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# The Prevalence and Associated Predictors for Diabetes Mellitus in Adult Patients With Thyroid Nodules

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## Abstract

**Background:** Diabetes mellitus (DM) and thyroid nodules (TNs) with the risk of malignancy are increasing globally. Hence, we conducted this study to evaluate the prevalence and the associated predictors for DM among adult patients with TNs in Royal Commission Hospital, Kingdom of Saudi Arabia (KSA).

**Methods:** A retrospective study was conducted between January 1, 2015 and December 31, 2021. Patients with documented TNs based on the American College of Radiology Thyroid Imaging Reporting and Data System (ACR TI-RADS) were recruited. Then the prevalence and associated risk factors for DM were assessed.

**Result:** Three hundred ninety-one patients who had TNs were recruited. The median (interquartile range (IQR)) age was 46.00 (20.0) years, and 332 (84.9%) of the patients were females. There was a high prevalence of DM (24.0%) among adult patients with TNs. In the univariate analysis, there were significant associations between diagnosed DM among adult patients with TNs and age, gender, 25-hydroxyvitamin D (25(OH)D) level, hypertension, bronchial asthma, free triiodothyronine (FT3), white blood cell count, low-density lipoprotein (LDL), high-density lipoprotein (HDL) and triglycerides. In the multivariate analysis, there were significant associations between diagnosed DM among adult patients with TNs and age (odds ratio (OR) 1.037 (95% confidence interval (CI) 1.012 - 1.062)), hypertension (OR 0.374 (95% CI 0.203 - 0.689)), FT3 level (OR 0.635 (95% CI 0.412 - 0.980)), LDL (OR 0.643 (95% CI 0.456 - 0.907)) and HDL (OR 0.654 (95% CI 0.465 - 0.919)).

**Conclusion:** There was a high prevalence of DM among patients with TNs. Age, hypertension, FT3, LDL and HDL were significantly associated with DM and TNs.

**Keywords:** Prevalence; Diabetes mellitus; Thyroid nodules; Predictors

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## Introduction

Diabetes mellitus (DM) is a group of metabolic disorders characterized by abnormal and elevated blood glucose levels, which is associated with increased morbidities, mortalities and higher medical care costs [1, 2]. Globally, it is estimated that one in 10 (573 million) people age 20 - 79 years have DM, and this figure is expected to jump to 783 million by 2045 [1]. Likewise, 541 million adults have impaired glucose tolerance, with a high risk of developing DM in the future [1]. Uncontrolled DM enhances generalized vascular damage, affecting vulnerable organs (the heart, eyes, kidneys, nerves and other organs), resulting in chronic and acute complications [1, 2]. According to the International Diabetes Federation, the total global healthcare expenditure for patients with DM is estimated at USD 966 billion (a 316% increase over the last 15 years) [1]. Additionally, DM was responsible for 6.7 million deaths worldwide in 2021: one death every 5 s [1, 2]. Meanwhile, in low- and middle-income countries, DM is prevalent (three in four adults); 73 million (one in six adults) are living with DM in the Middle East, and this figure is expected to reach 136 million by 2045 [1]. Unfortunately, in the Middle East and North Africa, one in three adults living with DM are undiagnosed, and an increased rate of prediabetes and hyperglycemia in pregnancy affects one in seven live births [1].

Thyroid nodules (TNs) are one of the most common thyroid diseases and are defined by the American Thyroid Association as a discrete lesion within the thyroid gland; besides being radiologically distinct from the surrounding thyroid parenchyma [3], they can be solitary, multiple, cystic or solid [4]. A high prevalence of TNs is reported in the general population [5] and among patients with DM [6-8], indicating close association [7, 9, 10]. TNs deserve medical attention and proper follow-up as some of these nodules have the potential to be malignant at certain stages [11]. The thyroid ultrasound, fine-needle aspiration report and the scoring systems are essential tools for assessing TNs with reliable diagnostic accuracy and prognostic value [12]. DM and thyroid gland disorders have bidirectional influence on each other, as addressed in some studies [13, 14]. While some studies reported a high prevalence of DM among patients with TNs [8, 11, 15], a higher prevalence of TNs was reported in patients with DM [6, 8, 16, 17]. Several factors, such as age, female gender, thyroid status, thyroid hormone level, lipid profile, metabolic syndrome components, chronic complications related to DM, environmental factors, diet and



