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Original Article

Thyroid Cancer Incidence and Risk Factors in Toxic Nodular Goiter Patients in a Tertiary Care Hospital

Muhammad Irfan Fazal,[1] Muhammad Zain Qamar,[1] Huria Asghar,[1] Maha Naseem,[2] Arslan Hamid[1], Faiza Qamar,[1] Muhammad Usman Fazal[1]

[1]Mayo Hospital, Lahore, [2]Central Park Hospital,Lahore

Abstract

Objective: In this specific research, patients with toxic nodular goiters were examined to determine the frequency and potential risk factors for malignant thyroid disease.

Methods: In this research, 98 patients with toxic nodular goiter, which includes both single toxic nodules (STN) and toxic multinodular goiter (TMNG), were examined. Gender, age, comorbidities, prior neck radiation, family history of thyroid cancer, type of disease, size of the largest nodule as determined by ultrasound, surgery's duration, and identification of a lymph node during surgery were some of the patient characteristics that the research gathered. The patients were divided into groups with benign and malignant conditions based on the results of the histopathological investigation.

Results: 21 people (21.43%) of the 98 TNG patients had a malignant thyroid disease diagnosis. Both the benign and malignant groups had a comparable age distribution, but males had a significantly higher likelihood of developing cancer. In contrast, TMNG was more prevalent in the malignant group. Medical problems and family histories of cancer were equally prevalent in both groups. No discernible differences between the two groups were found in the operational statistics, including operative time and lymph node detection. Male gender and TMNG appeared to be key indicators of malignancy in regression analysis. These results imply that the danger of malignant thyroid disease in patients with TNG can be anticipated by the male gender and TMNG, two important factors.

Conclusion: According to the research, malignant thyroid disease was found in 21.43 percent of TNG patients, indicating that thyroid hyperfunction does not offer protection against cancer. Additionally, these patients' MNG levels and being male were major risk factors for malignancy.

Keywords: Case-control study, Breast carcinoma, Risk factors, lifestyle, socio-demographic, Pakistan, and reproductive health.

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Corresponding Author: Dr. Muhammad Zain Qamar **Email:** qamarzain79@gmail.com

Introduction

Thyroid dysfunction is a prevalent endocrine disorder that has been increasing worldwide. It accounts for approximately 30 to 40 percent of patients who attend endocrine clinics.[1,2] According to research done in Egypt, thyroid dysfunction affected 30% of patients who visited endocrine clinics. The most common types were hyperthyroidism and subclinical hyperthyroidism, which accounted for 19.2% and 15.8% of cases, respectively.[2] Graves' disease, toxic multinodular goiter (TMNG), and a single toxic nodule (STN) are the primary causes of hyperthyroidism.[3,4]

Increased thyroid-stimulating hormone (TSH) levels have been linked to a higher chance of thyroid cancer and more advanced nodular thyroid disease, even when TSH levels are within the normal range, according to studies.[5] To manage well-differentiated thyroid cancer patients, one approach is to suppress this hormone, given that it promotes the development of healthy and well-differentiated neoplastic thyroid cells.[6]

Individuals who have primary toxic goiter typically exhibit lower levels of TSH. This may lead to a reduced risk of developing malignant disease due to the suppression of the associated oncogenes.[7] These findings have suggested that the occurrence of a hyperfunctioning thyroid disorder could potentially provide some degree

of protection against cancer. [4]

In the past, studies reported a low occurrence of thyroid cancer in individuals with hyperfunctioning thyroid nodules, with a recorded incidence of 3-5%.[8] Consequently, even the American Thyroid Association does not suggest performing a cytological evaluation for these nodules because the risk of malignancy is low.[3] However, recent findings have demonstrated a higher incidence of thyroid cancer in patients with toxic goiter, ranging from 12-18%, indicating that the risk of malignancy was previously underestimated.[4,9]

The aim of this study was to assess the occurrence and potential indicators of malignant thyroid disease in individuals with toxic nodular goiter (TNG).

Methods

A retrospective analysis involving 98 adult patients with toxic nodular goiter (TNG) who received surgical intervention between January 2018 and December 2020 was performed by the entire general surgical division at the Al-Azhar College of Medicine and Dentistry Hospitals. One or more thyroid nodules, decreased serum TSH, and normal or elevated T3 or T4 values were all considered to be toxic nodular goiters. The purpose of the study was to examine the medical characteristics and histopathological results of TNG patients who received surgical intervention.

