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DIFERENCIAS SEGÚN EL SEXO EN LA PREVALENCIA DEL CARCINOMA PAPILAR DE TIROIDES, LOS FACTORES DE RIESGO Y LAS CARACTERÍSTICAS POR IMAGEN: UNA REVISIÓN NARRATIVA DE LA LITERATURA

SEX DIFFERENCES IN THE PREVALENCE OF PAPILLARY THYROID CARCINOMA, RISK FACTORS, AND IMAGING FEATURES: A NARRATIVE LITERATURE REVIEW

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Resumen

Antecedentes: El carcinoma papilar de tiroides (CPT) es el tipo más frecuente de cáncer de tiroides diferenciado; su incidencia notificada ha aumentado en las últimas décadas, en gran medida debido a una mayor detección de microcarcinomas mediante ecografía de alta resolución y punción-aspiración con aguja fina (PAAF). Objetivo: Sintetizar la evidencia sobre la prevalencia del CPT y su distribución por sexo y edad, así como identificar los factores de riesgo asociados y las características de imagen relevantes para el diagnóstico y la estratificación del riesgo. Métodos: Se realizó una revisión narrativa de la literatura en PubMed, Scopus, SciELO y Web of Science, abarcando publicaciones en inglés y español entre 1990 y 2025. Se elaboró una matriz de evidencia que incluyó 28 documentos en la síntesis final. Resultados: Los estudios seleccionados mostraron una mayor incidencia de CPT en mujeres, un predominio en la edad adulta y un aumento en la detección incidental de tumores pequeños. Los factores de riesgo más consistentes fueron la exposición a radiación ionizante, los antecedentes familiares y las alteraciones moleculares. En cuanto a las pruebas de imagen, la marcada hipoecogenicidad, las microcalcificaciones, los márgenes irregulares y la morfología "más alto que ancho" fueron los hallazgos ecográficos más sugestivos de malignidad. La evaluación de los ganglios linfáticos cervicales y su integración con los sistemas TI-RADS/EU-TIRADS y Bethesda refuerzan la estratificación diagnóstica. Conclusión: Esta revisión permitió vincular con mayor claridad la epidemiología, los factores de riesgo y los hallazgos de imagen del CPT. La integración de la ecografía estandarizada y la citología sigue siendo esencial para equilibrar la detección oportuna con la reducción del sobrediagnóstico.

Palabras claves: cáncer de tiroides diferenciado; microcarcinoma; ecografía tiroidea; aspiración con aguja fina; diagnóstico por imagen; metástasis ganglionar.

Abstract

Background: Papillary thyroid carcinoma (PTC) is the most common type of differentiated thyroid cancer, and its reported incidence has increased in recent decades, largely because of greater detection of microcarcinomas using high-resolution ultrasonography and fine-needle aspiration (FNA). Objective: To synthesize the evidence on the prevalence of PTC and its distribution by sex and age, and to identify associated risk factors and imaging features relevant to diagnosis and risk stratification. Methods: A narrative literature review was conducted in PubMed, Scopus, SciELO, and Web of Science for publications from 1990 through 2025 in English and Spanish.

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An evidence matrix was developed comprising 28 documents included in the final synthesis. Results: The selected studies showed a higher incidence of PTC among women, predominance in adulthood, and increasing incidental detection of small tumors. The most consistent risk factors were ionizing radiation exposure, family history, and molecular alterations. On imaging, marked hypoechogenicity, microcalcifications, irregular margins, and a taller-than-wide shape were the ultrasonographic findings most suggestive of malignancy. Cervical lymph node assessment and integration with TI-RADS/EU-TIRADS and the Bethesda System strengthen diagnostic stratification. Conclusion: This review more clearly linked the epidemiology, risk factors, and imaging findings of PTC. The integration of standardized ultrasonography and cytology remains essential to balance timely detection with the reduction of overdiagnosis.

Keywords: differentiated thyroid cancer; microcarcinoma; thyroid ultrasonography; fine-needle aspiration; diagnostic imaging; lymph node metastasis.

