

## Original Research Article

# Serum BUN and creatinine estimation in patients of overt hypothyroidism: a case control study

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## ABSTRACT

**Background:** Hypothyroidism or underactive thyroid or low thyroid is a common endocrine disorder characterized by low serum T3 (triiodothyronine), T4 (thyroxine) and raised TSH (thyroid stimulating hormone). Thyroid hormones are involved in renal development and hemodynamic, kidney structure and GFR (glomerular filtration rate). Aim of this study was to see the alteration of basic renal markers in patients of hypothyroidism.

**Methods:** A total of seventy subjects were included in the study. Thirty-five were patients of hypothyroidism and thirty-five were age and sex matched normal controls. Serum T3, T4, TSH, creatinine and BUN (blood urea nitrogen) were estimated in both groups.

**Results:** Serum T3, T4 were significantly decreased and TSH was significantly raised among cases as compared to controls. Mean value of serum creatinine and BUN were within normal range in both the groups but these values were significantly raised among cases as compared to controls with p value 0.02 and 0.003 respectively. Also, there was positive correlation of TSH with BUN and creatinine among cases.

**Conclusions:** Hypothyroidism is associated with deranged renal function.

**Keywords:** BUN (blood urea nitrogen), Creatinine, GFR, Hypothyroidism

## INTRODUCTION

Triiodothyronine (T3) and thyroxin (T4) are tyrosine based hormones, partially made of iodine that is produced by thyroid gland. Ratio of T4 to T3 in human body is 14:1 to 20:1.

These hormones act on almost every cell of body, regulate metabolism of carbohydrate, protein, fat and vitamins.<sup>1,2</sup> Thyroid gland secrete T4 (prohormone)

which get converted to active form T3 in other organ by enzyme deiodinase, a selenium dependent enzyme. This active T3 binds to THR (thyroid hormone receptor) in nucleus of cell where it activates gene leading to production of specific protein.<sup>3</sup> T3 also bind on cell membrane to integrin  $\alpha\beta_3$ , stimulate sodium hydrogen antiporter, cell growth and angiogenesis.<sup>4</sup>

Overt hypothyroidism is caused by inadequate function of thyroid gland itself and iodine deficiency is the most

common cause. In areas where iodine is sufficient, Hashimoto's thyroiditis (chronic autoimmune thyroiditis) is the cause.<sup>5,6</sup> Overt primary hypothyroidism is diagnosed by low serum T3 and T4 and elevated TSH level.<sup>7</sup> According to study done by Allen Carle, life time risk of developing hypothyroidism is 2.3% with three times more prevalence in women than males.<sup>8</sup>

Hypothyroidism is associated with low sodium level in blood together with elevation in antidiuretic hormone as well as acute worsening of kidney function due to number of causes.<sup>9</sup> These hormones are essential for the growth of renal cells and for maintaining the homeostasis of fluid and electrolyte level.

So, renal system is adversely affected by hypothyroid state of body.<sup>10</sup> Thus, the aim of this study was to evaluate the renal markers, serum BUN and creatinine level in patients of hypothyroidism.

**METHODS**

This was a case control study conducted at, VIMS Pawapuri, Bihar, India, from August 2016 to May 2017. Study comprised a total of 70 subjects. 35 were patients of newly diagnosed cases of overt hypothyroidism attending the department of medicine. 35 were age and sex matched healthy controls, paramedical staffs and attendants of patients. Written informed consent was taken from all subjects after explaining them the whole research protocol. Study was conducted in accordance with Helsinki Declaration.

Age of patients in both groups ranged from 20-45 years. Diagnosis of hypothyroidism was based on raised T3, T4 level and decreased TSH level. T3, T4 and TSH were estimated by ELISA, Direct immunoenzymatic colorimetric method. Serum BUN was estimated by UREASE-GLDH method. Serum Creatinine was estimated by Jaffe's method.

