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Study of Serum Uric Acid level in Thyroid Disorders

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ABSTRACT

Background: Thyroid dysfunction affects hundreds of millions globally, serum uric acid (UA) elevation has been found to be related to thyroid dysfunction according to some studies. Thyroid dysfunction affects the purine nucleotide metabolism that may increase uric acid concentration, which is the end-product of purine metabolism and is a primary risk factor for development of gout.

AIM OF THE WORK: The aim of this study was to estimate the frequency of hyperuricemia in patients with thyroid dysfunction whether hypothyroid or hyperthyroid.

Patients and methods: This is a case control clinical study that was conducted in Internal Medicine Outpatient Clinic and Inpatient Department of Internal Medicine at Al-Azhar University Hospital, Damietta. The population of the study were classified into 50 hypothyroid patients (group I), 50 hyperthyroid patients (group II) and 50 normal as control (group III). All were subjected to full history, clinical examination and laboratory tests including, complete blood count, serum urea, serum creatinine, estimated glomerular filtration rate, lipid profile, thyroid stimulating hormone, free triiodothyronine and free thyroxine. Investigations included echocardiography, electrocardiography and thyroid ultrasound.

Results: There was significant elevation of body mass index, blood urea, createnine, VLDL, TG, cholesterol, Uric Acid, TSH in group I as compared to group II & III. Additionaly, there was statistically significant elevation of estimated glomerular filteration rate, FT4, FT3 in group II in comparison with groups I & III. Also, there was significant increase in IHD, pericardial effusion, in group I and statistically significant increase in pulmonary HTN in group II.

Conclusion: The uric acid level was elevated in both hypothyroidism and hyperthyroidism, the elevation was more in hypothyroidism concomitant with the elevation of other parameters that characterize chronic kidney disease such as creatinine, estimated glomerular filtration rate and blood urea indicating that the decreased excretion of uric acid was the leading pathogenesis to this elevation in hypothyroidism

Keywords: Hyperuricemia, Thyroid dysfunction, Gout, VAI.

INTRODUCTION

Thyroid dysfunction affects the purine nucleotide metabolism that may increase uric acid concentration, which is the end-product of purine metabolism and is a primary risk factor for development of gout. Uric acid has been considered as a non-specific finding, unless it is complicated by gout or renal stones [(1)].

Thyroid hormones including thyroid stimulating hormone, tri-iodothyronine and free thyroxine being essential for the optimal functioning of almost all body tissues, play a critical role in growth, cell differentiation and cellular metabolism [(2)]. Therefore, abnormal production of thyroid hormones results in various biochemical abnormalities leading to increased risk of metabolic syndrome, cardiovascular and musculoskeletal disorders [(3)].

Similar to thyroid dysfunction, the increased serum uric acid (SUA) levels are also associated with other co-morbid conditions including hypertension, metabolic syndrome, chronic kidney disease and type 2 diabetes mellitus [(4)]. The concurrence of deranged SUA levels in patients suffering from primary thyroid dysfunction may not only increase the risk of all mortality causes but can also affect the management and prognosis of the disease [(5)].

During the last few years, a growing attention has been paid to uric acid due to its involvement in "cardio-nephro-metabolic" disorders. Several epidemiological studies reported a relation between serum UA levels and traditional cardiovascular risk factors, including hypertension (HTN), metabolic syndrome and diabetes mellitus (DM), suggesting a possible pathophysiologic link between these conditions [(6)].

AIM OF THE WORK

The aim of this study was to estimate the frequency of hyperuricemia in patients with thyroid dysfunction whether hypothyroid or hyperthyroid.

SUBJECTS AND METHODS

This study is a case control clinical study that was carried out on one hundred and fifty individuals attending to Internal Medicine Outpatient Clinic and Inpatient of Internal Medicine Departement at Al-Azhar university hospital, Damietta. The population of the study were classified as follow:

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- Group I: fifty (50): patients diagnosed as hypothyroid.
- Group II: fifty (50): patitents diagnosed as hyperthyroid.
- Group III: fifty (50): apparently healthy individuals as controls.

Exclusion criteria:

- Patients with secondary thyroid dysfuction.
- History of Renal Or Hepatic disease.
- History of other endocrine disorder .
- History of medications that can affect serum uric acid or thyroid hormones level.

Methods

All were subjected to full history (history of hypert ension, DM, history of drug intake history of drug intake, any chronic illness and family history of thyroid disorders) and clinical examination. Anthropometric assessment; weight, he ight,W/H and BMI. Laboratory profiles: complete blood count (CBC), serum urea (S. Urea), serum creatinine (S. Cr), Estimated glomerular filtration rate (eGFR), lipid profile, thyroid stimulating hormone (TSH), free triiodothyronine (FT3) and free thyroxine (FT4). Investigations: echocardiography, electrocardiography (ECG) and Thyroid ultrasound.

Ethical approval:

The study was approved by the Ethics Board of Al-Azhar University and a signed written consent was obtained from each individual included in the study.

