Original Research Article

A study of thyroid profile in chronic kidney disease in tertiary care hospital in Chennai

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International Archives of Integrated Medicine, Vol. 7, Issue 10, October, 2020.
Available online at http://iaimjournal.com/
ISSN: 2394-0026 (P) **ISSN: 2394-0034 (O)**
Received on: 22-09-2020 **Accepted on:** 02-10-2020
Source of support: Nil **Conflict of interest:** None declared.
How to cite this article: K. Manickam. A study of thyroid profile in chronic kidney disease in tertiary care hospital in Chennai. IAIM, 2020; 7(10): 29-34.

Abstract

Background: Chronic kidney disease (CKD) is a global burden and is now recognized as a major public health problem worldwide. Patients with CKD have alterations in thyroid hormone metabolism. This study aims to evaluate the status of thyroid hormone profile in different stages of CKD.
Aim of the study: To study the prevalence of thyroid dysfunction in patients with chronic renal failure.
Materials and methods: This cross-sectional study was conducted in the year 2018, at Madha Medical College and Research Institute, Chennai. 50 patients were included in this study. Patients who fulfill the criteria for CRF and who were on conservative management were taken for the study. A thyroid profile was done in all patients who fulfill the criteria.
Results: The prevalence of low T3 syndrome was 54% (27 cases) and the low T4 syndrome was 22 % (11 cases). The prevalence of TSH in the hypothyroidism range was 4 % (2 cases). Mean T3, free T4, and TSH levels in various stages of CKD. The mean T3 was decreased significantly with reduced creatinine clearance. The free T4 was also significantly decreased in stage 5 CKD.
Conclusion: The number of patients with low T3 and T4 syndrome progressively increases with the severity of the renal failure. The serum level of total T3 and free T4 is directly proportional to the creatinine clearance level. Total T3 and free T4 correlated with the severity of the renal failure. TSH values will be useful to differentiate hypothyroidism from non- thyroidal illness due to CKD.

Key words

Chronic Renal Failure, Thyroxine Binding Globulin, Parathyroid hormone.

Introduction

Patients with chronic renal failure often have signs and symptoms suggestive of thyroid dysfunction. These findings include dry skin, sallow complexion, low temperature, cold intolerance, decreased basal metabolic rate, lethargy, fatigue, edema and hyporeflexia [1]. Various studies of thyroid functions in uremic patients have been carried out which have shown conflicting results. Hyperthyroidism, hypothyroidism and euthyroid state have all been reported by various workers. Serum triiodothyronine (T3) levels were consistently found to be low without any regard for the treatment of CRF. Serum total and free thyroxine (T4) concentrations have been reported as low, normal, or high [2]. 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. A reduction in total T3, but not in free T3 concentrations were associated with an increased all-cause and cardiovascular mortality in euthyroid CKD patients [3]. Total and free T3 behave as survival markers in patients with CKD both in HD and in PD [4]. The prevalence of hypothyroidism in end-stage renal disease (ESRD) has been estimated between 0 and 9%. There is also an increased prevalence of goiter in patients with ESRD. Though there are multiple factors which predicts the overall mortality and severity of the renal disease, one among the important factor is thyroid dysfunction. So it is prudent for the internist and treating physician to be aware of thyroid dysfunction so that early intervention can be instituted to improve the outcome [5].

Materials and methods

This cross-sectional study was conducted in the year 2018, at Madha Medical College and Research Institute, Chennai. 50 patients were included in this study. Patients who fulfill the criteria for CRF and who were on conservative management were taken for the study. A thyroid profile was done in all patients who fulfill the criteria.

Inclusion Criteria for Chronic Renal Failure:

- Symptoms of uremia for 3 months or more.
- Elevated blood urea, serum creatinine, and decreased creatinine clearance.
- Ultrasound evidence of chronic renal failure: Bilateral contracted kidneys – size less than 8 cm in male and female.
- Poor corticomedullary differentiation.
- Supportive laboratory evidence of CRF like anemia, low specific gravity, changes in serum electrolytes, etc.
- Radiological evidence of renal osteodystrophy.

Exclusion criteria:

- Patients underwent peritoneal dialysis or hemodialysis.
- Nephrotic range of proteinuria.
- Low serum protein especially albumin.

After selecting the patients, fulfilling the above criteria, about 5 ml of blood sample was collected in a non-heparinized serum bottle and sent for thyroid profile.

