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REVERSIBLE RENAL DYSFUNCTION IN PATIENTS WITH HYPOTHYROIDISM

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Abstract

Background: Hypothyroidism patients are more prone to get kidney disorders due to thyroid dysfunction. We aimed to determine the supplementation of thyroxine can reverse renal dysfunction in patients with hypothyroidism. **Methods:** This observational study, included A total 60 patients who were presented with hypothyroidism (30 were hypothyroidism with AKI and 30 were hypothyroidism with CKD). We estimated RFT, CPK, eGFR, T4, TSH and Urinary Proteins levels were measured before and after supplementation of thyroxine. **Results:** The age, urea, creatinine and urinary protein does not shown any significance between baseline and after supplementation of thyroxine in patients with hypothyroidism and AKI, CKD respectively P value is >0.05. The T4, TSH and eGFR shown a significant between baseline and after supplementation of thyroxine in patients with hypothyroidism and AKI respectively P value is 0.001**. The serum urea, creatinine, CPK, T4, TSH, eGFR and urinary protein shown a significant between baseline and after supplementation of thyroxine in patients with hypothyroidism and CKD, respectively P value is 0.001**. **Conclusion:** Based on study findings, the renal dysfunction occurs in moderate to severe hypothyroidism and it is reversible upon adequate thyroxine supplementation. Thyroid function testing should form an integral part of the first line blood investigations for patients with impaired renal function. Hypothyroidism should be considered as a cause for sudden deterioration in hitherto stable CKD.

Keywords: AKI, CKD, Hypothyroidism and Thyroxine.

Introduction

Hypothyroidism is a common metabolic disease due to defect in thyroid hormones. It can have major negative health repercussions and even cause death if left untreated (1). Thyroid-stimulating hormone (TSH) concentrations above the reference range and free thyroxine

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concentrations below the reference range are indicative of overt or clinical primary hypothyroidism (2). It has been demonstrated that thyroid dysfunction affects every organ system in the body, including the heart, muscles, and brain. Renal function is also impacted by thyroid state. In addition to having a direct impact on kidney function, the thyroid hormone can alter hemodynamics locally or systemically (3). Renal impairment occurring in hypothyroidism is subtle and frequently overlooked in clinical practice and arouses deep fear because of possible progression to End Stage Renal Failure (4). According to previous study findings, in patients with primary hypothyroidism, slightly reduced creatinine clearance was observed in all patients, while 54% of the patients had mildly elevated serum creatinine (5).

Thyroid dysfunction results in modifications to renal blood flow, glomerular filtration rate (GFR), tubular secretory and absorptive capacity, electrolyte pumps, and kidney shape. There have been reports linking different glomerulopathies to both hyper- and hypofunction of the thyroid (6-7). There are, however, few clinical research on thyroid dysfunction and its relationship to renal function, and little is understood about the impact of thyroid dysfunction on renal function (8). This has been proposed to cause structural changes such as truncated tubular mass, decreased kidney-to-body weight ratio, and altered glomerular architecture, as well as effects on cardiac output, intra-renal hemodynamics, and the renin-angiotensin-aldosterone system (RAAS) in patients with hypothyroidism (9-10). Many studies are conducted on animals and there are very few studies on humans. Based on this back ground, the present study to assess changes in renal function biochemical markers in individuals with thyroid dysfunction and to establish a correlation between these parameters and the thyroid profile of the patient.

Materials and Methods

This observational study was conducted in the Department of Endocrinology and Nephrology, BGS Global Hospitals, Bangalore and Sri Madhusudan Sai Institute of Medical Sciences and Research, Muddenahalli, Chikkaballapur, Karnataka. A total 60 patients who were presented with hypothyroidism (30 were hypothyroidism with AKI and 30 were hypothyroidism with CKD). The inclusion criteria age between 30 to 70 years and patients diagnosed with All had moderate to severe hypothyroidism (TSH 10 - >75 mIU/ml), Acute Kidney Injury (AKI) and Chronic Kidney Injury (CKI), for all the included subjects thyroxine was supplied. The participants with smoking, alcoholism, women with pregnancy, other types of thyroid diseases, kidney diseases, Type 1 and Type 2 diabetes mellitus, liver diseases, pancreatic diseases and whoever is not willing to participate in the were excluded. All the study was conducted after taken approval from Institutional Ethics Committee (IEC) and the participants were recruited after obtained consent form.

Five (5) mL of fasting venous blood sample was collected from all the subjects and transferred into plain vacutainer, allowed 10 minutes to clot. The serum samples were separated immediately by centrifugation at 3000 rpm for 10 minutes. The separated serum was transferred into appropriately labelled aliquots and stored at – 50 0 c until analysis was done. Additionally, we also collected spot urine sample, after collection immediately processed urinary proteins. Serum urea, creatinine, creatinine phospho kinase (CPK), T4 and TSH was determined by laboratory standard methods and eGFR was calculated by modification of diet in renal diseases (MDRD) formula.

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Statistical Analysis

Continuous variables were expressed as mean ± SD. The Kolmogorov-Smirnov test was used to evaluate the distribution of continuous variables. Data which were not normally distributed were expressed as or median (interquartile range). The analysis of variance (ANOVA) is used for comparison of study variables. The association between the variables was studied using Pearson correlation analysis. A p value<0.05 was considered as statistically significant. Statistical analysis was done using Microsoft excel spread sheets and SPSS version 20.0.

Results

Table 1 shows the comparison of study variables before and after thyroxine supplementation in patients with hypothyroidism and AKI. The age, urea, creatinine and urinary protein does not shown any significance between baseline and after supplementation of thyroxine in patients with hypothyroidism and AKI respectively P value is >0.05. The T4, TSH and eGFR shown a significant between baseline and after supplementation of thyroxine in patients with hypothyroidism and AKI respectively P value is 0.001**.

