ORIGINAL RESEARCH

Association of Thyroid Autoantibodies with Diabetic Nephropathy in Type 2 Diabetes Mellitus Patients

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ABSTRACT

Background • Diabetic nephropathy (DN) is one of the most common and severe complications in patients with type 2 diabetes mellitus (T2DM). Thyroid dysfunction has been associated with diabetes and its complications but the relationship between thyroid autoantibodies and T2DM-DN remains unclear.

Objective • The study aims to investigate the association between thyroid autoantibodies and diabetic nephropathy in patients with T2DM and analyze the expression of serum thyroid hormone levels in T2DM-DN patients and its prognostic value.

Methods • 117 patients with T2DM who visited our hospital from December 2020 to December 2022 were recruited and assigned to group A (65 patients with T2DM-DN) and group B (52 patients with T2DM without DN). Serum TH levels of patients with DN and normal diabetic patients were analyzed, and the prognosis of patients was evaluated.

Results • The results demonstrated that compared to group B, group A had higher serum cystatin C (cysC), serum creatinine (SCr), thyroglobulin antibody (TgAb), and urinary microalbumin/creatinine (UACR) levels, while the levels of free triiodothyronine (FT3), albumin (ALB), and estimated glomerular filtration rate (eGFR) were lower ($P < .05$). FT3 in group A2 was inferior to that in group A0 and group A1 ($P < .05$). After correction, the results demonstrated that the level of thyroid peroxidase antibody (TPOAb) in group A1 was superior to that in group A0 ($P < .05$). The positive rates of TPOAb (20%) and TgAb (23.08%) in patients with T2DM-DN were drastically superior to those in patients with T2DM without DN. Among the independent risk factors for DN, the OR of positive TPOAb was 8.125.

Conclusion • The level and positive rate of thyroid autoantibodies in patients with T2DM-DN were high and TPOAb positivity might be a risk factor for the occurrence of T2DM-DN. (*Altern Ther Health Med.* 2024;30(12):374-380).

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INTRODUCTION

Type 2 diabetes mellitus (T2DM) currently affects the majority of the diabetic population worldwide, accounting for approximately 90% of all cases.[1] Alarmingly, a large-scale global epidemiological study has projected that the global mortality rate associated with diabetes will exceed 7.7% by 2030.[2] The situation is particularly severe in China, where epidemiological data reveals a mortality rate of 11.6% due to hyperglycemia among individuals over 18 years old, corresponding to an estimated 114 million people affected by diabetes.[3]

Moreover, the coexistence of diabetes and thyroid dysfunction (TD) is prevalent among young individuals, with both conditions being common endocrine disorders. Metabolic disturbances involving insulin and thyroid hormone (TH) can potentially interfere with the proper functioning of each other.[4]

The key pathological characteristics of Type 2 diabetes mellitus (T2DM) include impaired insulin secretion and/or insulin resistance (IR). Diabetic nephropathy (DN) is a common microvascular complication of diabetes and is a significant factor in the development of end-stage renal disease (ESRD).[5] Although conventional treatments such as strict blood glucose control, protein intake reduction, hyperglycemia inhibition, and renin-angiotensin-aldosterone system antagonism can partially reduce the progression of DN in diabetic patients, they do not completely halt its progression. DN is typically characterized by damage to the glomeruli, interstitium, and capillaries; however, the specific causes and molecular mechanisms underlying these changes are not yet fully understood. Nonetheless, hyperglycemia, diabetes, and

proteinuria are recognized as major risk factors for the progression of DN.[6-8] Various factors contribute to the pathogenesis of DN, and thyroid dysfunction (TD) has recently emerged as a potential contributing factor. Previous studies have established a link between TD and diabetes, providing evidence that TD occurs more frequently in diabetic patients, particularly those with reduced thyroid function.[9]

Thyroid hormones (TH), including triiodothyronine (T3) and thyroxine (T4), play a crucial role in regulating metabolism and cellular functions throughout the body. Changes in TH levels can impact various physiological processes, including glucose metabolism, insulin secretion, and pancreatic function. Conversely, alterations in blood glucose levels can also affect thyroid function.[10] Therefore, the interaction between TH and DM has garnered significant attention.

