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Thyroid Carcinoma in Multinodular Goiter Systemic Review in Al-Imamin Al-Kadhimian Teaching Hospital

Dr. Kadhim Hatif Kamil [1]

Professor Dr. Haider Abdulhussein Ahmed [2]

Abstract

Background: Multinodular goiter (MNG) is a frequent thyroid disease which involves multiple thyroid nodules. Although MNG is usually benign, there is a high chance of malignancy, so its assessment and management is essential.

Aim: To determine the incidence of thyroid cancer in patients with MNG who undergo thyroidectomy at Al-Imamin Al-Kadhimian Teaching Hospital.

Methods: This observational study reviewed 100 cases of MNG that had thyroidectomy. Malignancy was diagnosed by histopathological tests. Demographic variables such as age, sex, body mass index (BMI), duration of goiter, nodule size, place of residence, family history, lymphadenopathy (LAP), dysphagia, shortness of breath (SOB), diabetes mellitus (DM) and hypertension (HT) were also evaluated.

Results: In a study of 100 cases, 19% were found to be malignant. Thyroid malignancies were of papillary (47.4%), follicular (36.8%), medullary (5.3%) and anaplastic (10.5%) types. The incidence of malignancy increased with age, with none in the age group below 40 years, 47.4% in 40-59 years and 52.6% in 60 years and older. Women were more likely to have a malignancy (57.9%). BMI was not found to be a risk factor. The mean duration and nodule size of malignant goiters were greater (5.21 years and 27.53 mm, respectively) than benign goiters. Rural patients (47.4%), those with family history (31.6%), LAP (26.3%), dysphagia (15.8%) and SOB (52.6%) had a higher risk of malignancy.

Conclusion: The findings of the study show a high risk of malignancy in MNG in elderly patients, women, and those with larger size and long duration of nodules. Risk factors include rural area, positive family history, LAP, dysphagia, and SOB. The results highlight the importance of careful work-up and management of MNG to facilitate early diagnosis and treatment of thyroid cancers.

Keywords: Multinodular goiter, thyroid malignancy, thyroidectomy, papillary carcinoma, follicular carcinoma.

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[1] M.B.CH.B.

[2] M.B.Ch.B, F.I.C.M.S., C.A.B.S, Consultant Surgeon

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1. Introduction

Thyroid hormones are essential for metabolism and endocrine function, and are produced by the thyroid gland. Multinodular goitre (MNG) is a relatively frequent thyroid condition, consisting of enlargement of the thyroid gland and the presence of multiple nodules. The incidence varies around the world, primarily based on iodine intake and environmental conditions, and is about 5% in iodine-replete regions and higher in iodine-deficient regions (1). While MNG is most commonly benign, the risk of co-existing thyroid cancer is of concern.

Thyroid cancer is rarer than benign thyroid disease but is increasing, likely due to better diagnostic techniques (2). The link between MNG and thyroid cancer is contentious, as some reports indicate that the risk of thyroid cancer in MNG may be similar to risk of thyroid cancer in solitary thyroid nodule (3). It is difficult to diagnose as multiple nodules can obscure malignancy. Thus, diagnosis relies on clinical examination, ultrasound characteristics, nodule growth and fine-needle aspiration biopsy (4).

Ultrasound features such as microcalcifications, hypoechogenicity, irregular margins and increased vascularity are suspicious features requiring further evaluation. Recent studies have shown that the incidence of malig-nancy in MNG ranges from 7-17% and primarily presents as papillary thyroid carcinoma (5). Risk factors for thyroid malignancy include exposure to radiation during childhood, a family history of thyroid disease, iodine deficiency and genetic mutations (6,7).

The current research seeks to report the prevalence of thyroid malignancy in patients who undergo thyroidectomy for multinodular goitre at Al-Imamin Al-Kadhimian Teaching Hospital, categorize the types of thyroid cancer and discuss the risk factors.

