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Pathology

Utility of Fine Needle Aspiration Cytology as a Low Cost Diagnostic Tool in the Diagnosis of Cervical Lymphadenopathy- An Institutional Based Study

Dr. Pranjali Sejwal[1], Dr. Rajesh Jaiswal[2*]
[1]Assistant Professor, Department of Pathology, Index Medical College, Indore, Madhya Pradesh, India
[2]Junior Resident, Department of Pathology, Index Medical College, Indore, Madhya Pradesh, India

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***Corresponding author**
Dr. Rajesh Jaiswal

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Abstract: To observe the cytomorphological patterns in patients presenting with enlarged cervical lymph nodes, diagnosed by fine needle aspiration cytology (FNAC); their distribution with respect to age and gender; and to determine the accuracy of FNAC as a diagnostic procedure in cases of cervical lymphadenopathy. Out of all patients presenting with cervical lymphadenopathy from June 2017 to June 2018, in the Department of Pathology, Index medical college, Indore, Madhya Pradesh, 100 consecutive cases were enrolled in this study, following exclusion of all cases where FNAC smears were inadequate or suboptimal for diagnostic interpretation. Histopathological examination was conducted on small excision biopsy specimens / radical neck dissection where ever possible and diagnostic efficacy of FNAC was evaluated. Overall age range of the enrolled patients, presenting with cervical lymph nodes was 1 to 72 years, mean age being 35.7 years with male-female ratio, 1.6:1. Out of 100 cases, benign and malignant lesions comprised 77 and 23 cases, respectively. Most common Benign lesion was reactive hyperplasia (29%), while squamous cell carcinoma was the most common malignant lesion. The overall sensitivity, specificity, positive predictive value, negative predictive value & the diagnostic accuracy was 100%, 91.67%, 92%, 100% and 95.7% respectively. FNAC in the diagnoses of inflammatory and neoplastic diseases serves as a reliable, low cost, rapid diagnostic tool of reasonably good accuracy that can influence patient management in terms of early diagnoses, initiation of medical intervention and prevention of unnecessary surgery in patients.

Keywords: Fine needle aspiration cytology, cervical lymphadenopathy, low cost diagnostic tool.

INTRODUCTION

Lymph nodes are discrete ovoid structures and part of peripheral immune system located along the course of lymphatics. They act as mirror of underlying disease process [1]. Lymphadenopathy refers to nodes that are abnormal in size, consistency or number. Cervical lymphadenopathy is one of the most common presentations in inflammatory and neoplastic disorders. In general, lymph nodes greater than 1 cm in diameter are considered to be abnormal [2]. In lymph node fine needle aspiration cytology was first used by Greig and Gray in 1904 to diagnose trypanosomiasis and Guthrie in 1921 systemically performed Fine Needle Aspiration on lymph nodes for diagnostic purpose and further was used as a diagnostic tool by Martin and Ellis in 1930 [3]. Fine needle aspiration cytology is a simple, safe and cost effective procedure which enables to reach the diagnosis in short time[4]. The Fine Needle Aspiration can be done in outpatient department without anesthesia and there is no disfigurement or scar on the skin[3]. The biopsy of the cervical lymph node is always the gold standard. However, it is more resource intensive than FNAC, requires anesthesia, strict asepsis, theatre time and often leaves a scar. In contrast, FNAC of the cervical node is relatively simpler and offers quick reliable results[5]. The present study was therefore undertaken to observe the cyto-morphological patterns, their distribution among various age groups and gender, and to evaluate FNAC as a diagnostic tool in the patients with cervical lymphadenopathy, admitted as well as those attending outpatient departments, Index medical college, Indore, Madhya Pradesh, India.

