the most common clinical manifestations of patients is enlargement of the cervical lymph nodes, which includes a number of conditions, from inflammation to malignant lymphoma or metastatic cancer. In patients with cervical lymphadenopathy, FNAC has a definite role in the initial diagnostic evaluation. It is a simple, low-cost, fast investigation procedure with minimal trauma and low risk of complications. In the cervical region, FNAC is a simple technique due to the patient's high compliance, the minimally invasive nature of the technique and the critical problem of avoiding surgery in situations such as non-neoplastic or inflammatory diseases, as well as metastatic tumors [1-3].

FNAC has become a well-accepted and widely used means of diagnosing cervical lymphadenopathy, being an easy, safe and cost-effective procedure. FNAC can distinguish between malignant, non-malignant and inflammatory cases, thus avoiding unnecessary surgery. Several study reports are available in literature, studies among population from coastal area, attending the rural medical college were facility for frozen section and MRI is lacking [4-6]. The aim of this research was to see if FNAC can accurately diagnose cervical lymphadenopathy, more precisely to analyze the cytological aspects of clinically enlarged lymph nodes, in order to diagnose tuberculosis, lymphoma and secondary malignancy.

Materials and Methods

The current study is a prospective study with the appropriate approval of the Institutional Research Committee and the Institutional Ethics Committee. Patient attending surgery OP with neck swellings identified by detailed medical history and clinical examination, were selected due to cervical lymphadenopathy. Data was obtained using a pre-structured proforma after the study participants gave their written informed consent. The research was conducted between September 2017 and July 2019 at the Govt. T D Medical College Hospital in Alappuzha, Kerala. The study involved the participation of 100 patients.

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Inclusion and exclusion criteria. The study included patients of both sexes with cervical lymphadenopathy, aged between 13 and 70 years. Patients under the age of 13 were referred for pediatric surgery. The study included all patients who had FNAC followed by surgery and histological examination. This study included FNAC from cervical lymphadenopathy revealed by clinical examination and confirmed by ultrasonography. In doubtful cases, CT scan of the neck was performed and, in such cases, FNAC was performed prior to CT scan. Cervical swelling that does not occur in the lymph nodes has been ruled out. The study also ruled out patients with inoperable tumors and those who were deemed unfit for surgery.

A thorough history and clinical examination were performed to find the aspiration lesion; an ultrasound of the neck was also performed. In some cases, a CT scan of the neck was also performed. The classification of cervical LNs by the American Academy of Otolaryngology and Head and Neck Surgery was used (AAO-HNS).

Direct aspiration of the percutaneous or transoral root was used. The aspiration was performed with a 23-gauge needle and a 10-cc disposable syringe, with the negative pressure needle moved in several directions for high swelling, with a multi-seat aspiration. The smears were prepared and fixed with ether-95% alcohol solution and stained with Papanicolaou's stain. All aspirations were done by the same team of cytotechnician and the examination of the lamellae was done by the same team of cytopathologist. After FNAC, patients were scheduled for surgery with adequate preoperative anesthetic control. Written informed consent was acquired in each case. The specimens were examined histopathologically. In cases of secondary lymph nodes from which FNAC was taken, they were removed along with the primary malignancy; those without a previous excision biopsy were identified postoperatively, labeled and sent separately for histopathological examination.

The diagnoses were compared histologically and cytologically. The sensitivity, specificity, positive predictive value and negative predictive value of FNAC were evaluated.

Results

The study comprised 100 individuals with cervical lymphadenopathy who had undergone FNAC before surgery and histopathological examination. Of which 46% were females and males were 54%, slight male preponderance in our study. Age between 13 and 70 were included in the study. Mean age of the patients is 36. Duration of swellings range from 3 months to 4 years; the mean duration was 7 months. Among the age group, 21-30 are more affected 26%, followed by 13-20 and 31-40 are 20% and 17% respectively.

Table 1. Age distribution and frequency (n=100)

Age	Male	Female	Frequency	Percentage
13 - 20	10	10	20	20
21 - 30	13	13	26	26
31 - 40	9	8	17	17
41 - 50	6	5	11	11
51 - 60	9	6	15	15
61 - 70	7	4	11	11
Total	54	46	100	100

Among the 100 cases FNAC showed, reactive lymphadenopathy was the commonest 42 cases, subsequently by tuberculous lymphadenopathy, granulomatous lymphadenopathy, metastasis from squamous cell carcinoma, metastasis from thyroid carcinoma, metastasis from adenocarcinoma then lymphoma are 23, 16, 10, 3, 2 and 4 cases, respectively.