2. Patients and Methods:

This is an observational study that involved a prospective study of patients who had thyroidectomy for multinodular goiter at Al-Imamin Al-Kadhimian Teaching Hospital, Baghdad, Iraq. Data was collected between April 2023 and April 2024. All patients who had been diagnosed with multinodular goiter and were treated by thyroidectomy during this period were included in the study, and the sample size was determined by the number of thyroidectomy cases that met the inclusion criteria during this period.

The inclusion criteria for patients in the study were those who had a diagnosis of multinodular goiter and who were treated with thyroidectomy during the study period. Those with a history of thyroid surgery or radioactive iodine therapy, or those with a solitary thyroid nodule and other non-multinodular thyroid diseases were excluded to maintain study sample homogeneity.

The study adhered to ethical guidelines. All subjects were verbally consented before the study. Confidentiality of patient data was ensured by denoting the records with code numbers, and the data were kept in password-protected computers for the purpose of research. We obtained administrative approval from the Council of Arabic Board for Health Specialization and the Department of Surgery of Al-Imamin Al-Kadhimian Teaching Hospital.

Variables were recorded using a standardised form from patient medical records. Demographic data included age, sex and body mass index. History included previous thyroid disease, radiation exposure, family history of cancer and other medical history. Clinical presentation included symptoms like neck swelling, swallowing difficulty and disease duration. Laboratory tests, including thyroid function tests, and ultrasonographic and fine-needle aspiration cytology results were reviewed. Postoperative

histopathological analysis of specimens provided definitive results such as presence and type of malignancy, tumor size and staging.

Surgery was carried out under general anesthesia via a cervical collar incision. The surgical approach involved dissection with recognition and preservation of recurrent laryngeal nerves and parathyroid glands, total thyroidectomy, and thorough cauterization. Care was taken to monitor for post-operative complications including hypocalcemia, bleeding and airway obstruction, including serial calcium levels and voice assessment.

Data analysis was done by Statistical Package for Social Sciences (SPSS) version 26. Data were presented as means and standard deviations or frequencies and percentages. The independent t-test and chi-square test were used for comparison of continuous and categorical variables, respectively. A p-value of ≤ 0.05 was considered statistically significant.

3. Results

In this study, we examined 100 cases of multinodular goiter, 19 cases (19%) were found to be malignant and 81 cases (81%) were benign (Figure 3-1). The cases diagnosed as malignant were detected on histopathological analysis after a thyroidectomy.

