



CO-RELATION OF THYROID DISORDERS IN CHRONIC KIDNEY DISEASE

Syed Najeemuddin, Oluseyi Abidoye^{*1}, Milisha Lal², Vrushali Dhongde³, Abdel Kareem Jamal Al Dabbas⁴,
Bhargav Muppaneni⁵, Rono Korra⁶

Medical Student at Mount Sinai Hospital.

¹Extern, Interfaith Hospital, New York.

²Physician, Bharati Vidyapeeth Hospital.

³Physician, Bharati Vidyapeeth Hospital.

⁴Extern, Heart Vascular Institute, Michigan.

⁵Extern, Chicago Lakeshore Hospital, Chicago.

⁶Observer, University of Oklahoma.

***Corresponding Author: Oluseyi Abidoye**

Extern, Interfaith Hospital, New York.

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ABSTRACT

Introduction: Thyroid hormones have a significant effect on the functioning of kidneys. This is due to pre-renal as well as renal effects on kidneys. Decreased GFR is seen in hypothyroidism and increase in GFR and increased Renin-Angiotensin-Aldosterone system is seen in hyperthyroidism. Many researchers have proposed a co-relation between incidence of primary hypothyroidism and subclinical hypothyroidism. In this study, we tried to find the co-relation of thyroid hormones in chronic kidney disease. **Methods:** In this study, we took 248 patients with GFR ranging from 90 to 30 mL/min/1.73m². Serum Creatinine and GFR was measured in all the participants. Patients with kidney transplants and patients on dialysis were excluded from the study. Proper physical examination etc was done of all the participants. All data was recorded and analyzed statistically. **Results:** A total of 248 participants were taken. TSH and T4 levels of all the participants were measured. TSH levels were used as diagnostic criteria for hypothyroidism. Hypothyroidism was defined when TSH levels were >4.5µg/dL or the patient was on taking any thyroid supplement. Subclinical hypothyroidism was measured by TSH levels >4.5µg/dL and total T4 levels as ≥4.5 µg/dL. Baseline characteristics are depicted in table 1. GFR and co-relation of GFR with thyroid levels are depicted in table 2. As GFR decreased, the prevalence of hypothyroidism increases. P value was calculated by multiple logistic regression analysis. P value is 0.0036. Hence, the co-relation is statistically significant. **Conclusion:** This study shows a positive co-relation between reduced GFR and higher prevalence of hypothyroidism along with subclinical hypothyroidism.

KEYWORDS: Thyroid, Creatinine, hypothyroidism.

INTRODUCTION

There is a strong co-relation between thyroid gland and kidneys.^[1] Thyroid dysfunction can lead to dysfunction of renal physiology and renal development and on the other hand, kidney dysfunction can also lead to thyroid dysfunction. There are many etiological factors where thyroid and kidney diseases co-exist. Thyroid hormones have pre-renal and direct renal effects on kidney. Thyroid hormones have cardiovascular effects and effects on renal blood flow. These effects are referred to as pre-renal effects. Apart from this, direct effects of thyroid hormones are due to its effect on glomerular filtration rate,^[2] and secretory and re-absorptive process. Thyroid hormones increase Na reabsorption at proximal convoluted tubule by increasing the activity of Na/K/ATPase.^[3] It also increases tubular potassium permeability.^[4] Thyroid hormones are also found to

regulate adrenergic receptors and dopaminergic receptors and calcium reabsorption. Thyroid hormones are also responsible for regulation of renin-angiotensin-aldosterone system.^[5]

HYPERTHYROIDISM AND RENAL FUNCTION

Hyperthyroidism results in increase in Renal blood flow and increase in Glomerular filtration Rate.^[6] Thyroid hormones also cause activation of renin-angiotensin-aldosterone system. All these leads to 18-25% increase in GFR in hypothyroid patients.^[7] Serum Creatinine is an inverse marker of GFR. It is significantly decreased in hyperthyroid patients. This is due to decrease in GFR as well as decrease in overall muscle mass.^[8]

HYPOTHYROIDISM AND RENAL FUNCTION

The effects of hypothyroidism are completely opposite to the effects of hyperthyroidism on renal functions. The renal blood flow is reduced due to decrease in cardiac output and increase in peripheral vascular resistance. In addition, glomerular basement membrane thickening and mesangial matrix expansion also leads to reduction in renal blood flow.^[9] GFR is reduced reversibly by about 40% in about half of the patients of hyperthyroidism.^[10] This is due to reduction in Renin release and decreased sensitivity of β -adrenergic stimulation. There is reduced proximal tubular absorption of sodium, water and chloride.^[11] This is due to reduced activity of Na/K/ATPase. There is net reduction in bicarbonate reabsorption as well. There is loss of medullary hyper tonicity and this is responsible for impaired urinary concentration ability of kidneys.

