

Renal function derangements in hypothyroidism: A clinical correlation between serum creatinine, urea and uric acid levels

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Abstract

Thyroid hormones (TH) are essential for an adequate development and kidney maturity. The dysfunction of thyroid causes striking changes in glomerular and tubular capacities and electrolyte and water homeostasis. Hypothyroidism is affiliated with a decline in glomerular filtration, hyponatremia, and a modification of the capacity for water extraction. Since various renal function derangements occur in hypothyroidism, therefore, present study has been intended to determine the various parameters (urea, creatinine and uric acid) related to renal function in hypothyroid patients and correlation of these parameters with thyroid hormones (T3, T4, TSH). The study was conducted on 200 hypothyroidisms. Age and sex matched healthy euthyroids were selected for the study. Serum was taken from each patient and control and was analyzed for T3 by competitive analog-based immunoassay, T4 by competitive analog-based immunoassay, TSH by 2 site chemiluminescent immunometric assay, creatinine by modified Jaffe's method, urea by urease method and uric acid by uricase method respectively. A total number of 300 cases that includes 200 hypothyroid patients (25% males and 75% females) and 100 controls (42% males and 58% females) were examined. The mean level of serum T3 (1.968 ± 0.1195 pg/ml), serum T4 (1.0152 ± 0.1235 pg/ml), serum urea (33 ± 5.570 mg/dl) of hypothyroids were significantly lower as compared to mean level of serum T3 (3.704 ± 0.1699 pg/ml), serum T4 (1.5764 ± 0.16230 pg/ml) and serum urea (35.12 ± 3.710 mg/dl) of euthyroids. The mean level of serum TSH (8.928 ± 0.9589 μIU/ml) serum Creatinine (2.192 ± 0.2566 mg/dl) and serum uric acid (4.224 ± 0.6554 mg/dl) of hypothyroids were significantly higher as compared to mean level of serum TSH (3.06 ± 0.4110 μIU/ml), serum Creatinine (0.852 ± 0.1396 mg/dl) and serum uric acid (3.772 ± 0.2975 mg/dl) of euthyroids. Hypothyroids serum T3 significantly correlated with positive person serum uric acid ($r = 0.343$). Hypothyroids serum T4 indicate noteworthy negative Pearson relationship with serum urea ($r = -0.367$) and creatinine ($r = -0.267$) Hypothyroids serum TSH indicate huge negative Pearson connection with serum uric acid ($r = -0.190$) and creatinine ($r = -0.344$). Elevated serum creatinine, serum urea and serum uric acid demonstrates renal capacity disturbances in hypothyroidism.

Keywords: Thyroid hormones, T3, T4, TSH, Serum creatinine, Serum uric acid.

Introduction

Hypothyroidism is a clinical state caused by any structural or functional derangement that interferes with the production of adequate levels of thyroid hormone.¹ Hypothyroidism has high prevalence among the elderly peoples. Among individuals over 60 years old, it affects 10% of women and 2% of men.²

THs are fundamental for a satisfactory development and advancement of the kidney. Thyroid brokenness causes exceptional changes in glomerular and tubular capacities and electrolyte and water homeostasis. Hypothyroidism is joined by a lessening in glomerular filtration, hyponatremia, and a modification of the capacity for water discharge. Over the top levels of TH create an expansion in glomerular filtration rate and renal plasma stream.³

For many decades it has been known that there is a close relationship between hypothyroidism and renal dysfunction. Hypothyroidism associated with altering systemic hemodynamic that affects both blood pressure and renal function. Thyroid hormones are necessary for maintenance of water and electrolyte homeostasis.

Many research studies have suggested that hypothyroidism should be evaluated in patients with kidney abnormalities.^{4,5}

Children with congenital hypothyroidism have an increased prevalence of congenital renal abnormalities.

Since various renal function derangements occur in hypothyroidism, therefore, present study has been intended to determine the various parameters (urea, creatinine and uric acid) related to renal function in hypothyroid patients and correlation of these parameters with thyroid hormones (T3, T4, TSH).

Materials and Methods

Study Design and Subjects: The study was conducted on patients with hypothyroidism on case control based investigation. Age and sex matched normal healthy controls were selected for the study. The study was conducted over a period of two years in the area of Ambedkar Nagar, Uttar Pradesh, India, with the investigation of M.R.A. Medical College, Ambedkar Nagar, Uttar Pradesh.

Inclusion Criteria: History, physical examination and elevated serum TSH level diagnosed 200 hypothyroid patients in the age group 30-60 years and 100 age and sex matched healthy subjects as controls.

