



## ROLE OF ULTRASOUND GUIDED FINE NEEDLE ASPIRATION CYTOLOGY AND NON ASPIRATION CYTOLOGY IN THYROID LESIONS- A CONTEMPORARY REVIEW

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**ABSTRACT** **BACKGROUND:** Fine needle aspiration cytology (FNAC) and Fine needle non aspiration cytology (FNNAC) are most widely employed diagnostic techniques in thyroid lesions. Both procedures have their own advantages and disadvantages. This review article is an attempt to evaluate the superiority of one test over the other based on available literature. **METHODS:** Primary relevant publications obtained from PubMed, Google Scholar, EMBASE, MEDLINE, Cochrane Database of systematic reviews (CDSR) were included. Duplicate copies of article in various databases were eliminated. The articles were reviewed based on cytological interpretation, role of ultrasound in cytology and comparison of FNAC and FNNAC. **RESULTS:** Both FNNAC and FNAC have similar diagnostic accuracy for a malignant thyroid lesion and superiority could not be established.

**KEYWORDS :** Thyroid, cytology, fine needle, aspiration, non- aspiration

### INTRODUCTION

Thyroid malignancy is one of the most common endocrine tumours with an incidence rate of 1% in male and 1.8% in females in India.<sup>1</sup> Due to the development and biopsy techniques incidence of thyroid lesion have tripled in the past 25 years.<sup>2</sup> Early diagnosis and appropriate treatment remains the corner stone in the management of the thyroid malignancy.

Since its time of inception, fine needle aspiration cytology remains the baseline investigations for pre- operative diagnosis. It is minimally invasive and has high sensitivity. The disadvantages include the negative pressure exerted during aspiration causing distortion in cellular morphology and blood in the background causing improper cytological interpretation.

In order to overcome these disadvantages fine needle non aspiration cytology was developed. As this technique is based on the capillary sampling, it eliminates bleeding and cellular distortion.<sup>3</sup> Inclusion of ultrasound in localising the lesion has significantly improved the diagnostic accuracy of these tests.

There are studies with conflicting results trying to establish superiority of one over other. In this review article we evaluate the performance of ultra sound guided FNAC and FNNAC in diagnosing thyroid lesion.

### METHODS

Relevant publications collected from PubMed, Google Scholar, EMBASE, MEDLINE, Cochrane Database of systematic reviews (CDSR) were included in the study. The key search words used were fine needle, aspiration, non-aspiration, capillary sampling, thyroid and cytology. No restriction based on date of publication was enforced. Duplicate copies of publications in multiple databases were eliminated. A brief contemporary overview of thyroid FNAC and FNNAC was prepared.

### REVIEW OF LITERATURE

The literature that has been available in the last 15 years has been reviewed under following headings

1. CYTOLOGY AND CYTOLOGICAL FEATURES OF THYROID LESION
2. REPORTING OF THYROID CYTOLOGY
3. FNAC
4. FNNAC
5. ROLE OF USG IN CYTOLOGY
6. COMPARITIVE STUDY IN FNAC and FNNAC

### CYTOLOGY

*Sidawy MK (2007)* in his book, Foundations in diagnostic pathology, has mentioned that identifiable swellings of the thyroid occur in 4% to 10% of the general population, of which only 5% are malignant.<sup>4</sup> Cytology provides a powerful tool to distinguish swellings which require surgery from those which don't require.

*Orell and Strett (2011)* in their book, on fine needle aspiration Cytology, have mentioned that thyroid cytology sample will be considered adequate for evaluation if it contains a minimum of six groups of well-visualized follicular cells, with at least ten cells per group, preferably on a single slide.<sup>5</sup>

The above criteria may not necessarily be applied for the following circumstances

- Solid nodules with cytological atypia- A sample that contains significant cytological atypia is never considered inadequate.
- Solid nodules with inflammation- Nodules in patients with lymphocytic (Hashimoto) thyroiditis, thyroid abscess, or granulomatous thyroiditis may contain only numerous inflammatory cells.
- Colloid nodules-Specimens that consist of an abundant thick colloid are considered benign and satisfactory for evaluation.<sup>6,7</sup>

