

## ASSESSMENT OF VARIATION IN BIOCHEMICAL MARKERS OF RENAL FUNCTION IN THYROID DISORDERS

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### ABSTRACT

#### Background

Thyroid disorders are one of the most common endocrine diseases which affect the physiological functioning of the body, mainly affecting the cardiovascular and the renal system. Hypothyroidism influences the metabolic pathways, RAS system and causes hemodynamic changes leading to reduced renal plasma flow and glomerular filtration rate. Hyperthyroidism increases purine turnover. Consequently, there occurs a rise in Serum urea, creatinine and uric acid levels. The study was conducted in Department of Biochemistry, Govt. Medical College, and Kota and attached group of hospitals. The duration of the study was January 2015 to October 2015. Levels of Serum TSH, Urea, Creatinine and Uric acid were measured. A total of 180 patients of ages between 25 – 60 years were included in the study.

#### Method

The estimation of TSH was done by chemiluminescence in Hormonal Assay Lab, and levels of serum urea, creatinine and uric acid were measured by fully auto analyzer EM360 in Biochemistry Lab, Department of Biochemistry, Govt. Medical College, and Kota. Among the total of 180 cases, 60 were hypothyroid (>10mU/L), 60 were hyperthyroid (< 0.05mU/L) and 60 were euthyroid (0.3-4.5mU/L).

#### Results

Analysis was done by Microsoft Excel. Mean  $\pm$  SD of TSH, Serum Urea, Creatinine and Uric acid were calculated in all cases. The results were compared by one - way ANOVA between hypothyroid, hyperthyroid, and euthyroid cases. P value was found to be < 0.05, which is highly significant.

#### Conclusions

Our study shows that disturbance of thyroid hormones is a risk factor for development of renal impairment, gout and renal stones. A significant increase in levels of serum urea, creatinine and uric acid is seen both in hypothyroidism and hyperthyroidism.

**KEYWORDS:** Creatinine, Glomerular Filtration Rate (GFR), Hyperthyroidism, Hypothyroidism, Renin-Angiotensin System (RAS), Thyroid Stimulating Hormone (TSH), Urea, Uric Acid

### INTRODUCTION

Thyroid gland is one of the largest endocrine gland of the body, which secretes tetraiodothyronine or thyroxin (T<sub>4</sub>)

and triiodothyronine (T3). The production of T4 and T3 is further regulated by the hypothalamus (Thyrotropin Releasing Hormone or TRH) and pituitary (Thyroid Stimulating Hormone or TSH). An increase or decrease in TSH levels is a very early biomarker of impending thyroid disorder (1). The main patterns of thyroid dysfunctions are hyperthyroidism and hypothyroidism (2). Thyroid hormones are necessary for growth and development of the kidney and for maintenance of water and electrolyte homeostasis. On the other hand, kidney is involved in the metabolism and elimination of thyroid hormones (3). Hyperthyroidism is also referred as “thyroid storm” or thyrotoxicosis (4). Hypothyroidism is a clinical syndrome caused due to deficiency of thyroid hormones (below the reference range) that causes the general slowing of the metabolic processes (1). Hyperthyroidism is the elevation of circulating thyroid hormones (above the reference range) that affects peripheral tissues leading to increased metabolic activities (5). Thyroid hormones (T3 and T4) regulate the rate of metabolism, affect the growth, modulate energy utilisation by increasing the basal metabolic rate (BMR), by increasing oxygen consumption and heat production (6).

Uric acid is a non-nitrogenous substance produced from purine metabolism, either due to breakdown of ingested purine nucleic acid or from tissue destruction. As thyroid hormones affect most of the metabolic pathways of the body, so purine metabolism is also affected by the disturbance in thyroid hormones, thus leading to hyperuricemia (7). There have been many epidemiological and experimental evidence supporting the hypothesis that uric acid may play direct pathogenic role in multiple diseases including renal diseases (8,9).

Creatinine is a cyclic anhydride of creatine that is produced as the final product of decomposition of phosphocreatine, secreted in urine. Measurement of plasma creatinine and its renal clearance are used as diagnostic indicators of kidney function (10).

Hypothyroidism leads to hemodynamic changes which may cause reduction in renal plasma flow and glomerular filtration rate, hence leading to increased serum uric acid, serum urea and serum creatinine (11,12). This is principally due to the generalised hypo dynamic state of circulatory system in hypothyroidism (13).

