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Original Research Article

Comparative Study of Diagnostic Accuracy of Minimally Invasive Pathological Techniques (FNAC) Impression Cytology with Clinical, Radiological and Histopathological Examinations in Diagnosis of Thyroid Nodule

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Abstract:

Introduction: Thyroid is one of the largest endocrine gland. Nervous system, endocrine System and immune system are connected physiologically and act in synchronized manner to mediate the body quick and precise response to environmental stress. Normal thyroid gland weighs 20-25 grams.

Aims: To determine and compare the diagnostic accuracy of clinical assessment, radiological assessment, FNAC before surgical management, impression cytology during surgery and histopathological examination after surgical removal of the thyroid nodule.

Materials and Methods: The present study was a prospective study. This Study was conducted from January 2017 to july 2018 at Department of surgery, NRS medical College & Hospital, Kolkata

Result: In this study, we have concluded that FNAC has 94.4% sensitivity, 83.3% specificity with accuracy of 90%. In our study USG was more reproducible than Clinical Examination, where the former had 47%sensitivity, 76.9% specificity, 72.7% positive predictive value (PPV), 52.6% negative. predictive value (NPV), and 60% accuracy, whereas the latter had 38.9% sensitivity, 75% specificity, 70% PPV, 45.00% NPV, and 53.3% accuracy. Ultrasonography had 47% sensitivity, 76.9% specificity, 72.7% positive predictive value (PPV), 52.6% negative predictive value (NPV), and 60% accuracy.

Conclusion: With respect to sensitivity, in our study FNAC has the highest sensitivity (94.4), followed by Ultrasonography (47.0) and Clinical Examinations (38.9). With respect to Specificity, in our study FNAC has the highest specificity (83.3), followed by Ultrasonography (76.9) and Clinical Examinations (75.0). With respect to Accuracy, in our study FNAC has the highest accuracy (90.0), followed by Ultrasonography (60.0) and Clinical Examinations (53.3). Impression smear also cannot detect the margin status in thyroid specimens.

Keywords: Histopathological, Thyroid Nodule and Radiological.

Introduction

Thyroid is one of the largest endocrine gland. Nervous system, endocrine System and immune system are connected physiologically and act in synchronized manner to mediate the body quick and precise response to environmental stress [1]. Normal thyroid gland weighs 20-25 grams. The functioning unit is the lobule, supplied by single arteriole and consists of 24-40 follicles lined with cuboidal epithelium. The follicle contains colloid in which thyroglobulin is stored. The arterial supply is rich and extensive anastomoses occur between the main thyroid arteries and branches of the trachea and oesophageal arteries. There is extensive lymphatic network within and around the gland. Although some lymph channels pass directly to the deep cervical nodes ,the subcapsular plexus drains principally to the central compartment juxta thyroid –'Delphian and paratracheal nodes and nodes on superior and inferior thyroid veins (level VI) and from there to deep cervical (level II, III, IV and V)and medistinal groups of nodes (level VII). The relationship between the recurrent laryngeal nerve (RLN) and thyroid is of supreme importance to the surgeons. A branch of vagus round the arch of aorta on the left and subclavian artery on the right. The clinical significance of this is that on left, the nerve has more distance in which to reach the tracheoesophageal groove and therefore runs in a

medial plane. On the right, there is less distance and the nerve runs more obliquely to reach the tracheoesophageal groove.

Approximately 2% of the nerve on the right are non-recurrent and will enter the larynx at the cricothyroid joint, at the level of Berry`s ligament. This is the point at which the nerve is at most risk of injury during surgery.

Embryology of thyroid underlies the anatomical position, anatomical variation and congenital condition of these structures and is therefore vital of surgery. The thyroglossal duct develops from the median bud of the pharynx. The foramen caecum at the junction of anterior two third and posterior one third of the tounge is the vestigial remnant of the duct. This initially hollow structure migrates caudally and passes in close continuity with, and sometimes through the developing hyoid cartilage. The parathyroid gland develops from third and fourth pharyngeal pouches. As it dedescends, the thymus takes the associated parathyroid gland with it, which explains why the inferior parathyroid which arises from third pharyngeal pouch normally lies inferior to the superior gland. The developing thyroid lobe amalgamates with the structures that arise in the 4th pharyngeal pouch, the superior parathyroid gland and ultimobranchial body. Parafollicular cell(C-cells) from neural crest reaches the thyroid via the ultimobranchial body. Thyroid gland is responsible for the production of the metabolic hormones-thyroxine (T4), triiodothyroxine (T3) and calcitonin.

