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Low Circulating Free Triiodothyronine Levels are Association with Progression Diabetic Nephropathy in Patients with Type 2 Diabetes

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ABSTRACT

Background: Diabetic nephropathy (DN) is a significant consequence of T2DM that causes CKD and ESRD. Recent investigations have linked thyroid hormones, particularly free triiodothyronine (FT3), to DN progression. Low FT3 levels are linked to lower outcomes in chronic illnesses, including renal failure. This study investigated the relationship between type 2 diabetes and low circulating free triiodothyronine levels and nephropathy development.

Methods: We enrolled ninety-eight type 2 diabetic patients. Patients with type 2 diabetes who were 18 years of age or older met the inclusion criteria. Patient interviews, medical records, and laboratory tests were used to gather data. FT3 levels were measured in blood samples, and estimated glomerular filtration rates (eGFR) and urine albumin excretion rates were used to gauge how far along DN was. The statistical analysis was done with SPSS 23.0.

Results: Of the 98 participants, 28.6% showed progression of diabetic nephropathy. Patients with low FT3 levels (<2.0 pg/mL) had a higher rate of nephropathy progression (52.9%) compared to those with normal FT3 levels (15.6%). Multivariate regression analysis revealed that low FT3 levels were significantly associated with nephropathy progression ($\beta = 1.47$, $p < 0.001$) after adjusting for confounders.

Conclusion: Patients with type 2 diabetes have a substantial correlation between the development of diabetic nephropathy and low levels of free triiodothyronine in the blood. Thyroid hormone monitoring may be essential for controlling the progression of DN.

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Recommendations: To investigate the underlying mechanisms and assess the possible advantages of treatment approaches aimed at thyroid function in people with diabetes, more research is required.

Keywords: *Diabetic nephropathy, Type 2 diabetes, Free triiodothyronine, Chronic kidney disease, Thyroid hormones*

INTRODUCTION

A serious consequence of type 2 diabetes mellitus (T2DM) is diabetic nephropathy (DN), which is typified by gradual loss of renal function and chronic albuminuria. It continues to be the primary cause of end-stage renal disease (ESRD) and chronic kidney disease (CKD) worldwide. The possible involvement of thyroid hormones, specifically free triiodothyronine (FT3), in the development of DN has been brought to light by recent studies.

Insulin sensitivity and glucose metabolism are two metabolic processes that are significantly impacted by thyroid hormones. Patients with diabetes may experience severe effects from changes in thyroid function, which may exacerbate issues like DN. Reduced levels of FT3, the thyroid hormone's active form, have been linked to poorer results in a number of chronic illnesses, including disorders of the kidneys [1].

Numerous recent investigations have examined the connection between thyroid hormone levels and DN development. For example, a research in euthyroid patients with T2DM identified a strong correlation between lower FT3 levels and the severity of DN [1]. Lower FT3 levels may be able to predict the development of renal impairment in diabetic patients, as this study showed that they positively connected with estimated glomerular filtration rate (eGFR) and negatively correlated with urine albumin-creatinine ratio (UACR) [2].

Furthermore, a different study emphasised FT3's defence against renal injury. Higher FT3 levels have been linked to a lower incidence of diabetic kidney disease (DKD), according to a study. Even after controlling for additional risk factors such age, the length of diabetes, and HbA1c levels, this protective effect persisted [3]. The results of these investigations highlight how crucial it is to keep an eye on thyroid hormone levels in diabetic patients as part of a comprehensive plan to control and slow the progression of DN.

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Research also indicates that thyroid dysfunctions, including both hypothyroidism and hyperthyroidism, can adversely affect renal function. For example, individuals with hypothyroidism are at an increased risk of CKD due to mechanisms such as reduced cardiac output and altered renal hemodynamics. Similarly, hyperthyroidism has been linked to an increased risk of reduced kidney function, although the associations are less consistent [4].

The study aims to investigate the association between low circulating free triiodothyronine levels and the progression of diabetic nephropathy in patients with type 2 diabetes.

METHODOLOGY

Study Design

A prospective cohort study.

