



Original Research Article

Efficacy of cytological examination in comparison with gold standard histopathology in various palpable & non-palpable lesions- A study of 483 cases in a tertiary care centre

Neha Rajan Jadhav^{1,*}, Neeru D Dave¹, Bansi Kavar¹

¹Dept. of Pathology, M. P. Shah Govt. Medical College & G.G.G Hospital, Jamnagar, Gujrat., India



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ABSTRACT

Background: It has become important to diagnose the pathology of any site in early stage to improve the prognosis of the disease process since there is limited resources in our country. Since FNAC is easy to perform, simple, cost effective procedure requiring minimal setup, we conducted this study to evaluate its diagnostic accuracy, sensitivity and specificity in comparison to histopathology.

Materials and Methods: This was a retrospective and prospective study carried out for a duration of 4 years and included total of 483 cases referred to Pathology Department. Biopsy was performed in all cases after FNAC and the findings were correlated.

Results: Of the 483 cases, patients belonged to age group of 10 to 70 years. In case of breast lesions all were females, in lymph node, lung & miscellaneous lesions there was male preponderance while in thyroid female preponderance was observed. The sensitivity & specificity of cytopathology in Breast was 98.87% & 78.26%, in Lung 98.18% & 86.66%, in Lymph node 93.93% & 85.71%, in Thyroid 93.18% & 85.71%, while in Miscellaneous 93.33% & 87.5% respectively.

Conclusion: FNAC can be used safely and can be relied upon in diagnosis of various pathologies even in centres with limited facilities & it can be set up at OPD level also, thus aiding in timely management of the patient. The overall Sensitivity and Specificity of cytopathological examination was good. PPV & NPV were within acceptable range.

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1. Introduction

Cytopathology is a branch of pathology that studies and diagnoses diseases at cellular level. This technique is generally used on samples of free cells or tissue fragments. This technique was first introduced by Martin and Ellis in 1930, for the diagnosis of different organ lesions.¹ Histopathology, on the other hand, studies the whole tissue. FNAC (Fine Needle Aspiration Cytology) is a useful technique for the initial diagnosis of various lesions as it is easy to perform, minimally invasive, cost effective, readily repeatable, provides early diagnosis and gives excellent patient compliance for Thyroid nodules² and other various lesions. FNAC procedures can be set up on OPD

basis as it does not require sophisticated instruments or set up. It not only confirms the presence of metastatic disease but also gives clues regarding the nature and origin of malignant tumor.³ This study was thus taken to evaluate the accuracy of cytopathology in comparison to histopathological diagnosis and also to validate the findings of other authors.

2. Aims and Objectives

1. To evaluate the diagnostic accuracy of FNAC by Cytopathology
2. To find out the sensitivity and specificity of FNAC of lesions of various site.
3. To estimate the Positive Predictive value and Negative Predictive value of various lesions.

* Corresponding author.

E-mail address: jadhavneha000@gmail.com (N. R. Jadhav).

3. Materials and Methods

This was hospital based analytic retrospective & prospective study carried out for duration of 4 years among patients attending TBCD, ENT, Surgery and Radiotherapy out-patient (OPD) and in-patient (IPD) department. This study included total 483 cases out of which 200 cases of breast, 140 of lung, 58 cases of thyroid, 47 of lymph node and 38 cases of other miscellaneous sites such as skin/soft tissue/salivary glands/prostate etc. were present. For all cases both FNAC and histopathological study was done.

Prior to FNAC, detailed clinical history, radiological findings and patient's informed consent was taken. All aseptic precautions and measures were followed. After positioning the patient, the lesion was thoroughly palpated, area was sterilized and lesion was fixed between fingers for the procedure (for superficial lesions) while for deeper and non-palpable lesions USG guided FNAC procedure was performed.

A 22-23-gauge needle with an 5cc or 10cc syringe was used without anesthesia. After piercing the lesion, to and fro method was applied and the tissue material was aspirated by negative suction. Smears were prepared then fixed in methanol and stained by Hematoxylin and Eosin, Pap stain and MGG stain. Ziehl and Nelson (Z.N.) stain for acid fast bacilli was done in cases suspected for tuberculosis. Subsequent biopsies/mastectomy specimens sent were grossed, processed by paraffin embedding and stained with Hematoxylin and Eosin.

