

**LIMITATIONS IN CYTODIAGNOSIS- AN INSTITUTIONAL STUDY**Prasad Uma<sup>1</sup>, K. Rajani<sup>2</sup><sup>1</sup>Associate Professor, Department of Pathology, Andhra Medical College, Vishakapatnam, Andhra Pradesh.<sup>2</sup>Assistant Professor, Department of Pathology, RIMS Medical College, Srikakulam, Andhra Pradesh.**ABSTRACT****BACKGROUND**

Fine needle aspiration cytology has replaced open biopsy in majority of the palpable lesions. Differentiation between benign and malignant lesions is possible with this procedure with low cost, but has certain limitations. In the present study, the limitations of cytodiagnosis in various palpable lesions in the body is analysed.

The aim of the study was to know the prevalence of various lesions which could be diagnosed on cytology, its limitations and need for histopathological examination.

**MATERIALS AND METHODS**

A prospective observational study was conducted in the Department of Pathology at tertiary care centre in rural area. 1200 cases attending for fine needle aspiration for a period of 2 years from January 2014 to December 2015 was taken up for the study. After obtaining informed consent from the patients, fine needle aspiration was performed using a 22 - 24 gauge needle with 10 mL syringe and long lumbar puncture needle for guided aspirations. Smears were fixed in 95% isopropyl alcohol and stained with Haematoxylin and Eosin. Air dried smears were stained with May-Grunwald stain and special stains were done wherever necessary. The tissue was subjected for histopathological examination wherever indicated and results tabulated. Overall diagnostic accuracy, sensitivity and specificity of cytology as a diagnostic procedure was calculated.

**RESULTS**

The overall accuracy of diagnosing granulomatous lymphadenitis and lymphoproliferative disorders on cytology was 65.71%. The overall accuracy of diagnosing fibrocystic disease of breast proliferative type was 80% and ductal carcinoma of breast was 100% on cytology. The overall accuracy of diagnosing follicular adenoma of thyroid was 36.20% and malignancy was 100% on cytology. The overall accuracy of diagnosing both benign and malignant lesions of salivary gland was 100% on cytology. The overall accuracy of diagnosing soft tissue tumours was 88.67% on cytology. In lesions of bone, skin and ultrasonographic-guided lesions of abdomen, the overall accuracy was 100%. On Pap smears, the overall accuracy was 84.48%.

**CONCLUSION**

In cases of granulomatous lymphadenitis without significant necrosis and negative AFB, fibrocystic disease of breast, follicular adenoma of thyroid, vascular tumours, soft tissue tumours with nuclear atypia and cases of atypical squamous cell of undetermined significance and high-grade intraepithelial lesions on Pap smears need histopathological examination for accurate diagnosis.

**KEYWORDS**

Cytodiagnosis, Limitations, Overall Accuracy, Various Lesions.

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**BACKGROUND**

Many of the clinicians feel that fine needle aspiration cytology (FNAC) remains the most important contribution of the technique from a practice point of view. It helps in differentiating benign and malignant lesions and offers specific diagnosis in inoperable cases as a guide to rational treatment. Although, the use of FNAC has widened, there are pressures for specialisation in this discipline with limitations.<sup>[1]</sup> The fundamental requirements on which the success of FNAC depends are representativeness and adequacy of the sample. Haematoma, infarction, capsule

pseudoinvasion and pseudomalignant reparative reactions cause real diagnostic difficulties.<sup>[2]</sup> The aims and objective of the study was to know the prevalence of various lesions, which could be diagnosed on cytology, limitations of cytodiagnosis in various lesions of lymph node, breast, thyroid, soft tissue, bone, salivary glands, skin, pap smears, ultrasonographic-guided intraabdominal aspirations and the need for histopathological examination.

**MATERIALS AND METHODS**

A prospective observational study was conducted in the Department of Pathology at a tertiary care centre in rural area. 1200 cases attending for fine needle aspiration in the rural hospital for 2 years from January 2014 to December 2015 was taken up for the study. After obtaining informed consent from the patients, fine needle aspiration was performed using a 22 - 24 gauge needle with 10 mL syringe and a long lumbar puncture needle for guided aspirations. Smears were fixed in 95% Isopropyl alcohol and stained with Haematoxylin and Eosin. Air dried smears were stained with May-Grunwald stain and special stains for acid fast bacilli and

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*Corresponding Author:*

Prasad Uma,

Q No.49-3-3, Lalithanagar,

Visakhapatnam-530016,

Andhra Pradesh.

E-mail: usha1966411@gmail.com

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fungus were done wherever necessary. Aspirations from lymph node, breast, thyroid, soft tissue, bone and joints, salivary glands, skin, Pap smears and ultrasonographic-guided intraabdominal lesions were analysed. The tissue was subjected for histopathological examination wherever indicated and results tabulated.

### Statistical Methods

To calculate overall diagnostic accuracy, sensitivity and specificity of cytology as a diagnostic procedure taking histopathology as a gold standard.

### RESULTS

A total of 1200 aspirates during this period were analysed. Lymph node aspirates were 30.83% (n= 370), breast aspirates were 12.91% (n= 155), thyroid aspirates were 20.08% (n= 241), soft tissue aspirates were 8.83% (n= 106), salivary gland aspirates were 2.08% (n= 25), bone and joint lesions were 1.41% (n= 17), skin aspirates were 2.08% (n=25). USG-guided aspirates from intraabdominal lesions were 3.08% (n= 37) and Pap smears were 9.66% (n= 116).

