



Risk factors associated with malignancy of thyroid nodules in adult women. A single-center observational study.

* Corresponding Author:

Vanessa Salazar Choez.

e-mail: mdsalazarch@gmail.com

Telephone: (04) 500 0950.

Address: km. 2.5 road to Samborondón. Faculty of Medical Sciences, UEES University.

Guayaquil, Ecuador

Conflict of interest: The authors declare no conflict of interest.

Received: May 24, 2023.

Accepted: July 10, 2023.

Posted: August 18, 2023

Editor: Dr. Lorena Sandoya.


Cite:

Salazar V, Valdés Y, Franco K. Risk factors associated with malignancy of thyroid nodules in adult patients. A single-center observational study. *Revista Oncología (Ecuador)* 2023;33(2):121-130.

ISSN: 2661-6653

DOI: <https://doi.org/10.33821/706>

SOCIEDAD DE LUCHA CONTRA EL CÁNCER-ECUADOR.

 Copyright 2023, Vanessa Salazar Choez, Yolanda Valdés Rodríguez, Kristell Franco Loor. This article is distributed under the [Creative Commons Attribution License BY-NC-SA 4.0](https://creativecommons.org/licenses/by-nc-sa/4.0/) terms, which permits use and redistribution, acknowledging the original author and source.

Vanessa Salazar Choez ^{1*}, Yolanda Valdes Rodriguez ^{PhD} ², Kristell Franco Loor ¹,

1. General Medicine Service, Complementary Health Network, Guayaquil, Ecuador.
2. Faculty of Health Sciences "Dr. Enrique Ortega Moreira," Espíritu Santo University of Specialties, Samborondón, Ecuador.

Abstract

Introduction: Although most thyroid nodules are benign, asymptomatic, and stable in the clinical history of a female patient, in ultrasound, cytological, and histopathological studies, it has been possible to obtain the subclinical characterization of lesions suggestive of malignancy. The current study aimed to evaluate the risk factors associated with the malignancy of thyroid nodules in adult patients.

Methodology: A descriptive, cross-sectional, retrospective, correlational study with a mixed approach was carried out in the endocrinology service of the Teodoro Maldonado Carbo Hospital between January and June 2019. The study population consisted of all patients diagnosed with thyroid nodules. The Bethesda system was used for reporting.

Results: There were 132 patients with thyroid nodules aged between 45 and 64 (57.6%). In a premenopausal state (52%), there was one pregnancy (12%), glucose ≥ 100 mg/dL (34%), BMI between 25.0 and 29.9 kg/m² (49%) and a family history of thyroid cancer (35%). Thirty patients had TSH values >4.00 μ UI/mL (23%). In the Bethesda system, 22 cases (17%) were category IV, 17 cases (13%) were category V, and 11 cases (8%) were category VI.

Conclusions: The most frequent thyroid cytological lesion found was a benign neoplasm. However, malignant lesions and indeterminate follicular lesions presented a prevalence of 8%. A significant association was found between malignant cytology nodules with elevated TSH levels and a family history of thyroid cancer.

Keywords:

DeCS: Thyroid nodule, Thyrotropin, Cytology, Pathology, Thyroid neoplasms

DOI: 10.33821/706

Introduction

At present and with technological advances in medicine, all the necessary tools are available to know and identify risk factors, diagnosis, and even modern treatments to treat certain diseases, including different pathophysiological alterations of the thyroid gland, with thyroid nodules being the most prevalent in the general population.

The detection of a tendency toward malignancy of a thyroid nodule has been increased due to the implementation of imaging techniques. The importance of recognizing the prevalence and incidence of thyroid nodules lies in stipulating a level of clinical significance [1]. The prevalence of thyroid nodules in the general population is 4-7% and 50-70%, as detected by palpation and ultrasound studies, respectively [2]. The vast majority of thyroid nodules present in patients are benign, and only 4-6.5% are malignant [3]. On the other hand, it has been estimated that at 60 years and older, approximately 50% of the general population will have at least one thyroid nodule, which indicates that it is essential to recognize it early [4].