In the context of DN, studies have explored the association between TH and the progression of renal damage in patients with T2DM. Subclinical hypothyroidism (SCH), characterized by normal thyroid function but elevated thyroid-stimulating hormone (TSH) levels, has been found to be more prevalent in T2DM patients with DN compared to those without DN. SCH has been directly linked to a decline in estimated glomerular filtration rate (eGFR) in T2DM patients.

Furthermore, research has indicated that increased TSH levels within the normal range are associated with a higher incidence of DN in T2DM patients.[11,12] However, studies specifically examining the relationship between TH and DN in individuals with normal thyroid function within the diabetic population are scarce. Most investigations have focused on DN progression in patients with hypothyroidism or SCH. However, some scholars believe that free triiodothyronine (FT3) levels in T2DM populations with thyroid function within the normal range have a negative correlation with the progression of DN.[13–15]

Research on the relationship between thyroid function and TH and DN in the normal diabetic population is of great significance for medical research on diabetes mellitus. For this reason, in this study, serum TH levels and prognosis were evaluated in patients with DN and normal diabetic subjects.

RESEARCH OBJECT AND METHOD

Research objects

A total of 117 patients with T2DM who visited Yiwu Central Hospital from December 2020 to December 2022 were recruited (the inclusion and exclusion criteria are shown in Table 1). Patients were enrolled into two groups based on the presence of DN (diagnostic criteria are shown in Table 1), and the basic clinical data of the patients were complete. Of these, there were 65 cases of T2DM-DN (group A) and 52 cases of T2DM without DN (group B). This study was approved by the Yiwu Central Hospital Ethics Committee, and all patients or family members signed an informed consent form.

DN was diagnosed according to the *China Clinical Guideline for Prevention and Treatment of Diabetic Nephropathy* (2019 Version): an increase in urinary microalbumin/creatinine (UACR) and/or an estimated decrease in eGFR, and other chronic renal diseases were excluded.

Table 1. Inclusion and Exclusion Criteria of Research Subjects

No.	Inclusion criteria
1	Typical symptoms of diabetes (including polydipsia, polyuria, polyphagia, and unexplained weight loss)
2	Random blood glucose ≥11.1 mmol/L
3	Fasting blood glucose (FPG) ≥7.0 mmol/L after at least 8 hours of fasting
4	Blood glucose ≥11.1 mmol/L 2 hours after oral glucose tolerance test
	Exclusion criteria
1	Subjects with history of primary or secondary renal disease other than DN
2	Subjects progressing to ESRD or requiring dialysis
3	Subjects with urinary system and other infected persons
4	Subjects with chronic consumptive disease such as malignant tumor and severe malnutrition
5	Subjects with severe acute and chronic diseases such as those affecting heart, lung, and liver
6	Subjects with history of other endocrine disorders (other than thyroid disease or diabetes)
7	Those currently taking drugs that affect thyroid function
8	Thyroidectomized patients
9	Pregnant or lactating patients

(1) Urine trace albumin was determined using a random urine test. Albuminuria could be diagnosed by random urine UACR ≥30 mg/g in two of the three random urine tests within 3–6 months, excluding infection and other interfering factors. Microalbuminuria: 30 mg/g≤ UACR ≤300 mg/g, and major albuminuria: UACR >300 mg/g.

(2) eGFR was tested. Age, sex, serum creatinine (SCr), cystatin C (cysC) concentration, and other parameters were used for calculation. The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation was adopted; when the eGFR of the patient was <60 mL min^{-1}.1.73 m^{-2}, a decrease in eGFR was diagnosed. The following conditions were excluded from being diagnosed as non-DN: (i) eGFR decreases rapidly; (ii) urine protein increases rapidly or nephrotic syndrome occurs; (iii) intractable diabetes; (iv) there is active urinary sediment (such as hematuria, proteinuria, white blood cells, and casts); (v) the disease is accompanied by symptoms or signs of other systemic diseases; (vi) over 30% reduction of eGFR after therapy with an angiotensin converting enzyme inhibitor or an angiotensin receptor antagonist within two to three months; and, (vii) ultrasound abnormality of the kidney.

