

Evaluation of Thyroid Hormones Levels in Libyan Patients with Chronic Renal Failure before and after Maintenance Hemodialysis

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Abstract

Data from recent studies revealed that kidney diseases might affect the thyroid function in various ways. A variety of alterations in thyroid hormone levels and metabolism have also been reported in patients with chronic renal failure (CRF) in some studied population. In addition, it was reported that serum levels of both T3 and T4 might alter immediately after a hemodialysis (HD) treatment than before. Therefore, this study was aimed to investigate the level of triiodothyronine (T3) and thyroxine (T4) in CRF Libyan patients before and after HD. This study was carried out on 46 CRF patients (30 males and 16 females) with a mean age of 47.46 ± 15.75 years. These patients were treated at the hemodialysis unit of Educational Central Zelitina Hospital, Zelitina, Libya. None of these patients apparently have any thyroid problems and no history of drug intake that may affect thyroid function. Blood samples were taken from each patient to measure serum levels of T3 and T4, before and after HD. In addition, the effects of several variables including age, gender, body mass index (BMI), presence of both hypertension and, diabetes mellitus and duration of kidney dialysis on serum levels of T3 and T4 before and after HD were also studied. After HD, there was a statistically significant increase in the serum levels of T3, T4. The age, gender, BMI, duration of kidney dialysis and the presence of hypertension and diabetes mellitus did not have any significant effect on the serum level of T3 and T4 before and after HD. However, the serum levels of T3 and T4 were still in the normal range in these examined patients either before or after HD. From these findings, it can be concluded that these CRF patients may be in a euthyroid state, because the serum levels of T3 and T4 were in the normal range. In addition, HD was seemed to improve the T3 and T4 thyroid hormone concentrations, suggesting that HD might activate the secretion of thyroid gland and catabolism. The other variables did not play any role in thyroid hormone levels in these patients either before or after HD. It is highly recommended that large scale

evaluation of thyroid hormone levels in Libyan CRF patients is performed by more patients, especially elderly patients.

Keywords

Chronic Renal Failure (CRF), Hemodialysis (HD), Triiodothyronine (T3) and Thyroxine (T4)

1. Introduction

The interaction between thyroid gland and the kidney in each other's functions is known for many years [1]. Thyroid dysfunction affects renal physiology and development, whereas kidney disease could result in thyroid dysfunction. The kidney normally plays an important role in the metabolism, degradation and excretion of several thyroid hormones. [2].

Thyroid gland is the largest endocrine gland in vertebrates located in the front of the neck, and just below the larynx. Thyroid glands can synthesize three important hormones, known as thyroxine (T4), triiodothyronine (T3) and calcitonin [3]. T4 and T3 are necessary for the normal growth, development, differentiation, and stimulate the rate of metabolism in most body tissue [4] [5]. Calcitonin is a potent hypocalcemic hormone, thought until recently to act predominantly on bone to inhibit osteoclastic bone resorption. There is also evidence for an action in the kidney to decrease tubular reabsorption of calcium, and in the brain and hypothalamus, where a number of actions have been reported [6].

Kidney function might be influenced or impaired by various factors, including infections, poisoning, tumors, stone formation and others [7] [8]. These factors might cause a decline in kidney function, and/or lead to kidney diseases or renal failure.

Renal failure is one of the most serious consequences of kidney diseases. Renal failure is a situation when the kidneys fail to function effectively and unable to maintain homeostasis of the blood. It can be divided into two forms: acute and chronic renal failure [9]. Whereas, there are other factors which may help to differentiate acute and chronic kidney disease including; the presence of anemia and the kidney size on ultrasound. Chronic kidney disease generally leads to anemia and small kidney size [10].

Patients with chronic renal failure (CRF) often have signs and symptoms indicative of thyroid dysfunction. These discoveries include dry skin, sallow complexion, low temperature, cold intolerance, decreased basal metabolic rate, sleep and tiredness. Various studies of thyroid functions in uremic patients have been carried out which have shown conflicting results [11].

However, CRF disease affects thyroid function in multiple ways, including low levels of circulating thyroid hormone concentration, altered peripheral hormone metabolism, disturbed binding to carrier proteins, possible reduction in tissue thyroid hormone content and increased iodine stores in the thyroid gland [12]. Thus, patients with renal failure may have various abnormalities of thyroid

function nevertheless; they are typically clinically euthyroid [13].

The aim of the present study was to evaluate the serum levels of thyroid hormones T3 and T4 levels in Zeletin city patients with chronic renal failure, before and after haemodialysis (HD).