Among the 42 cases of reactive lymphadenopathy proved by FNAC, 40 cases revealed the same diagnosis in HPR, the 2 different cases are lymphoma–1, metastasis thyroid carcinoma–1. Among the 23 cases of tuberculous lymphadenopathy proved by FNAC, 20 cases revealed the same diagnosis in HPR, the 3 different cases are reactive lymphadenopathies–2, granulomatous lymphadenopathies–1.

Among the 16 cases of granulomatous lymphadenopathy proved by FNAC, 15 cases showed the same diagnosis in HPR, the 1 different case is tuberculous lymphadenopathy – 1. Among the 10 cases of metastasis from squamous cell carcinoma and 3 cases of metastasis from thyroid carcinoma, all showed the same histopathology report.

Among the 2 cases of metastasis from adenocarcinoma, 1 showed the same diagnosis and another shows metastasis from squamous cell carcinoma. Among the 4 cases of lymphoma, 3 showed the same diagnosis, and different one was the reactive lymphadenopathy.

Post-operative histopathology diagnosis showed reactive lymphadenopathy in 43% cases, tuberculous lymphadenopathy in 21% cases, granulomatous lymphadenopathy in 16% cases, metastasis from squamous cell carcinoma in 11% cases, metastasis thyroid Ca. in 4% cases, metastasis from adenocarcinoma in 1% cases and lymphoma in 4% cases.

Among the 16 cases of carcinoma, most commonly affected age group is 51-60 followed by 61-70 and 21-30 (8 cases, 4 cases and 2 cases). Male are more affected than female 9:7. Most common lymph node group affected is level III, followed by level II, I B and V B. Among malignancy, most common is the secondary from squamous cell carcinoma – 11 cases (68.75%) followed by metastasis from thyroid carcinoma – 4 cases (25%) and metastasis from adenocarcinoma – 1 case (6.25%). Less than 40 years most common malignancy is metastasis from

thyroid carcinoma maximum number seen between the age of 21-30. In tuberculous lymphadenopathy, most notably affected age group is 21-30, followed by 13-20, 31-40, 41-50, 61-70, 51-60 are 6, 5, 4, 3, 2, 1 case, respectively. Females are more affected, M:F is 9:12. Most common group affected is level II, followed by V A, III and I B.

Lymphoma showed uniform distribution among all age group. Males are more affected 3:1. Most common group affected is level V B, followed by II and III with equal contribution. Lymphoma seen in 4% of cases, this is similar to study by Ahmad et al. [7].

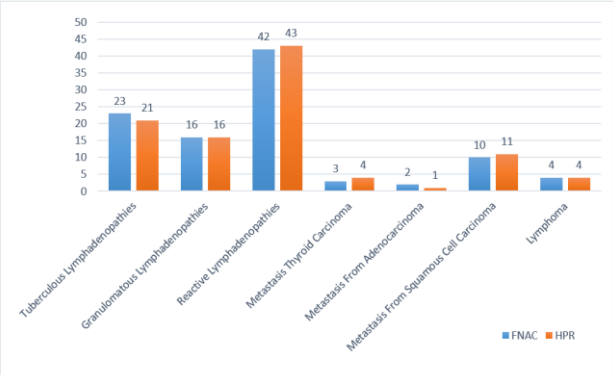

Figure 1. Study group disease distribution - FNAC and HPR (n=100)

Table 2. The comparison of FNAC and HPR (n=100)

CASES	No. (FNAC)	Same HPR	Different HPR	Different CASES
Tuberculous Lymphadenop.	23	20	3	Reactive Lymphadenopathies – 2 Granulomatous Lymphadenopathies - 1
Granulomatous Lymphadenop.	16	15	1	Tuberculous Lymphadenopathies - 1
Reactive Lymphadenop.	42	40	2	Lymphoma – 1 Metastasis from Thyroid Carcinoma - 1
Metastasis from Thyroid Carcinoma	3	3	0	
Metastasis from Adenocarcin.	2	1	1	Metastasis from SCC - 1
Metastasis from SCC	10	10	0	
Lymphoma	4	3	1	Reactive lymphadenopathies - 1

