ORIGINAL RESEARCH PAPER
Volume - 10 | Issue - 04 | April - 2021 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

SERUM CREATININE AND SERUM URIC ACID LEVEL IN SUBCLINICAL AND OVERT HYPOTHYROIDISM PATIENTS: A HOSPITAL BASED COMPARATIVE STUDY.

Biochemistry

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ABSTRACT

Objectives: This present study was to evaluate the association in the levels of TSH, FT3, FT4, serum creatinine and serum uric acid levels of various age group of subclinical and overt hypothyroidism patients. **Methods:** A sample of 5 ml venous blood was collected. After clotting it was centrifuged. fT3, fT4, TSH were estimated by using Erba Mannhein machine using CLIA method. Serum creatinine and uric acid were measured by auto-analyser Biosystem using their own kits. Creatinine was estimated by alkaline picrate method, and uric acid by uricase peroxidase method. **Results:** Most of the patients 28(35%) of hypothyroidism were belonged in age group of 41-50 years. 18(22.5%) patients were in age group of 31-40 years. Majorities of patients (62.5%) were females. Male and female ratio was 3:5. A statistically significant difference were seen in between the levels of FT3, FT4, TSH, serum creatinine and serum uric acid of subclincal to overt hypothyroidism patients respectively ($p \leq 0.05$). And, Significant association of TSH was seen with the levels of serum creatinine and uric acids between the patients of subclinical and overt hypothyroidism.
Conclusions: Thyroid dysfunction is commonly seen in middle age population. And it is more common in females than males. A statistically significant association was seen in TSH, FT3, FT4, serum uric acid and serum creatinine levels between the patients of subclinical and overt hypothyroidism. Serum creatinine and serum uric acid level was significantly higher in overt hypothyroidism as compared to subclinical hypothyroidism patients. Hence, the understanding of this association, hypothyroidism should be evaluated and treat by a multisystem approach. Assessment of thyroid function should be performed in patients presenting with deranged renal function.

KEYWORDS

Subclinical hypothyroidism, Overt hypothyroidism, Serum uric acid, serum creatinine

INTRODUCTION

Hypothyroidism is a common metabolic disorder in general population [1]. It is a clinical syndrome resulting from a deficiency of thyroid hormones leading to generalized slowing down of metabolic processes. It affects 2-15% of population worldwide and is one of the most common endocrine disorders in India. Women are more commonly affected compared to men [2]. The prevalence of primary hypothyroidism is 1:100 but it may be 5:100 if patients with subclinical hypothyroidism [normal T4, raised thyroid stimulating hormone (TSH)] are included (0.5–2.0% in female and 0.2% in male) [3]. Iodine deficiency is the most common cause of hypothyroidism worldwide [4]. In most parts of the world, iodine is a scarce component of soil, and hence it is little in food [5]. In area of iodine sufficiency, autoimmune disease (Hashimoto's thyroiditis) and iatrogenic causes are the most common causes of hypothyroidism [4].

Hypothyroidism is divided into overt and subclinical forms. Subclinical hypothyroidism is characterized by increased serum TSH and normal free triiodothyronine (fT3), free tetraiodothyronine (fT4) levels. Overt is characterized by increased TSH and decreased fT3, fT4 levels [6].

TSH elevation in subclinical hypothyroidism is modest with the values typically between 4 – 15 mU/ L5. It affects virtually every tissue in the body. This includes slowing of physical and mental activity [7]. Thyroid dysfunction causes remarkable changes in glomerular and tubular functions and electrolyte and water homeostasis [8]. It is associated with many biochemical abnormalities including increased serum creatinine levels. The serum creatinine concentration increases in hypothyroid patients due to reduction of glomerular filtration [9]. Studies suggests that in hypothyroidism there is decreased myocardial contractility and stroke volume with increased peripheral vascular resistance, which reduces the effective renal plasma flow and GFR, causing decreased clearance of creatinine and uric acid. This leads to elevation of serum creatinine and uric acid levels in hypothyroidism [10]. Objectives of our study was to evaluate the associations in the levels of TSH, FT3, FT4, serum creatinine and serum uric acid in subclinical and overt hypothyroidism patients.

MATERIALS & METHODS

This present study was conducted in Department of Biochemistry, VIMS Pawapuri, Nalanda, Bihar during a period from January 2020 to December 2020. Entire subject signed an informed consent approved by institutional ethical committee of VIMS was sought.

