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RESEARCH ARTICLE

OCCURRENCE OF MALIGNANCY IN SOLITARY THYROID NODULE AT TERTIARY CARE CENTRE

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ABSTRACT

Background: True solitary nodule occurs in 4-8% of the population and in autopsy it is seen in 50% of cases. The prevalence of thyroid nodule increases with age and women have a higher prevalence than men. Seventy percentage of solitary thyroid nodules are benign, indeterminate15%, malignant 5%, nondiagnostic in 15%. Increasing numbers of nodules are being detected serendipitously because of rising use of imaging technique. Solitary thyroid nodules being so prevalent in the general population, it is important to have clear strategy of assessing nodules and determining which will require surgery or can be managed conservatively.

Objectives of the study: 1. Primary aim in investigating thyroid nodules is to exclude possibility of malignancy.2. Analyzing the efficacy of clinical, biochemical, radiological and cytological evaluation of nodules. 3. Evaluating the management of solitary thyroid nodule, Identifying malignant nodule requiring surgery and its incidence and its outcome.

Methods: The study was conducted in ESI Model Hospital from January 2015 to June 2016. Patients satisfying inclusion criteria were enrolled. All the patients with solitary nodule thyroid are evaluated with thorough clinical examination, cytological, radiological and laboratory investigations. Appropriate thyroid surgery was performed and analyzed for histopathological examinations results.

Results : The commonest presentation of solitary thyroid nodule was asymptomatic swelling in front of the neck. The peak incidence of solitary nodule thyroid observed in 3rd to 5th decade, constituting 66.3% of the cases studied, Female predominance over male with ratio of 18:1 noted in occurrence of SNT. The common causes of solitary nodule was colloid goitre (50%), follicular adenoma (25%), adenomatous goiter (3%). Euthyroid state was noted in 95% of the cases. Incidence of malignancy in solitary thyroid nodule was 14.3%. The most common cause of malignancy was papillary carcinoma (72%) followed by follicular carcinoma (28%).

Conclusion: Solitary nodule of thyroid are more common among females and peak incidence in 3rd to 5th decade. Most of the patients presenting with solitary nodule of thyroid are euthyroid and only a small percentage of patient with toxicity or hypothyroidism . USG can be accurately used to detect patients with multinodular goiter who clinically present as solitary nodule of thyroid. Incidence of malignancy in male patients presenting with solitary nodule of thyroid is more when compared to female. The most common cause of malignancy in solitary nodule is papillary carcinoma followed by follicular carcinoma.

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INTRODUCTION

The solitary thyroid nodule is defined as a "palpably discrete swelling within an otherwise apparently normal gland" (Brander *et al.,* 1992). The prevalence of palpable nodules in general population is 4-7%, and in 13%–67% when ultrasound detection is used. In autopsy studies, they have a prevalence of approximately 50%. Solitary nodules of thyroid are about four times more common in women than in men .Most nodules are asymptomatic and are often discovered serendipitously by the patient or their primary medical practitioner when being examined for another problem (Cooper *et al.,* 2006).Thyroid cancers are rare, accounting for only 1.0% of all cancer in most populations and 0.5% of all cancer deaths, Nonetheless thyroid cancer occur in approximately 5% of all thyroid nodules independent of their size. The clinical importance of thyroid nodules rests with the need to exclude thyroid cancer, which occurs in 7%–15% of cases depending on age, sex, radiation exposure history, family history, and other factors (Miller *et al.,* 2004). In solitary thyroid nodules 70% are benign, indeterminate 15%, malignant 5%, nondiagnostic (Williams *et al.,* 2013). The risk of malignancy in cytological indeterminate thyroid lesion is high up to 42%. Atypical features and follicular neoplasm cytology have higher incidence of

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malignancy, these features urge us to recommend thyroidectomy (Inderbir Singh, 1996).

Aims and objectives

- To analyze the efficacy of clinical, biochemical, radiological and cytological evaluation of nodules.
- To identify malignant nodule requiring surgery and its incidence
- To evaluate the management of solitary thyroid nodule and its outcome.

