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RESEARCH ARTICLE

FINE NEEDLE ASPIRATION CYTOLOGY AND HISTOPATHOLOGICAL CORRELATION IN DIAGNOSING LYMPH NODE LESIONS

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ABSTRACT

Introduction: A lymph node is an oval or kidney-shaped organ of the lymphatic system, present widely throughout the body. Lymph nodes lie along the course of lymphatic vessels. Most lymphadenopathy is due to a benign self-limited disease such as viral infections, and adenopathy is secondary to an increase in normal lymphocytes and macrophages in response to an antigen. Other less common mechanisms responsible for adenopathy include lymphadenitis, neoplasia or storage diseases. Tubercular lymphadenitis is one of the commonest causes in developing countries. FNAC allows the pathologist to see the cells aspirated from the lesion. In contrast to large bore needle biopsy techniques, FNAC does not allow evaluation of the morphology. In some instances, aspirated cells can be evaluated by flow cytometry or with immunologic markers. ***Methods:*** This study was conducted at the Sher-i-kashmir Institute of Medical Sciences (SKIMS) Srinagar, Kashmir (India) in the Department of Pathology. The study was a prospective study of 2 years i.e. from June 2016 to May 2018. Cases presenting with lymphadenopathy where FNAC was done and underwent subsequent biopsy were studied. ***Results:*** This study included total of 120 patients who presented with lymphadenopathy. Out of 120 patients, there were 76(63.3%) males and 44 (36.7%) females. Male: Female ratio was 1.73:1. For Non-Hodgkin's Lymphoma FNAC showed sensitivity of 97.22%, specificity of 96.55%, positive predictive value of 92.11% and accuracy of 89.74%. For Hodgkin's Lymphoma FNAC showed sensitivity of 85.71%, specificity of 98.84%, positive predictive value of 92.31% and accuracy of 97%. For Metastatic tumors, FNAC showed sensitivity of 91.67%, specificity of 98.81%, positive predictive value of 97.06% and accuracy of 96.67%. For Benign Lesions, FNAC showed sensitivity of 93.94%, specificity of 97.73%, positive predictive value of 93.94% and accuracy of 96.69%. ***Conclusion:*** FNAC proved to be a safe, accurate, inexpensive and patient friendly in the effort to establish diagnosis in patients with lymphadenopathy.

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INTRODUCTION

A lymph node is an oval or kidney-shaped organ of the lymphatic system, present widely throughout the body. Lymph nodes lie along the course of lymphatic vessels. Lymph nodes have a highly cellular cortex and medulla which contains network of minute lymphatic channels (sinuses) through which lymph from afferent lymphatics is filtered, to be collected at hilum by efferent lymphatics (Roitt *et al.,* 2001). A young adult contains upto 450 lymph nodes of which 60-70 are found in head and neck, 100 in thorax, 250 in abdomen and pelvis. Lymph nodes are particularly numerous in the neck, mediastinum, posterior abdominal wall, abdominal mesenteries, pelvis, proximal region of limbs (Susan Stranding, 2005).

Lymph nodes are regional, and each group of them corresponds to a particular region of the body and reflects abnormalities in that region. Common areas where swollen lymph nodes are more prominent and therefore more readily noticeable are post auricular, cervical, supraclavicular, inguinal, sub mandibular and axillary regions. The etiology varies from an inflammatory process to a malignant condition (Hirachand *et al.,* 2009). Most lymphadenopathy is due to a benign self-limited disease such as viral infections, and adenopathy is secondary to an increase in normal lymphocytes and macrophages in response to an antigen. Other less common mechanisms responsible for adenopathy include lymphadenitis, neoplasia or storage diseases. Tubercular lymphadenitis is one of the commonest causes in developing countries (Shakya *et*