Another possible mechanism of action of thyroid hormone on renal function could be explained by its influence on maturation of the renin-angiotensin system (RAS). Thyroid hormones play major role in the growth and development of various tissues, including lungs and kidney, which are the major sites of synthesis of renin and angiotensin-converting enzyme (ACE) synthesis thus thyroid hormone disturbances in early stages affect the RAS components. The renin-angiotensin system consists of a cascade of reactions in which angiotensinogen, the substrate of RAS is cleaved by renin to generate the decapeptide angiotensin-I (A-I). Further the action of a membrane-bound metalloprotease, the peptidyl-dipeptidase, ACE converts A-I into an octapeptide angiotensin-II (A-II). Plasma renin activity and plasma levels of angiotensinogen, angiotensin-II and aldosterone are directly related to plasma levels of thyroid hormones. A-II is the most active peptide of RAS, acts on various tissues of the body via selectively binding to two major subtypes of G-protein-coupled receptors, namely A-II type 1 (AT<sub>1</sub>) and type 2 (AT<sub>2</sub>) receptors (14).

Hypothyroidism is associated with low plasma renin (15). In contrast, hyperthyroidism is accompanied by hyperactivity of RAAS (16). In 1989 Ford et al. (17), in contrast with previous reports (18, 19) demonstrated that hyperthyroidism can cause hyperuricemia by increasing the purine nucleotide turnover and decrease the renal urate excretion.

Normal level of TSH is 0.3 – 3.5 mU/L, in hyperthyroidism TSH level is <0.1 mU/L and in hypothyroidism, level

of TSH > 10mU/L (2).

## AIMS AND OBJECTIVES

To assess the levels of serum urea, creatinine and uric acids in hypothyroid, hyperthyroid and euthyroid cases and establish that biochemical markers of renal function are impaired with thyroid disorders.

## MATERIALS AND METHODS

The study was carried out in Govt. Medical College and attached group of hospitals, Kota, Rajasthan. The study period was from January 2015 to October 2015. A total of 180 patients of ages between 25 – 60 years were included in the study. Among the total of 180 cases, 60 were hypothyroid (>10mU/L), 60 were hyperthyroid (< 0.05mU/L) and 60 were euthyroid (0.3-4.5mU/L).

### Exclusion Criteria Were

- pregnancy
- hypertension and diabetes mellitus
- chronic renal disorders and liver disorders
- congestive heart failure
- dehydration
- bone disorders and muscle dystrophy
- glomerulonephritis and pyelonephritis
- eclampsia & preeclampsia
- Urinary tract obstruction and patients taking nephrotoxic drugs such as amino glycosides, cemitidine, cefoxitin, etc.
- age < 25 years , > 60 years and patients on treatment for hypothyroidism and hyperthyroidism

### Sample

After obtaining the consent of the patients, a overnight fasting sample of 5 ml was withdrawn. The samples were kept for 1hour to clot and then centrifuged at 3000 rpm for 10 minutes in Remi centrifugation machine. Further the serum samples were analyzed for TSH on Roche cobas e 411 by chemiluminescence in Hormonal Assay Lab and serum urea, creatinine and uric acid was done on fully auto analyzer EM360 in Biochemistry lab, New Medical College and Hospital, Department of Biochemistry, Govt. Medical College, Kota, Rajasthan.

The parameters measured on auto analyser were estimated by the following methods:

- Estimation of serum urea by Urease – Berthelot's method(20)
- Estimation of Creatinine was done by the modified Jaffe's method(21)(22)
- Estimation of serum uric acid by using uricase enzymatic method.

## STATISTICAL ANALYSIS

The statistical analysis was performed using Microsoft Excel Program. The results were expressed as Mean  $\pm$ SD. P value <0.05 was considered statistically significant. The results were compared between 3 groups (Euthyroid, Hypothyroid

and Hyperthyroid) by one- way ANOVA.

**RESULTS**

During the 10 months study period from January 2015 to October 2015, a total of 180 patients of both sexes were studied, out of which 60 were euthyroid, 60 were hypothyroid and 60 were hyperthyroid. Level of TSH was measured for the assessment of thyroid status. Thereafter levels of serum urea, creatinine and uric acid were measured as biochemical markers of renal functions. Levels of serum urea, creatinine and uric acid were raised in hypothyroid and hyperthyroid patients.