1. Introduction

Papillary thyroid carcinoma (PTC) is the most common malignant neoplasm of the thyroid gland and the predominant subtype of differentiated thyroid cancer (1,2). Although its overall prognosis is favorable, PTC exhibits substantial clinicopathological heterogeneity. Most patients have low-risk disease, whereas a subgroup develops local invasion, persistent or recurrent locoregional disease, and, less commonly, distant metastases (1,6-9). In recent decades, a sustained increase in the incidence of thyroid cancer, particularly PTC, has been reported. This trend is largely attributable to expanded access to high-resolution cervical ultrasonography and fine-needle aspiration (FNA), which has increased the incidental detection of microcarcinomas. Mortality, however, remains relatively low in most regions, intensifying the debate regarding overdiagnosis and overtreatment of very-low-risk tumors (14-17). From a diagnostic standpoint, ultrasonography is the first-line imaging modality for evaluating thyroid nodules and guiding decisions regarding FNA. Standardization through risk-stratification systems (e.g., ACR TI-RADS and EU-TIRADS), together with correlation with cytology using the Bethesda System, improves reproducibility, prioritizes FNA of nodules with a higher probability of malignancy, and reduces unnecessary procedures (3,11-13).

Synthesizing prevalence data and their distribution by sex and age provides key information for estimating the burden of PTC, guiding screening strategies and resource allocation, and interpreting the rise in reported cases in the context of overdiagnosis. Likewise,

integrating suspicious ultrasonographic findings with standardized reporting criteria and cytology can optimize timely diagnosis and risk stratification, particularly when cervical lymph node findings that may influence surgical planning are considered (5,11-13,26). In addition, identifying risk factors and prognostic variables (age, tumor size, extrathyroidal extension, and lymph node involvement) supports more individualized surveillance and management, with potential implications for recurrence and long-term outcomes (6-9,10).

The epidemiology of PTC shows a clear female predominance and a peak occurrence in adulthood (approximately 30-50 years), with geographic variation influenced by diagnostic practices and access to imaging technologies (14-16). At the biological level, molecular alterations involving BRAF and RAS have been described and contribute to PTC heterogeneity, with associations with distinct clinicopathological patterns (18). The best-established risk factors include exposure to ionizing radiation, particularly during childhood, as well as family history and certain predisposing syndromes. Other associations, such as thyroid autoimmunity or variations in iodine status, are heterogeneous across studies and should be interpreted in conjunction with the clinical context and ultrasonographic findings (19,25,28). On imaging, ultrasonography identifies suspicious features such as marked hypoechogenicity, microcalcifications, irregular margins, and a taller-than-wide shape; standardized reporting helps define thresholds for FNA and follow-up (11,12). Preoperative cervical lymph node assessment is also particularly relevant because of the frequency of lymphatic metastases and their association with a higher risk of recurrence, which may influence the extent of surgery and subsequent risk stratification (5,21).

However, important knowledge gaps remain because of methodological variability in prevalence estimates and the inconsistent correlation among imaging findings, histopathology, and clinical behavior in specific hospital settings, supporting the need for reviews that integrate the available evidence (3,5,14-17). Finally, although survival

in PTC is generally high, clinically meaningful recurrence has been reported in selected patients with very-low-risk disease. Accordingly, active surveillance has emerged as an alternative strategy aimed at reducing treatment-related morbidity without compromising oncologic outcomes (6-9,23,24). In this context, the objective of this review was to determine, based on the available literature, the prevalence of PTC and its differential distribution between women and men, and to synthesize the risk factors and imaging features relevant to timely diagnosis and risk stratification.

2. Methods

A narrative literature review was conducted. PubMed, Scopus, SciELO, and Web of Science were searched for publications in English and Spanish from 1990 through 2025. The search strategy combined terms related to "papillary thyroid carcinoma," "thyroid cancer," "prevalence," "risk factors," "ultrasound," "TI-RADS," "Bethesda," "fine-needle aspiration," and "lymph node metastasis" using the Boolean operators AND/OR. Priority was given to observational studies, pooled analyses, guidelines or consensus documents, and diagnostic classification systems that provided information on prevalence by sex and age, risk factors, imaging findings, the clinical utility of FNA, staging, and recurrence. General narrative reviews were retained as contextual support for the Discussion; however, the synthesis of results was structured around documents directly aligned with the objective of this review.

A total of 50 potentially relevant records were identified. Following review of titles, abstracts, and full texts, 28 documents were included in the final synthesis and organized into an evidence matrix according to document type, population or context, and main contribution. To maintain consistency with the final selection, references 1 and 2 were used solely as conceptual support for the Introduction, whereas references 3 through 30 comprised the analytical matrix (Table 1).

