

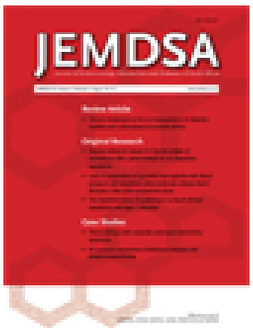
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Epidemiology spectrum and pathology of surgical thyroid resections in a metropolitan South African setting

Marquerit Van Der Merwe; Adam Botha; D van der Byl

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RESEARCH ARTICLE

Epidemiology, spectrum, and pathology of surgical thyroid resections in a metropolitan South African setting

M van der Merwe[1,2*], AR Botha[1,2] and D van der Byl[1]

[1]*Anatomical Pathology, National Health Laboratory Service, Chris Hani Baragwanath Academic Hospital, South Africa*
[2]*School of Pathology, Faculty of Health Sciences, University of the Witwatersrand, South Africa*
**Correspondence: marquerit.vdermerwe@nhls.ac.za*

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Background: Nodular thyroid disease is a common condition worldwide, and its prevalence is increasing. Surgical thyroid pathology includes non-neoplastic and neoplastic conditions. Patients may present with various thyroid pathologies. Given the multifactorial risk factors associated with these pathologies, such as age, gender, iodine deficiency, and prior radiation exposure, it is essential to understand the patient profile for each condition.
Objectives: This study aimed to describe the epidemiology, spectrum, and proportion of thyroid pathologies in patients who underwent thyroid resection in a metropolitan area in South Africa. It also examined the predisposing factors, types of surgeries performed, and their indications. Local and global statistics were compared to provide a broader understanding of the epidemiology, proportion, and spectrum of surgical thyroid pathology.
Methods: This study retrospectively examined 444 cases of thyroid resections that were performed at Chris Hani Baragwanath Academic Hospital over an eight-year period. Microscopic slide review was performed for 12% of the cases, which included at least one example of each diagnosis.
Results: A significant female predominance (91%) was noted. Thyroid pathologies affected a wide age range, with a mean of 48.26 years (standard deviation = 12.44). Amongst non-neoplastic conditions, nodular hyperplasia (48.87%) was the most common. The most common benign neoplasm was follicular adenoma (6.53%) and papillary thyroid carcinoma (29.05%) was the most prevalent malignancy. The study identified various papillary thyroid carcinoma (PTC) subtypes.
Conclusion: This study provides valuable insights into the epidemiology, spectrum, and pathology of non-neoplastic and neoplastic thyroid pathologies in a South African metropolitan setting.

Keywords: fine needle aspiration, neoplastic, non-neoplastic, thyroid nodule, thyroid resection

Introduction

Thyroid pathology is commonly encountered worldwide[1] and the prevalence of thyroid cancer is increasing.[2] This rise could be attributed to enhanced detection, followed by subsequent cytology, as well as multifactorial factors.[3,4] Due to its location, enlargement of the thyroid for any reason may be apparent early in the course of the disease. This location may also lead to compressive symptoms should the enlargement be significant. Therefore, various thyroid pathologies may present themselves to surgeons.[1]

Multiple diagnostic modalities are available, including molecular techniques; however, fine-needle aspiration (FNA) is the gold standard for initial diagnosis in solitary thyroid nodules.[5–7]

Thyroid disorders encompass non-neoplastic and neoplastic disorders. Non-neoplastic disorders include thyroiditis and hyperplastic disorders. Thyroiditis encompasses Hashimoto's thyroiditis (HT), de Quervain thyroiditis, and sub-acute lymphocytic thyroiditis.[8,9] Hyperplastic disorders include Graves' disease (GD) and nodular hyperplasia.[10]

Thyroid neoplasms are diagnosed based on the World Health Organization (WHO) classification of Endocrine and Neuroendocrine Tumours 5th edition, last updated in 2022, which includes benign and malignant neoplasms.[11] Benign neoplastic disorders include follicular thyroid adenomas (FTA) and Hürthle cell adenomas (HCA). The most commonly encountered malignant neoplasms include papillary thyroid carcinoma (PTC), follicular thyroid carcinoma (FTC), Hürthle cell carcinoma (HCC), medullary thyroid carcinoma (MTC), poorly differentiated thyroid carcinoma (PDTC), high-grade follicular cell-derived non-anaplastic thyroid carcinoma (HGFCDNATC), and anaplastic thyroid carcinoma (ATC). Figure 1 outlines the WHO's classification of follicular cell-derived neoplasms and thyroid C cell-derived carcinomas, which is of particular interest in this study.