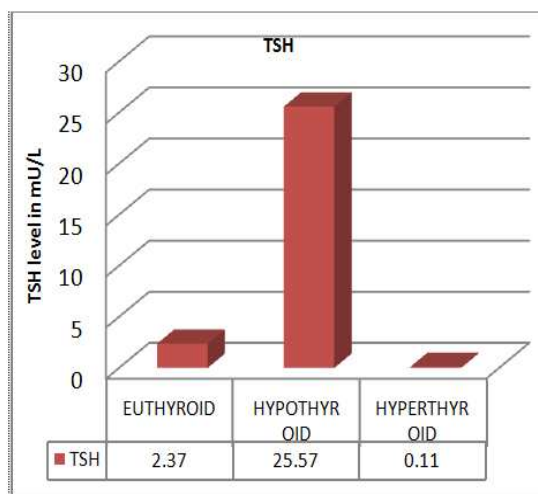
The Mean ± SD of ages (years) of cases in euthyroid was 43.75± 9.91, in the hypothyroid cases Mean ± SD was 37.48± 5.28 and in hyperthyroid cases the Mean ± SD was 47.92± 6.79.

The Mean ± SD of TSH in euthyroid cases was found to be 2.37 ± 0.96, in hypothyroid 25.57 ± 4.23 and in hyperthyroid 0.11± 0.04. The Mean ± SD of serum urea is 25.08 ± 7.13 in euthyroid cases and 57.83 ± 8.23 in hypothyroid and 53.81± 4.88 in hyperthyroid cases. The Mean ± SD of serum creatinine is 0.77 ± 0.09 in euthyroid cases and 1.91 ±1.34 in hypothyroid and 1.85± 0.27 in hyperthyroid cases. The Mean ± SD of serum uric acid is 5.14 ± 0.40 in euthyroid cases and 7.03 ±0.71 in hypothyroid and 6.59 ± 0.54 in hyperthyroid cases.

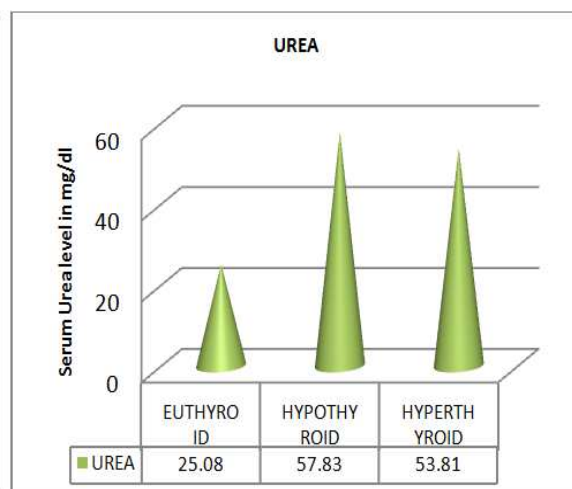
We found that serum urea, creatinine and uric acid levels were raised in cases of hypothyroidism and hyperthyroidism. P value was found to be <0.05, which is highly significant.

**Table 1: Showing Mean ± SD of Age Group, TSH, Serum Urea, Creatinine and Uric Acid in Euthyroid, Hypothyroid and Hyperthyroid Cases  
P Value<0.05 \*was Found to be highly Significant**

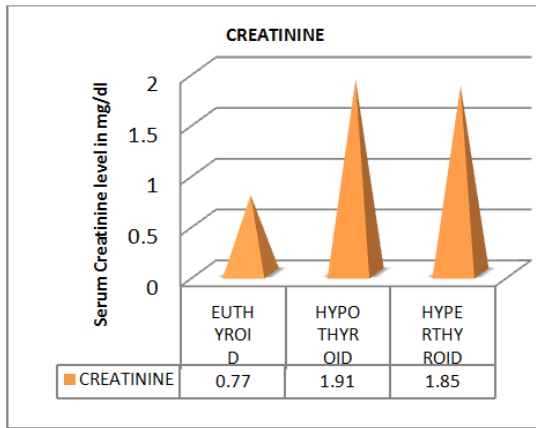
Parameters	Euthyroid (n=60) (Mean± SD)	Hypothyroid (n=60) (Mean± SD)	Hyperthyroid (n=60) (Mean± SD)	P Value
AGE (years)	43.75± 9.91	37.48± 5.28	47.92± 6.79	-
TSH ( mU/L)	2.37 ± 0.96	25.57 ± 4.23	0.11± 0.04	<0.05*
Serum Urea( mg/dl)	25.08 ± 7.13	57.83 ± 8.23	53.81± 4.88	<0.05*
Serum Creatinine( mg/dl)	0.77 ± 0.09	1.91 ±1.34	1.85± 0.27	<0.05*
Serum Uric Acid( mg/dl)	5.14 ± 0.40	7.03 ±0.71	6.59 ± 0.54	<0.05*



