

EVALUATION OF KIDNEY FUNCTION IN HYPOTHYROID SUBJECTS AND ITS CORRELATION WITH FT4 & TSH LEVEL

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Abstract

Background: The development of the kidneys, renal hemodynamics, glomerular filtration rate (GFR), electrolytes, and water balance are all affected by thyroid hormones. The objective of this study is to delineate the effects of thyroid hormonal status on kidney function by estimating serum creatinine, serum urea, albumin-to-creatinine ratio (ACR), and estimated glomerular function rate (eGFR) among primary hypothyroid patients. **Materials and Methods:** It was an Institution-based cross-sectional study done in the Department of Biochemistry in a Tertiary care Institute for a period of 1 year (Jan 2022 to Jan 2023). Renal function parameters, namely, serum creatinine, serum urea, urinary ACR, and eGFR among primary hypothyroid patients under treatment for more than 2 months were measured along with age- and sex matched controls. Apparently, healthy individuals of both male and female, without any previously known diseased condition or drug history in the age group of 25 to 55 years have been selected for the study. Among 130 individuals included in this study, 55 persons were controls and 65 individuals were primary hypothyroid patients. SPSS version 22 was used for analysis. **Result:** The study was done with female preponderance of 55%, while males were 45%. (F=70, M=60). The predominant age group was 25 to 40 years comprising 45% of study participants. The control group is having TSH mean value in normal range, i.e., $1.51 \pm 1.16 \mu\text{IU/mL}$ and primary hypothyroid patients on treatment having $3.66 \pm 1.61 \mu\text{IU/mL}$. Free T4 in control was $1.27 \pm 0.17 \text{ ng/dL}$ and in primary hypothyroid was $1.22 \pm 0.19 \text{ ng/dL}$. Pearson correlation analysis shows that serum creatinine, serum urea, and ACR are positively correlated with serum TSH value among patients with primary hypothyroidism ($n = 65$) regardless of their treatment status. **Conclusion:** In untreated primary hypothyroidism, renal function parameters may worsen significantly. Though the start of the treatment can cause the changed state of renal function to be reversed partially, still there is persistence of deterioration of renal function which is statistically significant.

INTRODUCTION

It has long been understood how the thyroid gland and the kidney affect each other's processes.^[1] Thyroid hormones impact both the kidney and liver throughout the embryonic stage and also in the matured state. Glomerular function, tubular secretory and absorptive capacities, electrolyte and water balance, as well as thyroid hormone-induced cardiovascular alterations, can all have a direct

impact. As a result, there are changes in clinically significant renal parameters like GFR, urine ACR, and indicators of tubular function in both hypo- and hyper-functioning thyroid glands.^[2,3] More than half of adults with hypothyroidism experience a decline in GFR and an increase in blood creatinine, even in cases of subclinical hypothyroidism cases. The presence of hyponatremia is also obvious. With the start of levothyroxine therapy, these changes return to normal.^[4]

The prevalence and pattern of thyroid problems depend on factors like iodine intake, sex, age, ethnicity, and geography. Except in hilly places and Terai regions, a well-balanced diet and drinking water normally suffice to meet a person's daily iodine needs.^[5] Even supplemental iodine may not be enough to meet the needs of the local population in such areas as the sub-Himalayan Terai regions due to the changing geographical situation.^[6] As a result, thyroid disorders, particularly hypothyroidism, are highly common in this area. Given the aforementioned information, the current study aims to correlate clearly the effects of thyroid hormones on renal functioning in a primary hypothyroid subject on treatment attending the outpatient clinic of a Tertiary Health Care centre.

MATERIALS AND METHODS

It was an Institution-based cross-sectional study done in the Department of Biochemistry in a Tertiary Health Care Institute for a period of 1 year (Jan 2022 to Jan 2023). Renal function parameters, namely, serum creatinine, serum urea, urinary ACR, and eGFR among primary hypothyroid patients under treatment for more than 2 months were measured along with age- and sex matched controls. Apparently, healthy individuals of both male and female, without any previously known diseased condition or drug history in the age group of 25 to 55 years have been selected for the study. Among 130 individuals included in this study, 55 persons were controls and 65 people were primary hypothyroid patients.