MATERIALS & METHODS

The present study was conducted in the Department of Pathology at Index medical college, Indore, Madhya Pradesh, India from June 2017-June 2018. A total of 100 consecutive cases were enrolled in the study for cytological evaluation, following exclusion of all cases where lymph node size was inappropriate for the procedure, inadequate/ suboptimal smears for diagnostic interpretation. Further 47 cases,

were enrolled for histopathological evaluation. All cases of cervical lymphadenopathy irrespective of gender and age, referred from various in-patient and outpatient clinical departments were evaluated for clinical features, physical examination and local examination. The procedure of aspiration was explained to the patient including limitations and complications and consent was taken. Under strict aseptic conditions lymph node was aspirated with 22 gauge needle attached to a 10ml syringe without local anaesthesia. Two smears were prepared from each patient, the alcohol fixed smears were stained with PAP stain and air dried smears were stained with MGG stain. Special stain like Z-N stain was done for all suspected cases of tuberculosis. Lymph node excision biopsies and radical neck dissection specimens were obtained wherever possible. Formalin fixed samples of lymph nodes were processed in an automatic tissue processor for paraffin block preparation. From each block, 2-3 micron thick sections were prepared by using rotatory microtome and all sections were stained with routine Hematoxylin & Eosin staining methods. All slides were evaluated for histomorphological features by three independent observers. Various cytomorhological pattern observed were compiled into frequency tables and data was analysed for the distribution of cases with respect to age, gender. The diagnostic efficacy of FNAC in cervical lymphadenopathy was evaluated in terms of sensitivity, specificity, positive predictive value, negative predictive value and accuracy, by comparing cytological diagnoses with histopathological diagnosis.

RESULTS

Table 1 represents the frequency distribution of benign and malignant lesions diagnosed by FNAC which comprised 77 benign and 23 malignant cases. Among benign lesion Reactive lymphadenitis (Figure 1) was most common comprising (37.66%, n=29), followed by Tubercular lymphadenitis (Figure 2) and Granulamatous lymphadenits (18.18%, n=14, each), Necrotizing lymphadenitis (15.58%, n=12), Acute suppurative lymphadenitis (9.09%, n=7) and a single case of Sinus histiocytosis (1.29%, n=1). Out of 23 malignant lesions metastatic carcinomas and lymphomas contributed 69.57% (n=16) and 30.43% (n=7) respectively. Among the metastatic carcinomas Squamous cell carcinoma (Figure 3) was the most common morphological type observed in this study comprising (87.5%, n=14) followed by one case each of Poorly differentiated carcinoma and Adenocarcinoma (6.25%, n=1)). Hodgkin's lymphoma (Figure 4) was more common (17.39%, n=4) than Non- Hodgkin's lymphoma comprising (13.04%, n=3) of the total malignant cases.

Figure 5 and 6 represent the frequency distribution of benign lesions with respect to age and gender. Overall, benign lesions were more common in the age group 11-20 years (27.27%, n=21). Males were slightly more affected than females, male-female ratio being 1.8:1. However, granulomatous lymphadenitis affected both equally. Acute suppurative lymphadenitis was the most common benign lesion in 1-10 years age group (5.19%, n=4), tubercular lymphadenitis (Figure 2) and reactive hyperplasia (Figure 1) in 11-20 years age group (9.09%, n=7 and 11.69%, n=9 respectively), granulomatous lymphadenitis in 31-40 yrs (6.49%, n=5) and necrotizing lymphadenitis in 41-50 years age group (6.49%, n=5).

Figure 7 and 8 represent the frequency distribution of malignant lesions with respect to age and gender. Overall, malignant lesions were more common in the age group 51-60 yrs (30.43%, n=7). Both males and females were almost equally affected (1.09:1). Metastatic carcinomas were more common (69.57%, n=16) followed by lymphomas (30.43%, n=7). Among metastatic carcinomas squamous cell carcinomas (Figure 3) was the most common (21.74%, n=5) morphological type in the age group 51-60 yrs affecting females slightly more than males. A single case of adenocarcinoma and poorly differentiated carcinoma was observed in the age group 31-40 yrs (4.35%, n=1) and 41-50 yrs (4.35%, n=1) respectively. Cases of Hodgkin lymphomas (Figure 4) were observed between the age group 11-30 yrs (8.70%, n=2) and 51-60 yrs (8.70%, n=2), affecting males more than females (M:F-3:1). Most common age group for Non-Hodgkin lymphoma was 41-50 yrs (8.70%, n=2) with male-female ratio 2:1.

In the present study out of 47 cases which were diagnosed by FNAC and histopathology both, 23 (true positive) were diagnosed malignant by both diagnostic methods while 2 cases (False Positive) were diagnosed malignant by FNAC and benign by histopathology. Twenty two cases (True Negative) were diagnosed benign by both methods. No case was diagnosed as false positive (Table 2).