Methods

Study design and setting

This study was a retrospective, observational, and non-interventional analysis that used archived histopathology reports from patients who underwent thyroid resections (lobectomy or thyroidectomy) between 1 January, 2014 and 31 December, 2021. Archived histopathology reports were analysed to utilise existing diagnostic information and to avoid further patient involvement. To ensure representation of all diagnoses, a minimum of 10% of cases (44 cases) were selected for microscopy slide review. To mitigate potential issues with slide retrieval due to misfiling, a larger list of 54 cases (10 additional cases) was compiled. Of these, slides from 53 cases were successfully retrieved, and all available slides were subsequently included in the review. The research was conducted at the Division of Anatomical Pathology, University of the Witwatersrand, and the National Health Laboratory Service

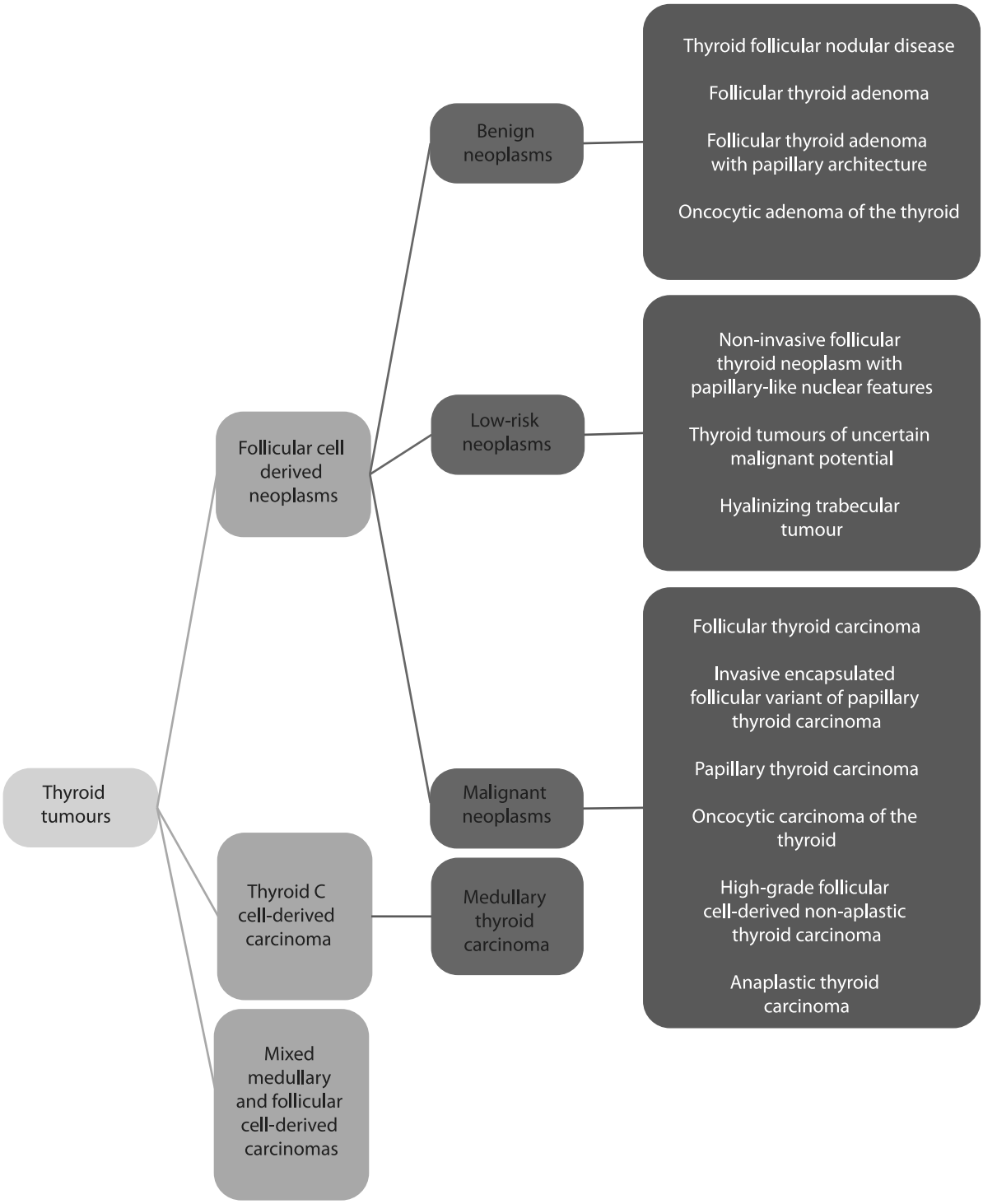


Figure 1: WHO classification of follicular cell-derived neoplasms and thyroid C cell-derived carcinomas.