Observation indexes

General data collected are as follows. Basic information and related medical history of the patient were included, such as sex, age, disease course, family history, smoking history, and cardiovascular and cerebrovascular disease history. Blood pressure was measured in the supine position using a standard mercury sphygmomanometer.

Detection indicators are shown as follows. All patients fasted for eight hours, and peripheral venous blood and clean middle section urine were drawn at 6:00 a.m. on the next day under a calm state. An automatic analyzer was employed to detect fasting blood glucose (FPG), glycated hemoglobin (HbA_{1C}), albumin (ALB), SCr, uric acid (UA), cysC, eGFR, total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL-C), low-density lipoprotein (LDL-C), urinary albumin-creatinine ratio (UACR), FT3, free thyroxine (FT4), TSH, thyroid peroxidase antibody (TPOAb), and thyroglobulin antibody (TgAb).

Statistical methodologies

All the data were statistically analyzed by SPSS 21.0. The normal or nearly normal distribution was denoted as the mean plus or minus standard deviation, while the skewed measurement data were indicated as medians (interquartile range). Count data were denoted as categories or percentages. For the comparison between different groups, if the measurement data conformed to the normal distribution and the homogeneity of variance, the independent sample *t* test or analysis of variance was adopted for processing; otherwise, the nonparametric test was used. If there was any difference between multiple groups, further pairwise comparisons were performed. Enumeration data were compared for differences using the chi-square test. A binary logistic regression analysis was utilized to explore the effects of different indicators on eGFR. All the results were considered to have considerable differences with $P < .05$.

RESULTS

Basic clinical data

In Table 2, 117 subjects were analyzed in total, including 64 males (54.7%) and 53 females (45.3%). The average age of the patients in the two groups was 57.26 ± 12.13 years old, and 65 patients (55.56%) had T2DM-DN. The analysis of general clinical data suggested that compared with group B, group A had substantial differences in terms of older adults, longer duration of diabetes, higher incidence of cardiovascular and cerebrovascular diseases, and higher systolic blood pressure (SBP) ($P < .05$). No great differences were found in the prevalence of diastolic blood pressure (DBP), diabetes, neuropathy, age, or smoking history ($P > .05$).

Biochemical index comparison

In Table 3, FPG, HbA_{1c}, UA, TC, TG, HDL-C, LDL-C, FT4, TSH, and TPOAb differed slightly between groups ($P > .05$). Relative to group B, group A had higher cysC, SCr, TgAb, and UACR, while FT3, ALB, and eGFR levels were lower ($P < .05$). After thyroid function was corrected by age, course of disease, history of cardiovascular and cerebrovascular diseases, smoking history, diabetes, ALB and cysC, the results demonstrated that TPOAb and TgAb in group A were superior to those in group B ($P < .05$) (Table 4).

Relationship between UACR and thyroid function

The patients were classified into A0 (UACR < 30 mg/g), A1 (30 mg/g≤ UACR ≤300 mg/g), and A2 (UACR > 300 mg/g) based on the UACR values. In Figures 1 and 2, the FT3 level in group A2 was inferior to that in groups A0 and A1 ($P < .05$). FT3 levels differed slightly between group A0 and group A1 ($P > .05$). No significant difference in the other four thyroid function indexes was revealed among the three groups of UACR ($P > .05$). After the index adjustment of age, course of disease, history of cardiovascular and cerebrovascular diseases, diabetes, smoking history, ALB, and cysC, the results demonstrated that TPOAb in group A1 was superior to group A0 ($P < .05$).

Table 2. Basic Clinical Data

Item		Group A (n = 65)	Group B (n = 52)	*P* value
Sex	Male (%)	34 (52.31%)	30 (57.69%)	.411
	Female (%)	31 (47.69%)	22 (42.31%)	.525
Age (years old)		59.94 ± 12.77	53.17 ± 11.05	<.050[a]
Course of disease (years)		11 (8-17)	9 (4-14)	<.050[a]
Disease history	History of cardiovascular and cerebrovascular diseases (%)	15 (23.08%)	4 (7.69%)	<.050[a]
	History of diabetes (%)	38 (58.46%)	28 (53.85%)	.433
Blood pressure	Systolic pressure (mmHg)	141 (122, 152)	127 (121, 142)	<.050[a]
	Diastolic blood pressure (mmHg)	81 (72, 86)	82 (71, 88)	.761
Smoking history (%)		26 (40.00%)	15 (28.85%)	.094
Neuropathy (%)		42 (64.62%)	34 (65.38%)	.758