Detailed history and clinical examination of all subjects were performed. 80 newly diagnosed hypothyroid cases with age group 20 years to >70 years were enrolled. Out of total 80 cases, 50 patients had subclinical hypothyroidism and 30 cases had overt hypothyroidism. Exclusion criteria of this study were the patients with chronic kidney diseases, gout, diabetes mellitus, hypertension, hypothyroid patients on treatment, hyperthyroid patients, muscular dystrophies, pregnant and lactating women. Patients on hypolipidaemias, antiepileptic drugs and women on oral contraceptives were also excluded from the study.

Procedures:

A sample of 5 ml venous blood was collected. After clotting it was centrifuged. fT3, fT4, TSH were estimated by using Erba Mannhein machine using CLIA method.[8] Normal value ranges for fT3 (1.2 - 4.1 pg/ml), fT4 (8.9-17.8 pg/ml), TSH (0.45-5.0 µIU/ml). Serum creatinine (0.6-1.4 mg/dL) and uric acid (2.7-6.5 mg/dL) were measured by auto-analyser Biosystem using their own kits. Creatinine was estimated by alkaline picrate method, and uric acid by uricase peroxidase method.

STATISTICAL ANALYSIS

Data was analysed by using IBM SPSS version 26 software. Mean ± standard deviations were calculated. Unpaired t -test was applied. P-value was taken less than or equal to 0.05 ($p \leq 0.05$) for significant differences.

OBSERVATIONS

A total of 80 patients of hypothyroidism with age group 20 years to greater than70 years were enrolled in this study. Among them 30 patients had overt hypothyroidism and 50 patients had subclinical hypothyroidism. Most of the patients 28(35%) of hypothyroidism were belonged in age group of 41-50 years. 18(22.5%) patients were in age group of 31-40 years. And 15(18.75%) patients were belonged in age group of 51-60 years. Male and female ratio was 3:5.

Table.1. Age wise distributions of hypothyroidism patients

Age group (years)	No. of patients	Percentage of patients
20-30	6	7.5%
31-40	18	22.5%
41-50	28	35%
51-60	15	18.75%
61-70	9	11.25%
>70	4	5%
Total	80	100%

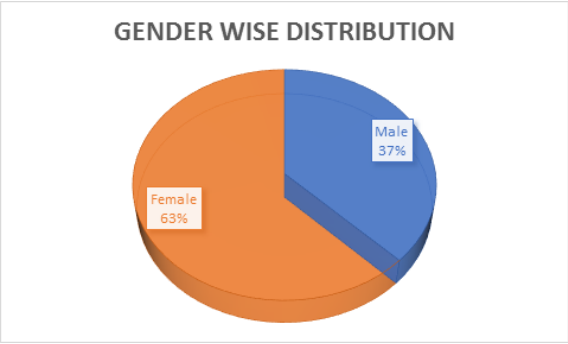

Figure.1. Gender wise distribution of hypothyroidism patients

Table.2. Thyroid parameters of subclinical and overt hypothyroidism patients.

Parameter	Subclinical hypothyroidism	Overt hypothyroidism	Mean differences	P-value
Ft3	2.54±0.98	1.02±0.22	1.52	<0.001
FT4	11.43±1.96	5.86±2.12	5.57	<0.001
TSH	22.42±13.10	86.11±19.65	63.69	<0.001
Serum creatinine	1.01±0.31	2.10±0.49	1.09	<0.001
Serum uric acid	5.64±0.81	7.47±1.46	1.83	<0.001

In this present study, when we compare the levels of FT3, FT4, TSH, serum creatinine and serum uric acid of subclincal hypothyroidism patients to overt hypothyroidism respectively. P-value was found to be less than 0.001. Which is statistically significant. But, greater mean differences was seen in TSH levels in patients with subclinical and overt hypothyroidism patients. And, Significant association of TSH was seen with the levels of serum creatinine and uric acids between the patients of subclinical and overt hypothyroidism.

DISCUSSIONS

The interactions between thyroid gland and renal functions are known for years [11]. Thyroid dysfunction can affect renal physiology and development, and on the other hand, kidney disorders can confluence thyroid function [12].

