fortune Journals

Research Article

FORTUNE JOURNAL OF HEALTH SCIENCES

ISSN: 2644-2906

Bronchial Asthma and Its Associated Risk Factors Among Adults with Thyroid Nodules

Imad R Musa

Abstract

Background: Bronchial asthma (BA) and thyroid nodules (TNs) are growing global health challenges. The present study thus aimed to investigate the prevalence of BA and its associated risk factors among adults with TNs in the eastern region of the Kingdom of Saudi Arabia (KSA).

Methods: A retrospective study was conducted at the Royal Commission Hospital in eastern KSA from January 1, 2015 to December 31, 2021. The participants' sociodemographic characteristics were assessed, and multivariate regression analyses were conducted to identify potential risk factors for patients with BA.

Results: A total of 391 adult participants with TNs were enrolled in this study, with a median (IQR) age of 46.00 (20.0) years. The majority of participants were female (84.9%), and the median (IQR) body mass index (BMI) was 30.27 (7.71) kg/m^2. The prevalence of BA among adult patients with TNs was 7.9%. A univariate analysis revealed a significant association between BA in these patients and age, platelet count (PLTc), neutrophil count, lymphocyte count, mean platelet volume, haematocrit, free triiodothyronine (FT3), low-density lipoprotein and high-density lipoprotein. However, there was no significant association between BA and gender, BMI, thyroid status, 25-hydroxyvitamin D (25[OH]D), white blood cell count, haemoglobin, red cell distribution width (RDW), total cholesterol, triglyceride, thyroid-stimulating hormone (TSH) and free thyroxine (FT4). Increased age (AOR = 1.046, 95% CI = 1.015–1.079), higher platelet count (AOR = 1.006, 95% CI 1.002–1.011), lower lymphocyte count (AOR = 0.492, 95% CI = 0.275–0.881) and elevated FT3 (AOR = 1.242, 95% CI = 1.043–1.480) were significantly associated with BA.

Conclusion: A relatively higher prevalence of BA was observed among adult patients with TNs compared to the general population in eastern KSA. Older age, elevated FT3, a higher PLTc and lower lymphocyte count were significantly associated with BA.

Keywords: Prevalence, bronchial asthma, thyroid nodules, Saudi Arabia

Introduction

Bronchial asthma (BA) is a chronic inflammatory condition of the airways characterised by bronchial hyperreactivity and evidence of a variable degree of airway obstruction [1]. Diagnosis of BA depends on the clinical history, physical findings, and pulmonary function tests: reversibility testing and

Affiliation:

Royal Commission Hospital at AL Jubail Industrial City, Al Jubail, Kingdom of Saudi Arabia

***Corresponding author:**
Imad R Musa, Royal Commission Hospital at AL Jubail Industrial City, Al Jubail, Kingdom of Saudi Arabia.

Citation: Imad R Musa. Bronchial Asthma and Its Associated Risk Factors Among Adults with Thyroid Nodules. Fortune Journal of Health Sciences. 6 (2023): 427-437.

Received: October 18, 2023
Accepted: October 26, 2023
Published: November 03, 2023