al., 2009). Fine needle aspiration cytology (FNAC) of lymph node has become an integral part of the initial diagnosis and management of patients with lymphadenopathy due to early availability of results, simplicity, and, minimal trauma with less complication (Keith *et al.,* 2007). FNAC is widely used as first line investigation for the diagnosis of lymphadenopathy. FNAC has been advocated as a useful method in comparison to more expensive surgical excision biopsies in developing countries with limited financial and health care resources (Das, 1999). It almost offers an accurate diagnosis for reactive lymphoid hyperplasia, infectious disease, granulomatous lymphadenitis, and metastatic malignancy. Thus, it can avoid the need for excisional biopsy in most cases and allow rapid onset of therapy (Howlett *et al.,* 2007). FNAC allows the pathologist to see the cells aspirated from the lesion. In contrast to large bore needle biopsy techniques, FNAC does not allow evaluation of the morphology. In some instances, aspirated cells can be evaluated by flow cytometry or with immunologic markers. In every circumstance, FNAC is a test and should be interpreted with the entire clinical circumstances. False negative and false positive FNAC results are reported in almost every series. Therefore, reliance upon FNAC findings at the expense of clinical, radiographic, or other findings is unsafe (Salgarelli *et al.,* 2009).

MATERIAL AND METHODS

This study was conducted at the Sher-i-kashmir Institute of Medical Sciences (SKIMS) Srinagar, Kashmir (India) in the Department of Pathology. The study was a prospective study of 2 years i.e. from June 2016 to May 2018. Cases presenting with lymphadenopathy where FNAC was done and underwent subsequent biopsy were studied. FNAC was performed using 20 ml syringe attached to a 22 gauge needle. The needle was allowed to move back and forth into different parts of the lymph node several times before withdrawal. The specimens were expelled on to cover glasses, air dried and stained with May Grunwald Giemsa stain and other stains like Papanicolaou (Pap) stain. For histopathology, biopsy specimens received were fixed in 100% formalin, studied grossly, photographed, processed and studied in detail using H&E and various special stains wherever indicated.

RESULTS

This study included total of 120 patients who presented with lymphadenopathy. Out of 120 patients, there were 76(63.3%) males and 44 (36.7%) females. Male: Female ratio was 1.73:1. In this study age ranged from 5 to 80 years. Mean age was 44 years. Maximum number of cases were seen in the age group 51-60 years (28 cases, 23.33%), followed by age group 21-30 years (24 cases, 20%), age group 61-70 years (20 cases, 16.67%), age group 41-50 years (19 cases, 15.83%), age group 31-40 years (17 cases, 14.17%), age group 11-20 years (9 cases, 7.50%), age group 71-80 years (2 cases, 1.67%), age group 01-10 years (1 case, 0.83%) respectively. Maximum no. of aspirations (Table 1.) were done from Cervical nodes 74 cases (61.67%) followed by Axillary nodes 19 cases (15.83%) followed by Supraclavicular nodes 15 cases (12.50%) followed by Inguinal nodes 9 cases (7.50%) followed by Retroperitoneal lymph nodes 2 cases (1.67%) respectively. Of the 120 patients subjected to FNAC, histological diagnosis revealed 36 cases of Non-Hodgkin's Lymphoma constituting 30% of all cases, Metastatic lesions in 36 cases constituting 30% of all cases, 34 cases turned out to be Benign constituting 28.33% of all cases, 14 cases of Hodgkin's Lymphoma constituting 11.67% of all cases.

Table 1. Distribution of cases according to site of lymphadenopathy

Site of lymphadenopathy	No. of Patients	Percentage
Cervical	74	61.67%
Axillary	19	15.83%
Supraclavicular	15	12.50%
Inguinal	10	8.33%
Retroperitoneal	2	1.67%
Total	120	100.0%

Correlation between FNAC and histopathology (Table 2)

1. Metastatic tumors (Fig 1,2,3&4)

Out of a total of 36 cases of metastatic tumors, FNAC and histopathology were concordant in 33 cases. Two cases of metastatic poorly differentiated carcinoma were misinterpreted in FNAC as Non-Hodgkin's Lymphoma and one case of metastatic poorly differentiated carcinoma was misinterpreted as hodgkins lymphoma. One case of hodgkins lymphoma was misinterpreted as metastatic poorly differentiated carcinoma. On statistical analysis, FNAC had a sensitivity of 91.67%, specificity of 98.81%, positive predictive value of 97.06% and accuracy of 96.67% for metastatic tumors.

2. Hodgkin's Lymphoma (Fig. 5 &6)

Out of a total of 14 cases of Hodgkin's Lymphoma, FNAC and histopathology were concordant in 12 cases. One case of Hodgkin's Lymphoma was misinterpreted in FNAC as Granulomatous Lymphadenitis and another one as metaststic poorly differentiated carcinoma. One case of metastatic poorly differentiated carcinoma was misinterpreted as hodgkins lymphoma. On statistical analysis, FNAC had a sensitivity of 85.71%, specificity of 98.84%, positive predictive value of 92.31% and accuracy of 97% for Hodgkin's Lymphoma.