### Lymph Node Lesions

Non-specific lymphadenitis and tuberculous lymphadenitis were the common lesions and on follow-up responded very well to antibiotics. In all the cases of metastatic lymph nodes, the primary tumour could be detected and treated appropriately [Table 1].

19 cases of granulomatous lymphadenitis without necrosis and negative for acid fast bacilli and 16 cases of lymphoproliferative disease were subjected for histopathological examination as they needed definitive diagnosis.

In 19 cases of granulomatous lymphadenitis on cytology: 7 cases were tuberculous lymphadenitis, 5 cases were fungal granulomas, 5 were Hodgkin's lymphoma and 2 cases were squamous cell carcinomatous deposits on histopathology.

In 16 cases of lymphoproliferative disorders on cytology: 11 were Non-Hodgkin's Lymphoma, 3 were non-specific lymphadenitis and 2 were Kikuchi's lymphadenitis on histopathology [Table 2]. Sensitivity, specificity and overall diagnostic accuracy of cytology in diagnosing lymph node lesions were 47.82%, 58.33% and 65.71% respectively.

### Breast Lesions

The commonest lesion on cytology was fibroadenosis (20.64%) followed by fibroadenoma (19.35%). Ductal carcinoma constituted 9.67% of cases and gynaecomastia in 7.74% of cases. Fibrocystic disease of proliferative type was 6.45% and atypical ductal hyperplasia in 9.67% of cases [Table 3].

There was 100% cytohistopathological correlation in cases of fibroadenoma of breast, ductal carcinoma and gynaecomastia. Fibrocystic disease of proliferative type showed 80% correlation, 2 cases showed atypical ductal hyperplasia on histopathology. In phyllodes tumour, 9 cases were benign phyllodes and 4 cases were of intermediate grade. In 73.33% cases of atypical ductal hyperplasia correlated on histopathology and 4 cases showed features of epithelial hyperplasia [Table 4]. Sensitivity, specificity and overall diagnostic accuracy of breast lesions were 100%, 100% and 89.47% respectively.

### Thyroid Lesions

Nodular goitre constituted 34.85% of cases, Hashimoto's thyroiditis (28.63%) and follicular neoplasm (24.06%) of cases [Table 5].

In malignant lesions, there was 100% cyto-histopathological correlation. The correlation percentage in cases of nodular goitre was 94%, 5 cases turned out to be papillary carcinoma on histopathology. The correlation percentage was 36.20% in follicular neoplasm. Out of 58 cases, 21 cases were diagnosed as follicular adenoma and 32 were adenomatoid goitre and 5 cases of follicular variant of papillary carcinoma [Table 6]. Sensitivity, specificity and overall diagnostic accuracy of cytology in thyroid lesions is 50%, 100% and 75.58% respectively.

### Salivary Gland Lesions

The common lesions in salivary gland aspirations were sialadenitis (32%), pleomorphic adenoma (32%) and adenoid cystic carcinoma (24%) [Table 7].

In cases of pleomorphic adenoma, the correlation percentage was 75%, 2 cases showed features of carcinoma ex-pleomorphic adenoma on histopathology [Table 8].

Sensitivity, specificity and overall diagnostic accuracy of salivary gland lesions were 81.81%, 100% and 88.23% respectively.

### Soft Tissue Lesions

Lipoma (63.20%) were the common lesions in soft tissue aspirates followed by neurofibroma (11.32%) [Table 9].

In ten cases of vascular tumours on cytology, 4 cases were haematoma on histopathology. Out of ten cases with diagnosis of benign spindle cell tumour, 2 cases showed intermediate grade lesion- dermatofibrosarcoma protuberans. Four cases with diagnosis of lipoma on cytology, 2 were atypical lipoma and 2 were liposarcoma. Two cases with diagnosis of neurofibroma on cytology were diagnosed as low-grade malignant peripheral nerve sheath tumour on histopathology [Table 10].

Sensitivity, specificity and overall diagnostic accuracy of soft tissue lesions are 46.66%, 100% and 88.67% respectively.

### Bone and Joint Lesions

The common lesions in aspirates from bone and joint were ganglion (58.82%) followed by 29.41% cases of giant cell tumour of bone [Table 11].

Sensitivity, specificity and overall diagnostic accuracy of cytology in bone and joint lesions were 100%, 100% and 86.66% respectively [Table 12].

### Skin Lesions, USG-Guided Intraabdominal Lesions and Pap Smears

Keratinous cysts were the commonest skin lesions. Sensitivity, specificity and overall diagnostic accuracy of cytology in skin lesions were 100% [Table 13, 14].

In USG-guided intraabdominal lesions, majority of the aspirates were from liver. Received biopsy only on malignant lesions. Sensitivity, specificity and overall diagnostic accuracy of cytology in USG-guided lesions were 100% [Table 15].

In 20 cases of Atypical squamous cell of undetermined significance (ASCUS) on Pap smears, 12 cases were chronic non-specific cervicitis with metaplastic change and 8 cases

were mild dysplasia on histopathology. In 25 cases with low grade squamous intraepithelial lesion (LSIL) on cytology 80% correlated with histopathology, but 5 cases turned out to be non-specific cervicitis on histopathology. In 18 cases with high-grade squamous intraepithelial lesion (HSIL), 8 cases showed severe dysplasia and 10 cases showed squamous cell carcinoma on histopathology. Sensitivity, specificity and overall diagnostic accuracy of cytology in Pap smears were 92.68%, 93.33% and 84.48% [Table 16].