Musa IR, et al., Fortune J Health Sci 2023
DOI:10.26502/fjhs.144

measurement of bronchial reactivity [1]. In 2019, the estimated global prevalence of BA is 9.8% in those aged 5–69 years, with the highest prevalence reported in Africa (11.3%) and the lowest documented in Southeast Asia (8.8%).[2]. Different prevalence of BA have been demonstrated in different regions worldwide [2–7]. Moreover, the burden of treating BA has continued to rise, with approximately 262.41 million cases reported across the globe in 2019 [8]. Several studies have pointed to an association between BA and pulmonary function tests and thyroid status and thyroid hormones [9,10]. In addition to the increased risk of hypothyroidism, hyperthyroidism and goitre among patients with BA [11–14]. Additionally, large goitres—particularly retrosternal goitre may mimic BA [15,16]. Similarly, symptomatic ectopic intratracheal thyroid is associated with breathing difficulty, cough, stridor and dysphagia [17]. Several risk factors for BA have been identified, including age, male gender, high body mass index (BMI), occupational asthmagens, smoking and thyroid dysfunction [8,11,18,19]. Nevertheless, TN is a growing global health problem that indicates the presence of an abnormal lesion within the thyroid gland tissue [20]. Females (36.51%) are more vulnerable to the condition than males (23.47%), and the estimated overall global prevalence of TNs is 24.83%, regardless of the diagnostic method adopted, based on a systematic review and meta-analysis study, conducted on 2022 [21]. Moreover, variations in the prevalence of TNs have been documented in different global regions [22]. TN malignancy risk warrants targeted and timely assessment and follow-up that will result in a better prognosis and a high cure rate [23]. Fortunately, the risk of malignancy in TNs is not markedly higher (27.5%) as most these nodules were benign [24]. Moreover, assessment of TNs has been improved considerably by thyroid ultrasound [25,26], sonography-guided fine needle aspiration cytology (FNAC) for TNs [26,27], the adoption of scoring systems for both thyroid ultrasound [27] and thyroid FNAC [28] in addition to the development of the facilities required to perform genetic and molecular testing [29]. Diagnostic accuracy and procedural safety have thus been achieved by reducing the rate of unindicated FNAC and thyroid surgeries [27,28].

TNs are identified as a growing medical and health problem in the KSA that may pose potential malignancy risks [24,30,31]: thyroid cancer has been identified as the third most common cancer among the Saudi population [32] and the second most common malignancy among Saudi women behind breast cancer [33]. TNs are linked to significant morbidity and mortality burdens in KSA [31]. Moreover, managing TNs is associated with higher financial costs in particular, those associated with aggressive thyroid cancer [34]. BA is considered a health challenge with a higher prevalence that is considerably higher than the prevalence reported in most countries using the European Community Respiratory Health Survey questionnaire [18]. It is more prevalent among children, with an overall prevalence of 8–25% [35], and males are more vulnerable to the condition than females [36]. A higher prevalence of BA was observed in southern Saudi Arabia (6.9%–19.5%) and in the capital Riyadh (11.3%–19.6%)[18,36]. In fact, the household out-of-pocket spending burden in KSA for chronic non-communicable diseases, including BA, remains high, with several disparities such as age, gender, education, employment and marital status [37]. Moreover, a higher percentage of adult patients with BA had uncontrolled disease (64%) [38]. Considering the significance of BA and TNs as growing medical health problems and the poor availability of published data on the coexistence of both medical conditions in the region, the present study aimed to investigate the prevalence and associated risk factors of BA among adult patients with TNs in the KSA.

Methods

A retrospective study was conducted at the Royal Commission Hospital in Al Jubail Industrial City between January 1, 2015 and December 31, 2021. The electronic medical files of adult patients (men and women) aged 18 years and older were retrieved. The study included those with documented TNs based on an ultrasound procedure performed in the hospital's radiology department of the hospital. Medical files with incomplete data or thyroid ultrasound reports for thyroid ultrasounds performed outside the hospital were excluded. The sociodemographic data, including each patient's age, gender, weight and height, were recorded. Common comorbidities were identified using a data collection sheet: thyroid status [euthyroid, hypo- or hyperthyroidism], diabetes mellitus (DM), hypertension and BA, obesity and anaemia. Similarly, laboratory tests performed simultaneously with TN evaluated were collected: complete blood count (WBCc, haemoglobin, PLTc and other haematological indices), vitamin D levels, lipid profiles [total cholesterol, low-density lipoprotein, high-density lipoprotein and triglycerides] and thyroid function [TSH, FT3 and FT4]. Each thyroid ultrasound procedure was performed by a radiology specialist in the hospital's radiology department. Each report was then reviewed and finally approved by a radiology consultant. The radiological department in the hospital adopted the American College of Radiology Thyroid Imaging Reporting and Data System (ACR TI-RADS) for evaluating TNs (Table 1) [39].

Table 1: (TI-RADS) Category definitions

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

ACR TI-RA
DS: American College of Radiology Thyroid Imaging Reporting and Data System.

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DOI:10.26502/fjhs.144

Definition of variables

TNs: TNs were diagnosed based on the definition of the American Thyroid Association (ATA) Guidelines [20].

Body mass index: BMI was calculated as body mass divided by the square of the body height; it is expressed in units of kg/m^2, resulting from mass in kilograms and height in metres [40].