3. Non-Hodgkin's Lymphoma (Figure 7 &8)

Out of a total of 38 cases of NHL, FNAC and histopathology were concordant in 35 cases. One case of NHL was misinterpreted in FNAC as reactive lymphadenitis. Besides there were two cases of metastatic poorly differentiated carcinoma misinterpreted as NHL and one case of granulomatous lymphadenitis misinterpreted as NHL in FNAC. On statistical analysis, FNAC showed sensitivity of 97.22%, specificity of 96.43%, positive predictive value of 92.11% and accuracy of 96.67% for Non-Hodgkin's Lymphoma

4. Benign Lesions (Fig 9&10)

Out of a total of 34 cases of benign lesions, FNAC and histopathology were concordant in 31 cases. Two cases of glandular tissue inclusions were misinterpreted in FNAC as lymphoepithelial lesion and another as reactive lymphadenitis. One case of granulomatous lymphadenitis was misinterpreted in FNAC as Non-Hodgkin's Lymphoma. Besides one case of Non-Hodgkin's Lymphoma was misinterpreted in FNAC as reactive lymphadenitis and another case of Hodgkin's Lymphoma was misinterpreted as granulomatous lymphadenitis in FNAC.

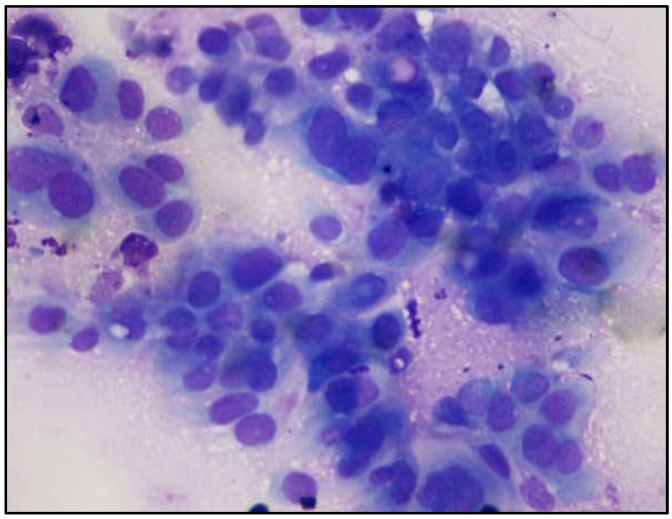

Fig. 1. Aspiration smear from a case of metastatic deposits of adenocarcinoma in lymph node showing acinar arrangement of malignant cells

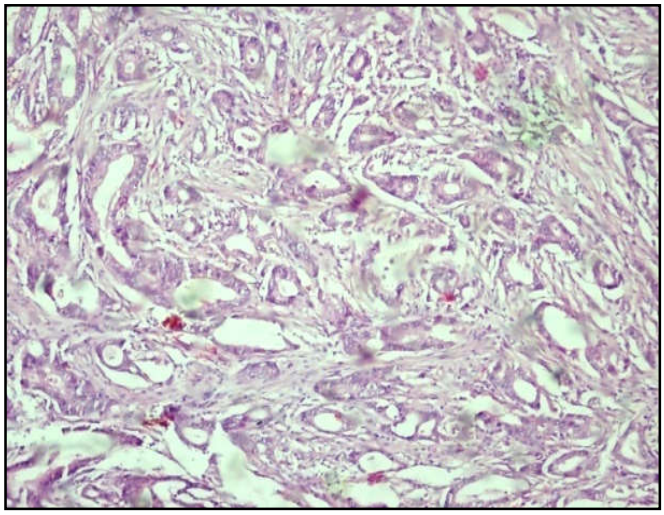

Fig. 2.Microphotograph of a section of metastatic deposits of adenocarcinoma showing glandular arrangement of malignant epithelial cells

