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Original Article

Frequency of Malignancy in Patients with Solitary Thyroid Nodule

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Abstract

Background: The thyroid gland is the largest endocrine gland in the human body and the most frequent site of primary endocrine malignancies. Solitary thyroid nodules (STNs) are clinically significant because of their malignant potential, with reported global malignancy risks ranging between 5% and 30%.

Objective: This study aimed to determine the frequency of malignancy in patients with STNs presenting at a tertiary care hospital in Swat, Pakistan.

Methodology: A cross-sectional study was conducted in the ENT Department of Saidu Group of Teaching Hospital, Swat, between January 2024 and May 2025. A total of 164 patients aged 20–65 years with ultrasonographically confirmed STNs (TIRADS ≥3) who underwent thyroid surgery were included. Fine-needle aspiration cytology (FNAC) was performed and classified using the Bethesda System, while histopathology of surgical specimens served as the diagnostic gold standard. Data were analyzed using SPSS v21, with chi-square tests applied for associations and logistic regression performed to adjust for confounders.

Results: The mean age of patients was 40.1 ± 11.4 years, with females comprising 68.9% of the cohort. Histopathology confirmed benign nodules in 82.3% (n=135) and malignancy in 17.7% (n=29). Among benign cases, colloid goiter (32.9%), follicular adenoma (26.2%), and nodular goiter (23.2%) were most frequent. Papillary carcinoma (13.4%) was the predominant malignant subtype, followed by follicular carcinoma (3.7%) and anaplastic carcinoma (0.6%). No statistically significant associations were observed between malignancy and patient age (p=0.109), gender (p=0.188), or residence (p=0.477). Bethesda categories V/VI were strongly predictive of malignancy.

Conclusion: Malignancy was identified in nearly one-fifth of surgically managed STNs, with papillary carcinoma being the most common subtype. These findings underscore the importance of FNAC and ultrasound-based risk stratification in preoperative evaluation to avoid unnecessary surgeries and optimize patient management.

Keywords: Fine-needle aspiration cytology, Papillary carcinoma, Solitary thyroid nodule, Thyroid malignancy.

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Introduction

The thyroid gland, the largest endocrine organ, is also the most frequent site for primary endocrine malignancies [1]. A solitary thyroid nodule (STN) is defined as a localized swelling or nodule in the thyroid gland where the remaining gland appears normal on palpation [2]. STNs account for 4–7% of thyroid disease presentations in adults, and their clinical importance lies in the increased risk of malignancy compared to multinodular goiters [3].

Globally, thyroid cancer constitutes less than 2% of all cancers in men and 1–5% in women [4]. The reported frequency of thyroid malignancy ranges between 0.9% and 13%, while the prevalence of thyroid nodules detected clinically is about 2–6%, and up to 68% when assessed with ultrasonography [5]. Although most thyroid nodules are benign, the risk of malignancy varies between 7% and 15%, depending on factors such as age, sex, history of radiation exposure, and family history [6]. The rising incidence of thyroid cancer is attributed both to advancements in diagnostic imaging and a true increase in papillary thyroid carcinoma [7].

Clinically, STNs are often discovered incidentally or during examination for unrelated medical conditions [8]. The risk of malignancy is higher in solitary nodules compared to multinodular goiters, and several studies have reported malignancy rates of 4–20% in STNs [9,10]. Historically, many clinicians opted for surgical removal of all solitary nodules to confirm histology; however, thyroid surgery carries risks, and current practice favors a selective approach, reserving surgery for nodules with a strong suspicion of malignancy [11].

Accurate preoperative assessment is therefore crucial in guiding management. Ultrasound risk stratification systems such as TIRADS and diagnostic modalities like fine-needle aspiration cytology (FNAC), reported according to the Bethesda System, play a central role in differentiating benign from malignant nodules and preventing unnecessary surgeries [12]. Given the limited data available from Pakistan, and considering the diagnostic and clinical challenges posed by STNs, this study was undertaken to determine the frequency of malignancy in patients presenting with solitary thyroid nodules at Saidu Group of Teaching Hospital, Swat.

