International Journal of Science and Research (IJSR)
ISSN (Online): 2319-7064
Index Copernicus Value (2015): 78.96 | Impact Factor (2015): 6.391

Correlation between Renal Function Tests and Thyroid Hormones in Sudanese Patients with Hypo- and Hyperthyroidism

Aalya Ibrahim Mohammed Osman[1], Adel Nasr Morsi[2]

[1]ALAMAL National Hospital, Khartoum North, Sudan

[2]Department of Chemical Pathology, Faculty of Medical Laboratory Sciences, University of Khartoum-Sudan

University of Khartoum, Faculty of Medical Laboratory Sciences, Chemical Pathology Department

Abstract: ***Background: Thyroid hormones affects functions of organ systems including the renal system, in which creatinine, blood urea nitrogen (BUN) and glomerular filtration rate (GFR) are affected. This study aimed to evaluate levels of creatinine, BUN and GFR in patients with hypo and hyperthyroidism and to correlate them with thyroid stimulating hormone (TSH), thyroxin (T4) and triiodothyronine (T3) levels. Methodology: A cross sectional descriptive study was conducted involving a total of 117 subjects in three groups: 37 hypothyroidism, 40 hyperthyroidism and 40 apparently healthy subjects as control. Plasma TSH, T4, T3, creatinine, blood urea nitrogen (BUN) and albumin were determined, glomerular filtration rate (GFR) was calculated according to MDRD equation. Results: Mean creatinine in hypothyroidism was 0.9±0.1 mg/dl, in hyperthyroidism was 0.7±0.2 mg/dl, while in control was 0.6±0.1 mg/dl, mean BUN in hypothyroidism was 11±2.9 mg/dl, and in hyperthyroidism was 14±2.5 mg/dl while in control was 10±3.2 mg/dl, mean estimated GFR in hypothyroidism was 100±17 ml/min, and in hyperthyroidism was 143±32 ml/min while in control was 163±23 ml/min. Correlation studies reveled that creatinine in hypothyroidism was significantly positive correlated with TSH and significantly negative correlated with T4 and T3, while in hyperthyroidism was significantly positive correlated with T4 and not correlated with TSH, BUN in hypothyroidism was significantly positive correlated with TSH but not correlated to T4 and T3 while in hyperthyroidism there is no correlation between BUN and thyroid hormones. GFR in hypothyroidism was significantly negative correlated with TSH and significantly positive correlated with T4 and T3 while in hyperthyroidism no correlation between GFR and thyroid hormones. Conclusion: Both overt hypo and hyperthyroidism significantly increase creatinine and BUN level while significantly decrease eGFR. Thyroid dysfunction significantly affects renal functions so normal functioning thyroid is needed for healthy kidney performance.***

Keywords: Overt, Hypothyroidism, Hyperthyroidism, Glomerular filtration rate

1. Introduction

Thyroid hormones include thyroxin (T4) and triiodothyronine (T3) are produced and secreted from thyroid gland under stimulation of thyroid stimulating hormone (TSH) from anterior pituitary gland which is controlled by thyrotropin-releasing hormone (TRH) from hypothalamus, thyroid hormones exert a negative feedback effect on TSH secretion from the pituitary[1,2]. Furthermore they induce considerable functional effects in organ systems including heart, brain, and muscles [3]. Renal system also affected by thyroid activity [4]. Thyroid disorders are common endocrine disease in humans [5]. During which histological [6,7], and physiological changes occur that will affect kidney structure, plasma hemodynamic, electrolytes homeostasis and glomerular filtration rate (GFR) [1,4]. Pathophysiological changes in hypothyroidism are seen to be opposite to that occur during hyperthyroid status [5]. That due to the generalized hypodynamic state of circulatory system [6]. These changes can be outlined by measuring plasma markers for effective renal assessment which includes: blood urea nitrogen (BUN), creatinine, uric acid and electrolytes as a routine analysis [8]. GFR can be calculated from serum creatinine as in creatinine clearance or measured by inulin clearance [4]. Modification Of Diet in Renal Disease (MDRD) equation estimate GFR relayed on multiple regression analysis of large data base [4,10]. Has been validated with the I^{125} – iothalamate (isotope) which is the gold standard method for clearance measurement [4], and it had been used by a number of studies to calculate GFR in patients with different conditions [4,11,12,13]. Creatinine, BUN and GFR had been measured to evaluate renal status in patients with hypo and hyperthyroidism in many different studies [4,6,9,16,18,22]. The objectives of the present study were to evaluate renal function tests and eGFR in patients with overt hypothyroidism and hyperthyroidism, and to correlate creatinine, BUN and eGFR with the thyroid function tests. GFR was estimated based on MDRD equation using serum urea, creatinine and albumin as variables.