- Normal range of serum T3 = 52-185 ng/ml
- T4 =5-15µg/dl
- TSH=0.39-6.16mIU/ml
- Creatinine= 0.6-1.4 mg/dl
- BUN=6-21mg/dl
- Urea = 2.14×BUN

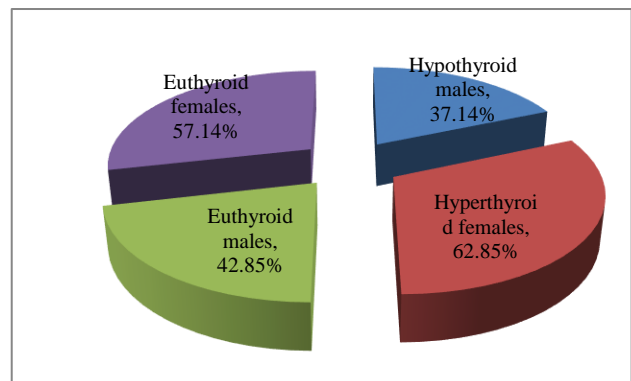
5ml of venous blood was collected from all 70 subjects under aseptic precaution after an overnight fast of 8 to 12 hours. Blood was left for half an hour to clot and then it was centrifuged and serum was separated. Patients with diagnosed kidney disease, previously diagnosed hypothyroid patients taking medication or any chronic illness were excluded from the study.

**Statistical analysis**

Data were represented as mean and standard deviation. Graph pad prism 5.0 statistical software was used for data analysis. Student's unpaired t test was applied to the result data correlation of TSH with BUN and Creatinine was done by Pearson's correlation coefficient. Results of the study were discussed at 95% confidence interval and p value < 0.05 was considered significant.

**RESULTS**

Mean age of hypothyroid patients was 38.08 ±13.09 and that of euthyroid subjects was 37.6±12.65 with p value 0.87. Among hypothyroid patients 13 (37.13%) were males and 22 (62.85%) were females. Among euthyroid subjects 15 (42.85%) were males and 20 were females (57.14%) as shown in Figure 1.



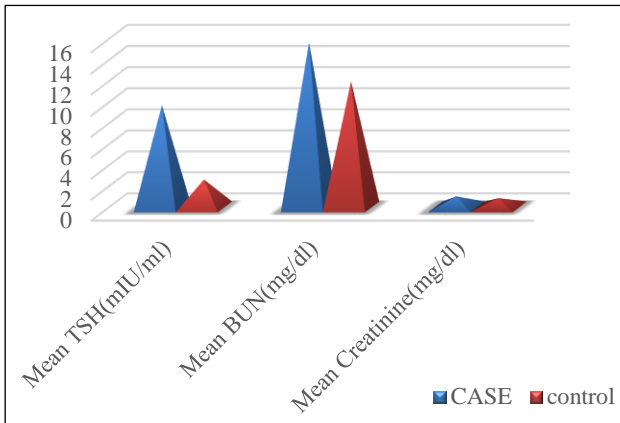
**Figure 1: Sex distribution among cases and control.**

T3 and T4 among cases were significantly decreased as compared to controls with p value <0.0001. TSH was significantly increased among cases as compared to controls with p value <0.0001 as shown in Table 1.

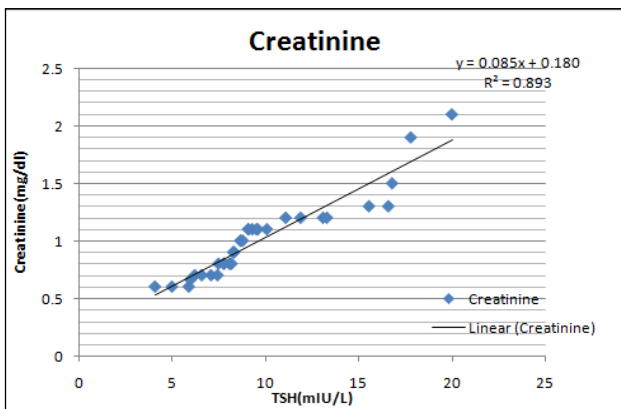
**Table 1: Mean value of different parameters among cases and control.**

Parameters	Case (hypothyroid patients) (Mean ± SD)	Control (euthyroid subjects) (Mean ± SD)	P value
T3 (ng/dl)	48.20±9.63	84.01±31.90	<0.0001
T4 (µg/dl)	4.72±0.74	10.90±2.66	<0.0001
TSH (mIU/ml)	9.71±3.75	2.62±1.08	<0.0001
BUN (mg/dl)	15.65±4.51	11.96±5.59	0.003
Creatinine (mg/dl)	1.007±0.33	0.84±0.24	0.02

