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Research Article

Association of TPO Gene (rs 2048722) Polymorphisms and Serum Level of Thyroid Hormones with Papillary Thyroid Cancer

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Abstract

Background: Papillary thyroid carcinoma (PTC) is the most prevalent form of thyroid cancer, making up about 80% of cases. It is influenced by both genetic and environmental factors, making it the most prevalent form of thyroid cancer. ***Objective***: Determine the connection between PTC and polymorphisms in the thyroid peroxidase gene (TPO, rs2048722) as a risk factor, as well as the changes in thyroid hormone serum levels. ***Methods***: The study involved 52 PTC patients and 48 healthy controls. We looked into the link between a type of TPO polymorphism and the risk of getting PTC by finding and genotyping TPO (rs2048722) C/T in healthy people and people who had PTC using T-ARMS-PCR and checking thyroid hormone levels in the Al-Diwaniyah Governorate. ***Results***: The polymorphism TPO (rs2048722) increased the PTC risk. According to multiple genetic models, homozygous TT genotypes increased the risk of PTC in the test by 4.03 times relative to other genotypes, and a heterozygous C/T genotype increased the risk by 2.09 times. Patients with PTC have elevated TSH. Patients over 50 exhibited greater mean values than the control group. In addition, T3 and T4 blood levels dropped significantly and increased overall. Compared to other groups, patients aged 50 and older had lower mean T3 levels. ***Conclusions***: In the Al-Diwaniyah Governorate, there was strong evidence that the TPO rs2048722 polymorphism was linked to a higher risk of PTC. This risk was affected by age, gender, and serum thyroid hormone levels.

Keywords: Papillary thyroid carcinoma, Risk factor, rs 2048722, TPO.

اقتران تعدد الاشكال لجين TPO (rs 2048722) ومستوى مصل هرمونات الغدة الدرقية مع سرطان الغدة الدرقية الحليمي

الخلاصة

الخلفية: سرطان الغدة الدرقية الحليمي هو الشكل الأكثر انتشارا لسرطان الغدة الدرقية، حيث يشكل حوالي 80٪ من الحالات ويتأثر بالعوامل الوراثية والبيئية، مما يجعله أكثر أشكال سرطان الغدة الدرقية انتشارا. **الهدف**: تحديد العلاقة بين PTC وتعدد الأشكال في جين بيروكسيديز الغدة الدرقية (rs204722) الدرقية كعامل خطورة، وكذلك التغيرات في مستويات المصل من هرمون الغدة الدرقية. **الطريقة**: شملت الدراسة 52 مريضا ب PTC و 48 شخصا من الأصحاء. نظرنا في العلاقة بين نوع من تعدد أشكال TPO وخطر الإصابة ب PTC من خلال إيجاد والتنميط الجيني C/T (rs2048722) TPO في الأشخاص الأصحاء والأشخاص الذين لديهم PTC باستخدام T-ARMS-PCR وفحص مستويات هرمون الغدة الدرقية في محافظة الديوانية. **النتائج**: زاد تعدد الأشكال TPO (rs2048722) من خطر PTC وفقا لنماذج جينية متعددة، وازدادت الأنماط الجينية TT متماثلة الزيجوت من خطر PTC في الاختبار بمقدار 4.03 مرة مقارنة بالأنماط الجينية الأخرى، وزاد النمط الجيني C/T غير المتجانس من الخطر بمقدار 2.09 مرة. المرضى الذين يعانون من PTC لديهم ارتفاع في مستوى TSH. أظهر المرضى الذين تزيد أعمارهم عن 50 عاما قيما متوسطة أكبر من المجموعة الضابطة. بالإضافة إلى ذلك، انخفضت مستويات الدم من T3 و T4 بشكل ملحوظ وزادت بشكل عام. بالمقارنة مع المجموعات الأخرى، كان لدى المرضى الذين تتراوح أعمارهم بين 50 وما فوق مستويات T3 أقل. **الاستنتاجات**: في محافظة الديوانية، كان هناك دليل قوي على أن تعدد الأشكال TPO rs2048722 كان مرتبطا بزيادة خطر الإصابة ب PTC. وتأثر هذا الخطر بالعمر والجنس ومستويات هرمون الغدة الدرقية في الدم.