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**Table 1.** ACR TI-RADS Category Definitions

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

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

nutritional patterns, and genetic factors have been reported as risk factors associated with thyroid nodular diseases and DM [10, 18-20]. Recently, published studies from the KSA showed a high prevalence of T2DM, which is considered a growing health problem [21-23], with direct expenditure on DM that comprises around 13.9% of the total health expenditure (25 billion riyals) [24]. In addition, recently, a high prevalence of TNs was reported among Saudi radiography technicians working in KSA hospitals and in a control group (34% versus 32%) [25]. Moreover, an increase in the thyroid cancer rate (11.7%) in the KSA was documented [26]. Given the importance of the two clinical entities, the potential coexistence of both conditions, and the meagre published data on the topic in the region, the current study aimed to investigate the prevalence the associated predictors for DM among adult patients with TNs in the Royal Commission Hospital in eastern region of the KSA.

## Materials and Methods

A retrospective study was conducted at the Royal Commission Hospital, lasting from January 1, 2015 to December 31, 2021. The files of adult patients (men and women) aged 18 years and older with documented TNs, based on the findings of an ultrasound procedure, were retrieved. The ultrasound procedures were conducted in the radiology department of the hospital. Medical records with incomplete data and thyroid ultrasound reports for thyroid ultrasounds performed in other hospitals were excluded. The sociodemographic data, including each patient's age, gender, weight, height, thyroid status and common comorbidities (T1DM and T2DM, hypertension and bronchial asthma), were gathered using a data collection sheet. Moreover, laboratory tests for complete white blood cell counts, thyroid function, lipid profiles and vitamin D levels were obtained. Each thyroid ultrasound procedure was conducted in the radiology department of the hospital by a radiology specialist, and each report was reviewed and approved by a radiology consultant. Thyroid ultrasound reports based on the American College of Radiology Thyroid Imaging Reporting and Data System (ACR TI-RADS) were adopted to evaluate the TNs (Table 1) [27].

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

### Definition of variables

*TNs*

TNs were diagnosed according to the 2011 version of the TI-RADS classification criteria for risk assessment of malignant TNs [28].

*Body mass index (BMI)*

BMI was calculated as the 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 meters.

*Vitamin D deficiency*

This variable is defined as a 25-hydroxyvitamin D (25(OH)D) level of < 30 ng/mL; levels equal or above this cutoff point are considered normal [29].

*DM*

This variable includes those who had documentation of DM (type 1 and 2), whether they were on diet control or on glucose-lowering drugs.

*Hypertension*

This variable includes patients diagnosed with hypertension and receiving treatment.

*Bronchial asthma*

This variable includes patients diagnosed with bronchial asthma based on their medical records.

### Statistical analysis

Data were analyzed using SPSS for Windows (version 22.0). Continuous data were assessed for normality using the Shapiro-Wilk test; all variables were not normally distributed. Data were expressed as proportions, medians with interquartile ranges (IQRs) or numbers and proportions, as applicable. A univariate analysis was performed with the diagnosed DM as the dependent variable. The independent variables were age, gender, BMI, thyroid status, hypertension, bronchial asthma, thyroid hormones, the 25(OH)D level, hemoglobin, white blood cell count, platelet count, lipid profile and ACR TI-RADS ultrasound score. A variable was analyzed using logistic regression if its univariate P-value was < 0.20, and backward stepwise likelihood ratio regression was selected for adjustment. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated, and P-values of < 0.05 were considered significant.

