

**MALIGNANCY INCIDENCE IN SOLITARY NODULE THYROID**JOSE V STANLEY<sup>1</sup>, MURALI TV<sup>2\*</sup>, SAM CHRISTIE MAMMEN<sup>1</sup>, MATHEW PHILIP PALLIKAMATTOM<sup>2</sup>, SHEEJA S<sup>3</sup><sup>1</sup>Department of General Surgery, Government Medical College, Kottayam, Kerala, India. <sup>2</sup>Department of Surgical Oncology, Government Medical College, Kottayam, Kerala, India. <sup>3</sup>Department of Pathology, Government Medical College, Kottayam, Kerala, India.

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**ABSTRACT**

**Objectives:** The incidence of thyroid cancer is rising in the state of Kerala. This study aimed to determine the incidence of malignancy in solitary nodule thyroid (SNT) cases operated on at our tertiary care hospital.

**Methods:** This is a retrospective register based study. All patients operated for SNT over 8 years from 2013 to 2020 were listed and pathological findings were evaluated.

**Results:** A total of 319 patients with SNT were included, with 75.5% being female. The mean age of patients was 42 years (standard deviation=±12.6). Histopathological analysis revealed malignancy in 16% (n=51) of cases. Other most common pathology observed in SNT cases was nodular colloid goiter (67.8%), followed by thyroid adenoma (13.2%), adenomatous nodule (1.9%), and thyroiditis. Among the 51 malignant cases, 70.5% were papillary carcinoma, 25.5% were follicular carcinoma, and one case each of medullary and poorly differentiated carcinoma was identified. A statistically significant association was found between age and malignancy diagnosis ( $p=0.011$ , Independent samples t-test). In addition, females had a higher incidence of cancer, with a  $p=0.021$  and an odds ratio of 2.7 (Chi-square test).

**Conclusion:** A solitary nodule has a 16% chance of malignancy, with papillary thyroid carcinoma being the most common type.

**Keywords:** Adenomatous nodule, Follicular carcinoma thyroid, Papillary carcinoma thyroid, Solitary Nodule thyroid, Thyroiditis.

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**INTRODUCTION**

A cross-sectional population survey in the state of Kerala indicates that the state is now iodine-sufficient, with a goiter prevalence of 12.2% [1]. Solitary nodule thyroid (SNT) are observed in approximately 4–7% of the population, while autopsy studies suggest their prevalence may be as high as 50% [2,3]. The incidence of cancer in Kerala is rising, and overdiagnosis could be a contributing factor [4]. At the Regional Cancer Center in Kerala, thyroid cancer ranks second among the most prevalent cancers in women [5].

Thyroid nodules are initially evaluated based on symptomatology, clinical examination, ultrasound, and fine-needle aspiration cytology (FNAC) [6]. These factors help assess the likelihood of malignancy, the presence of pressure symptoms, and hyperthyroidism – three key indications for surgical intervention in our region. In Kerala, benign multinodular goiter is the most common reason for thyroid surgeries, followed by malignancies and thyroiditis [7]. In our study, we analyzed the incidence of malignancy in all solitary thyroid nodules surgically treated at our tertiary care hospital in central Kerala.

**METHODS**

The objective of the study is to enumerate the incidence of malignancy in solitary thyroid nodules. It's retrospective register-based research on patients operated from 2013 to 2020 with a diagnosis of the solitary thyroid nodule. Departmental scientific committee and institutional review board approval were obtained for scientific content and ethical framework before the data collection.

Children below 12 years are excluded from the study. The pre-operative diagnosis by the clinician at admission for surgery is considered as the clinical diagnosis and all Solitary nodules are included. A diagnosis of dominant nodule of multinodular goiter in clinical evaluation is

excluded. Pre-operative evaluations suggested of malignancy or not are not considered for this post-operative data evaluation.