The overall sensitivity, specificity, PPV, NPV and diagnostic accuracy was 100%, 91.67%, 92%, 100% and 95.7% respectively, when cytopathological diagnosis was compared with histopathological diagnosis (Table 3).

Table-1: Frequency Distribution of various cervical lymph node lesions

Cytomorphological patterns	Types	No. of Cases (n)
Benign(n=77)	ASL	7
	TL	14
	GL	14
	NL	12
	RL	29
	SH	1
Malignant(n=23)	SCC	14
	PDC	1
	AdenoCa	1
	HL	4
	NHL	3

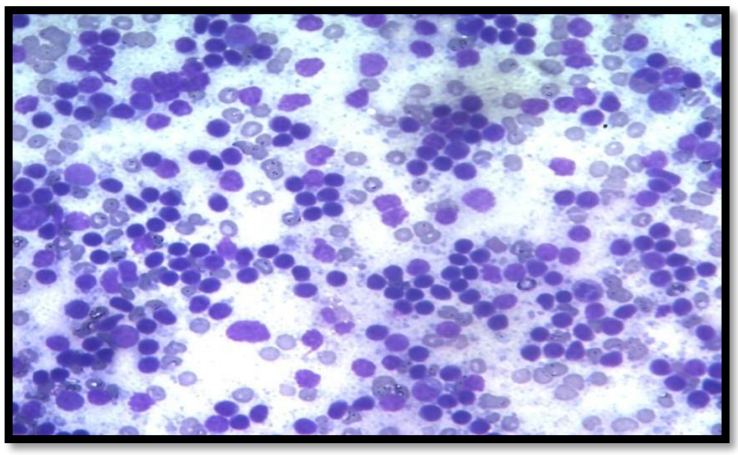

Fig-1: Reactive Lymphadenitis: Smears with heterogeneous population of lymphoid cells, presence of small and large lymphocytes, centrocytes, centroblasts, plasma cells, occasional immunoblasts and tingible body macrophages (MGG, 10X)

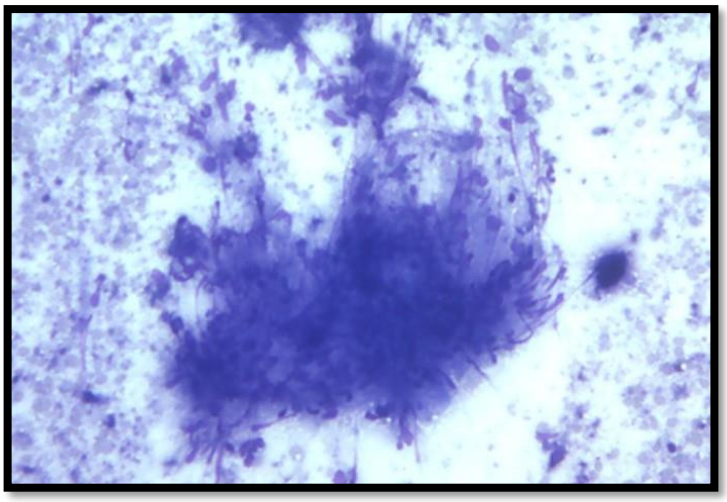

Fig-2: Tubercular lymphadenitis: Epitheloid cell granuloma in a background of caseous necrosis. AFB Positive (MGG, 10X)

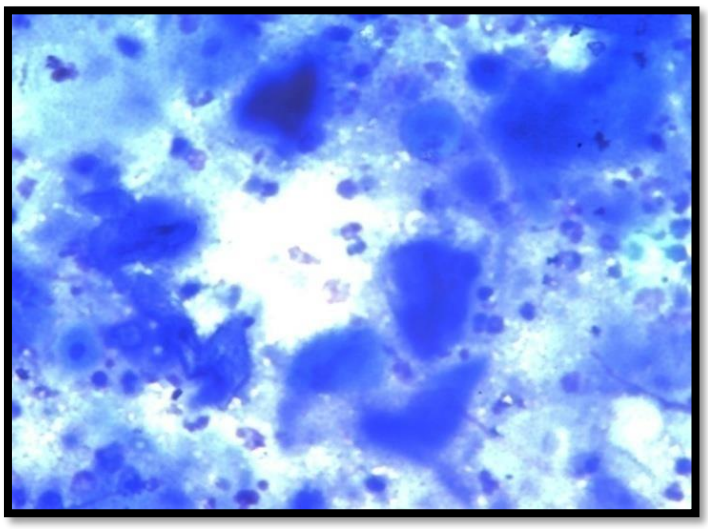

Fig-3: Squamous Cell Carcinoma. Polygonal cells with hyperchromatic enlarged nucleus, high N: C ratio, with abundant glassy blue cytoplasm(MGG, 40X)