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INTRODUCTION

Thyroid cancer is becoming more common every year, greater than all other cancers put together (including leukemia, pancreatic cancer, stomach cancer, and liver cancer). Typically, these thyroid cancers, originate from the papillaries, are small and remain contained. After 20 years, 99% of individuals diagnosed with these small, locally situated papillary thyroid cancers will still be alive [1]. Treatment options for numerous of these tumors include thyrotropin suppression treatment and radioactive iodine ablation. The research revealed the following findings: While these treatments are effective for more advanced thyroid cancers [2], the incidence of thyroid cancer in women is approximately three times higher than in men. Cancer, which affects women between the ages of 33 and 70, is quite

common. The study revealed a significantly greater risk of differentiated thyroid carcinoma (DTC) among participants older than 55 years (HR 1.78). PTC is a secondary malignancy in women diagnosed with thyroid cancer, which is concerning given the young average age at diagnosis and excellent survival rates. According to [3], women who have thyroid cancer often develop a PTC as a secondary cancer. The female thyroid cancer rate is around three times higher than the male thyroid cancer rate [4]. In recent years, evidence has mounted indicating genetic factors played a major role in PTC's etiology. Reference [5] used genome-wide association studies (GWAS) to find many SNPs in the PTC locus and other gene variations that increase susceptibility. The TPO gene, which specifies a protein-containing heme linked to the cell membrane, is found on the surface of every thyroid follicular cell. It plays a critical role in thyroid hormone production [6]. The TPO gene catalyzes iodide oxidation, TG iodination, and iodothyronine coupling [7]. Researchers have investigated a variety of thyroid disorders caused by changes in the TPO gene, including congenital hypothyroidism, autoimmune thyroiditis, and papillary thyroid cancer [8]. Researchers have conducted numerous studies to examine the ratios between various single nucleotide polymorphisms of the TPO. Many studies have also indicated the existence of a positive correlation. PTC, or papillary thyroid cancer, is the most prevalent type, based on the findings. The distribution of frequencies was significantly different when considering the co-dominant mode. The control and study groups differed in their genotypes. The research highlighted the homozygous TT genotype (OR = 4.03) and heterozygous C/T genotype (OR = 2.09) as important risk factors. This means that the risk of illness development is around four times higher for patients with the homozygous TT genotype than for those with other genotypes. Researchers reported a statistically significant difference when they compared the patient and control groups using dominant and recessive mode analyses [9]. Shen *et al*. (2023) observed an increased risk of papillary thyroid cancer (PTC) in a Kazakh population study that linked the risk of PTC susceptibility candidate gene 2 (PTCSC2) at locus rs965513; the study found that the TPO rs2048722, PTCSC2 rs925489, and SEMA4G rs4919510 polymorphisms were linked to a higher risk of THCA [10]. Other factors that played a role were gender, age, smoking, and alcohol intake.

METHODS

Study design and sampling

This case-control study comprises 100 blood samples obtained between September 2023 and January 2024. 52 patients with thyroid cancer and 48 healthy individuals without any chronic diseases, thyroid nodules, or thyroid hormone disorders provided the samples. This brings the total number of blood samples collected to 100. After their diagnosis, specialist oncologists at Al-Diwaniyah Teaching Hospital (Oncology Consultation), Al-Diwaniyah Governorate, took blood samples from individuals diagnosed with papillary thyroid carcinoma. After obtaining initial approvals from the Al-Diwaniyah Health Directorate and patient assent, we collected demographic information on each participant. The current study is divided into physiological (hormonal) and molecular sections. The chemiluminescence immunoassay system of the Mindray CL 900i device was used to measure the concentrations of the hormones TSH, T3, and T4 in patients' blood. The Tetra-ARMS-PCR method was used to perform genetic polymorphism for the TPO gene (rs2048722) C/T variation, using a specific set of primers. 5 ml of venous blood was drawn from the healthy subjects and TPC patients at Al-Diwaniyah Teaching Hospital from October 2023 until February 2023 in 2024 AD. Their ages were 33–75 years. 2 ml was placed in tubes containing the anti-seizure substance EDTA to conduct the genetic aspect of the study; it was stored at a temperature of -20 °C until a decision was made. For the hormonal aspect, the 3 ml were put in gel tubes and then at a temperature of 37 ºC for a period of 10 min, then the blood was centrifuged (3500 cycles/minute) for a period of five minutes; later, the levels of TSH, T3, and T4 were measured. The concentration of hormonal parameters (thyroid hormones) was measured by a chemiluminescence immunoassay system (Mindray CL 900i) (Shenzhen Mindray Biomedical Electronics Co., China). The CL-series T4 and T3 assay is a chemiluminescent immunoassay (CLIA) for quantifying free T4 and T3 in human serum or plasma.