Methodology

Study Design:

This was a hospital-based cross-sectional study designed to determine the frequency of malignancy in patients presenting with solitary thyroid nodules (STNs). The study focused on surgically managed cases to provide histopathological confirmation of diagnoses.

Ethics:

Prior to commencement, ethical approval was obtained from the Ethical Review Board of Saidu Medical College, Swat (Ref No: 91-ERB/023, dated 21/08/2023). Additional approval was secured from the College of Physicians and Surgeons of Pakistan (Ref No: CPSP/REU/ENT-2022-027-1388). All participants were informed about the study objectives, risks, and potential benefits, and written informed consent was obtained from each patient in accordance with the Declaration of Helsinki.

Setting:

The study was conducted in the Department of ENT at Saidu Medical College and Saidu Group of Teaching Hospital, Swat, Khyber Pakhtunkhwa, Pakistan, between January 1, 2024, and May 30, 2025.

Participants:

A total of 164 patients aged 20–65 years, both male and female, undergoing thyroid surgery for solitary thyroid nodules were included. Inclusion criteria required patients to have STNs confirmed on ultrasonography with a Thyroid Imaging Reporting and Data System (TIRADS) score ≥3. Patients with a history of prior neck irradiation, those younger than 20 or older than 65 years, and patients presenting with metastatic cervical lymphadenopathy of unknown primary origin were excluded.

Variables:

The primary outcome variable was malignancy status of the nodule (benign vs. malignant). Independent variables included demographic characteristics (age, gender, residence), comorbidities, TIRADS scores, and FNAC results.

Data Sources/Measurement:

All patients underwent ultrasonography of the thyroid gland, and nodules with TIRADS ≥3 were evaluated using ultrasound-guided fine-needle aspiration cytology (FNAC). FNAC results were reported using the Bethesda System for Reporting Thyroid Cytopathology. Surgical specimens obtained during thyroidectomy or lobectomy were subsequently subjected to detailed histopathological analysis, which was considered the gold standard for

diagnosis. Demographic and clinical data were recorded on a predesigned proforma.

Bias:
To minimize selection bias, consecutive non-probability sampling was employed, ensuring inclusion of all eligible patients during the study period. Observer bias was reduced by having FNAC and histopathological evaluations performed by independent pathologists blinded to clinical data. Recall bias was minimized as all demographic and clinical details were directly obtained at the time of hospital admission.

Study Size:
The sample size of 164 was calculated using OpenEpi sample size calculator, assuming a malignancy proportion of 4% in solitary thyroid nodules, with a 3% margin of error and a 95% confidence interval.

Quantitative Variables:
Quantitative variables such as age, height, and weight were summarized using means and standard deviations (Mean ± SD). Qualitative variables including gender, residence, and malignancy status were presented as frequencies and percentages.

Statistical Methods:
Data analysis was performed using IBM SPSS version 21. Descriptive statistics were used for baseline demographic and clinical characteristics. The prevalence of malignancy was calculated as a percentage of total cases. Stratification was performed by age, gender, and area of residence. The chi-square test was applied to evaluate associations between malignancy and categorical variables. A p-value of <0.05 was considered statistically significant. Additionally, multivariate logistic regression was performed to control for potential confounders such as age, gender, comorbidities, and TIRADS scores, with malignancy status as the dependent variable. Results were reported as adjusted odds ratios (AOR) with 95% confidence intervals.

Results

Participants
A total of 164 patients met the inclusion criteria and underwent surgical management for solitary thyroid nodules. The mean age of the participants was 40.1 years (±11.4). The age distribution revealed that 41.5% (n=68) of patients were between 35–49 years, 36.0% (n=59) were aged 20–34 years, and 22.6% (n=37) were in the 50–65 years group. Of the total participants, 113 (68.9%) were female and 51 (31.1%) were male. Most patients were from rural areas (65.2%, n=107), while the remaining 34.8% (n=57) were from urban settings.

Descriptive Data
Clinical and demographic variables were further analyzed to explore their relationship with nodule type (benign vs. malignant). However, no statistically significant associations were observed between malignancy and patient age (p=0.109), gender (p=0.188), or residence (p=0.477). This indicates that the distribution of benign and malignant lesions was fairly uniform across different demographic groups in this cohort.

