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# Solitary nodule thyroid: diagnosis and management

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## ABSTRACT

**Background:** Solitary nodule can be a true solitary nodule or a dominant nodule of multinodular goitre or ectopic thyroid or unilateral agenesis. Solitary nodule can be benign or malignant. Purpose of evaluation is to differentiate between the two.
**Methods:** A prospective study of solitary nodule thyroid (STN) patients presenting to ENT outpatient department, for a period of 3 years from September 2012 to 2015.
**Results:** Out of 67 patients enrolled into study, 53 patients had benign true STN, 9 patients had multinodular goiter (MNG) presenting as solitary nodule and 5 had malignant nodule (7.46%). Among the benign nodules, 25 patients had small solitary nodule (<4 cm size). They were treated medically and followed-up for a period of 1 year. 28 patients with large benign solitary nodules (>4 cm size) were taken up for surgery directly. Hemithyroidectomy was done in benign STN patients (39 patients) and total thyroidectomy was done in malignant nodule and MNG patients and followed-up by lifelong L-$T_4$ therapy.
**Conclusions:** Small benign solitary nodules regress with medical therapy alone. In large solitary nodules, and in those nodules not regressing with medical therapy, hemithyroidectomy is adequate. In MNG and malignant nodules, total thyroidectomy is advocated. Hemithyroidectomy and total thyroidectomy patients were followed - up with suppression and supplementation therapy respectively. This area being fluorotic belt, there is an increased prevalence of goiter. This study gives a concise guideline in evaluation and management of STN for goiter endemic areas.

**Keywords:** Solitary nodule, Thyroid nodule, Dominant nodule

## INTRODUCTION

Growths or lumps in the thyroid gland present as swellings in front of the neck moving with deglutition. Prevalence of these lumps depends on various factors like age, sex, diet, iodine deficiency, endemic areas, fluorosis belt and radiation exposure. High fluoride levels in drinking water and ground waters are known to interfere with iodine uptake by the thyroid gland and causes clinical hypothyroidism and nodule formation in thyroid gland.

Thyroid nodules may be single or multiple. Solitary nodules may be present in the lobes of the thyroid gland or in the isthmus. Solitary nodule can actually be a dominant nodule of multinodular goiter (23%), asymmetrical enlargement of one lobe of thyroid as in chronic lymphocytic thyroiditis (Hashimoto's thyroiditis), simple goiter, malignant nodule, unilateral agenesis, or rarely developmental errors such as ectopic tissue.[1,2] Solitary Thyroid nodules (STN) are seen in 4-7% of adult population. They are common among females (6.4%) as compared to male (1.5%).[2] Most of thyroid nodules are benign, only 5-20% of nodules are malignant.[2] Benign nodules are classified as adenomas, colloid nodules, cysts, infectious nodules, lymphocytic or granulomatous, hyperplastic nodules, thyroiditis, and congenital anomalies.[2] Malignant nodules can be classified into differentiated (papillary and follicular carcinomas), medullary carcinoma, undifferentiated

(small cell, giantcell, carcinosarcoma) and miscellaneous like lymphoma, sarcoma, squamous cell carcinoma, fibrosarcoma, mucoepidermoid carcinoma and metastatic tumour.

## METHODS

A prospective study of patients presenting as solitary thyroid nodule (STN) to ENT Outpatient department in Kamineni Institute of Medical Sciences, Narketpally, over a period of 3 years from September 2012- 2015.

### *Inclusion criteria*

Inclusion criteria were all patients who presented as STN clinically to ENT OPD during a period of 3 years from September 2012-2015 and age group from 20 to 70 years.

### *Exclusion criteria*

Exclusion criteria were age group <20 years and >70 years, those patients who presented clinically with multiple nodules in thyroid and diffuse thyromegaly, those who were not willing to undergo surgery or not willing for follow-up, syndromic presentations as part of MEN Syndromes.