4. Results: (Tables 1 and 2)

Total 483 cases were included in this study over the period of 4 years between 2016 to 2019, which had undergone Cytological/FNAC and Histopathological examination. Of these, 290 were female and 193 were male. Patients belonged to age ranging from 10 years to 75 years. All these cases were categorized on the basis of site of origin into lesions of Breast, Lung, Thyroid, Lymph node and miscellaneous (skin, soft tissue, salivary glands, prostate etc.) and were classified broadly into Benign and Malignant.

Table 1 shows the age wise distribution of various lesions. Maximum number of Breast occurred in 4th decade of life, maximum cases of lung pathology were observed in age group of 50-70 years, thyroid and other miscellaneous pathologies showed almost similar incidences in all age groups while in case of lymph node pathology, children and young adults were observed to be affected but more or less incidence was similar in other age groups as well. The overall incidence of pathological lesions was found to be common in the age group of 30-40 yrs.

Table 2 shows gender involvement in lesions of different sites. Breast pathologies showed involvement only in female. Male predominance was seen in lung, lymph node and miscellaneous group pathologies while female

predominance in case of thyroid lesions.

4.1. Breast

200 were of breast lesions and all the patients were female. Of these, 193 cases were concordant with histopathological findings whereas 07 cases had discordant results. 126 were benign and 74 were Malignant.

4.2. Lung

140 cases were of lung pathology. 123 patients were male while 17 female. Majority of the patients had a chronic history of smoking. 134 cases were concordant with histopathological diagnosis, while 06 cases were found to be discordant. 16 were benign, 123 malignant and 01 inconclusive.

4.3. Thyroid

58 cases belonged to lesions concerned with thyroid. 08 were male while 50 were female patients. 53 were concordant, whereas 05 cases were discordant with their histopathological diagnosis. 43 cases were Benign and 15 were malignant.

4.4. Lymph node

47 cases belonged to lesions of lymph node of mainly cervical, submandibular, axillary and inguinal lymph nodes. 33 patients were male while 14 were female patients. 43 were concordant with their histopathological findings, while 04 were discordant. 44 diagnosed as benign lesions and 3 were malignant.

4.5. Miscellaneous

This category included wide range of lesions of skin, soft tissue, salivary glands, liver, prostate etc. Total cases in this group were 38. Of these, 35 cases had diagnosis concordant with histopathology while 03 were discordant. Tables 3 and 4

4.6. Breast: (Tables 5 and 6)

Breast: Maximum number of concordant cases (96.5%) were from lesions of breast. There were 5 false positive and 2 false negative cases. Out of the 129 benign cases, 45 cases were diagnosed as Fibroadenoma, 22 with Fibrocystic disease of breast, 21 as Inflammatory conditions, 18 as Fibroadenoma with atypia, 21 benign ductal papilloma, 01 as sclerosing adenosis and 01 as Benign Phyllode tumor. From the remaining 71 malignant cases, 28 as ductal carcinoma in situ, 25 as Invasive Ductal carcinoma and 18 as Invasive lobular carcinoma.

Figure 1 a,b showing cytopathology & histopathology of Invasive Ductal Carcinoma of breast

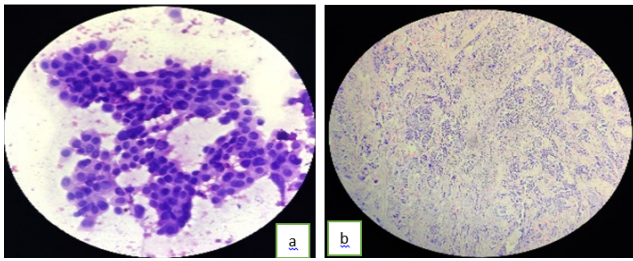


Fig. 1: **a:** H&E stained(40x) FNAC smear from breast lump diagnosed as Invasive Ductal Carcinoma, shows cluster of malignant ductal cells showing nuclear pleomorphism, nuclear hyperchromasia, high N:C ratio and nuclear overlapping; **b:** H&E stained(40x) section from lung biopsy diagnosed as Adenocarcinoma of lung showing large round cells with hyperchromatic nuclei, nuclear pleomorphism, high N:C ratio, at places prominent nucleoli and moderate amount of eosinophilic cytoplasm.

