



A STUDY OF CHANGES IN ELECTROLYTES AND CREATININE LEVELS IN HYPOTHYROID PATIENTS OF RIMS RANCHI JHARKHAND.

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ABSTRACT

INTRODUCTION: Hypothyroidism impacts renal function including deranged creatinine and electrolyte levels.

OBJECTIVES: To study levels of electrolytes and creatinine in hypothyroid patients attending RIMS Ranchi Jharkhand.

MATERIAL AND METHOD: 50 Patients and 50 control samples were taken. Thyroid estimation was done on ABOIT ARCHITECT i1000 SR IMMUNOASSAY machine. Creatinine was estimated on BECKMANN COULTER AU480. Electrolytes were estimated on ECOLYTE. Data was analysed using SPSS 20.

RESULT: Cases have higher creatinine & potassium and lower sodium as compared to control.

KEYWORDS : Creatinine, Electrolytes, Hypothyroidism

INTRODUCTION

The thyroid gland produces two related hormones, thyroxine (T4) and triiodothyronine (T3). Acting through thyroid hormone receptors α and β , these hormones play a critical role in cell differentiation during development and help to maintain thermogenic and metabolic homeostasis in adults.¹ Thyroid hormones are necessary for growth and development of the kidney and for the maintenance of water and electrolyte homeostasis. On the other hand, kidney is involved in the metabolism and elimination of thyroid hormones. Moreover, the decline of kidney function is accompanied by changes in the synthesis, secretion, metabolism, and elimination of thyroid hormones. Different treatments used in the management of patients with kidney and thyroid diseases may be accompanied by changes or adverse events that affect thyroid and kidney function respectively.²

Hypothyroidism is a clinical syndrome caused by deficiency of thyroid hormones (below reference range) that causes a generalized slowing of metabolic process.^{3,4} Primary hypothyroidism is a frequent syndrome, having prevalence of 0.5–2.0% among women and around 0.2% among men. According to several authors, recently the number of patients with autoimmune diseases with hypothyroidism have increased by 2.1%.⁵

Certain effects of hypothyroid state on the kidney are well established. Physiological effects include changes in water and electrolyte metabolism and reliable alterations of renal hemodynamics, including decrements in renal blood flow, renal plasma flow, glomerular filtration rate (GFR), and single nephron GFR.

The cause of decreased renal plasma flow and GFR observed is believed to be principally due to the generalized hypodynamic state of the circulatory system in hypothyroidism.^{6,7} Hypothyroidism is associated with many biochemical abnormalities including serum creatinine and electrolyte levels.

Creatinine is the cyclic anhydride of creatine that is produced as the final product of decomposition of phosphocreatine. It is excreted in urine. Measurement of plasma creatinine and its renal clearance are used as diagnostic indicators of kidney function. Hypothyroidism doesn't contribute to progression of CKD except mild to moderate reduction in GFR. Moreover, the effects of thyroid hormones on renal function and electrolyte balances have not been well established in RIMS RANCHI JHARKAND population.

Sodium and potassium are important components of the enzyme Na^+/K^+ ATPase, which is an enzyme present on the cell membrane

that helps in the transport of water and nutrients across the cell membrane.⁸ Thyroid hormones regulate the activity of sodium potassium pumps in most of the tissues.⁹ In the recent years research is focused on outcomes of patients with electrolyte disorders, mainly hypo- and hypernatraemia, which were found to be associated with increased mortality,¹⁰ but also disorders of potassium are shown to be the predictors for increased mortality.¹¹

With this background, the present study will be undertaken to assess the renal function and alterations in the level of serum electrolytes and creatinine in patients with thyroid dysfunction.

AIMS AND OBJECTIVES

1. To study levels of electrolytes and creatinine in hypothyroid patients of RIMS Ranchi Jharkhand.
2. To correlate electrolytes and creatinine levels in hypothyroid patient of RIMS Ranchi Jharkhand.