Lesions	No. of Cases	Percentage
Non-specific lymphadenitis	188	50.81
Tuberculous lymphadenitis	116	31.35
Granulomatous lymphadenitis	19	5.13
Metastatic lymph nodes	31	8.39
Lymphoproliferative disease	16	4.32
<b>Total</b>	<b>370</b>	<b>100</b>

**Table 1. Lymph Node Aspirates- 370 Cases**

Lesions	No. of Cases	Correlated with Histopathology	Not Correlated with Histopathology	% Correlation
Granulomatous lymphadenitis	19	12	7	63.15
Lymphoproliferative disorder	16	11	5	68.75
<b>Total</b>	<b>35</b>	<b>23</b>	<b>12</b>	

**Table 2. Cytohistopathological Correlation in Lymph Node Aspirates- 35**

Lesions	No. of Cases	Percentage
Chronic mastitis	19	12.29
Fibroadenoma	30	19.35
Fibroadenosis	32	20.64
Fibrocystic disease of non-proliferative type	9	5.8
Fibrocystic disease of proliferative type	10	6.45
Phyllodes tumour	13	8.38
Atypical ductal hyperplasia	15	9.67
Ductal cell carcinoma	15	9.67
Gynaecomastia	12	7.74
<b>Total</b>	<b>155</b>	<b>100</b>

**Table 3. Cyodiagnosis in Breast Lesions- 155**

Lesions	Number of Cases	Correlated with Histopathology	Not Correlated with Histopathology	% Correlation
Fibroadenoma	30	30	-	100
Fibrocystic disease of proliferative type	10	8	2	80
Phyllodes tumour	13	9	4	69.23
Atypical ductal hyperplasia	15	11	4	73.33
Ductal carcinoma	15	15	-	100
Gynaecomastia	12	12	-	100
<b>Total</b>	<b>95</b>	<b>85</b>	<b>10</b>	

**Table 4. Cytohistopathological Correlation in Breast Lesions- 95**

Lesions	No. of Cases	Percentage
Nodular goitre	84	34.85
Colloid cyst	10	4.14
Hashimoto's thyroiditis	69	28.63
Thyroglossal cyst	5	2.07
Follicular neoplasm	58	24.06
Hurthle cell neoplasm	5	2.07
Papillary carcinoma thyroid	8	3.31
Medullary carcinoma thyroid	2	0.82
<b>Total</b>	<b>241</b>	<b>100</b>

**Table 5. Cyodiagnosis in Thyroid Lesions- 241**

Lesions	Number of Cases	Correlated with Histopathology	Not Correlated with Histopathology	% Correlation
Nodular goitre	84	79	5	94
Colloid goitre	10	10	-	100
Thyroglossal cyst	5	5	-	100
Follicular neoplasm	58	21	37	36.20
Hurthle cell neoplasm	5	5	-	100
Papillary carcinoma thyroid	8	8	-	100
Medullary carcinoma thyroid	2	2	-	100
<b>Total</b>	<b>172</b>	<b>130</b>	<b>42</b>	

**Table 6. Cytohistopathological Correlation in Lesions of Thyroid- 172**

Lesions	No. of Cases	Percentage
Sialadenitis	8	32
Pleomorphic adenoma	8	32
Mucoepidermoid carcinoma	3	12
Adenoid cystic carcinoma	6	24
<b>Total</b>	<b>25</b>	<b>100</b>

**Table 7. Cyodiagnosis of Salivary Gland Lesions- 25**

Lesions	Number of Cases	Correlated with Histopathology	Not Correlated with Histopathology	% Correlation
Pleomorphic adenoma	8	6	2	75
Mucoepidermoid carcinoma	3	3	-	100
Adenoid cystic carcinoma	6	6	-	100
<b>Total</b>	<b>17</b>	<b>15</b>	<b>2</b>	

**Table 8. Cytohistopathological Correlation in Salivary Gland Lesions- 17**

Lesions	No. of Lesions	Percentage
Vascular tumours	10	9.4
Benign spindle cell tumours	10	9.4
Lipoma	67	63.20
Neurofibroma	12	11.32
Round cell sarcoma	4	3.77
Leiomyosarcoma	2	1.88
Extramedullary plasmacytoma	1	0.94
<b>Total</b>	<b>106</b>	<b>100</b>

**Table 9. Cyodiagnosis of Soft Tissue Lesions- 106**

Lesions	Number of Cases	Correlated with Histopathology	Not Correlated with Histopathology	% Correlation
Vascular tumours	10	6	4	60
Benign spindle cell tumours	10	8	2	80
Lipoma	67	63	4	94.02
Neurofibroma	12	10	2	83.33
Round cell sarcoma	4	4	-	100
Leiomyosarcoma	2	2	-	100
Extramедullary plasmacytoma	1	1	-	100
<b>Total</b>	<b>106</b>	<b>94</b>	<b>12</b>	

**Table 10. Cytohistopathological Correlation in Soft Tissue Lesions- 106**

Lesions	No. of Cases	Percentage
Ganglion	10	58.82
Giant cell tumour	5	29.41
Metastasis	2	11.76
<b>Total</b>	<b>17</b>	<b>100</b>

**Table 11. Cytodagnosis in Bone and Joint Lesions- 17**

Lesions	Number of Cases	Correlated with Histopathology	Not Correlated with Histopathology	% Correlation
Ganglion	10	8	2	80
Giant cell tumour of bone	5	5	-	100
<b>Total</b>	<b>15</b>	<b>13</b>	<b>2</b>	

**Table 12. Cytohistopathological Correlation in Bone and Joint Lesions- 15**

Lesions	No. of Lesions	Percentage
Keratinous cysts	11	44
Cold abscess	8	40
Lepromatous leprosy	2	8
Skin metastasis	1	4
Benign adnexal tumours	3	12
<b>Total</b>	<b>25</b>	<b>100</b>

