The prevalence and associated predictors for Bethesda III–VI for reporting thyroid cytopathology in Royal Commission Hospital, Kingdom of Saudi Arabia

Hussain Alyousif, Ishag Adam, Naser A. Alamin, Mona A. Sid Ahmed, Ayat Al Saeed, Abdulmuhsen Hussein Hassoni and Imad R. Musa

Abstract

Background: Thyroid cancer is increasing globally and is currently the most prevalent endocrine malignancy. Recent data show an increase in the incidence of thyroid cancer in the Kingdom of Saudi Arabia (KSA). Thyroid ultrasound and fine-needle aspiration cytology (FNAC) are the cornerstones in managing thyroid nodules. We conducted this study to evaluate the prevalence and the associated predictors for thyroid nodule Bethesda III–VI in eastern KSA.

Methods: A retrospective study was conducted between January 2015 and 31 August 2021. The participants were recruited patients who received a thyroid ultrasound and ultrasound-guided thyroid FNAC, using the thyroid imaging reporting and data system (TI-RADS) and the Bethesda Classification, respectively.

Result: Three hundred and ten patients who underwent thyroid FNAC were enrolled in the study. The median (interquartile, IQR) age was 47.0 (20.0) years, and 266 (85.8%) of them were females. The median (IQR) body mass index was 30.2 (7.6) kg/m². Out of these participants, 64.8% were euthyroid, 27.4% had hypothyroidism and 7.7% had hyperthyroidism. The ACR TI-RADS-3, 4 and 5 were 51.3%, 46.1% and 2.6%, respectively. The Bethesda outcome of thyroid FNAC I–VI was 5.2%, 63.9%, 15.5%, 5.8%, 3.5% and 6.1%, respectively. The risk for malignancy (Bethesda III–VI) was documented in 31.0% and atypia of undetermined significance was most prevalent (15.5%). A higher ACR TI-RADS score was associated with a higher risk of malignancy: ACR TI-RADS-3 (20.8%), ACR TI-RADS-4 (39.2%) and ACR TI-RADS-5 (87.5%). In a multivariate analysis, only the ACR TI-RADS score was significantly associated with the outcome of thyroid FNAC: ACR TI-RADS-4 [OR = 2.59 (95% CI = 1.54–4.36)] and ACR TI-RADS-5 [OR = 29.03 (95% CI = 3.44–245.07)].

Conclusion: There was a high prevalence of Bethesda III–VI and atypia of undetermined significance was most prevalent. A thyroid ultrasound report for TI-RADS was significantly associated with the outcome of thyroid FNAC and is a reliable tool in the absence of molecular testing for thyroid cancer.

Keywords: Bethesda, fine-needle aspiration cytology, predictors, prevalence

Introduction

The incidence of thyroid cancer continues to increase globally. Thyroid cancer is considered the most prevalent endocrine cancer worldwide. A marked increase in thyroid cancer was reported in gulf countries, including the Kingdom of Saudi Arabia (KSA). A thyroid nodule is defined as an abnormal lesion within the thyroid gland.
tissue. Thyroid fine-needle aspiration cytology (FNAC) is the cornerstone for assessing thyroid nodules. A thyroid ultrasound enhances the ability to manage thyroid nodule disorders by diagnosing nonpalpable thyroid nodules. Besides offering reliable classification of thyroid nodules that assists in the decision-making regarding the need for biopsy and directing the fine needle to target the most suspicious area of the nodule. Sonography-guided FNAC improves the accuracy and safety of the technique for diagnosing thyroid nodules. The Bethesda System for Reporting Thyroid Cytology (TBSRTC) is a very important tool for evaluating thyroid nodules with reliable diagnostic accuracy. Previous studies have recommended the TBSRTC as an effective tool for pre-operative diagnosis of thyroid nodules. Thyroid FNAC management was cost-effective compared with watchful management. Several factors – such as age, female sex, thyroid status, thyroid hormone level, thyroid autoantibodies, metabolic syndrome components, smoking and alcohol consumption, environmental factors, diet and nutritional pattern, and genetic factors – have been reported as risk factors associated with thyroid nodular diseases and cancers.