[a]indicates that the difference between groups was remarkable ($P < .05$)

Table 3. Contrast of Biochemical Indicators

Index	Group A (n = 65)	Group B (n = 65)	*P* value
FPG (mmol/L)	9.27 (6.54, 11.71)	7.94 (6.51, 9.45)	.351
HbA1c (%)	8.08 (6.15, 10.08)	6.34 (6.58, 8.52)	.115
ALB (g/L)	40.38 (37.74, 42.26)	41.55 (39.21, 44.22)	<.050[a]
UA (umol/L)	327.81 (264.58, 415.40)	301.28 (250.58, 347.84)	.169
cysC (mg/L)	0.95 (0.72, 1.15)	0.74 (0.68, 0.81)	<.050[a]
SCr (umol/L)	65.49 (53.20, 79.96)	60.67 (53.87, 68.71)	<.050[a]
TC (mmol/L)	4.42 (3.74, 5.63)	4.13 (3.86, 4.95)	.178
TG (mmol/L)	1.74 (1.16, 2.97)	1.39 (0.75, 3.12)	.265
HDL-c (mmol/L)	1.04 (0.76, 1.18)	0.87 (0.78, 1.11)	.877
LDL-c (mmol/L)	2.71 ± 1.02	2.54 ± 0.63	.264
UACR (mg/g)	81.45 (44.65, 143.77)	15.68 (10.05, 22.62)	<.050[a]
eGFR (mL/min/1.73m^2)	84.59 (61.69, 104.52)	101.82 (97.35, 109.66)	<.050[a]

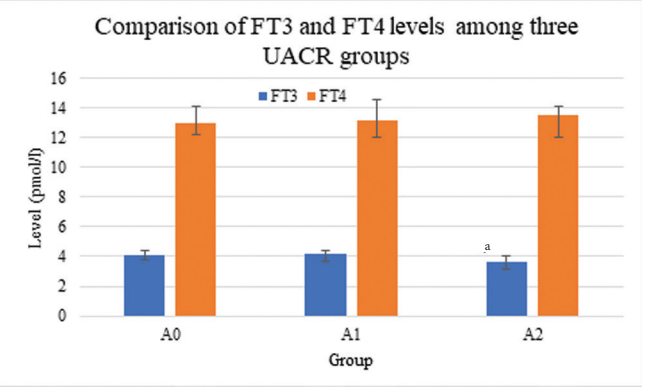
[a]indicates that the difference between groups was great ($P < .05$)

Table 4. Contrast of Thyroid Function

Index	Group A (n = 65)	Group B (n = 65)	*P* value
FT3 (pmol/L)	3.65 (3.16, 4.08)	4.23 (4.01, 4.55)	.089
FT4 (pmol/L)	13.65 (11.96, 14.43)	12.99 (12.14, 13.85)	.154
TSH (uIU/mL)	1.54 (1.02, 2.26)	1.41 (1.01, 2.24)	.223
TPOAb (IU/mL)	0.31 (0.15, 0.76)	0.23 (0.14, 0.41)	<.050[a]
TgAb (IU/mL)	1.57 (0.99, 3.58)	1.14 (0.73, 1.72)	<.050[a]

[a]indicates that the difference between groups was considerable ($P < .05$)

Figure 1. Comparison of FT3 and FT4 Levels Among the Three Groups of UACR.