Vitamin D deficiency: Vitamin D deficiency is defined by a (25(OH)D) level of < 30 ng/mL; levels equal to or above this cutoff point are considered normal [41].

Bronchial asthma: This variable includes individuals diagnosed with BA based on the documentation of their medical records.

DM: DM diagnoses is considered for those with documentation of DM (type 1 and 2), whether they were on diet control or on glucose-lowering drugs, during TN assessment.

Hypertension: This variable includes patients who had been diagnosed with hypertension and were receiving treatment during TN assessment.

Thyroid dysfunction: Indicates the documented diagnosis of hypothyroidism or hyperthyroidism based on thyroid function tests as documented in their medical records and as part of their treatment during TN assessment.

Statistical analysis

Data were input into a computer using IBM Statistical Package for the Social Sciences® (SPSS®) for Windows, version 22.0 (SPSS Inc., New York, United States). The proportions were expressed as frequencies (%). The Shapiro–Wilk test was used to determine the normality of continuous data (age, BMI, vitamin D levels, thyroid function test, haematological indices and lipid profile) and revealed a non-normal distribution. The non-normally distributed variables were expressed as the median (interquartile range [IQR]). A univariate analysis was performed for BA as the dependent variable with sociodemographic demographics (age, sex, age, BMI, vitamin D levels, thyroid function test, haematological indices, lipid profile, hypertension and DM) as independent variables. A multivariate analysis was also conducted for all variables with $p < 0.2$ to control for confounding variables. Adjusted odds ratios (AORs) and 95% confidence intervals (CIs) were calculated as they were applied, and a two-sided $p < 0.05$ was considered statistically significant.

Results

A total of 391 patients with documented TNs were enrolled in the study, and most of them were females (84.9%). The median (IQR) of the age was 46.00 (20.0) years, the median (IQR) of BMI was 30.27 (7.71) kg/m^2 and 25[OH)] D level was 14.5 (12.0) nmol/L. The median (IQR) for the thyroid function test was TSH 1.71 (2.43) mmol/L, FT4 1.12 (0.45) ng/dL FT3 2.69 (0.40) nmol/L. The median (IQR) for haematological indices was haemoglobin 12.6 (1.7) gm/dl, PLTc 276.15 (95.80) 10^9/L, WBCc was 7.01 (2.63) µL, neutrophil count 10^3/µL 3.740 (1.77), lymphocyte count 10^3/µL 2.500 (0.94), RDW (fL) 13.400 (3.10) haematocrit (L/L) 38.680 (5.50) and MPV (fL) 9.800 (2.83). The median (IQR) of lipid profile, total cholesterol, low-density lipoprotein, high-density lipoprotein and triglyceride were 5.8 (3.89) mmol/L, 3.76 (0.80) mmol/L, 3.00 (1.71) mmol/L and 1.78 (1.11) mmol/L, respectively. The prevalence of BA among adult patients with TNs was 7.9%. The outcome of thyroid ultrasound reports based on (ACR TI-RADS): ACR TI-RADS-1(2.6%), ACR TI-RADS-2 (18.4%) ACR TI-RADS-3 (40.7), ACR TI-RADS-4 (36.3%) and ACR TI-RADS-5 (2%) table (2).

Table 2: general characteristics of patients who had documented TNs in eastern region 2015-2021

Variables			
		Median	Interquartile range
Age, years		46	20
Body mass index, kg/m^2		30.27	7.71
Haemoglobin, gm/dl.		12.6	1.7
White blood cell, 10^3/µL.		7.01	2.63
Platelet, 10^9/L		276.15	95.8
Neutrophil count 10^3/µL		3.74	1.77
Lymphocytes count 10^3/µL		2.5	0.94
RDW femtoliters (fL)		13.4	3.1
MPV femtoliters (fL)		9.8	2.83
Hematocrit (L/L)		38.68	5.5
(25[OH)]D) levels, nmol/L		14.5	12
Thyroid-stimulating hormone, mmol/L		1.71	2.43
Free triiodothyronine, nmol/L		2.69	0.4
Free thyroxine, ng/dL		1.12	0.45
Total cholesterol, mmol/L		5.8	3.89
Low-density lipoprotein, mmol/L		3.76	0.8
High-density lipoprotein, mmol/L		3	1.71
Triglyceride, mmol/L		1.78	1.11
		Number	Proportion