Table 1: Comparison of study variables before and after thyroxine supplementation in patients with hypothyroidism and AKI.

Parameters	**Hypothyroidism with AKI Baseline**			**Hypothyroidism with AKI after thyroxine supplementation**			**P- Values**
	Mean ± SD			**Mean ± SD**			
Age	46.30	±	3.6	48.24	±	2.4	0.254
Serum Urea	36.24	±	2.7	34.16	±	1.6	0.671
Serum Creatinine	1.2	±	0.3	1.1	±	0.5	0.335
CPK	106.54	±	12.5	96.33	±	6.7	0.02*
T4	3.18	±	0.7	12.27	±	2.6	0.001**
TSH	100.84	±	13.6	0.87	±	0.4	0.001**
eGFR	56.27	±	4.3	72.09	±	1.5	0.001**
U. Protein	6.27	±	1.2	7.45	±	2.7	0.972

Table 1 shows the comparison of study variables before and after thyroxine supplementation in patients with hypothyroidism and CKD. The age does not shown any significance between baseline and after supplementation of thyroxine in patients with hypothyroidism and AKI respectively P value is 0.254. The serum urea, creatinine, CPK, T4, TSH, eGFR and urinary protein shown a significant between baseline and after supplementation of thyroxine in patients with hypothyroidism and CKD, respectively P value is 0.001**.

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Table 2: Comparison of study variables before and after thyroxine supplementation in patients with hypothyroidism and CKD.

Parameters	Hypothyroidism with CKD Baseline			Hypothyroidism with CKD after thyroxine supplementation			P- Values
	Mean ± SD			Mean ± SD			
Age	55.23	±	2.5	57.41	±	1.9	0.254
Serum Urea	61.55	±	1.8	56.34	±	2.6	0.001**
Serum Creatinine	2.9	±	0.5	1.8	±	0.2	0.001**
CPK	145.23	±	7.6	104.56	±	5.5	0.001**
T4	6.5	±	1.4	7.9	±	2.2	0.001**
TSH	29.78	±	3.3	4.32	±	1.9	0.001**
eGFR	35.56	±	1.4	56.71	±	0.6	0.001**
U. Protein	23.61	±	0.9	19.64	±	1.9	0.001**

Discussion

The present study aimed to investigate the potential influence of thyroid disease on laboratory markers of renal function. Specifically, biochemical indicators of renal function in patients with thyroid dysfunction were assessed and compared before and after treatment for thyroid disorders (11-12). The results showed that there are significant variations in renal function that are correlated with the degree of thyroid dysfunction. Serum creatinine and eGFR are the most frequently used biomarkers in routine clinical practice (13). Our research showed that while the mean eGFR significantly increased following treatment, the average blood creatinine level in the hypothyroid patients decreased statistically significantly after treatment compared to before treatment. The previous research has shown a reversible increase in serum creatinine in individuals with hypothyroidism (14-15).

In more than half of the hypothyroid population, the GFR is reversibly lowered. In hypothyroid individuals, the GFR reduction is caused by multiple causes. decreased renal response to vasodilators, decreased cardiac output, increased peripheral vascular resistance, intrarenal vasoconstriction, and decreased in hypothyroidism, production of renal vasodilators such as insulin-like growth factor-1 and vascular endothelial growth factor is involved in the decrease in renal blood flow (16-17). Pathologic changes to the glomerular structure in hypothyroidism, such as thickening of the glomerular basement membrane and expansion of the mesangial matrix, can also result in reduced renal blood flow (18). Reduced renin release, reduced angiotensin II, reduced sensitivity to adrenergic stimulation, and reduced renin-angiotensin system activity all contribute to the loss of GFR (19).

The glomerular surface area is limited, which imposes a structural constraint on filtration because of renal parenchymal growth retardation in hypothyroidism. Furthermore, there is less water, salt, and chloride absorbed via the proximal tubules. There is also a reduction in the expression of the renal basolateral chloride channel (20). Consequently, reduced chloride reabsorption raises the distal chloride supply, which in turn triggers tubuloglomerular feedback through the macula densa and reduces the activity of the renin-angiotensin system.

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Consequently, the GFR falls (21). Considering all of these findings, differences in serum creatinine observed in various thyroid disorders can be explained by the action of thyroid hormone on GFR. Even if they are slight, these differences can have an impact on certain patients. Patients receiving concomitant treatment with medicines having limited therapeutic range may experience toxicity due to GFR changes in hypothyroidism (22).

Hypothyroidism, for instance, has been linked to reduced renal-to-body weight ratio, shortened tubular mass, alterations in glomerular shape, reduced single nephron GFR, low renal plasma flow, and decreased glomerular transcapillary hydrostatic pressure, according to animal models (23). Further evidence from case series indicates that patients with hypothyroidism have lower renal plasma flow and GFR as determined by gold-standard isotope scans and creatinine-based estimation equations (24). Our research contributes to the expanding body of knowledge about the connection between renal function and thyroid status and may encourage screening of specific populations, like those with CKD. Based on study results suggest that treating hypothyroidism or reducing hypothyroid status may have an effect on renal function and the risk of chronic kidney disease.

Conclusion

Based on study findings, the renal dysfunction occurs in moderate to severe hypothyroidism and it is reversible upon adequate thyroxine supplementation. Thyroid function testing should form an integral part of the first line blood investigations for patients with impaired renal function. Hypothyroidism should be considered as a cause for sudden deterioration in hitherto stable CKD.

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