Genomic DNA extraction

After extracting the DNA from the blood samples according to the manufacturer's instructions, Gene Aid's gSYAN extraction of DNA kit for frozen blood (USA) was used to estimate genomic DNA. A DNA purity test was conducted to determine the concentration of DNA in the blood. The test was evaluated by reporting the readout at 260 and 280 nm with a nanodrop spectrophotometer (THERMO, USA). After that, the T-ARMS-PCR approach identified and mapped the TPO (rs2048722) C/T gene polymorphism in samples from both patients and healthy controls. We created the ARMS-PCR master mix with the GoTaq® G2 instrument. We used the Green Master Mix kit to construct a T-ARMS-PCR master mix. We followed the manufacturer's directions and ran two reactions on each sample with the PCR reaction mix using T-ARMS. We placed the PCR master mix components in an Exispin vortex centrifuge and spun them at 3000 rpm for three minutes. We next placed it in a PCR thermocycler (BioRad, USA). Examining T-ARMS-PCR End Results We used agarose gel electrophoresis to examine the T-ARMS-PCR products.

Statistical analysis

The Software for Social Science Statistics (SPSS) version 26 was used to conduct statistical analysis of the data. Variables were represented using numbers and percentages, with mean±standard deviation (SD) for normally distributed variables. The Chi-square test is used to estimate the dissimilarity in means between any two normally distributed variables, whereas the independent samples t-test and ANOVA test are used to compare differences in means between two or more groups. The level of significance was assessed using a p-value of less than 0.05.

RESULTS

In this study, we enrolled 52 subjects diagnosed with papillary thyroid carcinoma and 48 healthy subjects served as controls. Table 1 displays the demographics of both the patients and the control group subjects.

Table 1: Characteristics of patients with papillary thyroid cancer and healthy controls

Characteristic	Patients (*n*=52)	Controls (*n*=48)	*p*
Age (year)	49.40±8.80	47.20±12.62	0.313
Male	7(13.5)	12(25.0)	0.142
Female	45(86.5)	36(75.0)	
TSH mIU/L	9.70±1.48	2.54±0.177	<0.001
T3 nmol/L	0.93±0.044	0.98±0.047	0.421
T4 µg/dL	9.36±0.37	9.86±0.45	0.405

Values were expressed as frequency, percentage, and mean±SD.

According to age, the mean age of patients with papillary thyroid cancer was 49.40±8.80 years old and that of control subjects was 47.20±12.62 years old and there was no significant difference between both groups (p=0.313). Overall, the study included 19 (17.0%) males and 81 (81.0%) females. Patients with papillary thyroid cancer included 7 (13.5 %) cases of male gender and 45 (86.5%) cases of female gender, while control subjects included 12 (25.0%) cases of male gender and 36 (75.0%) cases of female gender, and there was no significant difference in the frequency distribution of patients and control subjects according to gender (p=0.142). Table 1 shows that TSH levels were significantly higher in people with papillary thyroid cancer compared to healthy controls (9.70±1.48 mIU/L vs. 2.54±0.177 mIU/L, p<0.001). Furthermore, T3 concentrations in patients with papillary thyroid cancer were non-significantly lower than in healthy control subjects (0.9±0.044 nmol/L and 0.98±0.047 nmol/L, respectively, p= 0.421). T4 levels were not significantly lower in people with PTC than in healthy control subjects (9.36±0.37 µg/dL *vs.* 9.86±0.45 µg/dL, p=0.405). Table 2 and Figure 1 display the receiver operating characteristic (ROC) we used. Analysis to find out how well thyroid hormone measures (TSH, T3, and T4) could distinguish between healthy control subjects and PTC patients. As long as the TSH level is higher than 3.65 mIU/L, the test is more sensitive (80.8%), specific (81.2%), positive predictive (82.4%), and negative predictive (79.6%).