(NHLS) based at Chris Hani Baragwanath Academic Hospital (CHBAH) in Johannesburg.

Ethical approval, data collection, and case selection

Ethical approval was obtained from the Human Research Ethics Committee (Medical) at the University of the Witwatersrand (certificate number: M220836). The study was registered with the Academic Affairs and Research Management System (AARMS) division at the NHLS and a search of the NHLS electronic database was conducted through the Corporate Data Warehouse (CDW). A total of 444 cases were identified by using a Systematized Nomenclature of Medicine (SNOMED) search with relevant terms provided by the investigators. Cases resected for non-thyroid pathology or where thyroid pathology was noted incidentally during post-mortem examinations were excluded.

Data extraction

Data were collected using a data collection sheet designed to capture parameters of statistical, pathological, and clinical significance. These parameters included gender, age, race, past medical history, presenting symptoms, type of surgery performed, indication for surgery, previous FNA results (if available), macroscopic description of the resection (weight,

smaller and larger dimensions, focality and laterality in the case of a tumour, and the presence or absence of parathyroid glands), histopathological diagnosis, and ancillary investigations. Information was gathered from the laboratory requisition forms completed by clinicians upon specimen submission. Patient hospital records were not accessed. Data from the data collection sheets were captured and coded in a Microsoft Excel© spreadsheet (Microsoft Corp, Redmond, WA, USA).

Data analysis

Statistical analysis was performed using Microsoft Excel©. Descriptive statistics were performed. The data that had a normal distribution were presented as mean ± standard deviation (SD) and the *t*-test was used to compare means. Categorical data were summarised as frequencies and percentages. A 95% confidence interval and a 5% margin of error were calculated for all variables.

Results

Epidemiology of surgical pathology

The study group consisted of 444 patients aged over eight years, of which 403 (91%) were females and 41 (9%) were males, resulting in a male-to-female ratio of 1:9.8 (Figure 2). Race was recorded in only 18% of cases, with 97.44% being African patients and 2.56% Caucasian patients. This low percentage of documented race did not allow for meaningful analysis or comparison. The age range of patients spanned from 8 to 94 years, with an overall mean age of 48.26 years (SD = 12.44). Considering the total number of male and female patients and the age ranges for the overall study period, a bell-shaped curve was depicted (Figure 3). The youngest patient, aged 8 years, was diagnosed with PTC, while the oldest patient, aged 94 years, was diagnosed with FTC.

Overall, non-neoplastic conditions had a mean age of 47.86 years (SD = 14.10), and neoplastic conditions had a mean age of 48.72 years (SD = 14.38). An F-test was used for the variance between the two groups (*p*-value of 0.195697402), indicating no significant difference in the variability of ages between non-neoplastic and neoplastic conditions. Table 1 outlines the mean age and SD for non-neoplastic and neoplastic thyroid conditions.

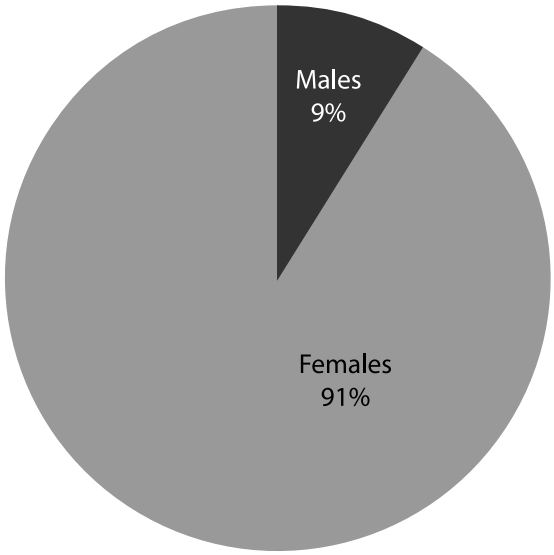


Figure 2: Percentage of females and males who underwent thyroid resection (total thyroidectomy/lobectomy) for both non-neoplastic and neoplastic thyroid pathology.