Objective of Research

Several factors have been shown to influence the results of thyroid function tests. These include the type of kidney diseases, the degree and duration of renal failure, the extent of malnutrition, diabetes mellitus, dietary factors, HD with heparin or CAPD, and renal transplantation [14] [15] [16]. Taken together, it appears from these previous studies, there is an evidence of relationship between the level of thyroid hormones and CRF. However, the issue of thyroid function in patients with CRF is still inconclusive due to the complexity of the system studied. Therefore, the goal of this research will be to examine the status of thyroid function in Zeletin city patients with CRF before and after the HD. According to our knowledge this study is the first study conducted on the Zeletin city populations.

2. Materials and Methods

2.1. Study Sample

Forty six Libyan CRF patients from Zeletin City were invited to participate in this study. The subjects were invited by using multistage, stratified cluster sampling by the gender (male and female) and age groups (≤ 40 , 41 - 65, and > 65 and years). Totally 46 patients (30 males and 16 females) where, apparently don't have any thyroid problems and no history of drug intake that affects thyroid function (e.g. beta blockers, thyroid hormone replacement therapy, thiouracil, neomercazole) were recruited to participate in the study. The verbal consents were obtained from each individual after explaining the aims and methods of this study.

2.2. Data Collection

Personal and socio-demographic data from the volunteers were collected in structured questionnaires consist of a series of questions. Gender, age, height, body weight, history of health problems were included in questionnaires (diabetes, blood pressure, and other diseases). Furthermore, the subjects were asked about the period of using HD treatment.

2.3. Blood Collection

Blood were collected from the volunteers of Libyan in Zelitin city. Five milliliters of venous blood was withdrawn before and after HD treatment from each recruited patient. The blood samples were taken in Serum-Separating Tubes (SSTs). That tube was used to provide the serum for measuring T3 and T4 hormones. However, the Libyan blood samples were collected in the hemodialysis unit of Educational Central Zelitin Hospital, and then kept at 4°C before transferred to their diagnostic lab.

2.4. Biochemical Analysis

The serum was separated from the blood samples. The samples were centrifuged at 3000 rpm for 5 min at 4°C. Serum total T3 and T4 hormone concentrations were assayed by Microparticle Enzyme Immunoassay (MEIA) using Abbott AxSYM system (AxSYM, Abbott Diagnostics, Abbott Park, IL), fully automated immunoassay analyzer and commercially available kits from Abbott, USA at Educational Central Zelitina Hospital lab in Libya.

2.5. Dependent and Independent Variables

Dependent variable: The level of T3 (ng/ml) in the blood was measured and divided into three main groups; under normal (<0.45), Normal (0.45 - 1.37), and Above normal (>1.37). The serum T4 (µg/dl) level was measured and divided into three main groups: Under normal (<4.5), Normal (4.5 - 12.0) and above normal (>12.0).

Independent variables: The following variables are identified to be predictors for thyroid functional hormone among the study patients:

Age: It was divided into three groups as the following: (≤40, 41 - 65, and >65 and years).

Gender: Male or female.

Body mass index (BMI): After measuring the height (meter) and body weight (Kg) of each patient, BMI was calculated for each subject by using the following formula ($BMI = \text{weight}/\text{Kg}/(\text{height}/\text{m})^2$) then it was divided into four categories as the following; (<19: Under weight, 19 - 25: Normal, >25 - 29.9: Overweight, ≥30: Obese).

Diabetes: No or Yes.

Blood pressure: No or Yes.

Duration of kidney dialysis (Years): It was divided into three groups as the following: (≤4, 5 - 9 and ≥10).

2.6. Data Processing and Statistical Analysis

Data were entered and analyzed by the Statistical Package for Social Sciences (SPSS) software version 11.0 (SPSS®: Inc., Chicago, IL, USA). Normality test was done to check the data. Percentages, cross tabulation, means and standard deviations were produced and calculated. In addition, McNemar-test was used for comparisons among paired dichotomous groups and Paired t test used for paired continuous parametric variables. Chi square test also was used to do comparison between before and after HD for Zelitina patients regarding the levels of T3 and T4 hormones. The level of significance was set at ($P \leq 0.05$).

3. Results

3.1. Introduction

The patients included in this study are 46 CRF patients from Zelitina city in Libya and their age, sex, duration of HD, BMI, presence or absence of both high blood

pressure and diabetes mellitus were investigated. thyroid hormones (T3 and T4) were measured for all of these patients before and after of hemodialysis (HD).

