

## Original Research Article

# Study of incidence in between benign and malignant tumors of solitary thyroid nodule

B. Hemashankara Rao<sup>1\*</sup>, K. Srinivasa Chakravarthy<sup>2</sup>

<sup>1</sup>Associate Professor, <sup>2</sup>Assistant Professor, Department of General Surgery, Maharajah's Institute of Medical Sciences, Nellimarla, Vizianagaram, Andhra Pradesh, 535217, India

**Received:** 29 September 2016

**Revised:** 03 October 2016

**Accepted:** 26 October 2016

### \*Correspondence:

Dr. B. Hemashankara Rao,

E-mail: drbhemashankarao@gmail.com

**Copyright:** © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

### ABSTRACT

**Background:** Accurate imaging characterization of a solitary thyroid nodule has been clearly problematic. The purpose of this study was to evaluate the role of the apparent diffusion coefficient (ADC) values in the differentiation between malignant and benign solitary thyroid nodules. Objective of the study was to study the clinico-pathological correlation of solitary thyroid nodule and the incidence of malignancy.

**Methods:** The study was conducted in MIMS (Maharajah's Institute of Medical Sciences). The study population was enrolled after fulfilling the selection criteria from OPD (Out Patient Department) of General Surgery. A total of 50 cases were studied who presented with complaint of thyroid swelling which was clinically confirmed as solitary thyroid nodule. Importance was given to detailed history; duration of swelling, pressure symptoms, and symptoms associated illnesses, previous exposure to neck irradiation, history of anti-thyroid drug use, positive family history. A detailed local examination was done in all cases followed by systemic examination.

**Results:** Out of 50 cases 10 cases were found to have malignant lesions with remaining 40 cases being benign lesions. The malignant nodules were significantly lower than those of benign ones ( $P = 0.0001$ ). There were no significant differences between the mean ADC values of various malignant thyroid nodules, but there were significant differences between the subtypes of benign thyroid nodules ( $P = 0.0001$ ).

**Conclusions:** The ADC value is a new promising non-invasive approach used for differentiating malignant from benign solitary thyroid nodules. The incidence of malignancy in solitary thyroid nodule is quite high. This warrants education to people to consult physicians for early diagnosis and adequate treatment without being passive as most of these swellings are asymptomatic for long duration.

**Keywords:** Benign tumors, Malignant, Solitary thyroid nodule

### INTRODUCTION

A discrete swelling in an otherwise impalpable gland is termed isolated or solitary. Dominant swelling in a gland is clinical evidence of generalized abnormality in the form of a palpable contralateral lobe or generalized mild nodularity.<sup>1</sup> About 70% of discrete thyroid swellings are clinically isolated and about 30% are dominant. Some 15% of isolated swellings prove to be malignant, and an

additional 30–40% is follicular adenomas.<sup>2</sup> The remainder are non-neoplastic, largely consisting of areas of colloid degeneration, thyroiditis or cysts.<sup>3</sup> Solitary palpable nodules are about four times more prevalent in women than in men. Solitary thyroid nodule is defined as palpably discrete swelling within the gland otherwise was probably normal gland; it has usually a benign lesions.<sup>4</sup> discrete swelling in one lobe with no palpable abnormality elsewhere is termed as isolated or solitary

thyroid nodule.<sup>5</sup> Solitary nodule of thyroid is a common way of presentation of thyroid disease. Management has changed in recent years but it was important differences of opinion remain over which nodules should be a surgically should be excised.<sup>6</sup> Solitary nodules in the thyroid are relatively common especially among adults, with an overall prevalence rate of 4-7 % in general population. Most of the thyroid nodules detected are being hyperplastic lesions and about 5-20 % of thyroid nodules are true malignant lesions.<sup>7</sup> Hence present main aim in evaluation of all solitary thyroid nodules which are suspicious and indeterminate is differentiation between benign and malignant lesions. Since solitary thyroid nodules represent a multitude of thyroid disorders, we have undertaken this study to thoroughly understand the epidemiology of thyroid disease which is of paramount importance and which contributes effectively in the management.<sup>8</sup> The frequency of thyroid nodules, about half of which are single on physical examination, increased throughout life. Single nodules are about 4 times more common in female than in male.<sup>9</sup>