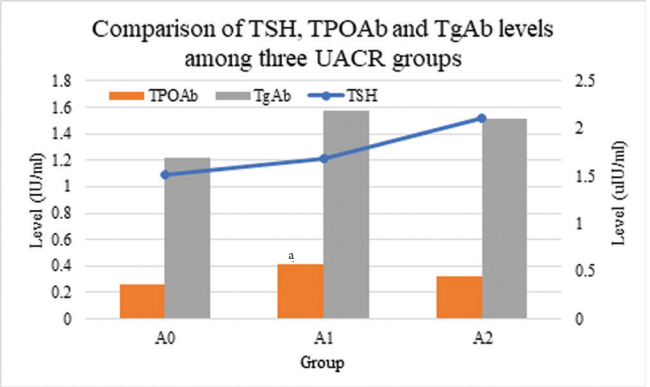


[a]Indicates drastic difference vs. the other two groups ($P < .05$)

Relationship between eGFR and thyroid function

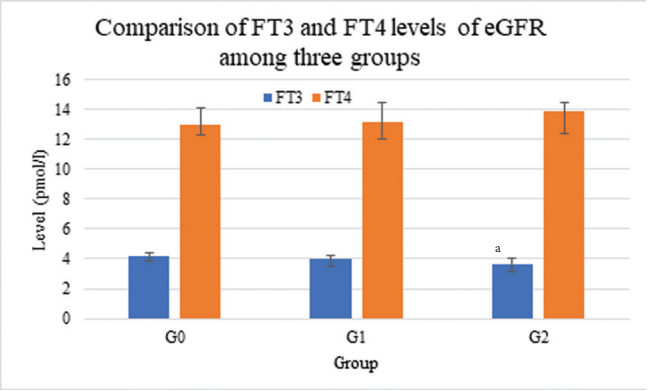
EGFR values were classified into the G0 group (eGFR ≥ 90 mL min^{-1}.1.73 m^{-2}), G1 group (60 mL min^{-1}.1.73 m^{-2} ≤ eGFR < 90 mL min^{-1}.1.73 m^{-2}), and G2 group (eGFR < 60 mL min^{-1}.1.73 m^{-2}). In Figures 3 and 4, the FT3 level in the G2 group was markedly inferior to that in the G0 group ($P < 0.05$). FT3 levels differed slightly between the G0 and G1 groups and between the G1 and G2 groups ($P > .05$). The

Figure 2. Comparison of Changes in TSH, TPOAb, and TgAb Levels Among the Three Groups of UACR.



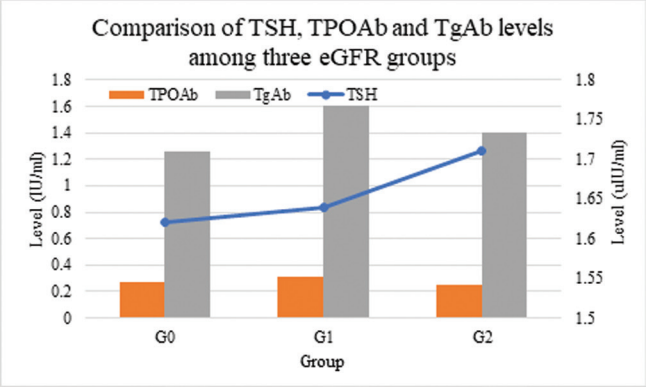
[a]Indicates marked difference vs. group A0 ($P < .05$)

Figure 3. Comparison of Changes in FT3 and FT4 Levels Among the Three eGFR Groups.



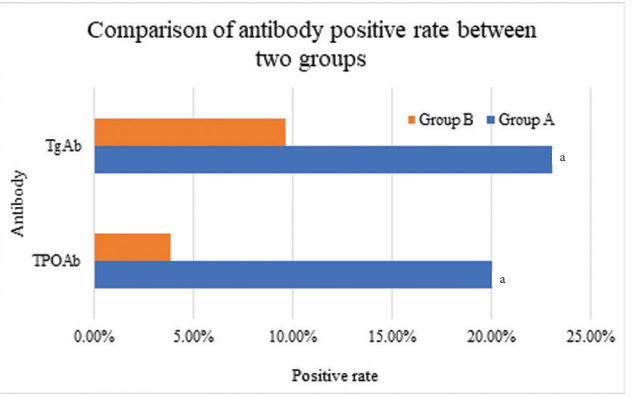
[a]Indicates marked difference vs. the other two groups ($P < .05$).

Figure 4. Contrast of TSH, TPOAb, and TgAb Levels Among the Three EGFR Groups.



other four thyroid function indicators showed no great differences among the three eGFR groups ($P > .05$). After the indexes such as age, course of disease, history of cardiovascular and cerebrovascular diseases, smoking history, diabetes, ALB, and cysC were adjusted, the results showed no marked difference in thyroid function among the various eGFR groups ($P > .05$).