In reactive lymphadenopathy, commonly seen in the younger age group, frequency in the age group of 13-20, 21-30, 31-40, 41-50, 51-60, 61-70 are 12, 12, 8, 4, 4, 3 in order. Male and female are 25 and 18. Most common group affected is level I B, followed by V A, I A, III and II, V B with equal contribution. Granulomatous lymphadenopathy commonly seen in the age group 21-30, followed by 31-40. Males and females affected equally. Most common group affected is level II, followed by V A, I B, III and I A, V B with equal contribution. Considering all cases most commonly affected lymph node group was V A 24%, followed by I B 23%, II 22%, III 18%, V B 7%, I A 6%.

Out of 100 cases 92 cases revealed the same diagnosis 8 cases showed different diagnosis. Out of 23 cases of tuberculous lymphadenopathies 21 cases revealed the same diagnosis in histopathology discordant cases are 2 cases of reactive lymphadenopathy and 1 case of granulomatous lymphadenopathy.

Among the 16 cases of granulomatous lymphadenopathy 15 cases revealed the same result and the discordant case was 1 tuberculous lymphadenopathy. In case of reactive lymphadenopathy, out of 42, 40 cases revealed the same diagnosis. Discordant cases were lymphoma and metastasis thyroid carcinoma 1 each. All the 3 cases of metastasis thyroid carcinoma showed same diagnosis.

Among the metastasis adenocarcinoma, out of 2 cases, 1 showed different diagnosis, discordant case was metastasis from squamous cell carcinoma. Among the metastasis from squamous cell carcinoma all the 10 cases revealed the same diagnosis. In lymphoma, 3 cases out of 4 showed same diagnosis, discordant case was reactive lymphadenopathy.

On statistical analysis of carcinomatous lesions there was 1 false negative, 1 case of metastatic thyroid carcinoma was diagnosed by cytology was reactive lymphadenopathy. Sensitivity, specificity was calculated as follows in the Table 3.

Table 3. Statistical analysis of Carcinomatous lesions (n=100)

Test evaluated (FNAC)	Histopathology positive	Histopathology negative	Total
FNAC positive	15 (True Positive)	0 (False Positive)	15
FNAC negative	1 (False Negative)	84 (True Negative)	85
Total	16	84	100
Sensitivity – 93.75%, Specificity – 100%, Positive predictive value – 100%, Negative Predictive value – 98.82%, Accuracy - 99%.			

On statistical analysis of lymphomatous lesions, found 1 false positive and 1 false negative, 1 case of lymphoma was diagnosed by cytology was reactive lymphadenopathy (false negative). 1 case of reactive lymphadenopathy was diagnosed by cytology was lymphoma (false positive). Sensitivity, specificity was calculated as follows in the Table 4.

Table 4. Statistical analysis of lymphomatous lesions (n=100)

Test evaluated (FNAC)	Histopathology positive	Histopathology negative	Total
FNAC positive	3 (True Positive)	1 (False Positive)	4
FNAC negative	1 (False Negative)	95 (True Negative)	96
Total	4	96	100

Sensitivity – 75.00%, Specificity – 98.96%, Positive predictive value – 75.00%, Negative Predictive value - 98.96%, Accuracy - 98%.

On statistical analysis of tuberculous lesions there was 3 false positive and 1 false negative. False positive cases are 2 cases of reactive lymphadenopathy and 1 case of granulomatous lymphadenopathy. False negative case is 1 granulomatous lymphadenopathy by cytology proved to be tuberculous lymphadenopathy.

Table 5. Statistical analysis of tuberculous lesions (n=100)

Test evaluated (FNAC)	Histopathology positive	Histopathology negative	Total
FNAC positive	20 (True Positive)	3 (False Positive)	23
FNAC negative	1 (False Negative)	76 (True Negative)	77
Total	21	79	100

Sensitivity – 95.24%, Specificity – 96.20%, Positive predictive value – 86.96%, Negative Predictive value - 98.70%, Accuracy – 96.00%.

Malignancy proved to be most prevalent in the level III and level V B lymph node groups. T.B. was proved to be most commonly and significantly involved with the level II, V A, and level I B groups. However, lymph node involvement in the level I A group was not proved to be related with any specific disease.