The development of thyroid cancer is related to a history of suffering from thyroid nodules, which can start with benign histology and, due to the influence of different factors, can become malignant. In this way, the incidence and prevalence of thyroid nodules in the population of adult women is high [5], for which the identification, study, and analysis are remarkable to make a timely and accurate diagnosis to grant patients a prioritization according to the severity of the clinical picture.

This study assessed the association between risk factors such as age, number of pregnancies, TSH value, fasting glucose, BMI, menopausal status, family history of thyroid cancer, and age. Bethesda system, with malignancy of thyroid nodules in adult women.

Materials and methods

Study design

The methodology used is a descriptive cross-sectional retrospective correlational study with a mixed approach.

Study area

The study was conducted in the endocrinology service of the Teodoro Maldonado Carbo Specialty Hospital of the IESS (Ecuadorian Institute of Social Security). We worked with adult women who attended the external consultation of the endocrinology service from January to June 2019.

Universe and Sample

The universe was made up of all the cases registered in the institution. The sample size was no probabilistic and discretionary, including all incident cases in the study period.

Participants

Cases of patients aged ≥ 18 years with thyroid nodules diagnosed by ultrasound, TSH test, and cytology were included. Cases of patients undergoing thyroid drug therapy, previous thyroid surgery, and other types of cancer were excluded.

variables

The variables were age, number of pregnancies, TSH value, fasting glucose, body mass index (BMI), menopausal status, family history of thyroid cancer, and Bethesda system.

Procedure, techniques, and instruments.

The data collection of the study sample was obtained through the AS400 system (MIS) from the review of medical records, explicitly using the information of the required variables such as age, family pathological history of thyroid cancer, number of pregnancies, BMI, and PAAF report. Coded diagnoses: E04.1 and C73 were used for the case investigation.

Avoidance of bias

To avoid study bias, the registration of medical records in a Microsoft Excel database was guaranteed, as well as a double checklist to include only the cases from the endocrinology outpatient service that met the eligibility criteria

Statistical analysis

The collected data were recorded in a form designed exclusively for this purpose. They were processed with SPSS 22.0 statistical software, where the frequency, distribution, and association statistical methods were applied.

Results

Participants

A total of 132 patients were included in the study.

Demographic characterization

The most prevalent age in women with thyroid nodules was the group between 45 and 64 years (57.6%), followed by periods between 18 and 44 years (22.7%), while patients ≥ 65 years presented in 19.7%. (Figure 1).

Regarding the variable "number of pregnancies," the group with the highest frequency was ≥ 2 deliveries with 81.1%, while 12.1% had only one pregnancy and 6.8% had no pregnancy. Regarding fasting glucose levels, a value < 100 mg/dl occurred in 65.9% of patients. In contrast to glucose values ≥ 100 mg/dl with 34.1%. Regarding the menopausal state, 51.5% of women were in the premenopausal period, and 48.5% were in the postmenopausal state. Based on the family pathological history of cancer, 34.8% of the patients had family members with a history of cancer.

Regarding the TSH value, it was determined that the range between 0.40 and 4.00 $\mu\text{UI/mL}$ was the most frequent, representing 74.2%, followed by high values > 4.00 $\mu\text{UI/mL}$ with 22.7%.

(Figure 2). Similarly, the BMI range between 25.0 and 29.9, corresponding to overweight, stood out in the patients studied, with 49.2% and type I obesity (18.2%) (Figure 3).

Figure 1. Age of patients with thyroid nodules.

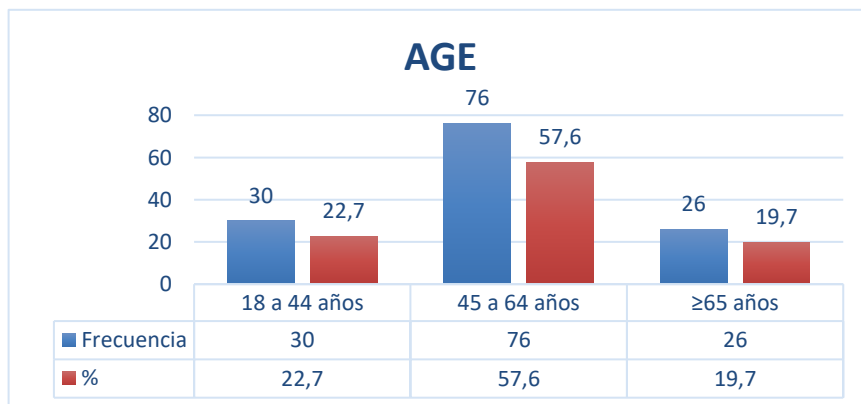


Figure 2. Risk factors associated with malignancy of thyroid nodules.

