Thyroid Profile in Chronic Kidney Disease Patients- A Study in Rims Hospital

L.Romesh Sharma¹,Mossang K²,Salam Ranabir³
¹Assistant professor, ²Post graduate trainee, ³Associate professor
Department of Medicine, Regional Institute of Medical Sciences, Imphal, Manipur, India.
Corresponding Author: Salam Ranabir

Abstract: Chronic kidney disease is an irreversible deterioration of renal function. The serum level and the function of most of the hormones are altered due to various mechanism including synthesis, transport, accumulation of inhibitors, target organ responsiveness and renal clearance. Our study aims to evaluate the thyroid profile in patients of chronic kidney disease. It is a cross-sectional study carried out at Department of Medicine, Regional institute of Medical Sciences, Imphal. Duration of study was from September 2014 to February 2016. Study Population includes 100 patients of CKD above 21 years of age. The commonest cause of CKD was found to be diabetes (35%), 21% patients had TSH level above the normal range (>5 µU/ml), 19% patients had low T3(<1.3 ng/ml) and 16% had low Thyroxin (T4) level.. The prevalence of Hypothyroidism and sub-clinical hypothyroidism were 18% and 4% respectively and the prevalence of hypothyroidism was found to be higher in patients with reduced GFR.

Date of Submission: 11-12-2019
Date of Acceptance: 26-12-2019

I. Introduction

Chronic kidney disease (CKD) is an irreversible deterioration of renal function, which results from diminished effective functioning of renal tissue. Ensuing impairment of excretory, metabolic and endocrine function of the kidney leads to the development of clinical syndrome of uremia.¹ Prevalence of CKD in India is estimated at 7572 per million and end stage kidney disease at 757 per million populations.² Cardiovascular disease is a major cause of morbidity and mortality among patients with CKD.³,⁴ Majority of patients die from cardiovascular system complications. In CKD, the serum level and the function of most of the hormones are altered because of several interplaying mechanisms. The mechanism may be synthesis, transport, accumulation of inhibitors, abnormality in target organ responsiveness and impaired renal clearance.⁵ Dialysis affects thyroid hormone metabolism minimally.⁶ Though regular dialysis is done in these patients, most of these uremic hormone abnormalities are not reversed, and some of them may even get worse.⁸⁹ Uraemia influences the function and size of the thyroid.¹⁰ Uraemic patients have an increased thyroid volume compared with subject with normal renal function and a higher prevalence of goitre, mainly in women.¹⁰,¹¹,¹² Also, thyroid nodules and thyroid carcinoma are more common in uraemic patients than in the general population.¹³ Most patients with end stage renal disease have decreased plasma level of free triiodothyronine (T3), which reflect diminished conversion of thyroxine T4 to T3 in the periphery.¹⁴,¹⁵ Chronic metabolic acidosis associated with the CKD may contribute in this effect.¹⁶ This abnormality is not associated with increased conversion to metabolically inactive reverse T3(rT3), since the plasma rT3 levels are typically normal. Although free and total T4 concentration may be normal or slightly reduced, sometimes freeT4 may be high due to the effect of heparin used in anticoagulation during haemodialysis (HD), which inhibit T4 binding to its binding proteins.¹⁷ The plasma concentration of thyroid stimulating hormone (TSH) is usually normal in CKD. However, the TSH response to exogenous thyrotrophic-releasing hormone (TRH) is often blunted and delayed, with a prolonged time required to return to baseline level.¹⁸,¹⁹ Reduced renal clearances may contribute to this delayed recovery, since TSH and TRH are normally cleared by the kidney. The kidney normally contributes to the clearance of iodide from the body. With advancing renal failure iodide excretion is diminished leading sequentially to an elevated plasma inorganic iodide concentration and an initial increment in the thyroidal iodide uptake. The ensuing marked increase in the intrathyroidal iodide pool results in diminished uptake of radiolabeled iodide by the thyroid in uraemic patients. Increases in total body inorganic iodide can potentially block thyroid hormone production (the Wolff-Chaikoff effect). These changes in iodide metabolism may account for reports of a slightly higher frequency of goitre and hypothyroidism in patient with CKD.²⁰,²¹ A study had reported reversion of thyroid function to normal after successful renal transplantation.²² This study was designed to evaluate the thyroid profile in CKD patient in RIMS Hospital, Imphal and to correlate the findings with different parameters.