Study Setting

The study was conducted over a duration of six months at GMERS Medical College in Gandhinagar, Gujarat.

Participants

A total of 98 participants were recruited for the study.

Inclusion and Exclusion Criteria

Inclusion criteria included patients aged 18 years and above, diagnosed with type 2 diabetes, and who provided informed consent to participate in the study. Exclusion criteria were patients with a history of thyroid disorders, recent thyroid surgery, or those on medications that could affect thyroid function. Additionally, patients with acute or chronic kidney disease unrelated to diabetic nephropathy, pregnant women, and individuals unable to comply with the study protocol were excluded.

Bias

To minimize selection bias, consecutive sampling was used to recruit participants. Information bias was mitigated by employing standardized data collection procedures and using calibrated instruments for biochemical measurements.

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Data Collection

Data were collected through patient interviews, medical record reviews, and laboratory investigations. Blood samples were obtained to measure free triiodothyronine levels and other relevant biochemical parameters.

Procedure

Participants were subjected to a detailed clinical examination. Blood samples were collected after an overnight fast and analyzed for free triiodothyronine levels using standardized assays. The progression of diabetic nephropathy was assessed based on urinary albumin excretion rates and estimated glomerular filtration rates (eGFR) at baseline and at the end of the study period.

Statistical Analysis

The statistical analysis was done with SPSS 23.0. The baseline characteristics of the subjects were compiled using descriptive statistics. Multivariate regression models were utilised to examine the correlation between the advancement of diabetic nephropathy and free triiodothyronine levels, whilst accounting for plausible confounding variables. Less than 0.05 was the threshold for statistical significance.

RESULT

The study comprised 98 individuals with type 2 diabetes in total. The gender distribution of the participants was 46 females (46.9%) and 52 males (53.1%), with a mean age of 58.3 ± 10.4 years. Table 1 provides a summary of the study participants' baseline characteristics.

Table 1: Baseline Characteristics of Study Participants

Variable	**Mean ± SD / n (%)**
Age (years)	58.3 ± 10.4
Gender (Male/Female)	52 (53.1%) / 46 (46.9%)
Duration of Diabetes (years)	12.5 ± 6.2

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HbA1c (%)	8.2 ± 1.3
Baseline eGFR (mL/min/1.73m²)	78.4 ± 20.5
Baseline Albuminuria (mg/g)	82.3 ± 35.7
Free Triiodothyronine (pg/mL)	2.5 ± 0.6

During the 6-month follow-up period, 28 participants (28.6%) showed progression of diabetic nephropathy as indicated by a decline in eGFR or an increase in albuminuria. The mean change in eGFR and albuminuria from baseline to the end of the study period are presented in Table 2.

Table 2: Changes in eGFR and Albuminuria

Variable	Baseline	6 Months	Mean Change
eGFR (mL/min/1.73m²)	78.4 ± 20.5	74.6 ± 22.3	-3.8 ± 5.1
Albuminuria (mg/g)	82.3 ± 35.7	95.4 ± 40.2	+13.1 ± 18.4

Participants were stratified into two groups based on their baseline free triiodothyronine levels: Low Free T3 Group (<2.0 pg/mL) and Normal Free T3 Group (≥2.0 pg/mL). The progression of diabetic nephropathy in both groups is shown in Table 3.

Table 3: Diabetic Nephropathy Progression by Free Triiodothyronine Levels

Variable	Low Free T3 Group (n=34)	Normal Free T3 Group (n=64)	p-value
Progression of Nephropathy (%)	18 (52.9%)	10 (15.6%)	<0.001
Mean Change in eGFR (mL/min)	-5.6 ± 4.2	-2.1 ± 3.8	0.003
Mean Change in Albuminuria	+20.5 ± 15.6	+8.7 ± 10.3	0.001

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(mg/g)			

Once possible confounders such as age, gender, length of diabetes, and HbA1c levels were taken into account, multivariate regression analysis showed that low circulating free triiodothyronine levels were critically linked to the development of diabetic nephropathy. Table 4 displays the regression coefficients and p-values for each of the model's variables.