4.7. Lung: (Table 7&8 Tables 7 and 8)

Lung: Out of the total 140 cases, 123 were malignant (including 02 cases which were suspicious for malignancy and considered as False negative), 16 Benign and 01 was inconclusive due to inadequate cellular material. There were 4 false positive and 2 false negative cases. On histopathology, 13 cases were confirmed as Tuberculosis, 02 diagnosed with Reactive changes and 01 as Pneumonitis. Out of the 123 malignant cases, 46 were confirmed as Squamous cell carcinoma, 51 as Adenocarcinoma, 18 as Small cell carcinoma, 06 as Small cell- Neuroendocrine carcinoma of lung and 02 as suspicious for malignancy. Total of 134 cases were concordant, while 06 were discordant with the histopathological diagnosis.

Figure 2 a,b showing cytopathology & histopathology of Adenocarcinoma of lung

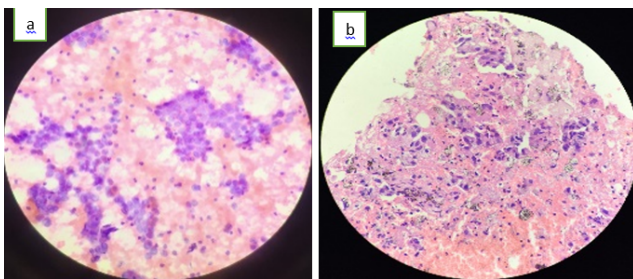


Fig. 2: **a:** H&E stained(40x) smear from Lung FNAC showing clusters of round pleomorphic cells with regular borders, cellular pleomorphism, prominent nucleoli and scant eosinophilic cytoplasm, diagnosed as Adenocarcinoma of Lung; **2b:** H&E stained(40x) section from lung biopsy diagnosed as Adenocarcinoma of lung showing large round cells with hyperchromatic nuclei, nuclear pleomorphism, high N:C ratio, at places prominent nucleoli and moderate amount of eosinophilic cytoplasm.

4.8. Thyroid:(Tables 9 and 10)

Thyroid: Out of the total 58 cases, 40 were diagnosed as benign lesions and 18 as Malignant. There were 02 false positive and 03 false negative on cytopathological examination. On histopathological examination, 15 cases were diagnosed as Colloid goiter, 07 as Thyroglossal cyst, 05 as granulomatous thyroiditis, 10 as Follicular adenoma, 03 cases as Hashimoto thyroiditis and 02 as Colloid goiter with secondary changes. Out of the 18 malignant cases, 10 were diagnosed as Papillary carcinoma thyroid, 05 as Medullary carcinoma thyroid and 03 as Hurthle cell carcinoma.

Figure 3 a,b showing cytopathological and histopathological features of Papillary carcinoma of Thyroid

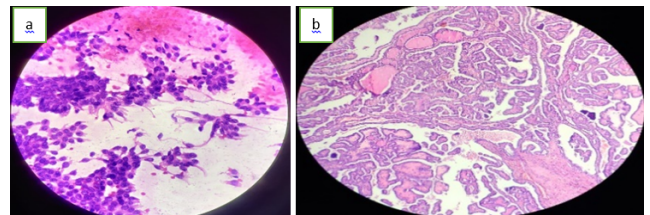


Fig. 3: **a:** H&E stained(40X) FNAC smear from thyroid lesion diagnosed as Papillary carcinoma thyroid, showing nuclear grooving; **3b:** H&E(10X) stained biopsy of same patient showing papillary pattern with glass ground opacity of nuclei in Papillary Thyroid Carcinoma.