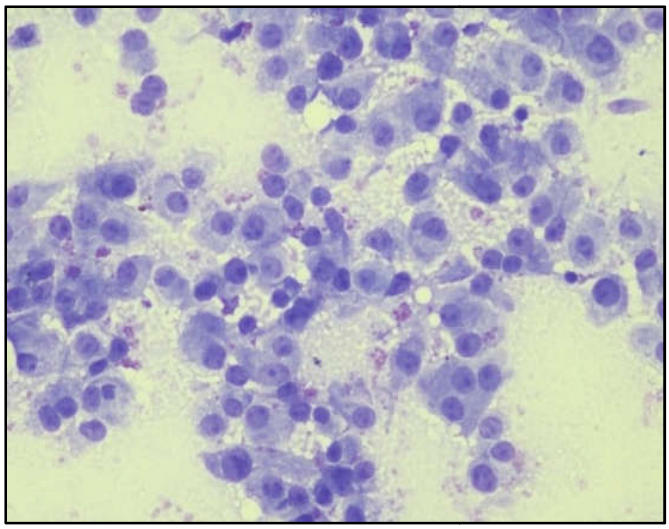

Fig. 3. Aspiration smear from a case of metastatic deposits of malignant melanoma in lymph node showing plasmacytoid cells with prominent nucleoli

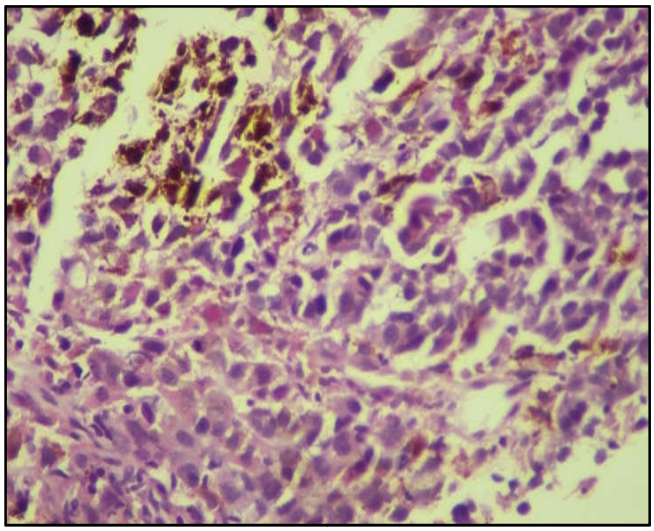

Fig. 4. Microphotograph of a section of metastatic deposits of malignant melanoma in lymph node showing pleomorphic nuclei with prominent nucleoli and pigment deposits

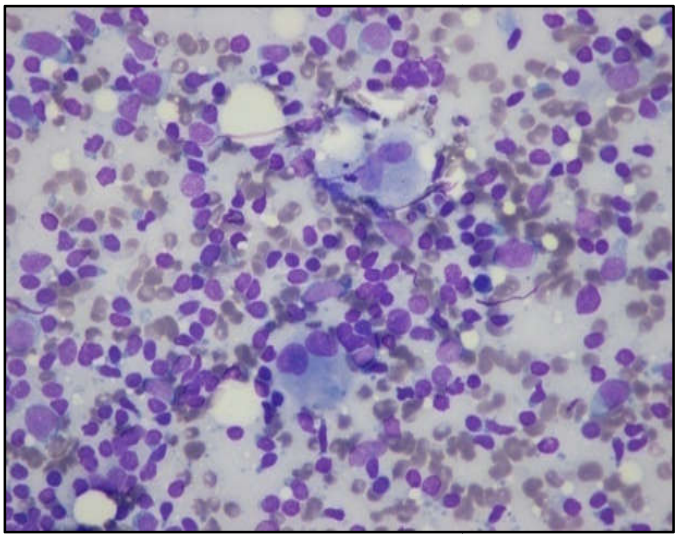

Fig. 5. Aspiration smear from a case of Hodgkin's lymphoma showing scattered binuclear Reed-sternberg cells with a background of lymphocytes