DOI: 10.9790/0853-1812106268
II. Material and Methods

It is a Cross-sectional study carried out at Department of Medicine, Regional institute of Medical Sciences, Imphal. Duration of Study was from September 2014 to February 2016. Study Population includes patients with CKD.

Inclusion criteria:

Patients of CKD above 21 years. Diagnostic criteria for CKD includes a) Clinical signs and symptoms of uraemia, b) The presence of CKD is established based on the presence of kidney damage and the level of kidney function (GFR) and c) Ultrasonographic evidence of bilateral shrunken kidney/ loss of corticomedullary differentiation.

Exclusion criteria:

1. Patients with history of alcohol consumption
2. Patients with thyroid and liver disease
3. Patients with Nephrotic syndrome
4. Patients on medication likely to affect thyroid function
5. Pregnancy.

Sample size:

A minimum of 100 CKD patients admitted in the Medicine ward, RIMS within the period of September 2014 to February 2016 were included in the study.

Methodology:

All the selected patients were subjected to detailed history and complete physical examination and data were noted in a pre-designed proforma. Blood sample was drawn (10ml) for assessing baseline electrolytes, hemogram, Liver function tests, Renal function tests and Thyroid function test. Haemogram was assessed by spectrophotometric method available in Department of pathology RIMS. Renal function test and liver function test was assessed by Roche auto-analyzer module P40 available in Department of Biochemistry, RIMS. All the laboratory methods was standardized with the coefficient of variation (CV) for all of the biochemical parameters varying from 1-5%. Ultrasonography of kidney was performed in department of Radiodiagnosis. The presence of CKD was established based on presence of kidney damage and level of kidney function (GFR). Markers of kidney damage included abnormalities in the composition of blood (elevated blood urea, serum creatinine) or urine abnormalities. Ultrasonogram showing Bilateral shrunken Kidneys (<8.5cm) with loss of corticomedullary differentiation was taken as indicative of chronic renal failure. Estimation of Total Thyroxine (T4) and Total triiodothyronine was carried out ELISA test as described by Chopra IJ et al. Serum TSH was estimated by ELISA micro plate immunoenzymometric assay as described by Hopton MR et al. Hypothyroidism was diagnosed by TSH >10 µIU/ml and low level of T4 and T3. Subclinical hypothyroid was diagnosed by normal level of T4 and T3 along with TSH >5 µIU/ml.

Statistical analysis of all the data was done by using SPSS 20 software. Chi square test, Pearson’s correlation coefficient and T test were used wherever applicable. The level \( P < 0.05 \) was considered as the cutoff value or significance. Informed consent was taken from the patient included in the study and the study was approved by Institutional Ethics committee.

III. Result

A total of 100 patients of CKD irrespective of cause, duration and stages were taken up for the study. The most common cause of CKD was Diabetic Nephropathy and Chronic Glomerulonephritis followed by Obstructive Uropathy (Table 1). The mean age of the patients ranged from 21 to 77 years (mean age 50.38±14.91 years). There were 62(62%) males and 38(38%) females. Maximum number of patients 29 (29%) were in the age group of 51 – 60 years. The total duration of disease ranged from 1 to 20 years (mean=4.85±3.51 years). Most patients (34%) had disease duration ranging between 4 to 5 years. The body mass index ranged from 13.04kg/m² to 30.50kg/m² with a mean of 21.68 ± 3.34kg/m². Most of the patients (70%) are in normal BMI range.