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DOI:10.26502/fjhs.144

Gender	Female	332	84.9
	Male	59	15.1
Diabetes mellitus	No	297	76
	Yes	94	24
Hypertension	No	303	77.5
	Yes	72	22.5
Bronchial asthma	No	360	92.1
	Yes	31	7.9
Obesity	No	189	48.3
	Yes	202	51.7
Thyroid status	Euthyroid	250	64
	Hypothyroidism	112	28.6
	Hyperthyroidism	29	7.4
Ultrasound	ACR TIRADS1	10	2.6
	ACR TIRADS2	72	18.4
	ACR TIRADS3	159	40.7
	ACR TIRADS4	142	36.3
	ACR TIRADS5	8	2

The univariate analysis revealed no significant association between BA in adult patients with TNs and gender, BMI, thyroid status, (25[OH)] D), white blood cell count, haemoglobin, red cell distribution width, total cholesterol, triglyceride, TSH or FT4. However, a significant association was observed between BA in these patients and age (AOR = 1.037, 95% CI = 1.009 –1.067), PLTc (AOR = 1.005, 95% CI = 0.275–0.881), neutrophil count (AOR = 1.217, 95% CI = 1.0161.457), lymphocyte count (AOR = 0.611, 95% CI = 0.3721.004), mean platelet volume AOR = 0.872, 95% CI = 0.275–0.881), haematocrit (AOR = 1.006, 95% CI = 1.001–1.012), FT3 (AOR = 1.197, 95% CI = 1.017–1.409), low-density lipoprotein (AOR = 1.040, 95% CI = 0.994–1.089) and high-density lipoprotein (AOR = 0.721, 95% CI = 0.481–1.081) (see Table 3).

The multivariate analysis indicated that DM, hypertension, neutrophils, haematocrit, mean platelet volume, low-density lipoprotein and high-density lipoprotein were not significantly associated with BA in patients with TNs. However, increased age (AOR = 1.046, 95% CI = 1.015–1.079), a higher PLTc, (AOR = 1.006, 95% CI 1.002–1.011), a lower lymphocyte count (AOR = 0.492, 95% CI = 0.275–0.881), and elevated FT3 (AOR = 1.242, 95% CI = 1.043–1.480), were highly significantly associated with BA in adult patients with TNs (Table 4).

Table 3: Univariate analysis of the predictors associated with bronchial Asthma among adult patients with TNs in eastern region, 2015-2021.

Variables		Adults without asthma **(n=360)**	Adults with asthma **(n=31)**	**OR (95.0 %CI**	**P**
		Median			
Age, years		46.00(21.0)	51.0 (17.00)	1.037(1.009 –1.067)	0.01
BMI		29.98(7.81)	32.46(8.92)	1.002(0.990– 1.014)	0.741
White blood cell, $10^3/\mu L$		6.9 (2.59)	7.87(2.53)	1.089(0.925– 1.281)	0.305
Haemoglobin, gm/dl.		12.60(1.70)	12.10(2.60)	1.004(0.956–1.054)	0.889
Platelet, 10^3/dl		276.15 (94.65)	304.1(112.0)	1.005(1.001–1.009)	0.022
Neutrophil count $10^3/\mu L$		3.70(1.76)	4.05(2.39)	1.217(1.0161.457)	0.033
Lymphocytes count10^3/mcL		2.50(0.98)	2.02(80.0)	0.611(0.3721.004)	0.052
Red cell distribution width(fL)		13.04(3.10)	12.97 (3.62)	0.998(0.976–1.020)	0.856
Mean platelet volume (fL)		9.81(2.77)	8.87(2.92)	0.872(0.715–1.063)	0.176
Hematocrit (L/L)		38.70(5.38)	37.80(9.60)	1.006(1.001–1.012)	0.023
TSH, mmol/L		1.72(2.40)	1.48 (2.59)	0.981(0.890–1.082)	0.7
FT3, nmol/L		2.69(0.40)	2.69 (0.71)	1.197(1.017–1.409)	0.031
FT4, ng/dL		1.12 (0.44)	1.15(0.52)	1.200(0.723–1.991)	0.481
Total cholesterol, mmol/L		5.80(3.90)	5.36(4.60)	0.885(0.733–1.068)	0.205
Low-density lipoprotein,mmol/L		3.76(0.80)	3.76(0.81)	1.040(0.994–1.089)	0.09
High-density lipoprotein,mmol/L		2.998 (1.68)	1.43 (1.80)	0.721(0.481–1.081)	0.113