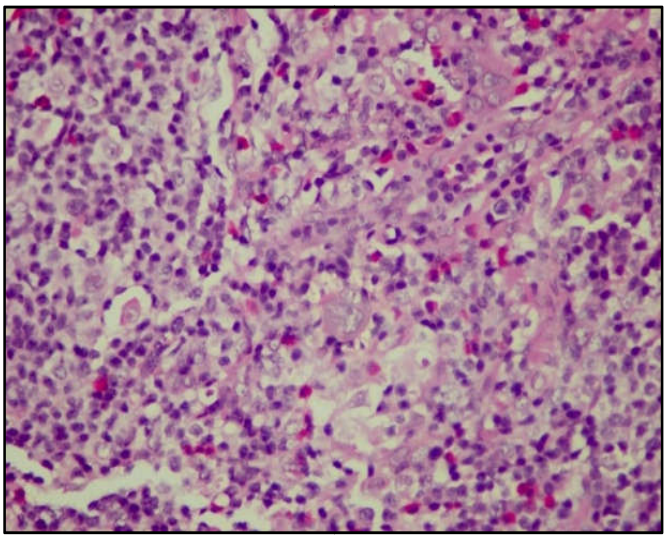

Fig. 6. Microphotograph of a section of Hodgkin's lymphoma showing binuclear and mono nuclear Hodgkin cells in a cellular background of lymphocytes and eosinophils

Table 2. Correlation between histopathology and FNAC

Diagnosis	Sensitivity (%)	Specificity (%)	PPV (%)	Accuracy (%)
Non-Hodgkin's Lymphoma	97.22	96.55	92.11	89.74
Hodgkin's Lymphoma	85.71	98.84	92.31	97.00
Metastatic tumors	91.67	98.81	97.06	96.67
Benign Lesions	91.18	97.67	93.94	95.83

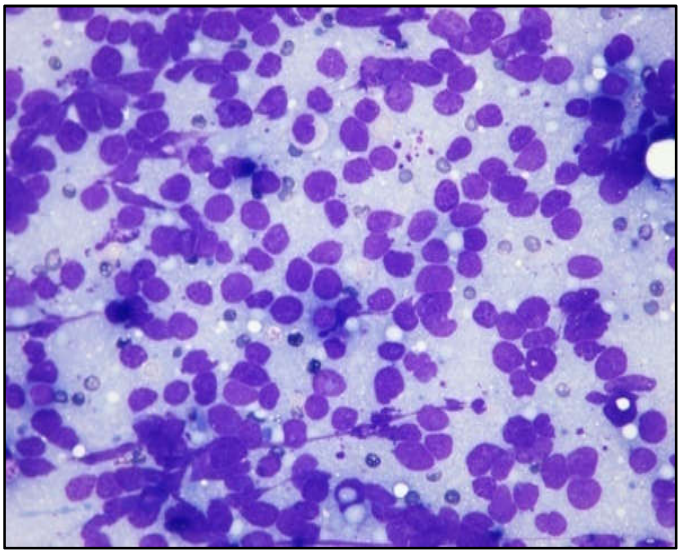

Fig. 7. Aspiration smear from a case of Non Hodgkin's lymphoma showing scattered monotonous population of cells with granular chromatin and scant cytoplasm

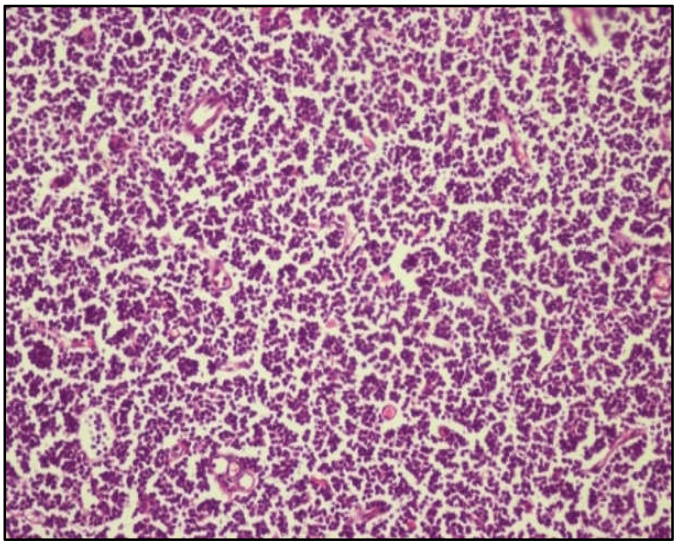

Fig. 8. Microphotograph of a section of Non Hodgkin's lymphoma showing diffuse architectural effacement of lymph node with infiltration by monomorphic population of cells