3. Results

The evidence from the 28 included documents clustered around four main domains (Table 1): population

epidemiology; risk factors and tumor biology; imaging and cytologic stratification; and prognosis, including recurrence and active surveillance. This structure provides a direct link between the statements made in the manuscript and the selected literature.

From an epidemiological perspective, global studies and trend analyses consistently showed a female predominance in PTC and a sustained increase in incidence, particularly driven by small tumors detected through ultrasonography and FNA. Likewise, the higher frequency among young and middle-aged adults supports a nonuniform distribution by sex and age and indicates that overdiagnosis accounts for a relevant proportion of the contemporary increase in reported cases (14-17).

With regard to risk factors, exposure to ionizing radiation, particularly at younger ages, family history, and molecular determinants were the most consistent findings in the evidence matrix. Genomic analyses of PTC demonstrated biological heterogeneity associated with alterations involving BRAF and RAS, while literature on tumor classification and recurrence helped contextualize the influence of tumor biology on clinical aggressiveness and recurrence (18-20,25,28,30). Additional associations were reported, including thyroid autoimmunity, population-level variation in iodine status, and coexistence with other developmental thyroid abnormalities; however, these findings were less consistent across studies and should be interpreted cautiously, with emphasis on their clinical, histopathological, and imaging correlation (19,26-29).

In diagnostic imaging, the selected evidence confirmed that high-resolution ultrasonography is the initial imaging modality for evaluating thyroid nodules. Features most strongly associated with suspicion of malignancy included marked hypoechogenicity, microcalcifications, irregular margins, a taller-than-wide shape, and selected signs of extrathyroidal extension. In addition, ACR TI-RADS and EU-TIRADS, together with the Bethesda System for cytology, provide a reproducible framework for determining indications for FNA and

follow-up (3,4,10-13). Cervical lymph node assessment was central to the evidence reviewed because ultrasonographic identification of suspicious lymph nodes influences staging and surgical planning. Cystic changes, microcalcifications, loss of the fatty hilum, a rounded morphology, and abnormal vascularity were repeatedly associated with metastasis, while staging documents and predictive models support their integration into the preoperative assessment (5,21,22). Finally, studies of recurrence and follow-up showed that extrathyroidal extension, lymph node involvement, and certain histopathological or molecular profiles are associated with a higher risk of persistent or recurrent disease. By contrast, in carefully selected patients with low-risk papillary thyroid microcarcinoma, active surveillance is a reasonable alternative when protocol-based ultrasonographic follow-up and appropriate institutional expertise are available (6-9,23,24,30).

4. Discussion

This evidence synthesis allowed clearer differentiation among findings derived from epidemiological studies, contributions from clinical research, and the role of diagnostic imaging. Across the included studies, the female predominance of PTC and its greater frequency in adulthood were consistently supported. However, interpretation of this pattern should account for the effect of differential access to ultrasonography and FNA on detection rates (14-17).

From an etiologic and pathophysiologic perspective, the strongest evidence continues to support exposure to ionizing radiation early in life and familial or molecular susceptibility. The incorporation of genomic data, particularly involving BRAF and RAS, not only explains part of the biological heterogeneity of PTC but also helps clarify why tumors with similar appearances may exhibit different clinical behaviors. Nevertheless, associations such as thyroid autoimmunity or variation in iodine exposure require critical interpretation because the magnitude of these associations is

not consistent across populations and study designs (18-20,25,28-30).

From a diagnostic perspective, this review confirms that the major strength of current practice does not lie in a single test, but rather in the structured integration of ultrasonography, cytology, and risk-stratification systems. Standardization with TI-RADS and EU-TIRADS improves reproducibility, while the Bethesda System provides a structured bridge between imaging suspicion and clinical management. This combination becomes even more valuable when cervical lymph node assessment is incorporated, because preoperative recognition of metastatic disease can modify staging, the extent of surgery, and subsequent follow-up (3-5,10-13,21,22).

The included studies suggest that recurrence is determined not only by tumor size but also by a constellation of clinical, nodal, histopathological, and biological variables. This finding supports more individualized surveillance strategies. At the same time, the feasibility of active surveillance for very-low-risk papillary microcarcinomas supports reconsideration of the traditional approach of immediate treatment in selected patients, favoring shared decision-making tailored to the patient's actual risk. In this regard, the principal clinical contribution of the present review is the integration of the epidemiology of overdiagnosis with concrete criteria for a more rational diagnostic and prognostic assessment (6-9,23,24).

