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# CO-RELATION OF THYROID DISORDERS IN CHRONIC KIDNEY DISEASE

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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/1.73m$^2$. 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 secretary 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 rennin-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/1.73m$^2$. 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 >4.5µg/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(c). All variables were compared statistically by multivariate regression analysis model.

**RESULTS**

**TABLE 1: BASELINE CHARACTERISTICS OF PARTICIPANTS.**

| | HYPOTHYRDOIDISM | NO HYPOTHYROIDISM |
|---|---|---|
| AGE (yrs) | 52.8 ±6.8 | 48.6 ±4.1 |
| **GENDER** MALE | 41 | 79 |
| FEMALE | 61 | 67 |
| TSH LEVELS(*µg/dL)* | 5.9 | 1.11 |
| TOTAL T4(*µg/dL)* | 9.1 ±2.8 | 8.2 ±3.1 |

**TABLE 2: GFR CO-RELATION IN PARTICIPANTS.**

| ESTIMATED GFR mL/min/1.73m$^2$ | HYPOTHYROIDISM | NO HYPOTHYROIDISM | P VALUE |
|---|---|---|---|
| ≥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 >4.5µg/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. 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 ± 6.8 years and in the euthyroid group was 48.6 ± 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 5.9µg/dL and 1.11µg/dL respectively. Total T4 levels were 9.1 ±2.8µg/dL in hypothyroid group and 8.2 ±3.1µg/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/1.73m$^2$ 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.

**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.

| | **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.

**REFERENCES**


1. Thyroid function in renal failure. Kaptein EM Contrib Nephrol, 1986; 50: 64-72.
2. Mechanism of impaired water excretion in the hypothyroid rat. Emmanouel DS, Lindheimer MD, Katz AI J Clin Invest, 1974 Oct; 54(4): 926-34.
3. Thyroid hormone upregulates Na, K-ATPase alpha and beta mRNA in primary cultures of proximal tubule cells. Lin HH, Tang MJ Life Sci., 1997; 60(6): 375-82.
4. Renal sodium- and potassium-activated adenosine triphosphatase and sodium reabsorption in the hypothyroid rat. Katz AI, Lindheimer MD J Clin Invest, 1973 Apr; 52(4): 796-804.
5. Thyroid hormone differentially regulates development of beta-adrenergic receptors, adenylate cyclase and ornithine decarboxylase in rat heart and kidney. Pracyk JB, Slotkin TA J Dev Physiol, 1991 Oct; 16(4): 251-61.
6. Correlation between severity of thyroid dysfunction and renal function. den Hollander JG, Wulkan RW, Mantel MJ, Berghout A Clin Endocrinol (Oxf), 2005 Apr; 62(4): 423-7.
7. Correlation between severity of thyroid dysfunction and renal function. den Hollander JG, Wulkan RW, Mantel MJ, Berghout A Clin Endocrinol (Oxf), 2005 Apr; 62(4): 423-7.
8. Correlation between severity of thyroid dysfunction and renal function. den Hollander JG, Wulkan RW, Mantel MJ, Berghout A Clin Endocrinol (Oxf), 2005 Apr; 62(4): 423-7.
9. Changes in glomerulotubular dimensions, single nephron glomerular filtration rates and the renin-angiotensin system in hypothyroid rats. Bradley SE, Coelho JB, Sealey JE, Edwards KD, Stéphan F Life Sci., 1982 Feb 15-22; 30(7-8): 633-9.
10. Changes in renal function in primary hypothyroidism. Montenegro J, González O, Saracho R, Aguirre R, González O, Martínez I Am J Kidney Dis., 1996 Feb; 27(2): 195-8.
11. Cardiorenal endocrine dynamics during volume expansion in hypothyroid dogs. Zimmerman RS, Ryan J, Edwards BS, Klee G, Zimmerman D, Scott N, Burnett JC Jr Am J Physiol, 1988 Jul; 255(1 Pt 2): R61-6.
12. Renal oxidative stress in medullary thick ascending limbs produced by elevated NaCl and glucose. Mori T, Cowley AW Jr Hypertension, 2004 Feb; 43(2): 341-6.