MATERIAL AND METHOD

The present study "A study of changes in electrolytes and creatinine levels in hypothyroid patients of RIMS Ranchi Jharkhand" was conducted in Department of Biochemistry, Rajendra Institute of Medical Sciences, Ranchi.

Prior approval from ethical committee was obtained.

STUDY DESIGN: Type of the study: Retrospective study.

Period of study: The period of study was from November 2016 to October 2017.

Sample size: 100

Selection of study subject included:

1. The cases comprised of patients coming to the Department of Biochemistry, Rajendra Institute of Medical Sciences, Ranchi for their thyroid profile test and were categorized as hypothyroid on the basis of their investigation report. The study group also comprised of patients assigned by the Department of Medicine after diagnosis of thyroid disorder.
2. The control group comprised of normal healthy euthyroid people living in and around the area of RIMS Ranchi.

Subjects were classified into 2 groups:¹²

1. Control: Euthyroid with normal thyroid profile
2. Case: Only primary hypothyroid patient having TSH ≥ 10 $\mu\text{IU/ml}$ and decreased FT3 and FT4 levels.

INCLUSION CRITERIA:

1. Age 18-60 yr.
2. Sex either male or female.

3. Should be fasting for at least 12 hours.
4. Should readily agree to participate in the study with an informed consent.
5. Only newly diagnosed and untreated cases of primary hypothyroidism.

Exclusion criteria:

- a) Pregnancy
- b) Paediatric age group (<18 yrs).
- c) Elderly age group (>60 yrs).
- d) Renal disorders.
- e) Hepatic disorders.
- f) Bone disorders.
- g) Diabetes, hypertension or any other systemic illness that may affect the renal function.
- h) Patients on drugs for treatment of thyroid disorders
- i) Any other medications that might affect renal function.

STUDY TOOLS:

1. Consent from the subject and an interview based on questionnaires.
2. Collection of blood samples :-an overnight fasting of at least 12 hour prior to blood collection with caution to avoid haemolysis and contamination.
3. Processing and biochemical analysis of blood samples:-
 (A)The serum creatinine was estimated by JAFFE'S method on BECKMAN COULTER AU480 machine.
 (B)The thyroid profile was estimated by Chemiluminescent Microparticle Immunoassay method on ABOTT ARCHITCT i1000SR IMMUNOASSAY machine.
 (C) Electrolytes were estimated by Ion Selective Electrode on ECOLYTE ESCHWEILER COMPACT ISE machine.

STATISTICAL ANALYSIS AND RESULTS

The results of present study were obtained from 100 subjects out of which 50 were control healthy individuals and 50 were cases of primary hypothyroidism. All results were expressed in Mean ± Standard deviation (Mean±SD). The data analysis was done using SPSS software (USA, Chicago, version 20.0). Unpaired student 'T' test was used for comparison between two groups. Pearson's correlation coefficient was used to test correlation between FT3, FT4 & TSH with sodium, potassium and creatinine in primary hypothyroid cases. 'p' value <0.05 was considered to be statistically significant.

Table 1: Age Wise Distribution of Study Population

Age groups (years)	Cases (Primary hypothyroids)	Control
10-20	5	6
21-30	17	13
31-40	18	12
41-50	5	13
51-60	5	6
Total	50	50

Table no 2: Sex wise Distribution of Study Population

Study group	Male	Female	Total
case	22%	78%	100%
control	22%	78%	100%

Table 3: Comparison of levels of TSH and ELECTROLYTES AND CREATININE between cases and controls:

Parameter	Control	Case	'p' value
TSH(µIU/ml) Values expressed as mean ± SD	2.08±1.14	60.24±34.33	0.000
Creatinine(mg/dl) Values expressed as mean ± SD	0.81±0.20	1.19±0.23	0.000
Sodium(mmol/L) Values expressed as mean ± SD	138.28±2.20	133.54±5.08	0.000
Potassium(mmol/L) Values expressed as mean ± SD	4.38±0.50	4.74±0.86	0.013