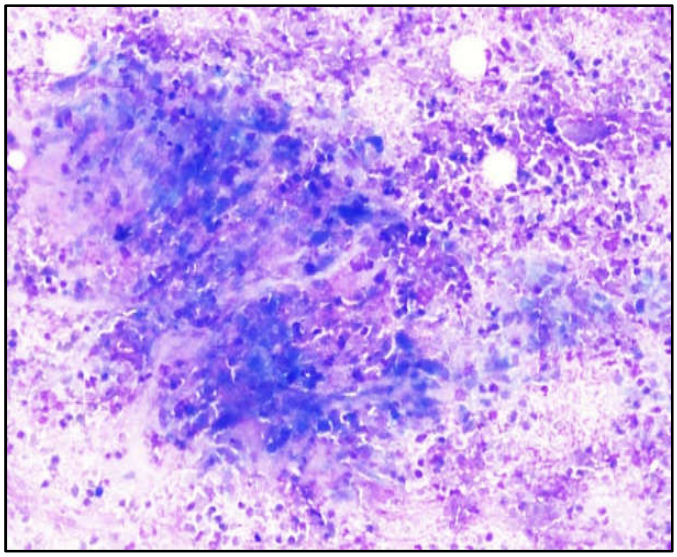

Fig. 9. Aspiration smear from a case of Granulomatous lymphadenitis showing well formed granuloma in a necrotic background

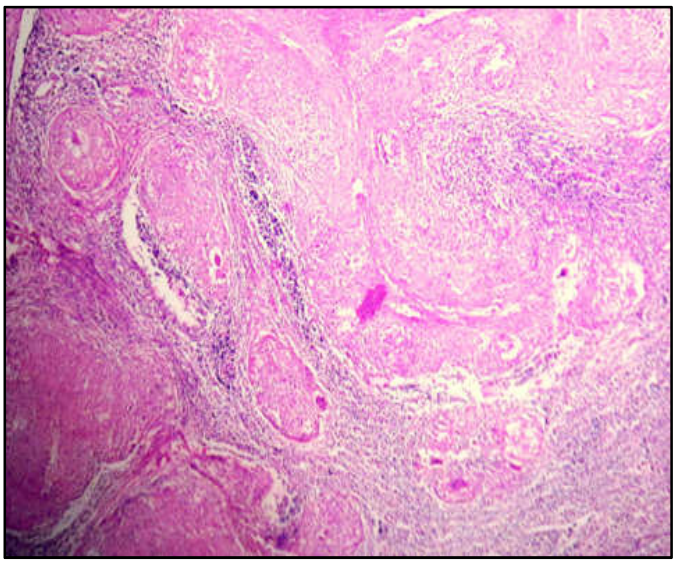

Fig. 10. Microphotograph of a section of Granulomatous lymphadenitis showing well formed caseating granulomas with giant cell formation

On statistical analysis, FNAC had sensitivity of 91.18%, specificity of 97.67%, positive predictive value of 93.94% and accuracy of 95.83% for benign lesions. For Non-Hodgkin's Lymphoma FNAC showed sensitivity of 97.22%, specificity of 96.55%, positive predictive value of 92.11% and accuracy of 89.74%. For Hodgkin's Lymphoma FNAC showed sensitivity of 85.71%, specificity of 98.84%, positive predictive value of 92.31% and accuracy of 97%. For Metastatic tumors, FNAC showed sensitivity of 91.67%, specificity of 98.81%, positive predictive value of 97.06% and accuracy of 96.67%. For Benign Lesions, FNAC showed sensitivity of 93.94%, specificity of 97.73%, positive predictive value of 93.94% and accuracy of 96.69%.

DISCUSSION

Lymphadenopathies are common presentation of patients of all ages and both sexes (Young *et al.,* 1981). Although the finding of lymphadenopathy sometimes raises fears about serious illness, it is usually a result of benign infectious causes. Most patients can be diagnosed on the basis of a careful history and physical examination. The causes may include various microbial infections, hematological diseases, neoplastic lesions (malignant or benign), and various connective tissue disorders (Mahbod *et al.,* 2002). FNAC of lymph node has become an integral part of the initial diagnosis and management of patients with lymphadenopathy due to early availability of