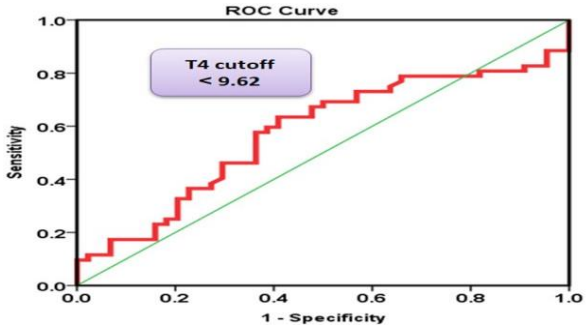

Figure 1: The TSH, T3, and T4 levels were analyzed using ROC curve to determine a potential diagnostic cutoff value. Curve in red represents TSH levels to differentiate between healthy control participants and patients with PTC. Green colored curve represents T3 level for PTC patient classification compared to healthy controls.

The area under the curve (AUC) value is 0.822 (95% CI, 0.731–0.914, p<0.001). Also, use an ideal T3 cutoff value below 0.95 nmol/L to tell the difference between PTC patients and healthy control subjects. This will give you a sensitivity of 57.7%, a specificity of 56.0%, a PPV of 60.0%, and an NPV of 58.3%. In Table 2, T4 level below 9.62 µg/dL can tell the difference between PTC patients and healthy control groups.

Table 2: Roc Curve of TSH, T3 and T4

Characteristic	TSH	T3	T4
Cutoff value	>3.65	<0.95	<9.62
p-value	<0.001	0.049	0.031
Sensitivity (%)	80.8	57.7	65.4
Specificity (%)	81.2	56.0	60.4
PPV (%)	82.4	60.0	64.2
NPV (%)	79.6	58.3	61.7
AUC (95% CI)	0.822 (0.7310.914)	0.553 (0.435-0.671)	0.625 (0.559-0.691)

CI: Confidence interval, AUC: Area under curve.

It has an AUC of 0.625 (0.559–0.691), a sensitivity of 65.4%, a specificity of 60.4%, a PPV of 64.2%, and an NPV of 61.7%. Table 3 displays the correlations between hormonal parameters and demographic characteristics.

Table 3: Correlations between hormones levels and demographic characteristics PTC patients

Parameters		TSH	T3	T4
TSH	*r*	1		
	p			
T3	*r*	-0.278	1	
	p	0.036		
T4	*r*	-0.347	0.470	1
	p	0.012	0.001	
Age	*r*	0.148	0.196	0.192
	p	0.296	0.165	0.174
Gender	*r*	0.130	0.197	-0.167
	p	0.360	0.161	0.236

r: correlation coefficient

Analysis of the TPO distribution (RS2048722) We used the T-ARMS-PCR method to identify a polymorphism in the C/T gene, which contains three genotypes: CC, CT, and TT. the C/T gene was found to have a polymorphism utilizing the T-ARMS-PCR technique. For the CT heterozygote, a 211-bp result showed both the C and T alleles. For the lane (TT)

mutant-type homozygote, a 250-bp T-ARMS-PCR product showed only the T allele. The 404bp T-ARMS-PCR product displayed an external control (Figure 2).