### WHO HISTOLOGICAL CLASSIFICATION OF THYROID TUMOURS (2017)<sup>6</sup>

- Follicular adenoma
- Hyalinizing trabecular tumour
- Other encapsulated follicular patterned thyroid tumours
- Tumours of uncertain malignant potential
- Noninvasive follicular thyroid neoplasm with papillary-like nuclear features
- Papillary thyroid carcinoma
- Follicular thyroid carcinoma
- Hurthle (oncocytic) cell tumours
- Poorly differentiated thyroid carcinoma
- Anaplastic thyroid carcinoma
- Squamous cell carcinoma
- Medullary thyroid carcinoma
- Mixed medullary and follicular thyroid carcinoma
- Mucoepidermoid carcinoma
- Sclerosing mucoepidermoid carcinoma with eosinophilia
- Mucinous carcinoma
- Ectopic thymoma
- Spindle epithelial tumour with thymus like differentiation
- Intrathyroid thymic carcinoma

- Paraganglioma and mesenchymal/stromal tumours
- Paraganglioma
- Peripheral nerve sheath tumours
- Benign vascular tumours
- Angiosarcoma
- Smooth muscle tumours
- Solitary fibrous tumour
- Hematolymphoid tumours
- Langerhans cell histiocytosis
- Rosai-Dorfman disease
- Follicular dendritic cell sarcoma
- Primary thyroid lymphoma
- Germ cell tumours
- Secondary tumours

#### FINE NEEDLE ASPIRATION CYTOLOGY (FNAC)

In 2003 *Das DK* published a review article addressing the origin and evolution of FNAC over the period of time. They have mentioned only during 19<sup>th</sup> and 20<sup>th</sup> century, surgical needles were used for diagnosis of the lesion. In 1912, a German Haematologist, Hans Hirschfeld reported the fine needle aspiration biopsy of cutaneous lymphomas and other tumors using cellular aspirates.<sup>8</sup> Later this technique was employed in various other lesions and was pioneered by Karolinska hospital (Lowhagen) at Sweden.

Minimum 6 aspirations are made. An adequate FNAC smear should have six aspirations with six groups of cells with each group containing 20 cells. Aspiration is graded as

- thy1- non diagnostic
- thy2- non neoplastic
- thy3- follicular
- thy4- suspicious of malignancy
- thy5- malignancy.

In 2009, *Magiorkinis et al* in their article commenting on the historical aspects of FNAC claims that the first use of fine needle thyroid biopsy was published by T.Tempka, Aleksandrowich and M.Tillin 1948.<sup>9</sup>

In 2015, *Witt et al* compared number of passes to obtain a satisfactory cytological result with on-site cytopathological interpretation is reduced with ultra sound guidance in a study conducted among 200 consecutive patients. There was 100% cytological adequacy and significantly fewer passes.<sup>10</sup>

#### FINE NEEDLE NON ASPIRATION CYTOLOGY

The cytologist consistently had problems while interpreting the prepared smear as it contained haemorrhagic background. Hence an alternative technique was attempted, called fine needle non aspiration cytology or cyto puncture, by *Briford et al*, for breast cancer.<sup>11</sup>

As the thyroid gland is highly vascular it usually yields aspirate with considerable amount of blood. So the smear prepared had blood in the background. This blood field often made the interpretation difficult. Another common problem encountered was dilution of thyroid cells by the aspirated blood. The basic principle behind FNNAC was filling of the cellular content within the lumen of the needle due to the capillary tension in the narrow channel. Both fluid and semi fluid contents ascends in to the lumen. The amount content that filled within the tube or capillary is inversely proportional to the diameter of the tube.<sup>12</sup> This technique was more patient friendly than other invasive techniques employed for pre-operative diagnosis.

In 2015, *Buzdugü et al* studied 309 patients with thyroid nodules in Endocrinology Clinic of the Iasi St. Spiridon. When mair's scoring system was used to assess the two sampling techniques, they found perception of tumor consistency was better with FNNAC.<sup>13</sup>

#### ROLE OF USG IN CYTOLOGY

Ultrasound is used to identify the number, size, vascularity and echogenicity of the nodule. It is also used to obtain cytology which is more accurate.

In 2017, *Dighe et al* in their elaborate study have established that Benign lesion is hyperechoic, often cystic with well-defined margin

and shows peripheral egg shell calcification with sonolucent rim (halo) around the nodule. Malignant lesion is hypo echoic with poorly defined margin, with high vascularity with micro calcification without any halo around them.<sup>14</sup>

In study conducted by *Degirmenciet al (2007)* sonogram guided fine needle biopsy was done for 232 solid thyroid nodules. The biopsy specimens were acquired after localisation of the lesion. Sufficient cytological material was obtained in 154 (66.4%). They concluded there was higher sufficient cytological material when sonogram was used and when finer needles were used.<sup>15</sup>