Table 1. Causes of CKD

<table>
<thead>
<tr>
<th>Underlying Disease</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetic Nephropathy</td>
<td>35(35%)</td>
</tr>
<tr>
<td>Chronic glomerulonephritis</td>
<td>35(35%)</td>
</tr>
<tr>
<td>Obstructive uropathy</td>
<td>23(23%)</td>
</tr>
<tr>
<td>Lupus Nephritis</td>
<td>6(6%)</td>
</tr>
<tr>
<td>ADPKD(Autosomal dominant polycystic kidney disease)</td>
<td>1(1%)</td>
</tr>
</tbody>
</table>
Thyroid stimulating hormone (TSH): TSH level ranged from 1-23 µIU/ml (mean 4.11±3.5 µIU/ml). Maximum patients 79 (79%) had TSH level in the normal range (0.25-5 µIU/ml) and 21 (21%) patients had TSH level above normal range (>5 µIU/ml) (Figure 1).

![Figure 1](image)

Tri-iodothyronine (T3): Tri-iodothyronine level ranged from 0.5-3.1 ng/ml (mean 1.63±0.63). Maximum patients 81 (81%) had T3 level in normal range (1.3-3.1 ng/ml) and 19 (19%) patients had low T3 (<1.3 ng/ml) (Figure 2).

![Figure 2](image)

Thyroxine (T4): Thyroxine (T4) level ranged from 39.60-158 µg/ml (mean 95.05±29.1). Most of the study patients (84) had Thyroxine (T4) level in the normal reference range (66-181 µg/ml) and 16 patients had low T4 (<66 µg/ml) (Figure 3).

![Figure 3](image)

The relation of mean serum TSH, T3 and T4 with stages of CKD are shown in Table 2. Mean TSH is significantly higher in CKD stage V as compared to stage IV and III and mean T3 and T4 were found to be higher in CKD stage III as compared to Stage IV and V although it was not statistically significant. Maximum patients (47%) in CKD Stage V had TSH in the normal range. Maximum patients (49%) in CKD Stage V had T3 in the normal range and Maximum patients (50%) in CKD Stage V had T4 in the normal range.
Table 2 showing relation between mean serum TSH, T3 and T4 with stages of CKD

<table>
<thead>
<tr>
<th>Stages of CKD</th>
<th>TSH µIU/ml</th>
<th>T3 ng/ml</th>
<th>T4 µg/ml</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CKD V (GFR&lt;15)</td>
<td>4.5±2.8</td>
<td>1.35±0.34</td>
<td>83.3±21.98</td>
<td>0.07</td>
</tr>
<tr>
<td>CKD IV (GFR15-29)</td>
<td>3.76±4.73</td>
<td>1.84±0.61</td>
<td>106.84±23.27</td>
<td>0.13</td>
</tr>
<tr>
<td>CKD III (GFR 30-59)</td>
<td>3.08±3.72</td>
<td>2.47±0.79</td>
<td>125.04±36.6</td>
<td>0.4</td>
</tr>
</tbody>
</table>

Abnormal thyroid function.

Out of 100 Chronic kidney disease patients, 18 (18%) had Hypothyroidism, 4(4%) had sub-clinical hypothyroidism and 78 (78%) were Euthyroid (TSH,T3 and T4 in normal range). None of the patients had hyperthyroidism (Figure 4).

Figure 4

Maximum number of hypothyroid patients i.e. 13 (72.2%) were in CKD stage V followed by 3 (16.6%) patients in CKD stage IV and 2 (11.2%) patients in CKD stage III.Maximum 3 (75%) patients of Sub-clinical Hypothyroidism occurred in CKD stage V and 1(25%) patients in CKD stage IV(Figure 5).

Figure 5

Amongst the cause of CKD, the prevalence of hypothyroid was maximum in Lupus Nephritis (33.3%) followed by obstructive uropathy (26%) and the prevalence of Sub-clinical hypothyroidism was maximum (5.7%) in Diabetes mellitus followed by Obstructive Uropathy (4.3%), (Table 3).

