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Prevalence of Thyroid Function Abnormalities in Patients with Chronic Renal Failure under Regular Hemodialysis

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ABSTRACT

Background: There are various changes in the thyroid gland and its function in end stage renal disease (ESRD). It is not surprising that impairment of kidney function leads to disturbed thyroid physiology.
Objective: Is to detect thyroid function abnormalities in hemodialysis patients.
Patients and Methods: 100 patients on maintenance hemodialysis (HD) were enrolled, they were excluded if they had the following criteria: history of thyroid disease, thyroid and parathyroid surgery, under interferon therapy, exposed to radiation, antithyroid drugs or thyroid replacement therapy, and those under 30 years. They were subjected to history taking, clinical examination and laboratory investigations including hepatitis C virological state, renal functions and thyroid functions.
Results: 92% of patients had normal thyroid-stimulating hormone (TSH) levels, 8% had abnormal TSH levels. Regarding fT3 levels, 67 % had normal fT3 while 33 % had abnormal fT3, and only 11 patients had abnormal fT4. In respect to the thyroid hormone status, only one was hyperthyroid, 92% were in euthyroid status, 2% were clinically hypothyroid, 5% were subclinically hypothyroid, and 1% was hyperthyroid. There was significant negative correlation between TSH levels and dialysis duration, 8 patients having abnormal thyroid functions ere females, and 60% had HCV positive status. No significant associations were found between HCV infection and the thyroid hormones levels. However, HCV positive patients experienced lower levels of T4 and TSH.
Conclusion: The average percentage of patients under regular hemodialysis with abnormal thyroid state is 8% with females having abnormal fT4 and TSH levels compared to males. TSH levels were inversely correlated with dialysis duration.
Keywords: Hepatitis C Virus, Free T3, Free T4, TSH, HD.

INTRODUCTION

Hypothyroidism has a more negative influence on kidney function. Peripheral vascular resistance is increased with intrarenal vasoconstriction, and cardiac output is decreased, causing decreased renal blood flow [(1)].

Various abnormalities in thyroid function were well documented, there is increase in prevalence of goiter and incidence of primary hypothyroidism in chronic renal failure. Diagnosis of primary hypothyroidism can only be made with confidence if plasma TSH is unequivocally elevated, measurement of free T4 may be helpful but can be unreliable. Diagnosis of hyperthyroidism in renal failure rests on the demonstration of elevated T4 concentration in the presence of suppressed TSH, although hyperthyroidism is extremely rare in patients with this condition [(2)].

Fortunately, most of the renal manifestations of thyroid disorders, which are clinically most significant with hypothyroidism, are reversible with treatment [(3)]. On the other hand, chronic kidney disease (CKD) is characterized by a low T3 syndrome which is now considered a part of an atypical nonthyroidal illness. CKD patients also have increased incidence of primary hypothyroidism and subclinical hypothyroidism [(1)]. It was also found that thyroid disorders are more common in patients on HD compared to general population [(4)].

Aim of the work is to detect thyroid function abnormalities in hemodialysis patients.

PATIENTS AND METHODS

Our study is a cross-sectional study. It was conducted on 100 patients on maintenance HD at

Mahalla General Hospital, excluding those with the following criteria: history of thyroid disease, thyroid and parathyroid surgery, under interferon therapy, exposed to radiation, antithyroid drugs or thyroid replacement therapy and those less than 30 years. They were subjected to careful history taking, clinical examination with special attention to the presence of symptoms and signs of hyperthyroidism, symptoms and signs of hypothyroidism and local examination of the thyroid gland. Laboratory investigations including serum creatinine, blood ureanitrogen [BUN], hemoglobin [HB], hepatitis C virological state and thyroid function tests by means of measurement of fT3, fT4, TSH.

Fasting blood samples were collected from patients under aseptic precautions by venipuncture; 5.0 ml were put in a vial. Two to three ml were left in test tube to clot for 15 minutes. The samples were then centrifuged for 10 minutes at 5000 rpm. The supernatant serum was separated then stored at -70 C till the time of analysis.