Presenting complaints are swelling in front of neck, dysphagia, dyspnoea, hoarseness of voice and Hypothyroid/ hyperthyroid features.<sup>10</sup> Carcinoma of the thyroid gland is an uncommon cancer but, none the less, is the most common malignancy endocrine system. It accounts for 10.5% of all malignant tumors of head and neck region.<sup>11</sup> Thyroid neoplasia can present either as discrete nodules or diffusely enlarged.

FNAC specimens are Benign (70%), Malignant (5%), suspicious (10%) and unsatisfactory (5%). Gland, although the former is most likely to be malignant Incidence of in thyroid malignancy in solitary thyroid nodule (STN) varies from 4.7-18.3%.<sup>12</sup>

Solitary thyroid nodules are benign and can be classified as Adenomas, Colloid nodules, Congenital abnormalities, Cysts, Infectious nodules, lymphocytic or granulomatous nodules and hyperplasia.<sup>13</sup> Thyroid carcinomas are classified according to the cell type from which they develop. The majority are nonmedullary thyroid cancers (NMTCs), which arise from the thyroid epithelial cells. These account for approximately 95% of tumors and are divided into four histologic subtypes: papillary (85%), follicular (11%), Hurthle cell (3%), and anaplastic (1%). Of these, 95% are sporadic tumors and the rest are thought to represent a familial origin, that is, familial nonmedullary thyroid cancer (FNMTC).<sup>14</sup>

Medullary thyroid cancers (MTCs) arise from the calcitonin-producing parafollicular cells of the thyroid and account for about 5% of all thyroid malignancies. In 20% they are familial and occur as part of the multiple endocrine neoplasias (MEN) syndromes. It is important to identify these patients, as pheochromocytomas are associated with MEN and need to be excluded prior to the patient receiving anesthetic. (15) FNMTCs are rare. Based on epidemiologic studies and kindred analysis, this

group of tumors is believed to result from a genetic inheritance, although environmental influences cannot be excluded. Inheritance is probably autosomal dominant with incomplete penetrance and variable expressivity. The diagnosis of FNMTC is made when thyroid cancer occurs in two or more first-degree relatives.<sup>16</sup> Clinically, FNMTCs can be divided into two groups. The first group includes familial tumor syndromes characterized by a preponderance of nonthyroidal tumors. These cancer syndromes include familial adenosis polyposis (Gardner syndrome), familial hamartoma syndrome (Cowden syndrome), and the Carney complex type 1. In the second group, NMTC predominates. Compared with sporadic NMTC, patients with FNMTC appear to present at an earlier age, have more benign thyroid nodules, have multifocal disease, and have a higher rate of locoregional recurrence.<sup>17</sup>

Benign thyroid nodule factors favouring Family history of Hashimoto's thyroiditis, Family history of benign thyroid nodule or goiter, Symptoms of hyperthyroidism or hypothyroidism, Pain or tenderness associated with a nodule, A soft, smooth, mobile nodule, Multi-nodular goiter without a predominant nodule (lots of nodules, not one main nodule), "Warm" nodule on thyroid scan (produces normal amount of hormone) and Simple cyst on an ultrasound.

Malignant nodule related about Age less than 20, Age greater than 70, Male gender, New onset of swallowing difficulties, New onset of hoarseness, History of external neck irradiation during childhood Firm, irregular, and fixed nodule, Presence of cervical lymphadenopathy (swollen, hard lymph nodes in the neck), Previous history of thyroid cancer, Nodule that is "cold" on scan (shown in picture above, meaning the nodule does not make hormone) and Solid or complex on an ultrasound.<sup>18</sup> Clinical examination of the thyroid should focus on whether the nodule is solitary or dominant in a multinodular goiter.

