

Determination of thyroid hormone levels in the serum of Non-dialyzed patients with chronic renal failure

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ABSTRACT

Thyroid hormones, triiodothyronine (T3) and thyroxin (T4) play an important role in growth, development, and physiology of the kidney. The kidney has a central role in metabolism and clearance of these hormones as well as thyroid – stimulating hormone (TSH). Chronic renal failure (CRF) is a state of irreversible deceleration in renal function results in alterations in internal milieu, which affects the synthesis and secretory rate of hormones. To evaluate the thyroid hormone levels in non-dialyzed patients with chronic renal failure (CRF); 24 patients with CRF aged 30-70 years, mean±S.d. (48.458 ± 13.569) and 48 healthy volunteers who served as controls aged 30-70 years (43.104 ± 12.387) were studied for their thyroid function status using enzyme-linked immunosorbent assay(ELISA). The study showed significant increase ($p < 0.05$) in the serum triiodothyronine (T3), thyroxin (T4) and thyroid stimulating hormone (TSH) levels in 25%, 20%, and 25% of CRF patients respectively as compared to the healthy groups; while 75% of CRF patients showed non significant low levels ($p > 0.05$) for both T3 and TSH and 80% for T4. Also there was a high positive relation between TSH, T3, T4 levels respectively with both age and gender of chronic renal failure patients. The results suggest that patients with CRF have a state of thyroid dysfunction.

Introduction

Thyroid hormones, triiodothyronine (T3) and thyroxin (T4) play an important role in the maturation and development of the skeleton and affect endochondral calcification and the entire process of cartilage growth (1). They also play an important role in growth, development, and physiology of the kidney; it is known that hypothyroidism decrease and hypothyroidism increases the kidney-to-body weight ratio by a not fully understood mechanism (2). The kidney has a central role in metabolism and clearance of these hormones as well as thyroid – stimulating hormone (TSH) (3).

Chronic renal failure (CRF) is a state of irreversible deceleration in renal function. When only less than 10% of renal function remains, it is termed as end stage renal failure, this permanent loss of renal function culminates in signs and symptoms termed uremia (4) .

Unlike acute renal failure, from which recovery is frequent, CRF is not reversible and may lead to a vicious cycle with progressive loss of remaining nephrons (5,6).

In addition, chronic renal failure results in alterations in internal milieu, which affects the synthesis and secretory rate of hormones (3). There are marked alterations in the concentrations in serum and the peripheral metabolism of thyroid hormones in chronic renal failure (CRF) (7,8).

A Secretion of thyroid hormones and their metabolism in humans are controlled at two levels:

The hypothalamic–pituitary–thyroid negative feedback axis controls thyroidal secretion, while extra-thyroidal tissues regulate the production of triiodothyronine (T3) and are responsible for thyroid hormone degradation (9). The thyroid gland produces thyroxin (T4) but only 20% of the most metabolically active thyroid hormone T3 and 5% to 8% of the calorigenically inactive reverse T3 (RT3) hormone and T4 in tissues such as liver, kidney and muscles

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(10,11). Patients with chronic renal failure often have signs & symptoms suggestive of thyroid dysfunction .These findings include dry skin, sallow complexion, low temperature, cold intolerance, decreased basal metabolic rate, lethargy, fatigue, edema & hyporeflexia(12). Serum (T3) levels were consistently found to be low without any regard to treatment of CRF; total & free thyroxin (T4) concentrations have been reported as low, normal or high. Serum thyroid stimulating hormone (TSH) levels were found to be normal in most patients of CRF even in those whose CRF is complicated by low T3 concentration. The incidence of goiter has also been variably reported in literature (13). However, Several factors such as the type of kidney disease e.g. protein –loosing ,nephropathies; treatment with immunosuppressive drugs ; the degree and duration of renal failure ; the extent of malnutrition ; dietary factors e.g. protein restriction ;drugs such as anti-hypertensive adrenergic blockers or corticosteroids ,and renal transplantation may all influence the results of thyroid function tests (14).

The objective of this study is to investigate association of thyroid hormone status with clinical severity and outcome in chronic renal failure.

Patients and Methods

Twenty four Patients with chronic renal failure (CRF) and with no history of thyroid abnormality aged 30-70 years, mean±S.d. (48.458 ± 13.569) and (48) healthy volunteers aged 30-70 years (43.104 ± 12.387) were taken as control group were included. The diagnosis of CRF was established on the basis of clinic profile and biochemical tests (serum urea, Creatinine and uric acid). Patients with CRF were carried out to measure serum T3, T4, and TSH levels by using enzyme-linked immunosorbent assay (ELISA); this was performed as described in the leaflet of the kit (Human, Germany).

