

Original Research Article

A study of the diagnostic effectiveness of repeated fine needle aspiration in thyroid and breast lesions

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ABSTRACT

Background: Fine needle aspiration cytology (FNAC) is a relatively safe diagnostic tool with high sensitivity and specificity. Due to lesion inherent properties and lack of proper technique, adequate cellularity is not yielded in some instances, resulting in an inconclusive report. In such instances we have to go for repeat FNA to make a proper diagnosis. Repeat aspirations impose unnecessary workload on the lab and are distressful to the patients. The issue of repeat aspiration is largely unaddressed. Objectives were to identify the proportion of repeated fine needle aspirations in breast and thyroid lesions turning out to be diagnostic and to identify and describe the common factors leading to repeat fine needle aspiration.

Methods: 190 cases of repeated FNA including both thyroid and breast lesions are included in the study. FNA done after an initial aspiration with inconclusive smear is considered as repeated FNA. History, clinical examination findings, findings in imaging studies, nature of aspirate obtained for each patient advised repeat FNA, are recorded. Proportion of repeat FNAs turning out to be diagnostic and the documented reasons for repeat were taken as the outcome measure.

Results: 78% of repeat FNA in thyroid lesions and 50% of the repeat FNA in breast lesions were diagnostic. Inadequate cellularity, haemorrhagic aspirate and cystic change are the most common factors leading to repeat FNA.

Conclusions: Since thyroid and breast are the most common sites where FNA is done and 64% of the total lesions are diagnostic, repeat FNA in all other sites are likely to yield a similar diagnostic outcome. Hence, repeat FNA is advisable in lesions which had initial non diagnostic result.

Keywords: Repeat FNA, Thyroid, Breast, Diagnostic, Inconclusive

INTRODUCTION

It was in 1950 and 1960s, FNAC as a technique began to flourish in the Europe. Soderstrom and Franzen in Sweden, Lopes Cardazo in Holland, Zajdela in France were the major proponents of FNA, studying thousands of cases each year.¹ In further years, FNAC had been established as a routine diagnostic tool used by pathologists and clinicians as it is a simple, cost effective and rapid technique. It is a relatively safe procedure with less procedure related complications. Nowadays FNAC is used as a first-line diagnostic test.

FNAC is a diagnostic tool with high sensitivity and specificity. But approximately 1–24% of FNAs yield a nondiagnostic result.² Due to lesion inherent properties and lack of proper technique adequate cellularity is not yielded in some instances, resulting in an inconclusive report. In such instances we have to go for repeat FNA to arrive at a proper diagnosis. Repeat aspirations impose unnecessary workload on the laboratory and the cytopathologist. It is also distressful to the patient and adds to their anxiety. According to Bethesda, nondiagnostic thyroid fine-needle aspirations are associated with 5-10% risk of malignancy.³ The risk of malignancy associated

with nondiagnostic results can be reduced with repeat FNA. The issue of repeat aspiration is largely unaddressed.

Thyroid and breast lesions are the most frequent lesions in which FNAC is done in our institute. Lymph nodes are the other common site in which FNA is done. Usually non aspiration technique is used in lymph nodes. Different lymph node groups have varying accessibility. Deep seated axillary lymph node groups are difficult to fix than the more superficial cervical lymph nodes. Hence, lymph nodes are not included in this study and is limited to thyroid and breast lesions. This study aims to find the diagnostic effectiveness of repeated FNA in thyroid and breast lesions and to describe the possible factors that lead to repeat.

METHODS

This is a descriptive study done on 190 cases of thyroid and breast lesions in which repeat FNA is done in the cytology lab, department of pathology, Government Medical College Kottayam during a period of 18 months from December 2018 to June 2020 after approval of Ethical Committee. The study was approved by the institutional review board (ethical committee) of Government Medical College, Kottayam (IRB No.127/2018).

Inclusion and exclusion criteria

Fine needle aspirations done after an initial aspiration with inconclusive smear is considered as repeated FNA. All thyroid and breast lesions in which repeated FNA was done during the study period are included in the study, while lesions in which image guided FNA was done, is excluded.

History, clinical examination findings, findings in imaging studies, nature of aspirate obtained for each patient advised repeat FNA, are collected and recorded as in the proforma. Proportion of repeat FNAs turning out to be diagnostic and the documented reasons for repeat were taken as the outcome measure. Common causes for repeat aspiration like inadequate cellularity, haemorrhagic aspirate and lesion related properties like cystic change/necrosis/others are entered in the proforma.