**Table 13. Cytodiagnosis of Skin Lesions- 25**

Lesions	Number of Cases	Correlated with Histopathology	Not Correlated with Histopathology	% Correlation
Keratinous cysts	11	11	-	100
Skin metastasis	1	1	-	100
Lepromatous leprosy	2	2	-	100
Benign adnexal tumours	3	3	-	100
<b>Total</b>	<b>17</b>	<b>17</b>	<b>-</b>	

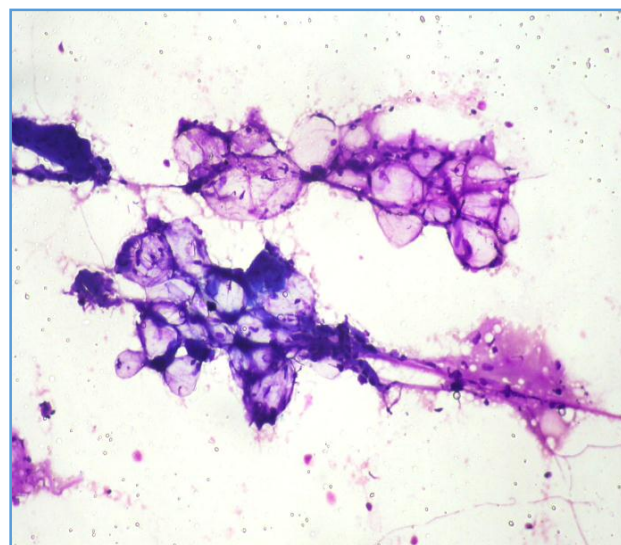
**Table 14. Cytohistopathological Correlation of Skin Lesions- 17**

Lesions	No. of Lesions	Percentage
<b>Liver</b>		
Hepatocellular carcinoma	4	12.90
Adenocarcinoma metastasis	7	22.58
Hepatic abscess	2	6.45
<b>GIT</b>		
Adenocarcinoma	12	38.70
<b>Retroperitoneum</b>		
Leiomyosarcoma	2	6.45
<b>Ovary</b>		
Serous carcinoma	4	12.90
<b>Total</b>	<b>31</b>	<b>100</b>

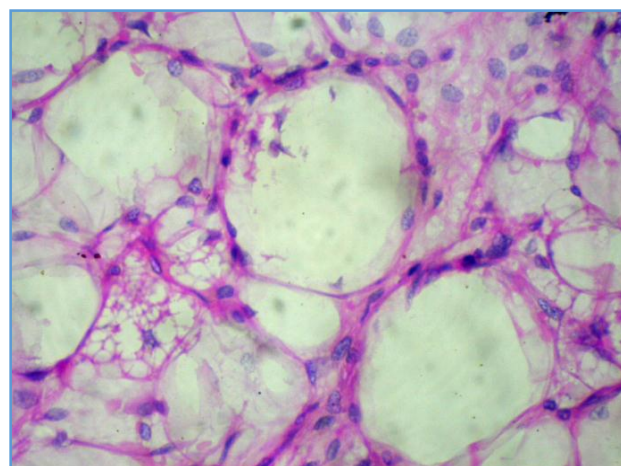
**Table 15. Ultrasonography Guided Intraabdominal Lesions- 31**

Lesions	No. of Lesions	Percentage
NILM	53	45.68
ASCUS	20	17.24
LSIL	25	21.55
HSIL	18	15.51
<b>Total</b>	<b>116</b>	<b>100</b>