## Results

Three hundred ninety-one patients who had TNs were enrolled in the study. The median (IQR) patient age was 46.00 (20.0) years, and 332 (84.9%) patients were females. The median (IQR) BMI and 25(OH)D level were 30.26 (7.71) $kg/m^2$ and 14.50 (12.0) nmol/L, respectively. The median (IQR) values for the thyroid function tests were as follows: thyroid-stimulating hormone (TSH), 1.72 (2.43) mmol/L; free triiodothyronine (FT3), 2.69 (0.40) nmol/L; free thyroxine (FT4), 1.12 (0.45) ng/dL. The median (IQR) lipid profile values for total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL) and triglycerides were 5.80 (3.89) mmol/L, 3.76 (0.80) mmol/L, 2.99 (1.71) mmol/L and 1.78 (1.11) mmol/L, respectively (Table 2). Most participants had normal thyroid function (64%), 28.6% had hypothyroidism and 7.4% were suffering from hyperthyroidism. The the patients' percentages according to ACR TI-RADS ultrasound scores (1, 2, 3, 4 and 5) were 2.6%, 18.4%, 40.7%, 36.3% and 2%, respectively (Table 2).

There was a high prevalence of diagnosed DM (24.0%) among adult patients with TNs.

In the univariate analysis, there was no association between diagnosed DM among adult patients with thyroid nodular disease and BMI, thyroid status, hematological index (hemoglobin and platelet), total cholesterol, thyroid-stimulating hormone, free thyroxine and thyroid ultrasound based on the ACR TI-RADS scoring system. However, there were significant associations between diagnosed DM among adult patients with TNs and age (OR: 1.069 (95% CI 1.048 - 1.092)), gender (OR 1.628 (95% CI 0.89 - 2.977)), 25(OH)D level (OR 1.020 (95% CI 1.000 - 1.041)), hypertension (OR 0.16 (95% CI 0.095 - 0.27)), bronchial asthma (OR 0.160 (95% CI 0.095 - 0.27)), FT3 (OR 0.649 (95% CI 0.459 - 0.919)), white blood cell count (OR 1.090 (95% CI 0.979 - 1.214)), LDL (OR 0.427 (95% CI 0.314 - 0.58)), HDL (OR 0.462 (95% CI 0.352 - 0.607)) and triglycerides (OR 0.665 (95% CI 0.463 - 0.954)) (Table 3).

In the multivariate analysis, gender, bronchial asthma, 25(OH)D level, and triglycerides and white blood cell counts were not significantly associated with diagnosed DM among adult patients with thyroid nodular diseases. However, there were significant associations between diagnosed DM among adult patients with TNs and age (OR 1.037 (95% CI 1.012 - 1.062)) (P = 0.004), hypertension (OR 0.374 (95% CI 0.203 - 0.689)) (P = 0.002), FT3 level (OR 0.635 (95% CI 0.412 - 0.980)) (P = 0.040), LDL (OR 0.643 (95% CI 0.456 - 0.907)) (P = 0.012) and HDL (OR 0.654 (95% CI 0.465 - 0.919)) (P = 0.015) (Table 4).