2. Materials and Methods

A cross sectional descriptive study was conducted in Khartoum state study duration from January 2017 until March 2017 involving a total of 117 subject divided into three group: group with hypothyroidism (n=37), group hyperthyroidism (n=40) and apparently healthly subjects (n=40) as control group. Patients included were newly overt hypo and hyperthyroidism of no history of diabetes, hypertension, malignancies

or kidney disease. Pregnant women and subclinical thyroid disorders were excluded. Blood samples were drawn for TFTs, urea, creatinine and albumin determination, GFR was calculated according to MDRD equation.

TSH was determined by immunoassay technique (Roche Hitachi Cobas e411 automated analyzer) where as total T4, and total T3 were determined by Enzyme linked ImmunoSorbent Assay (ELISA) using State Fax instrument (BIOS reagents). Plasma creatinine, urea, and albumin were determined by full automated instrument (Roche Hitachi Cobas c311 automated analyzer). GFR was calculated according to the MDRD (6 variable) equation: GFR= 170 × $(Pcr)^{-0.999}$ × $(Age)^{-0.176}$ × (0.762 if patient is female) × (1.180 if black) × $(BUN)^{-0.170}$ × $(Albumin)^{0.318}$ [4,12,13,14,15] (Where plasma creatinine (P.cr) concentration in mg/dl, blood urea nitrogen (BUN) in mg/dl and albumin in g/dl), urea was divided by 2.14 to give BUN concentration. The sample size was calculated and data were analyzed using SPSS (version17). Significance was defined by P. value <0.05.

3. Results

In hypothyroid group mean age was 40±9 years, mean TSH level was 12.1±2.5µIU/ml, mean T4 level 3.2±0.8 µg/dl, and mean T3 level was 0.6±0.3 ng/ml. In hyperthyroid group mean age was 40±9, mean TSH level was 0.08±0.06 µIU/ml, mean T4 level 14.4±2.74 µg/dl, and mean T3 level was 3.0±1.79 ng/ml. While in control group mean TSH level was 1.65±0.51 µIU/ml, mean T4 level 7.0±1.0 µg/dl, and mean T3 level was 1.87±0.58 ng/ml.

Creatinine, BUN and GFR levels showed significant difference in hypo and hyperthyroid groups when compared to control group. In hypothyroid group, creatinine level was significantly increased= 0.9±0.1 mg/dl, P=0.000, BUN level was significantly increased= 11±2.9 mg/dl, P=0.42 and eGFR level was significantly decreased= 100±17 ml/min, P=0.000. (Table (1)). While in hyperthyroid group, creatinine level was significantly increased= 0.7±0.2 mg/dl, P=0.39, BUN level was significantly increased= 14±2.5 mg/dl, P=0.000, eGFR level was significantly decreased=143±32 ml/min, P= 0.003. (Table (2))