**Table 16. Pap Smear Cytology- 116**

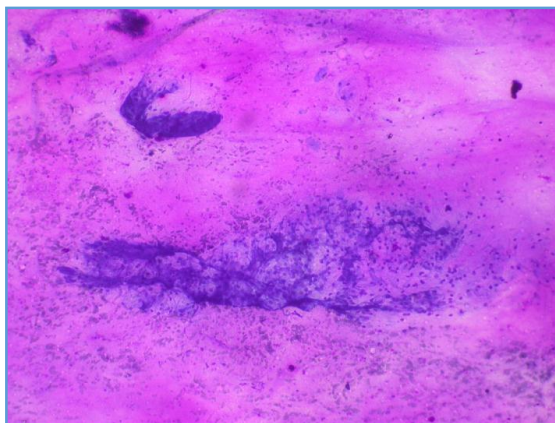


**Figure 1. Cytological Diagnosis of Lipoma (H and E, 100X)**

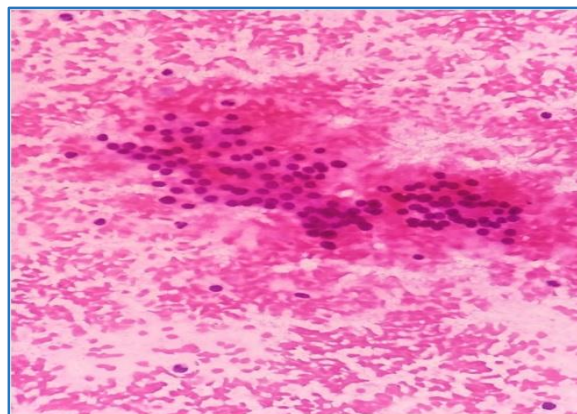


**Figure 1A. Histopathological Diagnosis of Atypical Lipoma (H and E, 400X)**

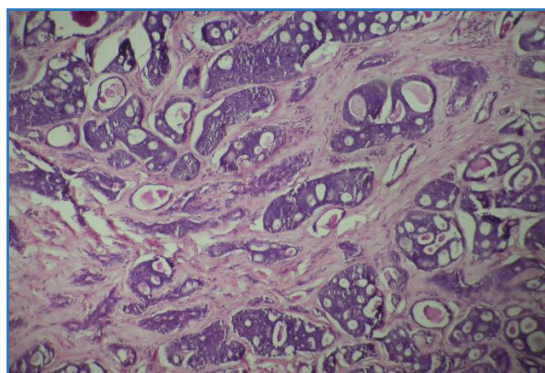




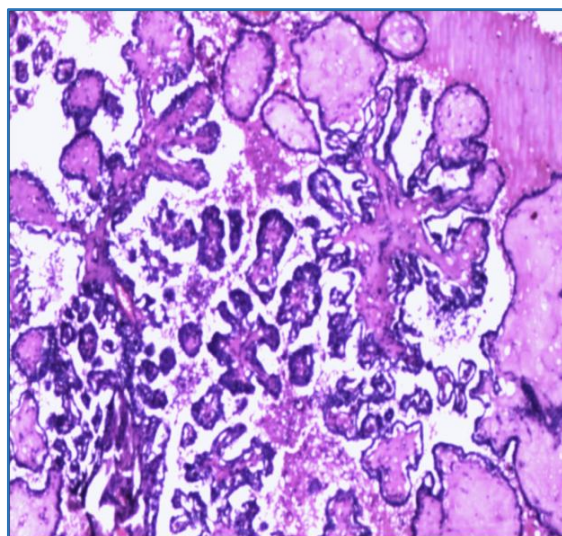
**Figure 2. Cytological Diagnosis of Pleomorphic Adenoma (H and E, 100X)**



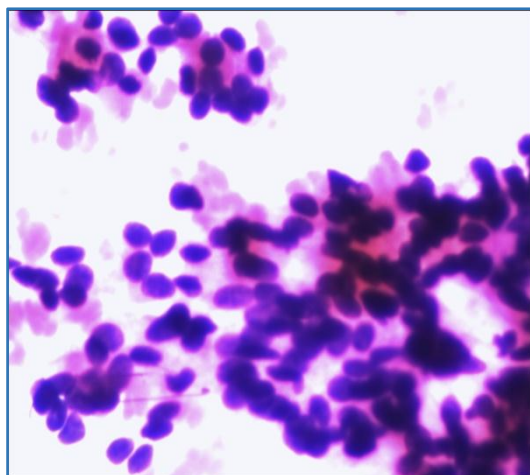
**Figure 4. Cytological Diagnosis of Nodular Goitre (H and E, 400X)**



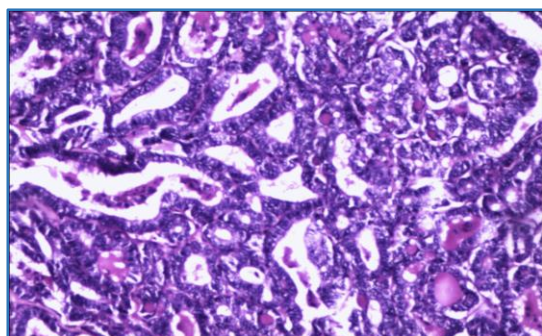
**Figure 2A. Histopathological Diagnosis of Adenoid Cystic Carcinoma (H and E, 100X)**



**Figure 4A. Histopathological Diagnosis of Papillary Carcinoma (H and E, 400X)**



**Figure 3. Cytological Diagnosis of Follicular Adenoma (H and E, 400X)**



**Figure 3A. Histopathological Diagnosis of Follicular Variant of Papillary Carcinoma (H and E, 400X)**

**DISCUSSION**

**Lymph Nodes**

The main purpose of doing an FNA examination is to decide whether surgical excision is needed in cases of abnormal peripheral lymphadenopathy. Cytological examination can decide whether the lymphadenopathy is due to reactive hyperplasia, metastatic malignancy, granulomatous inflammation and malignant lymphoma. In granulomatous lymphadenitis, the criteria for diagnosis is presence of epithelioid cells, multinucleated giant cells, both foreign body and Langhans giant cell and presence or absence of necrosis. Granulomatous lymphadenitis can be classified as non-infectious and infectious. Non-infectious causes are sarcoidosis and sarcoid-like reaction. Infectious causes can be classified as suppurative and non-suppurative. Suppurative granulomatous disorders include tularaemia, cat scratch disease, and Yersinia. Non-suppurative granulomatous disorders include tuberculosis, tuberculoid leprosy and syphilis.<sup>[3]</sup> Presence of caseous necrosis with clinical correlation goes in favour of tuberculous lymphadenitis. AFB stain may or may not show bacilli, negative images is sometimes seen. If smears show necrotic debris and plenty of polymorphs with histiocytes, negative AFB stain and culture with clinical diagnosis of tuberculous lymphadenitis poses a challenge to the pathologists. Infection

with atypical mycobacteria, cat scratch disease, lymphogranuloma venereum and HIV infection has to be considered depending on the site of lymph node involved. Granulomatous inflammation has been associated with metastatic lymphadenopathy and lymphoma. In such cases, interpretation on cytology should be done with great caution.