FNA is repeated mainly in inadequate or unsatisfactory smears. A specimen is considered “nondiagnostic” or “unsatisfactory” if it fails to meet the following adequacy criteria.

In case of thyroid lesions, criteria of adequacy is applied based on the Bethesda system for thyroid cytopathology. Thyroid FNA sample is considered adequate for evaluation if it contains a minimum of six groups of well visualized (i.e. well stained, undistorted, unobstructed) follicular cells, with at least ten cells per group, preferably on a single slide. In special circumstances this criteria is not required. A minimum number of follicular cells are not

necessary if the sample contains significant cytologic atypia. Nodules in patients with lymphocytic (Hashimoto) thyroiditis, thyroid abscess or granulomatous thyroiditis may contain only numerous inflammatory cells. Such cases are interpreted as benign and not non-diagnostic. A minimum number of follicular cells is not required in this case. Specimen that consist of abundant colloid are considered as benign and satisfactory for evaluation. A minimum number of follicular cells is not required if easily identifiable colloid predominates.

These are the scenarios considered as non-diagnostic: fewer than six groups of well preserved, well stained follicular cell groups with ten cells each (with exceptions given above), poorly prepared, poorly stained or significantly obscured follicular cells. Cyst fluid, with or without histiocytes and fewer than six groups of ten benign follicular cells. Occasionally aspirates from adjacent anatomical sites are obtained, like skeletal muscle and respiratory epithelium from trachea, which also has to be considered non-diagnostic. A repeat FNA can be recommended in all these cases. Non-diagnostic/unsatisfactory belongs to Bethesda criteria I and it carries a risk of malignancy of 5-10%.

In case of breast lesions, pauci cellular smears, poorly prepared smears with crush or drying artefacts or with cells trapped in clotted blood are considered as unsatisfactory. However, pauci cellular smears has to be evaluated based on clinical findings because lesions like fibrous mastopathy, sclerosed fibroadenoma, desmoplastic carcinoma or hypertrophic adipose tissue will naturally yield less number of cells.

Data management and analysis

Data is entered in Microsoft excel and analysed using IBM statistical package for the social sciences (SPSS) software. Proportion of repeat FNA in thyroid and breast lesions turned out to be diagnostic and probable causes for repeat in each category of lesions are analysed.

RESULTS

The present study was conducted on 190 cases of thyroid and breast lesions in which repeat FNA was done in the cytopathology lab, department of pathology, Government Medical College, Kottayam. The study period was from December 2018 to June 2020.

During this period, FNA was performed in 944 lesions including both thyroid and breast. Among that 23% lesions required repeat FNA. Total number of FNAs done in thyroid lesions alone were 629 and total number of FNAs done in breast lesions were 315. Among 629 thyroid lesions in which FNA was done, 140 required repeat FNA. Out of 140 patients, 118 patients actually repeated FNA. Among 315 breast lesions in which FNA was done, 85 required repeat FNA. Out of 85 patients, 72 actually repeated FNA (Table 1).

Table 1: Total number of FNA repeated in thyroid and breast lesions.

Organ	Total number of FNA done	Number of patients required repeat FNA	Number of FNA actually repeated
Thyroid	629	140 (22%)	118
Breast	315	85 (27%)	72

Among the 118 thyroid lesions in which FNA was repeated, 78% were diagnostic and 22% remained inconclusive (Table 2).

Among the 92 diagnostic lesions in thyroid, 83 were benign, 6 were follicular neoplasm and 3 were in AUS/FLUS category. Inadequate aspirate and hemorrhagic aspirate are the most common causes that led to repeat FNA in thyroid.

Among the 72 breast lesions in which FNA was repeated, 50% lesions turned out to be diagnostic, while 50% remained inconclusive (Table 2). The breast lesions turned out to be diagnostic include benign epithelial proliferative lesion (18), benign cystic lesion (4), epithelial proliferative lesion with atypia (4), carcinoma (9) and intramammary lymph node (1). Inadequate aspirate and cystic change were the most common causes that led to repeat FNA in breast. Out of the breast lesions that required FNA, 12.5% turned out to be malignancy.

