Diagnostic accuracy of fine needle aspiration cytology in neoplasms of solitary nodule in thyroid gland: a retrospective study

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ABSTRACT

Background: Common endocrine disorders like thyroid nodule may represent thyroid neoplasm either benign or malignant and are important to be diagnosed as they may progress and lead to thyroid dysfunction. Fine needle aspiration cytology (FNAC) has emerged as an economic, rapid, effective, simple and accurate strategy for diagnosing neoplastic thyroid nodules. The basic aim of the current investigation was to evaluate the diagnostic accuracy of FNAC in neoplasms of solitary thyroid nodules.

Methods: Current investigation was a retrospective diagnostic test evaluation study conducted on 60 patients who underwent total thyroidectomy for solitary nodule for a duration of one year. Routine blood investigation, thyroid function test, FNAC, chest X-ray, indirect laryngoscopy and ultrasound scanning of neck were done for all the patients. Collected data was coded and entered in excel sheets and was statistically analyzed using SPSS.

Results: Mean age of the participating patients was 45.51±7.2 years and age range was 24 to 68 years. Female patients were observed to be more than male patients. In majority of the patients duration of nodule was less than or equal to one to three years. Maximum number of patients underwent either total or hemithyroidectomy. FNAC diagnostic findings revealed patients with NCG, FN, LT, PC and MC. The results of FNAC findings resembled and were supported by HPR findings.

Conclusions: Current investigation findings revealed that fine needle aspiration cytology can be considered as potential, accurate, rapid and efficient diagnostic technique for rapid primary investigation of neoplasms of solitary nodules in thyroid gland.

Keywords: Diagnostic accuracy, Solitary thyroid nodules, Follicular neoplasm, Fine needle aspiration cytology, Malignant nodules, Benign nodules, Thyroid stimulating hormone, Thyroidectomy, Histopathology

INTRODUCTION

Thyroid nodules are considered to be common endocrine disorders globally.1,2 Thyroid nodules are defined as discrete thyroid gland lesions that can be solitary, cystic, solid or multiple according to the American thyroid association (ATA).3 Based on histological features thyroid nodules can be classified as hyperplastic lesions, adenomas or carcinomas.3,4 Epidemiological studies revealed that the prevalence rate of thyroid nodules in adults of iodine-sufficient regions is up to 7%.2,5 Thyroid nodules were observed to be more common in females with a prevalence rate of up to 6.8% compared to males with a prevalence rate of up to 1.5%.2,6 Cited gender disparity in prevalence rate of thyroid nodules may be due to hormonal influence.5,6

Thyroid nodules are clinically important to be diagnosed as they may lead to thyroid dysfunction or may represent thyroid cancer as evident in 6.5% of cases.7 Solitary nodules are also considered as significant indicators of multinodular goiter.7,8 Thyroid nodules may be neoplastic...
of benign or malignant type or non-neoplastic inflammatory or hyperplastic type.\textsuperscript{3,4} The hyperplastic thyroid nodules present as multiple nodular goitre whereas benign neoplastic nodules are most common but clinically insignificant.\textsuperscript{1,3} Follicular and papillary carcinomas that are types of malignant differentiated thyroid carcinomas represent 1\% of overall malignancies, whereas undifferentiated medullary thyroid carcinoma (MTC) represents 5\% of overall malignancies.\textsuperscript{4-7} It is observed and reported that clinically multinodular goitres (MNGs) are less common than solitary nodules which in turn are expected to harbour malignant disease.\textsuperscript{8,9} Obesity, smoking, alcohol consumption, increased levels of insulin-like growth factor-1, uterine fibroids, use of oral contraceptives and statins, metabolic syndromes, aging, female hormones, iron deficiency, hematopoietic stem cell transplantation, history of ionizing thyroid radiation and widespread use of modern imaging modalities are some of the causative factors for nonneoplastic or non-neoplastic thyroid nodules.\textsuperscript{5-11} It is observed and reported that prevalence rate of thyroid nodules depends on the identification or diagnostic techniques.\textsuperscript{2,3,8}