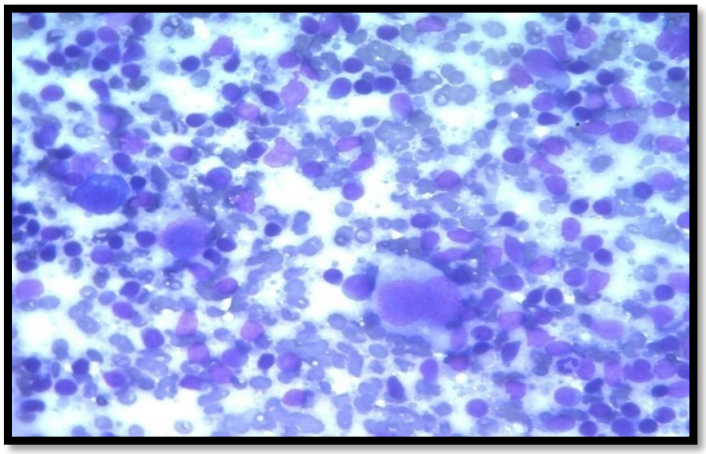

Fig-4: Hodgkin's Lymphoma: Binuclear Reed-Sternberg cells and mononuclear cells Hodgkin cells in a heterogeneous background of lymphoid cells (MGG stain, 40X)

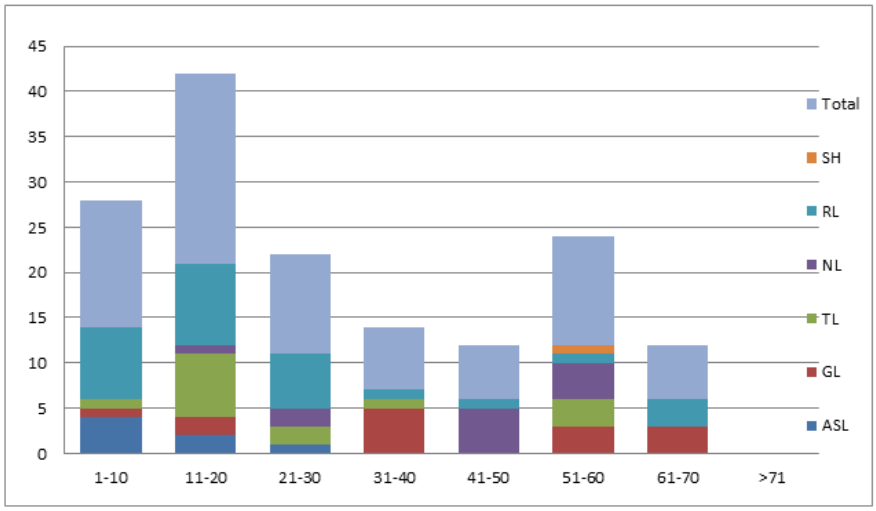

Fig-5: Frequency distribution benign cervical lymphadenopathy with respect to age
ASL: Acute suppurative lymphadenitis, GL: Granulomatous lymphadenitis, TL: Tubercular lymphadenitis, NL: Necrotizing lymphadenitis, RL: Reactive lymphadenitis, SH: Sinus Histiocytosis