Studies conducted in KSA reported an increase in the thyroid cancer rate (9–11.7%) with a significant geographical variation in the different regions of KSA. Despite the wide use and importance of such essential diagnostic tools, along with improvement in reporting system globally, there are few published data on the topic in the region. Hence, this study aimed to investigate the prevalence of thyroid FNAC based on Bethesda reporting and its associated predictors among adult patients in the Royal Commission Hospital in eastern KSA.

### Materials and methods

#### Study area

Jubail Industrial City, the World’s Largest Industrial City, was established in 1975 and situated on the Arabian Gulf, north of Dhahran, in the eastern Province of KSA. It has an area of 1016 square kilometres and includes industrial complexes and port facilities. Moreover, it contributes to about 7% of Saudi Arabia’s gross domestic product.

#### Methods

A retrospective study was conducted at the Royal Commission Hospital during 1 January 2015 through 31 August 2021. Royal Commission Hospital has a capacity of 217 beds and 200 physicians in all major specialties and most subspecialties. The records were retrieved of patients aged 18 years and above (males and females) with documented thyroid nodules based on ultrasound findings, who underwent ultrasound-guided FNAC in the hospital. Records of those with incomplete data, patients who underwent partial thyroid surgery without prior thyroid FNAC, patients diagnosed with thyroid cancer from lymph node biopsy, patients with known thyroid malignancy and reports from other hospitals were excluded. The sociodemographic data were gathered using a data collection sheet, including age, sex, body mass index (BMI), thyroid status, comorbidities, family history of thyroid cancer, smoking and exposure to radiation. Moreover, laboratory tests were performed for thyroid function, complete white blood count, lipid profile and vitamin D levels. A specialist conducted the thyroid ultrasound in the radiology department and a consultant radiologist revised and approved the report. Thyroid ultrasound reports based on the thyroid imaging reporting and data system [American College of Radiology thyroid imaging reporting and data system (ACR TI-RADS)] were adopted to assess the thyroid nodule (Table 1).

### Table 1. TI-RADS and category definitions.

| TI-RADS | Definition            |
|---------|----------------------|
| TI-RADS-1 | Benign               |
| TI-RADS-2 | Not suspicion        |
| TI-RADS-3 | Mildly suspicion     |
| TI-RADS-4 | Moderately suspicion |
| TI-RADS-5 | Highly suspicion     |

An expert radiologist conducted the thyroid FNAC under ultrasound guidance. Consent for the procedure was obtained after proper explanation. After the application of a local anaesthetic and under aseptic conditions, a 22-gauge needle was used with a 10-ml syringe. The tip of the needle-targeted areas presumed to contain the most cellular material of the thyroid nodule, under
Continuous low negative pressure was then applied simultaneously with a to-and-fro movement of the needle within the lesion to obtain the material in the needle hub. Mild pressure was applied to the site of the needle in order to prevent bleeding, and the patient was kept for 15 min before being reassured and discharged. One drop of aspirated material was forced onto each of several glass slides, and smears were prepared using a second glass slide similar to that adopted for the blood smears. Labelled slides were immediately wet fixed by placing them in an alcohol bottle before transferring them to the histopathology department in the hospital. A final cytopathology report was released after an expert pathologist studied each cell block. The ultrasound-guided thyroid FNAC and outcome were reported using TBSRTC, as shown in Table 2.

### Statistical analysis

Data were analysed with a computer using SPSS for Windows (version 22.0). Continuous data were checked for normality by the Shapiro–Wilk test, and all were not normally distributed. Data were expressed as proportions, median [interquartile range (IQR)] or number (proportion), as applicable. Moreover, the prevalence of the Bethesda categories was calculated. Univariate analysis was performed with the outcome of thyroid FNAC as the dependent variable. Independent variables were age, sex, thyroid status, exposure to radiation, thyroid function test, 25-hydroxyvitamin D (25[OH]D) levels, haemoglobin, white blood count, platelets, lipid profile, smoking and thyroid ultrasound report. Variables were shifted to the logistic regression analyses if their univariate \( p \) was \(<0.20\) and backward-stepwise likelihood ratio regression was used for adjustment. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated, and a \( p \) value of \(<0.05\) was considered significant.