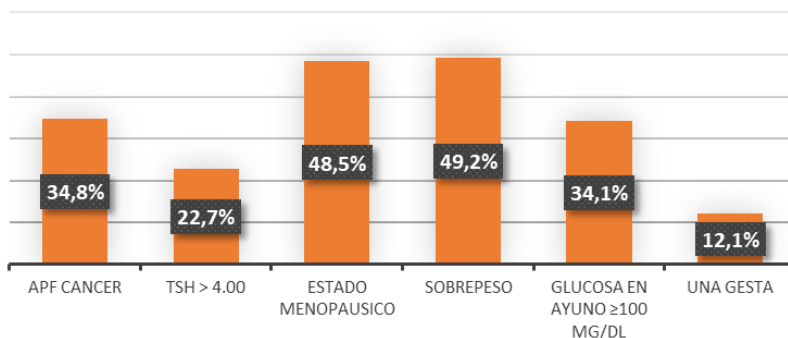
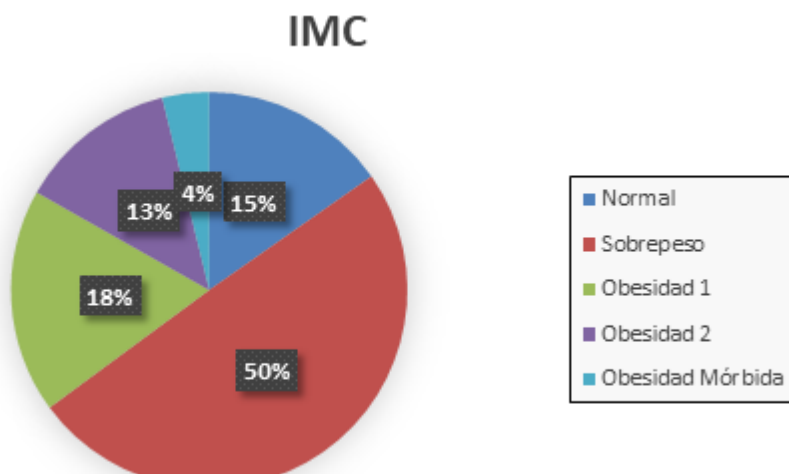
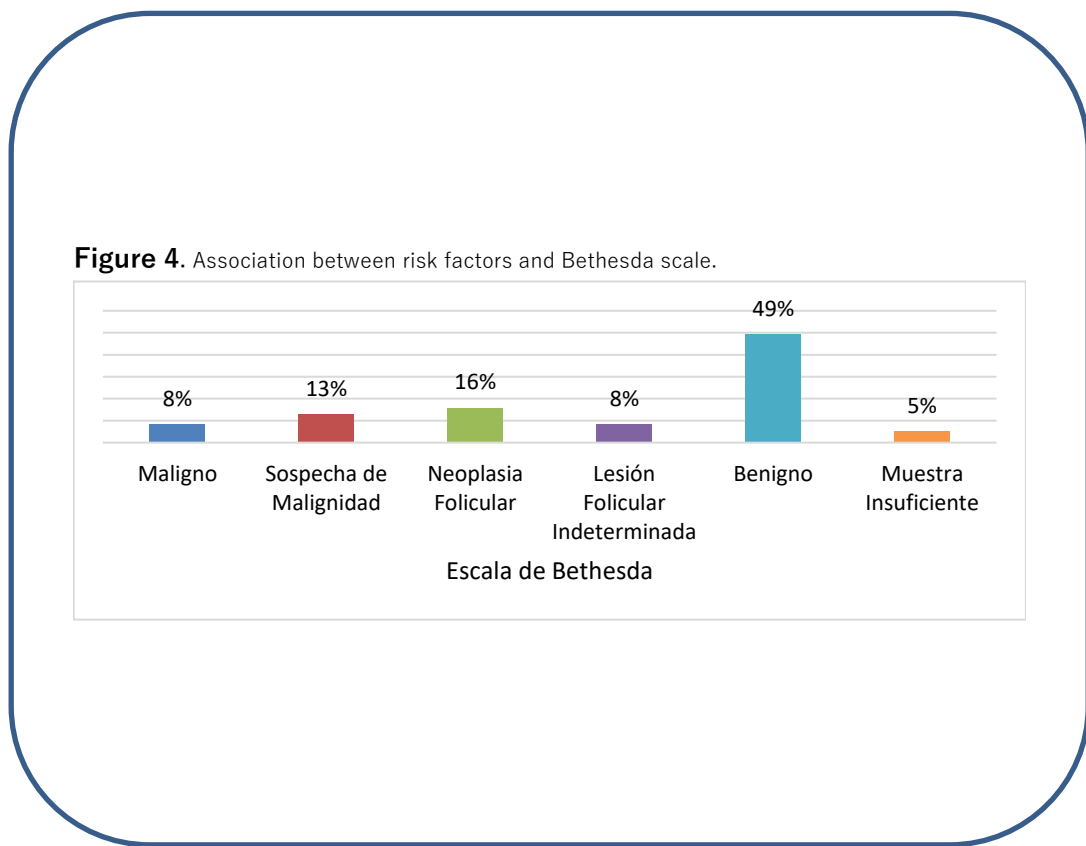