**Statistical evaluation**

With an estimated prevalence of solitary thyroid nodules at 7% in the general population, the minimum required sample size was calculated to be 101 patients, with a 95% confidence limit. Primary outcomes are reported as percentages, with the primary objective being the calculation of the malignancy rate among all surgically treated solitary nodules. Secondary objectives include determining the mean tumor size in malignant cases, assessing the association between age and malignancy incidence using the Independent Samples t-test, and evaluating the correlation between gender and malignancy incidence using the chi-square test. A  $p<0.05$  is considered statistically significant.

**RESULTS**

A total of 319 patients were included in this study, of whom 75.5% were female ( $n=241$ ) (Fig. 1). Over an 8-year period, the mean age of patients was 42 years (standard deviation [SD]=±12.6), ranging from 13 to 82 years (Fig. 2). Data on laterality were available 118 patients of which 44 (37.3%) were left-sided and 74 (62.7%) right-sided. Out of 319 patients, 32 patients do not have information on the type of surgery they underwent. The most common procedure done was hemithyroidectomy followed by total thyroidectomy (TT) (Table 1).

The final histopathology result of these procedures showed nodular colloid Goitre as the commonest diagnosis in 216 patients (67.8%). 51 patients (16%) had malignancy in SNT whereas, thyroid adenoma constituted 42 cases (13.2%) (Fig. 3). Three patients had toxic features in the solitary nodule. 66 patients (20.7%) had thyroiditis documented in the final histopathology. In 4 of them, thyroiditis was the only disease reported as causative of the nodularity and in the rest 62 it was a coexisting diagnosis to the primary pathology.

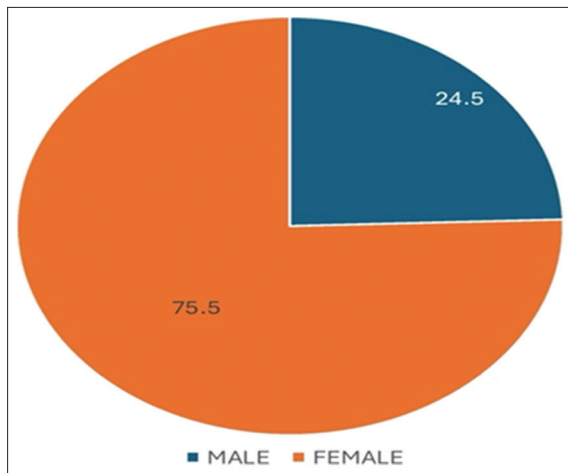


Fig. 1: Pie diagram showing gender distribution of all solitary nodular thyroid cases

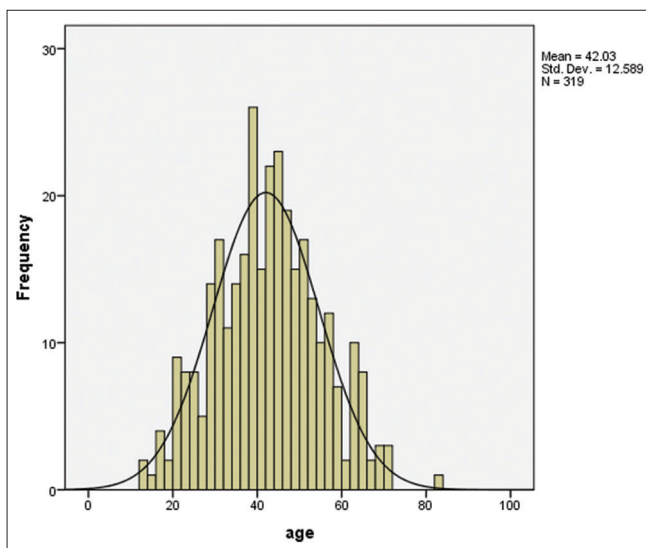


Fig. 2: Histogram showing age distribution of solitary nodular thyroid patients

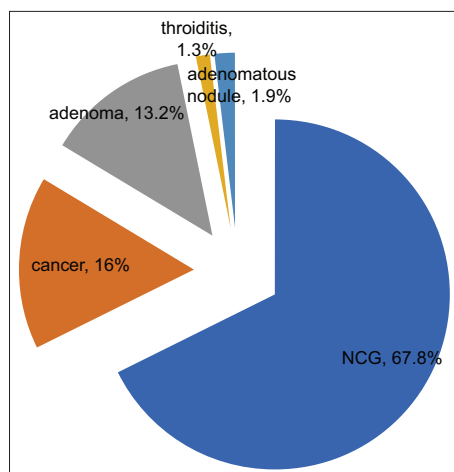


Fig. 3: Distribution of pathologies in solitary nodular thyroid in percentage of total. NCG: Nodular colloid goiter