*Inci et al (2013)* in their study between September 2010 and June 2012, 270 nodules were biopsied, 184 (68.1 %) specimens were considered as adequate CM and 86 (31.9 %) specimens were considered as inadequate CM. They concluded that the nodule size and needle size used for sampling did not affect the adequacy of FNAB and sonography improved the accuracy of cytological material obtained.<sup>16</sup>

#### COMPARISON OF FNAC VS FNNAC

In 2013 *Nisha et al* conducted a single blinded study comprising 144 patients with thyroid nodule. Those smears prepared were evaluated for cellular content, cellular dilution, with either blood or clot and cellular architecture, which facilitated better diagnosis of the lesion. Their study FNAC yielded better cellular material. Similarly, FNNAC yielded more diagnostically adequate smears. As expected the study points out smears prepared by FNAC had higher background blood than FNAC.<sup>17</sup>

In 1993, *Dey et al* in their single centre prospective study performed Fine needle aspiration (FNA) and non.suction fine needle sampling (FNS) consecutively in 107 lesions from 100 patients. The quality of diagnostic material was assessed using a scoring system based on the cellularity and amount of blood in the smear. The total score in the FNS group was significantly higher than that of FNA technique. They concluded that the FNS procedure is less traumatic and equally cost effective and can be safely undertaken in liver, orbital and thyroid lesions. However, this procedure cannot be advocated in cystic, bony and fibrous lesions.<sup>18</sup>

In 2003, *Haddadi-Nezhad et al* in their prospective study done Endocrinology and Metabolism Research centre, Tehran, studied 162 females and 38 males with thyroid lesions. Only those patients with thyroid lesion 1-4 cm were included in the study. All the patients were subjected to both FNNAC and FNAC. Even though specimen obtained from 43 patients were labeled as inadequate, the average score of all parameters studied revealed no statistical difference between them. They have concluded the study by mentioning that FNNA was not superior to FNAC.<sup>19</sup>

In 2015, *Song et al* in their meta-analysis assigned scored for each parameter used for assessing the slide. Their analysis included 16 studies involving 1842 patients and 2221 samples. They concluded that both the procedures were equally effective in diagnosing the lesion as there was no statistical difference in their respective diagnostic indices.<sup>20</sup>

In the study conducted by *Kaur et al (2014)*<sup>21</sup> to assess the diagnostic accuracy of FNAC over FNNAC, a single operator did procedures for 88 cases. Individual parameters such bloody background, content of cellular material, degree of cellular degeneration and trauma were considered. It was concluded samples obtained were diagnostically superior by FNNAC technique whereas FNAC produced more diagnostically adequate smears.

*Tauro et al (2012)*<sup>22</sup> in their prospective study 50 patients with thyroid nodule attending the FR Muller Medical College Hospital from May 2006 to April 2008 were subjected to both the cytological techniques; FNA and FNC. The specimen and results were compared and then correlated with the final histopathological findings wherever surgical specimens were available (38 cases). The FNC technique yielded 88% diagnostic superiority and adequate specimens compared to 94% by FNA. Sensitivity was 50% for FNC and 100% for FNA while specificity was 100% for both techniques; accuracy score was 97.4% for FNC and 100% for FNA in predicting malignancy. They concluded that if both test were done in tandem it can give better and accurate cytological diagnosis.

## LITERATURE REVIEW MATRIX

Table 1: Literature review matrix comparing similar articles and their results

S.No	INDICES OF SCREENING TEST	Nisha et al (2013) <sup>17</sup>		Kaur et al(2014) <sup>21</sup>		Tauro et al (2012) <sup>22</sup>		De Carvalho et al (2010) <sup>23</sup>		MC Elavanna et al (2010) <sup>24</sup>	
		FNAC	FNNAC	FNAC	FNNAC	FNAC	FNNAC	FNAC	FNNAC	FNAC	FNNAC
1.	SENSITIVITY	87.4%	85.6%	92.2%	95%	85%	100%	100%	50%	81%	81%
2.	SPECIFICITY	84%	88.2%	93%	94.2%	100%	100%	100%	100%	90%	77%
3.	POSITIVE PREDICTIVE VALUE	-	-	92%	-	-	-	100%	-		
4	NEGATIVE PREDICTIVE VALUE	-	-	-	96.2%	-	-	-	97.3%		
5.	ACCURACY	68.4%	64.5%	-	-	-	-	100%	97.4%	85%	77%

## CONCLUSION

Both FNNAC and FNAC have similar diagnostic accuracy for a malignant thyroid lesion. The choice of investigation depends on the investigators and the physician. Superiority of one test over other cannot be achieved based on the available literature.

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