Thyroid hormones (T4 and T3) regulate the rate of metabolism, affect growth, and modulate energy utilization by increasing the basal metabolic rate and increasing oxygen consumption, and facilitating heat production3. Long standing hypothyroidism can cause significant changes in renal function such as a decrease in sodium reabsorption in the proximal tubule, impairment in the concentrating and diluting capacities of the distal tubules, a decrease in the urinary urate excretion and a decrease in the renal blood flow and glomerular filtration rate (GFR) [13,14].

In this present study, a total of 80 patients of hypothyroidism with age group 20 to >70 years were enrolled. Among them 30 patients had overt hypothyroidism and 50 patients had subclinical hypothyroidism. Most of the patients 28(35%) were belonged in age group of 41-50 years and 18(22.5%) patients in age group of 31-40 years. Majorities of patients (62.5%) were females. Male and female ratio was 3:5.

According to Chaudhury et al., [15] the most common age group 30–39 years, the mean age of hypothyroid and controls were nearly same. However, hypothyroidism was found more common in the 25–35 years age group, similar to the study done by Rashead et al., [16] with highest percentage of people were in the age group 26–45 years. Among cases, 5 were males and 45 were females and in healthy controls 4 were males and 46 were females. The percentage rate of females was more than the percentage rate of males, similar to the study by Chaudhury et al., who recorded hypothyroidism that was more frequent in females. Qahtan et al. and Tejomani et al. [17] also observed that prevalence of hypothyroidism was higher among females.

Hypothyroidism, in turn, slows down all metabolic processes. One of these metabolic pathways is the purine metabolism pathway. Hypothyroidism by influencing this pathway causes changes in uric acid levels [18]. In hypothyroidism, due to decreased cardiac output, increased peripheral vascular resistance, vasoconstriction in the renal vasculature, reduced renal response to vasodilators, and decreased expression of renal vasodilators, such as vascular endothelial growth factor and insulin like growth factor 1, renal blood flow (RBF) is reduced. Glomerular filtration rate (GFR) also diminishes due to reduced sensitivity to beta-adrenergic stimuli and decreased renin secretion. Decreasing GFR and RBF along with rhabdomyolysis and myopathy induced by hypothyroidism increase serum creatinine [19]. Studies by Kreisman and Hennessey et al. [20], and Vaneet Kaur et al. [21] also point toward mean S.Creatinine level being significantly higher in hypothyroid cases. The serum Creatinine concentration increases in hypothyroid patients due to reduction of glomerular filtration rate because of hemodynamic changes in overt hypothyroidism12. Serum Creatinine level may also be increased due to hypothyroid myopathy. Hypothyroidism must be considered in patients presenting with acute renal failure and elevated muscle enzymes. The renal impairment could be due to reduced cardiac output and increased systemic and renal vasoconstriction leading to reduced renal blood and plasma flow and decreased GFR. A highly significant difference in values of uric acid, p value <0.001 was seen. Studies by Giordano et al13. showed 33.3% prevalence of hyperuricemia in patients with hypothyroidism. Similar studies were conducted by Erickson et al. [22] and Dariyerli et al. [23] and found hyperuricemia in patients with hypothyroidism. There is high prevalence of hyperuricemia and gout in hypothyroidism.

In our study, a very statistically significant differences were seen (p<0.001) in the levels of FT3, FT4, TSH, serum creatinine and serum uric acid respectively in patients with subclinical hypothyroidism as compared to patients of overt hypothyroidism.

In a similar study, Kaur et al. [24] examined the relationship between overt and subclinical hypothyroidism and renal function. In their research, 100 subjects in the control group, 50 in the overt hypothyroidism group and 50 in the subclinical hypothyroid group were studied. All participants in the study were between 20–70 years of age. At the end, they also concluded that subclinical hypothyroidism significantly increased serum creatinine (P<0.001), while they did not show significant increases in serum uric acid. Verhelst et al. [25] in a study that was designed to find out the relationship between serum creatinine and other Guanidino compounds in patients with thyroid dysfunction, concluded that in patients with subclinical hypothyroidism, serum creatinine levels increased.

CONCLUSIONS

Thyroid dysfunction is commonly seen in middle age population. It is more common in females than males. A statistically significant association was seen in TSH, FT3, FT4, serum uric acid and serum creatinine levels between the patients of subclinical and overt hypothyroidism. Serum creatinine and serum uric acid level was significantly higher in overt hypothyroidism as compared to subclinical hypothyroidism patients. Hence, the understanding of this association, hypothyroidism should be evaluated and treat by a multisystem approach. Assessment of thyroid function should be performed in patients presenting with deranged renal function.

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