Figure 5. Comparison of the Incidence of TPOAb and TgAb Between the Two Groups.



[a]Indicates remarkable difference vs. group B ($P < .05$)

Contrast of positive rates of TPOAb and TgAb

In Figure 5, there were 13 TPOAb-positive patients in group A, and the incidence rate was 20%. Whereas, there were two TPOAb-positive patients in group B, and the incidence rate was 3.85%. Group A had 15 TgAb-positive patients, with an incidence rate of 23.08%, while group B had 5 TgAb-positive patients which corresponded to an incidence rate of 9.62%. The chi-square test suggested that the positive rates of TPOAb and TgAb in group A were superior to group B ($P < .05$).

Risk forecast analysis

Binary logistic regression analysis suggested that TPOAb positivity was a risk factor for DN with an OR (95% CI) of 8.125 (0.77–54.33), thereby indicating that the incidence of DN in T2DM patients with TPOAb positivity was approximately 8 times superior to that in patients with TPOAb negativity. Additionally, there was no correlation between the thyroid function index and DN.

DISCUSSION

This study was a cross-sectional investigation that included 117 cases of Type 2 diabetes mellitus (T2DM) patients undergoing inpatient treatment. Specific inclusion and exclusion criteria were applied to select the participants. The findings of this research demonstrated that T2DM patients with diabetic nephropathy (T2DM-DN) exhibited a significant reduction in FT3 levels compared to T2DM patients without DN. Conversely, the TH levels were found to be higher in the T2DM-DN group. After adjusting for various factors such as age, disease history, cardiovascular and cerebrovascular disease history, smoking history, hypertension, albumin (ALB) levels, and cystatin C (cysC) levels, which may impact thyroid function, a reanalysis of thyroid function in T2DM patients revealed significantly elevated levels of thyroid peroxidase antibody (TPOAb) and TH in group A (T2DM-DN). Furthermore, when age, disease history, cardiovascular and cerebrovascular disease history, smoking history, hypertension history, ALB levels, and cysC levels were excluded as influencing factors, the research

results indicated that the microalbuminuria group had higher TPOAb levels. Additionally, due to reasons such as unadjusted age, disease history, cardiovascular and cerebrovascular disease history, smoking history, hypertension history, ALB levels, and cysC levels, the FT3 levels in group A were observed to decrease along with the decrease in estimated glomerular filtration rate (eGFR) levels. Among the subgroups in group A, the FT3 levels were the lowest in group A2). However, after adjusting for related influencing factors, none of these associations remained statistically significant.

Moreover, thyroglobulin antibody (TgAb) was found to be more prevalent in the population of T2DM-DN patients. Therefore, upon exploring the risk factors for T2DM-DN, the positive incidence rate of TPOAb was identified as an independent risk factor for the development of T2DM-DN, providing a valuable basis for the prevention of further progression of T2DM-DN.

Furthermore, our study revealed that patients in group A, compared to those with non-T2DM-DN, were characterized by older age, longer duration of onset, higher levels of thermistor, TPOAb, thyroglobulin antibody, and UACR, but lower levels of FT3 and eGFR. These findings are closely linked to the conclusion of our study. Previous research has demonstrated that when T2DM patients are categorized into subgroups based on UACR and eGFR levels, those in the large-scale albuminuria and low filtration group exhibit lower levels of FT3 and FT4, but higher levels of TSH.[16–18] In our study, we classified patients into three subgroups based on their UACR and eGFR levels. After adjusting for various factors related to thyroid nodule function, the results indicated that TPOAb levels were higher in certain microalbuminuria groups compared to the general proteinuria group. However, the TPOAb levels in most proteinuria groups were not significantly different, which may be attributed to the relatively small number of patients in the massive proteinuria group (the classification criteria for massive proteinuria include a urinary protein excretion of greater than or equal to 3.5 grams per day or a urine protein-to-creatinine ratio (UPCR) greater than or equal to 3000 mg/g (3.0 g/g) or 300 mg/mmol (0.3 g/mmol).