4.9. Lymph node: (Tables 11 and 12)

Lymph node: Out of the total 47 cases, 34 cases were confirmed as Benign and 13 were diagnosed as malignant. There were 2 false positive and 2 false negative cases. Amongst the benign conditions, 17 as Chronic Granulomatous lymphadenitis including Koch's lymphadenitis and sarcoidosis, 10 as Reactive lymphadenitis and 07 as Necrotizing lymphadenitis. Amongst the 13 malignant cases, 06 were metastasis to lymph node, 05 were diagnosed as Hodgkin lymphoma, 02 as Non-Hodgkin lymphoma. Out of the total 47 cases, 43 were concordant and 04 cases were discordant with their Histopathological diagnosis.

Figure 4 a,b showing cytopathological & Histopathological findings of Non Hodgkin lymphoma

4.10. Miscellaneous: (Tables 13 and 14)

Miscellaneous: Total 38 miscellaneous cases of skin, soft tissue, salivary glands, vascular, oral cavity, liver and Prostate lesions were included together in this category. 35 were concordant and 03 were discordant with histopathological findings. 34 were benign and 04

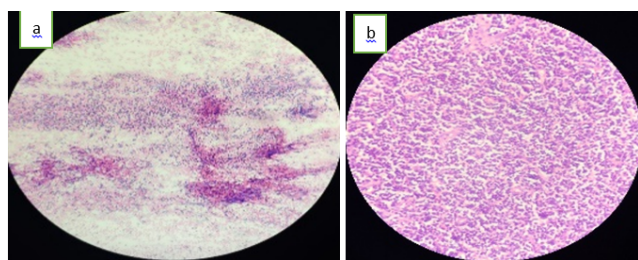


Fig. 4: **a:** H&E stain(10x) from cervical lymph node showing monomorphic population of lymphocytic cells, diagnosed as Non Hodgkin Lymphoma; **4b:** H&E stained section (40x) showing monomorphic population of lymphocytic cells in lymph node, diagnosed as Non Hodgkin Lymphoma

were malignant. There was 01 false positive and 02 false negative cases. Benign lesions included 07 of lipoma, 03 Pleomorphic adenoma, 03 sebaceous cyst, 02 Epidermal cyst, 03 Dermoid cyst, Dentigerous cyst and Odontogenic keratocyst were 01 each, 04 Chronic sialolithiasis + chronic sialadenitis, 02 Warthin tumor, 02 Hydatid cyst, 02 Benign prostatic hyperplasia, 01 Thymoma and 01 Schwannoma. Of the 04 malignant cases, 02 were mucoepidermoid carcinoma, 01 Acinic cell carcinoma, 01 Adenocarcinoma prostate and 01 was Carcinoma ex Pleomorphic adenoma.

Figure 5 a,b showing cytopathological & Histopathological findings of Acinic cell carcinoma of salivary gland.

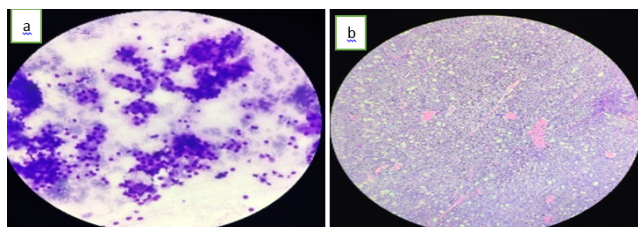


Fig. 5: **a:** MGG stained FNAC smear from salivary gland showing acinar like arrangement. Cells are mostly monomorphic having bland nuclear chromatin with fine vacuolated and granular cytoplasm, diagnosed as Acinic cell carcinoma; **5b:** H&E stained(10x) biopsy specimen showing large, polygonal cells with basophilic, granular cytoplasm and eccentric nuclei, diagnosed as Acinic cell carcinoma

5. Discussion: (Tables 15, 16, 17 and 18)

Similar studies have been conducted by Panjvani et al (2013)⁴ on 222 cases, Kujur P² on 106 cases and Damle et al (2019)⁶ on 273 cases, for cytological efficacy in breast lesions. In comparison to these studies, the present study conducted on 200 cases showed sensitivity (98.87%), specificity (78.26%), PPV (97%) and NPV (90%). The findings were observed to be in a closer range and the overall findings were comparable.

