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Madonna L. Aujero, MD John Michael P. Tagsa, MD Gleno Lon Q. Llamera, Jr., MD

Department of Otolaryngology-Head and Neck Surgery Southern Philippines Medical Center

Correspondence: Dr. Gleno Lon Q. Llamera, Jr.
Department of Otolaryngology- Head and Neck Surgery
Southern Philippines Medical Center
JP Laurel Ave., Bajada, Davao City 8000

Phone: +63 922 889 8114 Email: dmc_ent@yahoo.com

Philippines

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Association of Clinicodemographic Factors and Tissue Biopsy Results Among Patients with Thyroid Nodules at the Southern Philippines Medical Center

ABSTRACT

Objective: To compare selected clinicodemographic factors of patients with thyroid nodules who underwent thyroid surgeries with their tissue biopsy results and determine any association between clinicodemographic factors and tissue biopsy results.

Methods:

Design:Retrospective review of recordsSetting:Tertiary Government Training HospitalParticipants:251 patients with thyroid nodules

Results: Of 251 patients with thyroid nodules, the majority (218; 86.9%) were females while 33 (13.1%) were males. The average age in years was 41.5 ± 13.3 The same population also had malignant outcomes at 79.3%. Most of the patients did not have family history of thyroid malignancy (54%) and had no palpable cervical lymph nodes at presentation (75.9%). Furthermore, there was no distant metastasis at presentation for both lungs (97.7%) and bones (98.9%). There were no significant differences in tissue biopsy results when correlated with age (df=249; t=-.144; p = .886), duration of goiter (df=249; t=-.829; p = .408), and distant metastasis at presentation for lungs (Z=-5.977; p = .052) and bones (Z=-.457; p = .648). Significant differences were only evident for clinicodemographic factors such as sex (Z=-2.570; p = .010), family history (Z=-2.239; p = .020), palpable cervical lymph nodes at presentation (Z=-5.977; p = .000), and the following comorbidities: pulmonary tuberculosis (Z=-2.388; p = .017) and bronchial asthma (Z=-2.148; p = .032) and smoking history (Z=-3.455; p=.001). Furthermore, having no palpable cervical lymph nodes at presentation were associated with malignant tissue biopsy results (B=3.616; p=.001). Patients without palpable cervical lymph nodes at presentation were 37.204 times [OR=37.204] more likely to have benign biopsy results [95% CI: 4.705 – 294.168].

Conclusion: There are greater odds of having benign biopsy results for patients without palpable cervical lymph nodes at presentation.

Keywords: thyroid nodules; tissue biopsy; thyroid neoplasm; fine-needle aspiration biopsy

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In the general population, the prevalence of goiter is estimated to be 15.8% worldwide, 4.7% in the Americas and 28.3% in Africa. Iodine deficiency disorder (IDD) is the most common cause of goiter, affecting 30% of the world's population or more than 150,000 million people.² In the Philippines, the national prevalence of goiters was 3.7% in 1987 and 6.7% in 2019.3

To the best of our knowledge, based on a search of HERDIN Plus, the ASEAN Citation Index (ACI), Western Pacific Region Index Medicus (WPRIM), MEDLINE (PubMed; PubMed Central) using the keywords "thyroid nodules," "tissue biopsy," "thyroid neoplasm," "risk factors," and "fine-needle aspiration biopsy," there is a scarcity of research on the relationship between thyroid tissue biopsy results and such clinicodemographic factors as sex, age, duration of goiter, family history of goiter, palpable cervical lymph nodes at presentation, distant metastasis at presentation, associated comorbidities, and smoking history in the Philippines.

This study aims to compare the clinicodemographic profiles of patients with thyroid nodules who underwent thyroid surgeries with their tissue biopsy results and determine any association between selected clinicodemographic factors and tissue biopsy results.

METHODS

With Department of Health XI Cluster Ethics Review Committee (DOH XI CERC) approval (CERC Protocol Number P21060701), this retrospective series reviewed records of patients with thyroid nodules who underwent thyroid surgery at Southern Philippines Medical Center, Department of ENT-HNS from January 2017 (the year the Department of Pathology of SPMC adapted Bethesda Scoring) to December 2019.

Considered for inclusion were all patients 19 years old and above with thyroid nodules who underwent thyroid surgeries between January 2017 and December 2019. Those with no tissue biopsy results and incomplete medical records (which include the demographic profile, history of illness, physical examination, and metastatic workup for known malignant cases) were excluded.