MATERIALS AND METHODS

The study was conducted on patients with solitary thyroid nodule admitted in The Department of General Surgery, ESIC MC PGIMSR AND MODEL HOSPITAL, Rajajinagar, and Bengaluru-10 from JANAURY 2015 TO JUNE 2016. Prospective analysis of all the cases of solitary nodule thyroid in the specified period done. These cases were selected by random sampling method and studied in detail clinically and recorded as per the proforma. Routine investigations and specific investigations including Fine needle aspiration cytology (FNAC) of the nodule, Thyroid profile, indirect laryngoscopy, Plain X-ray neck, and Ultrasonography neck were done in all cases. Special investigations like radio-isotope scanning was not performed as the facilities were not available. All the patients were managed by surgery and diagnosis was confirmed by histo-pathological examination. The patients were grouped according to different variables like age , sex, size of the nodule, site of the nodule, functional thyroid status, FNAC reports and histopathological examination reports, Post-op complication of surgery then analyzed and compared with the previous similar studies conducted elsewhere. Finally conclusions were drawn accordingly.

Treatment

Pre-operative: Optimization of any co-morbidity of patients done prior to surgery and any other medications were prescribed based on individual status and was noted

Operative: Position of the patient, type of anesthesia, incision, type of operation planned, preoperative findings and type of operation performed were recorded.

Post-operative: Every patient was followed up post-operatively during the course of management in the hospital to note the development of if any complication and managed.

Follow-up: At the time of discharge, all the patients were advised to attend the surgical OPD regularly for follow up. Any recurrences or complications were noted. Thyroid functional status was assessed, accordingly thyroxine tablets prescribed if necessary.

RESULTS

Total of 77 cases of solitary nodule of thyroid were included studied

Age distribution: The age of the patients ranges from 20 years to 65 years, with peaks being in 3rd to 4th decades. The mean age of presentation is 40.13 years. Cases in 3rd to 4th decades constitutes 66.3% of the cases studied.

Sex distribution: Solitary nodule of thyroid are much more common in females. Out of 77 cases studied 73 were females and 4 were males, and the ratio comes to M: F = 1: 18.25. Also the malignant nodules are common in females. Malignancy noted in 11 cases, all belonged to female sex.

Table 1. Age wise distribution in SNT

Age in years	No. of Patients
0-9	0
10-19	0
20-29	12
30-39	34
40-49	17
50-59	8
60-69	6
TOTAL	77

Table 2. Sex distribution in SNT

Sex	No. of patients	Percentage
Males	4	5%
females	73	95%
Totals	77	100%

Clinical Features

All the cases in the present study presented with complaint of swelling in the region of the thyroid. Out of 77 cases, 68 patients presented with swelling alone (88%), 1 cases had pain, 2 cases had dysphagia and 1case had dyspnea. Also 3 patients had lymphadenopathy which was confirmed by ultrasonographic examination and 2 patient had features of hypothyroidism.

Duration of symptoms

In our study, duration of onset symptoms varied from 2 months to 4 years. Also duration of malignant nodules extend from 2 month to 4 years.

Table 3. Symptomatology in SNT

Duration of symptoms	No.of patients
<1month	0
1-3 month	27
4-6 month	38
7-12 month	6
1-2 years	5
>2 years	1

Site of the nodule

Out of 77 cases studied, 50 cases presented with nodule in right lobe of the thyroid gland and 27 cases in the left lobe of thyroid.

Size of the nodule

In the present study, on clinical examination size of the nodule, in its largest dimension, varies from 2cm to 7cm. Most of the patients presented with the size of about 4 to 6 cm. In the study, as such there is no correlation between the size of the nodule and the occurrence malignant nodule.

Table 4. Size of nodules in SNT

Size of the nodule	No. of patients	No of malignancy
<4 cm	27	5
>4 cm	50	6

Thyroid functional status

Out of 77 cases, two presented with hypothyroidism and rest all were in euthyroid state. Patients with hypothyroidism were treated with thyroxine.