For this purpose, normal reference range of thyroid hormones had been considered as follows: fT4 0.8 to 2.5 ng/dL, TSH 0.4 to 4.2 μ IU/mL. Individuals had been considered as hypothyroid patients, if TSH at diagnosis was $> 4.2 \mu$ IU/mL.^[7]

Methodology

Demographic details including thyroid hormonal status (serum TSH and fT4), serum creatinine, serum urea, and serum urea nitrogen, the values for eGFR and ACR have been gathered and categorized. The CKD-EPI equation and the four-

variable MDRD study equation were used to determine estimated GFR. For patients older than 18 years, these equations are the most frequently used IDMS traceable formulae for calculating GFR. Both formulae have been shown to be more accurate than the Cockcroft Gault creatinine clearance equation and incorporate variables for age, gender, and race.^[12-14]

MDRD study Equation^[8]

$$\text{GFR} = 175 \times (\text{sCr} - 1.154) \times (\text{age} - 0.203) \times (0.742 \text{ if female})$$

where sCr is serum creatinine in mg/dL.

CKD GPI Calculator^[9]

$$\text{GFR} = 141 \times \min(\text{sCr} / \kappa, 1)^\alpha \times \max(\text{sCr} / \kappa, 1) - 1.209 \times$$

$$0.993 \times \text{age} \times 1.018 \text{ (if female)} \times 1.159 \text{ (if black)}$$

where sCr is serum creatinine in mg/dL, κ is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of sCr/ κ or 1, and max indicates the maximum of sCr/ κ or 1.

Statistical Analysis

The statistical analysis was performed using SPSS version 22. The findings were present in number and percentage analyzed by frequency, percent. Chi-square test was used to find the association among variables. The critical value of P indicating the probability of significant difference was taken as <0.05 for comparison.

RESULTS

The study was done with female preponderance of 55%, while males were 45% (F=70, M=60). The predominant age group was 25 to 40 years comprising 45% of study participants. The control group is having TSH mean value in normal range, i.e., $1.51 \pm 1.16 \mu$ IU/mL and primary hypothyroid patients on treatment having $3.66 \pm 1.61 \mu$ IU/mL. Free T4 in control was 1.27 ± 0.17 ng/dL and in primary hypothyroid was 1.22 ± 0.19 ng/dL. Serum urea, CKD-EPI eGFR and MDRD e-GFR were higher in control group while serum creatinine and ACR were higher in hypothyroidism subjects.

Table 1: Comparison of Renal function parameters and Thyroid markers

	Control group (mean \pm SD)	Primary hypothyroid patients on treatment (mean \pm SD)
No. of cases	55	65
TSH (μ IU/mL)	1.51 ± 1.16	3.66 ± 1.61
Free T4 (ng/dL)	1.27 ± 0.17	1.22 ± 0.19
Serum creatinine (mg/dL)	0.75 ± 0.09	0.81 ± 0.11
Serum urea (mg/dL)	18.21 ± 2.44	16.26 ± 3.4
CKD-EPI eGFR (mL/min per 1.73 m ² body surface area)	102.53 ± 5.29	91.38 ± 11.62
MDRD eGFR (mL/min per 1.73 m ² body surface area)	91.22 ± 4.83	81.43 ± 10.74
ACR (mg/gm)	24.11 ± 3.43	45.96 ± 17.24

Table 2: Correlation analysis of serum TSH with renal function parameters

			Control group		Patients with primary hypothyroidism	
	Parameters correlated	r-value	Pearson's correlation significance		Pearson's correlation r-value significance	
Thyroid-stimulating hormone	Serum creatinine	0.21	0.23		0.65*	0.01
	Serum urea	-0.27	0.12		0.47*	0.01
	CKD-EPI eGFR	-0.11	0.51		-0.68*	0.01
	MDRD eGFR	0.01	0.99		-0.68*	0.01
	ACR	0.27	0.16		0.89*	0.01

As per [Table 2] Pearson correlation analysis shows that serum creatinine, serum urea, and ACR are positively correlated with serum TSH values among patients with primary hypothyroidism (n = 65) regardless of the treatment status. Moreover, eGFR values are negatively correlated with serum TSH values among them.

Table 3: Correlation analysis of serum free T4 with renal function parameters

			Control group		Patients with primary hypothyroidism	
	Parameters correlated	r-value	Pearson's correlation significance		Pearson's correlation r-value Significance	
Free T4	Serum creatinine	-0.05	0.77		-0.62*	0.01
	Serum urea	-0.05	0.71		-0.44*	0.01
	CKD-EPI eGFR	-0.25	0.14		0.69*	0.01
	MDRD eGFR	-0.14	0.41		0.62*	0.01
	ACR	-0.7	0.7		-0.60*	0.01

As per [Table 3], the serum fT4 values are negatively correlated with serum creatinine, serum urea, and ACR among patients with primary hypothyroidism (n = 65) regardless of the treatment status. Here the eGFR values are positively correlated with fT4 among them.