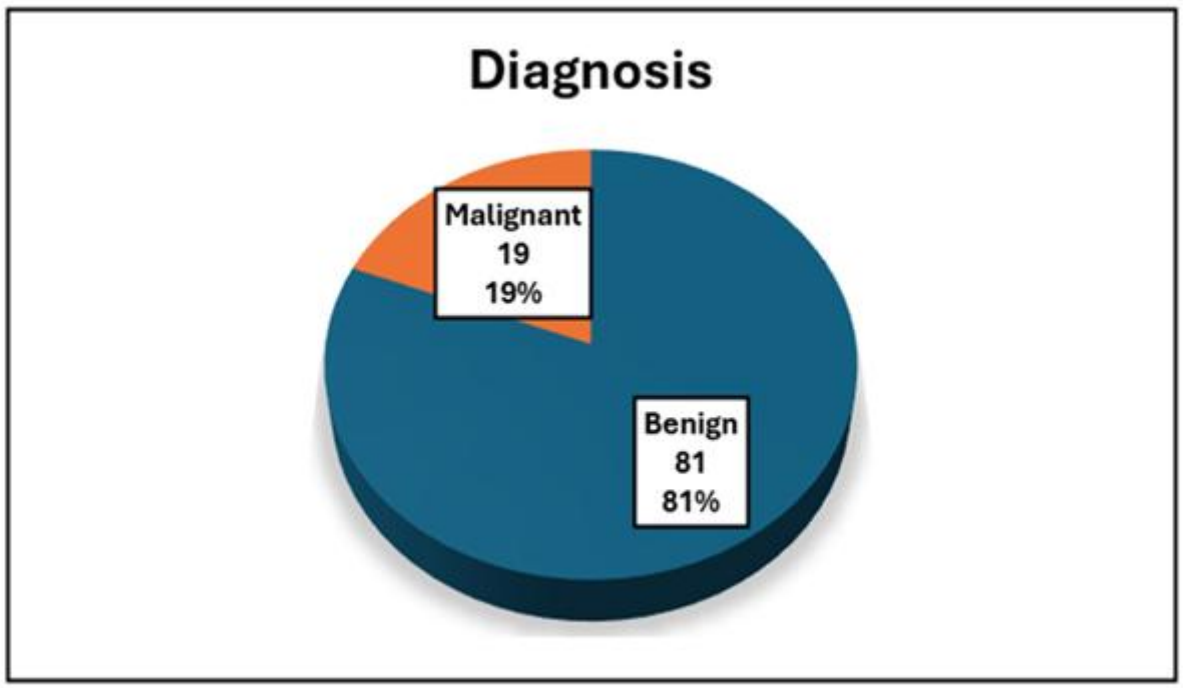


Figure 3.1: Distribution of cases according to diagnosis.

The types of thyroid malignancies are as following (Figure 3-2): Papillary carcinoma was present in 9 cases (47.4%). Seven cases (36.8%) were follicular carcinoma. Medullary carcinoma was found in 1 case (5.3%). Anaplastic carcinoma was present in 2 cases (10.5%).

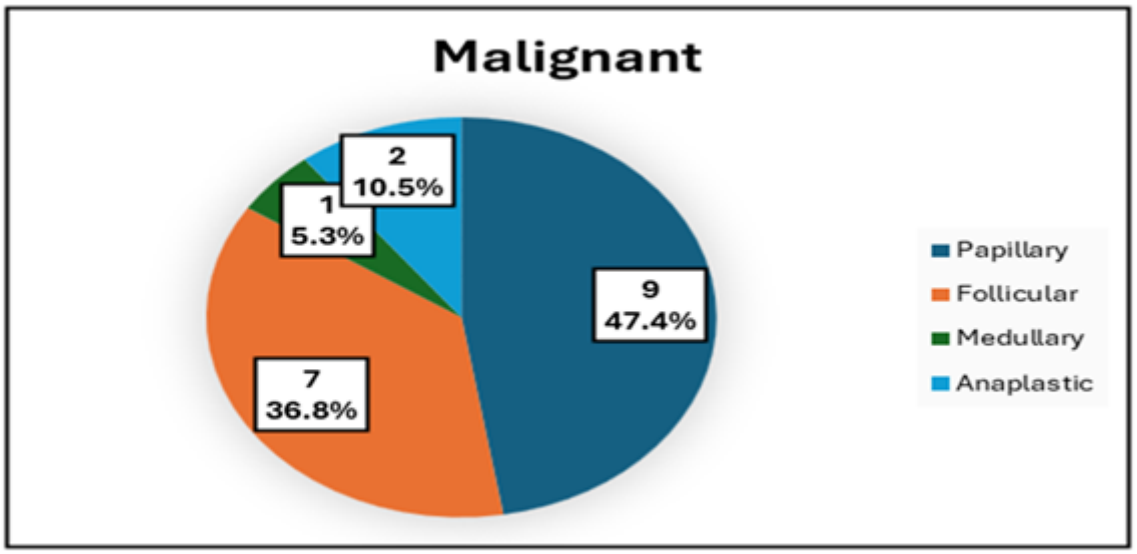


Figure 3.2: Type of malignancy found in the study.

Malignancy was significantly associated with age and sex. No malignant cases were found in patients below 40 years of age, while the proportion of malignancy increased considerably with age (47.4% in the 40-59 years age group and 52.6% in the ≥60 years age group, with all the latter group being malignant; $p < 0.001$). The proportion of females was higher in both malignant and benign cases, but a higher proportion of males was noted in malignant cases in comparison to benign cases, and the difference was statistically significant ($p = 0.001$). On the other hand, there was no significant difference in body mass index (BMI) between malignant and benign groups, suggesting that BMI is not related to malignancy ($p = 0.377$).