FNAC reports

Fine Needle Aspiration Cytology is the important investigation in the evaluation of solitary nodule of thyroid. All 77 cases were subjected to FNAC during the course of evaluation. FNAC reports are mainly categorized into 6 entities- Colloid goitre, follicular adenoma, Hyperplastic goiter, suspicious (of malignancy), malignant- Papillary and Follicular carcinoma, Hashimoto's thyroiditis, and cysts. In our study, out of 23 follicular neoplasms, 19 cases turned out to be follicular adenoma, 2 cases each were Hyperplastic nodule and Hashimoto's thyroiditis. One suspicious (of papillary carcinoma) case confirmed Follicular carcinoma on histopathological examination. Out of 5 cases 4 cases of papillary carcinoma were diagnosed preoperatively by FNAC alone and 3 cases were Lymph node positive. One case diagnosed as cysts by FNAC confirmed to be simple cysts on histopathological examination.

Table 5. FNAC dioagnosis in SNT

FNAC	No.of patients	Percentage
Colloid Goitre	46	60%
Follicular Adenoma	19	25%
Suspicious	1	1%
Hyperplastic Goitre	1	1%
Follicular carcinoma	4	5%
Papillary Carcinoma	5	7%
Simple cyst	1	1%

Table 6. Histopathological diagnosis

HPE Reports	No. of patients
Colloid goiter	38
Adenomatous goitre	2
Hyperplastic nodule	3
NEOPLASM	
Benign	
Follicular adenoma	19
Carcinoma	11
Papillary ca	(8)
Follicular ca	(3)
Hashimoto's thyroiditis	3
Simple cyst of thyroid	1
Total	77

FNAC and No.of patents		Histopatological diagnosis							
Diagnosis	No.of patients	Colloid goitre	Adenomatous goitre	Follicularadenoma	hyperplastic nodule	Papillary ca	Follicular ca	Hashimoto's thyroiditis	cyst
Colloid Goitre	46	37	2		1	3	2	1	
Follicular Adenoma	19			16	2			1	
Suspicious	1						1		
Hyperplastic Goitre	1					1			
Follicular carcinoma	4			3				1	
Papillary Carcinoma	5	1				4			
Simple cyst	1								1
Total	77	38	2	19	3	8	3	3	1

Table 7. Fnac and histopathology correlation

Histopathological examination of 77 cases revealed, About 38(50%) of the 77 patients were diagnosed with colloid goiter, followed by Follicular adenoma 19 (25%), Adenomatous goiter 2(3%) and Hashimoto's thyroiditis and Hyperplastic nodule 3 (4%) each, simple cyst 1(1%). Malignancy both follicular 3(4%) and papillary 8(10%)) was diagnosed in 11 out of the 77 cases. From the study, incidence of malignancy in solitary nodules is 14.29%.

Ultrasonography of SNT

Ultrasonography of 77 cases revealed, 14 cases were neoplastic out of it 8 cases were confirmed to be malignant in Histopatological examination, and 63 cases diagnosed as non neoplastic out of it 3 cases turned out be malignant. Out of 77 cases 66 (86%) patients nodules were benign, 11 were malignant (14.29%). From the study, out of carcinoma, 4 were papillary and 2 follicular carcinoma and no case of medullary or anaplastic or lymphoma was detected. Papillary carcinoma accounts to 73% and follicular carcinoma accounts to 27%. Depending upon the clinical diagnosis and FNAC features, all the 77 patients undergone surgery.

Table 8. Corelation of FNAC and HPE in neoplastic SNT

FNAC	Histopathological Diagnosis		Total
	Neoplastic	Non-neoplastic	
Neoplastic	24 (a)	5 (b)	29 (a+b)
Non-neoplastic	6 (c)	42 (d)	48 (c+d)
Total	30 (a+c)	47 (b+d)	77 (a+b+c+d)

Sensitivity, specificity, Accuracy of FNAC test was 84.6%, 93.7%, 92.2% respectively.

