A Retrospective Study Of Comparison Of Fine Needle Aspiration Cytology (FNAC) With Histopathological Diagnosis (HPE) In Thyroid Swelling: A Tertiary Care Hospital Experience.

Dr. Nipa Dalal*, Dr. Saurabh Gandhi, Dr. Devanshi Patel***, Dr. Sanket Shah***, Dr. Foram Parikh*****

*Associate Professor, **Assistant Professor,***2nd Year Resident Doctor, Department Of Otorhinolaryngology, N.H.L Municipal Medical College, Ahmedabad-380006, India.

Abstract: Background: Fine needle aspiration cytology (FNAC) has become the dominant method in the evaluation of thyroid nodules, being fast, reliable, safe, minimally invasive, cost effective. Its main role lies in differentiating between benign and malignant lesions which significantly affects decision making in treatment. This study was undertaken to establish the cytology –histopathology co relation. Material And Methods: This retrospective study was carried out in hospital attached with NHL Municipal Medical College, Ahmedabad having 125 cases in study. The statistical analysis included sensitivity, specificity, positive predictive value, negative predictive value and accuracy. Result: On cytological examination, 102/125were benign, 23 malignant or suspicious. On HPE, 97 were benign while 18 malignant from suspicious and malignant cases leaving 10 discordant cases. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy which was 78.26%, 95.09%, 78.26%, 95.09% and 92% respectively in our case series.Conclusion: FNAC is safe, simple procedure. It gives a reliable pre-operative cytological diagnosis based on which surgical procedures can be confidently executed. An attempt is made hereby to compare our results with worldwide documented literature. However pitfalls of this method should be kept in mind with careful observation and adequate clinical suspicion. [Dalal N Natl J Integr Res Med, 2020; 11(5):21-27]

Key Words: FNAC, HPE, Thyroid

Author for correspondence: Dr. Saurabh Gandhi, Department of ENT, SVP Hospital, N.H.L Municipal Medical College, Ashram Road, Ahmedabad-380006,Gujarat, India. E-Mail: saurabhgandhi8378@gmail.com Mobile: 9824613468

Introduction: Thyroid gland is unique among endocrine organs and first to develop in fetal life[1]. The Thyroid gland is the host to many diseases ranging from benign and malignant lesions to metabolic disorders to infectious and inflammatory diseases[2].

Thyroid swelling is very frequent. It is estimated that 4-7% adults have palpable enlargement of thyroid gland and 10 times more have impalpable nodules. Most of them are benign and fewer than 5% are actually malignant[3] still Thyroid cancer is commonest endocrine cancer accounting for more than 90% of all the endocrine cancers.

India is endemic for iodine deficiency disorders and it has been showed that prevalence of goiter in India is high as 40%. The development of goiter is a concern for both patient and clinician as many of benign may turn to malignant. Most of the goiter is benign but reports say that prevalence of malignancy in solitary thyroid nodule is around 10%[4].

Surgical Management of thyroid swelling requires careful preoperative decision making and planning. An expertly performed surgery for wrong reason is still a bad surgery. A multitude of diagnostic tests like ultrasound, thyroid nuclear scan, fine needle aspiration cytology (FNAC) and many more are available to evaluate goiter. Final diagnosis requires morphological examination of lesions for which FNAC and histopathological examination (HPE) becomes mandatory tests[6].

In 1883 Leyden described FNAC for the first time.7Martin and Ellis in 1930 used it first time for thyroid cytology[8]. Practice guidelines set forth by American Thyroid Association and National Comprehensive Cancer Network states that FNAC should be used as initial diagnostic test because of its superior diagnostic reliability and cost effectiveness[7].

FNAC is simple, cost effective and quick to perform in outpatient setting with excellent patient compliance6. It is usually performed without any previous preparation or anesthesia.
FNAC is considered to be the “Gold Standard” in the selection of the patient for surgery[9]. Aim of FNAC is to identify nodules that require surgery and those benign nodules that can be observed clinically and decrease the overall surgery[10].