Four key assessment parameters for diagnosis of thyroid nodules are clinical history and examination, serum levels of thyroid stimulating hormone (TSH), ultrasound examination and FNAC.\textsuperscript{6-12} Combination of TSH and thyroid scan with \textsuperscript{99}Tc scan help to differentiate between solitary nodule, MNG and inflammatory nodule due to thyroiditis or Grave’s disease.\textsuperscript{12,13} Other diagnostic techniques available for evaluation of thyroid nodule includes assessment of serum, genetic and immunohistochemical markers such as calcitonin, BRAF mutation, galectin-3, cyclooxygenase 2, cyclin D2, imaging studies like MRI, CT and 18FDG-PET and use of other radionuclides like iodine-123 that depicts thyroid function depending on its ability to trap iodine.\textsuperscript{1,3,5-7} Sensitivity and specificity of the available techniques is still debatable in the diagnosis of nodular thyroid disease in a euthyroid patient.\textsuperscript{12-14} Various cytological and clinical parameters such as age, gender, thyroid autoimmunity, nodularity, TSH level and ultrasound findings such as increased central nodular flow, irregular borders, hypo echogenicity and micro calcifications have been explored to enhance diagnostic accuracy in differentiating between benign and malignant thyroid nodules but it lacked sensitivity and specificity.\textsuperscript{2,6,7}

FNAC is a rapid, simple and safe strategy for diagnosing neoplastic thyroid nodules.\textsuperscript{12} FNAC is currently recommended for nodules with larger than 1 cm diameter and for suspicious nodules with less than 1 cm diameter with border irregularity, micro calcifications, hypo echogenicity and Doppler central flow.\textsuperscript{13,14} In FNAC each nodule is aspirated using disposable 10 ml plastic syringe with 25 gauge needle.\textsuperscript{13} Thyroid nodules are subjected to surgery or close monitoring with multiple repeat FNAC evaluation as 15-20\% of FNAC assessed thyroid nodules ultimately harbour malignancy.\textsuperscript{14,15} Few limitations that are reported for FNAC include partly cystic or cystic lesions yield insufficient cells for diagnosis and neither the size nor the colour of cyst aspirate is discriminatory also the cyst generally recurs.\textsuperscript{13-16} Follicular adenomas (FAs) cannot be distinguished from carcinomas and difficult to classify and large bore biopsy of FAs is often associated with side effects and possibilities of false negatives through FNAC.\textsuperscript{13-16}

\textbf{Objectives}

Primary objective of the current investigation was to evaluate the diagnostic accuracy of FNAC in neoplasms of solitary nodule in thyroid gland. The study was also directed towards determining the different histological types of solitary nodule of thyroid gland.

\textbf{METHODS}

\textbf{Study design, population, location and duration}

Current investigation was a retrospective diagnostic test evaluation study conducted on 60 patients who underwent thyroidectomy for solitary nodule at department of general surgery, Government TD medical college hospital, Alappuzha for the duration of year from 1 January to 31 December 2019.

\textbf{Inclusion criteria}

Inclusion criteria for current study were all patients admitted with clinically detected solitary nodule and who underwent thyroidectomy for 1 year of study period and all patients above 12 years and below 70 years of age.

\textbf{Exclusion criteria}

Exclusion criteria for current study were all patients clinically diagnosed with MNG or diffuse enlargement of the thyroid gland and patients with recurrent goiter.

\textbf{Sample size, sampling method and investigations}

Samples were collected through convenient sampling strategy from 60 patients who underwent thyroidectomies from January to December 2019. All patients admitted with a clinical diagnosis of solitary nodule of the thyroid underwent mandatory investigations such as routine blood investigation, thyroid function test, FNAC, chest X-ray, indirect laryngoscopy and ultrasound scanning of neck. Investigations like CT scan of neck and/or thorax and Technicium scan were optional and tailored according to individual patient needs.

\textbf{Procedure and data collection tool}

Records of patient who underwent thyroidectomy for solitary thyroid nodule were accessed from medical records library for the mentioned study duration after taking permission from medical superintendent of TDMCH. Preoperative details of patient including FNAC...
report and postoperative histopathology reports were entered in the proforma by the investigator. Observed data were entered in a data sheet. The data for the current investigation was collected through a formatted questionnaire.

Data analysis and statistical methods

Observed investigational data was coded and entered in excel sheets and was statistically analyzed using SPSS software version 17. The entire data was represented as frequency, proportion and percentage of co-relationship and compared using student t test or Chi square tests depending on the number of variables and p<0.05 was considered as level of significance.

RESULTS

Results of the current investigation conducted to assess the diagnostic accuracy of fine needle aspiration cytology in neoplasms of solitary nodules in thyroid gland on 60 patients revealed that all the 60 participating patients were diagnosed with solitary nodule thyroid and majority of the participating patients (85%) were in the age group of 31 to 60 years (Table 1). Mean age of the participating patients was observed to be 45.51±7.2 years and all the 60 participating patients fell in the age range of minimum 24 years to maximum 68 years.