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Serum thyroid stimulating hormone (TSH) (normal value: 0.39-3.55 µIU/ml) was measured using Accu-Bind ELISA kit (Monobind Inc. Lake Forest, CA 92630, USA). Serum free thyroxine (FT4) (normal value: 0.8-2 ng/dl) was measured using Accu-Bind ELISA kit (Monobind Inc. Lake Forest, CA 92630, USA). Serum free triiodothyronine (FT3) (normal value: 2.1-3.8 pg/ml) was measured using Accu-Bind ELISA kit (Monobind Inc. Lake Forest, CA 92630, USA). Free Thyroxine (FT4) or free triiodothyronine (FT3): Level in the serum samples was determined by using Accu-Bind ELISA kit (Monobind Inc. Lake Forest, CA 92630, USA). Serum thyrotropin (TSH) level in the serum samples was determined by using Accu-Bind ELISA kit (Monobind Inc. Lake Forest, CA 92630, USA).

Ethical approval and written informed consent:

An approval of the study was obtained from Ain Shams University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of the operation.

Statistical analysis

Recorded data were analyzed using the statistical package for the social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean±standard deviation (SD). Qualitative data were expressed as frequency and percentage.

The following tests were done:

- Independent-samples t-test of significance was used when comparing between two means.
- Chi-square (x^2) test of significance was used in order to compare proportions between two qualitative parameters.
- The confidence interval was set to 95% and the margin of error accepted was set to 5%. The p-value <0.05 was considered significant.

RESULTS

One hundred patients on regular hemodialysis (3 sessions per week) were enrolled in our study, 57 male and 43 female. Descriptive data of the patients is shown in table (1) as regards age, dialysis duration, thyroid function tests (fT3, fT4 and TSH), BUN, serum creatinine and hemoglobin; as for the virological status of the patients 60% were HCV positive and 40% were negative. As regards TSH, 92% of the patients had abnormal TSH and 8% had normal TSH, as for free T3; 67% of the patients were normal and 33% were abnormal, and as for free T4; 89% of the patients were normal and 11% were abnormal. There was positive correlation between HCV status of patients and both their age and duration of dialysis, while there was no correlation between HCV status of patients and other parameters as shown in table (2). There was positive correlation between TSH levels of the patients and their duration of dialysis as shown in table (3). There was no relationship between etiology of chronic renal failure and thyroid function tests as shown in table (4). There was no relationship between thyroid function tests and the virological state of the patients as shown in table (5). There was no relationship between the level of freeT3 and the TSH levels as shown in table (6). There was significant correlation between Free T4 levels and the TSH levels as shown in table (7). There was significant correlation between TSH levels and dialysis duration as shown in table (8).

Table (1): Descriptive data of the studied group

	Mean	±	SD
Age in years	56.920	±	5.293
Duration in years	6.140	±	1.039
HB (gm/dl)	9.377	±	1.570
Urea (mmol)	120.870	±	5.057
Creatinine (mg/dl)	9.530	±	2.692
T3 (µIU/ml)	2.138	±	0.793
T4 (µIU/ml)	1.413	±	0.379
TSH (µIU/ml)	2.602	±	0.487

Table (2): Correlation between HCV status and other parameters

	Virology						P-value
	Negative (N=40)			Positive (N=60)			
	Mean	±	SD	Mean	±	SD	
Age in years	49.075	±	15.999	62.150	±	12.397	**<0.001***
Duration in years	5.150	±	2.237	6.800	±	3.328	**0.007***
HB (mg/dl)	9.020	±	1.522	9.615	±	1.568	0.063
Urea (mmol)	117.075	±	30.666	123.400	±	7.741	0.379
Creatinine (mg/dl)	10.133	±	2.751	9.128	±	2.598	0.067
T3 (µIU/ml)	1.983	±	0.067	2.242	±	0.854	0.110
T4 (µIU/ml)	1.465	±	0.096	1.378	±	0.039	0.535
TSH (µIU/ml)	2.900	±	0.440	2.403	±	0.566	0.330