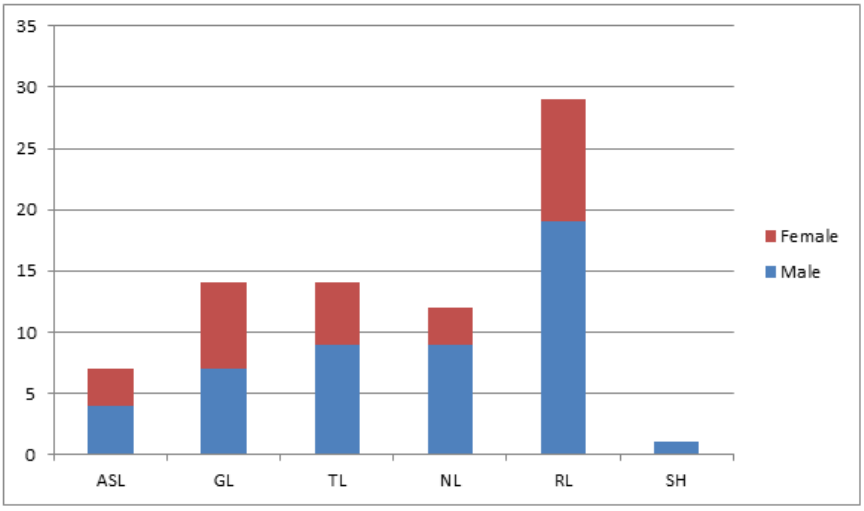

Fig-6: Frequency distribution of benign cervical lymphadenopathy with respect to gender

ASL: Acute suppurative lymphadenitis, GL: Granulomatous lymphadenitis, TL: Tubercular lymphadenitis, NL: Necrotizing lymphadenitis, RL: Reactive lymphadenitis, SH: Sinus Histiocytosis

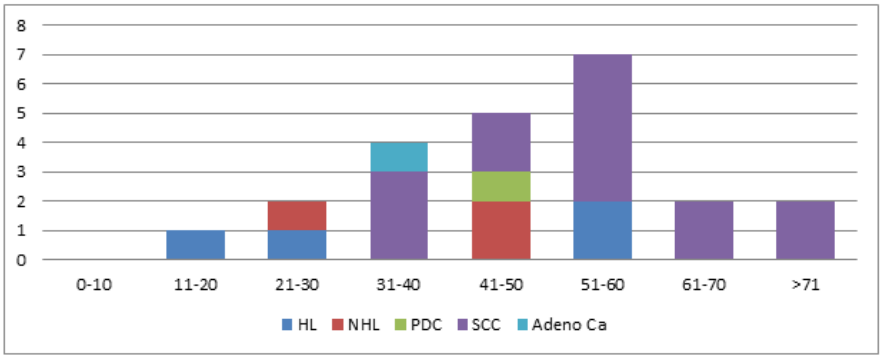

Fig-7: Frequency distribution of malignant cervical lymphadenopathy with respect to age.

HL: Hodgkin lymphoma, NHL: Non-Hodgkin lymphoma, PDC: Poorly differentiated Carcinoma, SCC: Squamous cell carcinoma, Adenoca: Adenocarcinoma

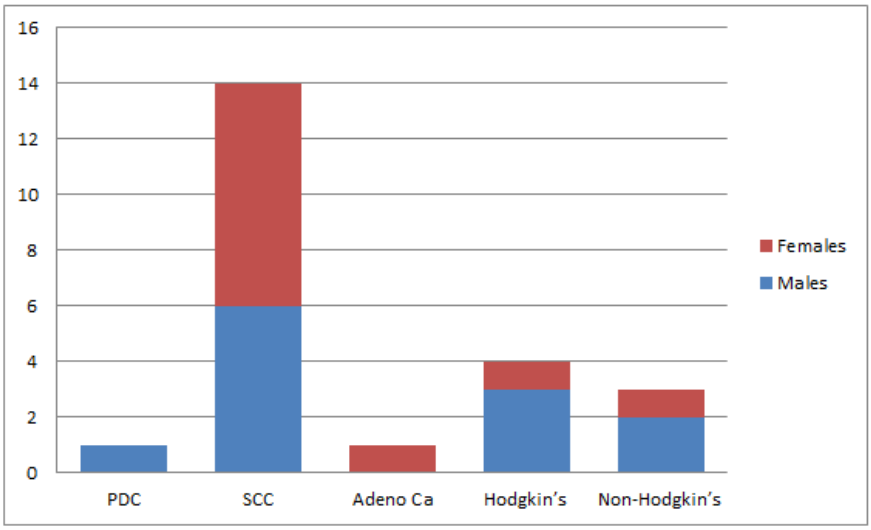

Fig-8: Frequency distribution of malignant cervical lymphadenopathy with respect to gender

HL: Hodgkin lymphoma, NHL: Non-Hodgkin lymphoma, PDC: Poorly differentiated Carcinoma, SCC: Squamous cell carcinoma, Adenoca: Adenocarcinoma

Table-2: Comparative analysis of cytological diagnoses by histopathological diagnoses in patients with cervical lymphadenopathy for benign and malignant cases.