CHRONIC KIDNEY DISEASE AND THYROID DYSFUNCTION

Hyperthyroidism accelerates the progression of chronic kidney disease. Hyperthyroidism causes intra-glomerular hypertension. This leads to hyper filtration. Hyperthyroidism also leads to proteinuria and this directly leads to renal injury. Hyperthyroidism also leads

to increased mitochondrial metabolism and this leads to down-regulation of superoxide dismutase and subsequently increase in free radicals and renal injury.^[12]

METHODS: In this study, we took 248 patients with GFR ranging from 90 to 30 mL/min/1.73m². Serum Creatinine and GFR was measured in all the participants. Patients with kidney transplants, patients on dialysis, pregnant women, patients receiving drugs that could contribute to hypothyroidism (Lithium, Amiodarone) and patients taking anti- thyroid medications were excluded from the study. Proper physical examination etc was done of all the participants. All data was recorded and analyzed statistically. TSH levels were measured by chemiluminescence immunometric assay. T4 levels were measured by radioimmunoassay. GFR was estimated by using the abbreviated Modification of Diet in Renal Disease(MDRD) equation(a,b). Hypothyroidism was defined when TSH levels were >4.5 μ g/dL or the patient was on taking any thyroid supplement. Subclinical hypothyroidism was measured by TSH levels >4.5 μ g/dL and total T4 levels as \geq 4.5 μ g/dL(c). All variables were compared statistically by multivariate regression analysis model.

RESULTS

TABLE 1: BASELINE CHARACTERISTICS OF PARTICIPANTS.

	HYPOTHYROIDISM	NO HYPOTHYROIDISM
AGE (yrs)	52.8 \pm 6.8	48.6 \pm 4.1
GENDER MALE	41	79
FEMALE	61	67
TSH LEVELS(μ g/dL)	5.9	1.11
TOTAL T4(μ g/dL)	9.1 \pm 2.8	8.2 \pm 3.1

TABLE 2: GFR CO-RELATION IN PARTICIPANTS.

ESTIMATED GFR mL/min/1.73m ²	HYPOTHYROIDISM	NO HYPOTHYROIDISM	P VALUE
\geq 90	4 (3.92%)	67 (45.89%)	0.0036
60-89	47 (46.07%)	62 (42.46%)	
45-59	27 (26.47%)	12(8.21%)	
30-44	19 (18.62%)	3(2.94%)	
<30	5 (4.9%)	2 (1.36%)	
TOTAL	102	146	

A total of 248 participants were taken. TSH and T4 levels of all the participants were measured. TSH levels were used as diagnostic criteria for hypothyroidism. Hypothyroidism was defined when TSH levels were >4.5 μ g/dL or the patient was on taking any thyroid supplement. Subclinical hypothyroidism was measured by TSH levels >4.5 μ g/dL and total T4 levels as \geq 4.5 μ g/dL. Baseline characteristics are depicted in table 1. In table 1, clinical hypothyroid participants and subclinical hypothyroid participants both are included in hypothyroidism group. The average age in the hypothyroidism group was 52.8 \pm 6.8 years and in the euthyroid group was 48.6 \pm 4.1 years. In hypothyroidism group, 41(40.96%), participants were males and 61(59.80%) participants were females. In euthyroid

group, 79(54.10%) participants were males and 67(45.89%) participants were females. Average TSH levels in hypothyroid group and euthyroid group was 5.9 μ g/dL and 1.11 μ g/dL respectively. Total T4 levels were 9.1 \pm 2.8 μ g/dL in hypothyroid group and 8.2 \pm 3.1 μ g/dL in euthyroid group.

GFR was measured in all the participants. GFR findings are mentioned in table 2. All units of GFR are in mL/min/1.73m² scale. For GFR 60-89, the prevalence of hypothyroidism was 46.07% and the prevalence of euthyroid state was 42.46%. For GFR 45-59, the prevalence of hypothyroidism was 26.47% and the prevalence of euthyroid state was 8.21%. For GFR 30-44, the prevalence of hypothyroidism was 18.62% and

the prevalence of euthyroid state was 2.94%. For GFR <30, the prevalence of hypothyroidism was 4.9% and the prevalence of euthyroid state was 1.36%. For every GFR variable, the prevalence was more in hypothyroidism like 4.9% vs 1.36% and 18.62% vs 2.94%. Multiple logistic regression analysis was done and it gave a p value of 0.0036 (<0.05). Hence, the difference in prevalence of decreased GFR in hypothyroidism and euthyroid state participants was statistically significant.

	Hyperthyroidism	Hypothyroidism
Serum creatinine	Decreased	Increased
Serum Cystatin C	Increased	Decreased
24- hour urine protein	Increased	Increased
Water load excretion	Increased	Decreased
Electrolyte imbalance	None	Hyponatremia

In our study, we took a total of 248 participants. 102 participants were found to have hypothyroidism and 146 participants were found to be euthyroid. In participants with hypothyroidism, there was a decrease in GFR as compared to the euthyroid participants. The p-value was 0.0036.

One study was done by Joan et al. It also showed that reduced glomerular filtration rate was associated with high prevalence of hypothyroidism.^[13]

CONCLUSION: This study shows a positive co-relation between reduced GFR and higher prevalence of hypothyroidism along with subclinical hypothyroidism.

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DISCUSSION

Thyroid hormone affects renal blood flow, glomerular filtration rate and tubular function, electrolyte homeostasis, and kidney structure. The clinical effects of hypothyroidism and hyperthyroidism on renal function tests are given in the table below.

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