Table 6. Etiological distribution of Lymph node (n=100)

Lymph Node	I A	I B	V A	II	III	V B	TOTAL	MALE	FEMALE
Tuberculous Lymphadenopathies		2	7	8	4		21	9	12
Granulomatous Lymphadenopathies	1	3	4	5	2	1	16	8	8
Reactive Lymphadenopathies	5	15	13	3	4	3	43	25	18
Metastatic Thyroid Carcinoma				3	1		4	1	3
Metastatic from Adenocarcinoma						1	1		1
Metastatic from Squamous Cell Carcinoma		3		2	6		11	8	3
Lymphoma				1	1	2	4	3	1
TOTAL	6	23	24	22	18	7	100	54	46

Table 7. Age and sex distribution of diseases (n=100)

Lymph Node	13-20		21-30		31-40		41-50		51-60		61-70		ALL AGE		
	M	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**TOTAL**
Tuberculous Lymphadenopathies	3	2	2	4	2	2	1	2	0	1	1	1	9	12	21
Granulomatous Lymphadenopathies	1	1	3	2	2	2	1	1	1	1	0	1	8	8	16
Reactive Lymphadenopathies	6	6	7	5	4	4	3	1	3	1	2	1	25	18	43
Metastatic Thyroid Carcinoma		1		2					1				1	3	4
Metastatic from Adenocarcinoma										1				1	1
Metastatic from Squamous Cell Carcinoma							1		4	2	3	1	8	3	11
Lymphoma			1		1			1			1		3	1	4
TOTAL	10	10	13	13	9	8	6	5	9	6	7	4	54	46	100

Table 8. Comparison with other studies - Carcinoma, Lymphoma, Tuberculosis.

CARCINOMA					
	Sensitivity	**Specificity**	**PPV**	**NPV**	**Accuracy**
Our Study	93.75%	100%	100%	98.82%	99%
Hodder et al. [8]	92%	83%	86%		
Hafez et al. [9]					100%
Prasad et al. [10]	97%	98.9%			
LYMPHOMA					
	Sensitivity	**Specificity**	**PPV**	**NPV**	**Accuracy**
Our Study	75%	98.96%	75%	98.96%	98%
Wang et al. [11]	93%	97%			
Petar et al. [12]	97.7%	85.7%			96%
TUBERCULOSIS					
	Sensitivity	**Specificity**	**PPV**	**NPV**	**Accuracy**
Our Study	95.24%	96.20%	86.96%	98.70%	96%
Gupta et al. [13]	100%	96.7%			
Prasad et al. [10]	83.3%	94.3%			

Discussion

At the head and neck unit, cervical lymphadenopathy is a common occurrence. Cervical lymph nodes are the most often enlarged and biopsied of all peripheral lymph nodes, according to numerous studies [3,4]. In our study, there is a male preponderance (54 male and 46 female) with female to male ratio 1:1.17. Most commonly affected age group is 21-30 followed by 13-20 and 31-40. This is comparable with study by Pandit et al. [14]. Most commonly affected age group in carcinoma is 51-60 followed by 61-70 and 21-30. This is similar to many studies which says, malignant metastasis to cervical node are seen commonly in older age group [14]. Similarly, Hafez and Tahoun [9] noticed that (77.4%) metastatic cases were seen over the age of 45 years.

In our study, cervical lymphadenopathy presents in all patients (100%), subsequently malaise (58%), fever (44%), weight loss (34%), anorexia (21%), difficulty in swallowing (4%), cough (4%), change in the voice (3%).

Commonest being the reactive lymphadenopathy (43%) subsequently by tuberculous lymphadenopathy (21%), granulomatous lymphadenopathy (16%), malignant lymphadenopathy (16%) and lymphoma (4%). This is comparable with Shakya et al. study [5], which indicated that in reactive hyperplasia, TB, malignancy, and granuloma, respectively, 50.4, 22.4, 4.8, and 10% of lymphadenopathy were involved. Khajuria et al. [6] found that reactive hyperplasia was most common (74.5%) in the first two life decades and lymph node due to tuberculosis common in second and third decades of life (58.9%).

Metastatic cervical lymphadenopathy constitutes 16% in decreasing order were metastasis from squamous cell carcinoma, thyroid carcinoma, adeno carcinoma.