Table 9. USG and histopathology correlation

USG	Histopathological Diagnosis		Total
	Neoplastic	Non-neoplastic	
Neoplastic	8 (a)	6 (b)	14 (a+b)
Non-neoplastic	3 (c)	60 (d)	63 (c+d)
Total	11(a+c)	66 (b+d)	77 (a+b+c+d)

Sensitivity, specificity, Accuracy of USG Examination was 72.7%, 90.9%, 88.3 respectively.

Among them, 60 patients had undergone hemithyroidectomy, 8 patients underwent total thyroidectomy, 3 cases undergone total thyroidectomy with MRND and 1 cases undergone total thyroidectomy with CLND. In 5 case, HPE after

hemithyroidectomy showed papillary carcinoma (Miller *et al*., 2004), follicular carcinoma (Cooper *et al*., 2006), and then completion of total thyroidectomy done. Post-operatively, suppressive dose of thyroxine was started for patients who had undergone total thyroidectomy. Three cases out of 17 cases of total thyroidectomy showed features of hypocalcemia on 2-4 post-operative day, hence, they are supplemented with oral calcium and vitamin D3. All the cases were followed up for 6 months, two cases had husky voice without any change in vocal cord movements one case had Temporary vocal cord palsy.

DISCUSSION

The observations and results of the present study were compared with the available previous similar studies.

Table 10. Mean age at presentation

Authors	Mean age(in years)
Gupta	38.7
Tai (2012)	43.22
Jena (2015)	36.8
Present study	40.13

In the study done by Gupta M (2010), Tai J D (2012), Jena A (2015) separately, reported the mean age at presentation as 38.7years, 43.22 years, 36.8 Years respectively. From the present study, the mean age at presentation found to be 40.13years, correlates with the previous studies. Most of the earlier series reported peak incidence of solitary nodule thyroid in the 3rd and 4th decades. In the present study, the peak incidence found to be 3rd to 4th decades, which constitutes about 66.3% of the cases studied. In our study Malignancy was noted in young patient at 27 year and older at 60 year, peak incidence in 3rd to 5th decades. Which correlates with previous study

Table 11. Sex distribution comparison to other studies

Authours	Sex incidence(M:F)
Gupta	1:11.5
Roti	1:5
Md Abdul Hussain (2014)	1:8
Present study	1:18

In the study done by Md Abdul Hussain (2014) and Gupta (2010) (1:11.5) reported ratio of sex incidence as 1:9 and 1:11.5 respectively. In the present study, it's found to be 1:18, even though ratio is more, which correlates with previous studies. And solitary thyroid nodules are more common in females as compared to males. Because of periods of fluctuations in the demands of the hormonal requirement in female in their life cycle (puberty, menstrual cycles, pregnancy, menopause), the chances of thyroid nodule formation are very high as compared with male counterparts.

Site of the nodule

Out of 77 cases studied, 50(65%) cases presented with nodule in right lobe of the thyroid gland and 27(35%) cases in the left lobe of thyroid. Tai *et al.,* (2012), in there study of 265 patients 163 patient presented with right sided SNT which correlates with our study (Tai *et al.,* 2012). And there was no increased risk of malignancy as compared to right with left side solitary nodule thyroid.

Size of the nodule

In 77 cases we studied, Nodules <4 cm were 27 (Malignant 5) and >4 cm were 50(Malignant 6), Lowest malignant nodule size was 2x1cm and Highest malignant size was 6x4cm. Tai *et al.,* 2012 and Jena *et al.,* (2015) in there study, revealed that there was no great significance between nodule size larger than 4 cm and nodule size less than 4 cm which correlated with our study. Nodule size is not a predictive risk factor for malignancy, but enlarging nodule over a short period may be an increased risk for malignancy in thyroid nodule.