DISCUSSION

Nearly every organ system in the human body is influenced by thyroid hormones, and the kidney is no exception of it. They have been involved in general tissue growth from embryogenesis, as well as kidney's glomerular filtration, tubular operations, and handling of electrolytes. In the current above-mentioned study, the altered renal function has been observed among thyroid patients who meet certain specified inclusion and exclusion criteria.

Hypothyroidism has been linked to increased serum creatinine levels, a decline in GFR, and decreased renal plasma flow. The GFR may be decreased 40% or more in hypothyroid people exactly as expected from animal model experiments.^[2,10-12] As soon as the hormone replacement for hypothyroidism is initiated, the falling trend in GFR is reversed. This is only feasible if the modifications to renal function do not result in long-term histological damage.^[2] Reduced cardiac output and circulation volume, reduced renin-angiotensin-aldosterone system activity, and hypothyroidism are all linked to a drop in the amount of atrial natriuretic factor,^[11] which could affect renal perfusion.^[2] In the current study, eGFR was considered as a crucial parameter for evaluating renal function. Estimated GFR had been computed using two distinct formulae employing age, gender, ethnicity, and serum creatinine levels, such as the CKD-EPI and four-variable MDRD eGFR. Since thyroidism itself affects how cystatin C

is metabolized, a cystatin C-based equation had not been used in this study.^[13,14]

The HUNT study conducted by Åsvold et al,^[15] was connected to a decreased GFR. They discovered that individuals with overt or subclinical hypothyroidism had decreased mean eGFR (79.3 mL/min per 1.73 m², p 0.001), (76.5 mL/min per 1.73 m², p 0.001) respectively in contrast to individuals whose TSH levels were in the lower third of the standard range (0.50-1.4 IU/mL; 83 mL/min per 1.73 m²). Contrarily, increased eGFR was linked with both subclinical and overt hyperthyroidism when compared to the reference group (mean 84.6 mL/min per 1.73 m², p = 0.04; 104.9 mL/min per 1.73 m², p 0.001). Their findings concur with those made earlier by Adrees et al and Woodward et al.^[16,17]

Also in cases of primary hypothyroidism, thyroxine therapy led to a reversible rise in GFR.^[2,4] Only a four-variable MDRD study was employed for GFR estimation in the HUNT investigation. The results of the current study are consistent with those of Svold et al.^[15]

Patients with considerably elevated serum creatinine values have been described in a hospital-based study by Arora et al vs euthyroid controls when compared to those with hypothyroidism (p 0.001). They kept track of 46 overt hypothyroid patients for 6 weeks while providing uninterrupted thyroid hormone replacement, and they discovered that the serum creatinine level dropped considerably after treatment compared to the baseline condition (p = 0.005).^[18]

Saini et al,^[19] investigated 77 patients with subclinical hypothyroidism in addition to 47 patients with overt hypothyroidism while performing a cross-sectional study on the Indian population. They discovered that there is a positive correlation between blood creatinine values and serum TSH among them (p 0.05).

In a study on the "correlation of thyroid dysfunction with serum creatinine", Attaullah et al.^[20] found that serum creatinine is positively correlated with TSH and negatively correlated with serum T4 in hypothyroid individuals (n = 191) (p 0.001 on both occasions). Additionally, they discovered that serum creatinine has a negative correlation with T4 in patients with hyperthyroidism (n = 195) (p 0.001).

CONCLUSION

Renal function alterations were observed in case of primary hypothyroid patients on treatment for more than 2 months in the foregoing institution-based observational study. In untreated primary hypothyroidism, renal function parameters may worsen significantly. Though the start of the treatment can cause the changed state of renal function to be reversed partially, still there is persistence of deterioration of renal function which is statistically significant.

Therefore, it may be inferred from these findings that patients should undergo a thyroid function screening, if they have any unexplained abnormal renal function. However, the potential long-term effects of impaired renal function among hypothyroid patients who remain untreated are still unknown. For patients with overt hypothyroidism who are untreated for long time, the risk of nephropathy in the near future should not be neglected because microalbuminuria is known to be a predictor of poor renal outcome even in nondiabetic subjects. Thus, it should be recommended to check for alteration in renal functions among both untreated hypothyroid patients as well as patients on treatment. Also it is advocated to take necessary actions in the form of beginning or continuing hormone replacement therapy to avoid any possibility of future nephropathy.

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