All the selected patients were first examined to make a clinical diagnosis of solitary nodule thyroid. Then the patient was evaluated by ultrasonography of thyroid gland and neck to check for the presence of non-palpable nodules in thyroid, whether the nodule is solid or cystic, assess vascularity, size and extent of nodule, and presence of neck nodes. FNAC was done to know the cytology of nodule. Thyroid profile was done to assess functional status of nodule. Patients in hypo or hyperthyroid status were made euthyroid by giving thyroxine or anti thyroid drugs respectively.

Patients presenting with small solitary nodule (<4 cm in size) were initially treated medically with suppressive doses of L-$T_4$ and were followed-up for a period of 1 year. If the nodule regressed, patient was continued on lifelong suppressive dose of L-$T_4$. If the nodule remained the same after 1 year follow-up, hemithyroidectomy was done. Large solitary nodule (>4 cm in size) reported as follicular adenomas, cystic nodules, colloid nodules on FNAC were posted for hemithyroidectomy directly. Multinodular goiter presenting as solitary nodules and thyroid nodules reported as suspicious for malignancy on FNAC was posted for total thyroidectomy. Those reported as papillary carcinoma on FNAC were posted for total thyroidectomy with or without neck dissection depending on involvement of neck nodes and $^{131}$I ablation therapy is reserved for recurrence of tumor in follow-up. Thyroid nodules reported as follicular carcinoma on histopathology were subjected to completion thyroidectomy. Patients who underwent hemithyroidectomy and total thyroidectomy were put on lifelong L-$T_4$ suppressive dose (25-50 µg per day) and supplementation dose (100-150 µg per day) respectively.

All patients were followed-up once in 6 weeks for 3 months followed by once in 3 months for 1 year. In their follow- up visits they were screened for thyroid hormone status, serum calcium levels and recurrence of the nodule.

## RESULTS

Out of 83 patients who reported to ENT OPD with solitary nodule, 16 were excluded from study as they abstained from follow-up. Total no of patients included in the study were 67. Nodule was showing a right lobe predilection (64%). 76% of STN were in younger age group (20-40 years) (Figure 1) and was showing a threefold female preponderance (female: male = 3:1).

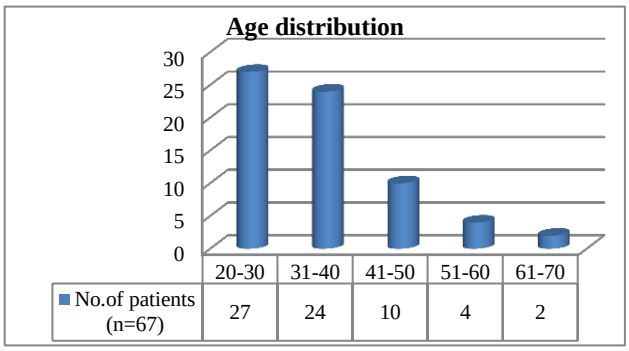


**Figure 1: Age distribution among the patients enrolled into study.**

Out of 67 patients, benign True solitary nodules were seen in 53 patients, 9 patients were multinodular goiter presenting as solitary nodule and 5 patients had malignant nodule. Among the 53 patients presenting as benign true solitary nodule, 17 patients were colloid goiter, cystic goiter was in 5 patients, and follicular adenoma was in 31 patients (58%) on cytology (Figure 2).

Thyroid profile revealed hypothyroid status in 17 patients and hyperthyroid in 8 patients and rest of 28 patients were euthyroid at initial presentation. The hypo or hyperthyroid patients were managed medically with L-$T_4$ and anti-thyroid drugs respectively till they all turned euthyroid. Among all euthyroid patients, small STN were present in 25 patients. They were treated with suppressive dose of L-$T_4$ therapy, following which nodules regressed in 14 patients; nodule remained the same in 11 patients who were taken up for hemithyroidectomy surgery. Large STN were seen in 28 patients, they were directly taken up for hemithyroidectomy.