Spectrum of surgical thyroid pathology

The spectrum of thyroid pathology included non-neoplastic and neoplastic conditions (Figure 4A and B). Non-neoplastic conditions accounted for 53.60% of cases, while neoplastic conditions made up 46.40%, with benign cases comprising 7.20% and malignant cases 38.20%.

Non-neoplastic pathologies encompassed HT (1.13%) and hyperplastic conditions, which comprised GD and nodular hyperplasia (52.25%). Benign neoplasms included FTA (6.53%) and HCA (0.68%). Malignant neoplasms included PTC (29.05%), FTC (4.73%), MTC (1.58%), ATC (0.45%), HCC (2.93%), and NIFTP (0.45%). There was a single case (0.22%) that showed only reactive cellular changes suggestive of previous radioactive iodine treatment.

Several PTC subtypes were noted and included: follicular, classic, solid, and tall cell subtypes; the frequencies of each of these subtypes are shown in Figure 5.

Past medical history

Past medical histories included radioactive iodine therapy (1%), pregnancy (0.2%), hypothyroidism (0.2%), hyperthyroidism (5%), hypertension (2%), diabetes mellitus (1.3%), and retroviral disease (1.6%).

Presenting symptoms

The most common presenting symptom for both non-neoplastic and neoplastic pathologies was a visible mass (79%). Other symptoms included: compression or obstructive symptoms (4.30%), overactive or underactive thyroid (4%), unresponsive to medical treatment (2.70%), metastatic disease (0.70%), and unknown (9.30%).

Indications for surgery

In non-neoplastic as well as benign neoplastic cases, the most common surgical indication was the presence of benign thyroid nodules (diagnosed based on clinical suspicion, radiological investigations, or FNA). For malignant neoplasms, Bethesda category VI on preoperative FNA was the most frequent indication, followed by a clinical suspicion of thyroid cancer or Bethesda category V.

Surgical intervention

Surgical interventions included lobectomies (24%), lobectomies and isthmusectomy (6%), and total thyroidectomies (70%).

FNA results

FNA results were documented on the request form for 70% of the patients. Bethesda category I was reported in 9% of cases and the final histopathological diagnoses included HT (3.70%), nodular hyperplasia (77.80%), and malignant neoplasms (18.50%). Bethesda category II accounted for 44.30% of cases, and a concordance rate of 76% was observed between the initial FNA findings and the final diagnosis. Bethesda category III represented 9.70% of cases, and had final diagnoses based on histopathological evaluation, which included HT (3.40%), GD (6.90%), nodular hyperplasia (48.30%), benign neoplasms (10.30%), and malignant neoplasms (31.10%). For Bethesda category IV, comprising 11% of cases, the concordance rate was 29.03%. Bethesda category V, which included 8% of the cases, had final histopathological diagnoses distributed as follows:

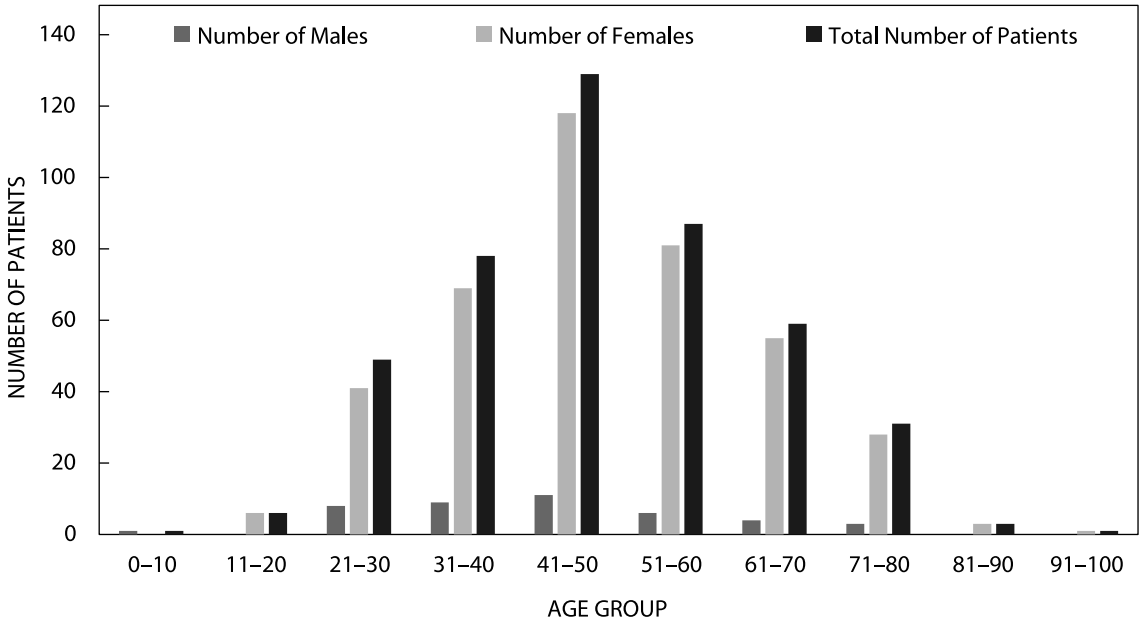


Figure 3: Distribution of male and female patients per age group over the study period.

nodular hyperplasia (12%), benign neoplasms (12%), malignant neoplasms (72%), and changes attributed to treatment effects from radioactive iodine therapy (4%). Bethesda category VI, representing 18% of cases, demonstrated a concordance rate of 93% between the FNA results and the final histopathological diagnosis. Figure 6 outlines the distribution of cytology results according to the Bethesda System for Reporting Thyroid Cytopathology. Figure 7 demonstrates the concordance between cytological and histological diagnoses for Bethesda II, IV, and VI categories.

Table 1: Mean age and standard deviation for non-neoplastic and neoplastic thyroid conditions

Diagnosis	Mean age (years)	Standard deviation (years)
Non-neoplastic thyroid conditions		
Hashimoto's thyroiditis	51.40	20.01
Graves' disease	37	11.28
Nodular hyperplasia	48.59	13.87
Neoplastic thyroid conditions		
Benign neoplastic thyroid conditions		
Follicular thyroid adenoma	46.02	13.38
Hürthle cell adenoma	48.67	6.13
Malignant neoplastic thyroid conditions		
Papillary thyroid carcinoma	47.40	15.29
Follicular thyroid carcinoma	52.38	17.59
Medullary thyroid carcinoma	48.43	21.97
Anaplastic thyroid carcinoma	65.50	0.71
Hürthle cell carcinoma	56.92	13.51
Non-invasive follicular thyroid neoplasms with papillary-like nuclear features	37	15.56
Treatment effect	33	Not applicable (single case)

Macroscopic pathological characteristics

Non-neoplastic pathologies, consisting of HT (126.8 mm) and hyperplastic disorders (GD and nodular hyperplasia) (123.8 mm), generally had the greatest dimensions of thyroid resections, followed by malignant neoplasms (110.07 mm), with benign neoplasms (103 mm) having the smallest resections. The average weight for HT, hyperplastic disorders, benign neoplasms, and malignant neoplasms was 157.6, 156.5, 95.23, and 130.2 g, respectively. The majority of neoplasms were unifocal. The presence of parathyroid gland tissue was noted in 5% of cases and was mostly present in specimens that had a malignant diagnosis.

Discussion

Spectrum and proportion of thyroid pathology

A range of non-neoplastic and neoplastic thyroid disorders are identified. Nodular hyperplasia affects nearly half (48.87%) of the study population. This finding aligns with local and global data, which report the frequency of nodular hyperplasia ranging from 1% to 90%, particularly in regions with iodine deficiency.[1,11,12] Among autoimmune thyroid disorders, which have a global prevalence of 0.30% to 1.20%, GD is the most common. This finding is consistent with our study, where GD occurred at a rate of 3.38%.[13] HT was observed in 1.13% and this is in line with local data from the Limpopo province, where HT occurred at a similar rate (1.10%).[1]

Overall, PTC accounted for 29.05% of cases and when considering only malignant thyroid disorders, PTC accounted for 74% of thyroid malignancies. FTC was the second most common thyroid malignancy (4.73%). These findings are consistent with international data, which consistently identify PTC as the most common thyroid malignancy.[14] However, a local study by Bhuiyan et al.,[1] conducted in the Limpopo province, reported a lower frequency of PTC (3.30%) compared with FTC (7.80%). In contrast to this, the study by Chagi et al.,[3]