It was observed through gender based distribution studies that females patients (81.66%) outnumbered the male patients (18.33%) participating in the current study (Figure 1). Patient history evaluation study revealed that in significant number of patients (85%) the duration of thyroid nodule was either less than a year or ranged between one to three years, very few patients (15%) were observed with thyroid nodules with duration of four years or more (Table 1).

Current study findings revealed that in significant number of patients; 53 (88.33%) patients out of total 60, there was no symptom of pain (Table 2). Out of total 60 participating patients in the current study, significant number of patients 45 (75%) did not exhibit pressure symptom (Table 2).

Results of the diagnostic investigation made through FNAC revealed that out of total 60 patients majority of the patients 37 (59.67%) patients were diagnosed with nodular colloid goitre (NCG), followed by patients 11 (17.74%) with follicular neoplasm (FN) (Table 3). Lymphocytic thyroiditis (LT), papillary carcinoma (PC) and medullary carcinoma (MC) were also diagnosed in 11.29%, 8.06% and 3.22% of participating patients respectively (Figure 2).

It was observed during the current investigational study that out of total 60 participating patients significantly high number of patients (32.81%) underwent total thyroidectomy (TT) and hemi thyroidectomy (HT) types of surgery (Table 4). Out of 60 patients total 13 (20.31%) patients underwent near total thyroidectomy (NTT) surgery.

| Parameters | Frequency | % | Chi square coefficient | P value | Significance |
|------------|-----------|---|-----------------------|---------|-------------|
| Age (in years) |           |    |                       |         |             |
| ≤30        | 2         | 3.33 |                       |         |             |
| 31-45      | 24        | 40.0 |                       |         |             |
| 46-60      | 27        | 45.0 |                       |         |             |
| ≥61       | 7         | 11.66 |                       |         |             |
| Mean age (in years) | | 45.51±7.2 |          |         |             |
| Age range (in years) | | 24 to 68 |          |         |             |
| Duration of thyroid nodules (in years) | | | | | |
| <1        | 21        | 35.0 |                       | 25.49   | 0.000012    | Significant |
| 1-3       | 30        | 50.0 |                       |         |             |
| 4-7       | 04        | 6.66 |                       |         |             |
| >7        | 5         | 8.33 |                       |         |             |
Table 2: Distribution of patients on the basis of pain and pressure symptoms.

| Symptoms | Frequency | %  | Chi square coefficient | P value  | Significance |
|----------|-----------|----|------------------------|----------|--------------|
| Pain     |           |    |                        |          |              |
| Yes      | 7         | 11.66 | 25.15                  | <0.00001 | Significant  |
| No       | 53        | 88.33 |                        |          |              |
| Pressure |           |    |                        |          |              |
| Yes      | 15        | 25.0 | 10.28                  | 0.001341 | Significant  |
| No       | 45        | 75.0 |                        |          |              |

Table 3: Distribution of patients on the basis of diagnosis done through FNAC.

| Diagnosis                       | Frequency | %     | Chi square coefficient | P value  | Significance |
|---------------------------------|-----------|-------|------------------------|----------|--------------|
| Nodular colloid goitre          | 37        | 59.67 |                        |          |              |
| Papillary carcinoma             | 5         | 8.06  |                        |          |              |
| Follicular neoplasm             | 11        | 17.74 |                        |          |              |
| Lymphocytic thyroiditis         | 07        | 11.29 |                        |          |              |
| Medullary carcinoma             | 2         | 3.22  |                        |          |              |

Table 4: Distribution of patients on the basis of type of surgery performed.

| Surgery type                       | Frequency | %     | Chi square coefficient | P value  | Significance |
|------------------------------------|-----------|-------|------------------------|----------|--------------|
| Total thyroidectomy                | 21        | 32.81 |                        |          |              |
| Near total thyroidectomy           | 13        | 20.31 |                        |          |              |
| Hemithyroidectomy                  | 21        | 32.81 |                        |          |              |
| Modified radical neck dissection   | 4         | 6.25  |                        |          |              |
| Subtotal thyroidectomy             | 5         | 7.81  |                        |          |              |

Table 5: Distribution of patients on the basis of HPR findings.