Complete enumeration of records of patients meeting inclusion and exclusion criteria was made, grouping the cases according to tissue biopsy outcomes as benign or malignant. Subsequently, selected clinicodemographic factors were rated according to the outcomes. The independent variables included in this study were sex, age, duration of goiter, family history of goiter, palpable cervical lymph nodes at presentation, distant metastasis in the bones and lungs, associated comorbidities (i.e., hypertension, diabetes mellitus, pulmonary tuberculosis, bronchial asthma, food and drug allergies, hyper/hypothyroidism, and other malignancies), and smoking history. The dependent variable was the tissue biopsy result.

All data were encoded using Microsoft Excel version 16.66.1 2016 (Microsoft Corp., Redmond, WA, USA) and were transferred to Statistical Package for Social Sciences (SPSS) version 21 software (IBM Corp., Armonk NY, USA) for data treatment. All statistical treatments were administered below a .05% level of significance. Categorical data were presented in frequencies and percentages, while mean and standard deviation were used for interval/continuous data. Data were analyzed with independent samples, a t-test for the comparison of parametric data, and a Mann-Whitney test for the comparison of non-parametric data. The study measured the difference in each selected clinicodemographic factor versus clinical outcomes: benign and malignant. Data were analyzed with logistic regression analysis to determine the factors associated with the clinical outcome of biopsy results.

RESULTS

A total of 251 patients with thyroid nodules who were operated on at Southern Philippines Medical Center during the study period, met inclusion and exclusion criteria. Table 1 shows the clinicodemographic profile of the patients using frequencies and percentages for categorical data and means and standard deviations for interval data. Most of the patients were females (86.9%) and had an average age of 41.5 \pm 13.3 years old. The average duration of the goiter was 104.4 ± 100 months.

Furthermore, most of the patients did not have family histories (63.7%), had no palpable cervical lymph nodes at presentation (90.8%), and no distant metastasis at presentation in the lungs (99.2%), and bones (99.2%). Most of the patients did not have hypertension (86.1%), had no diabetes mellitus (96%), no pulmonary tuberculosis (98.8%), no bronchial asthma (98%), no food and drug allergies (96%), no hypo/ hyperthyroidism (96%), nor other malignancies (99.6%), and no smoking histories (92%).

Of 251 biopsy results, 164 (65.3%) were benign while 87 (34.7%) were malignant. Table 2 shows the comparison of the clinicodemographic factors and benign and malignant biopsy results. The results were treated with independent sample t-tests for parametric data and Mann-Whitney tests for non-parametric data to determine whether there were significant differences in clinicodemographic profiles between biopsy results. Tested at a .05 level of significance, the results for age (df=249; t=-.144; p=.886), duration of goiter in months (df=249; t=-.829; p=.408), distant metastasis at presentation (lungs) (Z=-5.977; p=.052), distant metastasis at presentation (bones) (Z=-.457; p=648), hypertension (Z=-1.478; p=.139), diabetes mellitus (Z=-.315; p=.752), food and drug allergies (Z=-.315; p=.752), and other malignancies (Z=-1.373; p=.170), all favored accepting the null hypotheses. Thus, there were no significant differences between benign and malignant results and these clinicodemographic factors.

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Table 1. Clinicodemographic Profile of the Patients with Thyroid Nodules

		f	%	
Sex	Male	33	13.1	
	Female	218	86.9	
Age (X±SD)		41.5 ± 13.3		
Duration of goiter (in months) ($\bar{X}\pm SD$)		104.4 ± 100		
Family history	No	160	63.7	
	Yes	91	36.3	
Palpable cervical lymph nodes at presentation	No	228	90.8	
	Yes	23	9.2	
Distant metastasis at presentation (lungs)	No	249	99.2	
	Yes	2	0.8	
Distant metastasis at presentation (bones)	No	249	99.2	
	Yes	2	0.8	
Associated Comorbidities		0.0		
Hypertension	No	216	86.1	
	Yes	35	13.9	
Diabetes mellitus	No	241	96.0	
	Yes	10	4.0	
PTB	No	248	98.8	
	Yes	3	1.2	
Bronchial asthma	No	246	98.0	
	Yes	5	2.0	
Food and drug allergies	No	241	96.0	
	Yes	10	4.0	
Hypo/hyperthyroidism	No	241	96.0	
	Yes	10	4.0	
Other malignancies	No	250	99.6	
	Yes	1	0.4	
Smoking history	No	231	92.0	
	Yes	20	8.0	

Note: n = 251

However, there were significant differences in biopsy results for sex (Z=-2.570; p=.010), family history (Z=-2.239; p=.020), palpable cervical lymph nodes at presentation (Z=-5.977; p=.000), presence of pulmonary tuberculosis (Z=-2.388; p=.017), bronchial asthma (Z=-2.148; p=.032), and smoking history (Z=-3.455; p=.001).