All 9 patients with multinodular goiter were subjected to total thyroidectomy. Among 5 patients with malignant nodule, papillary carcinoma was detected in three patients, out of them 2 patients underwent total thyroidectomy with modified radical neck dissection because of presence of $N_+$ neck and total thyroidectomy

alone without neck dissection in 1 patient in view of $N_0$ neck. Follicular carcinoma was detected in histopathology of hemithyroidectomy specimens in 2 patients, they were taken-up for completion thyroidectomy. Total thyroidectomy patients were given lifelong L-$T_4$ supplementation therapy.

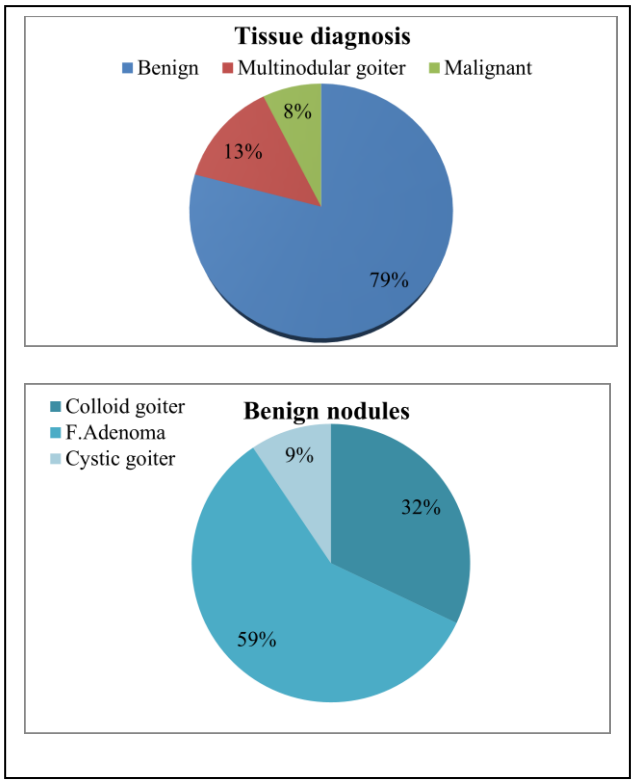


**Figure 2: Tissue diagnosis of patients with solitary nodule thyroid.**

Recurrent laryngeal nerve paresis was seen in 2 patients on 2nd postoperative day which recovered with steroid therapy within 7-10 days. Unilateral recurrent laryngeal nerve palsy developed in 1 patient. Recurrence of nodule was seen in 2 patients during follow-up who were taken-up for completion thyroidectomy followed by lifelong L-$T_4$ supplementation therapy.

## DISCUSSION

Evaluation of thyroid nodule is a challenge. Evaluation starts with a detailed history. Prior radiation exposure, male gender, past medical or family history suggestive of pheochromocytoma, hyperparathyroidism, chronic constipation and diarrhea, hypertension and episodes of nervousness or excitability suggests possibility of MEN 2a or 2b. Sengupta et al did a prospective study among 178 patients of incidentally detected thyroid swelling, identified highest incidence of thyroid swelling (75.84%) in 20-40 year age group, with a fourfold female preponderance.[3] In our study also, solitary nodules were common in 20-40 year age group (76.1%) with a threefold female preponderance. In Sengupta et al study, thyroid nodules were more commonly located on right lobe, our study also gave right sided preponderance (64%). In Sengupta et al study, most of the patients presented in euthyroid state (90%), but in our study patients presented in euthyroid state were 62.6% only as this being goiter endemic area.

