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Research Article

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The Effect of Chronic Renal Failure on Thyroid Hormones Specificity Measured fT3 in a Sample of Iraqi Patients

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Abstract

Background: *Chronic renal failure (CRF) affects thyroid function in multiple ways, including low circulating thyroid hormone concentration, altered peripheral hormone metabolism, disturbed binding to carrier proteins, possible reduction in tissue thyroid hormone content, and increased iodine store.*

Objective: *To evaluate of thyroid Gland Function in patients with chronic renal failure and an attempt to find a relationship between chronic renal failure and thyroid dysfunctions.*

Subjects and Methods: *A total number of 96 subjects with age range from 15-67 years old (56 males and 40 females) were included in this study. Total number was divided into two groups according to their number Group A. Study group: haemodialysis (HD) consists of 48 patients and Group B. Control group: consists of 48 subjects.*

T3, T4, TSH, fT3, Urea, Creatinine, Albumin and TSP were measured in each of the two groups.

Results: *The results revealed statistically significant reduction serum level of tT_3, fT_3 more than tT_4 in Chronic Renal Failure group in comparison with normal levels in control group while there is no statistically significant difference seen between case and control groups in regard to TSH.*

Conclusion: *There is a decrease serum level of tT_3, tT_4 and fT_3 but the decreased of tT_3 and fT_3 more than tT_4 in Chronic Renal Failure group in comparison with normal levels in control group.*

Keywords: Thyroid hormones, Haemodialysis (HD) patients

Introduction

The thyroid gland produces two major related hormones thyroxine and triiodthyronine, commonly called T_4 and T_3, respectively. Both of these hormones profoundly increase the metabolic rate of the body. Complete lack of thyroid secretion usually causes the basal metabolic rate to fall 40 to 50 percent below normal, and extreme excesses of thyroid secretion can increase the basal metabolic rate to 60 to 100 percent above normal [1,2]. The embryonic thyroid gland develops from endoderm at foramen cecum that migrates downward and elongates to form two clusters of spherical follicles. The follicles proliferate to form the lobes of the thyroid gland. It is a butterfly-shaped or located in the neck. Its main function is to produce thyroid hormones, which control the body's metabolic rate of the thyroid gland [3,4].

Chronic renal failure, or end- stage renal disease (ESRD), is a progressive, irreversible deterioration in renal function in which the body's ability to maintain metabolic, fluid and electrolyte balance fails, resulting in uremia or azotemia (retention of urea and other nitrogenous wastes in the blood) [5,6]. ESRD may be caused by many factors, systemic diseases, such as diabetes mellitus (leading cause); hypertension chronic glomerulonephritis; pyelonephritis obstruction of the urinary tract; hereditary lesion, as in polycystic kidney disease; vascular disorders; infections; medications; or toxic agents [7].

Chronic renal failure affects thyroid function in multiple way, including low circulating thyroid hormone concentration, altered peripheral hormone metabolism, disturbed binding to carrier proteins, possible reduction in tissue thyroid hormone content, and increase iodine store in thyroid glands, Both plasma triiodothyronine (T3) and Thyroxin (T4) are reduced [8].

There are two important general principles laboratory assessment of thyroid functions [9,10].

- Thyroid function should not be assessed in seriously ill patients unless there is a strong suspicion of thyroid dysfunction.
- When thyroid dysfunction is suspected in critically ill patients,

measurement of serum TSH along is in adequate for the evaluation of thyroid function.

Chronic kidney disease defines as either kidney damage or a decreased kidney glomerular filtration rate (GFR) of less than 60 ml/min/1.73 m^2 for 3 or more months [11-13]. Renal function affects the thyroid gland in many ways. Disturbances in homeostasis and inflammation are common complication of kidney diseases [14,15].

The kidney normally plays an important role in the metabolism, degradation and excretion of several thyroid hormones. It is not surprising therefore that impairment in kidney function lead to disturbed thyroid physiology. All levels of the hypothalamic-pituitary-thyroid axis may be involved, including alteration in hormone production, distribution, and excretion. As a result, abnormalities in thyroid function tests are frequently encountered in uremia. However, the overlap in symptomatology between the uraemic syndrome and hypothyroidism requires a cautious interpretation of these testes. Never the less, it is ordinarily possible in the individual uraemic patient to assess thyroid states accurately by Physical Diagnosis and thyroid function testing. Epidemiologic data suggests that predialysis patients with chronic renal dysfunction have an increased risk of hypothyroidism; many cases are subclinical [15,16].

Most patients with end stage renal diseases have decreased plasma levels of free T_3, which reflects diminished conversion of T_4 to T_3 in the periphery [17]. Low levels of total T_3 may also reflect metabolic acidosis and reduced protein binding [18]. With respect to the latter, circulating thyroid hormones are normally bound to thyroid hormone binding globulin (TBG) and, to a lesser extent to pre albumin and albumin. Although circulating TBG and albumin levels are typically normal in uremia (in the absence of the nephrotic syndrome), retained substances in renal failure may inhibit hormone binding to these proteins.