Outcome Data
Histopathological evaluation of excised specimens demonstrated that 135 patients (82.3%) had benign nodules, whereas 29 patients (17.7%) were diagnosed with malignant lesions. Among the benign cases, colloid goiter was the most common finding (40.0% of benign, 32.9% overall), followed by follicular adenoma (31.9% of benign, 26.2% overall) and nodular goiter (28.1% of benign, 23.2% overall). In the malignant group, papillary thyroid carcinoma was the predominant type (75.9% of malignant, 13.4% overall), followed by follicular carcinoma (20.7% of malignant, 3.7% overall), while anaplastic carcinoma was rare (3.5% of malignant, 0.6% overall).

Main Results
The study findings suggest that malignancy was present in nearly one-fifth of patients with solitary thyroid nodules undergoing surgical management, which is within the upper range of global estimates (5–30%). Papillary carcinoma emerged as the most frequent malignant subtype, consistent with worldwide epidemiological patterns. Further analysis of ultrasound and FNAC findings indicated variable predictive accuracy: Bethesda Categories V/VI strongly correlated with malignant histopathology, while Categories II/III and IV demonstrated lower predictive values. Multivariate logistic regression revealed no significant independent association between malignancy and age, gender, or residence after adjustment for confounders. These results highlight that demographic characteristics alone are not strong predictors of malignancy in solitary thyroid nodules, and that structured diagnostic approaches, including TIRADS and FNAC, remain essential for risk stratification and surgical decision-making.

Table 1. Demographic Characteristics and Their Association with lesion Type (Malignant vs. Benign)

Variable	Category	Malignant	Benign	Total	Percentage of Total (%)	P-value	Interpretation
Age Group	20–34 years	13	46	59	35.98%	0.109	No significant association between age and tumor type
	35–49 years	7	61	68	41.46%		
	50–65 years	9	28	37	22.56%		
Gender	Male	12	39	51	31.10%	0.188	No significant association between gender and tumor type
	Female	17	96	113	68.90%		
Residence Area	Rural	16	91	107	65.20%	0.477	No significant association between residence and tumor type
	Urban	11	46	57	34.80%		

Table 2 . Types of Thyroid Lesions and Their Corresponding Percentages of Benign and Malignant Cases

Lesion Type	**Lesion Count**	**% of Total**	**% of Benign**	**% of Malignant**
Benign Lesions (135; 82.32%)				
Colloid goiter	54	32.93%	40.00%	—
Nodular goiter	38	23.17%	28.15%	—
Follicular adenoma	43	26.22%	31.85%	—
Malignant Lesions (29; 17.68%)				
Papillary carcinoma	22	13.41%	—	75.86%
Follicular carcinoma	6	3.66%	—	20.69%
Anaplastic carcinoma	1	0.61%	—	3.45%

Table 3. Correlation of FNAC Bethesda Categories with Final Histopathology Results

Bethesda Category	Benign n=135	Malignant (n=29)	Total	PPV	NPV	Sensitivity	Specificity	Accuracy
II/III (Benign)	98 (72.6%)	2 (6.9%)	100	2.0%	98.0%	6.9%	72.6%	68.3%
IV (Follicular Neoplasm)	28 (20.7%)	6 (20.7%)	34	17.6%	82.4%	20.7%	79.3%	71.3%
V/VI (Suspicious/Malignant)	9 (6.7%)	21 (72.4%)	30	70.0%	30.0%	72.4%	93.3%	87.8%

(PPV: Positive Predictive Value; NPV: Negative Predictive Value)

Table 4. Adjusted Odds Ratios for Age, Gender, and Residence in Predicting Malignancy of Thyroid Lesions

Predictor	AOR	95% CI	p-value
Age (35–49 yrs vs 20–34 yrs)	0.39	0.14 – 1.10	0.074
Age (50–65 yrs vs 20–34 yrs)	1.13	0.40 – 3.23	0.815
Gender (Female vs Male)	0.83	0.36 – 1.90	0.667
Residence (Urban vs Rural)	1.15	0.48 – 2.75	0.749

Foot Note: {Adjusted Odds Ratio (AOR)}

Discussion

This cross-sectional study was conducted to determine the frequency of malignancy in solitary thyroid nodules (STNs) among surgically managed patients at Saidu Group of Teaching Hospital, Swat. Out of 164 patients, 17.68% were diagnosed with malignancy, while 82.32% were found to have benign pathology. Papillary carcinoma was the most common malignant type, followed by follicular carcinoma and the rare anaplastic carcinoma. These findings fall within the global malignancy risk for STNs, which ranges from 5% to 30% [7,12,14].

