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SERUM URIC ACID LEVEL IN PRIMARY HYPOTHYROIDISM

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Abstract :

Hypothyroidism is a clinical condition characterised by transient or progressive impairment of biosynthesis of thyroid hormones with compensatory thyroid enlargement. Thyroid hormone exerts its action on every cell of the body, by influencing the rate of general metabolic processes. It is involved in brain maturation and tissue development. Hyperuricemia can result from increased production or decreased excretion of uric acid or from a combination of two processes. In Primary hypothyroidism, renal plasma flow is reduced in accordance with the changes in cardiovascular hemodynamics that causes decreased glomerular filtration.AIM AND OBJECTIVES- The aim of the study is to estimate the level of Serum Uric acid in Primary hypothyroid cases and to compare it with normal, healthy control groups (age and sex matched) and to correlate the relationship between Serum Uric acid level with Serum Creatinine, Blood Urea, Total Cholesterol and fasting Glucose.

MATERIALS AND METHODS:

-Study population composed of 50 patients with Primary hypothyroidism and 50 healthy control groups (age and sex matched). Blood samples from both the groups were analysed for serum Uric acid, thyroid profile, renal function test, total cholesterol and fasting blood glucose. Uric acid was estimated by Uricase method. Thyroid profile was done by ELISA. RESULTS- The mean S.Uric acid level was significantly high in the study group (10.4 plus or minus 1.71 mgdl) when compared to the control group (5.37 plus or minus 0.95 mgdl) and the p value is statistically significant. Our study showed decreased level of S.T3 and S.T4 and increased S.TSH in the study group when compared to that of control group. CONCLUSION- To conclude, our study showed increased level of Serum Uric acid in patients with Primary Hypothyroidism when compared to normal healthy controls. Increase in S.Uric acid levels in hypothyroid patients may be due to increased production from excess ADP and decreased renal clearance.

If thyroid status is corrected, Uric acid level returns to normal and an improvement of renal status occurs in patients with Primary hypothyroidism.

Keyword : Primary Hypothyroidism, Thyroid hormones, Uric acid, Creatinine clearance.

Hypothyroidism is a clinical condition characterised by transient or progressive impairment of biosynthesis of thyroid hormones with compensatory thyroid enlargement.Hypothyroidism commonly occurs in 2-15% of the general population. It is associated with weight gain, fatigue, hoarseness of voice, cold intolerance, constipation and depression.Hypothyroidism is a risk factor for atherosclerosis and cardiovascular disease (1). Thyroid dysfunction also causes remarkable changes in renal functions, electrolyte and water homeostasis. Primary hypothyroidism is the state due to deficiency of thyroid hormones usually due to impaired function, damage to, or surgical removal of thyroid gland.Primary hypothyroidism accounts for 99% of cases of hypothyroidism. Primary Hypothyroidism is a common endocrine disorder where the thyroid gland produces less than the normal amount of thyroid hormones (T_3 & T_4) with the clinical and biochemical manifestations of thyroid hormone deficiency (2).Thyroid hormone exerts its action on every cell of the body, by influencing the rate of general metabolic activity(3).It is involved in brain maturation, tissue development and heat production(4). In Thyroid gland, hormones are derived from thyroglobulin(Tg), a large iodinated glycoprotein. Tg is iodinated on tyrosine residues and subsequently proteolysed to release newly synthesized T_4 and T_3 .A peripheral deiodinase in target tissues such as pituitary, kidney, and liver selectively removes $I^-$from T_4 to make T_3, which is a muchmore active molecule. T_4 can be thought of as a prohormone, though it does have some intrinsic activity (5). Thyroid hormones are essential for an adequate growth and development of the kidney.The kidneys are not only an organ for metabolism and elimination of thyroid hormones but also a target organ of iodothyronines action.Synthesis of thyroglobulin and hormones of the thyroid gland are regulated by the hypothalamic –hypophyseal mechanism (6). Hypothyroidism is accompanied by a decrease in glomerular filtration, hyponatremia and an alteration of the ability for water excretion (7,8).Impaired water excretion is associated with decreased creatinine clearance, increased serum creatinine levels and increased serum uric acid level(9,10).The plasma osmolality is lower in these patients(11).It is consistent and reversible(12,13). Uric acid (2,6,8- trihydroxypurine) is the end product of catabolism of purine nucleosides adenosine and guanosine. Uric acid has the property ofprotection against ageing and oxidative stress.The daily synthesis of uric acid is approximately 400 mg and dietary sources contributes to another 300 mg. Approximately 70% of the uric acid is excreted by the kidneys and the rest by the gut. Renal handling of uric acid is complex and involves four sequential steps:

(1) glomerular filtration of virtually all the uric acid in capillary plasma entering the glomerulus

(2) reabsorption in the proximal convoluted tubules of about 98 to 100 % of filtered uric acid

(3) subsequent secretion of uric acid into the lumen in the distal portion of the proximal tubules

(4) further reabsorption in the distal tubules. The net urinary excretion of uric acid is 6 to 12% of the amount filtered.