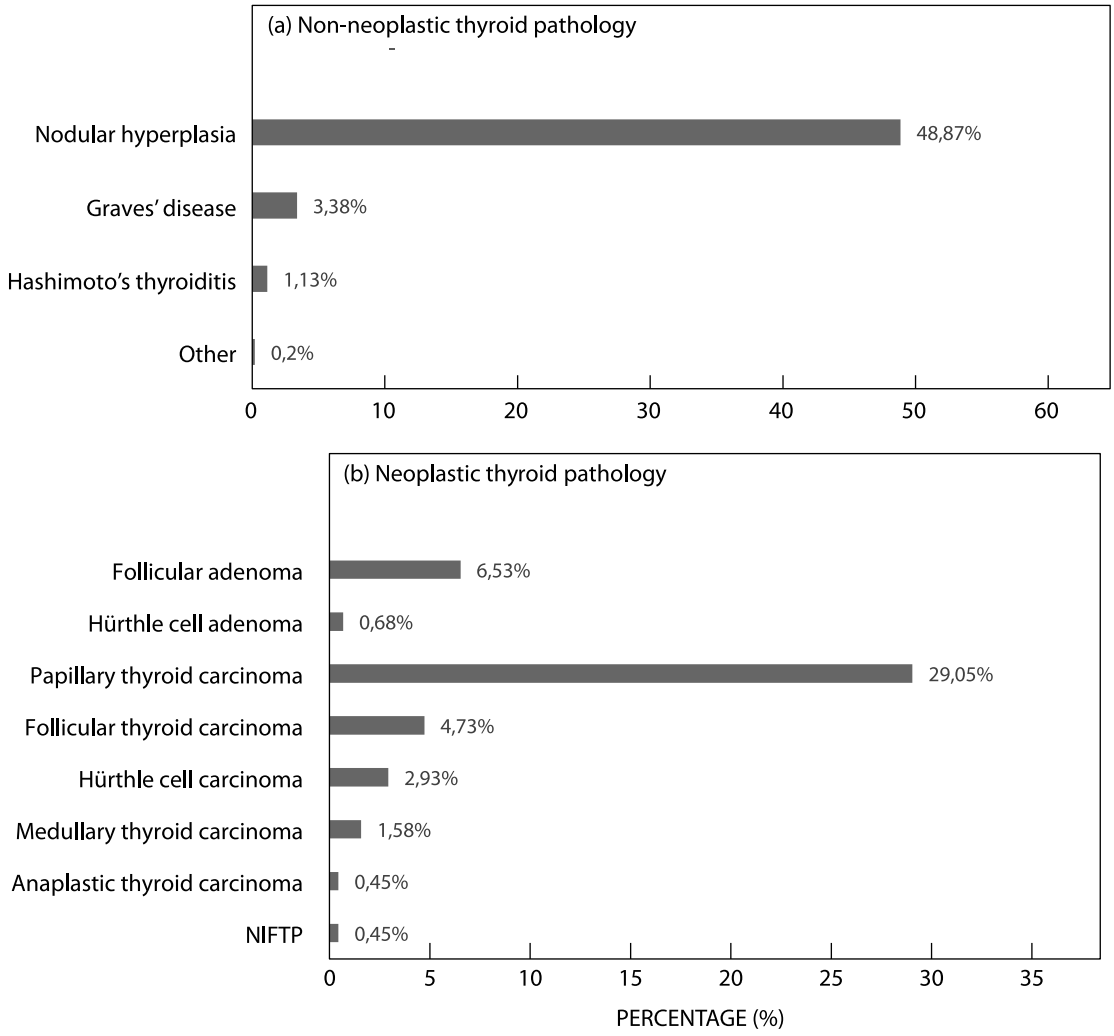


Figure 4: A and B: The spectrum of (A) non-neoplastic and (B) neoplastic surgical thyroid pathology.

from the same region as our study, also found PTC to be the predominant thyroid malignancy, with a rate of 65%.

The WHO recognises several PTC subtypes.[15–20] This study identified four of these subtypes: follicular (77.50%), classic (20.20%), solid (1.50%), and tall cell (0.8%). Our findings are in contrast to the global patterns, where the classic subtype is more prevalent.[15,16] The reason for this is unclear and requires further research.

Other malignancies represent a smaller proportion and include: HCC (2.93%), MTC (1.58%), ATC (0.45%), and NIFTP (0.45%).