#### Table 2. Bethesda’s system for reporting thyroid cytopathology.

| Category | Description |
|----------|-------------|
| I. Nondiagnostic or Unsatisfactory | Cyst fluid only, virtually acellular specimen and other (obscuring blood, clotting artefact, etc.) |
| II. Benign | Consistent with a benign follicular nodule [includes adenomatoid nodule, colloid nodule, etc.], consistent with lymphocytic [Hashimoto] thyroiditis in the proper clinical context or consistent with granulomatous [subacute] thyroiditis. |
| III. Atypia of Undetermined Significance | Follicular Lesion of Undetermined Significance. |
| IV. Follicular Neoplasm | Suspicious for a Follicular Neoplasm or specify if Hürthle cell (oncocytic) type. |
| V. Suspicious for Malignancy | Suspicious for one of these cancers; papillary carcinoma or medullary carcinoma or metastatic carcinoma or lymphoma or other cancer. |
| VI. Malignant | Diagnostic for one of these: papillary thyroid carcinoma, poorly differentiated carcinoma, medullary thyroid carcinoma, undifferentiated (anaplastic) carcinoma, squamous cell carcinoma, carcinoma with mixed features (specify), metastatic carcinoma, nonHodgkin lymphoma or other. |
Result

General characteristics

Three hundred and ten patients who underwent thyroid FNAC were enrolled in the study. The median (IQR) age was 47.0 (20.0) years, and 266 (85.8%) of them were females. Out of the participants, 297 (95.8%) were not smokers, 8 of them were exposed to radiation and 9 had a family history of thyroid cancer. The median (IQR) BMI was 30.28 (7.6) kg/m², and 25[OH]D level was 14.65 (10.8) nmol/l. The median (IQR) levels for the thyroid function test were as follows: thyroid-stimulating hormone (TSH) 1.70 (2.38) mmol/l, free thyroxine (FT4) 1.12 (0.40) ng/dl and free triiodothyronine (FT3) 2.67 (0.42) nmol/l. The median (IQR) of lipid profile, total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL) and triglyceride were 5.68 (3.92), 3.75 (0.80), 2.99 (1.70) and 1.73 (1.12) mmol/l, respectively. The median (IQR) of haemoglobin was 12.6 (1.9) gm/dl, platelet was 275.90 (96.6) 10⁹/l and white blood cell count was 6.87 (2.4) 10⁹/l, as shown in Table 3.

Most of the participants were euthyroid (201) (64.8%), 85 had hypothyroidism (27.4%) and 24 had hyperthyroidism (7.7%). The thyroid ultrasound report for TI-RADS-3, 4 and 5 was 51.3%, 46.1% and 2.6%, respectively. The outcome of the thyroid FNAC based on the Bethesda reporting system was nondiagnostic or unsatisfactory in 5.2%, benign in 63.9%, atypia of undetermined significance in 15.5%, follicular neoplasm in 5.8%, suspicious for malignancy in 3.5% and malignant in 6.1%.

The finding of high risk for malignancy (Bethesda III–VI) was 31.0% and atypia of undetermined significance was most prevalent (15.5%). The risk for malignancy was directly correlated with the increased ACR TI-RADS score: ACR TI-RADS-3 (20.8%), ACR TI-RADS-4 (39.2%) and ACR TI-RADS-5 (87.5%).

In the univariate analysis, there was no association between the age, sex, BMI, smoking, exposure to radiation, 25[OH]D levels and thyroid FNAC across the group. Similarly, there was no significant association between thyroid status, family history of thyroid cancer and the thyroid function test of TSH and FT3. There was no association between the outcome of the thyroid FNAC and comorbidities (diabetes mellitus, hypertension and bronchial asthma). There was no significant association between total cholesterol, LDL, HDL and triglyceride nor haematological indices, including haemoglobin, platelets and white blood cell count. There was, however, a significant association between the thyroid FNAC and FT4 [OR = 1.22 (95% CI = 1.01–1.46)] and the ultrasound findings based on TI-RADS: ACR TI-RADS-4 [OR = 2.45 (95% CI = 1.47–4.09)] and ACR TI-RADS-5 [OR = 26.72 (95% CI = 3.17–224.91)], as shown in Table 4.