Low plasma fT_3 levels may also be associated with decreased survival overall and the presence of the malnutrition - inflammation syndrome [19,20]. There is substantial clinical overlap between chronic renal failure and hypothyroidism. In addition to low total and (fT_3) levels, there are a number of symptoms that are common to both conditions including: cold intolerance, puffy appearance, dry skin, lethargy, fatigability and constipation. Furthermore, the frequency of goiter is markedly increased in ESRD [21]. Despite these findings, most uraemic patients are considered to be euthyroid as evidenced by normal plasma concentration of TSH and free T4, and normal basal metabolic rate and tendon relaxation time [17].

Subjects and Methods

This study was conducted at the Department of physiological chemistry, Collage of Medicine, University of Baghdad during the period of December 2007 through to March 2008. A total number of 96 subjects with age ranging from 15-67 years old (38.98 ± 12.22; mean ± SD, 56 males and 40 females) were included in this study. Test groups subjects were randomly selected from the patients attending dialysis unit in five artificial kidney centers: (Al-Yarmook Teaching Hospital, Baghdad Teaching Hospital, Al-Karama Teaching Hospital, Al- Kadhymia Teaching Hospital, and Al- Kindey Teaching Hospital). Subjects recuperate to full fill the criteria of being nonthyroidal illness (NTI) at least 3 months history of haemodialysis, not due to thyroid gland dysfunction, While 48 healthy subjects with normal thyroid function tests (28 male and 20 females) were selected from patient's relatives, medical staff of Al- Yarmook hospital and other hospitals.

Total number was divided into two groups according to their number.
Group A. Study group: (haemodialysis HD) consists of 48 patients
Group B. Control group: consists of 48 subjects
Also they were divided according to gender:
Group I: Male (n=56)
Group II: Female (n=40)

To compare the significance of the difference in the mean values in comparison groups, student -Pearson chi-square test was applied; $p< 0.05$ was considered statistically significant.

The correlation coefficient [r] test is used to describe the relation between the different studied continuous parameters; $p< 0.05$ was considered statistically significant. Patients were excluded from the study if they had a history of systemic illness which causes low fT3 like Ischemic heart disease including myocardial infarction, sepsis, recent big surgery, infection, and Diabetic mellitus [22]. Or Patients on heparin or any drug which cause T3 displacement from binding globulin like diuretic [23]. Or Patients who are on β-blocker drugs. Or Patients that have diseases which cause low protein such as starvation, nephrotic syndrome, hepatic insufficiency or protein losing entropathy [24]. Or Patients taking regularly iodine by drugs or foods [25,26]. Or Patients with Thyroid disease such as hypothyroidism, hyperthyroidism and goiter [27]. Or Patients on thyroid replacement Therapy (Thyroxine) or anti-thyroid medication (carbimazole) [28]. Five ml of venous blood were aspirated from control group and CRF patients at 8:00 - 9:00 am. Blood samples were collected into plain test tubes and centrifuged after 30 minutes of collection for 10 minutes at 3000 rpm. Serum was frozen at -20 C0 till used in determination of T3, T4, TSH, fT3, urea, creatinine, S.alb. and TSP.

Results and Discussion

Table (1) shows the (mean ± SD) of T3, T4, TSH, fT3, urea, creatinine, albumin and total serum protein concentrations in sera of patients with chronic renal failure and control group, in which $p< 0.05$ was considered statistically significant.

Table 1: Levels of T3, T4, TSH, fT3, urea, creatinine, albumin and total serum protein concentrations in sera of patients with chronic renal failure and control group

Subjects	Control (n=48)	Patients (n=48)	t -Test
T3(ng/ml)	(0.40-3.70)	(0.20-3.10)	(P < 0.0001
T4(µg/ml)	(0.90-13.20)	(0.80-9.90)	P < 0.0001
TSH (µIU/ml)	(0.10-8.50)	(0.50-8.70)	P > 0.05
fT3(ng/ml)	(0.60-12.10)	(0.40-6.70)	P < 0.0001
Urea (mg/dl)	(25.03-50.0)	(72.72-181.92)	P < 0.0001
Creatinine (mg/dl)	(0.40-1.20)	(2.8-9.8)	P < 0.0001
Serum Albumine (g/dl)	(3.45-5.53)	(2.00-5.00)	(2.00-5.00)
Total Serum Protein (g/dl)	(6.00-9.30)	(3.60-8.70)	P < 0.0001

This study shows highly significant difference in mean T_3 between CRF and control groups.