Representative sample from desired diseased area and experienced cytologist to interpret the result are must for successful diagnosis. So limitations of FNAC are related to specimen adequacy, sampling technique, skill of performing

aspiration, interpretation of aspirate and overlapping cytological features between benign and malignant follicular neoplasm and also in detecting some papillary carcinoma from other benign diseases. The ultimate answer lies in Histopathological examination (HPE). And this raise the question that how much corroborative is FNAC and HPE[6]. Many studies are available comparing the results of FNAC and HPE in western countries and some in India too. We did this study to find out efficacy of FNAC in comparison to HPE at our institute.

Aim And Objective: To find out the efficacy of FNAC in thyroid lesions in comparison to HPE. To find out the accuracy of FNAC in terms of sensitivity, specificity, positive predictive value and negative predictive value in comparison with HPE. Compare the results of our study to that of various other studies.

Material & Methods: This retrospective study was carried out in hospital attached with N.H.L Municipal Medical College, Ahmedabad, Gujarat.

Inclusion Criteria: All the patients operated for thyroid surgery during study period.
Exclusion Criteria: Patient treated conservatively for inflammatory or other thyroid diseases. Patients unfit for surgery. Patients who refused for surgery. Patients with inoperable tumors Patients fulfilling inclusion criteria were taken into the study. Permission for the study was obtained from department head of unit. Total 125patients were evaluated by thorough clinical examination of neck swelling along with vocal cord mobility and relevant clinical examination. They were evaluated with TFT, USG Neck (CT Neck in selected cases), and other preoperative profile along with FNAC.

FNAC was carried out by pathologist with 23G needle, smears were fixed with ether 95% alcohol solution and staining was performed using Papanicolaou's stain. According to FNAC report patients were operated for thyroid surgery, specimen was excised, processed in automated tissue processing units and sent for histopathological examination. Indications for surgery were proven or suspicious FNAC reports, pressure symptoms or cosmetic problems etc.

The report of FNAC and HPE were compared and validity of FNAC was assessed. FNAC diagnosis was done on Bethesda System of diagnosis (2017)[11]. Statistical Analysis: Statistical analysis was done using SPSS software to determine the specificity and sensitivity of FNAC and results were tabulated.

Results: Total 125 patients operated for thyroid surgery were taken into the study out of them only12 were males while female (113) were predominant with share of (90.4) % in the study. The age distribution shows that though it was seen in all age groups, 21-30, younger age group was most commonly involved with having share of 33.6% while other commonly involved age group was 31-4 and 41-50 with share of around 18.5% each.

Chart 1: Age Distribution

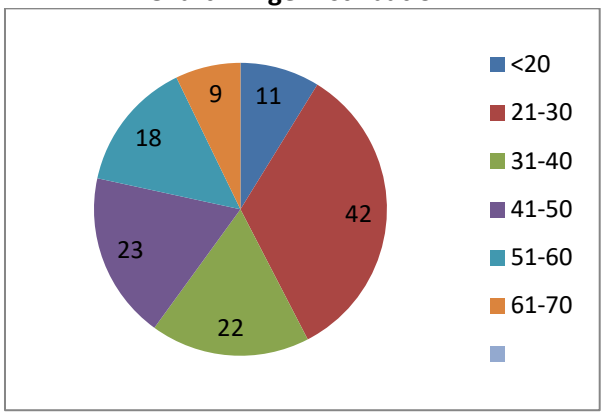
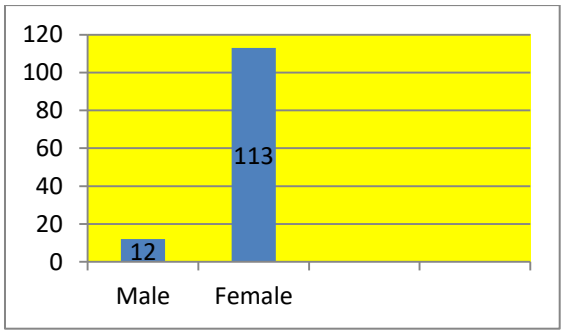


Chart 2: Sex Ratio



All patients FNAC report was described as Bethesda system and also subclassified according to clinical cytology of the lesion. According to Bethesda Grading suggested thyroid surgery was planned and HPE diagnosis was made. Majority of Thyroid lesion were (>80%) were benign in our study with benign colloid goitre being the commonest as evident from Table 1. Around 20% of them were either malignant, suspicious or follicular lesion Total 23 cases were either suspected or malignant on cytology. Follicular neoplasm (10 cases) was most common in suspected cases as diagnosed by cytology and papillary carcinoma (6 cases) was most common malignancy suggested by FNAC.