We compared our present study of 140 cases, with other similar studies by Modi et al (2016)⁷ and Ghildiyal et al (2018)⁸ and carried out on 70 and 99 cases respectively. The present study showed highest sensitivity (98.18%), concordance (95.71%), PPV (96.42%) and NPV (92.85%) as compared with other two studies with lowest Discordance (4.28%) and specificity in comparable range.

The present study was compared with 3 other studies done by Pandey et al (2012)⁹ on 112 cases, Bamanikar et al (2014)¹⁰ on 300 cases and Ramteke et al (2017)¹¹ on 385 cases. Though the present study had lower number of cases compared to others, a humble effort was made to cover all criteria with regard to age, sex and previous or family history if any. Present study showed highest sensitivity (93.18%) as compared to others. Accurate diagnosis on cytopathological examination was seen to be challenging due to presence of colloid material on aspiration and chances of missing out on small neoplastic focus, which were observed on Hemi/Total thyroidectomy specimens.

Study conducted by Malhotra et al (2017)¹² was on total 238 cases but only 113 were followed by histopathological examination and hence only those findings were compared and included in the discussion. Same with study by Pathy (2017)¹³ with total cases being 1129 but only 399 followed up for histopathology. The present study showed close similarity with other studies in case of sensitivity (93.33%) and PPV (93.33%). Overall giving good comparison with other two.

6. Conclusion

FNAC is a simple, cost effective, rapid and fairly accurate method for diagnosing various palpable and deep-seated lesions, providing a high diagnostic accuracy. Hence it can be used safely and conveniently and can be relied upon in diagnosis of various pathologies even in centres with limited facilities. According to our study out of total 483 cases 396 were concordant and 87 were discordant with histopathological diagnosis. Hence, the overall Sensitivity and Specificity of cytopathological examination in present study was calculated to be 96.16% and 80.43% respectively while Positive Predictive value (96.47%) and Negative Predictive value (87.20%).

7. Acknowledgement

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8. Source of Funding

None.

Table 1: Age distribution for various lesions (n=483)

Age	Breast	Lung	Thyroid	Lymph Node	Miscellaneous	Total
10-19	18	00	06	13	06	45
20-29	50	04	17	08	09	88
30-39	73	05	10	11	05	104
40-49	41	07	15	10	11	84
50-59	12	48	07	02	04	73
60-69	06	52	02	01	01	60
>70	00	24	01	02	02	29
Total	200	140	58	47	38	483

Table 2: Gender wise distribution of cases (n=483)

Site	Male	Female	Total
Breast	00	200	200
Lung	123	17	140
Thyroid	08	50	58
Lymph node	33	14	47
Miscellaneous	29	09	38
Total	193	290	483

Table 3: Distribution of Concordant and Discordant cases (n=483)

Site	Concordant	Discordant	Total	Sensitivity	Specificity
Breast	193	07	200	98.87%	78.26%
Lung	134	06	140	98.18%	86.66%
Thyroid	53	05	58	93.18%	85.71%
Lymph node	43	04	47	93.93%	85.71%
Miscellaneous	35	03	38	93.33%	87.5%
Total	458	25	483	96.16%	80.43%

Table 4: Positive & Negative Predictive Value (n=483)

Site	Total cases	Positive Predictive value	Negative Predictive value
Breast	200	97.00%	90.00%
Lung	140	96.42%	92.85%
Thyroid	58	95.34%	80 %
Lymph node	47	93.93%	85.71 %
Miscellaneous	38	96.55%	77.77%
Total	483	96.47%	87.20%

Table 5: Concordant cases on Cytopathology & Histopathology (Breast): (n=193)