Table 12. Efficacy of fnac comparison to other studies

Authours	Sensitivity	Specificity	Accuracy
Afroze *et al*	61.9	99.3	94.5
Kessler *et al*	79	98.5	87
Gupta *et al*	80	86.6	84
Muratli *et al*	87.1	64.6	77.3
Present study	84.6	93.7	92.2

In our study, out of 23 follicular neoplasms, 19 cases turned out to be follicular adenoma, 2 cases each were Hyperplastic nodule and Hashimoto's thyroiditis. One suspicious (of papillary carcinoma) case confirmed as Follicular carcinoma on histopathological examination. Out of 5 cases, 4 cases of papillary carcinoma were diagnosed preoperatively by FNAC alone. Five cases diagnosed as colloid goiter turned out be malignant in HPE. Thus even though FNAC diagnosis of malignancy is highly significant and such patients should be subjected to surgery, A benign FNAC diagnosis should be viewed with caution as false negative results do occur.

Table 13. Efficacy of usg in snt comparison to other studies

Authours	Sensitivity	Specificity	Accuracy
Koike *et al*	86.5	92.3	88.7
Lokhande *et al*	71.43	90.62	87.18
Kapali *et al*	88.4	73.3	80.3
Present study	72.7	90.9	88.3

From the present study, Ultrasonography of 77 cases revealed, 14 cases were neoplastic, out of it 8 cases were confirmed to be malignant in Histopathological examination, and 63 cases diagnosed as non neoplastic out of it 3 cases turned out be malignant. 4 cases presented with Micro calcification, 3cases with cervical lymphadenopathy which proven to be malignant on HPE. Sensitivity, specificity and accuracy of Present study is 72.7%, 90.9%, 88.3% respectively which are comparable with previous studies by Lokhande *et al*. 2015 and Kapali *et al.* 2016. Ultrasound is a sensitive and specific modality in assessment of thyroid nodules with good overall accuracy. The most sensitive parameter in suspecting malignancy is hypo echogenicity of the nodule, the most specific features are lymphadenopathy followed by microcalcifiation.

Table 14. Aetiological incidence (in percentage)

Series	Adenoma	Carcinoma	Colloid goitre	Others	Total no. of cases
Khairy	53	24	63	32	172
Gupta	18	12	42	3	75
Tai	148	97	20	-	265
Anitha	53	20	20	10	103
Present study	21	11	38	7	77

From the present study, commonest cause of solitary nodule is Colloid goitre, which is comparable with the studies done by Khairy *et al*. 2004, Gupta *et al* and Anitha *et al.,* 2016. The common causes of Adenoma are follicular adenoma and adenomatous goitre.

Table 15. Distribution of non-neoplastic and neoplastic lesions diagnosed by HPE

Authours	Non-Neoplastic	Neoplastic	Ratio
Khairy	77	95	0.82:1
Hurtado Lopez	80	50	1.6:1
Gupta	45	30	1.55:1
Jena	45	58	1.23:1
Anitha	30	73	0.5:1
Present study	45	32	1.40:1

In the present study, neoplastic conditions include adenomas and all malignant lesions. From the study, the ratio of non-neoplastic to neoplastic cases is about 1.40:1, which is comparable to the studies done earlier like Gupta (2010), Hurtado Lopez (2005), Jena A (2015).

Table 16. Incidence of carcinoma comparison to other studies

Study	Year	Percentage
Gupta *et al*	2010	20.0%
Tai *et al*	2012	33.6%
Md Abdul Hossain *et al*	2014	28.0%
Jena	2015	39.7%
Anitha *et al*	2016	18.51%
Khairy	2004	14.0%
Present study	2016	14.3%

From the literature, the incidence of malignancy in thyroid nodule ranges from 5% to 30%. From the present study, the incidence found to be 14.3%, which is comparable with the study done by Khairy *et al*. 2004, Anitha *et al.* 2016, and Gupta *et al.* 2010.

Conclusions

Solitary nodule of thyroid is more common in females and more common in the age group of 30-50years. Most of the patients with solitary nodule of thyroid present with swelling alone. Nodule size is not a predictive risk factor for malignancy, but enlarging nodule over a short period may be an increased risk for malignancy in thyroid nodule. FNAC is the investigation of choice in the evaluation of solitary nodule of thyroid. It detects papillary carcinoma in a solitary nodule with high sensitivity and specificity. In ultrasound, the most sensitive parameter in suspecting malignancy is hypo echogenicity of the nodule, the most specific features are lymphadenopathy followed by microcalcifiation.

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