Table 3.1: Distribution of study sample according to demographics.

Variables		Malignant	Benign	P value
		No. (%)	No. (%)	
Age	<40	0 (0)	33 (40.7)	**<0.001**
	40-59	9 (47.4)	48 (59.3)	
	≥60	10 (52.6)	0 (0)	
Sex	Male	8 (42.1)	9 (11.1)	**0.001**
	Female	11 (57.9)	72 (88.9)	
BMI	18.5-24.9	8 (42.1)	35 (43.2)	0.377
	25-29.9	7 (36.8)	38 (46.9)	
	≥30	4 (21.1)	8 (9.9)	

Goiters' Duration: The mean duration of goiter in malignant cases was 5.21 years (SD: 2.78 years) while in benign cases, it was 3.93 years (SD: 2.08 years) (Figure 3-3). This implies that malignant goiters might have a longer duration than benign goiters

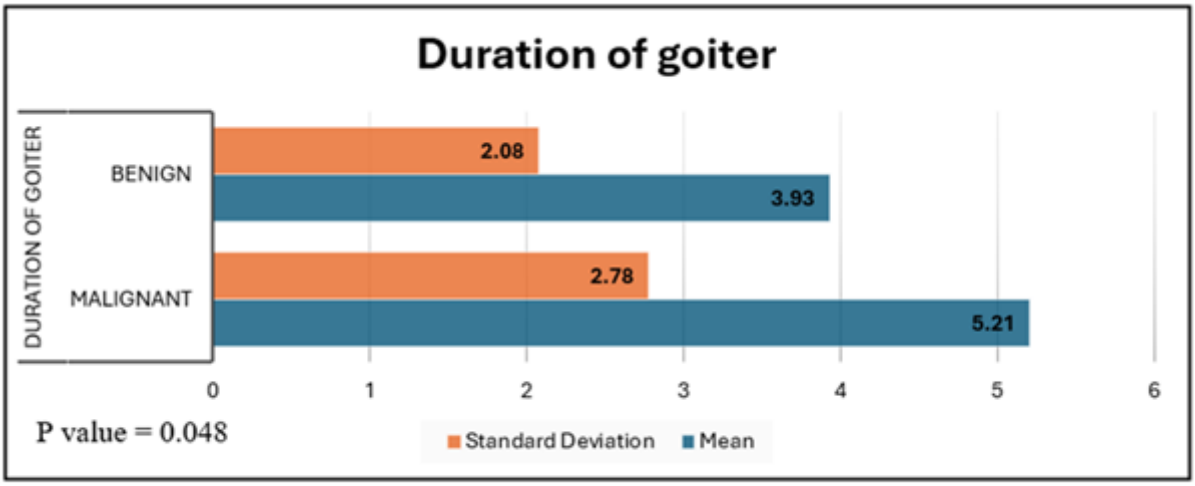


Figure 3.3: Duration of goiter in years.

The mean size of the nodule in malignant cases was significantly greater 27.53 mm (standard deviation 4.19 mm) than in benign cases 9.3 mm (standard deviation 2.42 mm) (Figure 4). This was found to be statistically significant (p = <0.001).