Limitations

This review has limitations inherent to its narrative design. The evidence matrix included observational studies, pooled analyses, guidelines, and classification documents, resulting in methodological and conceptual heterogeneity across the included sources. In addition, the absence of formal quantitative data extraction precluded estimation of pooled measures of association or diagnostic performance. Although the group of analyzed documents was more clearly defined, the possibility of selection and publication bias remains.

5. Conclusions

PTC continues to show a clear female predominance and is more frequently diagnosed in adulthood, in a context in which overdiagnosis associated with ultrasonography and FNA accounts for part of the observed increase in incidence. The evidence matrix indicated that the most consistent risk factors are ionizing radiation exposure, familial predisposition, and molecular heterogeneity of the tumor. In diagnostic imaging, structured ultrasonography using TI-RADS/EU-TIRADS, complemented by Bethesda cytology and cervical lymph node assessment, provides the strongest diagnostic framework for guiding FNA, staging, and follow-up. The explicit organization of the included literature strengthens the traceability of the findings and improves the academic coherence of the manuscript.

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Conflicts of interest

The authors declare no conflicts of interest.

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Table 1. *Evidence matrix of the documents included in the narrative synthesis (n = 28).*

Reference	Type of evidence	Population / context	Main contribution
3	Meta-analysis	Thyroid nodules / ultrasound risk stratification	Evaluates the performance of ultrasound risk-stratification systems for papillary carcinoma.
4	Retrospective comparative study	PTC subtypes according to the 2022 WHO classification	Compares ultrasonographic findings among histological subtypes of papillary carcinoma.
5	Retrospective predictive model	PTC with cervical lymph node assessment	Proposes ultrasound-based risk stratification for cervical lymph node metastasis.
6	Retrospective study	Patients with PTC	Identifies prognostic factors for survival and recurrence.
7	Retrospective study	4,085 patients with PTC	Defines clinicopathological predictors of recurrence.
8	Retrospective study	Patients with PTC	Analyzes prognostic factors associated with recurrence.
9	Model development and validation	Patients with PTC	Develops a predictive model for recurrence.
10	ATA clinical guideline	Adults with thyroid nodules and differentiated thyroid cancer	Summarizes recommendations for diagnosis, staging, and management.
11	Consensus / white paper	Thyroid nodules in adults	Establishes ACR TI-RADS criteria for risk stratification and FNA.
12	European guideline	Thyroid nodules in adults	Presents EU-TIRADS for ultrasonographic stratification of malignancy risk.
13	Cytopathology consensus	Thyroid FNA cytology	Standardizes the Bethesda System and its clinical correlation.

14	Global epidemiological study	Global burden of thyroid cancer, 2022	Provides estimates of incidence and mortality.
15	Global epidemiological study	36 cancers in 185 countries	Places the relative burden of thyroid cancer in a global context.
16	Epidemiological analysis	Global trend	Highlights the impact of overdiagnosis on the increase in reported cases.
17	Global trend analysis	Global trend	Reinforces the relationship between rising incidence and overdiagnosis.
18	Integrated genomic characterization	Papillary thyroid carcinoma	Describes molecular alterations and tumor heterogeneity.
19	Review / 2022 WHO update	Thyroid tumors	Summarizes classification changes relevant to PTC.
20	Conceptual review of the 2022 WHO classification	Thyroid tumors	Describes new concepts in nomenclature and classification.
21	Staging update	Differentiated and anaplastic thyroid cancer	Explains the changes introduced in the 8th edition of the AJCC/TNM staging system.
22	Staging review	Thyroid cancer	Discusses the scope and limitations of the 8th edition of the AJCC/TNM staging system.
23	Clinical review	Low-risk papillary thyroid microcarcinoma	Summarizes evidence supporting active surveillance.
24	Clinical review	Papillary thyroid microcarcinoma	Supports active surveillance in selected cases.
25	Pooled analysis of 12 studies	Childhood exposure to external radiation	Confirms the association between radiation exposure and thyroid cancer.
26	Descriptive clinical article	PTC and thyroglossal duct cyst	Explores their coexistence and the clinical significance of this association.
27	Clinical review	Thyroid cancer	Provides general clinical context for the Discussion.
28	Systematic review with meta-analysis	Adults with PTC	Synthesizes associated risk factors.
29	Narrative review	Papillary thyroid carcinoma	Summarizes general clinical and imaging features.
30	Observational study	Patients with PTC and recurrence	Describes risk factors associated with recurrence.