Table 2: Proportion of repeat FNA turned diagnostic in thyroid and breast lesions.

Thyroid	Breast
78%	50%

DISCUSSION

Outcome of FNA in 944 lesions of thyroid and breast together were analysed. 23% lesions required repeat FNA in total. Among 629 thyroid lesions in which FNA was done, 22% required repeat FNA. 118 patients actually underwent repeat FNA.

Among 315 breast lesions in which FNA was done, 27% required repeat FNA and 72 really underwent repeat FNA. In a study conducted by R Goyal et al, number of repeat FNA required was 18.3% in thyroid lesions and 12% in breast lesions (Table 5).⁴

Among the 118 thyroid lesions in which FNA was repeated, 78% were diagnostic and 22% remained inconclusive (Figure 1 and Table 2). In a study conducted by Israel et al, FNA was repeated in 106 patients with thyroid swelling who had initial non diagnostic result.⁵ FNA was done under ultrasound guidance and only 58% of the lesions turned diagnostic (Table 6). This is less compared to the proportion of diagnostic lesions in the present study.

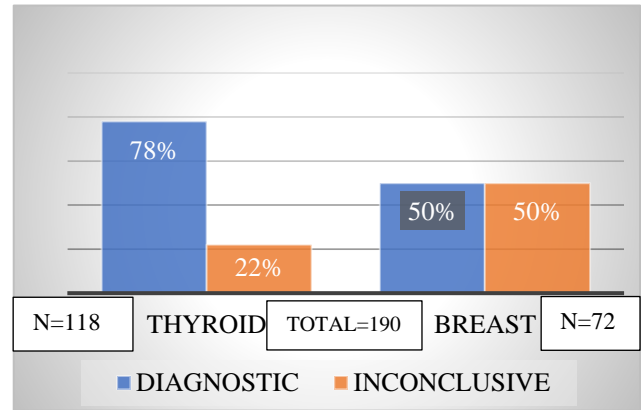


Figure 1: Outcome of repeated FNA in thyroid and breast lesions.

In another study conducted by Graciano et al, FNA was repeated in 237 patients with thyroid swelling who had initial non diagnostic FNA.⁶ 70.2% of the repeat FNA turned out to be diagnostic. This figure is comparable to the proportion of diagnostic FNA in the present study. According to Bethesda, repeating the FNA results in a diagnostic interpretation in up to 60-80% of cases, primarily in lesions with a smaller cystic component.⁷

Among the 92 diagnostic lesions in thyroid, 83 were benign, 6 were follicular neoplasm and 3 were in AUS/FLUS category (Figure 2). Benign lesions are requiring repeat FNA the most. It may be due to its increased incidence. Benign follicular nodules showed features of cystic degeneration in 15 lesions, hurthle cell change in 2 lesions and features of thyroiditis in 11 lesions.

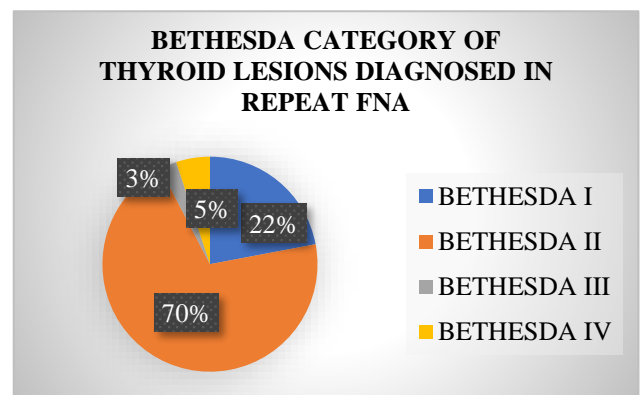


Figure 2: Bethesda category of thyroid lesions diagnosed in repeat FNA.

Table 3: Benign thyroid lesions diagnosed in repeat FNA.

Diagnosis	Number of lesions
Colloid nodule	18
Benign follicular nodule	47
Lymphocytic thyroiditis	18

Table 4: Diagnosis made in breast lesions after repeat FNA.