**Table 2.** General Characteristics of Adult Patients With Thyroid Nodules in Eastern Region 2015 - 2021

| Variables | Median | Interquartile range |
|---|---|---|
| Age, years | 46.00 | 20.0 |
| Body mass index, $kg/m^2$ | 30.26 | 7.71 |
| Vitamin D, nmol/L | 14.50 | 12.00 |
| Thyroid-stimulating hormone, mmol/L | 1.71 | 2.43 |
| Free triiodothyronine, nmol/L | 2.69 | 0.40 |
| Free thyroxine, ng/dL | 1.12 | 0.45 |
| Total cholesterol, mmol/L | 5.8 | 3.89 |
| Low-density lipoprotein, mmol/L | 3.76 | 0.80 |
| High-density lipoprotein, mmol/L | 2.99 | 1.71 |
| Triglyceride, mmol/L | 1.78 | 1.11 |
| | Number | Proportion |
| Gender | | |
| Female | 332 | 84.9 |
| Male | 59 | 15.1 |
| Diabetes mellitus | | |
| No | 297 | 76 |
| Yes | 94 | 24.0 |
| Hypertension | | |
| No | 303 | 77.5 |
| Yes | 88 | 22.5 |
| Asthma | | |
| No | 360 | 92.1 |
| Yes | 31 | 7.9 |
| Thyroid status | | |
| Euthyroid | 250 | 64.0 |
| Hypothyroidism | 112 | 28.6 |
| Hyperthyroidism | 29 | 7.4 |
| Ultrasound based on ACR TI-RADS | | |
| ACR TI-RADS 1 | 10 | 2.6 |
| ACR TI-RADS 2 | 72 | 18.4 |
| ACR TI-RADS 3 | 159 | 40.7 |
| ACR TI-RADS 4 | 142 | 36.3 |
| ACR TI-RADS 5 | 8 | 2 |

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

## Discussion

Our study showed a high prevalence (24%) of diagnosed DM among patients with thyroid nodular disease, which was higher than that obtained in studies from China (11.6% [15] and 14.24% [8, 11]). To our knowledge, our study is the first to assess the prevalence of DM among individuals with thyroid nodular diseases in the region. Many studies have, however, evaluated the prevalence of thyroid nodular diseases in patients with DM: A higher prevalence of TNs among patients with DM compared to the control group was reported in Po-


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**Table 3.** Univariate Analysis of the Factors Associated With Diabetes Mellitus in Adult Patients With Thyroid Nodules in Eastern Region 2015 - 2021

| Variables | DM (n = 94), median (IQR) | No DM (n = 297), median (IQR) | OR (95.0% CI) | P |
|---|---|---|---|---|
| Age, years | 56.00 (15.0) | 43.00 (20.0) | 1.069 (1.048 - 1.092) | < 0.000 |
| Body mass index, kg/m$^2$ | 32.87 (9.47) | 29.58 (7.00) | 1.004 (0.995 - 1.013) | 0.399 |
| Vitamin D | 15.73 (11.82) | 14.00 (10.6) | 1.020 (1.000 - 1.041) | 0.047 |
| Thyroid-stimulating hormone, mmol/L | 2.0750 (2.32) | 1.63 (2.42) | 1.004 (0.997 - 1.011) | 0.278 |
| Free triiodothyronine, nmol/L | 2.691 (0.40) | 2.691 (0.41) | 0.649 (0.459 - 0.919) | 0.015 |
| Free thyroxine, ng/dL | 1.19 (0.45) | 1.10 (0.46) | 0.902 (0.743 - 1.095) | 0.298 |
| Hemoglobin, g/dL | 12.70 (1.86) | 12.50 (1.80) | 0.99 (0.942 - 1.041) | 0.695 |
| White blood cell, $10^9$/L | 7.40 (2.65) | 6.9 (2.79) | 1.090 (0.979 - 1.214) | 0.114 |
| Platelet, $10^3$/dL | 275.58 (99.5) | 276.2 (85.70) | 0.999 (0.996 - 1.001) | 0.289 |
| Total cholesterol, mmol/L | 4.85 (1.94) | 6.27 (3.69) | 1.001 (0.995 - 1.008) | 0.702 |
| Low-density lipoprotein, mmol/L | 3.145 (1.66) | 3.76 (0.44) | 0.427 (0.314 - 0.58) | < 0.000 |
| High-density lipoprotein, mmol/L | 1.39 (1.89) | 3.00 (1.51) | 0.462 (0.352 - 0.607) | < 0.000 |
| Triglyceride, mmol/L | 1.44 (0.84) | 2.26 (1.07) | 0.665 (0.463 - 0.954) | 0.027 |
| Gender | | | | |
| Male | 19 (20.2) | 40 (13.5) | Reference | 0.114 |
| Female | 75 (79.8) | 257 (86.5) | 1.628 (0.89 - 2.977) | |
| Thyroid status | | | | |
| Euthyroid | 57 (60.6) | 193 (65.0) | Reference | |
| Hypothyroidism | 32 (34.0) | 80 (26.9) | 1.418 (0.517 - 3.89) | 0.497 |
| Hyperthyroidism | 5 (5.3) | 24 (8.1) | 1.92 (0.674 - 5.47) | 0.222 |
| Hypertension | | | | |
| No | 47 (50.0) | 256 (86.2) | Reference | 0.000 |
| Yes | 47 (50.0) | 41 (13.8) | 0.16 (0.095 - 0.27) | |
| Bronchial asthma | | | | |
| No | 83 (88.3) | 277 (93.3) | Reference | 0.125 |
| Yes | 11 (11.7) | 20 (6.7) | 0.160 (0.095 - 0.27) | |
| Ultrasound | | | | |
| ACR TI-RADS 1 | 3 (3.2) | 7 (2.4) | Reference | |
| ACR TI-RADS 2 | 19 (20.2) | 53 (17.8) | 3.000 (0.248 - 36.325 | 0.388 |
| ACR TI-RADS 3 | 33 (35.1) | 126 (42.4) | 2.509 (0.289 - 21.756) | 0.404 |
| ACR TI-RADS 4 | 38 (40.4) | 104 (35.0) | 1.83 (0.218 -15.428) | 0.577 |
| ACR TI-RADS 5 | 1 (1.1) | 7 (2.4) | 2.556 (0.305 - 21.479) | 0.387 |