Statistical analysis

The analytical data was interpreted by students unpaired and students proportion‘t’ test. The relations between the related biochemical variable in CKD were analyzed and interpreted by the point biserial correlation coefficient (r_{p1bis}). The correlation between the thyroid indices was analyzed and interpreted by Karl Pearson’s coefficient(r). The above analysis and interpretation of statistical procedures were performed by the statistical package S.P.S.S. [13]. The value of $P < 0.05$ was considered significant.

Results

The prevalence of low T3 syndrome was 54% (27 cases) and the low T4 syndrome was 22% (11 cases). The prevalence of TSH in the hypothyroidism range was 4% (2 cases). Among the males, 48.6% of patients had low T3 syndrome. And among the females was 62.2%.

The difference was not statistically significant P>0.05. The prevalence of low T4 among the males was 18.9% and among the females was 30.8%. The difference among the sexes was not statistically significant i.e. P>0.05. The prevalence of TSH in clinical hypothyroidism range among males was 2.7%. And among the females was 7.7%. The prevalence of the sexes was not statistically significant (P>0.05) (**Table – 1**).

Table - 1: Sex wise prevalence of thyroid dysfunction in CKD patients.

Thyroidhormones	Level of hormone	No	Males, n=37		Females=13		't'	Significance
			Frequency	%	Frequency	%		
T3	low	27	18	48.6	9	69.2	1.354	P>0.05
	normal	23	19	51.4	4	30.8		
T4	low	11	7	18.9	4	30.8	0.830	P>0.05
	normal	39	30	81.1	9	69.2		
TSH	high	2	1	2.7	1	7.7	0.636	P>0.05
	normal	48	36	97.3	12	92.3		

Table - 2: Distribution of total T3, free T4 and TSH in various stages of CKD.

Stages of CKD	Frequency	Mean Total T3	Mean free T4	Mean TSH
1-3	5	103.4±30.7	1.25±0.1	1.8±1.9
4	16	91±36.6	1.1±0.2	1.2±0.8
5	29	68.8±24	0.9±0.3	4.5±13.7

Table - 3: Relationship between creatinine clearance with total T3, free T4, and TSH.

Relation with Cr. Clearance	r	Significance
Total T3	0.320	P<0.05
Free T4	0.381	P<0.01
TSH	-0.133	P>0.05

Table - 4: Correlation of total T3 with creatinine clearance.

Creatinine clearance (ml/min)	T3 dysfunction		Normal		Total		rp1bis	d.f.	Significance
	No.	%	No.	%	No.	%			
60-89	0	0	1	4.3	1	2			
30-59	1	3.7	3	13	4	8			
15-29	6	22.2	10	43.5	16	32			
<15	20	74.1	9	39.1	29	58	-	48	P<0.05
Total	27	100	23	100	50	100	0.316		
Mean±S.D	12.2±8.6		20±14.8		15.8±12.3				
't'	2.338								
Significance	P<0.05								

Table - 2 reveals the mean T3, free T4, and TSH levels in various stages of CKD. The mean T3 was decreased significantly with reduced creatinine clearance. The free T4 was also significantly decreased in stage 5 CKD.

Table - 3 shows a positive correlation between total T3 and Creatinine clearance and it was statistically significant. The free T4 and creatinine clearance showed a positive correlation and it was statistically significant. **Table – 3** shows a negative correlation of TSH with

creatinine clearance and it was not statistically significant.

The mean creatinine clearance in low T3 syndrome was 12.2±8.6 ml and in normal patients was 20±14.8 ml. The difference between the patients was statistically significant i.e. P<0.05. The r_{p1bis} determines the direction between the creatinine clearance with low total T3 patients. The dysfunction with creatinine clearance was negatively correlated i.e. r_{p1bis} = -0.316. Statistically explain the negative relationship between them significantly i.e. P<0.05 (**Table – 4**).

Table - 5: Relationship between creatinine clearance with free T4.

Creatinine clearance (ml/min)	**FREE T4 dysfunction**		**Normal**		**Total**		**r_{p1bis}**	**d.f.**	**Significance**
	No.	**%**	**No.**	**%**	**No.**	**%**			
60-89	0	0	1	2.6	1	2	-0.340	48	P<0.05
30-59	0	0	4	10.3	4	8			
15-29	1	9.71	15	38.5	16	32			
<15	10	90.4	19	48.6	29	58			
Total	11	100	39	100	50	100			
Mean±S.D	7.9±4		18±13		15.8±12.3				
't'	2.518								
Significance	P<0.05								

Table - 6: Prevalence of goiter in chronic kidney disease patients.