In multivariate analysis, age, diabetes mellitus, FT4, FT3 and tobacco were not significantly associated with the outcome of the thyroid nodule FNAC. The thyroid ultrasound report based on TI-RADS was significantly associated with the outcome of the thyroid nodule FNAC: ACR TI-RADS-4 [OR = 2.60 (95% CI = 1.55–4.36)] and ACR TI-RADS-5 [OR = 29.03 (95% CI = 3.44–245.07)], as shown in Table 5.

Discussion

The prevalence of thyroid FNAC in this study based on the Bethesda reporting system was nondiagnostic or unsatisfactory (5.2%), benign (63.9%) and those with potential risk for malignancy (Bethesda III–VI) (31%): atypia of undetermined significance (15.5%), follicular neoplasm (5.8%), suspicious for malignancy (3.5%) and malignant (6.1%). The high risk of malignancy (Bethesda III–VI) was considerably higher than that obtained in Riyadh, the capital of KSA (10.2%), and in Qassim (10.8%), which is in the centre of KSA. It was slightly lower than the outcome of Bethesda III–VI reported in the southwestern region of KSA (36.5%), however. Interestingly, a markedly higher rate of potential risk for malignancy (Bethesda III–VI) was reported in the eastern region (Johns Hopkins Aramco Healthcare) (62.6%) and in Jeddah (western region) (62.1%). Atypia of undetermined significance (15.5%) was the most prevalent among the group at high risk for malignancy and in the Qassim region, which is in the central part of KSA (4%). Follicular neoplasm (16.1%), however, was prevalent in the southwestern and eastern regions (28.2%), those suspicious for malignancy (5.2%) were prevalent in Riyadh, and malignant (23.5%) was prevalent in Jeddah. Interestingly, our results and result of literature review study showed almost similar findings regarding the benign, Bethesda III–VI, and the
Table 3. General characteristics of patients who underwent thyroid FNAC in eastern region 2015–2021.

| Variables                              | Median  | Interquartile range |
|----------------------------------------|---------|---------------------|
| Age, years                             | 47.00   | 20.0                |
| Body mass index, kg/m²                 | 30.28   | 7.6                 |
| Haemoglobin, gm/dl                     | 12.60   | 1.9                 |
| White blood cell, 10⁹/l                | 6.87    | 2.4                 |
| Platelet, 10⁹/l                        | 275.90  | 96.6                |
| Thyroid-stimulating hormone, mmol/l    | 1.70    | 2.38                |
| Free triiodothyronine, nmol/l          | 2.67    | 0.4                 |
| Free thyroxine, ng/dl                  | 1.12    | 0.4                 |
| Total cholesterol, mmol/l              | 5.68    | 3.9                 |
| Low-density lipoprotein, mmol/l        | 3.75    | 0.8                 |
| High-density lipoprotein, mmol/l       | 2.99    | 1.7                 |
| Triglyceride, mmol/l                   | 1.73    | 1.12                |
| 25-hydroxyvitamin D (25[OH]D) levels, nmol/l | 14.65  | 10.8                |
| Thyroid status                         |         |                     |
| Euthyroid                              | 201     | 64.8                |
| Hypothyroidism                         | 85      | 27.4                |
| Hyperthyroidism                        | 24      | 7.7                 |
| Sex                                    |         |                     |
| Female                                 | 266     | 85.8                |
| Male                                   | 44      | 14.2                |
| Tobacco                                |         |                     |
| Never                                  | 297     | 95.8                |
| Current/former                         | 13      | 4.2                 |
| Exposure to radiation                  |         |                     |
| No                                     | 302     | 97.4                |
| Yes                                    | 8       | 2.6                 |
| Family history of thyroid cancer       |         |                     |
| No                                     | 301     | 97.1                |
| Yes                                    | 9       | 2.9                 |