The result in present study is in agreement with that published by (Hussein Saied, 2005 et al.) and (G Avasthi, 2001 et al.) [29,30]. This may be due to poor peripheral conversion from T_4 to T_3 which is the main source for production of T_3 on peripheral level, may be due to weak affinity of deiodinases enzymes due to drug such as heparin, beta-blocker, anticonvulsants and furosemide drugs competition to thyroid nuclear receptors which affect transcription and damage to DNA, also drugs affect TBG, may be explained by cleavage of thyroxine – binding – globulin (TBG) by protease enzyme causes a conformational change that reduce the affinity of TBG.

It was found previously that there was a normal or slightly decreased T4 levels in dialyzed patient [31,32]. This finding was compatible with (Hussein Saied, 2005 et al.) and (HJ Mehta, 1991 et al.) [29,33]. TSH level showed no significant difference between mean of CRF and control groups. These results are compatible with previous studies done by (Hussein Saied, 2005 et al.), (Carmine Zoccali, 2005 et al.) and (Serhat Aytug, 2007 et al.) [29,34,35].

Measurement of fT_3 was emphasized in our study. This measurement was taken in consideration in a sample of Iraqi CRF patients for up the first time knowledge.

Statistically analysis values of fT_3 level indicate significant difference between CRF and control group.

This study agreed with what was reported in literature (Hussein Saied, 2005 et al.), (HJ Mehta, 1991 et al.) and (Hamdy Abo-Zenah, 2008 et al.) [29,33,36].

fT3 correlates positively with T4 [r = 0.349, p = < 0.05] (Figure 1).

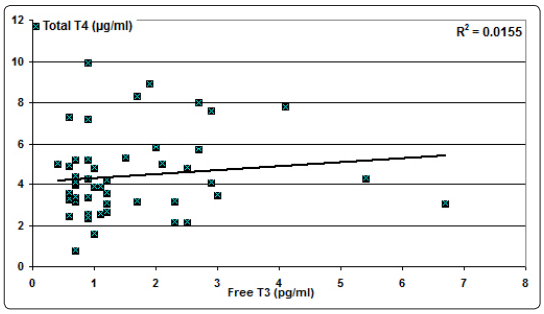

Figure 1: The correlation between free T_3 and the total T4 of CRF patients included in the study

fT3 correlates positively and strongly with total serum protein [r = 0.437, p = < 0.01] (Figure 2).

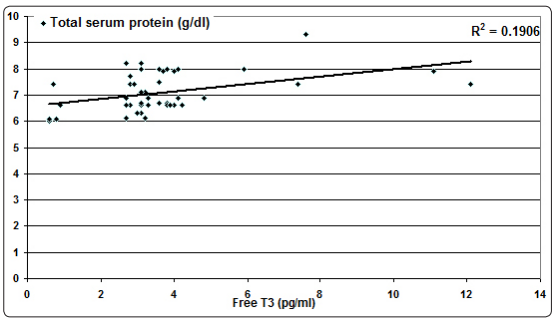

Figure 2: The correlation between free T_3 and the TSP of controls included in the study

Levels of tT_3 and fT_3 suffer further reductions in CRF, which is thought to be due to impairment in deiodenation of T_4, a principle process by which T_3 is produced at peripheral levels [33]. There was a highly significant elevation of S.urea and S.creatinin between CRF and control group respectively.

TSP contains two types (albumin and globulin); Serum globulin regarding the main types of protein those binding thyroid hormones. It was found that there is a decreased in the (TSP) level in CRF group.

Statistically analysis revealed there is a high significancy of TSP between CRF and control group. Albumin is another protein that binds hormones but the binding with thyroid hormones is less than globulin binding thyroid hormones.

There is a highly significant of serum albumin between CRF and control groups. There is in agreement with other studies (Jan Robertson, 2006 et al.) [37,39].

In the present study reveals that 34 patients (70.83%) had duration of CRF between 1-4 years, while 10 patients (20.83%) had duration between 5-9 years and only 4 patients (8.33%) had duration 10 years or more. The mean duration of CRF was between 3.75 ± 3.75 (Figure 3).

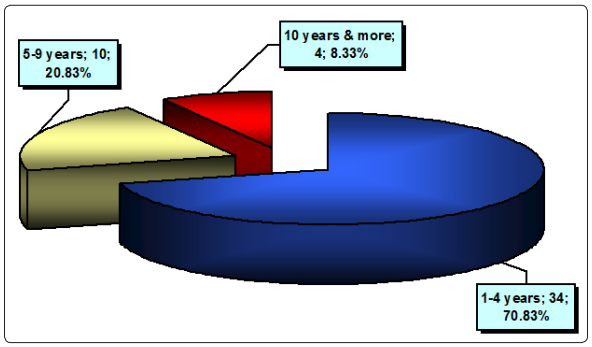

Figure 3: The duration (years) of CRF of patients included in the study [Mean±SD (Range); 3.75±3.72 (1.00-17)]

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