The observed rate is higher than some local studies reporting around 4% malignancy [10,11], but comparable to international data where selective surgical cohorts are examined [15]. Differences may arise due to selection bias, since only patients undergoing surgery were included. Surgical populations often represent higher-risk nodules, particularly those with suspicious features on ultrasonography or FNAC. Additionally, regional factors, such as iodine deficiency in rural areas of Swat, may further elevate the risk of malignancy [9,17].

In terms of histological distribution, papillary carcinoma accounted for the majority of malignant nodules, which is consistent with global literature documenting papillary carcinoma as the most frequent thyroid cancer [7,14,15]. Follicular carcinoma was less frequent, and anaplastic carcinoma remained rare, in agreement with reports highlighting its low prevalence but highly aggressive clinical course [16].

Demographically, most patients were female, supporting the well-documented female predominance in thyroid disease [17,18]. However, statistical analysis revealed no significant association between malignancy and age, gender, or residence, suggesting that these demographic factors alone are not reliable predictors of malignancy [3,6]. Instead, accurate diagnosis requires structured diagnostic tools.

The role of FNAC, classified according to the Bethesda system, was reaffirmed. Categories V/VI showed strong predictive value for malignancy, while Categories II/III and IV were less predictive, consistent with previous findings

[2,12,13]. This underlines the importance of combining FNAC with ultrasonography-based risk stratification systems such as TIRADS to optimize patient selection for surgery [5,12].

Taken together, the results align with global trends and emphasize the continued importance of early detection, structured evaluation, and selective surgical management of STNs [7,14].

Limitations

This study has several limitations. Firstly, it was a single-center study, limiting the generalizability of findings to other populations. Secondly, only surgically managed cases were included, introducing selection bias and likely overestimating malignancy rates compared to the general population of STNs [11]. Thirdly, the absence of long-term follow-up data prevented evaluation of recurrence rates, response to therapy, or survival outcomes. Furthermore, the iodine-deficient status of the study population in rural Swat may have influenced the results, making comparisons with iodine-sufficient populations less precise [17,18]. Lastly, reliance on a cross-sectional design limited causal inference, though the study provided valuable prevalence data and diagnostic insights.

Conclusion

Malignancy was present in 17.68% of solitary thyroid nodules in this surgically managed cohort, with papillary carcinoma being the predominant histological subtype. These findings are consistent with international literature and highlight the clinical importance of accurate preoperative risk assessment. The combination of ultrasound features, TIRADS, and FNAC remains critical for distinguishing benign from malignant nodules and avoiding unnecessary surgeries. While the malignancy frequency observed in this study likely reflects a higher-risk surgical population, it provides valuable insight into the regional burden of thyroid disease. Broader, multicenter, and population-based studies including conservatively managed nodules are needed to refine malignancy risk estimates in Pakistan.

Authors' Contributions

All authors meet the ICMJE criteria for authorship. They have reviewed and approved the final version of the manuscript and agree to be accountable for all aspects of the work.

Author 1: Substantial contribution to conception and design, drafting the manuscript, final approval, agreed to be accountable for all the work.

Author 2: Substantial contribution to conception and design, data acquisition, drafting the manuscript, final approval, agreed to be accountable for all the work.

Author 3: Analysis and interpretation of data, drafting the manuscript, final approval, agreed to be accountable for all the work.

Author 4: Analysis and interpretation of data, critical revision, final approval, agreed to be accountable for all the work.

Author 5: Substantial contribution to conception and design, drafting the manuscript, final approval, agreed to be accountable for all the work.

Author 6&7: Substantial contribution to conception and design, data acquisition, drafting the manuscript, final approval, agreed to be accountable for all the work.

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