To gather data, patients' medical histories were taken, clinical examinations were conducted, and regular preoperative blood tests, such as TSH, T-3, and T-4, were performed, along with neck ultrasonography. The nodules detected were categorized using the British Thyroid Association's classification, and only individuals with a U2 classification were included, while those with U3, U4, or U5 nodules, a previous history of neck radiation, and/or Graves' disease were excluded. Thyroid scans were performed only on patients with a single nodule to confirm hyperfunction.

Before surgery, patients were counseled about the potential benefits, risks, and difficulties of the procedure, and informed consent was obtained, following ethical standards consistently. A total thyroidectomy was performed once the patient's thyroid function had normalized. The thyroid specimen removed during surgery was sent for histopathological analysis, and incidental thyroid cancer was diagnosed if no clinical features of malignancy were present.

At Al-Azhar University Hospitals, routine thyroid evaluation involved analyzing and selecting one sample section from every 1 cm of the residual tissue of the thyroid, along with all dominant nodules. Patients were divided into two categories, benign and malignant, based on the final histopathological report. The information gathered comprised demographics such as age and gender of patients, the existence of any associated medical conditions, whether there was any thyroid cancer in the family, radiation exposure in the neck region in the past, the form of the disease (multinodular or single), the size of the dominant nodule as detected through ultrasound, the duration of the operation, and any recognition of noteworthy lymph nodes while undergoing the operation.

Statistical Analysis

The data that was gathered for this study were subjected to statistical analysis using the Statistical Package for the Social Sciences (SPSS 26) software developed by IBM/SPSS Inc. in Chicago, IL. The results of this analysis were then reported using basic demographic statistics, such as frequencies and percentages, or mean values with standard deviations. To compare two independent sets of qualitative data, the chi-square test was utilized. Meanwhile, the independent-samples t-test and Mann-Whitney U test were used to compare quantitative data. Moreover, the study also employed univariate and multivariate logistic regression analysis to examine the potential risk factors associated with a binary categorical outcome. To determine statistical significance, a p-value of 0.05 or less was set as the threshold. By utilizing a combination of these methods, the study was able to gain valuable insights into the data and draw meaningful conclusions from the results.

Results

Patients with thyroid nodules were included in the research, and the characteristics of the benign and malignant groups were contrasted. Patients in the benign group had an average age of 47.13 years, whereas those in the malignant group had an average age of 48.67 years; the difference between the two categories was not statistically significant. Despite the fact that there were more females in both groups, men had a significantly greater correlation with cancer. Between the two research groups, there were no appreciable differences in the prevalence of chronic liver disease, diabetes, or hypertension. Additionally, both groups were uncommonly affected by an existing family history of malignancy of the thyroid.

In the research, TMNG and STN thyroid nodules were compared. The former was more common in the normal group than the malignant group. The dominant nodule's size, as determined by ultrasound, did not, however, vary significantly among the two different groups. In Table 1, the study's findings are displayed.

Among both malignant and benign groups, there was no discernible variation in the length of the operation. During surgical exploration, no major lymph nodes were found in either group. Table 2 contains additional

details about the operative statistics.

Table 1: *Preoperative Data*

Variable		Benign Group (n=77)	Malignant Group (n=21)	p-value
Age (Years)		47 ± 11.94	48.67 ± 10.66	0.594
Gender	Male	12(15.58%)	8 (38.1%)	0..023*
	Female	65(84.42%)	13 (61.90%)	
Comorbidities				
Diabetes Mellitus		9 (11.69%)	3 (14.24%)	0.748
Hypertension		9 (11.69%)	4 (19.05%)	0.378
Chronic Liver Disease		2 (2.6%)	0 (0%)	0.456
Family history of cancer Thyroid		1 (1.3%)	0 (0%)	0.600
Preoperative diagnosis	TMNG	44(57.14%)	17 (80.95%)	0.046*
	STN	33(42.86%)	4 (19.05%)	
Size of the dominant nodule (mm) by the US		32.29±12.93	35.67 ± 14.43	0.303

Table 2: *Operative Findings*

Variable	Benign Group (n=77)	Malignant Group (n=21)	p-value
Operative Time	87.17 ± 19.30	93.29 ± 19.90	0.204
Detected lymph nodes	0 (0%)	0 (0%)	1

Table 3: *Regression analysis to detect risk factors of malignancy in TNG*

Variable	Univariate analysis	OR	Multivariate analysis 95% CI for OR	p-value
Age	0.590			
Male gender	0.028*	2.713	1.207-8.423	0.043
Diabetes	0.748			
Hypertension	0.383			
Chronic Liver Disease	0.999			
Family History of cancer thyroid	0.999			
TMNG	0.001*	3.530	1.642-11.965	0.022
Size of the Nidules	0.301			

In individuals with thyroid nodules, regression analysis was used to determine possible risk variables related to malignancy. Male gender and TMNG were found to be substantial indicators of carcinoma in TNG patients in both univariate and multivariate analyses. Further details can be found in Table 3.