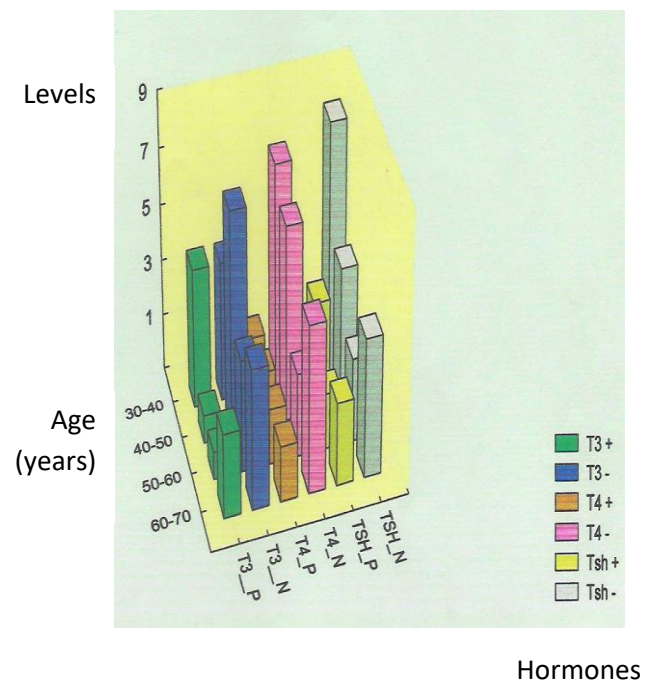
Statistical analysis

The statistical analysis used included t- test, F-test, chi –square test(x²). The statistical package for social science (SPSS for windows) and statistica program were used. A p value < 0.05 was considered statistically significant (15).

Results

The demographic study showed a highly significant differences (P<0.05) in the level of TSH, T3, and T4 hormones respectively when compared with the same age of CRF patients as illustrated in figure 1; similarly there were a highly significant differences (P<0.05) in the level of TSH, T3, T4 hormones when compared with the gender of those patients as it illustrated in figure 2.

Serum thyroid hormone profile in CRF patients and healthy subjects are given in table 1. Our findings showed that serum T3 and TSH levels in 6 cases (25%) of CRF patients were significantly higher (p<0.05) (5.450±0.426) and (7.865±2.332) respectively than their levels in control groups (0.681±0.319) and (0.725±0.625) respectively; while 18 cases (75%) of CRF patients showed non significant low levels of both hormones (p>0.05) (0.629±0.399) and (0.471±0.591) respectively as compared with the controls. Similarly, a high significant increase of T4 levels showed in 4 cases (20%) of CRF patients (p<0.05)(15.662±2.322) than the control group(2.197±0.749); while non significant decrease were shown in T4 levels in 20 cases (80%) of CRF patients (1.939±1.177) compared with the control



group(2.196±0.749).

Figure 1: Serum thyroid hormone profile in CRF patients according to age groups

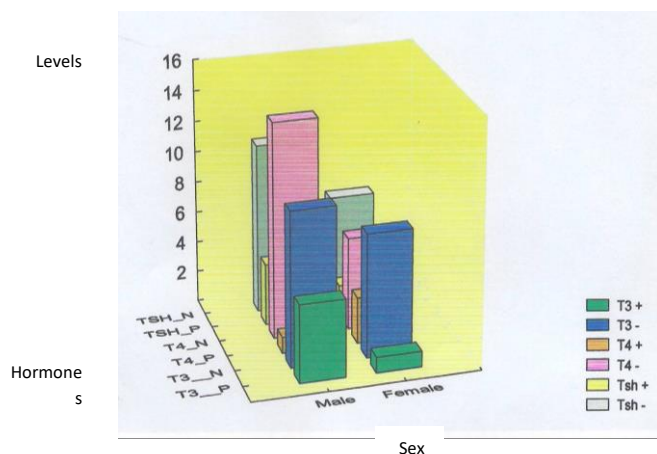


Figure2: Serum thyroid hormone profile in CRF patients according to gender

Table (1): Mean distribution of serum T3, T4, TSH levels in CRF patients and controls

Studied group	N	Mean	S.d	F- test	t-test (sig.at 0.05)	
T3 ng/ml	positive	6	5.450	0.426	1.791 NS	4.48
	negative	18	0.629	0.399	1.57 NS	
	control	48	0.681	0.319		
T4 µg/dl	positive	4	15.662	2.322	9.597 HS	11.35
	negative	20	1.939	1.177	2.094 NS	
	control	48	2.197	0.749		
TSH mIU/l	positive	6	7.865	2.332	13.899 HS	7.74
	negative	18	0.471	0.591	1.120 NS	
	control	48	0.725	0.625		

NS=not significant, HS=high significant

Discussion

A large number of hormonal systems are affected by CRF, yet it remains unclear to what extent these changes are responsible for manifestations of uremic syndrome (13).the present study demonstrate the thyroid function states in chronic renal failure not yet dialysis therapy. Our results are agreement with Joseph *et al.*, who showed that patients of CRF, had low T3, T4 and free T4 (fT4) but had high TSH levels suggesting maintenance of pituitary-thyroid axis (16). The likely explanations for low levels of both T3 & T4 could be defective release in response to TSH. FT4 is the most active biological fraction, constituting 0.03% of T4 and its levels are unaffected by variations of concentration of carrier proteins and hence, reflects thyroid status accurately. In nonthyroidal illness, reduced T3 Levels are due to decreased peripheral conversion of T4 to T3, while thyroid gland production of T3 is normal and T3 clearance rates are normal or decreased, as in other nonthyroidal illness (17). It is suggested that low T3 is associated with worse neurological outcome and the severity of low T3 may be a predictor of functional improvement in CRF (18).