| Findings                           | Frequency | %     | Chi square coefficient | P value  | Significance |
|------------------------------------|-----------|-------|------------------------|----------|--------------|
| Nodular colloid goitre             | 30        | 46.87 |                        |          |              |
| Papillary carcinoma thyroid        | 13        | 20.31 |                        |          |              |
| Lymphocytic thyroiditis            | 8         | 12.50 |                        |          |              |
| Follicular carcinoma thyroid       | 4         | 6.25  |                        |          |              |
| Hurthle cell change                | 1         | 1.56  |                        |          |              |
| Medullary carcinoma                | 2         | 3.12  |                        |          |              |
| Follicular adenoma                 | 6         | 9.37  |                        |          |              |

Figure 2: Distribution of patients on the basis of diagnosis done through FNAC.
Figure 3: Distribution of patients on the basis of type of surgery performed.

Figure 4: Distribution of patients based on type of thyroid nodule findings.

Figure 5: Distribution of patients on the basis of HPR findings.
Total 5 (7.81%) patients and 4 (6.25%) patients underwent modified radical neck dissection (MRND) and subtotal thyroidectomy (STT) surgeries respectively (Figure 3). It was observed in current investigation that few patients also underwent a combination of either TT and MRND or HT and MRND surgeries.

It was depicted through the diagnostic findings of FNAC that out of total 60 participating patients almost half of the patients 33 (55%) were observed to have solitary nodule thyroid (SNT) whereas 25 (41.66%) of patients were observed to have MNG and 2 (3.33%) of patients were observed to have cyst (Figure 4).

HPR study findings revealed that out of total 60 patients 30 (46.87%) had NCG, 13 (20.31%) patients had PCT, 8 (12.50%) patients had LT, 4 (6.25%) patients had follicular carcinoma thyroid (FCT), 2 (3.12%) patients were with MC, 6 (9.37%) patients had FA and 1 (1.56%) patient exhibited HCC (Hurthle cell change) (Table 5) (Figure 5). HPR findings in current investigation also revealed a few cases with combination of PCT and LT or LT and HCC.

**DISCUSSION**

Age based distribution of all 60 patients participating in current investigation revealed that majority of the patients with thyroid nodules were mid aged and the mean age of the patients in current study was observed to be 45.51±7.2 years, age of all participating patients ranged between minimum 24 years to maximum 68 years. The age based observations of current study were in close resemblance to published reports by Monib et al and Jena et al who reported the mean age of patients with thyroid nodules to be 33.5±9.1 years and 39±14.1 years respectively and age range between 22 to 55 years. Current study revealed that prevalence of thyroid nodule was observed to be more in females than in males, which resembled to study reports published by Tai et al and Arena et al.23,24 Current study findings also revealed that in majority of the patients duration existence of thyroid nodule was not more than one year or between one to three years, the observation resembled to the study reported by Maia et al and Delbridge et al.21,22

It was observed in current investigation that majority of the patients of solitary thyroid nodule exhibited no pain and pressure symptoms. Current study findings revealed that majority of solitary thyroid nodule investigated through FNAC exhibited nodular colloid goitre followed by follicular neoplasm. Some patient also exhibited lymphocytic thyroiditis, papillary carcinoma and MC the observation made in current study were in close agreement in study reports published by Das et al and Norris et al.23,24

Current study findings revealed that most of the patients who exhibited solitary thyroid nodules underwent TT or hemic thyroidectomy surgeries. Solitary thyroid nodule patients also underwent near TT, modified radical neck dissection or STT types of surgeries. The observations made in current investigation were supported by the reports published by Gagner et al, Singer and Adwok.18,25-27 Results of FNAC findings in the current investigation confirmed solitary nodule thyroid in majority of patients, FNAC findings also revealed multinodular goitre and cyst in some of the participating patients. Results of HPR investigation in current study revealed that most of the participating patients with solitary thyroid nodules represented with nodular colloid goitre followed by PCT. Alternatively cases of LT, FCT, HCC, MC and FA were also observed in solitary nodule patients participating in current study.

**Limitations**

Small sample size of only 60 patients was the limitation of the current investigations, more concrete and adequate conclusion could have been drawn with a larger sample size of study participants.

**CONCLUSION**

From results and observation made through current study findings it can be concluded that FNAC can be considered a potential, accurate and efficient diagnostic technique for investigating neoplasms of solitary nodules in thyroid gland. Current investigation also reveals nodular colloid goitre, PCT, LT, FCT, HCC, MC and FA as different histological types of solitary nodule of the thyroid gland.

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