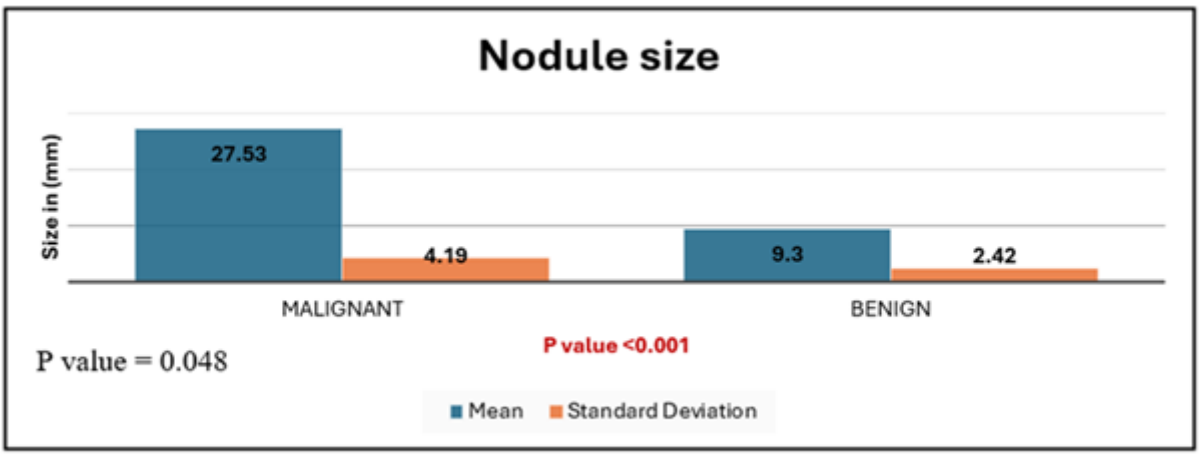


Figure 3.4: Nodule size according to study groups.

Demographic information was also significantly associated with malignancy of multinodular goiter. Rural residence was significantly associated with malignancy (p = 0.002). The presence of family history of thyroid disease was also significantly associated with malignancy (p = 0.001). The presence of lymphadenopathy, dysphagia and shortness of breath were all significantly associated with malignant cases, with lymphadenopathy and shortness of breath being highly significant (p < 0.001) and dysphagia also significant (p = 0.017). However, other medical conditions such as diabetes and hypertension were not significantly associated with malignancy (p = 0.087 and p = 0.774, respectively).

Table 3.2: Distribution of risk factors of thyroid cancer.

Variables		Malignant	Benign	P value
		No. (%)	No. (%)	
Residency	Urban	10 (52.6)	69 (85.2)	**0.002**
	Rural	9 (47.4)	12 (14.8)	
Family history	Yes	6 (31.6)	5 (6.2)	**0.001**
	No	13 (68.4)	76 (93.8)	
LAP	Yes	5 (26.3)	2 (2.5)	**<0.001**
	No	14 (73.7)	79 (97.5)	
Dysphagia	Yes	3 (15.8)	2 (2.5)	**0.017**
	No	16 (84.2)	79 (97.5)	
SOB	Yes	10 (52.6)	7 (8.6)	**<0.001**
	No	9 (47.4)	74 (91.4)	
Diabetes	Yes	6 (31.6)	12 (14.8)	0.087
	No	13 (68.4)	69 (85.2)	
Hypertension	Yes	5 (26.3)	24 (29.6)	0.774
	No	14 (73.7)	57 (70.4)	

4. Discussion

Our study finds a significant incidence of cancer in multinodular goiter. of the 100 patients, 19% were found to be malignant on histopathological analysis after thyroidectomy, compared to 81% benign. This incidence is consistent with other studies which report that although multinodular goiters are generally benign, they do have a high incidence of malignancy, and require close scrutiny.

Papillary carcinoma was the most common type of malignant pathology among the cases, accounting for 47.4% of the cases. This was followed by follicular carcinoma (36.8%), medullary carcinoma (5.3%) and anaplastic carcinoma (10.5%). The results reflect the nature of the malignant cases in multinodular goiters, which are mostly differentiated thyroid cancers (papillary and follicular) as is the case in the world.

A high incidence of differentiated thyroid carcinoma was reported in the study of Ghadhban et al(8) in patients with multinodular goiter. They found that 40.8% of patients suffered from colloid goiter, 17.5% from micro-papillary carcinoma and 37.5% from follicular adenoma.

There was a strong association between age and malignancy. There were no patients under 40 who had malignant goiters. In contrast, the incidence of malignancy was much higher in older patients with 47.4% of patients in the age range of 40-59 years and 52.6% of those aged 60 years or older being diagnosed with malignant goiters. This finding of an increased risk of malignancy with age in patients with multinodular goiters suggests cautious management of older patients.