Table – 1 Cytological (FNAC) Diagnosis Of Thyroid Swelling

Bethesda Grade	Subtype	No. Of Patients	Percentage
I	Non Diagnostic	0	0%
II	Colloid Goitre	44	80.80%
	Adenomatous Nodule	8	
	Benign Follicular Lesion	10	
	Thyroiditis	4	
	Cystic Goitre	27	
	Nodular Goitre	8	
III	Follicular Lesion Of Undetermined Significance	1	0.80%
IV	Follicular Neoplasm	8	8%
	Suspicious For A Follicular Neoplasm	1	
	Hurthle Cell Neoplasm	1	
V	Suspicious For A Malignancy	4	3.20%
VI	Malignant: Papillary Carcinoma Medullary Carcinoma Anaplastic Carcinoma	 6 2 1	7.20%
		125	100%

In the present study the cases reported as 'suspicious' on cytology were included in the malignant category for statistical analysis because both lead to surgical management as far as the treatment is concerned This allows for an easier comparison and clearer final results. All the reports of FNAC were compared with final HPE diagnosis and the results are evident in Table 2.

Table 2- Cyto-Histopathological Correlation Of All Cases

Cytological Diagnosis	Histopathological Diagnosis	Discordant Cases
Benign (N=102)	Benign (N=97) [Tn]	5[Fn]
Malignant (N=9)	Malignant(N = 9)[Tp]	0[Fp]
Suspicious (N=14)	Benign (N=5)	5[Fp]
	Malignant(N=9)[Tp]	

N = Total Number, TN=True Negative, TP =True Positive, FN=False Negative, FP=False Positive

In HPE all the 9 cases of malignancy diagnosed by FNAC were malignant only while out of 14 suspicious cases,9 were malignant in which 3 were papillary carcinoma,2 were medullary carcinoma,2 non-invasive follicular neoplasm,1 invasive follicular neoplasm and 1 case was of Hurthle cell neoplasm and 5 turned out to be benign one-false positive(3 goitre ,1 Hurthle cell adenoma and 1 thymoma).

Out of 102 cases diagnosed benign by FNAC,97 were benign while 5 cases were discordant to be

malignant-false negative (2papillary,1 medullary, 1 follicular and 1 maltoma). From this result statistical analysis of results of FNAC was done as following:

1) Sensitivity: Probability when test result will be positive when disease is present-true positive rate)
2) Specificity: Probability that attest result will be negative when the disease is not present-true negative rate
3) Positive Predictive Value: probability that disease is present when the test is positive.
4) Negative predictive value: probability that disease is not present when test is negative.
5) Accuracy: accuracy is the portion of correct results, true positive and true negative in relation to all cases studied. The results of this indicator are shown in chart 3 which were compared with the results of similar studies done by other researchers as shown in table 4.

Table-3 Details Of The Discordant Cases

Discordant Cases (No.)	Cytological Diagnosis	Histopathological Diagnosis
5	Benign	Malignant
		1 - Medullary Carcinoma
		1 - Maltoma
		2 - Papillary Carcinoma
		1 - Follicular Carcinoma
0	Malignant	-
5	Suspicious	Benign
		1 - Hurthle Cell Adenoma
		2 - Multinodular Goitre
		1- Colloid Goitre
		1 - Thymoma