Table 3 shows the factors associated with biopsy results treated with logistic regression analysis. Having a model-fit logistic regression (p=.000), the results revealed the following: sex (B=.305; p=.552), age (B=-.012; p=.394), duration of goiter (B=.001; p=.405), family history (B=.542; p=.091), distant metastasis at presentation (bones) (B=18.796; p=.999), distant metastasis at presentation (lungs) (B=-3.482; p=.079), hypertension (B=.347; p=.480), diabetes mellitus (B=-.857; p=.456), pulmonary tuberculosis (B=20.718; p=.999), bronchial asthma (B=2.187; p=.058), food and drug allergies (B=-.257; p=.752), hyper/hypothyroidism (B=-.021; p=.979), and other malignancies (B=17.416; p=1.000) favored accepting the null hypotheses. Hence, these abovementioned factors are not associated with biopsy results.

However, having no palpable cervical lymph nodes at presentation (B=3.616; p=.001) was associated with biopsy results. Patients without palpable cervical lymph nodes at presentation were 37.204 times (OR=37.204) more likely to have benign biopsy results (95% CI: 4.705 – 294.168).

DISCUSSION

The purpose of this study was to determine which among selected clinicodemographic factors were associated with benign biopsy results in patients with thyroid nodules. Our analysis provided interesting information that suggest significant differences in various clinicodemographic factors when grouped according to biopsy results. Most of the patients were females, which reflects findings of previous studies like those of Mulder⁴ and Russel⁵ where thyroid diseases occur more commonly in women than men, in part because of the autoimmune nature of many thyroid disorders.

The average age of patients with thyroid nodules in our study was 41.5 years old, which is lower than the findings of Girardi⁶ that thyroid problems were common among the elderly with peak occurrence between 51 to 60 years old. However, these results are consistent with statements of the American Society of Clinical Oncology (ASCO) that thyroid cancer can occur at any age, but about two-thirds of all cases are found between the ages of 20 and 55.7 Our average duration of goiter was 104.4 months (8.6 years), much shorter than the findings of Medeiros-Neto⁸ that the average duration of goiter was 17 years.

Most of the patients with thyroid nodules in our study did not have family histories. This neither denies nor confirms the findings of Bomeli *et al.*⁹ that thyroid diseases are often hereditary. The more family members that have thyroid disease, the greater the likelihood that there is a hereditary root and the higher the chances the patient will experience a thyroid problem. At the very least, our findings reflect the American Cancer Society's information that several inherited conditions have been linked to different types of cancer, but most people who develop thyroid cancer do not have an inherited condition or a family history of the disease.¹⁰

Most of our patients had no palpable cervical lymph nodes at presentation. Our results are also consistent with the review of Bazemore and Smucker that the prevalence of malignancy is quite low among primary care patients with lymphadenopathy.¹¹

Most of our patients had no distant metastasis at presentation for both lungs and bones, which is congruent with the findings of Song *et al.*,¹² that distant metastasis is rare and diagnosed in only 1% to 4% of patients, and Nixon *et al.*,¹³ that lung lesions identified on postoperative chest computed tomography imaging are uncommon among patients with malignant thyroid nodules.

Table 2. Comparison of Clinicodemographic Factors and Biopsy Results

		Tissue Biopsy Resu			lts		
Clinicodemographic Profile		Benign (n = 164) f %		Malignant (n = 87)		t, Z	р
Sex	Male Female	15 149	9.1 90.9	18 69	20.7 79.3	-2.570	.010
Age (X±SD)		41.2 ± 12.5		41.7 ± 14.9		144	.886
Duration of goiter (in months) $((\overline{X}\pm SD))$		100.6 ± 96.9		111.6 ± 105.9		829	.408
Family history	No Yes	113 51	68.9 31.1	47 40	54.0 46.0	-2.329	.020
Palpable cervical lymph nodes at presentation	No Yes	162 2	98.8 1.2	66 21	75.9 24.1	-5.977	.000
Distant metastasis at presentation (lungs)	No Yes	164 0	100.0 0	85 2	97.7 2.3	-1.946	.052
Distant metastasis at presentation (bones)	No Yes	163 1	99.4 0.6	86 1	98.9 1.1	457	.648
Associated Comorbidities							
Hypertension	No Yes	145 19	88.4 11.6	71 16	81.6 18.4	-1.478	.139
Diabetes mellitus	No Yes	157 7	95.7 4.3	88 3	96.6 3.4	315	.752
PTB	No Yes	164 1	100.0 0.6	86 4	95.4 4.6	-2.388	.017
Bronchial asthma	No Yes	163 1	99.4 0.6	83 4	95.4 4.6	-2.148	.032
Food and drug allergies	No Yes	157 7	95.7 4.3	84 3	96.6 3.4	315	.752
Hypo/hyperthyroidism	No Yes	158 6	96.3 3.7	83 4	95.4 4.6	361	.718
Other malignancies	No Yes	164 0	0	86 1	98.9 1.1	-1.373	.170
Smoking history	No Yes	158 6	96.3 3.7	73 14	83.9 16.1	-3.455	.001