Luo et al(9) examined the risk factors for malignancy in multinodular goiter. They found that an increased age was associated with an increased likelihood of thyroid cancer

Females (57.9%) were more likely to have a malignant goiter than males (42.1%) (significant). But the incidence of benign goiters was higher in females (88.9%), meaning that although there is a greater incidence of multinodular goiters in females, there's a significant chance for these to be malignant. This variation in thyroid cancer incidence between males and females is also evident in the literature on thyroid disease, where there is a female predominance for benign and malignant thyroid disease.

Likewise, Khan et al(10) calculated the incidence of thyroid carcinoma in patients with multinodular

goiter. They found that the incidence of thyroid carcinoma was significantly greater in women with a female to male ratio of 4:1. They concluded that although multinodular goiters are more prevalent in females

There was no significant correlation with BMI. There was no significant difference in the occurrence of malignant vs benign cases across BMI classes, indicating that BMI is not a strong predictor of malignancy in patients with multinodular goiters. Our results are consistent with some reports with conflicting findings on the association between BMI and thyroid cancer risk.

Gąsior-Perczak et al's study(11) examined the effect of BMI on clinical evolution, response to therapy and clinical outcome in patients with differentiated thyroid cancer (DTC). They found that BMI is not significantly associated with more aggressive clinicopathological features of thyroid cancer. High BMI was not associated with advanced stage of cancer, extrathyroidal extension or lymph node metastases. This again supports that BMI has no significant effect on the risk of malignancy of thyroid cancer

Goiters with malignancy had a longer duration (5.21 years) compared to benign goiters (3.93 years), suggesting that the duration of goiter is a risk factor for malignancy. Moreover, the size of the malignant nodules (27.53 mm) was larger than that of benign nodules (9.3 mm), suggesting nodule size is a risk factor for malignancy. These findings are important in clinical practice, and should guide clinicians to more closely investigate the possibility of malignancy in patients with longer durations and larger-sized nodules.

Luo et al(9) suggested that the size of nodules and duration of goiter are the risk factors of malignant multinodular goiter. They emphasised the importance of nodule size and duration of goiter as predictors of malignancy, as we found.

Gąsior-Perczak et al(11) identified the size of the nodule was a key determinant of the risk of malignancy in patients with thyroid nodules. There was a greater risk of malignancy in larger nodules, and this applied to all thyroid diseases.

There was a significant increase in the rate of malignancy in patients living in rural (47.4%) vs urban (52.6%). This could be due to disparities in health care, environmental or genetic factors. A family history of thyroid disease was also significantly associated with high malignancy rate (31.6%), highlighting the importance of genetic predisposition in thyroid cancer.

Huston-Paterson et al(12) reported differences in the outcomes of thyroid cancer in rural and urban areas. This study assessed that rural patients were more likely to be diagnosed with distant disease and had a greater disease specific mortality. It's important to note that the rural patients in this study were mostly from Al-Tagi district, so there may be an environmental component that could lead to a significant increase in the rate of thyroid malignancy.

Lymphadenopathy (LAP) and symptoms of dysphagia and shortness of breath (SOB) were associated with malignant. LAP was significantly more prevalent in cases with malignancy (26.3% in malignant cases vs 2.5% in benign cases), and suggests that the presence of LAP should alert to the possibility of cancer. Likewise, SOB was significantly associated with malignancy, likely as a result of the larger size of the nodule leading to compressive symptoms.

There was no significant association between diabetes mellitus and hypertension and malignant cases. This indicates that these factors, while significant comorbidities, do not predict malignancy in patients with multinodular goiter.

5. Conclusions

Our findings demonstrate the complex interactions of various factors contributing to the risk of malignancy in patients with multinodular goiter, including age, gender, size of nodule, duration of goiter, rural living, family history, lymphadenopathy and compressive symptoms. This study underscores the value of a risk-based, multifaceted approach to evaluate and detect thyroid cancer at an early stage. The

increased incidence of malignancy in rural patients, especially in Al-Tagi district, leads to the speculation of common environmental risk factors that may play a role in this elevated risk, which needs to be explored further.

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