Chart-3 Statistical Analysis Of FNAC Results

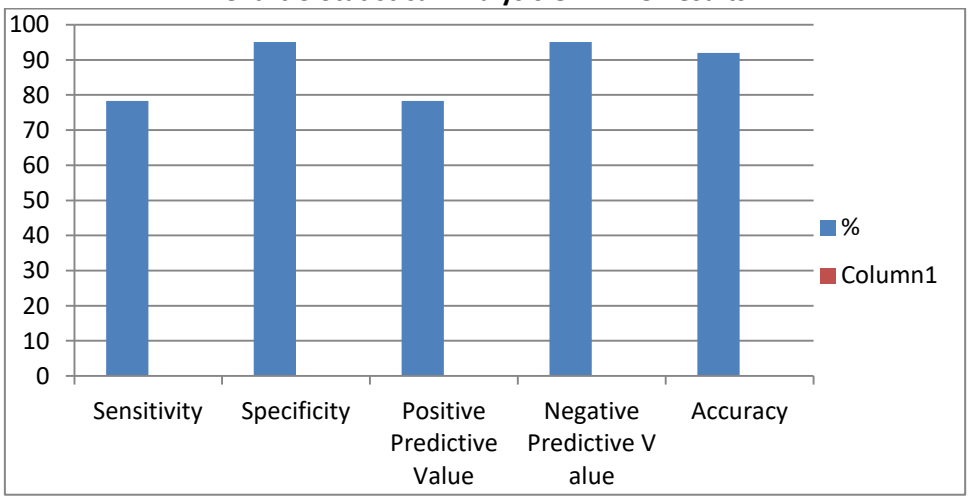


Table-4 Comparison With Other Studies

Authors	No. Of Cases	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
Luis Lopez et al12	872	90%	99.8%	98%	99%
Mojghan Amrikachi et al13	6226	93%	96%	92%	99%
Muhammad Saddique et al14	90	75%	95.83%	81.81%	93.81%
Mohd.Arif et al2	150	84.48 %	78.26 %	90.74	66.67%
Our Study	125	78.26%	95.09%	78.26%	95.09%

Discussion: Numerous Investigations like radio iodine scan, ultrasound scan, Thyroid suppression tests, hormone analysis and many others while leading the Surgeon along a uncertain path towards the diagnosis and thus towards a surgical

strategy have proven to be unreliable to a large extent when the final diagnosis of histopathology is obtained, all in spite of the cost the patient incurs.[15] Fine needle aspiration cytology examination introduced by our Scandinavian Colleagues in the nineteen fifties is a reliable, cost effective and simple procedure which has stood the vigorous assault of all its critics among both the surgeons and the physicians and has proved to be the single most important factor in achieving a pre-operative diagnosis there by aiding or altering the surgical strategy or in other forms of management of thyroid pathology (Charles V. Mann et al, Ikram M. et al 1999, Harsoulis P. et al 1986).[15]

Primary aim of our study was to establish the efficacy of FNAC in diagnosis of various thyroid lesions in comparison to gold standard investigations i.e. histopathological examination

which is only being done after surgery and choice of surgery or even indications of surgery will largely depends upon pre-operative diagnosis.

Our study showed highest incidence of thyroid lesions in age group of 21-30 which has almost 35% of case while other most common age group was 31-40 and 41-50, both having 18 % share of each.

The results are comparable with other studies like Mohd.Arif et al[2] in which 54.6% cases were seen in 21-40 age group.Similiar findings were seen in Tazeen Jilani et al in a series of 400 cases where 52% cases were found in 21-40 age group[16].

Female preponderance is very well known in all thyroid lesions which was also reflected in our study with male female ratio of 1:9.4. Mandekar et al. (1995)[17] reported a male female ratio of 1:6.1 in their study of 238 cases of various thyroid lesions. Male female ratio in the study conducted by Sirpal Y (1996)[18] on 1123 cases was 1:1.4 which is comparatively less. Al Rikabi et al. (1998)[19] observed a male female ratio of 1:5.2 in their study on 125 cases of various thyroid lesions.

The reporting systems for thyroid cytology vary among institutions and include 4 category system[20], 5 category system[21] or 6 category systems[11]. The most widely used ones are the Bethesda system[11] (6 category) and the Royal College of Pathologist (5 category) system.[21] Our institute employed Bethesda System of diagnosis with 6 standard categories as described in literatures. More than 80% of cases in our series were benign according to cytology with goitre being most common benign pathology accounting for share of around 56.8% of total cases.7% cases in our series were found to be malignant with Papillary Carcinoma being most common while almost 11% cases were kept in suspicion of malignancy or in follicular neoplasm group.