Figure 3. Body mass index in the study group.





Cytological characterization

Cytological lesions, according to the Bethesda scale, showed that 64 Bethesda II cases (48.5%) presented benign lesions, 22 Bethesda IV cases (16.7%) where follicular neoplasms were found, and 11 Bethesda III cases (8.3%) indicating indeterminate follicular lesions, the same as the Bethesda VI cases (8.3%) with malignant lesions (Figure 4).

The association between the family pathological history of thyroid cancer and the Bethesda grade had moderate grade of association ($r= 0.449$) with a favorable significance of $P < 0.001$, which would determine that both variables are related.

Finally, an analysis of the relationship between the Bethesda grade and the TSH value was performed, where a positive association of 0.298 was observed with a statistically significant $P = 0.001$ (Table 1).

Table 1 . Correlation coefficient between the variables.

No.=132		APF Cancer	Bethesda	TSH
APF Cancer	R.		0.449 **	
	Next (bilateral)		<0.001	
Bethesda	R.	0.449 **		0.298*
	Next (bilateral)	<0.001		0.001

* Two-tailed correlation. Pearson's correlation coefficient.

Discussion

The importance of histopathological lesions in thyroid nodules lies in the tendency toward malignancy that could develop. Advances and the greater availability of sensitive and easily accessible images for diagnosis have contributed to the increase in incidence, including ultrasonography and FNA [6]. According to clinical guidelines on managing thyroid nodules, different factors have been described for later use as determinants of malignancy risk, ranging from clinical, laboratory, ultrasound, and histopathological characteristics [7].

Similarly, Bernet and Chindris state that between 7 and 15% of asymptomatic thyroid nodules have a risk of malignancy. Additionally, they describe that after an initial diagnosis, the execution of a clinical follow-up, based on the use of ultrasound images, would be indicated in the majority of thyroid nodules, in contrast to the fact that surgical intervention would be relevant in those with clinical risk factors, presence of local symptoms and malignant cytology [8].

The presentation of thyroid nodules in females has stood out compared to that in males, and the influence of hormonal factors has been described as a possible cause. Based on the above, the effect exerted by estrogens on the growth of thyroid cancer cells would be carried out through a pathway mediated by alpha and beta estrogen receptors [9].