(Continued)
most prevalent among them (atypia of undetermined significance) which were 68.8%, 21.1% and 12.4%, respectively.\(^3\)\(^8\) The high prevalence of Bethesda III–VI might be explained by the global increase of thyroid cancer,\(^1\)\(^2\) in gulf countries\(^3\)\(^4\) and in KSA.\(^5\)\(^2\)\(^7\)\(^3\)\(^9\) Moreover, this could be explained by the improvement of high-quality ultrasounds and screening for thyroid nodules – enhancing detection and diagnosis of thyroid cancers – and a possible increase in exposure to risk factors.\(^3\)\(^2\)\(^8\) A significant geographical variation in the incidence of thyroid cancer throughout the KSA was documented in 2013.\(^5\)\(^3\) This geographical variation pointed to different risk factors contributing to thyroid cancer: nutritional patterns, together with excessive weight gain,\(^1\)\(^9\) high consumption of processed chicken and fresh and processed fish products\(^2\)\(^5\) and environmental carcinogens, such as pollutants and radiation exposure.\(^2\)\(^4\) Furthermore, the differences in the genetic backgrounds of the study groups and the polygenetic factors – activation of oncogenes such as Rat sarcoma (RAS), human gene that encodes a protein called B-Raf (BRAF), receptor tyrosine kinase/phenylthiocarbamide (RET/PTC) and the overstimulation of the phosphatidylinositol 3-kinase/protein kinase \(B\) (PI3K/AKT) pathway – are involved in thyroid tumorigenesis.\(^2\)\(^6\) In addition, the thyroid FNAC procedure is operator dependent,\(^4\)\(^0\) and the influence of different methodology adopted for these studies.

Our results of ultrasound findings based on TI-RADS reporting were significantly associated with the ultrasound-guided thyroid FNAC and the Bethesda reporting system. This aligned with the results of many studies, demonstrating that ultrasound findings using TI-RADS reporting can predict the thyroid FNAC with reasonable specificity and sensitivity.\(^8\)\(^9\) Ultrasonography reliably classifies thyroid nodules, and thus can assist in the decision-making of whether to proceed for a thyroid FNAC.\(^9\) This was in concordance with the result of ARC TI-RADS obtained in this study: ACR TI-RADS-3 (20.8%), ACR TI-RADS-4 (39.2%) and ACR TI-RADS-5 (87.5%). This study showed that age was not a significant predictor for the outcome of Bethesda III–VI. This goes with the nonsignificant association obtained in recently published data.\(^1\)\(^8\)\(^4\)\(^1\) One study identified age as an independent predictor for thyroid malignancy, however.\(^1\)\(^7\) This study along with one conducted in the eastern region showed no significant association between sex and the outcome of a thyroid FNAC, despite the fact that females represented the majority of cases.\(^1\)\(^8\) Likewise, most clinical data demonstrated that females were more vulnerable to thyroid cancer.\(^3\)\(^4\) This may reflect the imbalance between the two oestrogen receptor isoforms, \(\alpha\) and \(\beta\), as triggering factors and might be responsible for cell proliferation.\(^4\)\(^2\) This study showed no significant association between metabolic syndrome

### Table 3. (Continued)

| Variables       | Median | Interquartile range |
|-----------------|--------|---------------------|
| Diabetes mellitus |        |                     |
| No              | 208    | 67.1                |
| Yes             | 89     | 28.7                |
| Hypertension    |        |                     |
| No              | 238    | 76.8                |
| Yes             | 72     | 23.2                |
| Asthma          |        |                     |
| No              | 289    | 93.2                |
| Yes             | 21     | 6.8                 |

FNAC, fine-needle aspiration cytology.
Table 4. Univariate analysis of the predictors associated with Bethesda III–VI in eastern region, 2015–2021.