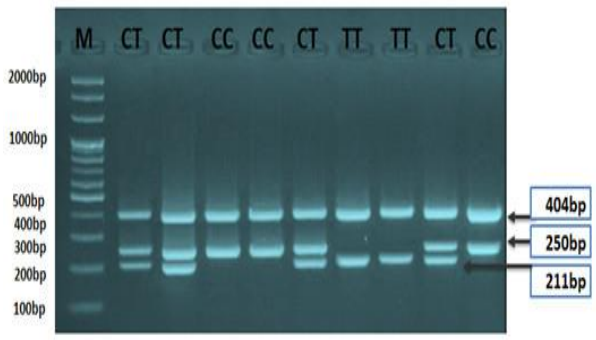

Figure 2: Agarose gel electrophoresis of the T-ARMS-PCR product, which was used to analyze the TPO (rs2048722) C/T gene polymorphism. M stands for the marker. For the CC wild type homozygote lane, the 250 bp T-ARMS-PCR result showed only the C allele. In the lane (TT) mutant type homozygote, the 211bp T-ARMS-PCR product alone showed the T allele, whereas in the (CT) heterozygote, both the 250bp and 211bp products showed the C and T alleles. The T-ARMS-PCR fragment exhibited the external internal control at 404 base pairs.

All study groups maintained Hardy-Weinberg equilibrium in relation to the genotype distribution. The frequencies of TT genotypes were higher in PTC patients than in their controls, with a statistically significant difference (p=0.044). In Table 4, the T allele of TPO (rs2048722) C/T was more frequently observed with PTC compared to healthy subjects (p=0.002). In particular, after a systematic comparison between TPO (rs2048722) C/T genotypes and thyroid hormone levels, the current results show the mean levels of serum TSH hormone were higher in patients with the TT genotype in comparison with other groups, but the difference was non-significant (p=0.602).

Table 4: TPO (rs2048722) C/T POLY genotype frequency in TPC patients and healthy subjects

Mode	*TPO (rs2048722)*	Patients (n=52)	Controls (n=48)	p	OR	95% CI
Co-dominant	TT	12(23.1)	4(8.3)		4.03	1.17-13.9
	C/T	14(26.9)	9(18.8)	0.044	2.09	0.78 -5.57
	CC	26(50.0)	35(72.9)			Reference
Dominant	TT+C/T	26(50.0)	13(27.1)	0.018		Reference
	CC	26(50.0)	35(72.9)		0.371	0.16-0.85
Recessive	TT	12(23.1)	4(8.3)	0.044	3.3	1.1-11.6
	C/T+CC	40(76.9)	44(91.7)			Reference
Alleles	T	38(36.5)	17(17.7)	0.002	2.67	1.38-5.17
	C	66(63.5)	79(82.3)			Reference

Values were expressed as frequency and percentage

The mean levels of serum T3 hormone were 1.48±0.57 for people with the CC genotype, 0.94±0.113 for people with the CT genotype, and 0.92±0.066 for people with the TT genotype. People with the TT genotype had lower mean levels of serum T3 hormone than people in the other groups, but the difference wasn't statistically significant (p=0.643). Furthermore, in comparison to other groups, patients with the TT genotype had lower mean levels of serum T4 hormone, but the difference was non-significant (p=0.794) (Table 5).

Table 5: The association between ARMS-PCR finding and hormonal levels in PTC patients

Hormones	ARMS-PCR finding			p*
	CC genotype (n=26)	*CT genotype* (n=14)	*TT genotype* (n=12)	
TSH				
Mean	10.43±2.16	7.22±2.63	10.98±3.25	0.602
Range	0.14–37.22	0.17–30.02	0.43–27.05	
T3				
Mean	1.48±0.57	0.94±0.113	0.92±0.066	0.643
Range	0.44–15.88	0.56–1.40	0.47–1.80	
T4				
Mean	10.24±0.88	9.95 ± 0.64	9.38 ± 0.96	0.794
Range	4.68–15.32	1.60–15.88	3.18–14.33	

Values were expressed as mean±SE. * Analyzed using ANOVA.