Correlation studies between creatinine, BUN and GFR and thyroid hormones in hypothyroid group showed that; creatinine was significantly positive correlated with TSH level (r=0.86, P=0.000) and significantly negative correlated with both T4 (r=-0.76, P=0.000) and T3 level (r=-0.67, P=0.000). while in hyperthyroid group Creatinine was significantly positive correlated with T4 (r=0.43, P=0.005) and T3 (r=0.37, P=0.018) and not correlated with TSH level (r=-0.28, P=0.08), while BUN level in hypothyroid group show significant positive correlation with TSH (r=0.23, P=0.046), no correlations were found between T4, T3 and BUN level. In hyperthyroid groups BUN not correlated with thyroid function tests. GFR in hypothyroid group was significantly negative correlated with TSH (r=-0.839, P=0.000) and significantly positive correlated with both T4 (r=0.75, P=0.000) and T3 level (r=60, P=0.000) while in hyperthyroid group no correlation between GFR and thyroid hormones level. (Table (3) and (4)).

Table 1: Comparison of Creatinine, BUN and GFR between control and hypothyroidism:

Variables	Hypothyroidism mean	Control mean	P. value
Creatinine	0.9 ± 0.1	0.6 ± 0.1	0.000**
BUN	11 ± 2.9	10 ± 3.2	0.005*
GFR	100± 17	163 ± 23	0.000**

Table 2: Comparison of Creatinine, BUN and GFR between control and hyperthyroidism:

Variables	Hyperthyroidism mean	Control mean	P. value
Creatinine	0.7 ± 0.2	0.6 ± 0.1	0.039*
BUN	14 ± 2.5	10 ± 3.2	0.000**
GFR	143 ± 32	163 ± 23	0.003**

Table 3: Correlation between renal parameters and thyroid hormones in of hypothyroid group:

Variables	Coefficient	TSH	T4	T3
Creatinine	R	0.860	-0.760	-0.670
	P	0.000*	0.000**	0.000ns
BUN	R	0.230	-0.171	-0.086
	P	0.046ns	0.136ns	0.450ns
GFR	R	-0.839	0.750	0.600
	P	0.000**	0.000*	0.000ns

Table 4: Correlation between renal parameters and thyroid hormones in of hyperthyroid group:

Variables	Coefficient	TSH	T4	T3
Creatinine	R	-0.279	0.431	0.372
	P	0.082ns	0.005**	0.018*
BUN	R	-0.100	0.001	0.149
	P	0.541ns	0.998ns	0.360ns
GFR	R	0.297	-0.280	-0.220
	P	0.063ns	0.080ns	0.172ns

**: significant at 0.01 level of probability, ns: no significant difference

4. Discussion

Significantly elevated plasma creatinine level was found in hypothyroid group (P=0.000) which was in agreements with study performed at 2012 by Saini V et al, in which creatinine level was significantly increased [18]. Close similar result was found in study done at 2011 by Stojanoski S et al, where creatinine was increased and equal 115 µmol/l (1.3 mg/dl) [22]. Another study carried in Sudan at 2006 by Khalid et al, showed that creatinine was significantly elevated and equal 1.18 mg/dl and (P= 0.000) [4]. The result also consistent with study done at 2003 by Fricker M et al, where creatinine was increased to 86 µmol/l (0.97 mg/dl) [9]. Also study done at 1999 by Kreisman SH et al, where creatinine was also significantly elevated (1.17mg/dl with P value of < 0.001) [6]. Also closely similar results was found in study carried out at 1997 by Verhelst J et al [16]. Plasma creatinine level was also significantly elevated in hyperthyroid subjects (P=0.039) this completely disagree with previously mentioned studies [22,9,16]. Blood Urea Nitrogen level was significantly elevated in hypothyroidism (P=0.005) this closely agree with study performed at 2012 by Saini V et al [18]. In hyperthyroid group significantly elevated BUN was

found (P=0.000). In this study, glomerular filtration rate was calculated using MDRD equation, in hypothyroid group eGFR was significantly decreased (P=0.000) being also consistent with study performed in Sudan at 2006 by Khalid et al in which eGFR was significantly decreased (GFR= 67.5 ml/min, P=0.002) [4]. GFR also significantly decreased in hyperthyroidism (P=0.003) although our study lacked the use of gold standard method for GFR estimation, the results of hypothyroid group were in close agreements with the study that used the standard method for GFR estimation which was carried at 2011 [22]. And also agree with other studies that used different methods and equations except in that the level of eGFR in hyperthyroid subjects in other studies was significantly increased [9,20].