Naggada H.A et al. (2006)[22] also observed that the most common benign lesion in thyroid was nodular goitre followed by follicular adenoma. Fernandes H et al. (2009)[23] observed that the commonest lesion encountered in thyroid gland was nodular goitre and among the malignant neoplasms papillary carcinoma was the most common lesion noted.

Malignant to benign ratio in our series was 1:4.4 which was 1:1.27 in Tazeen Jialni et al[16] series. Attavilla et-al. (1990)[24] observed malignant to benign ratio of 1: 59.1.Mandrekar et al (1995)[17] observed malignant to benign ratio of 1:51.9. Al Rikabi et al. (1998)[19]observed malignant to benign ratio of 1:14.8.

We did not have any case in undiagnosed category; the reason behind it was the routine procedure of repeating FNAC in patients of that category. Repeat FNAC was done after a period of week to supress any hematoma because of first FNAC.The reasons behind more number of goitre operated in our series were large size, compression symptom or cosmetic demands of the patients.

While comparing with HPE it was seen that 97 cases out of 102 benign detected by FNAC were benign only while 5 cases turned out to be malignant as discussed in results part.100% cases diagnosed as malignant by FNAC were malignant in HPE.In suspicious case series there was discrepancy in 5 cases. From this data statistical analysis of efficacy of FNAC was done in form of sensitivity, specificity, positive predictive value, negative predictive value and accuracy which was 78.26%, 95.09%, 78.26%, 95.09% and 92% respectively in our case series.

False negative diagnosis can occur due to inadequate sampling or due to aspiration of fluid from cystic lesions of thyroid with an underlying malignancy[25]. Among all the thyroid cancers, Papillary Carcinoma tends to undergo marked haemorrhagic degenerative changes.

Sampling of this haemorrhagic fluid with sparse tumour cells may result in false interpretation as a benign cyst. This could be the reason in 2 cases who were diagnosed benign initially and turned out to be papillary carcinoma in final HPE diagnosis.

Although, fine-needle biopsy is the best predictor of malignancy in either cystic or solid thyroid lesions, it is slightly less reliable when a thyroid lesion is fluid filled rather than solid[26]. Sampling error occurs in 7.5% to 46%of cases documented in literature. This is high in cases where the size of nodule is more than 4 cm or less than 1cms, when there is haemorrhage into a nodule, or, it is multinodular[2].

A False Positive Diagnosis Can Be Given If:

a) Cellular colloid goitre is mistaken for neoplasms.
b) Chronic Lymphocytic thyroiditis can be misdiagnosed as malignant lymphoma[2]

The sensitivity of FNAC in study by Chetna Sharma[25] in case series of 724 cases was 89.5% and specificity was 98%.The comparable studies in literature report sensitivity in the range of 82–93.4% and specificity of 74.9–96%. The positive predictive value in Chetna[25] series was 84.6% compared to 85.7–98.6% in other studies[27-29-30].

The negative predictive value in that series was 98.6% as compared to 91.8–94% in similar studies in literature[28-29-30]. The accuracy of FNA in detecting malignancy in thyroid lesions in her study was 97%[25] which reinforces that FNAC can be used as a reliable tool to detect thyroid malignancy. Other studies in the literature report accuracy ranging from 83.6% to 93.6% and support our results[28-29-30].

Comparison of all this indicators along with few other studies in which cases range from around 100 to more than 6000 as shown in table 4 in results have similar type of data.

FNAC diagnosis is reliable to such an extent that frozen section used extensively can be limited to for pathologies detected as suspicious on FNAC.

While follicular neoplasm definitely needs histological examination to rule out carcinoma, rest of the FNAC confirmed pathologies do not need frozen section routinely and surgical management can be planned based on FNAC report alone (Chow et al, 1999)[31].