Exclusion Criteria: Patients with renal diseases, chronic renal failure and other systemic diseases.

Sample Collection: All the samples were collected after overnight fasting for 8 hours about 5 ml of venous blood was drawn with aseptic precaution from antecubital vein of the entire subject and dispensed into plain vials.

Analysis of Sample: Serum separated from plain vial after centrifugation was used for estimation of serum T3 (pg/ml) by competitive analog-based immunoassay, serum T4 by (pg/ml) by competitive analog-based immunoassay, serum TSH (μ IU/ml) by 2 site chemiluminescent immunometric assay, creatinine (mg/dl) by modified Jaffe's method, urea (mg/dl) by urease method and uric acid (mg/dl) by uricase method.

Statistical Analysis

Mean \pm SD were calculated for all the parameters analyzed and were compared by Student's t-test (paired) and correlated by Pearson correlation using SPSS 16.0 for windows. The levels of significance were denoted as P-values ($P < 0.05$ – As significant and $P < 0.001$ – As highly significant).

Results

A total number of 300 cases that includes 200 hypothyroid patients (25% males and 75% females) and 100 controls (42% males and 58% females) were examined.

The mean level of serum T3 (1.968 ± 0.1195 pg/ml), serum T4 (1.0152 ± 0.1235 pg/ml), serum urea (33 ± 5.570 mg/dl) of hypothyroids were significantly lower as compared to mean level of serum T3 (3.704 ± 0.1699 pg/ml), serum T4 (1.5764 ± 0.16230 pg/ml) and serum urea (35.12 ± 3.710 mg/dl) of euthyroids.

The mean level of serum TSH (8.928 ± 0.9589 μ IU/ml) serum Creatinine (2.192 ± 0.2566 mg/dl) and serum uric acid (4.224 ± 0.6554 mg/dl) of hypothyroids were significantly higher as compared to mean level of serum TSH (3.06 ± 0.4110 μ IU/ml), serum Creatinine (0.852 ± 0.1396 mg/dl) and serum uric acid (3.772 ± 0.2975 mg/dl) of euthyroids.

Hypothyroids serum T3 show significant positive Pearson correlation with serum uric acid ($r = 0.343$) but not with serum urea and creatinine. Hypothyroids serum T4 show significant negative Pearson correlation with serum urea ($r = -0.367$) and creatinine ($r = -0.267$) but not with serum uric acid. Hypothyroids serum TSH show significant negative Pearson correlation with serum uric acid ($r = -0.190$) and creatinine ($r = -0.344$) but not with serum urea.

Table 1: Characteristics of study subjects

Hypothyroids			Euthyroids		
Sex	Number	Percentage	Sex	Number	Percentage
Males	50	25%	Males	42	42%
Females	150	75%	Females	58	58%
Total	200		Total	100	

Table 2: Shown the various parameters of renal function in hypothyroids and controls

Parameters		Urea	Uric acid	Creatinine
Serum T3	Pearson Correlation	-0.008	0.343**	-0.027
	Sig. (2-tailed)	0.905	0.000	0.707
	N	200	200	200
Serum T4	Pearson Correlation	-0.103	-0.190**	-0.344**
	Sig. (2-tailed)	0.147	0.007	0.000
	N	200	200	200
Serum TSH	Pearson Correlation	-0.367**	0.112	-0.267**
	Sig. (2-tailed)	0.000	0.116	0.000
	N	200	200	200

Table 3: Correlation of different variables (TSH, T3, and T4) with urea, creatinine and uric acid

Parameters	Hypothyroids (Mean \pm SE)	Euthyroids (Mean \pm SE)	Z- value	P-value
T3 (pg/ml)	1.968 ± 0.1195	3.704 ± 0.1699	91.479	0.000
T4 (pg/ml)	1.0152 ± 0.1235	1.5764 ± 0.16230	30.354	0.000
TSH (μ IU/ml)	8.928 ± 0.9589	3.06 ± 0.4110	74.102	0.000
Urea (mg/dl)	33 ± 5.570	35.12 ± 3.710	3.918	0.000
Creatinine (mg/dl)	2.192 ± 0.2566	0.852 ± 0.1396	58.525	0.000
Uric acid (mg/dl)	4.224 ± 0.6554	3.772 ± 0.2975	8.208	0.000

**Correlation is significant at the 0.01 level (2-tailed).

Discussion

The present case-control based investigation assessed the biochemical parameters of renal capacity in hypothyroid subjects and contrasted the outcomes and those of euthyroid and also the connection of different renal parameters with thyroid hormones (T3, T4 and TSH). This examination demonstrates that there is a huge increment in serum creatinine and serum uric acid levels in hypothyroid patients when contrasted with euthyroid while there is a huge abatement in serum urea in hypothyroid when contrasted with euthyroid. Serum urea demonstrates a huge negative connection with serum TSH and uric corrosive show noteworthy positive relationship with serum T3 and huge negative connection with serum T4 while serum creatinine indicates critical negative connection serum T4 and serum TSH.