Correlation studies between renal parameters and thyroid functions reveled that in hypothyroid group plasma creatinine had a significant positive correlation with TSH and significant negative with both T4 and T3 level (P=0.000 in each), meant that creatinine increased as TSH increase and T4 and T3 decrease this results consistent with study done at 2015 in Pakistan by Attaullah S et al in which TSH had a significant positive correlation with creatinine and T3 and significant negative correlation with T4 (P= 0.000 for each) [21]. Also consistent to some extend with study performed at 2012 by Saini V et al, in which TSH in hypothyroidism showed significant positive correlation with creatinine [18]. In hyperthyroid subjects plasma creatinine level had a significant positive correlation with T4 (P=0.005) and T3 (P=0.018) became increased as they increase, this disagree with the Pakistanian study in which creatinine had significant negative correlation with TSH, T4, and T3 during hyperthyroidism [21]. BUN in hypothyroid group had a significant positive correlation with TSH (P=0.046) only while in hyperthyroidism BUN not correlated to TSH, T4 and T3 level. eGFR in hypothyroid had a significant negative correlation with TSH and significant positive correlation with T4 and T3 (P=0.000 for each) meant that it increased as TSH decrease, and decreased as T4 and T3 decrease while in hyperthyroid eGFR not correlated to thyroid hormones level. Increased plasma creatinine, blood urea nitrogen and decreased eGFR in hypothyroid subjects believed to be related to the generalized hypodynamic circulatory system, results of hypothyroid obtained also reflect that these changes in creatinine and eGFR strongly related to TSH and T4 and T3 level, unlike hyperthyroid subjects results which were inconsistent and totally disagree with most studies performed considering renal parameters in hyperthyroidism and these discrepancy may due to initiation of treatment in most hyperthyroid subjects.

5. Limitations

Limitations were related to hyperthyroid patients samples as most were obtained during treatment course.

6. Conclusion

The present study illustrated that overt hypo and hyperthyroidism cause significant increased creatinine and blood urea nitrogen while decreased estimated glomerular filtration rate. Correlations were found between creatinine, eGFR and thyroid hormone levels. BUN level exhibit different relationships with thyroid function tests depending on the type of thyroid dysfunction. Strict observation of renal function parameters to manage those patients accordingly is highly recommended because normal functioning thyroid is needed for healthy kidney performance.

7. Acknowledgment

I like to express my deepest gratitude to Chemical Pathology Department, Faculty of Medical Laboratory Sciences University of Khartoum.

References

[1] Mariani LH, Berns JS. The renal manifestations of thyroid disease. Journal of the American Society of Nephrology. 2012 Jan 1;23(1):22-6.
[2] Koller KJ, Wolff RS, Warden MK, Zoeller RT. Thyroid hormones regulate levels of thyrotropin-releasing-hormone mRNA in the paraventricular nucleus. Proceedings of the National Academy of Sciences. 1987 Oct 1;84(20):7329-33.
[3] Vadstrup S. Comparative aspects of iodine conservation in mammals. Comparative Biochemistry and Physiology Part A: Physiology. 1993 Sep 1;106(1):15-7.
[4] Khalid, A. S., M. I. Ahmed, H. M. Elfaki, N. Hassan, and S. M. Suliman. "Renal Function in Hypothyroidism." (2006).
[5] Vargas F, Moreno JM, Rodríguez-Gómez I, Wangensteen R, Osuna A, Álvarez-Guerra M, García-Estañ J. Vascular and renal function in experimental thyroid disorders. European Journal of Endocrinology. 2006 Feb 1;154(2):197-212.
[6] Kreisman SH, Hennessey JV. Consistent reversible elevations of serum creatinine levels in severe hypothyroidism. Archives of Internal Medicine. 1999 Jan 11;159(1):79-82.
[7] Davis RG, Madsen KM, Fregly MJ, Tisher CC. Kidney structure in hypothyroidism. The American journal of pathology. 1983 Oct;113(1):41.
[8] Gowda S, Desai PB, Kulkarni SS, Hull VV, Math AA, Vernekar SN. Markers of renal function tests. N Am J Med Sci. 2010 Apr 1;2(4):170-3.
[9] Fricker M, Wiesli P, Brändle M, Schwegler B, Schmid C. Impact of thyroid dysfunction on serum cystatin C. Kidney international. 2003 May 31;63(5):1944-7.
[10] Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Annals of internal medicine. 1999 Mar 16;130(6):461-70.