Studies have found that the FT3 level of patients with T2DM-DN has a positive correlation with the eGFR value. However, thyroid function was not found to be associated with eGFR after the interfering factors were corrected by the partial correlation method.[19] Therefore, our study yielded results that were inconsistent with previous research, likely due to the presence of numerous confounding factors that could have influenced thyroid function, leading to potential mixed analysis bias. Nevertheless, after adjusting for confounding components such as disease, age, hypertension, and albumin (ALB) levels, the impact of mixed analysis bias on the accuracy of the conclusions was mitigated. However, it is important to note that in recent years, there have been varying experimental findings regarding the positive rates of extra thyroid autoantibodies in different nephrotic populations. The study also highlighted that in the non-chronic dialysis nephrotic population, where all patients exhibited healthy serum free thyroxine (FT4) levels, the positive rate of thyroid autoantibodies in the serum increased as the estimated glomerular filtration rate (eGFR) value decreased.[20–22]

The findings of the study suggest that the positive rates of TPOAb (20%) and thyroglobulin antibody (23.08%) in patients with T2DM-DN were greatly superior to those in patients with T2DM without DN. However, in contrast, the results from a horizontal analysis study indicated that mean *in vivo* serum FT3 and FT4 levels in ESRD patients were greatly inferior to those in normal healthy subjects, while the TPOAb levels were not different from the mean thyroglobulin antibody levels. Therefore, DN developing into ESRD should be excluded when topics related to thyroid nodules and autoantibodies and DN are explored because ESRD may strongly interfere with the host's immunity.[23] Some research results have also pointed out that the level of TPOAb is greatly related to impaired glucose tolerance in patients with β-thalassemia.[24] Other researchers have shown that positive expression of TPOAb increases the risk of gestational diabetes mellitus in early pregnancy.[25,26] It is also believed that high-level TPOAb may be the main risk factor for the progression of diabetic small vessel diseases as a whole (including DN, diabetic retinopathy, and diabetic peripheral neuropathy) in type 2 diabetic patients with SCH and normal functional people. Nevertheless, relevant research results on the adverse impact of TPOAb positivity to T2DM-DN in the type 2 diabetic group without defining normal functional people are still unclear. In our study, logistic regression analysis was adopted to determine the result. Among all the independent risk factors for DN, the OR value of TPOAb positivity was 8.125, indicating that the risk of nephropathy in TPOAb-positive T2DM patients was approximately eight times superior to TPOAb-negative patients.[27–29]

However, the specific mechanism of DN due to thyroid autoantibody dysfunction is currently unclear. The latest basic research results show that, according to the chip data analysis provided by the Gene Expression Technology (GEO) system, three long-chain noncoding RNAs (lncRNAs), including Growth and Apoptosis Coherent Genome 15 (PEA15), Multigene Nonprotein Decoded RNA472 (LINC00472), and microRNA22 (MIR22 22), are potential detection markers of DN,[30–32] and the functional analysis is carried out based on the coding genome for its co-expression. The results demonstrated that most of these genomes were related to autoimmune thyroid diseases such as type 1 diabetes. Investigations have shown that 22.3% of patients with T2DM have many pancreatic autoantibodies, including glutamic acid decarboxylase antibody (GADA) and zinc transporter-8 antibody (anti-ZnT8), associated with autoimmune thyroid nodule lesions, and their anti-ZnT8 has become the main risk factor for immune cells to tolerate renal replacement therapy.[33,34] Furthermore, data suggested that the presence of the endothelin-1 (EDN1) rs1800541

(T-1370G) G allele and rs57072783T allele in white patients with Type 2 diabetes mellitus (T2DM) was closely associated with a decreased risk of diabetic nephropathy (DN). However, other data indicate that the levels of thyroid peroxidase antibody (TPOAb) and thyroglobulin antibody were higher in patients with the EDN1G5665T GG genotype compared to those carrying the T allele, and the TPOAb levels in individuals carrying the EDN1T-1370GG allele were also lower than those with the TT genotype. These findings suggest a potential cross-relationship between the occurrence of T2DM-DN and the development of thyroid autoantibodies with the EDN1 gene.[35–37]

The findings of our study provide important insights into the relationship between thyroid function and diabetic nephropathy (DN) in patients with normal thyroid function. We observed significant differences in serum thyroid hormone (TH) levels between patients with T2DM-DN and those with T2DM without DN, indicating a potential association between TH and the development and progression of DN. Here, we will discuss the implications of these findings, explore potential underlying mechanisms, address study limitations, and suggest directions for future research.