Triglyceride, mmol/L		1.80 (1.10)	1.44 (1.27)	0.997(0.951–1.045)	0.9
(25[OH)]D) levels, nmol/L		14.60(12.22)	14.05(8.90)	0.978(0.939–1.019)	0.275
		Number			
Gender	Female	304(84.4)	28 (90.3)	0.582(0.171–1.979)	0.386
	Male	56 (15.6)	3 (9.7)	Reference	
Diabetes Mellitus	No	277 (76.9)	20 (64.5)	Reference	0.125
	Yes	83 (23.1)	11 (35.5)	0.545(0.251–1.183)	
Hypertension	No	283 (78.6)	20 (64.5)	Reference	0.076
	Yes	77 (21.4)	11 (35.5)	0.495(0.227–1.077)	
Thyroid status	Euthyroid	231 (64.2)	19 (61.3)	Reference	
	Hypothyroid	104 (28.9)	8 (25.8)	0.514(0.162–1.631)	0.259
	Hyperthyroid	25 (6.9)	4 (12.9)	0.481(0.134–1.724)	0.261

Table 4: Multivariate analysis of the predictors associated with bronchial asthma in patient with thyroid nodules in eastern region 2015-2021

Variables	OR (95.0 %CI	P
Age, years	1.046 (1.015–1.079)	0.04
Diabetes Mellitus	0.594 (0.229–1.536)	0.282
Hypertension	0.814 (0.295–2.250)	0.692
Platelet, 10^3/dl	1.006 (1.002–1.011)	0.006
Neutrophil count 10^3/µL	1.166 (0.951–1.429)	0.141
Lymphocytes count 10^3/µL	0.492 (0.275–0.881)	0.017
Mean platelet volume (fL)	0.960 (0.789 –1.168)	0.681
Hematocrit (L/L)	1.005 (1.000 –1.011)	0.061
FT3, ng/Dl	1.242 (1.043–1.480)	0.015
Low-density lipoprotein, mmol/L	1.034 (0.982–1.088)	0.202
High-density lipoprotein, mmol/L	0.831 (0.507–1.362)	0.463

Discussion

Among the study's main findings is the higher prevalence (7.9%) of BA among adult patients with TNs. The prevalence obtained in this study is considerably higher than that reported by a national household survey conducted among the general population in 2013 (4.05 %) and in the eastern region of KSA (4.15–4.36%), where this study was conducted [42]. Meanwhile, a markedly higher prevalence of BA was observed among the Saudi population in the southern region of KSA (19.5%) and in Riyadh (11.3%–19.6%) [18,36]. The prevalence reported in the present study is significantly lower than the global prevalence of BA in the general population aged 5–69 years (9.8%), with the highest prevalence recorded in Africa (11.3%) and the lowest in Southeast Asia (8.8%) [2]. Moreover, it is within the range of prevalence that was documented in the Gulf region (4.7% to 30.0%), with the highest prevalence recorded in the United Arab Emirates and the lowest in KSA [43]. The current prevalence, as documented in the present study, is close to that recorded among adults in America (7.0–7.7%) [3,5], higher than that reported in Germany (5.35%) [4] and lower than that demonstrated in Finland (10.3–11.2%) [6,7].