| Variables                        | High risk for malignancy (n = 96) | Low risk for malignancy (n = 214) | OR (95% CI)             | p     |
|----------------------------------|------------------------------------|-----------------------------------|-------------------------|-------|
| Median                           |                                    |                                   |                         |       |
| Age, years                        | 44.0 [22.5]                        | 47.0 [18.0]                       | 0.98 [0.96–1.01]        | 0.085 |
| Body mass index, kg/m²            | 29.5 [7.1]                         | 30.57 [7.5]                      | 0.97 [0.94–1.01]        | 0.206 |
| haemoglobin, gm/dl                | 12.6 [1.7]                         | 12.6 [1.9]                       | 1.02 [0.98–1.06]        | 0.324 |
| White blood cell, 10⁹/l           | 6.99 [2.4]                         | 6.83 [2.4]                       | 0.97 [0.86–1.09]        | 0.665 |
| Platelet, 10⁹/dl                  | 275.45 [105]                       | 275.9 [90.5]                     | 1.00 [0.99–1.01]        | 0.933 |
| Thyroid-stimulating hormone, mmol/l | 1.6 [2.47]                        | 1.71 [2.37]                     | 1.002 [0.949–1.05]      | 0.946 |
| Free triiodothyronine, nmol/l     | 2.69 [0.42]                        | 2.69 [0.4]                      | 0.75 [0.52–1.08]        | 0.129 |
| Free thyroxine, ng/dl             | 1.13 [0.44]                        | 1.11 [0.39]                      | 1.22 [1.01–1.46]        | 0.036 |
| Total cholesterol, mmol/l         | 5.62 [4.12]                        | 5.7 [3.8]                       | 0.98 [0.91–1.06]        | 0.758 |
| Low-density lipoprotein, mmol/l   | 3.75 [0.91]                        | 3.75 [0.6]                       | 0.99 [0.95–1.04]        | 0.981 |
| High-density lipoprotein, mmol/l  | 2.99 [1.83]                        | 2.99 [1.6]                       | 0.90 [0.70–1.15]        | 0.410 |
| Triglyceride, mmol/l              | 1.69 [1.09]                        | 1.76 [1.1]                       | 0.97 [0.85–1.12]        | 0.760 |
| 25-hydroxyvitamin D [25(OH)D] levels, nmol/l | 14.45 [11.6]                   | 14.7 [10.9]                       | 1.01 [0.98–1.03]        | 0.541 |

| Number                           |                                    |                                   |                         |       |
|----------------------------------|                                    |                                   |                         |       |
| **Sex**                          |                                    |                                   |                         |       |
| Female                           | 80 [83.3]                          | 186 [86.9]                         | 1.32 [0.68–2.59]        | 0.404 |
| Male                             | 16 [16.7]                          | 28 [13.1]                         | Reference               |       |
| **Thyroid status**               |                                    |                                   |                         |       |
| Euthyroid                        | 57 [59.4]                          | 144 [67.3]                        | Reference               |       |
| Hypothyroid                      | 32 [33.3]                          | 53 [24.8]                         | 1.26 [0.49–3.23]        | 0.635 |
| Hyperthyroid                     | 7 [7.3]                            | 7 [7.9]                           | 1.57 [0.59–4.23]        | 0.369 |
| **Tobacco**                      |                                    |                                   |                         |       |
| Never                            | 90 [93.8]                          | 207 [96.7]                        | Reference               | 0.156 |
| Current/ former                  | 6 [6.2]                            | 7 [3.3]                           | 2.09 [0.75–5.77]        |       |

(Continued)
components (diabetes mellitus, hypertension, BMI and lipid profile) and the outcome of the Bethesda reporting system, thereby supporting similar findings of one study conducted in the eastern region. Some studies reported metabolic syndrome was an independent risk factor for the increased prevalence of thyroid nodular disease and cancer in both sex, however. This study demonstrated that the thyroid status and thyroid function test were not significant predictors for the thyroid FNAC outcome. A similar result was obtained in a recently published study conducted in the same region. In contrast to this finding, some studies documented that both hyperthyroidism and hypothyroidism were associated with a higher risk of thyroid cancer either a suppressed or elevated TSH. Interestingly, vitamin D level was not a significant predictor for the risk of thyroid cancer in this study, because vitamin D deficiency was prevalent in the studied group (91.0%). Moreover, vitamin D levels were not significantly associated with thyroid disorders. Our result was in concordance with another study, revealing that haemoglobin levels, platelet and white blood counts were not significant predictors for thyroid nodule FNAC.