T4 is a pro hormone requiring 5'-monodeiodination to produce the most active thyroid hormone T3 (6). The liver, kidney and muscle supply more than 80% of plasma T3 (19). Impaired conversion of T4 to T3 may be related to malnutrition and humoral factors including cytokines that are generally associated with CRF (20).

In agreement with a number of other reports we observed decreased serum T4 concentration in CRF patients not on hemodialysis (7, 9, 21, and 22). Low total T4 values in chronic renal failure patients may be primarily related to impaired T4 binding to serum carrier proteins; it has been reported that many inhibitors of T4 binding to serum carrier proteins are present in CRF patients and thus contributing to the decreased levels of T4 in CRF(6).

In our study, there was a significant increase in the mean serum TSH in patients with CRF when compared to healthy group, a result that is in accordance with the result of many studies (6, 13, 23).The increase in serum TSH in the study may be attributed to the increase in half – life of TSH in CRF and /or non significant low serum T3 levels in these patients. Normal or slightly increased serum TSH concentrations, as determined by radioimmunoassay, have been reported in CRF (24).A recent study showed

the critical role of the pore-forming α subunit (KCNQ1) for proper function of thyroid gland; it participate in the regulation of cell volume and cell proliferation. TSH stimulates cell proliferation and the increased numbers of T3/T4 secreting cells augment the release of the hormones (25). However an elevated TSH level is the most useful index of hypothyroidism (4), while TSH was not elevated in uremic patients in a separated study (8). Possible mechanism of action of thyroid hormone on renal function could be explained by its influence on maturation of the rennin-angiotensin system (RAAS). Plasma rennin activity and plasma levels of angiotensinogen, angiotensin II and aldosterone are directly related to plasma levels of thyroid hormones (26, 27).

These thyroid hormone changes may be mediated in part by cytokines or other inflammatory mediators, acting at the level of the hypothalamus and pituitary, the thyroid gland, and the hepatic deiodinase system, as well as on binding of thyroxin to thyroid binding globulin. The degree of thyroid function disturbance correlates with disease severity and low levels of thyroid hormones predict a poor prognosis in several illnesses (28).

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تقدير مستوى هورمونات الغدة الدرقية في مصول مرضى الفشل الكلوي المزمن غير الخاضعين للديال الدموي

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الخلاصة

تؤدي هورمونات الدرقية T4, T3 دورا مهما في تطور ونمو و وظيفة الكلى . ولللكلى دور مهم ايضا في ايض هذه الهورمونات وتخليص الجسم من الفائض منها وكذلك الحال بالنسبة للهرمون المحفز للدرقية TSH . ولغرض التحري عن أمراض الغدة الدرقية في المرضى المصابين بالفشل الكلوي المزمن تم قياس مستويات هرمون الدرقية TSH, T4, T3 في مصول المرضى الذين لم يخضعوا للديال الدموي (غسيل الكلى) باستخدام تقنية الامتزاز المناعي المرتبط بالإنزيم الاليزاز . خضع لهذه الدراسة 24 مريضا بالفشل الكلوي تراوحت أعمارهم بين 30-70 سنة و 48 من المتطوعين الأصحاء تراوحت أعمارهم بين 30-70 سنة أيضا. أظهرت النتائج وجود زيادة معنوية عالية ($P < 0.05$) في مستويات هرمون T3 و T4 و TSH في 25% و 20% من مرضى الفشل الكلوي على التوالي مقارنة بمجاميع الأصحاء . في حين شهدت مستويات كل من T3 و TSH انخفاضا في 75% من المرضى الا انه لم يكن معنويا من الناحية الاحصائية. كذلك هنخفض مستوى هرمون T4 في 80% من مصول المرضى ولم يكن الانخفاض معنويا عند مقارنته مع مجموعة الأصحاء . كانت هناك علاقة ايجابية معنوية ($P < 0.05$) بين مستويات كل من TSH و T3 و T4 مع كل من أعمار وأجناس المرضى . وعلى ضوء نتائج الدراسة، فإن نسبة من المرضى المصابين بالفشل الكلوي المزمن يعانون من أمراض الغدة الدرقية ذاتية المناعة و التي تكون لعبت دورا في تطور المرض.