Statistical methods

Data were collected, coded, revised and entered t o the Statistical Package for Social Science (IBMSP SS) version 23. The data were presented as number a nd percentages for the qualitative data. Mean, standa rd deviation and ranges for quantitative data with parametric distribution and median with inter quartile range (IQR) for the quantitative data with non parametric distribution. ***Chisquare test*** was used in the comparison between two groups with qualitative data and ***Fisher exact test*** was used instead of the Chisquare t est when the expected count in any cell was found to be less than 5. The comparison between two groups with with quantitative data and parametric distribution were done by using ***One Way Analysis of Variance (ANOVA) test*** and ***Kruskall- Wallis test*** was used in the comparison between more than two groups with quantitative data and non-parametric distribution.

RESULTS

Table (1): Comparison between group I, group II & control group as regards anthropometric measures

	Group I		Group II		Control group		One way ANOVA	
	Mean	SD	Mean	SD	Mean	SD	f	P value
BMI (Kg/m²)	33.56	6.95	22.04	1.84	23.56	1.61	108.423	<0.001
Ht/m	1.78	0.11	1.74	0.10	1.67	0.07	16.049	<0.001
Wt/kg	93.42	17.55	67.22	9.62	74.28	8.20	58.909	<0.001

There was statistically significant increase in group I in comparison with group II and control group regarding anthropometric measure.

Table (2): Comparison between group I, group II & control group as regards clinical examination

		Group I		Group II		Control group		Chi square test	
		No	%	No	%	No	%	X^2	P value
Clinical examination	DM	12	24.0%	16	32.0%	6	12.0%	5.781	0.055
	HTN	17	34.0%	15	30.0%	7	14.0%	5.821	0.054
	Chronic illness	10	20.0%	5	10.0%	4	8.0%	3.736	0.154
	Other AID	5	10.0%	6	12.0%	1	2%	6.082	0.053
	History of smoking	8	16.0%	15	30.0%	6	12.0%	5.728	0.053
	F H of thyroid D	31	62.0%	21	42.0%	20	40%	5.929	0.051
	Duration of thyroid dys (yr) Mean ± SD	3.65 ± 3.61		3.52 ± 3.61		--	--	0.032**	0.858
	Gout	10	20.0%	11	22.0%	0	0.0%	12.292	0.002
	Goiter	18	36%	25	50.0%	0	0.0%	1.999	0.157
	Pressure symptoms	10	20.0%	12	24.0%	0	0.0%	0.233	0.629

There was no statistically significant difference concerning DM, HTN, chronic illness, other autoimmune disease, goiter and pressure symptoms. However, there was statistically significant increase of gout in group I in comparison with group II and control group.

Table (3): Comparison between group I, group II & control group as regards laboratory investigations

	Group I		Group II		Control group		One way ANOVA	
	Mean	SD	Mean	SD	Mean	SD	f	P value
eGFR (mL/min/1.73m²)	88.66	12.68	104.19	13.23	100.75	9.16	23.774	0.001
Blood urea (mg/dl)	31.48	10.97	24.02	6.35	24.02	6.35	13.859	0.001
Createnine (mg/dl)	1.22	0.14	0.82	0.17	0.96	0.17	79.907	0.001
AST (U/L)	36.78	9.04	37.72	10.00	33.94	8.68	2.260	0.108
ALT (U/L)	37.80	10.42	35.20	9.42	33.22	8.04	3.021	0.062
HDL(mg/dl)	44.38	11.22	51.30	7.75	50.38	7.60	0.270	0.764
VLDL (mg/dL)	28.84	10.50	23.40	9.96	18.40	6.92	15.888	0.001
TG (mg/dL)	147.16	12.37	125.10	18.02	123.82	14.84	37.010	0.001
Cholesterol (mg/dL)	205.86	24.17	161.92	25.92	116.52	31.02	134.916	0.001
Uric Acid (mg/dl)	7.59	1.18	7.25	1.26	5.19	0.85	68.160	0.001
FT4 (pmol / L)	8.68	1.36	27.26	1.62	15.10	2.88	1047.647	0.001
FT3 (pmol / L)	3.14	0.78	8.71	1.53	4.81	0.93	319.869	0.001
TSH (ul /ml)	9.78	3.62	0.11	0.11	4.08	0.64	261.538	0.001
Platelet	267.86	58.02	268.02	59.18	267.34	58.66	0.002	0.998
HB	11.62	1.54	11.41	1.60	11.58	1.35	0.279	0.757
WBCS	6.74	1.63	6.72	1.65	6.73	1.60	0.003	0.997

There was statistically significant increase in blood urea, createnine, VLDL, TG, cholesterol, uric acid and TSH in group **I** in comparison with group **II** and control group. While, there was statistically significant increase in eGFR, FT4 and FT3 in group **II** in comparison with group **I** and control group.