The characteristics of the nodule, including size, consistency (e.g., soft, firm, woody, or hard), and involvement with adjacent structures, should also be defined. Examination of the cervical lymph nodes, including the central compartment (level VI) and the lateral neck (levels I–V). Suggestion of involvement of lateral neck lymph nodes will change the extent of preoperative investigation required in these patients.

## METHODS

The sonographic features that suggested malignancy include microcalcifications, an irregular or microlobulated margin, marked hypoechogenicity, and a shape that was taller than it was wide. The presence of one or more of these features indicated classification as (malignant). The absence of all of these features indicated classification as (benign). Presence of an anechogenic cystic nodule classification as (benign).

**Inclusion criteria**

All the data of the 50 cases which were studied in MIMS (Maharagah’s Institute of Medical Sciences). The study population was enrolled after fulfilling the selection criteria from OPD (Out Patient Department) of General Surgery.

**Exclusion criteria**

All the required investigations for the study were done routinely during the admission period. FNAC and Thyroid function tests were done in all cases. Ultrasound scan, X-ray necks were also done in all cases who presented with thyroid swelling.

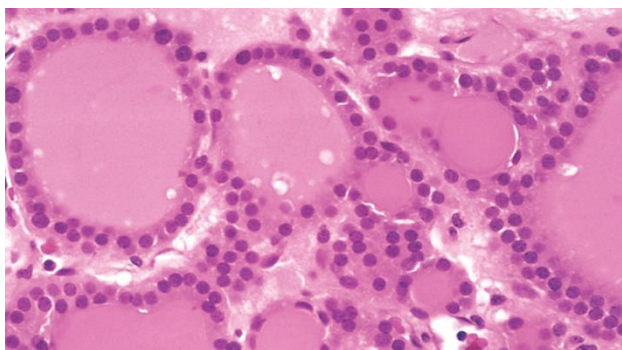
3 guage needles, multiple passes, ideally from periphery of lesion, Reaspirate after fluid drawn, immediately smeared and fixed and Papanicolaou stain common. Importance was given to detailed history, duration of swelling, pressure symptoms; these symptoms associated illnesses, previous exposure to neck irradiation, history of anti-thyroid drug use, positive family history. A detailed local examination was done in all cases followed by systemic examination.

**Statistical analysis**

Using SPSS software version 12 statistical analyses was done. The benign and malignant solitary thyroid nodule variables using student ‘t’ test.

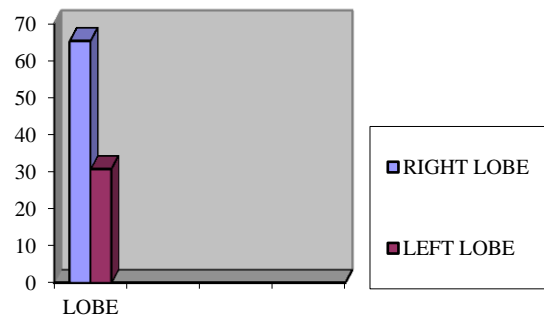
**RESULTS**

In this present study total of 50 cases were studied who presented with complaint of thyroid swelling which was clinically confirmed as solitary thyroid nodule. Out of 50 cases 10 cases were found to have malignant lesions with remaining 40 cases being benign lesions. The malignant nodules were significantly lower than those of benign ones (P = 0.0001). There were no significant differences between the mean ADC values of various malignant thyroid nodules, but there were significant differences between the subtypes of benign thyroid nodules (P = 0.0001).



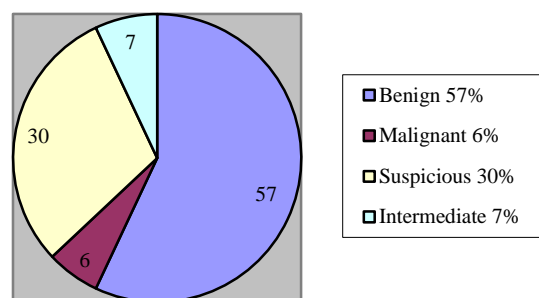
**Figure 1: Follicular adenoma: well-differentiated follicles resemble normal thyroid parenchyma.**

The ADC value is a new promising noninvasive approach used for differentiating malignant from benign solitary thyroid nodules. The incidence of malignancy in solitary thyroid nodule is quite high. There were significant differences between cystic and solid thyroid nodules (adenomatous nodules and follicular adenomas), with (P= 0.0001). The cystic or hemorrhagic thyroid nodule did not benefit from diffusion-weighted MR imaging. There is a higher incidence of colloid goiter (38.3%) followed by follicular adenoma (29.1%) among all the solitary nodule of thyroid cases were studied.