In this study, the peak incidence of malignant lesions was in the 5th decade. This is identical to study by Ahmad et al. and Sarda et al. [7,15]. In this study most common cancers in younger than 40 years were thyroid cancers (4 cases) and lymphoma (4 cases). In this study, among the malignancy most commonly affected is metastasis from squamous cell carcinoma, which is similar to [7,16]. Males are more affected in this study than female in malignant secondary lymph nodes. Female -7 and male – 9. This is similar to study by Naeimi Mohammad et al. [17]. Reason may be, more addiction in male. In malignancy lymph node group, most commonly affected is level III.

In the present study, the size of malignant nodes was over 2 cm, benign nodes were less than 2 cm, in 79% cases and 83% cases respectively. These results were similar to that of Tilak et al. [18]. In this study tuberculous lymphadenopathy constitutes 21%. Females are more affected than male, M:F - 9:12. Most commonly affected age group is 21-30. These findings were in accordance with study by Biswas et al. [19]. Lymph node most commonly affected is level II followed by, V A. This is similar to Samar et al. [20] and Dandapat et al. [21]. Greater part of patients was with unilateral cervical lymph nodes, bilateral nodes are seen only in 12% cases.

In this study lymphoma constitutes 4%. Seen in all age group. Males are more affected than females 3:1. Commonly affected lymph node is V B, followed by II and

III. There was 1 case (25%) of Hodgkin's lymphoma and 3 cases (75%) of non-Hodgkin's lymphoma. The bulk of diagnostic issues documented in the literature stem from the inability to distinguish low-grade lymphomas from one another and from reactive lymphadenitis, as well as the inability to distinguish high-grade lymphomas from metastases [22-24].

In this study reactive lymphadenopathy is the commonest constituting 43% the total lymphadenopathy. Male-female ratio is 25:18. Commonly affected lymph node is I B followed by, V A. Age group affected is 13-20 and 21-30 with 12 cases in each category followed by 31-40. This is in accordance with study by Khajuria Ruchi et al. [6] which says in 1st two decades of life most common is reactive hyperplasia (74.5%). In this study granulomatous lymphadenopathy commonly seen in the 2nd and 3rd decade, equally affecting both sexes. Lymph node group affected are II, V A, I B, III, followed by I A, V B.

Rammeh et al. investigated the factors that influence the rate of non-diagnosis FNA and discovered that it is affected by the size of the lymph node (less than 1 cm), its submandibular location, and the aspirator's experience [25]. According to Ahn D et al., surgeons can achieve a low insufficient sampling rate and good diagnostic accuracy by receiving training and handling at least 100 ultrasound-guided FNAC patients [26].

On analyzing carcinomatous lesions, there was 1 false negative result and no false positive result. In this study for carcinomatous lesions, Sensitivity – 93.75%, Specificity – 100%, Positive predictive value – 100%, Negative Predictive value – 98.82%, Accuracy - 99%. On analyzing lymphomatous lesions, there was 1 false negative result and 1 false positive result. In this study for lymphomatous lesions, Sensitivity – 75.00%, Specificity – 98.96%, Positive predictive value – 75.00%, Negative Predictive value - 98.96%, Accuracy - 98%. On analyzing tuberculous lesions, there was 1 false negative result and 3 false positive results. In this study for tuberculous lesions, Sensitivity – 95.24%, Specificity – 96.20%, Positive predictive value – 86.96%, Negative Predictive value - 98.70%, Accuracy – 96.00%.

Limitations

FNAC has several limitations - sampling error. In these situations, repeat FNAC is recommended. Cytotechnologist and cytopathologist must be well trained and experienced.

Conclusions

FNAC is a highly accurate and specific first-line investigation study of cervical lymphadenopathy. FNAC is accurate and simple technique for the diagnosis. In the largest portion of instances, tubercular lymphadenitis can be figured out from reactive and granulomatous lymphadenitis. As a result, we'll be able to design our treatment accordingly. It can tell the difference between a lymphoma and a malignant lesion, avoiding unnecessary surgery. It is safe without any major complications and can be repeated if needed. For the screening of cervical lymphadenopathies, FNAC can be used as a low-cost diagnostic test.

Conflict of interest disclosure

There are no known conflicts of interest in the publication of this article. The manuscript was read and approved by all authors.

Compliance with ethical standards

Any aspect of the work covered in this manuscript has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

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