On the other hand, Fiore and Vitti noted in a clinical review that the serum TSH value and risk of papillary thyroid cancer in nodular thyroid diseases with elevated TSH values were associated with an increase and an advanced stage of thyroid cancer. Patients in settings III and IV showed higher mean TSH values between 4.9 ± 1.5 mIU/l compared to patients in stages I and II, who led to a mean value of 2.1 ± 1.5 mIU/l [10].

Regarding the Bethesda scale, category III includes indeterminate follicular lesions that represent a 10 to 30% risk of thyroid cancer. Thus, Teixeira et al. demonstrated in a retrospective study with 197 patients who underwent FNA and obtained a result of indeterminate follicular lesions that the incidence of thyroid cancer was 16.2%. With the data shown by the study, the performance of surgical interventions in patients within Bethesda category III was considered to make a histopathological diagnosis and rule out malignancy [11].

Nandedkar et al. studied a total of 606 patients with thyroid lesions, where the main objective was to correlate the results obtained by FNA with the thyroid histopathology of the patients. Based on the Bethesda scale, 501 patients presented benign lesions, 5 were indeterminate follicular lesions, 55 were diagnosed with follicular neoplasms, seven patients had lesions suspected of malignancy, and 12 cases were malignant. A cytohistopathological correlation was performed in 148 benign and 18 malignant lesions, and the sensitivity of FNA was 85.7%, the specificity was 98.6%, and the diagnostic accuracy was 97.7% [12].

Conclusions

The most frequent thyroid cytological lesion found was a benign neoplasm. However, malignant lesions and indeterminate follicular lesions presented a prevalence of 8%. A significant association was found between malignant cytology nodules with elevated TSH levels and a family history of thyroid cancer.

Abbreviations

BMI: Body mass index.

PAAF: fine needle aspiration puncture.

TSH: thyroid stimulating hormone.

Administrative information

Additional Files

None declared by the authors.

Acknowledgments

We thank the directors and staff of the Teodoro Maldonado Carbo Hospital of the Ecuadorian Institute of Social Security, where the study was conducted.

Author contributions

Vanessa Salazar: Conceptualization, formal analysis, research, project management, resources, software.

Yolanda Valdes Rodriguez: Conceptualization, methodology, validation, visualization.

Kristell Franco: Conceptualization, methodology, validation, visualization, writing review, and editing.

All the authors have read and approved the final version of the manuscript.

Financing

The researchers funded the study. The authors did not receive any financial recognition for this research work.

Availability of data and materials

Data are available upon request to the corresponding author. No other materials are reported.

Statements

Ethics committee approval

No studies of databases or medical records were needed.

Consent for publication

It is not required when images, resonances, or tomographic studies of specific patients are not published.

Conflicts of interest

The authors declare that they have no conflicts of competence or interest.