Table (4): Comparison between group I, group II & control group as regards echocardiography

		Group I		Group II		Control group		Chi square test	
		No	%	No	%	No	%	X^2	P value
Echocardiography	IHD	10	20.0%	12	24.0%	3	6.0%	6.432	0.040
	Peri. Effusion	3	6.0%	0	0.0%	0	0.0%	6.122	0.047
	Pulmonary. Htn	3	6.0%	6	12.0%	0	0.0%	6.383	0.041
	Cardiomyopat	2	4.0%	6	12%	1	2.0%	5.185	0.074

There was statistically significant increase in IHD and pericardial effusion in group **I** in comparison with group **II** and control group. While, there was significant increase in pulmonary hypertension in group **II** in comparison with group **I** and control group.

DISCUSSION

In the present study elevated serum uric acid level was observed in 68% of the cases. The significant increase was in group I ($P < 0.001$) (76% 38 out of 50 patients). This finding is in agreement with **Khan *et al.*** [7] and **Giordano *et al.*** [8].

On the contrary and according to **Raber *et al.*** [9] who conducted a screening study on a large number of patients suffering from various degrees of thyroid dysfunction including hyperthyroidism and hypothyroidism, they couldn't find any association between serum uric acid level and TSH. Therefore, they didn't warrant routine estimation of serum uric acid level in such patients. Also, **Abebe *et al.*** [10] reported low serum uric acid levels in both hypothyroid and hyperthyroid patients. The disagreement between these finding and our results can be explained by the differences in the studied population and in sample size.

The relationship between uric acid level and thyroid dysfunction has been investigated in several studies, which provided conflicting results. Mean serum uric acid level in our study was higher in hypothyroid patients as compared to hyperthyroid and this is consistent with the previous studies. The significant elevation in group I was attributed to reduced renal perfusion and impaired glomerular filtration rate, and so such patients should also be monitored closely for chronic kidney disease in addition to gout and coronary heart disease. In this regard decreases in uric acid excretion, increase in creatinine and a decrease in creatinine clearance have been described in hypothyroid patients.

It was found that, the administration of levothyroxine in these hypothyroid hyperuricemic patients resulted in the normalization of TSH, FT4, serum and urinary uric acid levels as well as creatinine and creatinine clearance values. This fact

suggests that hypothyroid hyperuricemia could be secondary to a reduction in renal plasma flow and glomerular filtration. Thus the reduction in serum uric acid level that was observed under replacement therapy with levothyroxine could be theoretically due to improvement in its renal excretion.

In this study, there was significant increase in ischemic heart disease (coronary heart disease) in group I and group II as compared to control group. This finding is consistent with **McQuade *et al.*** [(11)] who conducted a study on a group of patients in cardiology clinic and found a high prevalence of coronary heart disease among patients suffering from hypothyroidism in addition to moderate subclinical hypothyroidism. This can be explained by the presence of several CHD risks, which were common in hypothyroid patients as hypercholesterolemia, hypertriglyceridemia and high fibrinogen level leading to premature atherosclerosis.

Also in our study, there was a statistically significant increase in both serum urea and serum creatinine in group I in comparison with group II & III, in agreement with this, **Sidhu *et al.*** [(12)], documented that there was significant increase in serum level of both urea and creatinine in hypothyroidism as compared to hyperthyroidism. **Saini *et al.*** [(13)] also, reported the same results, but in contrast to that **Qahtan *et al.*** [(14)] didn't find this association.

Our study, showed significant increase in serum creatinine level in group I with p value < 0.001 and this is in consistence with **Khan *et al.*** [(15)] **and Vaneet *et al.*** [(16)]**.** The explanation of this is the decrease of glomerular filtration rate or hypothyroid myopathy.

In this study, serum total cholesterol, triglycerides and very low density lipoprotein were significantly increased in group I. In agreement with our results, **Shashi & Sharma** [(17)] reported the presence of hypercholesterolemia and hypertriglyceridemia in clinical hypothyroidism and also the contributive role of subclinical hypothyroidism in causing dyslipideamia. In addition, **Fox *et al.*** [(18)] found that total cholesterol & very low density lipoprotein to be increased in hypothyroidism. According to **Lee *et al.*** [(19)] **& Teixeira *et al.*** [(20)] clinical hypothyroid patients may present with increased triglycerides associated with increased levels of very low density lipoproteins and occasionally fasting chylomicroneamia. **Abbas *et al.*** [(21)], explained this by the decrease in LDL receptors activity resulting in decreased catabolism of LDL and intermediate density lipoproteins. **Nikkila and Kekki** [(22)] explained that by a decrease in lipoprotein lipase activity decreasing the clearance of triglyceride rich lipoproteins.

CONCLUSION

The uric acid level was elevated in both hypothyroidism and hyperthyroidism. The elevation was more in hypothyroidism concomitant with the elevation of other parameters that characterize chronic kidney disease such as creatinine, estimated glomerular filtration rate and blood urea indicating that the decreased excretion of uric acid was the leading pathogenesis to this elevation. On the other hand, gout was more in hyperthyroidism that was explained by the hyper catabolic state that increase the urate crystal deposition in the tissues. In addition, the increase of incidence of ischemic heart disease in hypothyroidism with elevation of uric acid can provide evidence of participation of uric acid in the pathogenesis of IHD in hypothyroidism.

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