Of the patients diagnosed with malignancy, papillary cancer was the most common type. Papillary cancer and its follicular variant accounted for 42.86% and 33.33%, respectively, of the overall number of malignant cases. The confidence interval for these results is presented in Section 3.1.

Out of the total number of cases under study, five were diagnosed with the follicular type, accounting for 23.81% of the cases. (This particular information was not included in the tables presented in the study.)

Discussion

In past hyperthyroid state in patients of TNG was considered a protective factor for malignancy.[11] nonetheless recent evidence have made this belief contraversial[6] some studies reported low incidence[8] contrary to others reporting higher incidence[4]. The objective of the research was to look into the causes and likelihood of thyroid cancer in people with toxic nodular goiter (TNG). The findings of the study revealed that 21.43% of patients diagnosed with TNG also had thyroid malignancies, which is consistent with previous researches[4]. However, the variation in the incidence rates among different studies may be attributed to variations in patient selection criteria, the underlying cause of hyperthyroidism, the type of surgical procedure used, or the degree of histopathological investigation[6]. Therefore, further studies are necessary to validate these outcomes and identify the underlying factors that influence the prevalence of thyroid cancer among TNG patients.[8]

Interestingly, the researchers discovered that among TNG patients, male sexual orientation was a significant indicator of malignancy. This is in line with previous studies.[4] This may be due to hormonal or genetic differences that predispose males to a higher risk of thyroid cancer. To validate this association and examine the underlying mechanisms, more study is required.

The research discovered that, in contrast, the probability of malignancy in TNG patients did not significantly change if there was a relative with a history of thyroid cancer.[4] This indicates that routine thyroid cancer screening may not be necessary for TNG individuals who have a familial history of thyroid carcinoma. However, this finding requires validation in larger studies with a more diverse population.

Intriguing results from the study also indicate that, in contrast to previous studies, the dimension of the domi-

nant nodule on the thyroid is not a major risk factor for malignancy.[6] This finding could be explained by the fact that all of the research participants had hyperfunctioning lumps, which could display distinct characteristics and behaviors from non-functioning nodules. Overall, the study results highlight the need for further research to better understand the risk factors associated with thyroid malignancy in TNG patients.

Moreover, the study found that thyroid Multi-Nodular goiter (TMNG) poses a substantial risk for thyroid malignancy, consistent with prior studies that reported a higher prevalence of tumors in TMNG individuals as opposed to those with single thyroid nodules (STN). This discrepancy could be attributed to the differing pathology between TMNG, which is characterized by multiple nodules, and STN, which is characterized by a single dominant nodule. Nonetheless, we urge the researchers to investigate the underlying mechanisms of this association and determine the optimal management strategy for patients diagnosed with TMNG.

In conclusion, this study sheds important light on the prevalence of thyroid cancer and the risk factors linked with it in people who have thyroid nodular goiter (TNG), emphasizing the significance of early detection and proper management of TNG patients. According to the study's findings, TMNG and male gender may both offer sizable risks for thyroid cancer among TNG patients, whereas familial history of thyroid cancer might not. To confirm these results and determine the best method for treating patients with TNG, additional study is required.

Conclusion

Previous research has indicated that having an overactive thyroid gland does not offer any protection against cancer. The current study has also shown that around 20% of cases of thyroid nodules with the potential to produce excessive hormones exhibit malignancy. Furthermore, the study has found that males and those with toxic multiple nodular goiter (TMNG) are significant risk factors for developing malignancy in patients with thyroid gland nodules with the potential to produce excessive hormones (TNG). Early detection of malignancy is critical for patients with a solitary nodule with the potential to produce excessive hormones (SNG) and risk factors for cancer. For these patients, surgery should be investigated as soon as possible to identify the disease at its earliest stage, which may influence the need for additional procedures if thyroid cancer is found. Therefore, based on the study's findings, we recommend that patients with dominant nodules, even with toxicity, undergo preoperative fine-needle aspiration (FNA) to exclude the possibility of malignancy. This would allow for early detection and the timing of surgery.

Conflict of Interest: None

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