Table (3): Correlation between T3, T4, TSH and other parameters

Correlations				
		T3	**T4**	**TSH**
Age in years	**r**	-0.117	-0.095	-0.175
	P-value	0.246	0.345	0.082
Duration in years	**r**	0.104	0.001	- 0.252
	P-value	0.304	0.995	0.029*
HB (mg/dl)	**r**	0.096	0.016	0.002
	P-value	0.343	0.873	0.985
Urea (mmol)	**r**	-0.094	-0.078	0.084
	P-value	0.354	0.441	0.404
Creatinine (mg/dl)	**r**	-0.193	0.026	0.052
	P-value	0.054	0.800	0.606

Table (4): Correlation between the etiology of chronic renal failure and TSH levels

Etiology	**Normal TSH**		**Abnormal TSH**		**Total**		**P- value**
	N	**%**	**N**	**%**	**N**	**%**	
Hypertension	36	39.13	4	50.00	40	40.00	0.454
Diabetes mellitus	22	23.91	3	37.50	25	25.00	
Congenital Polycystic kidney	10	10.87	1	12.50	11	11.00	
Obstructive uropathy	9	9.78	0	0.00	9	9.00	
Systemic lupus erythematosus	9	9.78	0	0.00	9	9.00	
Recurrent UTI	6	6.52	0	0.00	6	6.00	
Total	92	100.00	8	100.00	100	100.00	

Table (5): Correlation between HCV status of the patients and their TSH levels

Virology	**Normal TSH**		**Abnormal TSH**		**Total**		**P-value**
	N	**%**	**N**	**%**	**N**	**%**	
C-Negative	36	39.13	4	50.00	40	40.00	0.557
C-Positive	56	60.87	4	50.00	60	60.00	
Total	92	100.00	8	100.00	100	100.00	

Table (6): Correlation between Free T3 level and TSH level

FT3	**Normal TSH**		**Abnormal TSH**		**Total**		**P-value**
	N	**%**	**N**	**%**	**N**	**%**	
Normal	64	69.57	3	37.50	67	67.00	0.064
Abnormal	28	30.43	5	62.50	33	33.00	
Total	92	100.00	8	100.00	100	100.00	

Table (7): Correlation between Free T4 levels in patients and their TSH levels

FT4	**TSH**						**P-value**
	Normal TSH		**Abnormal TSH**		**Total**		
	N	**%**	**N**	**%**	**N**	**%**	
Normal	84	91.30	5	62.50	89	89.00	
Abnormal	8	8.70	3	37.50	11	11.00	
Total	92	100.00	8	100.00	10	100.00	

Table (8): Correlation between TSH and other parameters

	RESULTS						P-value
	Normal TSH			Abnormal TSH			
	Mean	±	SD	Mean	±	SD	
Age (in years)	57.674	±	15.081	48.250	±	16.051	0.095
Duration(in years)	5.946	±	2.906	8.375	±	3.815	**0.029***
HB (mg/dl)	9.383	±	1.561	9.313	±	1.776	0.904
Urea (mmol)	121.054	±	5.675	118.750	±	28.828	0.860
Creatinine (mg/dl)	9.598	±	2.736	8.750	±	2.110	0.396
T3 (µIU/ml)	2.179	±	0.076	1.663	±	0.047	0.077
T4 (µIU/ml)	1.437	±	0.069	1.138	±	0.046	0.234

DISCUSSION

In the present study, the included patients had a mean age of 56.92 ± 15.29. They comprised 57 females and 43 males. By the end of the study, a total of 42.2% were found to be anti-HCV reactive. This discrepancy may be explained by the variable HD duration in different studies and the subsequent variable exposure to HCV infection.