Sachin A Badge et al,<sup>[4]</sup> in their study documented tubercular lymphadenitis in 48.70% of cases. All showed bacilli with ZN stain followed by granulomatous lymphadenitis in 32.90%, reactive hyperplasia in 8.06% and metastatic carcinoma in 3.87%. The chances of finding AFB are greater when pus or caseous material is aspirated.<sup>[5]</sup>

Those cases lacking the typical finding and showing scattered epithelioid cells with or without granuloma or only necrotic material with neutrophilic infiltration were diagnosed as tuberculous lymphadenitis, even though AFB was negative in majority of the studies.<sup>[6]</sup> Excisional biopsy is potentially hazardous, as it gives rise to sinus formation. In developing countries, tuberculous infection is the commonest and even in the absence of typical cytological features trial of antituberculous therapy can be done.<sup>[7]</sup> In a region where tuberculous infection is common and other granulomatous diseases are rare, the presence of a granulomatous feature in FNAC is highly suggestive of tuberculosis. The literature on the use of FNAC to diagnose tuberculous cervical lesions is mainly from the developing countries, where mycobacterial infections are prevalent.<sup>[7]</sup>

In the present study analysed 370 cases of lymph node aspiration, 50.81% were non-specific lymphadenitis, 31.35% cases were tuberculous lymphadenitis with typical features of caseous necrosis and epithelioid granulomas. Positive bacilli on ZN stain and on follow-up responded to antituberculous therapy. Nineteen cases of granulomatous lymphadenitis with few epithelioid granulomas, no necrosis and negative for bacilli on ZN stain were subjected for histopathological examination: 7 were due to tuberculous lymphadenitis, 5 cases were due to fungal infection, 5 cases were offered the diagnosis of Hodgkin's lymphoma and 2 cases showed metastatic deposits.

In the study by Sachin A Badge et al,<sup>[4]</sup> lymph node aspirates (3.87%) showed metastatic deposits in 3.87% of cases. In studies by Patel et al and Ghartimagar et al, metastatic deposits were seen in 27.06% and 18% of cases respectively.<sup>[8,9]</sup> In the study by Sachin A Badge et al,<sup>[4]</sup> Lymphomas constituted only 0.96% cases. This was in accordance with the study by Khan et al (2%).<sup>[10]</sup> Although, their prevalence is low, they pose a great diagnostic challenge. Age of the patient and polymorphous population of cells and atypical cells should raise a suspicion of Hodgkin's lymphoma. Inadequate samples and fibrosed nodes in advanced disease may be the cause of lack of Reed-Sternberg cells.

In the present study, metastatic lymphadenitis was seen in 8.37% of cases and lymphoproliferative disorders in 4.32% of cases. All the 16 cases with cytological diagnosis of lymphoproliferative disorder was subjected to histopathology and 11 cases turned out to be Hodgkin's lymphoma and 3 cases infectious mononucleosis and 2 cases with diagnosis of Kikuchi's disease with sensitivity of 47.82%, specificity of 58.33% and diagnostic accuracy of 65.71%.

## Breast

Fine needle aspiration cytology of breast in the hands of experienced cytopathologists have high degree of diagnostic accuracy.<sup>[11,12]</sup> In the present study for easy interpretation, reporting of breast lesions was divided into 5-tier system: C1- for inadequate smears, C2- for benign lesions, C3- suspicious probably benign, C4- suspicious probably malignant and C5- malignant breast lesions.

Inadequate smears were not seen in the present study as the aspiration was repeated at least twice, which yielded adequate material for interpretation. C2 category is for smears that are usually cellular showing the characteristic patterns of different benign lesions. No atypical or malignant features are present. Usually duct configurations, myoepithelial cells and bipolar nuclei are visible. Inflammatory background may or may not be seen. In this group the lesions were chronic mastitis (10.96%), fibroadenosis (20.64%), fibrocystic disease with non-proliferative epithelium (5.8%), fibroadenoma (19.35%), phyllodes tumour (8.38%) and gynaecomastia in 7.74% of cases. The commonly encountered cytological features of fibroadenoma are fibromyxoid stroma, staghorn clusters and numerous single bare nuclei being seen in 90%, 78.6% and 64.6% of cases, respectively. The absence of any components of the diagnostic triad and low cellularity are the common pitfalls in the diagnosis of fibroadenoma. Similar features were recorded by SM Kollur et al.<sup>[13]</sup>

Category C3 and C4 are the grey zones. In C3 category benign ductal epithelial cells are seen but with crowding, pleomorphism and discohesion. C4 is reserved for aspirate where atypical features are obvious, but there are features of hypocellularity. Apocrine cells, macrophages and ductal cells are the characteristic features of a non-proliferative type of fibrocystic changes, which yields only scanty materials. Fibrocystic disease of proliferative type, there are sheets and clusters of ductal epithelial cells, presence of atypia in these cellular clusters and nucleoli. Presence of nipple discharge, the diagnosis goes in favour of intraductal papilloma. In the present study, 10/155 (6.45%) were given the diagnosis of fibrocystic disease with proliferative activity.

C5 category consists of cellular aspirate with evidently malignant cytologic features. It is not always possible to label the exact subtype especially tubular carcinoma, medullary carcinoma and mucinous carcinoma which have excellent prognosis, and usually squamous cell carcinoma and metaplastic carcinoma have bad prognosis. In the present study, carcinoma breast constituted 9.67% of cases and were diagnosable on FNAC. The type encountered was ductal carcinoma, was NOS type confirmed on histopathology. Sensitivity, specificity and overall diagnostic accuracy of breast lesion was 100%, 100% and 89.47% respectively.