ACR TI-RADS: American College of Radiology Thyroid Imaging Reporting and Data System; CI: confidence interval; DM: diabetes mellitus; IQR: interquartile range; OR: odds ratio.

land (48% versus 28%) [16]; in two studies from China: a cross-sectional study with 121,702 participants (50.1% versus 32.5%) [8] and a systematic review analysis (60% versus 43%) [6]; and in the Czech Republic (62% versus 50%) [17], respectively. Interestingly, a high prevalence of TNs was reported among individuals with prediabetic range of blood sugar levels in different countries (42.9-66%) [6, 8, 17, 30]. Furthermore, the significant association between DM and TNs was documented in many studies across the globe: Turkey [30, 31], China [6, 11, 15, 18, 32], Korea [32], Poland [16], Argentina [33], Italy [7], and the Czech Republic [17]. Not only was the significant association demonstrated but so was the fact that the presence of DM can predict thyroid gland volume, nodule size [9, 16, 30, 31, 33], the risk of cancer and poor prognosis [11]. Additionally, the duration of DM [9, 19], glycemic control [13, 33], family history of DM [18] and diabetic nephropathy [10, 19] were independent risk factors for TNs in patients with DM. The high prevalence of DM found among partici-

**Table 4.** Multivariate Analysis of the Factors Associated With Diabetes Mellitus in Adult Patients With Thyroid Nodules in Eastern Region 2015 - 2021

| Variables | OR (95.0% CI) | P |
|---|---|---|
| Age, years | 1.037 (1.012 - 1.062) | 0.004 |
| Free triiodothyronine, nmol/L | 0.635 (0.412 - 0.980) | 0.040 |
| Vitamin D, nmol/L | 1.007 (0.995 - 1.020) | 0.248 |
| Low-density lipoprotein, mmol/L | 0.643 (0.456 - 0.907) | 0.012 |
| High-density lipoprotein, mmol/L | 0.654 (0.465 - 0.919) | 0.015 |
| Triglyceride, mmol/L | 0.920 (0.710 - 1.192) | 0.526 |
| White blood cell, $10^9$/L | 1.128 (0.991 - 1.284) | 0.068 |
| Hypertension | | |
| No | Reference | |
| Yes | 0.374 (0.203 - 0.689) | 0.002 |
| Bronchial asthma | | |
| No | Reference | |
| Yes | 0.741 (0.281 - 1.949) | 0.543 |
| Gender | | |
| Male | Reference | |
| Female | 0.645 (0.284 - 1.465) | 0.295 |