DISCUSSION

Papillary thyroid carcinoma (PCT) is one of the most common forms of thyroid cancer and affects people all over the world. As shown in Table 1, the age group of adults over 50 years old comprises the biggest percentage (49.40%) of the patients, according to the present findings. This corresponds to the findings, which demonstrated that papillary thyroid cancer (PTC) is more common in older patients, particularly those over the age of 50. It also agrees with the findings of Díez *et al*. [11] regarding patients diagnosed with papillary carcinoma of the thyroid with advanced-stage disease (III/IV) who are 55 years of age or older. Stage III/IV indicates that the cancer has spread to other sensitive areas of the body, such as the lungs and bones, or that there is spasm in the external tissues, including the large blood vessels. Worldwide, the incidence rates of thyroid cancer have been steadily rising for decades, with a greater increase in papillary carcinomas compared to other forms and a higher increase in females than males. The causes of the rising incidence and gender disparities in thyroid cancer are unclear, and the only known risk factor is the female gender [9]. There were 45 females (86.5% of the total) and 7 males (13.5%) among the patients with papillary thyroid carcinoma in the present study's demographic analysis, as shown in Table 1. The results of this investigation agreed with a previous study that suggested the gender difference in PTC may be attributed to the fact that a woman's hormone levels change during pregnancy and the menstrual cycle [10]. The majority of women reach or enter menopause between the ages of 40 and 49, which also happens to be the peak incidence of papillary thyroid cancer in this age group [9]. It is well

established that sex hormones are significant carcinogens for breast and prostate cancers. Hormone-specific nuclear receptors control gene expression and tumor cell biology by regulating the actions of sex hormones, particularly estrogen [12]. The α- and β-estrogen receptors, which regulate the effects of estrogen, are expressed in papillary thyroid cancer [13]. Polymorphisms in estrogen receptors may be a risk factor for thyroid cancer, as stated by [14]. Estrogen, in contrast to male sex hormones, can greatly accelerate cell proliferation in thyroid cancer cell lines [15]. It alters the expression of subtypes of estrogen receptors in cell lines that have been developed from thyroid carcinoma. The effects of estrogen on thyroid cancer cell lines are type-specific, as stated by [16]. The levels of estrogen receptor-α are considerably increased in papillary thyroid carcinoma. According to Krashin *et al*. [17], estrogen dramatically increases the migratory rate, invasive characteristics, and proliferation rate of thyroid cancer cell lines. The findings show that the TSH hormone level was greater in the patient group when compared with the healthy control group. At 9.70±1.48 mIU/L, the average TSH level was found. Reference [18] confirmed what other studies had already shown: that individuals with PTC who had high TSH levels were more likely to develop papillary thyroid cancer. TSH is a key regulator of thyroid function because it controls thyrocyte proliferation. There is a strong association between blood TSH and the risk of thyroid cancer once it binds to its receptor on the membrane of thyroid follicular cells [19]. The fact that DTCs have a reduction in surface receptor TSHRs due to a drop in mRNA level was first recognized more than twenty years ago. Further, the cancer's aggressiveness is inversely related to the mRNA level of these receptors [20]. Differentiated thyroid cancer (DTC), which encompasses both papillary and follicular types of thyroid cancer, is marked by an increase in blood TSH levels due to decreased expression of the TSHR surface receptor. In terms of prognosis [21], we found evidence that higher TSH levels before surgery are associated with PTC. Organization, iodine intake, and thyroid hormone production and release are all regulated by TSH, which also promotes thyroid growth [22]. Furthermore, research suggests that levothyroxine, which inhibits TSH, can slow the disease's advancement, recurrence rates, and cancer-related death in patients with well-differentiated thyroid carcinoma [23]. The current findings provide credence to the theory that TSH is probably a carcinoma propagator, enhancing the growth and aggressiveness of thyroid cancer. It has been observed in recent years that elevated serum TSH is linked to a higher incidence of thyroid cancer and advanced-stage disease, and the average TSH rises with age. Knowing if elevated TSH in thyroid cancer patients happens independently of age is crucial because being older than 50 years old is a recognized prognostic factor for thyroid cancer. The current findings are in agreement with the study conducted by [24], which found that the mean serum TSH levels in individuals less than 40 years old, 40-49 years old, and above 50 years old were 8.94±2.27, 10.40±3.42, and 11.20±3.01, respectively. Patients older than 50 years old had higher mean TSH levels compared to younger patients; this finding is consistent with previous research showing that age is a significant prognostic indicator in staging systems for papillary thyroid cancer. This study confirms the findings of [15], which found that male patients had an average serum TSH level of 5.65±2.95 and female patients had an average level of 10.68±1.77. Interestingly, the results showed that female patients had higher mean levels than male patients. Who displayed the upper-level feminine? The cells have estrogen alpha and estrogen beta receptors because estrogen hormones are vital in the increase of TSH hormone. Neoplastic thyroid tissue expresses estrogen receptors and has the potential to release estrogen; its thyrotrophs, pituitary cells responsible for thyroid regulation, also have estrogen receptors, which lead to a shift in TSH secretion. They increase TSH production in response to estrogen activation. TSH increases the gland's production of thyroid hormone, which in turn promotes thyroid cancer. The current findings demonstrate that the average serum T3 levels in patients younger than 40 years were 1.00±0.07, in those aged 40–49 years old they were 0.89±0.072, and in those aged 50 and above they were 0.80±0.071. Patients older than 50 had the lowest average levels. Age categories were compared to other categories, and the average levels of serum T4 in males were 11.02±0.75 and in females were 9.68±0.51. The average levels were lower in female patients compared to male patients, but this difference was not statistically significant (p=0.318). Based on numerous studies, it has been shown that patients with papillary thyroid cancer (PTC) have elevated TSH levels due to a lack of the T3 hormone [25]. There was an increased risk of PTC associated with higher TSH levels than usual. The odds ratio (OR) was 1.58, with a 95% confidence interval (CI) ranging from 0.97 to 2.56, indicating statistical marginal significance. An increased risk of PTC was not significantly associated with serum concentrations of TT3, TT4, and FT4, which were either below or above the normal range. While there was no dose-response association for TT4 and FT4, the risk of PTC decreased as TSH levels increased (p= 0.0001) and TT3 levels decreased (p= 0.031) within the normal ranges. [26] The production of thyroid hormones is dependent on TPO. TPO, located on the top surface of thyroid follicular cells, facilitates iodide oxidation. According to [10], mutations in TPO are the leading cause of congenital hypothyroidism, a condition where the body does not produce enough thyroid hormone because of a permanent iodine organization malfunction. This study found that many Iraqi individuals have similar genetic variations within the TPO that put them at risk for PTC. Functional findings demonstrated that the TPO enzyme malfunction corroborated the functions of TPO rs2048722 polymorphisms in PTC in earlier investigations [10]. This study's findings provide new evidence linking TPO and PTC, which has been suggested by multiple research groups in