S. No.	Diagnosis	No. of Cases	Percentage
1.	Inflammatory (Mastitis)	19	9.5%
2.	Fibroadenoma	43	21.5%
3.	Fibrocystic breast disease	22	11%
4.	Fibroadenoma with atypia	18	9%
5.	Benign ductal papilloma	21	10.5%
6.	Ductal carcinoma in situ	28	14%
7.	Invasive ductal carcinoma	24	12%
8.	Invasive lobular carcinoma	18	9%
	Total	193	96.5%

Table 6: Discordant cases (Breast) (n=07)

S. No.	Cytopathological diagnosis	Histopathological diagnosis	No. of cases	Percentage
1.	Fibrocystic disease of breast with hyperplasia with atypia	Intraductal carcinoma	01	0.5%
2.	S/o Ductal carcinoma	Sclerosing adenosis	01	0.5%
3.	S/o Ductal carcinoma	Inflammatory condition	02	01%
4.	Ductal carcinoma	Cellular fibroadenoma	02	01%
5.	Fibroadenoma	Intraductal carcinoma	01	0.5%
	Total		07	3.5%

Table 7: Concordant cases on Cytopathology & Histopathology (Lung): (n=134)

S. No.	Diagnosis	No. of Cases	Percentage
1.	Tuberculosis	13	9.28%
3.	Squamous Cell carcinoma	46	32.85%
4.	Adenocarcinoma	51	36.42%
5.	Small cell Carcinoma	18	12.85%
6.	Small Cell-Neuroendocrine Carcinoma	06	4.28%
	Total	134	95.72%

Table 8: Discordant cases of Lung (n=06)

S. No.	Cytopathological diagnosis	Histopathological diagnosis	No. of cases	Percentage
1.	Adenocarcinoma	Reactive changes	02	1.42%
3.	Small cell carcinoma	Inconclusive	01	0.71%
5.	Non-small cell carcinoma	Pneumonitis	01	0.71%
6.	Negative for malignancy	Suspicious for malignancy	02	1.42%
	Total		06	4.28%

Table 9: Concordant cases on Cytopathology & Histopathology (Thyroid) (n=53)

S. No.	Diagnosis	No. of Cases	Percentage
1.	Colloid Goiter	13	22.41%
2.	Thyroglossal Cyst	07	12.06%
3.	Hashimoto's Thyroiditis	03	5.17%
4.	Granulomatous thyroiditis	05	8.62%
5.	Follicular Adenoma	10	17.24%
6.	Hurthle Cell Carcinoma	02	3.44%
7.	Papillary Thyroid carcinoma	08	13.79%
8.	Medullary Carcinoma	05	8.62%
	Total	53	91.37%

Table 10: Discordant cases of Thyroid (n=05)

S. No.	Cytopathological diagnosis	Histopathological diagnosis	No. of cases	Percentage
1.	Bethesda category IV	Colloid goitre with secondary changes	01	1.72%
2.	Bethesda category II	Papillary carcinoma of thyroid	02	3.44%
3.	Suspicious for malignancy (Bethesda category V)	Colloid goitre with secondary changes	01	1.72%
4.	Bethesda category II	Hurthle cell carcinoma	01	1.72%
	Total		05	8.62%

Table 11: Concordant cases on Cytopathology & Histopathology (Lymph node) (n=43)

S. No.	Diagnosis	No. of Cases	Percentage
1.	Chronic Granulomatous inflammation	15	31.91%
2.	Reactive Lymphadenitis /Hyperplasia	10	21.27%
3.	Necrotizing Lymphadenopathy	07	14.89%
4.	Metastasis	06	12.76%
5.	Hodgkin Lymphoma	03	6.38%
6.	Non-Hodgkin Lymphoma	02	4.25%
	Total	43	91.48%

Table 12: Discordant cases of Lymph Node (n=4)

S. No.	Cytopathological diagnosis	Histopathological diagnosis	No. of cases	Percentage
1.	Non-Hodgkin lymphoma	Necrotizing granulomatous lesion TB	01	2.13%
2.	Small cell neuroendocrine carcinoma	Non caseating granulomatous sarcoidosis	01	2.13%
3.	Reactive lymphadenitis	Hodgkin lymphoma	01	2.13%
4.	Chronic granulomatous inflammation	Nodular lymphocyte prominent Hodgkin lymphoma	01	2.13%
	Total		04	8.52%