CI: confidence interval; OR: odds ratio.

pants with TNs in our study may be explained by the global rise in DM [1, 2] and the higher overall prevalence of DM that was documented among Saudi females (27.6%) [22] and males (23.7-34.1%) [21, 22]. Likewise, the World Health Organization has reported DM as a growing health problem in the KSA; it ranked the second highest in the Middle East and the seventh highest in the world for the rate of DM in 2016. It is estimated that around 7 million Saudi Arabians are suffering from DM and that almost 3 million have a prediabetic range of blood sugar levels [23]. While insulin resistance plays an important role in the pathogenesis of T2DM, thyroid function is associated with insulin resistance even in subjects with a normal glucose tolerance [34, 35]. Likewise, the effect of both hyperthyroidism and hypothyroidism on insulin resistance, through different mechanisms, indicates the close link with DM [36]. This may reflect the influence of lower and higher levels of TSH in both conditions, respectively [32, 37]. Insulin resistance is associated with the insulin-like growth factor 1 signalling pathway that is involved in the proliferation of thyroid cells, an effect enhanced by TSH [37]. Similarly, many studies demonstrated the effect of insulin resistance on thyroid tissue proliferation and increases in nodule formation and goiter size [6, 9, 30, 38]. Likewise, the polymorphism in a single nucleotide (type 2 deiodinase (Dio2) results in a threonine change to alanine (Thr92Ala) at codon 92, the enzyme responsible for the conversion of T4 to T3, indicating close relationship to increased insulin resistance, T2DM and increased BMI [39, 40]. Additionally, genetic factors have an important influence: insulin resistance can reduce the rate of insulin-stimulated glucose transfer caused by a translocation of the glucose transporter type 2 (GLUT2) gene, leading patients to develop subclinical hypothyroidism with stimulatory effects of TSH [41]. On the other hand, novel missense variations in Thr92Ala are associated with insulin resistance [41]. Likewise, high levels of serum growth differentiation factor 15 were independently associated with TNs in patients with T2DM, in particular those over 60 years of age [6, 42]. This may reflect the close association between the two conditions and their potential effects on each other. The difference in the prevalence of DM among patients with TNs between our study and those conducted in other countries may be explained by the difference of lifestyle and dietary habits [36], a multifactorial etiology resulting from both genetic predisposition and the individuals' environment interactions [43] and the methodology adopted for each study. There was bidirectional influence between DM and thyroid diseases, including thyroid nodular diseases. Therefore, failure to recognize inadequate thyroid hormone levels in patients with DM and insulin resistance among those with thyroid disorders might be associated with poor management in both conditions [41]. Hence, screening for the presence of the other disease if the patient has either DM or thyroid disorders is highly recommended for proper management and better outcomes [13]. Interestingly, some medications (metformin and thyroxine) have positive and beneficial effects on both T2DM and thyroid diseases, and other medications (sulfonylureas, thiazolidinediones and antithyroid drugs such as methimazole) can negatively impact both, respectively [13]. In contrast, some clinical studies reported no significant influence of insulin resistance on the pathogenesis of TNs; hence, some other pathological mechanisms may be more prominent during TN formation and carcinogenesis [17, 44]. Our study and many current clinical studies revealed that advanced age is a significant predictor for DM in patients with TNs conducted in China [8-10, 38], Turkey [31] and Korea [32]. This may be explained by the fact that thyroid dysfunction is common in the elderly, which may take on different clinical conditions: clinical and subclinical hypo- and hyperthyroidism, thyroid nodular diseases and thyroid cancer [45]. Similarly, the multimorbidity of thyroid diseases and elements of metabolic syndrome (DM, hypertension and dyslipidemia) are quite common in the elderly [19, 46]. TNs in advanced age were associated with changes in the thyroid gland that accompany aging [47]. The age-related changes in the thyroid gland include the degeneration of thyroid cells, leading to fibrosis, infiltration of inflammatory cells, thyroid follicle alteration, and thyroid nodular diseases [47]. Thus, screening for TNs in female and elderly individuals, especially among patients with DM, is of paramount value. Our study demonstrated a significant association between the presence of hypertension and T2DM in patients with TNs. Similarly, a significant association was obtained in recently published data [8, 15, 18]. This may be related to a strong association between thyroid diseases and metabolic syndrome elements, as documented in some studies across the globe: China [19, 46], Korea [32], Turkey [31], Italy [7] and Argentina[33]. Likewise, metabolic syndrome is characterized by insulin resistance that enhances the proliferation of thyroid cells and TNs with an increased risk of progression to carcinoma [37, 48]. Additionally, isolated systolic hypertension was observed in patients with thyroid cysts [49] as well as in those without evidence of atherosclerosis and who were not taking medications for hypertension [50]. The current study showed a significant association between DM and both LDL and HDL among patients with TNs. Moreover, higher levels of LDL were significantly higher in participants with DM than in those without, indicating that it may have significant risk for developing thyroid nodular diseases among patients with DM. This result coincides with similar outcomes of significant association from some studies regarding LDL [18, 51, 52]. On the other hand, our study demonstrated significant higher levels of HDL among patients with DM and thyroid nodular disease, as reported in one study [53]. While HDL emerged as a significant protective factor in these patients [54, 55], other studies documented a nonsignificant association [10, 38]. The current study and recently published studies revealed that both cholesterol and triglyceride levels were not significantly associated with DM and TNs [10, 38]. Interestingly, statin therapy was associated with a decrease in the dominant TN volume among patients with DM, which might be attributed to the antiproliferative effects of statin therapy on the TNs [51, 52]. The current study showed that lower levels of T3 were a significant predictor for DM for patients with thyroid nodular diseases. This result was strengthened with a similar significant association of lower levels of T3 with the risk of developing T2DM [56] and gestational DM [57]. This may be explained by the influence of Dio2, the enzyme responsible for the conversion of T4 to T3 [40], which is associated with an increased risk of increased insulin resistance and T2DM [39]. The results of the present study are in accordance with the outcomes of many studies that have shown no significant associations between DM and other associated predictors (gender, FT4, TSH, thyroid status, hematological indices, vitamin D levels and the ACR TI-RADS scoring system) [38, 58-60].