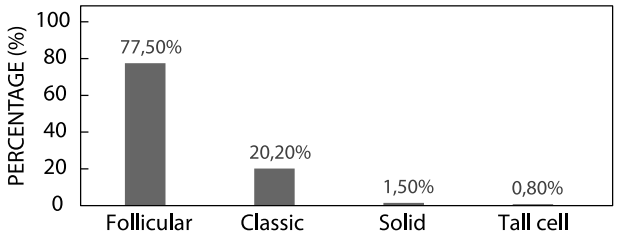


Figure 5: Frequency of the subtypes of papillary thyroid carcinoma encountered.

Benign thyroid tumours include FTA (6.53%) and HCA (0.68%), which are less common than malignancies. This aligns with global statistics (3–4.30%).[21] This is in contrast to local data

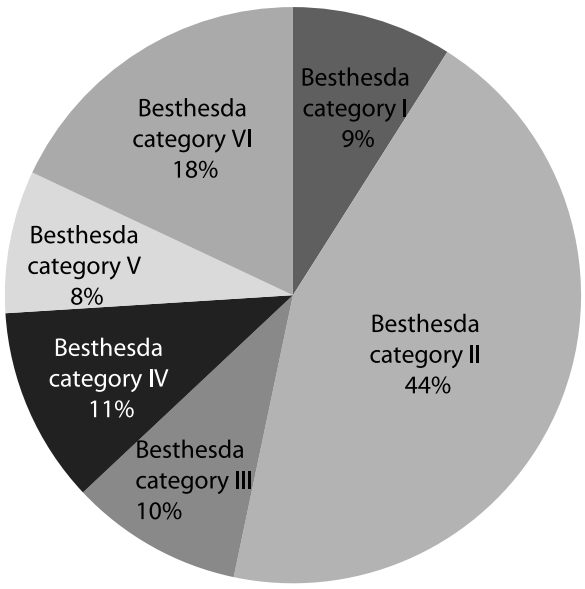


Figure 6: Distribution of cytology results according to the Bethesda System for Reporting Thyroid Cytopathology.

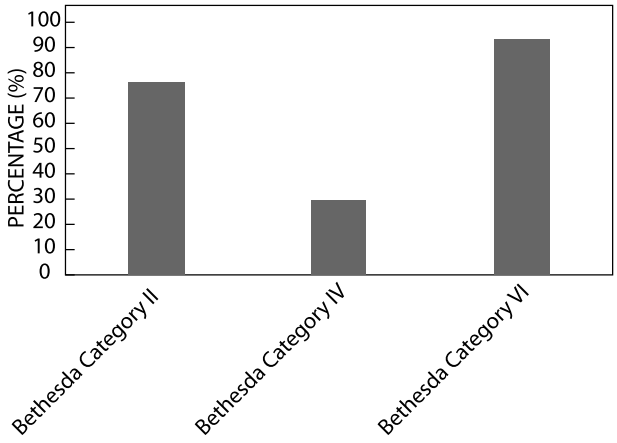


Figure 7: Concordance between cytological and histological diagnoses for Bethesda II, IV, and VI categories.

from the Limpopo study, which reported that benign tumours represented the majority (57.80%) of their cases.[1]

Gender and age distribution

Overall, there is a significantly higher prevalence in females (91%) compared with males (9%), with a male-to-female ratio of 1:9.8. This finding is consistent with both local and global data, which show a female predominance in both neoplastic and non-neoplastic thyroid disorders. This pattern may be attributed to hormonal, genetic, and immunological differences between males and females.[14,22–24] Notably, the ratio of benign-to-malignant pathologies is 0.16:1 in females and 1:21 in males. This indicates that malignant thyroid diseases are significantly more common than benign neoplastic diseases in both male and female genders, but the disparity is particularly notable in males.

The age distribution ranges from 8 to 94 years and the overall mean age is 48.26 years (SD = 12.44), aligning with local data.[1,5,25,26] Patients with non-neoplastic conditions have a mean age of 47.86 years (SD = 14.10), while those with neoplastic conditions have a mean age of 48.72 years (SD = 14.38). There is no significant difference in age distribution between the two groups. The highest mean age was noted in ATC (65.5 years [SD = 0.71]) and the lowest mean age in GD (37 years [SD = 11.28]) and NIFTP (37 years [SD = 15.56]). This suggests that ATC tends to occur in older individuals, while GD and NIFTP occur in relatively younger patients.

The SD is slightly higher for neoplastic conditions, indicating more variability in the ages of patients with neoplastic conditions. MTC has the highest age variability (21.97 years), compared with ATC, which has the lowest age variability (0.71 years). High variability in age indicates a wide range of ages among patients and low variability suggests patients are of similar age. Nodular hyperplasia and PTC are the most common diagnoses overall, occurring in middle-aged individuals, with an age variability of 13.87 and 15.29 years respectively.