Note: Significant at p < .05

Table 3. Factors Associated with Biopsy Results

Clinico de mographic Profiles	В	95% CI	OR	р
Sex (male)	.305	.496 - 3.705	1.356	.552
Age	012	.962 - 1.015	.988	.394
Duration of goiter	.001	.998 - 1.005	1.001	.405
Family history (no)	.542	.917 – 3.227	1.720	.091
Palpable cervical lymph nodes at	3.616	4.705 – 294.168	37.204	.001
presentation (none)				
Distant metastasis at presentation (lungs)	18.761	0	1.4x108	.999
Distant metastasis at presentation (bones)	-3.482	.670 - 1578.225	.031	.079
Hypertension	.347	.540 – 3.705	1.415	.480
Diabetes mellitus	857	.045 – 4.033	.424	.456
Pulmonary tuberculosis	20.718	0	9.9x108	.999
Bronchial asthma	2.187	.927 – 85.672	.112	.058
Food & drug allergies	257	.157 – 3.819	1.293	.752
Hyper/hypothyroidism	021	.205 – 4.672	1.021	.979
Other malignancies	17.416	0	-	1.000
Smoking history	1.115	.775 – 11.994	.321	.111

Note: Significant at p < .05

Most of our patients with thyroid nodules did not have hypertension. Our results differ from those of Malyszko et al., that reported hypertension as one of the most common comorbidities in patients with malignancy, particularly in the elderly, 14 and Shimizu et al., 15 that thyrotoxic problems cause hypertension usually through an increase in systolic blood pressure by decreasing systemic vascular resistance, increasing heart rate, and raising cardiac output.

Most of our patients did not have diabetes mellitus, unlike the findings of Zhang et al.16 that nearly a quarter of the adult population with documented thyroid problems have diabetes. Luo et al. found that malignant thyroid nodules are not associated with diabetes.¹⁷ Pulmonary tuberculosis was not prevalent either in our study, although Falagas et al. found that pulmonary tuberculosis is a risk factor for the development of a malignant tumor.18

Family history significantly varies between benign and malignant thyroid nodules. In the study of Kust et al., 19 the difference between

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benign and malignant thyroid diagnosis was found to be statistically significant. Family history plays a significant role in the development of thyroid cancer, and having first-degree relatives with not only medullary but also papillary thyroid cancer strongly predicts the risk of developing malignant thyroid disease. In contrast, benign thyroid disorders in family history do not lead to the development of thyroid cancer.

Palpable cervical lymph nodes at presentation significantly vary between benign and malignant thyroid nodules. The majority of thyroid nodules are asymptomatic and benign and most of the time, do not have palpable cervical lymph nodes at presentation. However, the majority of malignant thyroid nodules have palpable cervical lymph nodes at presentation. These are consonant with the findings of Mohseni *et al.*, that cervical lymph nodes are involved more often than the other lymphatic regions. Generally, it is due to infections, but most of the supraclavicular lymphadenopathies are associated with malignancy. Having no palpable cervical lymph nodes at presentation was associated with benign biopsy results.

Smoking histories significantly varied between benign and malignant thyroid nodules. Most of the patients with malignant thyroid nodules had smoking histories. Current smokers had a 36% lower risk of thyroid cancer than nonsmokers; the risk was lower, especially if they were less than 65 years old. Past smokers and never smokers had a

similar risk. The amount or duration of smoking did not affect the risk.²²

Our study has many limitations. As a review of records, our data was secondary and may not reflect the actual histories, physical exam findings, and laboratory results of the actual patients. Inter-recorder variability and issues of recall and interpretation must therefore be considered, and inaccuracies in our data allowed for. Our sampling of patients with thyroid nodules who underwent surgery reflects a sampling bias that discounts patients with thyroid nodules who did not undergo surgery, thereby preventing the generalizability of our findings to all patients with thyroid nodules. Our sample size itself was based on convenience – with preset temporal parameters rather than a sample size calculation. Our study focused on selected factors associated with biopsy results among patients with thyroid nodules admitted to a tertiary hospital. We recommend other risk factors such as exposure to radiation, insulin dependence, visceral obesity, and nodule size be considered in future studies. Finally, we recommend expanding the sample size through multicenter research by collaborating with other major hospitals in the Davao Region.

In conclusion, our study suggests that there are greater odds of having benign biopsy results for patients without palpable cervical lymph nodes at presentation.

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