Table 13: Concordant cases on Cytopathology & Histopathology (miscellaneous): (n=35)

Sr. No.	Diagnosis	No. of Cases	Percentage
1.	Lipoma	07	18.42%
Cystic lesions			
2.	Benign cystic lesion (Dermoid cyst)	03	7.89%
3.	Benign cystic lesion (Epidermal cyst)	02	5.26%
4.	Hydatid cyst (Liver)	02	5.26%
6.	Dentigerous cyst	01	2.63%
7.	Benign cystic lesion (Sebaceous cyst)	03	7.89%
8.	Odontogenic keratocyst	01	2.63%
Inflammatory lesions			
9.	Chronic sialolithiasis	03	7.89%
10.	Benign prostatic hyperplasia	02	5.26%
Benign lesions			
11.	Thymoma	01	2.63%
13.	Schwannoma	01	2.63%
14.	Warthin tumor	01	2.63%
15.	Pleomorphic adenoma	03	7.89%
16.	Capillary hemangioma	02	5.26%
Malignant lesions			
17.	Mucoepidermoid carcinoma	02	5.26%
18.	Acinic cell carcinoma	01	2.63%
	Total	35	92.11%

Table 14: Discordant cases of miscellaneous (n=3)

S. No.	Cytopathological diagnosis	Histopathological diagnosis	No. of cases	Percentage
1.	Benign prostatic hyperplasia	Adenocarcinoma of prostate	01	2.63%
2.	Possibility of low grade mucoepidermoid carcinoma	Warthin's tumor of parotid	01	2.63%
3.	Pleomorphic Adenoma	Carcinoma ex pleomorphic adenoma	01	2.63%
	Total		03	7.89%

Table 15: Comparison study of Breast cases:

Studies	No. of cases	Sensitivity	Specificity	PPV	NPV	Concordance
Panjvani et al (2013) ⁴	222	97.82%	100%	100%	97.85%	98.90%
Kujur P (2015) ⁵	106	96.15%	96.29%	96%	96.29%	-
Damle et al (2019) ⁶	273	100%	97.77%	91.53%	100%	98.16%
Present (2020)	200	98.87%	78.26%	97%	90%	96.5%

Table 16: Comparison Study of Lung Cases:

Studies	No. of cases	Sensitivity	Specificity	PPV	NPV	Concordance	Discordance
Modi et al (2016) ⁷	70	91.5 %	72.5%	94.7%	61.5%	88.5%	11.5%
Ghildiyal et al (2018) ⁸	99	81.48%	93.33%	93.62%	80.77%	85.85%	14.5%
Present study (2020)	140	98.18%	86.66 %	96.42%	92.85%	95.71%	4.28%

Table 17: Comparison study of thyroid cases:

Studies	No of cases	Sensitivity	Specificity	PPV	NPV	Concordance	Discordance
Pandey et al (2012) ⁹	112	57.14%	90%	70.58%	83.33%	80.28%	19.71%
Bamanikar et al (2014) ¹⁰	300	50%	100%	100%	100%	94.2%	5.7%
Ramteke et al (2017) ¹¹	385	92.31%	97.01%	85.71%	98.48%	96.25%	-
Present study (2020)	58	93.18%	85.71%	95.34%	80%	91.37%	8.62%

Table 18: Comparison Study of Lymph node cases:

Study	No. of cases	Sensitivity	Specificity	Positive Predictive value
Malhotra et al (2017) ¹²	113	94.49%	91.15%	96.26%
Pathy et al (2017) ¹³	399	93.88%	94.64%	99.8 %
Present study (2020)	47	93.33%	85.71%	93.33%

9. Conflict of Interest

None.

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Author biography

Neha Rajan Jadhav IIIrd Year Resident

Neeru D Dave Associate Professor

Bansi Kavar IInd Year Resident

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