3.2. Characteristic of Studied Patients

The samples consist of 30 males forming 65.2% and 16 females forming 34.8%. Their ages ranged from 20 to 90 years. The samples divided into three groups as shown in **Table 1**.

3.3. Medical History of Sample

In current study, CRF patients of Zelitina were suffered from additional diseases. Whereas, 10 persons (12.7%) were suffered from diabetes mellitus and 34 persons (73.9%) were had hypertension. The duration of kidney dialysis among the studied patients is different and was divided into three groups; 1 to 4 years, 5 to 9 years, and more than 10 years. The mean and SD value of duration of kidney dialysis was 6.76 and 4.18 years, respectively (**Table 2**).

Table 1. Distribution of socio-demographic and personal data of sample (N = 46).

Variable	Libyan (N = 46) N(%)
Age	
≤40	16 (34.8)
41 - 65	25 (54.3)
>65	5 (10.9)
Mean ± SD	(47.28 ± 14.79)
Gender	
Male	30 (65.2)
Female	16 (34.8)
BMI	
Under weight (<19)	7 (15.2)
Normal (19 - 25)	20 (43.5)
Over weight (>25 - 29.9)	10 (21.7)
Obese (≥30)	9 (19.6)

Table 2. Distribution of medical history of sample (N = 46).

Variable	Libyan (N = 46) N(%)
Diabetes mellitus	
Yes	10 (21.7)
No	36 (78.3)
Hypertension	
Yes	34 (73.9)
No	12 (26.1)
Duration of kidney dialysis (Years)	
≤4 years	17 (37.0)
5 - 9	18 (39.1)
≥10	11 (23.9)
Mean ± SD	(6.76 ± 4.18)

3.4. The Hormonal Status at Times before and after HD Samples

Table 3 shows the mean serum levels of T3 and T4 hormones for the 46 patients with CRF, before and after HD. The mean serum levels of T3 were 110 ng/ml and 121 ng/dl before and after HD, respectively. This study also revealed that 34 patients were had normal serum level of T3 (45 - 137 ng/dl) before HD, but their number decreased to become 29 patients after HD. In addition, before HD, the serum level of T3 in 2 cases was lower than the normal range and 10 cases were higher than the normal range. After HD, only 1 case had serum level of T3 lower than the normal range and 16 cases had serum level of T3 above the normal range. Statistically, the mean values of serum level of T3 in patients with CRF showed significant change after HD ($P < 0.05$).

Furthermore, of the 46 HD patients with CRF entered in the study, the mean values of serum level of T4 were 4.5 μ g/dl before HD and 5.9 μ g/dl after HD. The number of the patients before HD who had normal serum level of T4 (4.5 - 12.0 μ g/dl) were 19 (41%) patients and this number had increased to 41 (89%) patients after HD. Whereas, the number of the patients who had under normal serum level of T4 before HD were decreased from 27 (58.7%) to 5 (10.9%) (**Table 3**). Statistical analysis revealed that there was a significant difference on the mean serum levels of T4 in CRF Libyan patients before and after HD ($P < 0.001$).

Table 3. The serum levels of T3 and T4 hormones in 46 patients with chronic renal failure, before and after HD.

Variable	Patients		P-value
	Before HD	After HD	
	N (%)	N (%)	
T3 (ng/dl)			$P < 0.05$
Under normal (<45)	2 (4.3)	1 (2.2)	
Normal (45 - 137)	34 (73.9)	29 (63.0)	
Above normal (>137)	10 (21.7)	16 (34.8)	
Mean \pm SD of T3 level	110.0 \pm 32	121.0 \pm 37	
T4 (μ g/dl)			$P < 0.01$
Under normal (<4.5)	27 (58.7)	5 (10.9)	
Normal (4.5 - 12.0)	19 (41.3)	41 (89.1)	
Above normal (>12)	0	0	
Mean \pm SD of T4 level	4.5 \pm 1.14	5.9 \pm 1.31	

Data are shown as N (%). Patients are divided into two subgroups on the basis of T3 and T4 level: under normal, normal, above normal. Significant differences were observed on serum level of T3 and T4 before and after HD.

4. Discussion

The serum thyroid hormone was used as indicator to determine the level of the hormones both before and after the kidney dialysis. The thyroid hormones level; T3 and T4 were analyzed and measured for all recruited patients in the study

from Zelin city in Libya. large number of hormonal systems are affected by CRF, until now CRF disease remains unclear to what extent these changes are responsible for aspects of uraemic syndrome. Patients with CRF often have signs and symptoms suggestive of thyroid dysfunction. Therefore, the diagnoses of thyroid disease in these patients have obvious prognostic implications [11].