**Figure 2: Location of nodule comparison of lobe.**

The preponderance of solitary thyroid nodule is higher in females than in males with younger age groups of <40 years being affected mostly. The internal content of a nodule was categorized according to the ratio of the cystic portion to the solid portion in the nodule: predominantly solid (<50% cystic) and predominantly cystic (≥50% cystic). Incidence of Malignancy is Malignant Lesions 23% and 78% (Benign Lesions).



**Figure 3: FNAC report.**

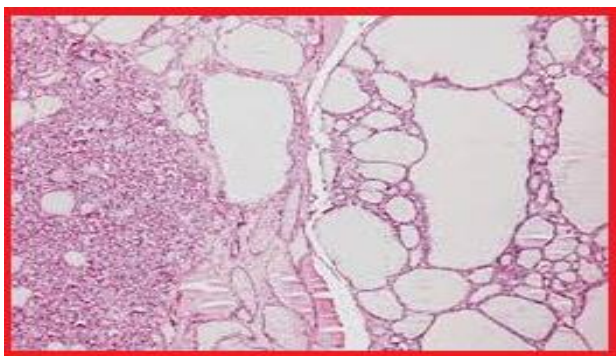
A spongiform appearance was defined as the aggregation of multiple microcystic components in more than 50% of the volume of the nodule. The shape of the nodule was categorized as follows: ovoid to round (when the anteroposterior diameter of the nodule was equal to or less than its transverse diameter on a transverse or longitudinal plane), taller than wide (when the anteroposterior diameter of a nodule was longer than its

transverse diameter on a transverse or longitudinal plane), or irregular (when a nodule was neither ovoid to round nor taller than wide). The margin of a nodule was categorized as well-defined smooth, spiculated, or ill-defined.

**Table 1: Type of operation performed.**

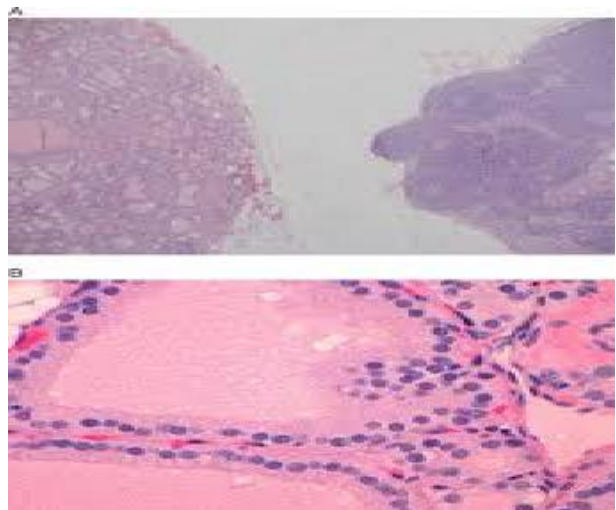
Operation	No. of cases in percentages
Hemithyroidectomy alone	85.12%
Near total thyroidectomy	9.5%
Total thyroidectomy	2.6 %
Total thyroidectomy with LN dissection	4.1%

Distributions of symptoms are seen swelling in the thyroid region, pain in the nodule, pressure symptoms, toxic symptoms and metastatic symptoms are rare. Swelling in front of the neck was the commonest symptom present in all the cases. The other symptoms present were pain and pressure symptoms.



**Figure 4: Histology slideshow thyroid tumor.**

Hemithyroidectomy i.e., removal of ipsilateral lobe with isthmus was the operation done for 68 cases.