Conclusion: Following conclusions were made by our study:

1. FNAC is safe, quick and patient friendly procedure for diagnosis of various thyroid lesions.
2. It is reliable with high level of accuracy for differentiating various benign and malignant lesions of thyroid.
3. Correct Sampling technique and proper reporting system adapted will increase the efficacy of this method.
4. Modalities of treatment or type of surgery can be decided on the basis of results of FNAC in thyroid swellings.
5. Some patients can be kept conservatively on basis of FNAC but close observation and clinical suspicion is necessary.
6. Some type of malignancy like follicular variant of papillary carcinoma and detection of follicular neoplasm will require HPE.

References:

1. Chandanwale S, Singh N, Kumar H. Clinicopathological correlation of thyroid nodules. Int J Pharm Biomed Sci. 2012; 3:97-102.
2. Arif M, H Sunil. Benefits and limitations of FNAC in thyroid diseases: our institutional experience. Int J Res Med Sci 2013; 1:435-40.
3. Esmaili HA and Taghipour H. Fine- Needle Aspiration in the Diagnosis of Thyroid Diseases: An Appraisal in Our Institution. ISRN Pathology. 2012; doi:10.5402/2012/912728.
4. Rojeski MT, Gharib H. Nodular thyroid disease. Evaluation and management. New Eng. J Med. 1985; 313:428-36
5. Goldstein RE, Netter Ville JL et al., Implications of follicular neoplasms, atypia and lesions suspicious for malignancy diagnosed by fine needle aspiration of thyroid nodules. Annals of Surgery. 2002; 235: 656-664.
6. Gupta M, Gupta S, and Gupta VB. Correlation of Fine Needle Aspiration Cytology with Histopathology in the Diagnosis of Solitary Thyroid Nodule. J Thyroid Res. 2010; doi:10.4061/2010/379051
7. Das D, Sharma MC, Sharma A, Datta TK, Lahiri SK. A Comparative study between fine needle aspiration cytology and histopathological examination in the diagnosis of neoplastic and non-neoplastic lesions of the thyroid gland. Indian J Prev Soc Med. 2012; 43(1):72-5.
8. Orell SR, Vielh P. The techniques of FNA cytology. In: Orell SR, Steratt FG, eds. Fine needle aspiration cytology. 5th edn. Elsevier; 2012: 10.
9. Polyzos SA, Kita M, Avramidis A. Thyroid nodules - Stepwise diagnosis and management. Hormones (Athens) 2007; 6:101- 19
10. Gupta M, Gupta S. Correlation of Fine Needle Aspiration Cytology with Histopathology in the Diagnosis of Solitary Thyroid Nodule. SAGE Hindawi Access to Research Journal of Thyroid Research Volume 2010, Article ID 379051,doi:10.4061/2010/379051
11. Edmund S, Syed Z. The 2017 Bethesda System for Reporting Thyroid Cytopathology.