In our study, 40 patients (40%) had chronic renal failure due to hypertension; 25 patients (25%) due to diabetes mellitus; 11 patients (11%) due to congenital polycystic kidney; 9 patients (9%) due to obstructive uropathy; 9 patients (9%) due to systemic lupus erythematosus; and 6 patients (6%) due to recurrent urinary tract infection.

In the current study, 92% of patients had normal TSH levels while 8% had abnormal TSH levels. This figure is close to that found by **Horáček *et al.*** [5], who worked on 167 hemodialysis ESRD patients. TSH and thyroid hormone levels (T4, fT4, T3 fT3, rT3) were determined. The patients were then prospectively followed up for up to 5 years and the possible impact of any observed abnormalities on their mortality was studied. The TSH was found to be normal in 85% of the studied patients.

Regarding T3 levels, the present study found that 67% of the studied patients had normal T3 while the remainder 33% had abnormal T3. In addition, only 11 patients had abnormal T4. This is in harmony with the study of **Shamsadini *et al.*** [6] who found that only 15 out of 57 HD (26.3 %) patients while 3 cases out of 57 had abnormal T4 (5.3 %). However, in the study of **Ozen *et al.*** [7], who investigated the prognostic value of serum fT3 levels on survival in HD, low T3 was reported in 71.7% of the cases. This may be explained by the different laboratory techniques, different patients characteristics of different reference ranges used for diagnosis of the thyroid hormone state.

In respect to the thyroid hormone status in the studied patients, we found that only one hyperthyroid patient "has got low TSH level", 92% of our patients were in euthyroid status "have got normal TSH levels", 2% were clinically hypothyroid "have got high TSH levels and low T4 levels", 5% were subclinically hypothyroid "have got high TSH levels with normal T4 levels and they were not complaining of hypothyroidism". These data are similar to what was found by **Rhee *et al.*** [8] who found that among the studied HD patients, 87.1% were in the euthyroid state. Also, in the study of **Chonchol *et al.*** [9], 9.5 % of the studied patients had subclinical hypothyroidism. In addition, the study of **Kutlay *et al.*** [10] reported hyperthyroidism in 1.14% in ESRD patients under HD.

In our study females were found to have significantly higher T3 and TSH levels while no significant differences were found between males and females regarding T4. However, in the study of **Meuwese *et al.*** [11] no significant differences were found between thyroid hormone levels in males and females. The difference detected in our study may be explained by the fact that the only hyperthyroid patients in our study is a female.

In the present study, no significant associations were found between HCV infection and the thyroid hormone levels, which is similar to **Ibrahim *et al.*** [12] results. However, HCV +ve patients experienced lower levels of T4 and TSH. This is supported by the study of **Bini and Mehandru** [13] who found that among 225 patients, overt thyroid disease developed in 6.7%, and subclinical thyroid disease was diagnosed in 4%. Most of the patients with thyroid dysfunction completed HCV therapy, and thyroid disease resolved in 10 of the 12 patients with overt hypothyroidism and 2 of the 3 with overt hyperthyroidism. Thus HCV had only a minor contribution to the development of thyroid dysfunction in HD patients.

Regarding the correlations between thyroid hormones and the various clinical and laboratory data, we found only a significant direct correlation between TSH level and duration of hemodialysis. This is in accordance with **Sanai *et al.*** [14] who found successive decrement of TSH with increasing dialysis duration.

In our study, no significant associations were found between etiology of renal failure and TSH, which is in agreement with **Meuwese *et al.*** [11] who found no significant associations between thyroid function and

the clinical data including diabetes and hypertension. In this study, patients with abnormal TSH had significantly higher frequency of abnormal T4 but not T3. This was confirmed by subsequent correlation analysis and it is in agreement with the study of **Horáček *et al.* [5].**

CONCLUSION

The average percentage of patients under regular hemodialysis with abnormal thyroid state is 8% with females having abnormal fT4 and TSH levels compared to males. TSH levels were inversely correlated with dialysis duration.

Conflict of interest: On behalf of all authors, the corresponding author states that there is no conflict of interest.

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