Earlier, similar result for serum creatinine has also reported.^{6,7} Relatively comparable changes in serum creatinine with hypothyroidism have been accounted for in segregated contextual investigations and couple of different examinations having lesser number of hypothyroid patients.⁸ Indeed, even newborn children with intrinsic hypothyroidism have demonstrated higher serum creatinine levels in the extent of the seriousness of hypothyroidism, however, no impacts were seen on serum urea levels. The consistency of raised serum creatinine in this investigation with different examinations.⁹ Hypothyroidism influence renal bloodstream, GFR, tubular function, electrolytes homeostasis, and electrolyte pump capacities, and kidney structure.¹⁰

Essential hypothyroidism is related to a reversible height of serum creatinine in both adults¹¹ and children.¹² The expanded serum uric acid in hypothyroid shows either expanded creation because of myopathy related with hypothyroidism or because of diminished renal discrepancy of uric acid.¹³ Histopathological changes in cellular film thickening in nephrons have been exhibited in both hypothyroid inrats¹⁴ and humans.¹⁵

Physiological impacts incorporate changes in water and electrolyte homeostasis, strikingly hyponatremia, and adjustments of renal hemodynamics¹⁶ incorporating decrements in renal bloodstream, renal plasma stream, glomerular filtration rate (GFR), and single nephron GFR. The reason for the diminished renal plasma stream and GFR watched is accepted to be basically due to the summed up hypodynamic condition of the circulatory framework in hypothyroidism. GFR esteems in myxedematous patients are by and large 33% lower than the qualities in euthyroid individuals.¹⁷

Other conceivable component thyroid hormone activity on renal capacity could be clarified by its impact on the development of the renin-angiotensin framework (RAAS). Plasma renin movement and plasma levels of angiotensinogen, angiotensin II and aldosterone are specifically identified with plasma

levels of thyroid hormones.¹⁸ Hypothyroidism is related to low plasma rennin.¹⁹ This examination affirms that the hypothyroid state is related to a predictable elevation in the serum creatinine and uric acid levels, apparently because of a decline in the GFR or modification in RAAS.

A noteworthy connection between's thyroid capacity and purine nucleotide digestion has been built up in hypothyroidism. Giordano et al. contemplated 28 patients with essential hypothyroidism and found a critical increment in the occurrence of both hyperuricemia and gout in the hypothyroid patients.²⁰ Erickson and associate have tentatively assessed that the 54 patients with a recorded gouty joint inflammation for the nearness of hypothyroidism.²¹

The prevalence of hypothyroidism was significantly higher in patients with gouty arthritis. Overall, 15% of these patients, 25% of women and 12% of men, had hypothyroidism. These rates were 2.5-fold greater in women and six fold greater in men than found in the controls. Moreover, our study showed that hyperuricemia in hypothyroidism is related to elevated serum creatinine and diminished creatinine discrepancy. This reality recommends that hypothyroid hyperuricemia is optional to a lessening in renal plasma stream and glomerular filtration, officially very much showed in thyroid hormone lack disorders.

Hypothyroidism-related kidney brokenness is by all accounts more related to the decrease in thyroid hormone levels as opposed to with thyroid autoimmunity.²² Among the instruments engaged with hypothyroidism-related kidney confusions are immediate impacts of TH on the cardiovascular framework (expanded fringe protection and lessening of myocardial contractility and stroke volume) and digestion (hyperlipidemia), and backhanded impacts through paracrine or endocrine middle people, for example, insulin-like development factor write 1 (IGF-1) and vascular endothelial development factor.²³

The reversible relationship amongst hypothyroidism and elevated serum creatinine and uric acid are critical for a clinician. This data maintain a strategic distance from pointless examinations, treatment cost and stress in patients giving either expanded creatinine or gout with undetermined thyroid status. The appraisal of thyroid capacity ought to be routinely completed for assessment of patients giving unhinged renal capacity.

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Conflict of Interest: All the authors have declared that, there has been no conflict of interest at any stage of the study.

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