The spherical thyroid follicular unit is composed of a single layer of cuboidal follicular cells that encompass a central depository of colloid filled mostly thyroglobulin (Tg), the protein in which T4&T3 are synthesized and stored. In between these units are parafollicular cells or C-cells that generate calcitonin. When hormones are required, the complex is reabsorbed into the cells and thyroglobulin is broken down. T3&T4are liberated and enter the blood, where they are bound to serum proteins; albumin, thyroxine binding globulin(TBG) and thyroxine binding prealbumin (TBPA). The small amount hormone that remains free in the serum is biologically active [2,3].

Material and Methods

Study Area: Indoor ward, Department of surgery, NRS medical College & Hospital, Kolkata

Study Population: Patient admitted at indoor in a single unit Department of surgery, NRSMCH, Kolkata

Study Duration: January 2017 to July 2018

Sample Size: 30 patients admitted with thyroid nodue in surgical ward of NRSMCH, Kolkata

Sample Design: simple random sampling

Study Design: A prospective study

Parameters to Be Studied:

- Demographic parameter: Age , sex, BMI, family History
- Clinical parameters: History vitals and detailed examination of thyroid swelling and its others signs.
- Pathological parameters: FNAC impression cytology of resect specimen
- Radiological parameters: ultrasonography (USG),

Study Tools:

- History taking
- Clinical thyroid nodule examination
- Minimally invasive pathological techniques i.e. FNAC
- Radiological parameters neck Xray lateral view, CXR PA view, USG, CT, and MRI in selected cases.
- Impression cytology of the resected specimen from resected surface
- Histopathological examination of the specimen

Study Technique: After proper case selection, the patients can undergo clinical examination, FNAC, USG, Radiography of neck and chest CT and MRI in few selected cases. In clinical examination, local examination is done by inspection and palpation of thyroid swelling. Followed by examination of regional lymphnodes. FNAC is performed from thyroid swelling and reports are studied. USG of the swelling is done and reports are collected. Radiography neck lateral view and CXR PA view are done.

During surgery when the specimen of thyroid swelling is resected impression cytology technique is used to determine cellular diagnosis and margin status of the resected specimen. The specimen is then evaluated by histopthological examination

Inclusion Criteria:

- Patients above the age of 12 years
- Patients having thyroid nodule
- Patient having euthyroid status

Exclusion Criteria:

- Children aged less than 12 years
- Pregnant patients
- Patients unable to undergo gold standard diagnostic procedure i. e. excision biopsy
- Patient having hypo or hyper thyroid status.

Result

Table 1: Distribution of patients according to the duration of thyroid swelling/nodule in months

Row Labels	Count of Duration (months)	Percent
<6	7	23.3
6-11	13	43.3
12-17	4	13.3
18-23	3	10.0
24-29	2	6.7
30-36	1	3.3
Grand Total	**30**	**100**

Table 2: Distribution of cervical lymph node metastasis

Row Labels	Count of Cervical Lymph Nodes	Percent
No	27	90
Yes	3	10
Grand Total	**30**	**100**

Table 3: Distribution of patients according to the family history of thyroid nodule

Row Labels	Count of Family History	Percent
Absent	26	86.7
Present	4	13.3
Grand Total	**30**	**100**

Table 4: Distribution of patients according to the side of thyroid nodule

Row Labels	Count of Family History	Percent
Right	15	50
Left	15	50
Grand Total	**30**	**100**

Table 5: Distribution of patients according to the skin changes

Row Labels	Count of Skin Changes	Percent
Absent	27	90.0
Present	3	10.0
Grand Total	**30**	**100**

Table 6: Distribution of patients according to fixity to deeper structures

Row Labels	Count of Fixity to Deeper Structure	Percent
No	24	80
Yes	6	20
Grand Total	**30**	**100**

Clinical Examination:

Table 7: Frequency of Clinical Examination

		Frequency	Percent
Clinical Examination	FN	11	36.7
	FP	3	10.0
	TN	9	30.0
	TP	7	23.3
	Total	**30**	**100.0**

FN= False Negative; FP= False Positive; TN= True Negative; TP= True Positive

Therefore, Sensitivity = 7/(7+11) = 7/18 = 38.9, Specificity = 9/(9+3) = 9/12 = 75.0, Positive Predictive Value = 7/(7+3) = 70.0, Negative Predictive Value = 9/(9+11) = 45.0, Accuracy = (7+9)/30 = 53.3.