Firstly, our study demonstrated that patients with T2DM-DN had higher levels of thyroglobulin antibody (TgAb) and thyroid peroxidase antibody (TPOAb) compared to patients with T2DM without DN. These findings suggest that the presence of thyroid autoantibodies may play a role in the development of DN in patients with normal thyroid function. TPOAb positivity, in particular, was identified as an independent risk factor for DN. This indicates that autoimmune processes targeting the thyroid gland may contribute to the pathogenesis of DN.

Secondly, we observed lower levels of FT3 in patients with T2DM-DN compared to those without DN. This finding suggests a possible association between decreased FT3 levels and the development of DN. Thyroid hormones, including FT3, play crucial roles in regulating metabolism and cellular functions. Altered thyroid hormone levels may impact insulin sensitivity, glucose metabolism, and renal function, all of which are relevant to the development and progression of DN.

The observed differences in serum cystatin C (cysC), serum creatinine (SCr), urinary microalbumin/creatinine ratio (UACR), estimated glomerular filtration rate (eGFR), and albumin (ALB) levels further support the association between TH and DN. Higher cysC, SCr, and UACR levels, along with lower eGFR and ALB levels, were found in patients with T2DM-DN compared to those without DN. These markers reflect renal function and the extent of renal damage, indicating that TH may influence the progression of DN through its effects on the kidneys.

The mechanisms underlying the relationship between thyroid function and DN are likely multifactorial. One potential mechanism involves the interaction between thyroid hormones and renal hemodynamics, including alterations in glomerular filtration rate, renal blood flow, and tubular function. Thyroid hormones can affect the renin-angiotensin-aldosterone system and endothelial function, thereby influencing renal function. Additionally, the autoimmune component suggested by the presence of thyroid autoantibodies may contribute to the development of renal inflammation and damage in DN.

Despite the clinically significant findings, it is important to acknowledge the limitations of our study. Firstly, the sample size was relatively small, which may affect the generalizability of the findings. A larger-scale study involving a more diverse patient population would enhance the robustness of the results. Secondly, the cross-sectional design of our study limits our ability to establish causality. Longitudinal studies are needed to determine the temporal relationship between TH alterations and the development of DN. Furthermore, our study focused on patients with T2DM, and the findings may not be directly applicable to other types of diabetes.

Future research can build upon our findings to further elucidate the relationship between thyroid function and DN. Mechanistic studies are warranted to investigate the precise pathways through which thyroid hormones and autoantibodies influence renal function and the progression of DN. Additionally, prospective studies with larger sample sizes are needed to validate our results and explore the predictive value of thyroid function markers in identifying individuals at risk for DN. Interventional studies evaluating the impact of thyroid hormone modulation on DN outcomes could provide valuable insights into potential therapeutic strategies.

In summary, thyroid nodule function is associated with T2DM-DN. Therefore, the content and positive rate of TPOAb and thyroglobulin antibodies in the population with T2DM-DN are high, and TPOAb positivity is also a major risk factor for T2DM-DN. Hence, it is necessary to use further large-scale randomized clinical comparative experiments and prospective studies to further explore the relationship between TH level and the development of DN, in particular to study the effect of the positive rate of TPOAb on the generation and transmission of DN, thus indicating an effective method for the early treatment and diagnosis of DN.

CONCLUSION

In this study, the latest diagnostic criteria for DN were applied. By exploring the relationship between thyroid autoantibodies and DN in hospitalized patients with T2DM, we found that the positive expression of TPOAb had a certain significance for the occurrence of T2DM-DN. In patients with T2DM-DN, the level and positive rate of thyroid autoantibodies were high. Moreover, regression analysis suggested that the positive expression of TPOAb might be a risk factor for the occurrence of T2DM-DN.

AUTHOR DISCLOSURE STATEMENT

The authors declare that they have no competing interests.

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