References

1. Araque KA, Gubbi S, Klubo-Gwiezdzinska J. Updates on the Management of Thyroid Cancer. *Horm Metab Res.* 2020 Aug;52(8):562-577. doi: [10.1055/a-1089-7870](https://doi.org/10.1055/a-1089-7870). Epub 2020 Feb 10. PMID: 32040962; PMCID: [PMC7415555](https://pubmed.ncbi.nlm.nih.gov/PMC7415555/).
2. Moon JH, Hyun MK, Lee JY, Shim JI, Kim TH, Choi HS, Ahn HY, Kim KW, Park DJ, Park YJ, Yi KH. Prevalence of thyroid nodules and their associated clinical parameters: a large-scale, multicenter-based health checkup study. *Korean J Intern Med.* 2018 Jul;33(4):753-762. doi: [10.3904/kjim.2015.273](https://doi.org/10.3904/kjim.2015.273). Epub 2017 Jul 7. PMID: 28859466; PMCID: [PMC6030422](https://pubmed.ncbi.nlm.nih.gov/PMC6030422/).
3. Tala H, Díaz RE, Domínguez Ruiz-Tagle JM, Sapunar Zenteno J, Pineda P, Arroyo Albala P, Barberán M, Cabané P, Cruz Olivos F, Gac E P, Glasinovic Pizarro A, González HE, Grob F, Hidalgo Valle MS, Jaimovich R, Lanás A, Liberman C, Lobo Guíñez M, Madrid A. Estudio y manejo de nódulos tiroideos por médicos no especialistas. Consenso SOCHED [Study and management of thyroid nodes by non specialist physicians: SOCHED consensus]. *Rev Med Chil.* 2017 Aug;145(8):1028-1037. Spanish. doi: [10.4067/s0034-98872017000801028](https://doi.org/10.4067/s0034-98872017000801028). PMID: 29189861.
4. Paschou SA, Vryonidou A, Goulis DG. Thyroid nodules: A guide to assessment, treatment and follow-up. *Maturitas.* 2017 Feb;96:1-9. doi: [10.1016/j.maturitas.2016.11.002](https://doi.org/10.1016/j.maturitas.2016.11.002). Epub 2016 Nov 9. PMID: 28041586.
5. Gharib H, Papini E, Garber JR, Duick DS, Harrell RM, Hegedüs L, Paschke R, Valcavi R, Vitti P; AACE/ACE/AME Task Force on Thyroid Nodules. American Association of Clinical Endocrinologists, American College of Endocrinology, and Associazione Medici Endocrinologi Medical Guidelines for Clinical Practice for the diagnosis and management of thyroid nodules--2016 UPDATE. *Endocr Pract.* 2016 May;22(5):622-39. doi: [10.4158/EP161208.GL](https://doi.org/10.4158/EP161208.GL). PMID: 27167915.
6. Kitahara CM, Sosa JA. The changing incidence of thyroid cancer. *Nat Rev Endocrinol.* 2016 Nov;12(11):646-653. doi: [10.1038/nrendo.2016.110](https://doi.org/10.1038/nrendo.2016.110). Epub 2016 Jul 15. PMID: 27418023.
7. Gilmartin A, Ryan M. Incidence of Thyroid Cancer among Patients with Thyroid Nodules. *Ir Med J.* 2018 Sep 10;111(8):802. PMID: 30547520.
8. Bernet VJ, Chindris AM. Update on the Evaluation of Thyroid Nodules. *J Nucl Med.* 2021 Jul;62(Suppl 2):13S-19S. doi: [10.2967/jnumed.120.246025](https://doi.org/10.2967/jnumed.120.246025). PMID: 34230067.
9. Caini S, Gibelli B, Palli D, Saieva C, Ruscica M, Gandini S. Menstrual and reproductive history and use of exogenous sex hormones and risk of thyroid cancer among women: a meta-analysis of prospective studies. *Cancer Causes Control.* 2015 Apr;26(4):511-8. doi: [10.1007/s10552-015-0546-z](https://doi.org/10.1007/s10552-015-0546-z). Epub 2015 Mar 10. PMID: 25754110.
10. Fiore E, Vitti P. Serum TSH and risk of papillary thyroid cancer in nodular thyroid disease. *J Clin Endocrinol Metab.* 2012 Apr;97(4):1134-45. doi: [10.1210/jc.2011-2735](https://doi.org/10.1210/jc.2011-2735). Epub 2012 Jan 25. PMID: 22278420.
11. Teixeira GV, Chikota H, Teixeira T, Manfro G, Pai SI, Tufano RP. Incidence of malignancy in thyroid nodules determined to be follicular lesions of undetermined significance on fine-needle aspiration. *World J Surg.* 2012 Jan;36(1):69-74. doi: [10.1007/s00268-011-1336-8](https://doi.org/10.1007/s00268-011-1336-8). PMID: 22057754.
12. Nandedkar SS, Dixit M, Malukani K, Varma AV, Gambhir S. Evaluation of Thyroid Lesions by Fine-needle Aspiration Cytology According to Bethesda System and its Histopathological Correlation. *Int J Appl Basic Med Res.* 2018 Apr-Jun;8(2):76-82. doi: [10.4103/ijabmr.IJABMR_169_17](https://doi.org/10.4103/ijabmr.IJABMR_169_17). PMID: 29744318; PMCID: [PMC5932928](https://pubmed.ncbi.nlm.nih.gov/PMC5932928/).

Editor's note

The Journal Oncología (Ecuador) remains neutral regarding jurisdictional claims on published maps and institutional affiliations.