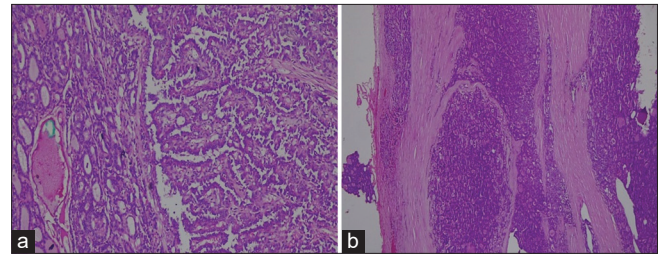


Fig. 4: (a) Papillary carcinoma histopathology H and E, (b) Follicular carcinoma with vascular and capsular invasion

Table 1: Type of procedures done for data available 287 SNT patients

Type of surgery	Number of patients	Percentage
Total thyroidectomy	102	35.5
Total+CCC	9	3.1
Hemithyroidectomy	166	57.8
Endoscopic hemithyroidectomy	2	0.7
Subtotal thyroidectomy	8	2.8
Data not available	32	Not considered
Total	319	100

SNT: Solitary nodule thyroid

Table 2: Types of malignancy in SNT

Type of cancer	Frequency	Percentage
Papillary carcinoma thyroid	36	70.5
Follicular thyroid	13	25.5
Medullary thyroid carcinoma	1	2.0
Poorly differentiated	1	2.0
Total	51	100

SNT: Solitary nodule thyroid

Out of 51 malignancies diagnosed, papillary carcinoma was the predominant variant with 36 cases (70.5%) (Fig. 4). Follicular carcinoma constituted 13 cases (25.5%) followed by one case of poorly differentiated carcinoma and medullary thyroid carcinoma each (2% each) (Table 2). The tumor size information was available for 35 out of the 51 cancer cases and the mean size was 2.5 cm (SD±1.5). Out of this 14.3% were microcarcinomas (<1 cm size).

The mean age of malignancy-diagnosed SNT patients is 37.9 years (SD±13.7) and all other benign diagnosis together has a mean of 42.8 years (SD±12.2). Age and malignancy diagnosis had a statistically significant association ( $p=0.011$ , Independent samples t-test). In females, SNT showed a malignancy incidence of 18.7% and in males 7.7% only. This correlation was statistically significant with a  $p=0.021$  and an odds ratio of 2.7 in a Chi-square test.

## DISCUSSION

Thyroid nodules are distinct lesions within the thyroid parenchyma, possessing a noteworthy potential for malignancy. They are frequently identified in clinical practice, often as incidental findings [8]. Solitary thyroid nodules carry a higher risk of carcinoma compared to multinodular goiter [9,10]. Ultrasound and FNAC are the two universally available tools used in the initial evaluation of a nodule in the thyroid. Solid or cystic, shape, multinodular or not, color flow patterns, echogenicity, margins of the nodule, fine punctate calcifications, taller than wider, associated lymph nodes are the commonest ultrasound parameters evaluated in a thyroid nodule to

rule out malignancy [11,12]. Even the location of nodule in the gland is of importance [13,14].