Serum Uric acid level depends on purine content of the diet, rate of purine synthesis, degradation and salvage pathway.Hyperuricemia is defined by serum uric acid concentrations greater than 7.0 mg/dl in men or greater than 6.0 mg/dl in women

(14). Hyperuricemia can result from increased production or decreased excretion of uric acid or from acombination of two processes (15).Renal plasma flow is reduced in accordance with the changes in cardiovascular hemodynamics.

AIM AND OBJECTIVES:

1 Toestimate the level of Serum Uric acid in Primary hypothyroid patients and to compare it with normal and healthy control groups(age and sex matched).

2To correlate the relationshipbetween Serum Uric acid level with other parameters such as Serum Creatinine, BloodUrea, Total Cholesterol and fasting Glucose in patients with Primary hypothyroidism.

MATERIALS AND METHODS:

This Study was conducted at our medical college hospital. Written informed consent was obtained from the participants.Study population composed of 50 patients with Primary Hypothyroidism and 50 healthy control groups (age and sex matched). Blood samples from both the groups were analysed for serum Uric acid, thyroid profile, routine renal function test,total cholesterol and fasting blood glucose.

INCLUSION CRITERIA:

Patients with Primary Hypothyroidism

EXCLUSION CRITERIA:

Patients with Chronic inflammatory disease, Renal disease and Acute infections.

SAMPLE COLLECTION:

5 ml of fasting venous blood was collected. Blood samples were allowed to clot for half an hour and then centrifuged. Serum samples were stored at -20C for T_3,$T_4$and TSH estimation. Other parameters such as uric acid, serum creatinine, urea, total cholesterol and fasting glucose weremeasured. Creatinine clearance (C)was calculated using Cockcroft-Gault formula.

ESTIMATION OF URIC ACID:

METHOD: URICASE – TRINDER, END POINT Uric acid + O_2 + H_2O----------->Allantoin + CO_2 + H_2O_2 TOOS + 4AAP + H_2O_2---------->Quinoneimine dye +4 H_20 The intensity of the colour formed is proportional to the uric acid concentration.

Mixed and incubated for 5 minutes at 37° C. The absorbance read at 540nm against reagent blank.

CALCULATIONS:

Uric acid (mg/dl) = Abs of Test

X Concentration of Standard (mg/dl)

Abs of Standard Uric acid (Standard)=6 mg/dl

ESTIMATION OF OTHER PARAMETERS:

Serum creatinine was estimated by Jaffe's method. Blood urea was estimated by Urease – Glutamate Dehydrogenase method. Fasting blood glucose was estimated by Glucose Oxidase and Peroxidase method. Serum total cholesterol was estimated by Cholesterol Oxidase and Peroxidase method.

ESTIMATION OF THYROID PROFILE:

Thyroid profile T_3, T_4 and TSH was estimated by Sandwich ELISA.

ASSAY PROCEDURE:			
Pipette into tubes marked	Blank	Standard	Test
Working Reagent	1000µl	1000µl	1000µl
Distilled Water	25µl	-	-
Standard	-	25µl	-
Sample	-	-	25µl

REFERENCE VALUES:	
Serum/Plasma	mg/dl
Women	2.5-6.8

ESTIMATION OF THYROID PROFILE:

Thyroid profile T_3, T_4 and TSH was estimated by Sandwich ELISA.

CALCULATION OF C:

cr

COCKCROFT-GAULT FORMULA:

For males,

C = [140-Age(years)]xWeight(kg)

cr

72x S.creatinine(mg/dl)

For females,

C =[140-Age(years)]x Weight (kg) x0.85

c r

72x S.creatinine(mg/dl)

DISCUSSION:

Primary Hypothyroidism is characterised by myopathy and decreased water excretion. Serum creatinine is increased and creatinine clearance is slightly decreased in patients with hypothyroidism (16). In our study, we measured serum Uric acid in Primary hypothyroid patients and compared the same with the normal healthy individuals. The mean S.Uric acid level was significantly high in the study group (10.4 ± 1.71mg/dl) when compared to the control group (5.37± 0.95mg/dl) and the p value is statistically significant. S.Uric acid level depends on purine content of the diet, rate of purine synthesis, degradation and salvage pathway. Since 75% of Uric acid is eliminated through kidneys, in patients with hypothyroidism impaired renal function is one of the etiology for hyperuricemia. In Primary

RESULTS AND STATISTICAL ANALYSIS:

TABLE: 1

DESCRIPTIVE STATISTICS

PARAMETERS	Control (n=50)				Study (n=50)			
	Min.	Max.	**Mean**	S.D	Min.	Max.	**Mean**	S.D
URICACID	3.60	7.00	**5.37**	0.95	6.00	14.0	**10.4**	1.71
T3(ng/ml)	0.52	2.00	**1.44**	0.38	0.12	0.69	**0.32**	0.13
T4(g/L)	58.00	112.0	**87.76**	15.41	22.0	52.0	**41.1**	7.69
TSH(IU/ml)	0.55	3.40	**2.01**	0.84	4.85	27.50	**11.71**	5.076

TABLE: 2

DESCRIPTIVE STATISTICS

PARAMATERS	Control (n=50)				Study (n=50)			
	Min.	Max.	**Mean**	S.D	Min.	Max.	**Mean**	S.D
UREA	18.0	39.0	**27.82**	6.38	22.0	48.0	**31.82**	6.01
CREATININE	0.46	0.90	**0.68**	0.10	1.00	1.80	**1.32**	0.21
GLUCOSE (F)	58.0	111	**85.5**	11.92	65.0	105	**87.86**	9.84
T.CHOLESTEROL	140	210	**179.22**	19.21	168	302	**252.3**	34.6
C_{cr}(ml/min)	122	147	**120.3**	9.611	58.9	125.0	**85.5**	17.49

TABLE: 3

STUDENT'S t –TEST ANALYSIS OF S.URICACID VALUES BETWEEN CONTROL AND STUDY GROUP

Sample	Mean	S.D	Statistical inference
Control (n=50)	5.3700	.95260	T=-18.136
Study (n=50)	10.4000	1.71429	.0001< 0.05 Significant

TABLE: 4

STUDENT'S t-TEST ANALYSIS OF T3,T4,TSH VALUES BETWEEN CONTROL AND STUDY GROUP

Sample	Mean	S.D	Statistical inference
T3			
Control (n=50)	1.4478	.38145	T=19.613 .0001<0.05 Significant
Study (n=50)	**0.3220**	.13870	
T4			
Control (n=50)	87.7600	15.41608	T=19.132 .0001<0.05 Significant
Study (n=50)	**41.1400**	7.69577	
TSH			
Control (n=50)	2.0160	.84466	T=-13.326

TABLE: 5

STUDENT'St –TEST ANALYSIS OF CREATININE AND C_{cr} BETWEEN CONTROL AND STUDY GROUP

Sample	Mean	S.D	Statistical inference
CREATININE			
Control (n=50)	.6810	.10628	T=-18.896 .0001<0.05 Significant
Study (n=50)	**1.3220**	.21504	
C_{cr}			
Control (n=50)	120.3984	9.61188	T=12.350 .0001<0.05 Significant
Study (n=50)	**85.5348**	17.49471	

TABLE: 6

PEARSONS CORRELATION

PARAMETERS	URIC ACID	STATISTICAL INFERENCE
T3	-.817(**)	P<0.01 significant
T4	-.773(**)	P<0.01 significant
TSH	.686(**)	P<0.01 significant
UREA	.229(*)	P<0.05 significant
CREATININE	.789(**)	P<0.01 significant
T.CHOLESTEROL	.738(**)	P<0.01 significant
C_{cr}	-.684(**)	P<0.01 significant
N	100	

hypothyroidism, renal plasma flow is reduced in accordance with the changes in cardiovascular hemodynamics and glomerular filtration rate is decreased (17).Maximal urinary flow rate and free water clearances were similarly reduced in these patients. So S.Uric acid level is increased. Further, hyperuricemia is also due to increased production of uric acid due to myopathy. In hypothyroid patients, there is an excess ADP which is degenerated to xanthine. Xanthine is a substrate for Xanthine oxidase resulting in increased Uric acid production (18, 19). Our study showed decreased level of T_3 and T_4 and increased TSH in the study when compared to that of control group. This is due to decreased synthesis of thyroid hormones and loss of negative feedback control when compared to healthy individuals. Pearsons correlation studies revealed a positive correlation between serum Uric acid and TSH and a negative correlation between serum Uric acidand T_3 & T_4. If thyroid status is corrected, Uric acid level returns to normal and an improvement of renal status occurs in Primary hypothyroid cases(20).

CONCLUSION:

To conclude, our study shows increased level of Serum Uric acid in patients with Primary Hypothyroidism when compared to normal healthy controls. Increase in Uric acid levels in hypothyroid cases may be due to increased production from excess ADP and decreased renal clearance.

REFERENCES:

1.Hypothyroidism and thyroiditis, page 377-382, Williams Textbook of Endocrinology, edited by HenryM. Kronenberg, Shlomo Melmed, Kenneth S.Polonsky and P.Reed Larsen, 11th edition, published bySaunders Elsevier.