Cytopathological diagnosis	Histopathological diagnosis	
	Malignant	Benign
Malignant	23 (TP)	2 (FP)
Benign	0 (FN)	22(TN)

TN: true negative cases; FN: false negative cases; FP: false positive cases; TP: true positive cases.

Table-3: Diagnostic validity of cytopathological diagnosis of cervical lymph nodes as compared with histopathological diagnosis in patients with cervical lymphadenopathy

Statistical parameters	Percentage (%)	95% CI (%)
Sensitivity	100	85.18-100
Specificity	91.67	73.00-98.97
PPV	92.0	73.97-99.02
NPV	100	84.56-100
Diagnostic Accuracy	95.7	76.54-100

Table-4: Comparison of sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of present study with different studies

Study / Year	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Diagnostic Accuracy (%)
Present study	100	91.67	92	100	95.7
Babu *et al*. [4]	89.5	100	100	90.5	91
Qadri *et al*. [13]	94.5	90.5	96.6	85.2	92.4
Qasmi *et al*. [10]	79.5	47.6	78	50	70
Hafez *et al*. [9]	90.9	67.2	82.6	81.3	100
Rakshan *et al*. [8]	75.8	96.6	94	85.1	88

DISCUSSION

The age of patients presenting with cervical lymphadenopathy ranged from 1year to 72 years which was almost in agreement to the observations of Patel *et al*.[6] (2 to 82 yrs)**,** Rahman *et al*. **[**7] (2 to 85 yrs) and Rakshan *et al*.**[**8] (1 to 87 yrs). The mean age of all patients observed was 35.7 years which was closely similar to that reported by Patel *et al*.[6] and Singh *et al*. [3]. Most common age group for cervical lymphadenopathy in this study was 11-20 yrs which was slightly lower in comparison to Hafez *et al*. [9] & Patel *et al*. [6]. In present study, the male to female ratio observed was 1.8:1 similar to that reported by Patel *et al*. [6]. Almost similar results were reported by Rakhshan *et al*.[8] Slightly higher ratio was observed by Qasmi *et al*. [10]. Reactive lymphadenitis was the most common lesion comprising 37.66% of total benign lesion and 29% of all the cases diagnosed by FNAC. Almost similar distribution of reactive lymphadenitis was reported by Patel et al.[6] and Singh et al.[3] out of total cases in their study. Next in order among benign lesion was tubercular lymphadenitis and granulomatous lymphadenitis each comprising 18.18% of the total benign lesion and 14% each of the total selected cases. Almost similar distribution of tubercular lymphadenitis was reported by Uwimama et al.[11] (18.1%) while much higher numbers were reported by Kumar et al.[5] and Aslam et al.[12] of the total cases in their study. Out of 23 malignant lesions metastatic carcinomas and lymphomas contributed 69.57% and 30.43% respectively however among all the 100 cases diagnosed by FNAC they comprised 16% and 7% respectively. Almost similar distribution of metastatic carcinoma was reported by Hafez et al.[9] while much of lower numbers were reported by Patel et al.[6], Singh et al.[3] of the total cases in their studies. Compared to the present study Aslam et al.[12] reported much higher number of metastatic carcinoma (34.6%) while almost similar distribution of lymphomas was reported by them (7.7%). In studies conducted by Aslam et al.[12] and Singh et al.[3] cases diagnosed as lymphoma were less than that observed in this study comprising 5.5% and 5.45% respectively. Among the metastatic carcinomas squamous cell carcinoma was the most common morphological type observed in this study as also reported by Singh et al.[3] (75%), Pavithra et al.[1] (56.25%), Hafez et al.[9] (45.20%), Rahman et al.[7] (33%) and Qadri et al.[13] (32.20%) although in varying numbers. In the present study metastatic adenocarcinoma and poorly differentiated carcinomas comprising 6.25% each out of metastatic lesions while 1% of the total cases diagnosed by FNAC. Qadri et