**Figure 5: Histopathology of thyroid tumor.**

FNAC was able to confirm the diagnosis whether benign or malignant in 68.2% of the cases studied. 88% of the solitary thyroid nodule cases which were studied underwent Hemithyroidectomy alone and 85% of the patients who were studied with solitary thyroid nodule had a firm consistency of the swelling.

**Table 2: Present study histopathological reports.**

Histopathological report	Percentage of reports
Nodular colloid goiter	50.3%
Follicular adenoma	28.4%
Papillary carcinoma	11.5%
Follicular carcinoma	3.7%
Medullary carcinoma	-
Thyroiditis	1.6%
Multi nodular goiter	7.8%

**DISCUSSION**

Present findings support previous study of results that suggest a taller-than-wide shape is very specific for differentiating malignant thyroid nodules from benign ones. This result conveys the fact that malignant nodules (taller than wide) grow across normal tissue planes, while benign nodules grow parallel to normal tissue planes. This study shows higher incidence of colloid goiter followed by adenoma of thyroid nodule among all solitary thyroid nodule cases studied. We have divided our FNAC cases into four groups into Benign, Malignant, Follicular and Indeterminate groups which helps in further management.

Indeterminate FNAC results were due to adenomas, follicular neoplasms and overlapping cytological features.<sup>10</sup> With sensitivity and specificity of 88-92% of FNAC and its safety, reliability, minimally invasive, high diagnostic accuracy, economicity makes it a invaluable tool in the management of solitary thyroid nodule. The use of ultrasound guided FNAC has improved tissue sample collection in small thyroid nodules, difficult access especially in those with large areas of cystic degeneration or necrosis and in cases of suspicious and inadequate sampling cases.<sup>17</sup> To accurately determine a cancerous nodule is challenging especially in suspicious nodules. After HPE, about 78.3% of suspicious nodules turn out to be benign in nature. Among the thyroid nodules in the present study, 16.7% were found to be cystic.

Most thyroid cysts are formed by the degeneration of adenomas. A thyroid cyst has the highest ADC value because it may contain serous fluid or may be a colloid cyst with high thyroglobulin concentration. One patient had a hemorrhagic cyst that was misdiagnosed as a malignant tumor with a low ADC value.<sup>12</sup> The cause of this decrease in ADC value was the presence of hemorrhage within the cyst with subsequent restricted diffusion and a low ADC value. It can be seen that

solitary thyroid nodules are common in 3<sup>rd</sup> and 4<sup>th</sup> decades of life. The youngest patient in this study was 15 years old and the oldest being 65 years. There is a female preponderance with sex ratio being 6:1 but nodules in males have higher risk for malignancy if present. There were significant differences between cystic and solid thyroid nodules (adenomatous nodules and follicular adenomas), with  $P=0.0001$ . The cystic or hemorrhagic thyroid nodule did not benefit from diffusion-weighted MR imaging. This clearly states that fairly large numbers of patients are subjected to surgery, which still remains the only way to rule out thyroid malignancy, which is not so beneficial.

## CONCLUSION

We concluded that the ADC value is a new promising noninvasive imaging approach that can be used for characterization of solitary thyroid nodules and differentiation between benign and malignant ones. The prevalence of 4-7% of solitary thyroid nodule in general population, with majority being benign lesions requires a thorough clinical as well as histopathological approach in the evaluation and management of solitary thyroid nodules. 5% of these nodules being malignant and significant number of suspicious lesions mandate FNAC & HPE of these nodules, which remains the corner stone in the management of solitary thyroid nodule. Diffusion-weighted MR imaging does not help to differentiate among different types of malignant thyroid nodules but does reliably differentiate among various benign nodules.

Fine needle aspiration cytology has become an invaluable, minimally invasive, reliable tool in the pre-operative assessment of patients with suspicion. Overall, the 97% negative predictive value of FNA is useful in selecting patients who do not require surgery. We conclude that the current work up was unable to prevent unnecessary surgeries for benign suspicious nodules, which later were confirmed by HPE as benign lesions. Further studies are needed to determine whether diffusion-weighted MR imaging could be added to the routine imaging technique used for differentiating malignant from benign solitary thyroid nodules. A patient with an FNA result that is suspicious or clearly malignant should also be counseled to undergo surgery, even in the absence of other risk factors. Hence we suggest improvement of diagnostic process using immune histochemistry and / imaging techniques.