2.Hypothyroidism and Myxedema coma, page 1613, Endocrinology Adult and Pediatric, edited by J. Larry Jameson, Leslie J. De Croot et al,Volume II, 6th edition, published by Saunders Elsevier.

3 Thyroid, page 949-959, Clinical Chemistry, edited by Lawrence A.Kaplan and Amadeo J.Pesce, 5 th edition, published by Mosby Elsevier.

4 The Thyroid Gland, page 492, Clinical Chemistry, edited by Michael L. Bishop, Edward P. Fody, Larry E. Schoeff,6th edition, published by Wolters Kluwer/ Lippincott Williams and Wilkins.

5 The Diversity of the Endocrine System, page 489-491, Harper's Illustrated Biochemistry, edited by Robert K. Murray, Peter J. Kennelly, David A.Bender, Victor W.Rodwell, Kathleen M.Botham and P. Anthony Weil, 29th edition, published by Mc Graw- Hill Medical.

6.TheThyroid, page 1195-1206, Principles of Biochemistry, edited by Abraham White, Philip Handler, Emil L.Smith, Robert L.Hill and I.Robert Lehman, 6th edition, published by-Tata Mc Graw- Hill .

7 Derubertis FR Jr, Michelis MF, Bloom ME, Mintz DH, Field JB and Davis BB , Impaired water excretion in myxedema, American Journal of Medicine, 1971 Jul, 51(1):41-53.

8 Allon M, Harrow A, Pasque CB and Rodriguez M, Renal sodium and water handling in hypothyroid patients: the role of renal insufficiency, Journal of American Society of Nephrology.1990 Aug; 1(2):205-210.

9.Montenegro J, González O, Saracho R, Aguirre R, González O and Martinez I, Changes in renalfunction in primary hypothyroidism, American Journal of Kidney Diseases, 1996 Feb; 27(2): 195-198.

10 del-Rio Camacho G, Tapia Ceballos L, Picazo Angelin B, Ruiz Moreno JA, Hortas Neito ML and Romero González J, Renal failure and acquired hypothyroidism, Pediatric Nephrology. 2003 Mar; 18(3):290-292.

11 Liu XM, Bai Yand Guo ZS, Study on urinary function and metabolism of water and electrolytes in primary hypothyroidism, Zhonghua Nei Ke Za Zhi, 1990 May; 29(5): 299-302,318.

12 Kreisman SH and Hennessey JV, Consistent reversible elevations of serum creatinine levels in severe hypothyroidism, Archieves of Internal Medicine, 1999 Jan 11; 159(1): 79-82.

13 Mooraki A, Broumand B, Neekdoost, Amirmokri P and Bastani B, Reversible acute failure associated with hypothyroidism, Nephrology (Carlton) 2003 Apr; 8(2): 57-60.

14 Kidney Function Tests, page 686-689, Tietz Text book of Clinical Chemistry and Molecular Diagnostics, edited by Carl A. Burtis, Edward R. Ashwood et al, 5th edition, published by Saunders Elsevier.

15 Disorders of Purine and Pyrimidine Metabolism, page 3182-3184, Harrison's Principles of Internal Medicine, edited by DanL. Longo, Anthony S.Fauci , Dennis L.Kasper, Stephen L.Hauser, J.Larry Jameson and Joseph Loscalzo, Volume II, 8th edition, published by Mc Graw Hill.

16 KaranikasG,Schütz M, Szabo M, Becherer A, Weisner K, Dudczak R and Kletter K, Isotopic Renal Function Studies in Severe Hypothyroidism and after Thyroid Hormone Replacement Therapy, American Journal of Nephrology 2004,24:41-45.

17 Hypothyroidism and pregnancy - and growth- related thyroid disorders, page 523, Oxford Textbook of Endocrinology and Diabetes, edited by John A.H. Wass and Paul M. Stewart, 2nd edition, published by Oxford University Press.

18.T.Sharmila Krishna, D.Pavani Priyanka and E.Venkat Rao, Alterations of Serum Uric acid concentrations in subjects with Hypothyroidism, International Journal of Applied Biology and Pharmaceutical Technology, 2011; 2 (2):322-326.

19 Giordano N, Santacroce C, Mattii G, Geraci S, Amendola A and GennariC, Hyperuricemia and gout in thyroid endocrine disorders, Clinical and Experimental Rheumatology. 2001 Nov-Dec; 19(6):661-665.

20 Nakahama H,Sakaguchi K, Horita Y, Sasaki O, Nakamura S, Inenaga T and Takishita S, Treatment of severe hypothyroidism reduced serum creatinine levels in two chronic renal failure patients, Nephron 2001 Jul; 88 (3): 264-267.