Ultrasonography:

Table 8: Frequency of Ultrasonography

		Frequency	Percent
Clinical Examination	FN	9	30.0
	FP	3	10.0
	TN	10	33.3
	TP	8	24.7
	Total	**30**	**100.0**

FN= False Negative; FP= False Positive; TN= True Negative; TP= True Positive

Therefore, Sensitivity = 8/(8+9) = 8/17 = 47.0, Specificity = 10/(10+3) = 10/13 = 76.9, Positive Predictive Value = 8/(8+3) = 72.7, Negative Predictive Value = 10/(10+9) = 52.6, Accuracy = (8+10)/30 = 60.0.

FNAC:

Table 9: Frequency of FNAC

		Frequency	Percent
Clinical Examination	FN	1	3.3
	FP	2	6.7
	TN	10	33.3
	TP	17	56.7
	Total	**30**	**100.0**
FN= False Negative; FP= False Positive; TN= True Negative; TP= True Positive			

Therefore, Sensitivity = 17/(17+1) = 17/18 = 94.4, Specificity = 10/(10+2) = 10/12 = 83.3, Positive Predictive Value = 17/(17+2) = 89.5, Negative Predictive Value = 10/(10+1) = 90.9, Accuracy = (17+10)/30 = 90.0.

Discussion

Accurate preoperative diagnosis of thyroid nodule is most important prerequisite not only for proper counseling but management also. The type of management solely depends on this. For surgical point of view, type of surgery whether hemithyroidectomy, subtotal thyroidectomy, near total or total thyroidectomy will be performed, depends on proper diagnosis of the nodule, which is not possible before surgery with certainty without histopthological examination.

To compare tests fairly, Clinical examination, FNAC and USG should be done fo thyroid nodule, and later surgically excised for definitive histology. The aim of our study was to determine and compare the diagnostic accuracy of clinical assessment, radiological assessment, FNAC, thyroid function test before surgical management, impression cytology during surgery and histopathological examination after surgical removal of the thyroid nodule.

The low cost and easy availability, enabling a Fine needle aspiration biopsy (FNAC) is the most important step in the workup of the thyroid nodule, as cytology is the primary determinant in whether thyroidectomy is indicated.

FNAC is widely available and well tolerated, with a low risk of complications. Its use has dramatically decreased the number of thyroidectomies performed. FNAC can be performed with or without ultrasound guidance, but diagnostic accuracy is improved using sonographic needle localization due to a decreased number of inadequate specimens and false negative results [4].The only malignant pathology reliably diagnosed through fine needle aspiration is papillary thyroid carcinoma, as features such as 'Orphan Annie' nuclei, nuclear grooves, intra-nuclear inclusions, and psammoma bodies can be sufficient for a diagnosis.

Medullary carcinoma, anaplastic carcinoma, lymphoma, poorly differentiated carcinoma, and metastatic disease have also been reported to be classified on the basis of cytology. Benign and malignant follicular neoplasms and oncocytic (formerly called Hurthle cell) adenomas and carcinomas cannot be distinguished on the basis of cytology alone, as tissue architecture is required to make the diagnosis of malignancy through observation of capsular or angiolymphatic invasion.

While this has historically been true, recent advances in the application of molecular markers to FNAC are changing these principles. Clinical Examination is also a noninvasive predictor of the thyroid nodule, whether it is malignant or benign and is relatively simple and inexpensive, but accuracy is lower 53.3%, compared with other parameters. In this study, we have concluded that FNAC has 94.4% sensitivity, 83.3% specificity with accuracy of 90%.

There was no reported complication during procedure in all 30 cases described in our study. In a study conducted by Fatemeh Hajmanoochehri and Elham Rabiee named "FNAC accuracy in diagnosis of thyroid neoplasms considering all diagnostic categories of the Bethesda reporting system: A single-institute experience", FNAC diagnosis had 95.2% sensitivity, 68.4% specificity, 83.3% positive predictive value, 89.6% negative predictive value, and 85.14% accuracy [5]. In another study conducted by Ajay Kumar B, Sreejayan MP and Vaisagh Remin at Department of General Surgery, Government Medical College, Kerala, India, Sensitivity of FNA for diagnosis of neoplasm is 81.6%. Specificity of FNA for diagnosis of neoplasm is 92%.These values are in agreement with the values of our study [6].