THYROID Volume 27, Number 11, 2017 Mary Ann Liebert, Inc.DOI: 10.1089/thy.2017.0500
12. Luis H. Lopez, Jorge A. Canto, Miguel F. Herrera, Armando Gamboa-Dominguez, et al; Efficacy of Fine-Needle Aspiration Biopsy of Thyroid Nodules: Experience of a Mexican Institution; World J. Surg. 21, 408–411, 1997.
13. dsMojghanAmrikachi, Ibrahim Ramzy, Sheldon Rubén Feld, Thomas M Wheeler, Accuracy of Fine-Needle Aspiration of Thyroid .A Review of 6226 Cases and Correlation With Surgical or Clinical Outcome, Arch Patho Lab Med. 125;484–488; 2001.
14. Muhammad saddique, Umair-ul-islam, Pervez iqbal, Qamaruddinbaloch; Fnac: A reliable diagnostic tool in solitary thyroid nodule and multinodular goitre; patients. Journal of surgery, 24(3); 2008. \
15. Ikram M, Hyder J, Muzaffar S, Hasan SH. Fine Needle Aspiration cytology (FNAC) in the management of thyroid pathology – the Aga Khan University Hospital experience. J Pak Med Assoc 1999; 49(6):133-5.
16. Tazeen J,Danish R et al Histopathological and Cytological Correlation of Thyroid Nodules with Emphasis on Bethesda System for Reporting Thyroid Cytology-A 7 Year Study. International Journal of Contemporary Medical Research 2018; 5(1):28-31
17. Mandreker, SR., Nadkarni, NS, Pinto, RG and Menezes, S. Role of fine needle aspiration cytology as the initial modality in the investigation of thyroid lesions. Acta Cytologica. 1995; 39: 898-904
18. Sirpal YM. Efficacy of fine needle aspiration cytology in the management of thyroid diseases. Indian J Patho Microbiol. 1996; 39: 173-8.
19. Al-Rikabi, AC, Al-Omran, M., Cheema, M, El-Khwsky F. and Al-Nuaim A. Pattern of thyroid lesions and role of fine needle aspiration cytology (FNA) in the management of thyroid enlargement: a retrospective study from a teaching hospital in Riyadh. APMIS. 1998; 106:1069–1074.
20. Amrikachi M, Ramzy I, Rubenfeld S, Wheeler TM. Accuracy of fine-needle aspiration of thyroid. Arch Pathol Lab Med 2001; 125:484–8
21. Cross PA, Chandra A, Giles T, Johnson S, Kocjan G, Poller D, Stephenson T. Guidance in the reporting of thyroid cytologyspecimen2009[Internet].Availableat:< http://www.rcpath.org/resources/pdf/g089guidanceonthereportingofthyroidcytologyfinal.pdf
22. HA Naggada, AB Musa, BM Gali et al.Fine needle aspiration cytology of thyroid nodule(s): a Nigerian tertiary hospital experience. The Internet Journal of Pathology. 2006; 5:7.
23. Fernandez H, D'Souza C R S, et al, FNAC Head and Neck Masses. Journal of Clinical and Diagnostic Research. 2009;3: 1719-1725
24. 24 Attavilla G, Pascale M, Nenci I. Fine needle aspiration cytology of thyroid gland diseases. Acta Cytol 1990; 34: 251-6.
25. C.Sharma. Diagnostic accuracy of fine needle aspiration cytology of thyroid and evaluation of discordant Cases. Journal of the Egyptian National Cancer Institute (2015) 27, 147–153
26. de los Santos ET, Keyhani-Rofagha S, Cunningham JJ,Mazzaferri EL. Cystic thyroid nodules. The dilemma of malignant lesions. Arch Intern Med 1990; 150:1422–7.
27. Sangalli G, Serio G, Zampatti C, Bellotti M, Lomuscio G. Fine needle aspiration cytology of the thyroid: a comparison of 5469cytological and final histological diagnoses. Cytopathology2006; 17:245–50.
28. Borgohain R, Lal RK, Chatterjee P, Brahma N, Khanna S. A study of cyto-histological correlation in the diagnosis of thyroid swelling. IOSR J Dent Med Sci 2014; 13(11):46–9, e-ISSN: 2279–0853, p-ISSN: 2279–0861, Ver. IV,
29. Sinna EA, Ezzat N. Diagnostic accuracy of fine needle aspiration cytology in thyroid lesions. J Egypt Natl Cancer Inst 2012;24:63–70.
30. Jarwani PB, Patel S. Fine-needle aspiration cytology (FNAC) of the thyroid: a cytohistologic correlation with critical evaluation of discordant cases. GCSMC J Med Sci 2013; 2:5–12.
31. Chow T.L, Venu. V. Kwok S.P. Use of FNAC and frozen section in diagnosis of thyroid nodules. Australia – New Zealand Journal of Surgery 1999; 69(2):131-133.

Conflict of interest: None

Funding: None

Cite this Article as: Dalal N, Gandhi S, Patel D, Shah S, Parikh F. A Retrospective Study Of comparison Of Fine Needle Aspiration Cytology (FNAC) With Histopathological Diagnosis (HPE) In Thyroid Swelling: A Tertiary Care Hospital Experience. Natl J Integr Res Med 2020; Vol.11(5): 21-27