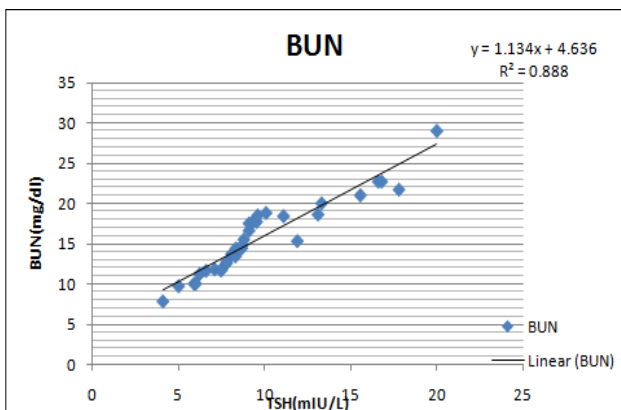
**Figure 2: Mean value of serum TSH, BUN and creatinine among cases and control.**



Mean value of serum BUN and Creatinine among cases and control were in normal range. However mean value of BUN and Creatinine were significantly higher in cases as compared to controls with p value 0.003 and 0.02 respectively as shown in Table 1. Comparative mean value of serum TSH, serum BUN and serum Creatinine among cases and control is shown in Figure 2.



**Figure 3: Positive correlation between serum TSH and creatinine among cases.**



**Figure 4: Positive correlation between serum TSH and BUN among cases.**

Study also found a positive correlation between serum TSH and serum creatinine level among hypothyroid patients as shown in Figure 3. Same positive correlation was found between serum TSH and serum BUN among hypothyroid patients as shown in Figure 4.

**DISCUSSION**

This study was carried out to show the association of rising TSH level with creatinine and BUN (blood urea nitrogen) in patients of hypothyroidism. T3 and T4 hormones by their pre-renal and intrinsic effects, increase renal perfusion and GFR (glomerular filtration rate).<sup>11</sup> Decreased T3 and T4 (as in case of hypothyroidism) results in decreased renal perfusion and GFR.

Functioning renal mass is measured as kidney to body mass ratio. This ratio is decreased in hypothyroid patients.<sup>12</sup> It has been reported that GFR is reversibly reduced by 40% in 55% case of hypothyroidism.<sup>13</sup> It is due to decreased responsiveness to β adrenergic stimuli leading to decreased rennin release, decreased angiotensin II and altered RAAS (renin-angiotensin-aldosterone) activity, all causing decreased GFR.<sup>14</sup> The study, published in nephrology dialysis transplantation (2015;30:282-287), also found that a 10 mL/min/1.73 m2 lower eGFR was associated with a 0.11 mIU/L higher serum level of thyrotropin (TSH).

Serum creatinine is reversibly raised in patients of hypothyroidism. It is due to decreased GFR and associated myopathy and rhabdomyolysis. Moreover, poor circulation results in lower blood flow to the kidneys and so lessens its ability to clear the urea leading to raised urea level in blood.<sup>15</sup> The reason behind decreased renal plasma flow and GFR is hypodynamic state of circulatory system in hypothyroid patients.<sup>16</sup>

Increased level of creatinine and BUN in patients of hypothyroidism is a reversible change and can be reverted by correcting thyroid hormone deficiency.<sup>17</sup>

Present study shows that both renal markers i.e. creatinine and BUN are increased in patients of hypothyroidism and there exists a positive correlation of TSH with creatinine and BUN. Present study matched with Sidhu GK et al who had also shown raised creatinine and urea in patients of hypothyroidism.<sup>18</sup> Present study also matched with Kaur V et al who has shown raised urea and creatinine in patients of subclinical and overt hypothyroidism and has established a positive correlation of TSH with these markers.<sup>19</sup> The study done by Qahtan A et al has shown positive correlation between TSH and creatinine in hypothyroid patients like present study and negative correlation with urea unlike present study.<sup>20</sup>

**CONCLUSION**

From this study, it is concluded that hypothyroidism is associated with decreasing renal function. The greater the

degree of hypothyroidism, the greater is the renal impairment. So, this study is a helpful guide to the clinicians that every hypothyroid patient must be screened for renal function so that any impairment can be diagnosed at an early stage and precautions taken. Limitation of present study was that our sample size was small. Further studies are needed taking larger number of subjects which could give a more acceptable result.

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*Ethical approval: The study was conducted in accordance with Helsinki declaration*

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