Diagnosis	Number of lesions
Benign cystic lesion	4
Benign epithelial proliferative lesion	18
Intramammary lymphnode	1
Epithelial proliferative lesion with atypia	4
Carcinoma	9

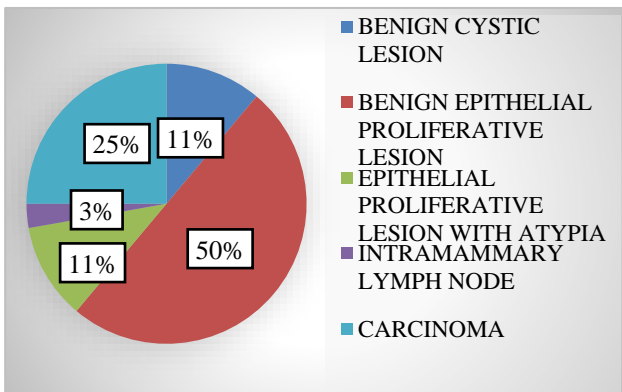


Figure 3: Diagnosis in breast lesions after repeat FNA.

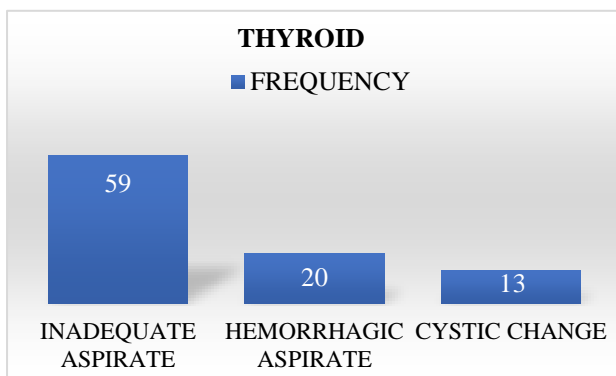


Figure 4: Probable cause that lead to repeat in thyroid lesions.

In a study conducted by Ferreria et al, the diagnosis after repeat FNA falls into the Bethesda categories as, 43.6% lesions remained inconclusive after repeat FNA, which was far more than the present study. 0.4% of the lesions turned to malignancy in repeat FNA (Table 7).⁸

While analysing the nature of aspirate in the thyroid lesions that required repeat FNA, 50 yielded scanty bloodstained aspirate, 22 yielded hemorrhagic aspirate and 21 yielded colloid in the first attempt. Inadequate aspirate and hemorrhagic aspirate are the most common causes that led to repeat FNA in thyroid (Figure 5). Inadequate aspirate can be due to poor experience of the aspirator. Hemorrhagic aspirate may be due to increased vascularity of the lesions as in lymphocytic thyroiditis.

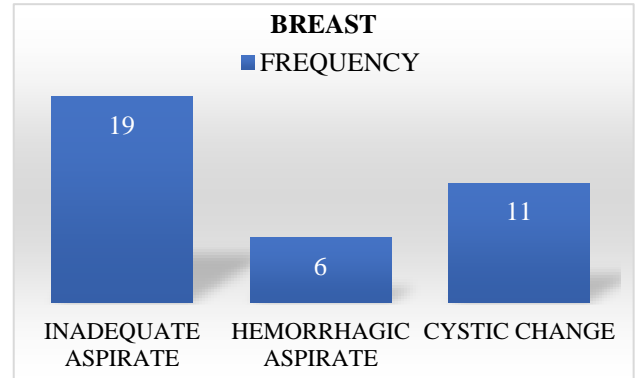


Figure 5: probable factors that led to repeat FNA breast lesions.

Table 5: Number of thyroid and breast lesions in which FNA was required: comparison with other study.

Study	Number of repeat FNA required in thyroid lesions	Number of repeat FNA required in breast lesions
Present study	140/629 (22%)	85/315 (27%)
Goyal et al (2014)	76/415 (18.3%)	86/716 (12%)

Table 6: Proportion of repeated FNA turned diagnostic in thyroid lesions: comparison with other studies.

Study	Number of thyroid lesions in which repeat FNA is done	Proportion of repeated FNA turned diagnostic (%)
Present study	118	78
Israel et al (2007)	106	58
Graciano et al (2014)	237	70.2
Ferreria et al (2014)	771	56.4

Among the 72 breast lesions in which FNA was repeated, 50% lesions turned out to be diagnostic, while 50% remained inconclusive (Figure 1). This was comparable to study of Kooistra et al.⁹ In this study repeated FNA yielded 54.8% diagnostic results in breast lesions (Table 8).