In our study USG was more reproducible than Clinical Examination, where the former had 47%sensitivity, 76.9% specificity, 72.7% positive predictive value (PPV), 52.6% negative predictive value (NPV), and 60% accuracy, whereas the latter had 38.9% sensitivity, 75% specificity, 70% PPV, 45.00% NPV, and 53.3% accuracy.

Ultrasonography had 47% sensitivity, 76.9% specificity, 72.7% positive predictive value (PPV), 52.6% negative predictive value (NPV), and 60% accuracy. In study conducted by Alper Ozel, Sukru Mehmet Erturk, Alkin Ercan, Banu Yılmaz, Tulay Basak, Vito Cantisani, Muzaffer Basak, Zeki Karpat titled" [7]. The diagnostic efficiency of ultrasound in characterization for thyroid nodules: how many criteria are required to predict malignancy?" For the nodules greater than one centimeter, the calculated diagnostic performances including sensitivity, specificity, positive predictive value and negative predictive value were 62.5%, 91.5%, 30.3% and 97.7%, respectively. The diagnostic accuracy of US score for nodules larger than one centimetre was found; 89.9%. For the nodules smaller or equal to one centimetre the corresponded values for the sensitivity, specificity, positive predictive value, negative predictive value and accuracy were 83.3%, 94.9%, 62.5%, 98.2% and 93.8%, respectively (table II).

The presence and absence of each US feature of the evaluated nodule – shape taller than wide, irregular margin, hypoechogenicity, microcalcification, and intranodular vascularity – were scored 1 and 0, respectively. In the other study permormed by Ganesh Manikantan, Ragendu G. Ravi, Meer M. Chisthi titled "Diagnostic accuracy of ultrasonography in goiters: a tertiary centre experience" [8], for detection of malignancy ultrasound has a sensitivity of 87.2%, specificity of 79.2%, positive predictive value of 89.1 %, negative predictive value of 76% and an overall accuracy of 84.5%, which is not in concordance with literature.

In the study conducted by Dhanadia A et al, for detection of malignancy ultrasound had sensitivity of 83.3%, specificity 72.7%, PPV 29.4%, NPV 96.9%. [9]. this difference in result may be due to differences in data selection, sample size or parameters taken for considering malignancy. This difference may also be due to lack of uniform reporting and this is operator dependent. We have followed TIRADS (Thyroid Image Reporting And Data System), which is a risk stratification system for classifying thyroid lesions and was recently recognized in an American College of Radiology (ACR) .I have discussed it in detail in review of literature. But one thing is in accordance with our finding is that it is the second most accurate modality for thyroid nodule.

When comparing the sensitivity, specificity, PPV, NPV, and accuracy of clinical examination, radiological diagnosis(USG), and miniinvasive (FNAC) diagnosis, our results showed that sensitivity was 38.9%, 47%, and 94.4%; specificity was 75%, 76.9%, and 83.3%; PPV was 70%, 72.7%, and 89.5%%; NPV was 45%, 52.6%, and 90.9%%; and accuracy was 53.3%, 60%, and 90%, respectively.In our study, the false-positive rate of FNAC was 6.7%, whereas the false-negative rate of FNAC was 3.3%.

The sensitivity, specificity, and accuracy of FNAC for thyroid nodule ranged from 80% to90%, 65%to85% and85%to95% respectively available in literatures. In our study, FNAC of thyroid nodule lesions showed a sensitivity of 94.4%, a specificity of 83.3%, and an accuracy of 90%. The PPV was 89.5% and the NPV was 90.9%. These results are in agreement with many other reports that have shown the high diagnostic value of this technique.

Conclusions

- With respect to sensitivity, in our study FNAC has the highest sensitivity (94.4), followed by Ultrasonography (47.0) and Clinical Examinations (38.9).
- With respect to Specificity, in our study FNAC has the highest specificity (83.3), followed by Ultrasonography (76.9) and Clinical Examinations (75.0).
- With respect to Accuracy, in our study FNAC has the highest accuracy (90.0), followed by Ultrasonography (60.0) and Clinical Examinations (53.3).
- Impression smear also cannot detect the margin status in thyroid specimens

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