TABLE NO 4: Correlation of TSH with sodium potassium and creatinine in primary hypothyroid cases:

TSH	Parameters	r value	p value
	Creatinine	0.310	0.028
	Sodium	-0.334	0.018
	Potassium	0.459	0.001

DISCUSSION

Hypothyroidism is a condition in which the body suffers from insufficiency of thyroid hormone. Thyroid hormones are involved in controlling various metabolisms, more importantly renal and electrolytes metabolism. Thyroid hormones play as a central regulator of body hemodynamics, thermoregulation and metabolism. Therefore, it has an influence on renal hemodynamics, glomerular filtration and electrolyte handling.¹³ Hypothyroidism is a very common condition and is seen more commonly in women than in men. Earlier statistics also have suggested that hypothyroidism is more common in women than in men.^{14,15} The higher prevalence of thyroid disease in women suggests that estrogen might be involved in the pathophysiology of thyroid dysfunction. Estradiol has an antagonistic effect on the hormones T3 and T4. The reason being, estradiol competes with T3 and T4 for binding sites on the receptor proteins.¹⁶ Estradiol also limits the thermogenic action of T4 and promotes storage of fat.

The goal of this study was to compare the levels of FT3, FT4, TSH and to evaluate creatinine and electrolytes in primary hypothyroid patients and finding correlation between them.

In the present study prevalence of hypothyroidism was found to be high in patients. Although all age group presented with a high prevalence of hypothyroidism, higher number of subjects was observed between age group of 21-40 years of age. This is in accordance with study done by Tayal D et al 20097 (Table no 1)

Prevalence of primary hypothyroidism was high in females with about 78 % cases. (Table no 2). This is in accordance with studies done by Sheikh BA et al 200914 and Ali M N et al 2008.15

There was a statistically significant (p=0.000) increase in mean TSH in cases (60.24±34.33) compared to controls (2.08±1.14) (Table no 3). These findings were in accordance with study by Tayal D et al 2009.7

Rodrigo C et al 201117 showed that there are several case reports of renal damage in untreated hypothyroidism. The pathogenesis is multifactorial. There is a possible link between thyroid hormones and kidney injury which may be due to reduced cardiac output causing a decreased plasma flow and glomerular filtration rate due to the hypodynamic circulation. The hypodynamic circulatory state causes prerenal insufficiency which may be aggravated by other multi-systemic effects of hypothyroidism such as reduced cardiac output, low volume state, and increased peripheral resistance due to the arterial wall stiffness. Primary glomerular and tubular dysfunction in hypothyroidism has been observed with supportive histological evidence from biopsy specimens with thickening of glomerular and tubular basement membranes and inclusions in cell cytoplasm. Rhabdomyolysis, another rare manifestation of hypothyroidism can also result in acute kidney injury. These are reversible with thyroxine treatment.

In the present study, there was statistically significant (p=0.000) increase in serum creatinine in cases (1.19±0.23) as compared to controls (0.81±0.20) (Table no 3) and is in accordance with the study of Tayal D et al 20097, which also showed a significant increase in serum creatinine in hypothyroid patients compared to euthyroid. Another study done by Kreisman and Hennessey 199918 also found that mean serum creatinine level in hypothyroid cases was significantly greater in comparison to euthyroid value. In another study by Schmid C et al 200419 on 14 newly diagnosed hypothyroid patients in Switzerland, mean serum creatinine level was found

elevated and decreased after thyroxine replacement therapy. Some more study done by Khan MAH et al 2005²⁰ in the Biochemistry department of Bangabandhu Sheikh Mujib Medical University, serum creatinine value was found significantly higher in cases compared to controls. Serum creatinine concentration in hypothyroid patients increases due to reduction of glomerular filtration rate because of hemodynamic changes in severe hypothyroidism.