Table 7: Diagnosis of thyroid lesions in repeat FNA: comparison with other studies.

Study	Percentage of non-diagnostic (Bethesda I)	Percentage of benign (Bethesda II)	Percentage of AUS/FLUS (Bethesda III)	Percentage of follicular neoplasm (Bethesda IV)	Percentage of suspicious for malignancy (Bethesda V)	Percentage of malignancy (Bethesda VI)
Present study	22.1	70.3	2.5	5.1	-	-
Ferreria et al (2014)	43.6	49.3	-	6.2	0.4	0.4

Table 8: proportion of repeated FNA turned diagnostic in breast lesions: comparison with other studies.

Study	Proportion of repeated FNA turned diagnostic in breast lesions (%)
Present study	50
Kooistra et al (2009)	54.8

The proportion of diagnostic lesions in breast were less compared to the proportion of diagnostic lesions in thyroid. This may be due to lesion inherent properties. In case of sclerosed fibroadenoma, desmoplastic carcinoma, hypertrophic adipose tissue and fibrous mastopathy, smears will be naturally paucicellular.

The breast lesions turned out to be diagnostic include, benign epithelial proliferative lesions, benign cystic lesions, epithelial proliferative lesion with atypia, carcinoma and intramammary lymph node (Figure 3). Nature of the aspirates in these lesions were haemorrhagic aspirate, fluid and scanty bloodstained material in the initial aspiration. Inadequate aspirate and cystic change were the most common causes that led to repeat FNA in breast (Figure 5).

Usually fluidy aspirate is obtained in case of fibrocystic disease of breast. In our study, 1/9 malignant breast lesions yielded fluidy aspirate. This indicates that cystic lesions should be further investigated for malignancy especially in the older age group. We should repeat FNA in the residual lesion, if the cyst remains uncollapsed after initial aspiration of fluid. The smears from benign cystic lesion showed macrophages, inflammatory cells and often a few ductal epithelial cells and myoepithelial cells. Most of the smears that were inconclusive showed stromal elements and adipocytes.

Out of the breast lesions that required FNA, 12.5% turned out to be malignancy. It shows the importance of repeating FNA in breast lesions that was inconclusive in the initial FNA. Positive predictive value of FNAC for malignancy was comparable with core needle biopsy i.e. 99 to 100%.¹⁰ In breast lesions that required repeat FNA, calcification (4%) and cystic change (9%) were noted in ultrasonography (USG).

23.6% of the breast lesions that required repeat FNA were of size less than 1 cm. Out of that, 82% remained inconclusive even after repeat FNA. It shows that it is better to advise USG guided FNAC for sub-centimetric lesions as it is difficult to localize and fix the small lesions. It will avoid unnecessary apprehension and stress to the patient and also avoid delay in the treatment plans. In one study, 21% of false negative breast FNAC was due to non-palpable tumours.⁹ An inadequacy rate as high as 34–58% and lowest inadequacy rate of 10% has been reported previously in non-palpable breast lesions.^{11,12} It is comparable to the percentage of non-diagnostic results in lesions less than 1cm in the present study.

In a few cases, in which a benign diagnosis was made after initial FNA, repeat FNA was done in view of high clinical suspicion for malignancy. In those lesions, we obtained more sample and confirmed the benign diagnosis.

Limitations

Only repeat FNA from thyroid and breast lesions are included in the study as they are the most common lesions in which FNA is done in our institute. Since our hospital is a teaching institution, residents having varying years of experience are doing FNA. The experience of aspirators may affect the yield of FNA. FNA taken by more experienced person may get better yield. But it is difficult to assess their expertise. USG guided FNA samples are not included in the study as it is not comparable with palpation guided FNA.

CONCLUSION

This study was conducted to identify the proportion of repeated fine needle aspiration in breast and thyroid lesions turning out to be diagnostic. 78% of the repeat FNA in thyroid lesions and 50% of repeat FNA in breast lesions were diagnostic. Inadequate aspirate, hemorrhagic aspirate and cystic change were the common factors leading to repeat fine needle aspiration. Since thyroid and breast are the most common sites where FNA is done and 64% of the total lesions are diagnostic, repeat FNA in all other sites is likely to yield a similar diagnostic outcome. Hence, repeat FNA is advisable in lesions which had initial non diagnostic result. Repeat FNA also helps to reduce false negative results.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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