### Table 4. (Continued)

| Variables                        | High risk for malignancy (n = 96) | Low risk for malignancy (n = 214) | OR (95% CI) | p     |
|----------------------------------|-----------------------------------|-----------------------------------|-------------|-------|
| Exposure to radiation            |                                   |                                   |             |       |
| No                               | 93 [96.9]                         | 209 [97.7]                        | Reference   | 0.687 |
| Yes                              | 3 [3.1]                           | 5 [2.3]                           | 1.348 [0.32–5.76] |       |
| Family history of thyroid cancer |                                   |                                   |             |       |
| No                               | 93 [96.9]                         | 209 [97.7]                        | Reference   | 0.691 |
| Yes                              | 3 [3.1]                           | 5 [2.3]                           | 1.342 [0.31–5.74] |       |
| Diabetes mellitus                |                                   |                                   |             |       |
| No                               | 59 [61.5]                         | 149 [69.6]                        | Reference   | 0.158 |
| Yes                              | 37 [38.5]                         | 65 [30.4]                         | 1.438 [0.87–2.38] |       |
| Hypertension                     |                                   |                                   |             |       |
| No                               | 74 [77.1]                         | 164 [76.6]                        | Reference   | 0.931 |
| Yes                              | 22 [22.9]                         | 50 [23.4]                         | 0.98 [0.55–1.73] |       |
| Asthma                           |                                   |                                   |             |       |
| No                               | 92 [95.8]                         | 197 [92.1]                        | Reference   | 0.229 |
| Yes                              | 4 [4.2]                           | 17 [7.9]                          | 0.50 [0.16–1.54] |       |
| Ultrasound                       |                                   |                                   |             |       |
| ACR TI-RADS-3                    | 33 [34.4]                         | 126 [58.9]                        | Reference   |       |
| ACR TI-RADS-4                    | 56 [58.3]                         | 87 [40.7]                         | 2.46 [1.48–4.09] | 0.001 |
| ACR TI-RADS-5                    | 7 [7.3]                           | 1 [0.5]                           | 26.727 [3.18–224.92] | 0.003 |

ACR TI-RADS, American College of Radiology thyroid imaging reporting and data system; CI, confidence interval; OR, odds ratio.
Table 5. Multivariate analysis of the predictors associated with Bethesda III–VI in eastern region 2015–2021.

| Variables                        | OR (95% CI)       | p    |
|----------------------------------|-------------------|------|
| Age, years                       | 0.99 (0.97–1.01)  | 0.139|
| Free thyroxine, ng/dl            | 1.08 (0.88–1.34)  | 0.463|
| Free triiodothyronine, nmol/l    | 0.74 (0.51–1.09)  | 0.131|
| Tobacco                          |                   |      |
| Never                            | Reference         |      |
| Current/former                  | 2.83 (0.94–8.48)  | 0.063|
| Diabetes mellitus                |                   |      |
| No                               | Reference         |      |
| Yes                              | 1.507 (0.88–2.60) | 0.139|
| ACR TI-RADS scoring system      |                   |      |
| ACR TI-RADS-3                   | Reference         |      |
| ACR TI-RADS-4                   | 2.60 (1.55–4.36)  | 0.000|
| ACR TI-RADS-5                   | 29.03 (3.44–245.07) | 0.002|

ACR TI-RADS, American College of Radiology thyroid imaging reporting and data system; CI, confidence interval; OR, odds ratio.

...that thyroid cancer is under the influence of multifactorial aetiology.

The limitations
The study was retrospective. Other factors – such as thyroid antibodies, iodine levels, nutritional pattern, genetic analysis and environmental factors – were not assessed.

Conclusion
There was a considerably high prevalence of Bethesda III–VI, atypia of undetermined significance being the most prevalent among them, and the TI-RADS reporting was the most significant predictor for thyroid FNAC in Royal Commission Hospital. ACR TI-RADS and Bethesda are reliable tools to evaluate thyroid nodules in the absence of molecular testing facilities.

Declarations

Consent for publication
Not applicable.

Author contributions

Hussain Alyousif: Data curation; Methodology; Writing – original draft; Writing – review & editing.
Ishag Adam: Conceptualization; Formal analysis; Writing – original draft; Writing – review & editing.
Naser A. Alamin: Conceptualization; Data curation; Investigation; Writing – original draft; Writing – review & editing.
Mona A. Sid Ahmed: Data curation; Investigation; Methodology; Writing – review & editing.
Ayat Al Saeed: Data curation; Investigation; Methodology; Writing – review & editing.
Abdulmuhsen Hussein Hassoni: Data curation; Investigation; Methodology; Writing – review & editing.
Imad R. Musa: Conceptualization; Formal analysis; Writing – original draft; Writing – review & editing.
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ORCID iD
Imad R. Musa https://orcid.org/0000-0002-1138-0710

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