*Funding: No funding sources*

*Conflict of interest: None declared*

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

## REFERENCES

1. Silver CE, Brauer RJ, Schreiber K. Cytologic evaluation of thyroid nodules. New criteria for surgery. NY State J Med. 1984;84(3):102-9.
2. Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ, et al. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer: the American Thyroid Association (ATA) guidelines taskforce on thyroid nodules and differentiated thyroid cancer. Thy. 2009;19(11):1167-214.
3. Lindsay S, Sheline GE, Potter GD, Chaikoff IL. Induction of neoplasms in the thyroid gland of the rat by x-irradiation of the gland. Cancer research. 1961;21(1):9-16.
4. Chopra S, Knight MA, Vega-Lopez F. Dermatological problems. Manson's Tropical Diseases. 2009;22:333-71.
5. Tarrar AM, Wahla MS, Ilyas S, Khan OU, Waqas A, Raza A. Solitary thyroid nodule; frequency of malignancy at combined military hospital Rawalpindi. Prof med J. 2010;17(4).
6. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE et al. 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: the Ame Thy Asso gui task force on thyroid nodules and differentiated thyroid cancer. Thy. 2016;26(1):1-133.
7. Mohamed S. Histopathological Characteristics of thyroid tumors among sudanese Patients (Doctoral dissertation, UOFK). Available at: <http://khartoumspace.uofk.edu/handle/123456789/8896>.
8. Razi M, Hassan A, Khalid N, Ali SM, Khan AI, Hussain R, et al. Survival analysis of papillary thyroid carcinoma in relation to stage and recurrence risk - 20 year experience in Pakistan. Radi Soc Pak. 2015;12:115.
9. Fogelfeld L, Wiviott MB, Shore-Freedman E, Blend M, Bekerman C, Pinsky S, et al. Recurrence of thyroid nodules after surgical removal in patients irradiated in childhood for benign conditions. N E J Med. 1989; 30;32(13):835-40.
10. Siddiqui, Mustaqeem A., Morie Gertz, Diana Dean. Amyloid goiter as a manifestation of primary systemic amyloidosis. Thy. 2007;17(1):77-80.
11. Stiller, Charles A. International patterns of cancer incidence in adolescents. Can trea rev. 2007;33(7):631-45.
12. Bomeli SR, LeBeau SO, Ferris RL. Evaluation of a thyroid nodule. Oto cli of N Ame. 2010;43(2):229-38.
13. Neki NS, Kazal HL. Solitary thyroid nodule-an insight. J Ind Acad Clin Med. 2006;7(4):328-3.
14. Yeung, Meei J, Serpell JW. Management of the solitary thyroid nodule. The oncologist. 2008;13(2):105-12.
15. Güler EN, Bozkurt MF, Ozbas S, Yalcin S. Thyroid Cancer 21. Neuroendocrine Tumours: Diag and Manag. 2015;(27):353.
16. Win AK, Buchanan DD, Rosty C, MacInnis RJ, Dwyer JG, Dite GS, et al. Role of tumor molecular

and pathology features to estimate colorectal cancer risk for first-degree relatives. *Gut.* 2015;64(1):101-10.

17. Nosé V. Familial follicular cell tumors: classification and morphological characteristics. *Endocrine pathology.* 2010;21(4):219-26.
18. Chetan VR, Veeresalingam B, Kumar MK, Durbesula PT, Rao PS. A study on the clinical

manifestations and the incidence of benign and malignant tumors in a solitary thyroid nodule. *Int J res Med Sci.* 2013;1(4):429-34.

**Cite this article as:** Rao BH, Chakravarthy KS. Study of incidence in between benign and malignant tumors of solitary thyroid nodule. *Int J Res Med Sci* 2016;4:5288-93.