recent years [27], and provide support for the importance of TPO polymorphisms in disease development. Several SNPs in TPO are well-known. Thus, TPO (rs2048722) was chosen, and its genetic connections with PTC risk were assessed using Tetra-ARMS-PCR analysis. The goal was to find out if rs2048722 genetic variants could be a genetic marker for PTC susceptibility. In this study, the genotype frequencies of TPO (rs2048722) were measured in 52 patients with PTC and 48 healthy controls. Table 4 shows that there are statistically significant differences in the distribution of these frequencies between the two groups (p=0.044). The results showed that there is a higher vulnerability to PTC associated with the TPO (rs2048722) polymorphism. These findings are in line with those of [10], who demonstrated that in a stratified examination of Chinese individuals aged 44 and younger who smoked, the rs2048722 gene in TPO was likewise identified as a major risk gene for THCA. According to [28], there was another study that discovered that the case group had a greater frequency of the TT genotype and T allele of TPO (rs2048722) compared to the control group. However, the difference in frequency was not statistically significant.

Study limitations

The medical condition of thyroid cancer patients was an obstacle, as we faced difficulty in the blood collection process.

Conclusions

This results showed a strong link between variations in the TPO gene and papillary thyroid cancer (PTC), especially in people who had the homozygous TT genotype of the TPO gene (rs2048722). This suggests that the risk of disease development is around four times higher for patients with the homozygous TT genotype compared to people with other genotypes, and our results show that thyroid cancer rates rise with age, particularly among those aged ≥55 years.

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Conflict of interests

No conflict of interests was declared by the authors.

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Data sharing statement

Supplementary data can be shared with the corresponding author upon reasonable request.

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