About 23% of solitary thyroid nodules are actually the dominant nodules of a multinodular goiter and although the risk of malignancy in each individual nodule within a multinodular goiter is lower than that of a true solitary thyroid nodule, the cumulative malignancy risk – when adjusted for all nodules – approaches that of a solitary nodule [9]. Differentiated thyroid cancer is the commonest and among it, papillary carcinoma thyroid leads the incidence followed by follicular similar to our findings [15]. Our series has a malignancy incidence that matches the literature [16]. In this study, all solitary nodule cases were analyzed together, regardless of whether there was pre-operative evidence of malignancy. As a result, the surgical approach varied among patients, with some undergoing TT, others undergoing hemithyroidectomy, subtotal thyroidectomy, and a subset receiving TT with central compartment dissection.

Though the reason is not fully understood, females have more chance of thyroid cancer [17]. As per literature, a nodule in male has more chance of being malignant than one in female but recent publications refute this finding suggesting near equal probabilities [18]. In our study, the risk of malignancy is more for females in SNT which is statistically significant. Diet environmental factors or common somatic mutations are not the reasons for the gender predilection of thyroid cancer and this subject requires further research [19].

Chronic lymphocytic thyroiditis or Hashimoto's thyroiditis is an autoimmune destruction of follicular cells and it is the most common cause of hypothyroidism in developed countries [20]. The prevalence of this disease is 7.5% globally and females are 4 times more commonly affected than males [21]. Nodules are one of the clinical manifestation of thyroiditis [22,23]. In our series, 20.7% of SNT patients had thyroiditis and in four of them that were the only pathology described, showing that thyroiditis alone can produce a solitary nodule-like clinical presentation.

Tumor size in differentiated thyroid cancer is a predictor of disease-free survival following treatment [24]. In the United Kingdom, management guidelines doesn't recommend FNAC on nodules <1 cm unless there is a lymph node associated [25]. The <10 mm papillary carcinomas are called as micropapillary carcinomas and it is possible to get higher risk features even in these when operated [26,27]. Our patient population also had 14.3% of <10 mm carcinomas, though the mean size was 2.5 cm.

Some solitary thyroid nodules or dominant nodules associated with multinodular goiter can be highly cellular and form proliferative nodules without being true neoplasms. Many pathologists prefer to use the less definitive term adenomatoid nodule or adenomatous hyperplasia for these lesions. Although they are well-circumscribed, they lack complete encapsulation. Key distinguishing features include compressed thyroid tissue at the periphery and a uniform appearance within the lesion, which differentiates them from follicular adenomas [28].

Adenomatoid nodules retain several characteristics of nodular colloid goiter and may undergo degeneration, fibrosis, or Hürthle cell changes. Conventionally, benign-appearing follicular tumors that are completely surrounded by a fibrous capsule are classified as follicular adenomas, whereas circumscribed but unencapsulated tumors are considered hyperplastic nodules. However, studies indicate that adenomatous nodules arising from a background of nodular hyperplasia are monoclonal in nature, leading some to classify them as follicular adenomas [29,30]. In our study, we have considered these nodules as a distinct entity.

### Limitations

This study does not include pre-operative evaluations for malignancy diagnosis. In addition, missing data have led to varying denominators across the analyzed variables.

### CONCLUSION

Nodular colloid goiter is the most common cause of a solitary thyroid nodule. The overall malignancy incidence in solitary thyroid nodules is 16%, with papillary carcinoma being the most prevalent type. Thyroiditis can also present as a solitary nodule. Females have a higher incidence of thyroid cancer, and there is a significant association between patient age and the likelihood of malignancy in SNT cases.

### TAKE HOME MESSAGE

SNT has a 16% chance of being malignant.

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### AUTHOR'S CONTRIBUTION

The 1<sup>st</sup> and 2<sup>nd</sup> authors did data collection. The 3<sup>rd</sup>–5<sup>th</sup> authors were involved in planning and result analysis. The 5<sup>th</sup> author was involved in pathology result evaluation. The 3<sup>rd</sup> and 4<sup>th</sup> authors were key persons in statistical analysis. The 1<sup>st</sup>, 2<sup>nd</sup>, and 5<sup>th</sup> authors prepared the manuscript. All authors did the manuscript corrections and have agreed to the final version.

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