Table 4: Multivariate Regression Analysis for Nephropathy Progression

Variable	Regression Coefficient (β)	Standard Error (SE)	p-value
Low Free T3 (<2.0 pg/mL)	1.47	0.43	<0.001
Age	0.12	0.05	0.03
Gender (Male)	-0.08	0.07	0.25
Duration of Diabetes	0.09	0.03	0.01
HbA1c	0.15	0.06	0.02

The findings suggest that lower levels of circulating free triiodothyronine are significantly associated with the progression of diabetic nephropathy in patients with type 2 diabetes.

DISCUSSION

The study's findings show a strong correlation between type 2 diabetic patients' developing diabetic nephropathy and low levels of free triiodothyronine (T3) in the blood. During the six-month study period, a decrease in estimated glomerular filtration rate (eGFR) and an increase in albuminuria were indicative of the progression of nephropathy in 28.6% of the individuals. Compared to individuals with normal baseline levels (≥2.0 pg/mL), those with lower baseline levels of free T3 (<2.0 pg/mL) were more likely to experience the progression of nephropathy.

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Specifically, 52.9% of patients in the low free T3 group exhibited nephropathy progression, compared to only 15.6% in the normal free T3 group. Additionally, the low free T3 group had a greater mean decline in eGFR (-5.6 ± 4.2 mL/min) and a more substantial increase in albuminuria (+20.5 ± 15.6 mg/g) compared to the normal free T3 group, which had a mean eGFR decline of -2.1 ± 3.8 mL/min and an albuminuria increase of +8.7 ± 10.3 mg/g. These differences were statistically significant, indicating a robust relationship between low free T3 levels and worsening kidney function.

Multivariate regression analysis further supported these findings, showing that low free T3 levels were a significant predictor of nephropathy progression after adjusting for confounding factors such as age, gender, duration of diabetes, and HbA1c levels. The regression model revealed that low free T3 levels had a regression coefficient (β) of 1.47 ($p < 0.001$), indicating a strong independent association with the progression of diabetic nephropathy.

Overall, the study shows that in patients with type 2 diabetes, low levels of free T3 in the blood are substantially linked to the development of diabetic nephropathy. These results imply that controlling and maybe slowing the development of diabetic nephropathy in persons with diabetes may depend on the measurement and treatment of thyroid hormone levels. To investigate the underlying mechanisms and assess the possible advantages of treatment approaches aimed at thyroid function in this patient group, more investigation is necessary.

According to a study, people with DN had considerably lower serum FT3 levels than type 2 diabetic controls. Thyroid hormone levels tended to decline as DN progressed, and there was a negative correlation found between FT3 levels and the likelihood of developing DN [5]. According to the results of another study, DN in euthyroid individuals with type 2 diabetes was substantially correlated with relatively low levels of thyroid hormones, especially FT3 [6].

A study comprising 452 individuals diagnosed with type 2 diabetes revealed a robust correlation between low FT3 levels and the onset and advancement of diabetic kidney disease (DKD). According to the study, FT3 levels gradually dropped as DKD got worse [7]. Reduced FT3 levels were found to be substantially linked with diabetic nephropathy in a study of people with type 2 diabetes who had recently received their diagnosis. The majority of the patients had low FT3 syndrome, and low FT3 has been found to be a separate risk

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factor for DN [8]. In patients with type 2 diabetes, a lower FT3/FT4 ratio is an independent predictor of DKD, according to an exploratory investigation. The study discovered notable variations in DKD prevalence and glycaemic control between various FT3/FT4 ratio groups [9].

CONCLUSION

Low free triiodothyronine (FT3) levels were linked to type 2 diabetic nephropathy (DN) progression in the study. Patients with low FT3 levels (<2.0 pg/mL) had a faster progression of nephropathy than those with normal levels. The multivariate regression analysis showed that low FT3 levels independently predict DN progression. These data show that monitoring thyroid hormone levels, particularly FT3, may help type 2 diabetics manage and maybe prevent diabetic nephropathy. Further research is needed to understand the causes and assess the advantages of thyroid function therapy in this population.

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