al.[13] and Hafez et al.[9] reported adenocarcinoma as the second most common metastatic tumor comprising 21.9% and 25.8% of the metastatic lesions. Poorly differentiated carcinoma was reported in 14.6% and 22.6% of the metastatic lesions diagnosed by them. In contrast to the present study and other studies Pavithra et al.[1] reported poorly differentiated carcinoma (25%) as the second most common morphological type than adenocarcinoma (9.5%). Among lymphomas, Hodgkin's lymphoma was more common in the present study comprising 17.39% of the total malignant cases and 4% of the total cases diagnosed by FNAC findings being in agreement to that reported by Sen et al.[14] and Singh et al.[3] although in varying numbers who reported 8% and 4% cases of hodgkin lymphoma respectively. In contrast to the present study and several other studies Pavithra et al.[1], Hafez et al.[9], and Qadri et al.[13] reported non-Hodgkin lymphoma as the common morphological type out of total cases in their study comprising 0.63%, 2.6% and 2% respectively.

In the present study for the diagnosis of malignant and benign lesions fine needle aspiration cytology had an overall diagnostic sensitivity of 100% and specificity of 91.67%. The positive predictive value was 92.0% and Negative predictive value was 100%. The overall diagnostic accuracy of FNAC in patients with cervical lymphadenopathy for malignant and benign lesions was 90%. These values were compared with the studies of different authors Rakshan *et al*.[8], Hafez *et al*.[9], Qasmi *et al*.[10], Qadri *et al*.[13] and Babu *et al*.[4] (Table 4).

In present study, one false negative case was diagnosed as poorly differentiated carcinoma on cytology and Non-Hodgkin's lymphoma on histopathology because of pseudoaggregation of tumor cells leading to misinterpretation of clusters as seen in cases of carcinomas, such cases may be misdiagnosed as Non-Hodgkin's lymphoma non representative sampling can lead to presentation of singly scattered large pleomorphic cells which causes difficulty in diagnosis on FNAC. On the contrary Hafez *et al*.[9] reported a case as NHL, large cell type on cytology which was diagnosed as metastatic undifferentiated large cell carcinoma on histopathology, so they concluded that the presence of lymphoid globules (cytoplasmic fragments) in the smear background as well as lobulated nuclei favoured the diagnosis of lymphoma and some degree of cell aggregation favoured the metastatic carcinoma diagnosis but immunostaining was required in such cases to reach the definite diagnosis. In the present study, two false positive cases were reported which were diagnosed as NHL on cytopathology and reactive on histopathology because of non-representative sampling from germinal centre which can lead to misdiagnosis of Non-Hodgkin's lymphoma specially centrocytic and centroblastic type because in both conditions cells with centroblasts and centrocyte like features present as the predominant cell population. The study supports the view of Bhasker *et al*.[15] that the most difficult area in the diagnosis of lymph node diseases by FNAC is Non-Hodgkin lymphoma. Complete clinical work up, immunocytochemistry and flow cytometry can enhance the accuracy of the procedure in the diagnosis of lymphoma. Rakhshan *et al*.[8] also suggested that anicillary methods such as IHC in the evaluation in aspiration smear can optimize the accuracy of the method. Weiss *et al*.[16] suggested that immunohistochemical and other special studies may be very helpful in distinguishing reactive follicular hyperplasia and follicular lymphoma. Determination of bcl-2 is the single most useful ancillary study, being consistently negative in reactive follicular hyperplasia, but positive in about 90% of cases of follicular lymphoma.

CONCLUSION

In the present study, Reactive hyperplasia, tubercular and granulomatous lymphadenitis were observed as the common causes of benign cervical lymphadenopathy while metastatic squamous cell carcinoma was the most common cause of malignant cervical lymphadenopathy. Fine needle aspiration cytology is a simple, easy, diagnostic tool with reasonable good sensitivity and specificity in the diagnosis of benign and malignant lesions of lymph nodes. The procedure has low diagnostic accuracy in differentiating benign and malignant lesions. However, for typing of lesions with fine needle aspiration cytology may be difficult in certain cases specially lymphomas, therefore, it may be used as the initial investigation tool which can be followed by histopathology and immunohistochemistry for confirmation. Negative results on fine needle aspiration cytology does not rule out a neoplastic pathology which may be due to non-representative sampling and should be followed by biopsy for for definitive diagnosis by histopathological evaluation.

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