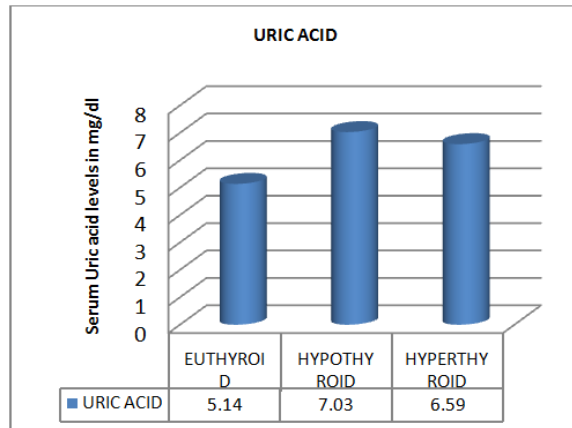
**Graph 1**



**Graph 2**



Graph 3



Graph 4

Graph 1, 2, 3 and 4: Showing the Mean of Serum TSH, Serum Urea, Serum Creatinine and Serum Uric acid in Euthyroid, Hypothyroid and Hyperthyroid Cases

**DISCUSSIONS**

The present study shows that there is a noteworthy rise in the levels of biochemical markers of renal function in thyroid disorders. The cases of both hypothyroidism and hyperthyroidism showed that there is a disturbance in the renal functions, which may be attributed to the pathological changes that occur due to effects of elevated or decrease thyroid hormones. Histological changes in nephrons especially basement membrane thickening has been demonstrated in hypothyroidism (23). Physiological effects include changes in water and electrolyte metabolism notably hyponatremia and alterations in renal hemodynamic(24,25).The cause of decreased renal plasma flow and GFR observed is due to the generalized hypo dynamic state of the circulatory system in hypothyroidism(13). Thyroid hormones also induces relaxation of blood vessels resulting in reduction in vascular resistance and increase serum levels of renin activity and angiotensinogen concentration(26). There may be a possible inter-relationship between purine nucleotide metabolism and thyroid disorders.s

The serum uric acid levels are significantly increased in the hyperthyroidism cases which may be attributed to the increased levels of thyroid hormones, this agrees with study of Jeff 2008(27). The increased levels of thyroid hormones lead to increased metabolic fate of purine metabolites, hence causing increased production of uric acid in the blood. The level of production of uric acid exceeds the renal capacity to excrete uric acid, which may accumulate in joints causing gout or may get deposited causing renal stones.(28). In hypothyroidism, the reduced renal plasma flow and decreased GFR caused due to low levels of thyroid hormones may lead to hypothyroid hyperuricemia. In a study conducted by Schmid et al (29) among 14 newly diagnosed cases of hypothyroidism, mean serum creatinine level was found to be elevated and decreased after thyroid replacement therapy. The changes of serum urea and creatinine levels develop rapidly and appear to be reversible.

**CONCLUSIONS**

Our study shows that disturbance of thyroid hormones is a risk factor for development of renal impairment, gout and renal stones. A significant increase in levels of serum urea, creatinine and uric acid is seen both in hypothyroidism and hyperthyroidism. Thyroid gland being one of largest endocrine gland of the body influences almost all the major systems of the body. Elevated or decreased levels of thyroid hormones profoundly affect the renal system. The assessment of

thyroid functions should be routinely carried out in patients with altered biochemical renal markers and vice versa. We emphasize on the routine investigation of cases with thyroid disorders.

### LIMITATIONS OF THE STUDY

- There is a need to explore this study further.
- TPO antibodies could not be measured due to certain limitations.
- Thyroid scan was not done due to limitations.

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