[11] Lin J, Knight EL, Hogan ML, Singh AK. A comparison of prediction equations for estimating glomerular filtration rate in adults without kidney disease. Journal of the American Society of Nephrology. 2003 Oct 1;14(10):2573-80.
[12] Vukobrat-Bijedic Z, Husic-Selimovic A, Mehinovic L, Junuzovic D, Bijedic N, Sofic A, Bjelogrlic I, Mehmedovic A. Estimated Glomerular Filtration Rate (eGFR) Values as Predictor of Renal Insufficiency in Advanced Stages of Liver Diseases with Different Etiology. Medical Archives. 2014 Jun;68(3):159.
[13] Chen YW, Chen HH, Wang TE, Chang CW, Chang CW, Wu CJ. Difference between CKD-EPI and MDRD equations in calculating glomerular filtration rate in patients with cirrhosis. World J Gastroenterol. 2011 Oct 28;17(40):4532-8.
[14] Hallan S, Astor B, Lydersen S. Estimating glomerular filtration rate in the general population: the second Health Survey of Nord-Trondelag (HUNT II). Nephrology Dialysis Transplantation. 2006 Jun 1;21(6):1525-33.
[15] Kuan Y, Hossain M, Surman J, El Nahas AM, Haylor J. GFR prediction using the MDRD and Cockcroft and Gault equations in patients with end-stage renal disease. Nephrology Dialysis Transplantation. 2005 Nov 1;20(11):2394-401.
[16] Verhelst J, Berwaerts J, Marescau B, Abs R, Neels H, Mahler C, De Deyn PP. Serum creatine, creatinine, and other guanidino compounds in patients with thyroid dysfunction. Metabolism. 1997 Sep 1;46(9):1063-7.
[17] Montenegro J, González O, Saracho R, Aguirre R, González Ó, Martínez I. Changes in renal function in primary hypothyroidism. American Journal of kidney diseases. 1996 Feb 1;27(2):195-8.
[18] Saini V, Yadav A, Arora MK, Arora S, Singh R, Bhattacharjee J. Correlation of creatinine with TSH levels in overt hypothyroidism—A requirement for monitoring of renal function in hypothyroid patients?. Clinical biochemistry. 2012 Feb 29;45(3):212-4.
[19] Villabona C, Sahun M, Gómez N, Gómez JM, Soler J, Roca M, Mora J, Puchal R. Blood volumes and renal function in overt and subclinical primary hypothyroidism. The American journal of the medical sciences. 1999 Oct 1;318(4):277-80.
[20] Iglesias P, Diez JJ. Thyroid dysfunction and kidney disease. European journal of endocrinology. 2009 Apr 1;160(4):503-15
[21] Attaullah, S., Haq, B.S. and Ahmed, Z., 2015. Correlation of thyroid dysfunction with serum creatinine.
[22] Stojanoski S, Pop Gjorceva D, Gruev T, Ristevska-Miceva S, Ristevska N. Impact of thyroid dysfunction on serum cystatin C, serum creatinine and glomerular filtration rate. Maced J Med Sci. 2011 Mar 1;4(1):25-30.

Author Profile

Adel Nasr Morsi

Aalya Ibrahim Mohammed