In this study, 29 (63%) out of 46 cases of patients were had normal serum levels of T3 after HD and 41 (89%) out of 46 cases had normal serum levels of T4 after HD. The mean value before and after HD for T3 level in patients were 110 ± 32 ng/dl and 121 ± 37 ng/dl, respectively. Similarly, the mean values of serum level of T4 were 4.5 μ g/dl before HD and 5.9 μ g/dl after HD. There was a significant change in serum levels of T3 and T4 before and after HD. Taken together, our data revealed that the HD treatment increase the serum levels of both T3 and T4 hormones. Based on these data, it is possible to suggest that HD might activate the secretion of thyroid gland and catabolism. This can be explained by the normal negative feedback regulation of the pituitary thyroid axis or the thyroid hormones and thyrotropes form a negative feedback loop. This means when the serum level of T3 and T4 increase, the production of TSH must decrease, because of no need to stimulate thyroid gland to secrete more T3 and T4 hormone.

Taken together, HD seem to contribute positively to the thyroid function, because the serum levels of T3 and T4 in most of patients included in this study were in the normal range after HD. Uremia has been reported to cause a reduction in peripheral conversion of T4 to T3, producing a functionally hypothyroid state [17]. On other hand, a previous study done by El-Reshaid and colleagues showed that, after iron depletion, thyroid abnormalities improved in 8 cases out of 9 cases in patients with iron overload [18]. Based on these data, it is possible to suggest that regular HD treatment may also lower morbidity and mortality among Zeletin city patients with CRF.

The opposite of our finding was illustrated by Hershman *et al.* They reported a decrease in serum T4 hormone level after HD [19]. Similarly, two later studies done by Kayima *et al.* and by Hardy *et al.* reported that patients with CRF had low serum levels of T4 in adults after HD [20] [21]. In addition, Xess and co-workers also reported that patients with CRF had significant decrease in total T3 level [22]. These reports indicated that the CRF patients were in a subclinical hypothyroid state. It has been suggested that the low serum T3 levels is due to presence of dialyzable toxins in uremic plasma that might impair T3 transcriptional activity or extra-thyroidal T4 to T3 conversion [23]. While the low level of T4 is due to the presence of circulating inhibitors.

In agreement with our study, it had been demonstrated that TSH level on CRF Japanese patients were not significantly changed before and after HD [24]. Shamsadini and colleagues demonstrated that there was a significant change in serum levels of T3 and T4 before and after HD in 57 Iranian patients with CRF [25]. Similarly, Alsaran *et al.* also reported that there was a significant difference in free-T3 and free-T4 hormone levels before and after HD and no significant

difference between before and after HD for TSH level in 40 Saudi Arabia patients with end stage renal disease [26].

This study provides an evidence that the presence of diabetes mellitus and hypertension showed no effect on serum levels of T3 and T4 in CRF patients before and after HD. Similarly, the duration of HD exhibited no effect on serum levels of T3 and T4 in CRF patients before and after HD. By contrast, In addition, a study conducted by Zoccali *et al.* concluded that low FT3 is frequently shown in inflammatory illnesses, and the similar association also observed in chronic kidney disease patients as well as in patients with end stage renal disease [27]. Thus, these findings suggested that these variable factors such as presence diabetes mellitus, hypertension or duration of HD did not contribute to change that observed in levels of thyroid hormones.

5. Conclusions

The results of the present study demonstrated that some Libyan CRF patients had serum levels of T3 and T4 lower than the serum normal range before HD, then after HD, they had normal serum levels of T3 and T4 hormones. For this reason we conclude, there is a novel interaction of kidney with thyroid hormones in patients with CRF. Also, HD might participate in the regulation of thyroid hormone synthesis (T3 and T4). On the other hand, thyroid gland levels seem to be dependent on renal function.

However, the results of the present study demonstrate that most CRF patients have lower than the normal range of T3 and T4 hormones before kidney dialysis, then after kidney dialysis they have normal levels of T3 and T4 hormones.

Finally, kidney dialysis may have a positive feedback effect on thyroid gland secretions. The thyroid gland hormones increase catabolic activities resulting in an increase in T3 and T4 hormone levels, which in turn switch off the secretion of thyroid hormones by a feedback mechanism.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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