There was a positive correlation between TSH and creatinine among hypothyroids with $r = 0.310$ and also statistically significant $p = 0.028$ (Table no 10). These studies were in accordance with Tayal D et al 2009⁹ and Prakash A et al 2006.²¹

Hyponatremia is the most common electrolyte abnormality encountered in clinical practice in hypothyroidism as shown by Kargili et al., 2010.²² Our study demonstrated a statistically significant ($p=0.000$) low level of serum sodium in cases (133.54 ± 5.08) than controls (138.28 ± 2.20) (Table no 3), and also statistically significant ($p=0.013$) increased levels of potassium in cases (4.74 ± 0.86) as compared to controls (4.38 ± 0.50). (Table no 3).

According to Saruta T et al, 1980²³ Plasma Renin Activity (PRA) and Plasma Aldosterone (PA) may be suppressed in hypothyroidism probably due to dysfunction of juxtaglomerular cells and glomerulosa cells respectively and the possibility that suppression of PRA and PA in patients with hypothyroidism is related to exaggerated sodium excretion and decrease in potassium excretion.

Study done by Christoph Schwarz et al 2012²⁴ observed association between thyroid hormones and electrolyte disorders. In his study there was decreased sodium and increased potassium levels in hypothyroidism. According to him electrolyte abnormalities are relevant only in marked hyper and hypothyroidism. Our study is in conformity with the study done by Christoph where we too observed electrolyte changes in hypothyroidism. Study done by Murgod et al 2012⁸ observed electrolyte changes and lipid abnormalities in hypothyroidism. In their study they found decreased sodium and decreased potassium levels along with lipid abnormality in hypothyroidism. However our study was not in conformity with the study done by Murgod et al 2012. In the present study along with decreased sodium there was increased potassium. According to them, Thyroid hormones regulate the activity of sodium potassium pumps in most of the tissues by regulating Na⁺-K⁺ ATPases and in hypothyroidism because of low potassium levels, and because of deficiency of thyroid hormones, this enzyme is affected, resulting in accumulation of water inside the cells and causing edema. This is said to be one of the mechanisms responsible for weight gain seen in hypothyroid patients⁹. Hyponatremia was recently shown to be associated with an increased risk of falls and fractures, making the subject more relevant for patients prognosis, especially the elderly.²⁵

In the present study it showed negative correlation between TSH and serum sodium with $r = -0.334$. (Table no 4). In case of potassium it showed, positive correlation $r = 0.459$ with TSH (Table no 4). Potassium correlation was statistically significant with TSH.

CONCLUSION

This study was undertaken to study the levels of FT3, FT4, TSH and their effect on different biochemical parameters such as creatinine, sodium and potassium in primary hypothyroid patients.

This study showed that in cases of hypothyroidism TSH level were increased and levels of FT3 and FT4 were on lower side.

The current study showed that there was increase in levels of serum creatinine in cases of hypothyroidism as compared to normal healthy people which were statistically significant in case as compared with controls.

It also showed decrease in serum sodium and increase in serum potassium in cases as compared to controls, which were statistically significant.

With increase in TSH there was increase in creatinine and potassium and was also associated with decrease in sodium. These were statistically significant in hypothyroid patients.

This study concludes that as the severity of thyroid hormone deficiency increases, renal as well as cardiovascular system is involved more and more and electrolyte imbalance becomes more prominent.

Last but not the least this study also suggests that hypothyroid patients should take early initiatives including periodic monitoring of serum electrolytes, renal profile and thyroid profile and appropriate intake of thyroxine for prevention of long term complications like renal failure and hyponatremia.

Although the finding of this study may be utilized for the prospective management of hypothyroid cases, further studies involving larger sample size of hypothyroid cases along with their follow up studies are needed to explore the actual differences in the effects of thyroid hormones in primary hypothyroid patients.

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