results, simplicity, and, minimal trauma with less complication. FNAC has also been advocated as a useful method in comparison to more expensive surgical excision biopsies in developing countries with limited financial and health care resources (Hafez and Tahoun, 2011). In our study malignant lymphadenopathy constituted the majority of cases. overall 86 (71.67%) of cases were malignant. Benign lesions constituted the remaining 34(28.33%) cases. In the study by Al Aiwan *et al.* (1996) benign cases comprised of 55.3% of all cases, while malignant involvement was observed in the remaining 44.7%. In the study by Qadri *et al.* (2012) profile of lymphadenopathy in kashmir valley, the cytological features were observed to be benign in 798 cases (50.5%), and malignant in 738 cases (46.7%). This high number of malignant cases as compared to other studies, where benign cases comprise the majority of cases, may be explained by the fact that a majority of cases which underwent FNAC were non malignant, however only those cases where on cytology, smears were suggestive of or suspicious of malignancy and subsequently underwent histopathological examination were included. Our study did not include those cases of FNAC whose subsequent histopathological examination was not done. Besides our institute is the only Regional Cancer Centre in the state due to which we receive large number of cases of malignant lymphadenopathy. Out of 86 patients with malignant lymphadenopathy (including Hodgkin's lymphoma and non-Hodgkin's lymphoma), FNAC of 81 cases were confirmed histologically, showing an overall accuracy of 91.67%, sensitivity of 95.29%, specificity of 82.86% and a positive predictive value of 93.10%. In the study by Al Aiwan *et al.* (1996) they found an overall accuracy of 89.6% for malignant lymphadenopathy which is almost the same as in our study (91.67%). In our study there were a total of 36 cases of non-Hodgkin's lymphoma, FNAC and histopathology were concordant in 35 cases. One case of non-Hodgkin's lymphoma was misinterpreted in FNAC as reactive lymphadenitis. Besides there were two cases of metastatic poorly differentiated carcinoma misinterpreted as non-Hodgkin's lymphoma and one case of granulomatous lymphadenitis misinterpreted as non-Hodgkin's lymphoma in FNAC. On statistical analysis, FNAC showed sensitivity of 97.22%, specificity of 96.55%, positive predictive value of 92.11% and accuracy of 89.74% for non-Hodgkin's lymphoma. In the study by Al Aiwan *et al.* (1996) they found an overall accuracy of 88.5% for non-Hodgkin lymphoma which is almost the same as in our study(89.74%).

In the study by Madan *et al.* (2014) sensitivity of FNAC in diagnosing NHL was 100% where as specificity was 95.7% which is consistent with our study. Out of a total of 14 cases of Hodgkin's Lymphoma, FNAC and histopathology were concordant in 12 cases. One case of Hodgkin's Lymphoma was misinterpreted in FNAC as Granulomatous Lymphadenitis and another one as metastatic poorly differentiated carcinoma. One case of metastatic poorly differentiated carcinoma was misinterpreted as Hodgkin's lymphoma. On statistical analysis, FNAC had a sensitivity of 85.71%, specificity of 98.84%, positive predictive value of 92.31% and accuracy of 97% for Hodgkin's Lymphoma. In the study of Al Aiwan *et al.* (1996), accuracy of FNAC in diagnosing Hodgkin's lymphoma was 76.9%. In the study by Madan *et al.* (2014), FNAC showed a sensitivity of 78.6% in diagnosing HL whereas the specificity was 100% which is consistent with our study. Out of a total of 36 cases of metastatic tumors, FNAC and histopathology were concordant in 33 cases. Two cases of metastatic poorly differentiated carcinoma were misinterpreted in FNAC as Non-Hodgkin's Lymphoma and one case of metastatic poorly differentiated carcinoma was misinterpreted as Hodgkin's lymphoma. One case of Hodgkin's lymphoma was misinterpreted as metastatic poorly differentiated carcinoma. On statistical analysis, FNAC had a sensitivity of 91.67%, specificity of 98.81%, positive predictive value of 97.06% and accuracy of 96.67% for metastatic lesions. In the study of Al Aiwan *et al.* (1996) Accuracy of FNA in diagnosing metastatic tumours was 96.0% which is almost the same as in our study (96.67%). In the study by Singh *et al.* (2017), sensitivity and specificity of FNAC in metastatic carcinoma proved to be 97.5% and 100% respectively which is consistent with our study.

Conclusion

FNAC proved to be a safe, accurate, inexpensive and patient friendly in the effort to establish diagnosis in patients with lymphadenopathy

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