Symptoms such as pain in the thyroid gland, sudden increase in size of the gland, stridor or respiratory distress, dysphagia, dysphonia increases the clinical suspicion of a malignancy. However in our study, none of the patients presented with these symptoms. Examination is done to look for all characteristics of thyroid swelling along with specific features like high vascularity (bruit), fluctuation test to check for cystic nature, extent of swelling into thoracic inlet (retrosternal goiter), consistency of nodule and pressure symptoms of nodule on adjacent structures. Both benign and malignant solitary thyroid nodules can be soft or firm, smooth or irregular on examination. But hard or variable consistency, size larger than 4cm, fixation to or invasion of surrounding structures and presence of palpable lymph nodes suggests malignancy. Vocal cord paralysis is not a reliable indicator of malignancy as it can occur in benign disorders also.[4] Excision of nodule followed by histopathology confirms malignancy in solitary nodules. Incidence of malignancy was 20.9% among 91 patients in the study done by Kendall; incidence of malignancy in the present study was 7.46%.[5]

Many investigations including diagnostic imaging studies, radio iodine scans, serological tests, cytogenetics and cytological studies like fine needle aspiration cytology (FNAC) are available. Out of all these investigations, FNAC has become investigation of choice initially due to its diagnostic ability and cost effectiveness.[6] In addition some studies reported that, fine needle aspiration only was used as initial treatment in 53% of thyroid nodules.[7]

Imaging studies include ultrasonography of neck, CT scan and radioactive iodine scan. Ultrasonography of thyroid and neck, is done to see whether the nodule is a true solitary nodule, presence of non-palpable nodules, solid or cystic, vascularity of nodule, extent of the nodule, and presence of lymphadenopathy in the neck. Nodules less than 1 cm are not palpable clinically unless they lie in anterior part of gland. About 50% of them are detected by ultrasonography.[8] Other imaging modalities include CT Scan of Neck, and thyroid scan. Radioactive Iodine scan helps to determine the functional activity of the thyroid nodule. Most of benign nodules like cysts, colloid nodules, benign follicular lesions, hyperplastic nodules and nodules of Hashimoto's thyroiditis present as cold nodules. But studies report that isotopically cold nodules are considered suspicious of malignant potential.[9] Warm or hot nodules indicate hyperfunctioning nodule. Radio iodine scanning and clinical examination of thyroid nodule are not reliable indicators to differentiate benign thyroid nodule from malignant.[5] Other limitations of radio iodine scanning is inability to detect thyroid

nodules at periphery of gland and at isthmus and misinterpretation is possible if normal functioning thyroid tissue overlaps the cold solitary nodule or if thyroid gland is asymmetrical.[4]

A concise and practical guideline is established for solitary nodule thyroid for diagnosis and management (Figure 3).

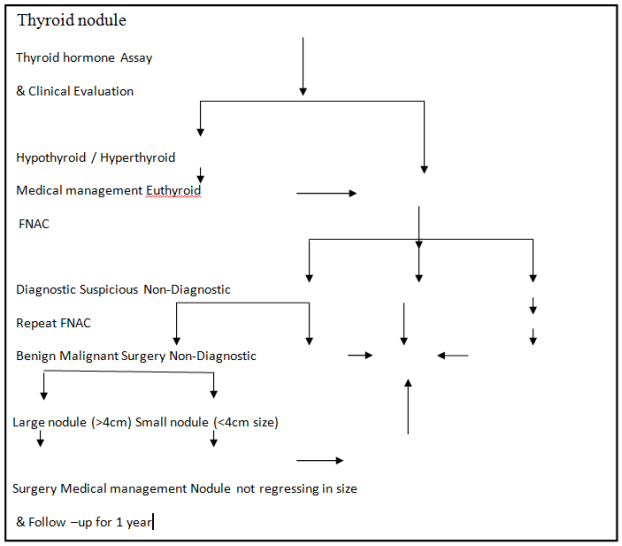


**Figure 3: Algorithm for the evaluation of thyroid disorders.**

As iodine deficiency is the cause for enlargement of thyroid particularly in endemic areas, iodine supplementation therapy seems to be an adequate approach. A controversial trial of supplementation of iodine conducted in endemic areas revealed increased incidence of thyrotoxicosis in predisposed individuals due to sudden increase in uptake of iodine by thyroid gland, and iodine therapy also increased the incidence of papillary carcinomas and lymphocytic thyroiditis [10]. Due to these drawbacks, Iodine therapy is refrained from use. Currently three modalities of treatments are available. They are L $-T_4$ suppressive therapy, surgery and $^{131}I$ therapy.