Pre-existing and chronic conditions

A variety of pre-existing chronic conditions and risk factors are observed, including pregnancy, hypothyroidism, hyperthyroidism, hypertension, diabetes mellitus, epilepsy, asthma, and retroviral disease. Patients with a history of radioactive iodine therapy were diagnosed with nodular hyperplasia and FTA. Although previous radiation therapy, especially to the head and neck region, is a known risk factor for developing neoplastic thyroid pathology, particularly PTC, no patients with PTC in this study had a documented history of prior radiation exposure.[2,4,24,27]

Presenting symptoms

The most common presenting symptom for both non-neoplastic and neoplastic thyroid pathologies is the presence of visible masses (79%), which is in line with a South African multi-institutional review that also found a visible mass (67.20%) to be the most common presenting symptom.[28] Other symptoms included masses that cause compressive or obstructive symptoms (4.30%), symptoms of overactive or underactive thyroid (4%), unresponsive to medical treatment (2.70%), metastatic disease (0.70%), and unknown (9.30%).

FNA results

FNA results were available for 70% of patients, allowing assessment of concordance with final histopathological diagnoses, which varied across Bethesda categories. Category I (9%) had limited predictive value, with outcomes ranging from HT to nodular hyperplasia and malignancy, emphasising the need for repeat sampling or further evaluation. Category II, the most common (44.3%), showed a high concordance rate of 76%, with most cases diagnosed as nodular hyperplasia, consistent with the benign nature of this category. Category III (9.7%) showed a wide range of outcomes – including HT (3.4%), GD (6.9%), nodular hyperplasia (48.3%), benign neoplasms (10.3%), and malignancies (31.1%) – highlighting the diagnostic uncertainty of this indeterminate group. Category IV (11%) had a low concordance rate of 29.03%, reflecting the limitations of FNA in distinguishing between follicular adenomas and carcinomas, which require histological assessment. Category V (8%) was predominantly malignant (72%), with smaller proportions of benign neoplasms (12%), nodular hyperplasia (12%), and post-treatment changes (4%), supporting its high-risk classification and the need for timely intervention. Category VI (18%) showed a 93% concordance rate, confirming the high diagnostic accuracy of FNA in clearly malignant cases. Bethesda categories II, IV, and VI show better concordance with final histopathology because they are associated with more definitive cytological features and clearer clinical interpretations compared with categories I, III, and V.

Overall, these findings support the predictive value of the Bethesda System, especially in categories II and VI, while illustrating the diagnostic challenges in indeterminate cases. Integration of cytological, clinical, and radiological data remains essential for optimal thyroid nodule management.

Surgical intervention

Surgical intervention remains a cornerstone of thyroid disease management, particularly for cases with high suspicion of malignancy or compressive or obstructive symptoms. Total thyroidectomy was the most common surgical procedure performed for both non-neoplastic and neoplastic disorders, accounting for 70% of all surgeries.

Macroscopy of thyroid resections

Larger thyroid glands are more commonly associated with non-neoplastic conditions, while smaller thyroid glands are more likely to be linked to neoplastic pathologies.

Implications for clinical practice

A thorough understanding of the prevalent non-neoplastic and neoplastic thyroid conditions within a specific population can lead to quicker accurate diagnosis and treatment, ultimately improving patient outcomes and possibly reducing the risk of metastasis. A high index of suspicion should be maintained when evaluating thyroid nodules, regardless of the patient's age.

Limitations

As this was a retrospective study, we relied on existing medical records and histopathology reports, which may lack completeness. The study was conducted at a single institution, CHBAH, which may not reflect the diversity of thyroid pathologies in other regions.

Conclusion

This study provides valuable insights into the epidemiology, spectrum, and pathology of thyroid disease in a South African metropolitan setting. The findings highlight the importance of context-specific management approaches, the need for ongoing research to refine diagnostic and therapeutic strategies, and the potential benefits of personalised approaches to thyroid disease management based on local epidemiological patterns. The study also highlights the complexity of thyroid pathology and the need for a multidisciplinary approach to ensure optimal patient outcomes.

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ORCID

M van der Merwe http://orcid.org/0000-0002-2317-1238
Ar Botha http://orcid.org/0000-0002-7083-7602
D van der Byl http://orcid.org/0000-0001-5915-3966

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