The difference in prevalence of BA among adults with TNs may be explained by the variation across KSA's different regions [42] as well as the fact that the prevalence of BA among Saudi adults is under-investigated [18]. The higher prevalence of BA in this group of patients may reflect a close association between the two medical conditions. Several studies have reported that patients with BA have a higher risk of developing thyroid dysfunction, including thyroiditis, hypothyroidism, hyperthyroidism and diffuse or nodule thyroid goitre [11–13]. A recently published study demonstrated a significant relationship between serum total immunoglobulin E (IgE) levels and TN formation [44]. This corroborates the finding that IgE production is a primary marker for the diagnosis and monitoring of allergic asthma, and higher levels of IgE are associated with poor prognosis: persistent symptoms, exacerbations of BA and a poor quality of life [45]. Moreover, hypothyroidism increases BA episodes, diminishes the possibility of remission, and exacerbates BA due to the lack of thyroid hormones [14]. Hyperthyroidism similarly impacts BA remission and increases the serum IgE and interleukins (IL4/IL1) ratio, leading to deterioration of BA control as a result of Type 2 helper T (Th2)-response excessive stimulation [14].

Moreover, thyroid functions varied in patients with BA without impairing pulmonary function [10]. Although hyperthyroidism and hypothyroidism clinically represent different thyroid function entities, the pathogenesis of Graves' disease and Hashimoto thyroiditis involves the Th-17 pathway and the IL-17 family cytokines pathway [46,47] as well as non-type 2 asthma and airway remodelling in patients with BA [11,48]. This accords with the present study's finding that a higher prevalence of thyroid dysfunction

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DOI:10.26502/fjhs.144

(hypo-hyperthyroidism) among patients with TNs (36%) and BA (38.7%). Interestingly, the severity of BA and goitre are significant predictors for the risk of developing cancers in general, and in particular, thyroid papillary cancer among patients with BA [49]. Additionally, certain medications used to control BA, such as Dupilumab, a fully human monoclonal antibody that blocks IL-4 and IL-13 are associated with painless thyroiditis, leading to transient hyperthyroidism and hypothyroidism and recovery without anti-thyroid treatment [50]. Similarly, nonspecific β blockers used to control palpitation of overactive thyroid may exacerbate BA attacks [51].

The present study identified a significant association between increased age and BA in adult patients with thyroid nodular diseases, corroborating several studies that have identified increased age as a significant predictor for risk of developing BA [3,4,6,19,52]. Ageing is associated with a decline in lung function owing to a reduction in compliance, elastic recoil of the lung, a reduction in respiratory muscle strength and increased residual volumes [53]. Furthermore, increased prevalence of airway hyper-responsiveness may occur in elderly patients with BA compared to younger subjects as a result of differences in the pathophysiological determinants of airway hyper-responsiveness with ageing [54]. Moreover, the signification association between ageing and BA may relate to elderly people's vulnerability to asthma induced by non-IgE-mediated allergy [52]. Similarly, ageing is associated with a chronic low-grade inflammation called inflamm-ageing [55] and altered adipokine levels in patients with BA [56]. Additionally, the multimorbidity associated with asthma, such as gastro-oesophageal reflux, chronic rhino-sinusitis, obstructive sleep apnoea and heart conditions, increases with age [57].

Some of these comorbidities in the elderly and the medications required to treat them may increase asthma exacerbation's and negatively affect its control [19]. Meanwhile, TNs in advanced age are related to changes in the thyroid gland that accompany ageing: the degeneration of thyroid cells, leading to fibrosis; infiltration of inflammatory cells; thyroid follicle alteration; and eventually thyroid nodular diseases [58]. The prevalence of both medical conditions (BA and TNs) is expected to increase with age to justify its significant association in this study.

The present study demonstrated a significant association between elevated FT3 and BA, as reported in several earlier clinical trials [9,59,60]. Interestingly, elevated FT3 in patients with BA is reversible, and it is a protective mechanism against stress response [9]. Low FT3 was significantly associated with higher mortality rates and a significantly longer duration of mandatory ventilation[59,60]. Moreover, the correlation between FT3 and pulmonary function is directly related to changes in thyroid enzymology: hypoxia reduces step-up deiodinase activity, and the retention of carbon dioxide markedly reduces thyroid hormone levels [9].

This indicates that hypoxia leads to type 1 thyroid allostasis via different mechanisms that are unrelated to the negative effect of hypothyroidism on pulmonary function [9]. On the other hand, elevated FT3 levels may be associated with hot nodules of toxic adenomas and multinodular goitre [61]. Moreover, inflammation accelerates the development of TN disease by means of an indirect effect, inhibiting the synthesis of thyroid hormones, which eventually leads to elevated TSH [62]. Not only is elevated FT3 protective against BA but it is also associated with a reduced risk of thyroid cancer [63] and lowers the risk of recurrence [64]. A significant association was observed between PLTc and BA among TN patients in the present study. A similar significant association with elevated PLTc was observed among patients with BA compared to the control group [65][66]. Similarly, significantly high PLTc was observed among the patients during exacerbation and asymptomatic periods compared with the control group [67].