## Thyroid

FNAC of the thyroid has become increasingly popular as a diagnostic technique as it provides a sensitive, economical method of obtaining cytologic material for examination with distinct advantages which includes accurate diagnosis, excellent patient acceptance and minimal or no morbidity. The sensitivity of the thyroid FNAC ranges from 65% to 99% and its specificity from 72% to 100%.<sup>[14]</sup> Various studies have shown diagnostic accuracy of 80% and 100%. Only a small percentage of patients with benign cytological findings

undergo surgery, it is difficult to know true frequency of false negative results.<sup>[15,16]</sup>

Pinki Pandey et al<sup>[17]</sup> in their study documented colloid goitre in 67.94% cases followed by thyroiditis in 20% cases, 1.47% adenomatous goitre and 1.17% thyroglossal cysts. Among the neoplastic group, 3.52% cases were reported as follicular neoplasm, 2.05% cases as Hürthle cell neoplasm and 1.17% as malignant tumours. FNA revealed a sensitivity of 62.5%, a specificity of 90.74% and diagnostic accuracy of 82.35%. Presence of Hürthle cell metaplasia, hyperplastic nodules and papillary hyperplasia were responsible for the false positive diagnoses.

Karen E et al<sup>[18]</sup> compared Ultrasound-guided sampling of the thyroid and non-aspiration technique of FNA; comparison of these two techniques showed no significant difference with regard to specimen adequacy. No significant difference in diagnostic accuracy was found on comparison of the two techniques.

In the present study, the malignant lesions showed 100% cytohistopathological correlation. The correlation percentage in cases of nodular goitre was 94%, 5 cases with long-standing goitre with large size showed foci of papillary carcinoma on histopathology. The correlation percentage is 36.20% in follicular neoplasm. Out of 58 cases 21 cases were diagnosed as follicular adenoma, 32 were adenomatoid goitre and 5 cases of follicular variant of papillary carcinoma. Sensitivity, specificity and overall diagnostic accuracy are 50%, 100% and 75.58% respectively.

#### Soft Tissue and Bony Lesions

FNA biopsies from soft tissue and bone are difficult to interpret as the aspirates have lot of blood or are scanty cellular due to fibrosis. Despite these difficulties, FNA cytology is being used as a diagnostic modality for initial diagnoses, for recurrences and metastases of soft tissue and bone lesions in many centres due to its simplicity, low morbidity, cost-effectiveness and ability to issue rapid diagnoses.<sup>[19]</sup>

In the study by Arul P et al<sup>[20]</sup> the sensitivity, specificity, accuracy of FNAC for diagnosing malignant soft tissue tumours was 91.7%, 97.7% and 97% respectively. Sensitivity and specificity of soft tissue and bone lesions by FNA in the study by Khalbuss et al<sup>[21]</sup> was 97% and 98% respectively, Kitagawa et al<sup>[22]</sup> showed 100% sensitivity and specificity and Hirachand et al<sup>[23]</sup> showed sensitivity and specificity of 25% and 100% respectively. There is wide variation in the sensitivity and specificity of soft tissue and bone lesions, probably due to variable aspirates obtained due to fibrosis and haemorrhage.

In the present study sensitivity, specificity and overall diagnostic accuracy in diagnosing soft tissue tumours on cytology was 46.66%, 100% and 88.67% respectively. Sensitivity, specificity and overall diagnostic accuracy of cytology in bone and joint lesions were 100%, 100% and 86.66% respectively.

#### Skin, Salivary Glands, USG-Guided Aspiration of Intraabdominal Lesions and Pap Cytology

In the study by Rajat Gupta et al,<sup>[24]</sup> the most common lesions were epidermal inclusion cysts (25.8%) and ganglions (6.5%). Among the malignant neoplastic cases, maximum were metastatic deposits of cancer. In USG-guided

aspirations, liver was the common site for FNAC in the study done by Tasleem Ahmed et al<sup>[25]</sup> and Adhikari RC et al.<sup>[26]</sup> Adenocarcinoma was the most common malignant type in the study made by Shamshad et al.<sup>[27]</sup>

McGrath et al<sup>[28]</sup> in his article stated that ASCUS on pap smears has to be differentiated from low-grade SIL (LSIL) and marked reactive changes. High interobserver and intraobserver variability is well documented in the literature on Pap smears regardless of years of training or level of expertise. Tamboli et al<sup>[29]</sup> documented sensitivity of 90.65% and diagnostic accuracy of 90.4% on Pap smears.

In the present study sensitivity, specificity and overall diagnostic accuracy in diagnosing salivary gland lesions is 81.81%, 100% and 88.23% respectively. Sensitivity, specificity and overall diagnostic accuracy of cytology in USG-guided intraabdominal lesions and skin lesions were 100%. Sensitivity, specificity and overall diagnostic accuracy of cytology on Pap smears were 92.68%, 93.33% and 84.48%.

#### CONCLUSION

**Cytology Plays a Great Role in Diagnosing Various Lesions but has Limitations. The Lesions in the Grey Zone are-**

1. Granulomatous lymphadenitis without caseous necrosis and negative for acid fast bacilli.
2. Lymphoproliferative disorders.
3. Fibrocystic disease of breast of proliferative type.
4. Atypical ductal hyperplasia.
5. Phyllodes tumour of breast.
6. Follicular neoplasm of thyroid.
7. Long-standing large size goitres.
8. Long-standing large size pleomorphic adenoma of salivary gland.
9. Soft tissue tumour, larger than 10 cm.
10. Vascular tumours.
11. ASCUS and HSIL on Pap smears.

All these lesions need histopathological examination to further sub-categorise the lesions.