Disease	**No.**	**%**
Goiter	2	4
Goiter with pleural effusion	1	2
No evidence	47	94

The mean creatinine clearance with low free T4 dysfunction and normal patients was 7.9±4 and 18±3 ml respectively. The difference between the mean was statistically significant i.e. P<0.05. The point biserial correlation coefficient i.e. r_{p1bis} = -0.340 illustrated the negative correlation (**Table – 5**).

Among the 50 patients 47(94%) patients had no evidence of goiter. With the remaining 3 patients, 2(4%) patients had exclusively goiter, 1 (2%) patients had goiter with pleural effusion. The total prevalence of goiter in our study was 6% (**Table – 6**).

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 the uremic syndrome. Patients with CRF often have signs and symptoms suggestive of thyroid dysfunction and hence the diagnosis of thyroid disease in these patients has obvious prognostic implications. The data reported deals primarily with the biochemical parameters [6]. In our study, out of 50 patients, 27 patients (54%) had low T3 syndrome. The prevalence of low T3 in stage 1- 3 is 20 %, for stage 4 is 38%, and stage 5 is 70%. This observation is consistent with Ikeda K, et al. in which the prevalence of low T3 will be increased according to the increase in the stage of CKD. In our study, there is a positive correlation between Total T3 and creatinine clearance and it is statistically significant P<0.05 [7]. This shows serum T3 levels were associated with the severity of CKD even in the normal TSH level. There was a higher frequency of reduced free T4 values in our study (22%) which is consistent with Kaptein E, et al. study but it is not statistically significant [8]. In our study, there is a positive correlation

between Free T4 and creatinine clearance and it is statistically significant P<0.05. Out of the 50 uremic patients, 2 patients show TSH >10 µIU/ml. The high serum TSH level is > 75 µIU/ml. Both these patients had very low serum T3 concentrations which can be explained by the normal feedback regulation of the pituitary thyroid axis. One patient is having both goiter and pleural effusion [9]. Katz AI, et al. who studied 175 patients of CRF who had low T3, T4, fT4 but had high TSH levels suggested maintenance of the pituitary thyroid axis. 48 patients i.e. 96% reported a normal level of serum TSH ≤5 µIU/ml [10]. Out of 48 patients, 25 patients had low T3 and 9 patients had low total T3 and free T4. So these 25 patients had a normal level of serum TSH despite low serum T3 level. They demonstrated abnormality in the hypophyseal mechanism of TSH release in uremic patients as the TSH response to TRH was blunted [10]. In Kayima JK, et al. study low TT3, FT3, and TT4 values are seen in clinically euthyroid CKD patients. However, finding of normal T4 values and TSH would indicate functional euthyroid status. It can be presumed that free T4 values would fall if these patients develop hypothyroidism and TSH values would rise simultaneously. Thus Free T4 and TSH levels combined can be used for the diagnosis of hypothyroidism in presence of CKD. Subjects with TSH > 10 µIU/ml and free T4 below the reference range have overt primary hypothyroidism and should be treated with thyroid hormone replacement [11]. The prevalence of primary hypothyroidism in CKD ranges from 0- 9.5% as evidenced in previous studies. The prevalence of hypothyroidism in our study is 4%. This is consistent with the results of Li Bok N, et al. reported a high prevalence of goiter in CRF patients especially those on chronic dialysis. Incidences were increased in end-stage renal disease. The possible explanation is due to the accumulation of iodides in the thyroid gland due to decreased renal clearance in CRF patients [12]. In our study, 3(6%) patients had evidence of goiter. Out of 3 patients, 1(2%) had clinical and biochemical features of hypothyroidism. The remaining 2 patients had low T3 level with normal TSH and T4 [13]. As stated previously, Hemodialysis and continuous ambulatory peritoneal dialysis have shown to affect the thyroid profile independently of CRF. Also, drugs like heparin, furosemide used during dialysis will affect the thyroid profile. Vaamonde CA has conducted studies regarding the effect of dialysis on CRF patients with thyroid dysfunction [14]. This study showed no significant improvement in thyroid profile after repeated hemodialysis. But in the patients who have undergone renal transplant surgery, most of the thyroid function parameters returned to normal with TSH below normal [15].

Conclusion

The prevalence of thyroid dysfunction in patients with CKD is 54%. Number of patients with low T3 and T4 syndrome progressively increases with the severity of the renal failure. Serum level of total T3 and free T4 is directly proportional to the creatinine clearance level. Total T3 and free T4 correlated with the severity of the renal failure. TSH values will be useful to differentiate hypothyroidism from non- thyroidal illness due to CKD. Only 6% of the study population had evidence of goiter. Alteration in the values of T3 and T4 occurs as a part of the body adaptation mechanism to conserve energy.

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