Moreover, a higher PLTc was reported in thyroid nodular diseases and is an independent predictor for severity of inflammation and the presence of papillary thyroid cancer [66,68,69]. Not only was elevated PLTc documented during episodes of BA but the platelet indices were also altered during the exacerbation phase, compared with the stable phase and control group [70]. This may point to the role of platelets in the inflammation process during BA attacks [71]. The potential mechanism may be attributablee to IL-6-induced thrombocytosis associated with increased thrombopoietin level, which is a platelet production stimulator [72]. Another possibility is that paraneoplastic thrombocytosis results from the stimulation of malignant cells to increase platelet production and platelet activation and aggregation [68,69]. Both plasma levels of platelet factor 4 and platelet-activating factor among patients with an asthma attack were significantly higher than those of the controls [73], which results in the release of platelets from bone marrow haematopoietic stem or via a spleen-dependent mechanism, respectively [74,75].

The present study identified a significant association between low lymphocyte counts and BA among adult patients with TNs. Other studies have observed a similar significant association [76,77]. Likewise, a significant decrease in the lymphocyte subgroup—human peripheral blood gamma delta T cells—was reported in adult patients with both mild and severe BA [78,79]. The lower lymphocyte count in patients with BA is of prognostic significance, as it is negatively associated with the severity of BA and normalized after remission of asthmatic events [77]. This may be explained by the role that B and T lymphocyte attenuator (BTLA) plays in the proliferation, recruitment and survival of T cells in response to inhaled allergen; hence, the regulation of cell

death through BTLA signalling is the main determinant of the inflammatory response in the lung[80]. The newly approved biological agents may be associated with lymphopenia, as the lymphocyte count before the biological agent treatment was statistically higher than the value at 3 and 6 months of treatment [81]. Similar CD4+ T-cell lymphopenia was observed with alefacept therapy, which inhibits the activation and proliferation of T cells by blocking LFA-3/CD2 interaction and induction of apoptosis in activated memory T cells [82]. Nevertheless, a recently published study reported a significant association with lower lymphocyte count and TNs [83,84]. Moreover, it is a predictor for TN cancer, as a lower lymphocyte count was observed in malignant TNs than in benign samples [84].

Likewise, T-cell lymphopenia in patients with thyroid cancer was considered a significant indicator for the aggressiveness of tumour behaviour and might determine future therapeutic options [85]. T-cell lymphopenia may be due to increased T-cell apoptosis, which was associated with head and neck cancer [86] or possibly concomitant decreased homeostatic proliferation of T cells, reduced thymic output and redistribution of T cells to the tumour site [85]. The other variables assessed in this study demonstrated a non-significant association with BA among patients with TNs. This may be explained by the fact that BA is a complicated, multifactorial illness with hereditary and environmental influences [87] as well as thyroid nodular diseases [88]. The study's main limitation is that it was retrospective and collected data from only one centre. Other factors, such as thyroid antibodies, iodine levels, smoking, alcohol consumption, physical activity, nutritional patterns, drug history, genetic analysis and environmental factors, were not assessed.

Conclusion

A higher prevalence of BA was observed among adult patients with TNs than among the general population in eastern KSA. Older age, elevated FT3, a higher PLTc and lower lymphocyte count were significant predictors of BA in this group of patients.

Declarations

Availability of data and Material

Data are available upon request.

Ethics approval and consent to participate

The study was approved by the Institutional Review Board of the Royal Commission Hospital, KSA (IB-RCH-012), which waived verbal or written consent from the participants. It was conducted in compliance with the ethical standards of the responsible institution on human subjects as well as with the Helsinki Declaration.

Consent for publication

Not applicable.

Conflicts of Interest

The author has no conflicts of interest to declare.

Disclosure

No funding received.

ORCID iD: Imad R. Musa https://orcid.org/0000-0002-1138-0710

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