In diffuse goiters without autonomous degeneration, TSH suppression by treatment with thyroid hormones is known to slow down or even revert the growth. A goiter reduction of 15-40% is expected within 3 months of therapy, but it reverts back to pretreatment size on withdrawal.[10] Treatment with $T_3$ alone or combination with L-$T_4$ is almost same as with L-$T_4$ alone, but L-$T_4$ gives more pronounced suppression of serum TSH than Iodine. It is recommended in endemic euthyroid goiters to give 200 µg of iodine combined with 100 µg of L-$T_4$ for at least 6 months followed by iodine supplementation alone.[10] Berghout et al divided non –toxic multinodular goitre patients into two groups,one treated with L-$T_4$ and other is a control group, given only placebo.[11] Goiter volume was reduced by 45% within 9 months period with L-$T_4$ therapy and returned to baseline volume of gland after 9 months of discontinuation of L-$T_4$. In placebo group, the goiter continued to increase in size by more than 20% during 9 months. Lifelong treatment with L-$T_4$ suppression therapy may be required to avoid goiter recurrence. In case of large goiters, subclinical or frank hyperthyroidism can be the consequence when treated with L-$T_4$. So, L-$T_4$ therapy is not recommended in large goiters or goiters with suspicion of malignancy, surgery is preferred as it causes significant reduction in size and prompt relief of symptoms and gives definitive tissue diagnosis.[10] Hemithyroidectomy was the predominant intervention (55.06%) in the study done by Sengupta et al, in our study also hemithyroidectomy was predominant intervention, done in 39 patients (58.2%) out of 67 patients.[3] Complication rates for thyroidectomy are minimal in skilled hands but in retrosternal extension of goiters complication rates are high even in skilled hands like post-operative tracheomalacia, necessitating reintubation in postoperative period. Reccurent laryngeal nerve palsy and injury to parathyroids account to less than 1% during thyroidectomy.[10] Recurrent laryngeal paresis in the present study, developed in 2 patients who developed paresis on 2$^{nd}$ post-operative day and recovered in 7-10 days of steroid therapy, and paralysis developed in 1 patient which amounts to 1.88%.

Recurrence in nontoxic multinodular goiter is seen in 15-40% of patients in study done by Berghout et al seen in long term follow-up.[11] Recurrence was seen in 2 patients (2.98%) in the present study. Recurrence rates are directly proportional to the volume of the thyroid tissue left back during surgery particularly in multinodular goiters and in endemic areas. Recurrence rates do not depend on age of the patient, duration of goiter and serum levels of TSH during follow-up. Postoperative supplementation with L-$T_4$ is useful particularly in endemic areas to prevent recurrence. Complication rates are ten times more in revision thyroidectomies, so $^{131}I$ ablation of recurrent goiters is preferred to surgical management.[10]

## CONCLUSION

Single nodule within the thyroid gland on examination can be a true solitary nodule, a multinodular goiter presenting as solitary clinically, or a malignant nodule. Purpose of evaluation of solitary nodule is to differentiate between benign and malignant nodules. Ultrasound examination of neck and FNAC helps to differentiate benign from malignant nodules. Small solitary nodular goiters are treated with L-$T_4$ Suppression therapy, but surgery is done in nodules not regressing with medical therapy. Recurrence of nodules in multinodular goiter depends on volume of thyroid tissue left back during surgery. So, total thyroidectomy is preferred in them. Total thyroidectomy with or without neck dissection is done in malignant nodules. Periodic follow- up of the patients with L-$T_4$ therapy post operatively, particularly

in endemic areas is known to prevent recurrence of benign nodules in thyroid gland.

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