#### REFERENCES

- [1] Hajdu SI, Melamed MR. Limitations of aspiration cytology in the diagnosis of primary neoplasms. *Acta Cytol* 1984;28(3):337-45.
- [2] Chan JKC, Tang SK, Tsang WYW, et al. Histologic changes induced by fine-needle aspiration. *Advances Anat Pathol* 1996;3:71-90.
- [3] Khajuria R, Goswami KC, Singh K, et al. Pattern of lymphadenopathy on fine needle aspiration cytology in Jammu. *JK Sci* 2006;8:157-9.
- [4] Badge SA, Ovhal AG, Azad K, et al. Study of fine needle aspiration cytology of lymph node in rural area of Bastar District, Chhattisgarh. *Med J DY Patil Univ* 2017;10(2):143-8.
- [5] Prasoon D. Acid-fast Bacilli in fine needle aspiration smears from tuberculous lymph nodes. Where to look for them. *Acta Cytol* 2000;44(3):297-300.
- [6] Paul PC, Goswami BK, Chakrabarti S, et al. Fine needle aspiration cytology of lymph nodes: an Institutional study of 1448 cases over a five year period. *J Cytol* 2004;21:187-90.

- [7] Lau SK, Wei WI, Hsu C, et al. Efficacy of fine needle aspiration cytology in the diagnosis of tuberculous cervical lymphadenopathy. *J Laryngol Otol* 1990;104(1):24-7.
- [8] Patel MM, Italiya SL, Dhandha ZB, et al. Study of metastasis in lymph nodes in FNAC: our institutional experience. *Int J Res Med Sci* 2013;1(4):451-4.
- [9] Ghartimagar D, Ghosh A, Ranabhat S, et al. Utility of fine needle aspiration cytology in metastatic lymph nodes. *J Pathol Nepal* 2011;1:92-5.
- [10] Khan AH, Hayat AS, Baloch GH, et al. Study of FNAC in cervical lymphadenopathy. *World Appl Sci J* 2011;12(11):1951-4.
- [11] Bukhari MH, Arshad M, Jamal S, et al. Use of fine needle aspiration in the evaluation of breast lumps. Article ID 689521, *Pathology Research International* 2011;2011: p. 10.
- [12] Panjvani SI, Parikh BJ, Parikh SB, et al. Use of fine needle aspiration cytology in the evaluation of breast lesions. *Journal of Clinical and Diagnostic Research* 2013;7(12):2777-9.
- [13] Kollur SM, El Hag IA. FNA of breast fibroadenoma: observer variability and review of cytomorphology with cytohistological correlation. *Cytopathology* 2006;17(5):239-44.
- [14] Caraway NP, Sneige N, Samaan NA. Diagnostic pitfalls in thyroid fine needle aspiration: a review of 394 cases. *Diagn Cytopathol* 1993;9(3):345-50.
- [15] El Hag IA, Kollur SM, Chiedozi LC. The role of FNA in the initial management of thyroid lesions: 7 year experience in a district general hospital. *Cytopathology* 2003;14(3):126-30.
- [16] Kumori T, Shinya H, Satomi T, et al. Management of nodular goiters and their operative indications. *Surg Today* 2003;30:722-6.
- [17] Pandey P, Dixit A, Chaturvedi V, et al. Usefulness of fine-needle aspiration in the diagnosis of thyroid lesions: an institutional experience of 340 patients. *Otolaryngology Online Journal* 2013;3(4):1-17.
- [18] Schoedel KE, Tubulin ME, Pealer K, et al. Ultrasound-guided biopsy of the thyroid: a comparison of technique with respect to diagnostic accuracy. *Diagnostic Cytopathology* 2008;36(11):787-9.
- [19] Nagira K, Yamamoto T, Akisue T, et al. Reliability of fine-needle aspiration biopsy in the initial diagnosis of soft-tissue lesions. *Diagn Cytopathol* 2002;27(6):354-61.
- [20] Arul P, Masilamani S. Fine needle aspiration cytology of soft tissue tumors with its histopathological correlation in a rural hospital of south India: a retrospective study. *Clin Cancer Investig J* 2016;5(2):146-50.
- [21] Khalbuss WE, Teot LA, Monaco SE. Diagnostic accuracy and limitations of fine needle aspiration cytology of bone and soft tissue lesions: a review of 1114 cases with cytological-histological correlation. *Cancer Cytopathol* 2009;118(1):24-32.
- [22] Kitagawa Y, Ito H, Sawaizumi T, et al. Fine needle aspiration cytology for soft tissue tumours of the hand. *J Hand Surg Br* 2003;28(6):582-5.
- [23] Hirachand S, Lakhey M, Singha AK, et al. Fine needle aspiration (FNA) of soft tissue tumours (STT). *Kathmandu Univ Med J (KUMJ)* 2007;5(3):374-7.
- [24] Gupta R, Gupta R, Dewan D, et al. Fine needle aspiration cytology as a diagnostic tool in nodular skin lesions. *Int J Med Sci Public Health* 2016;5(6):1229-32.
- [25] Reyaz TA, Summyia F, Isma N, et al. USG guided fine needle aspiration cytology of intra-abdominal and pelvic masses in Kashmir: a study at tertiary care hospital. *International Journal of Medical Research & Health Sciences* 2016;5(4):169-75.
- [26] Adhikari RC, Tuladhar A, Shrestha S, et al. Deep-seated thoracic and abdominal lesions: usefulness of ultrasound guided fine needle aspiration cytology, a 3 year experience. *Nepal Medical Coll J* 2010;12:20-5.
- [27] Ahmed SS, Akhtar K, Akhtar SS, et al. Ultrasound guided fine needle aspiration biopsy of abdominal masses. *JK Science* 2006;8(4):200-4.
- [28] McGrath CM. ASCUS in papanicolaou smears. Problems, controversies and potential future directions. *Am J Clin Pathol* 2002;(Suppl 117):S62-S75.
- [29] Tamboli GD. Accuracy of cytological findings in abnormal cervical smear by cyto-histological comparison. *Journal of Medical Education & Research* 2013;3(2):19-24.