### Limitations

The study was retrospective and from one center. Other factors, such as thyroid antibodies, iodine levels, type of DM, glycemic control, the duration of DM, nutritional patterns, exposure to radiation, genetic analysis and environmental factors, were not assessed.

### Conclusion

There was a high prevalence of DM among patients with thyroid nodular disease. Age, hypertension, FT3, LDL and HDL were significant predictors for DM among patients with TNs in eastern region of the KSA.

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## Conflict of Interest

The authors declare that there is no conflict of interest.

## Informed Consent

Not applicable.

## Author Contributions

Conceptualization: IRM, AMK and HA. Methodology: FHA, NME, SH and MAS. Data curation: FHA, MAS, SH, AMK and NME. Formal analysis: IRM and HA. Investigation: FHA, MAS, SH, AMK and NME. Writing - original draft preparation: IRM, HA and AMK. All contributors reviewed the manuscript.

## Data Availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

## Abbreviations

KSA: Kingdom of Saudi Arabia; DM: diabetes mellitus; T2DM: type 2 diabetes mellitus; TNs: thyroid nodules; FT4: free thyroxine; FT3: free triiodothyronine; T3: hormone triiodothyronine; T4: thyroxine; TSH: thyroid-stimulating hormone; 25(OH)D: 25-hydroxyvitamin D; LDL: low-density lipoprotein; HDL: high-density lipoprotein; AOR: adjusted odds ratio; IQR: interquartile range; BMI: body mass index; CI: confidence interval; SD: standard deviation; ACR TI-RADS: The American College of Radiology Thyroid Imaging Reporting and Data System

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