Table 3 showing thyroid status and etiologies of CKD

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Hypothyroid(%)</th>
<th>Subclinical Hypothyroid(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DM</td>
<td>8.5%</td>
<td>5.7%</td>
</tr>
<tr>
<td>OBU</td>
<td>26%</td>
<td>4.3%</td>
</tr>
<tr>
<td>CGN</td>
<td>20%</td>
<td>2.8%</td>
</tr>
<tr>
<td>ADPKD</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>
IV. Discussion

A total of 100 patients of CKD irrespective of cause, duration and stages were taken up for the study. Diabetic nephropathy (35%) and Chronic glomerulonephritis (35%) was the commonest cause of CKD. In a study of 30 CKD patients by Avasthi G et al 37, Chronic glomerulonephritis (30%) was the commonest cause followed by Obstructive uropathy (6%). In a study by Mittal S et al 26, the commonest cause of CKD in India was Chronic glomerulonephritis. According to third annual report of CKD registry of India by Indian society of Nephrology 27, the commonest cause of CKD was diabetic nephropathy (30%), followed by undetermined cause (15.6%). In a study by Gibi J et al 38 conducted in RIMS Hospital in 2002, the commonest cause of CKD was Chronic glomerulonephritis (48.64%) followed by Obstructive uropathy (15.54%). But we found that diabetes has overtaken Chronic glomerulonephritis as the commonest cause of CKD. Our study shows that diabetic nephropathy and Chronic glomerulonephritis are the commonest cause of CKD which agrees with other studies.

The body mass index ranged from 13.04 to 30.50 kg/m² (mean of 21.68 ± 3.34). In this study most of the patients 70 (70%) had normal BMI, 14 (14%) were underweight and 14 (14%) were overweight. Bjorn O A et al 39 in their study found that mean body mass index (kg/m²) of the patients were 26.5 which is similar to the present study. Maheshwari et al 40 in their study found that 48% of patients on maintenance haemodialysis had BMI <18.5 kg/m² and 42% had normal BMI. Our study also shows that most of the patients of CKD had normal BMI.

In our study TSH level ranged from 1.23 µIU/ml (mean 4.11±3.5 µIU/ml). Maximum patients 79 (79%) had TSH level in the normal range (0.25-5 µIU/ml) and 21 (21%) patients had TSH level above normal range (>5 µIU/ml) and there were no patients with low level of TSH. Avasthi G et al 37 in their study of 30 patients of CKD showed that mean TSH level and free T4 was significantly increased in patients of CKD as compared to controls (4.73±2.60 µIU/ml vs 2.69±3.44 µIU/ml p<0.05). Mehta H J et al 41 in their study measured the level of TSH, Total T3, free T3, Total T4 and free T4 in 127 patients of CKD and found that the patients on conservative management for CKD the serum TSH and FT4 were not significantly altered. Patients with low T3, T4 and free T4 showed a high TSH suggesting maintenance of pituitary thyroid axis in CKD patients which is similar to our study and mean TSH was not high and TSH response to TRH was distinctly blunted, suggesting possibility of pituitary dysfunction as well.

Tri-iodothyronine (T3) level ranged from 0.5-3.1 ng/ml (mean 1.63±0.63). Maximum patients 81 (81%) had T3 level in normal range (1.3-3.1 ng/ml) and 19 (19%) patients had low T3 (<1.3 ng/ml). Among these patients (19) with low T3 level, CGN had maximum 10 (52.6%) patients, followed by 7 (36.8%) of Diabetic nephropathy and 2 (10.5%) obstructive uropathy. Ramirez G et al 42 in their study showed that in patients on dialysis, mean serum thyroxin and triiodothyronine levels are lower than normal. Spector D A et al 43 studied thyroid function and metabolic status in 38 patients with chronic renal insufficiency who were in a dialysis programme. They found mean serum total triiodothyronine (T3) concentration to be normal but 43% of the group had low serum T3 and 54% had low serum free T3 concentrations. Serum TSH concentrations were normal in all but four subjects who had very slight elevations. In our study, the findings are comparable with other previous studies showing decrease level of T3 in uremic patients.

Thyroxine (T4) level ranged from 39.60-158 µg/ml (mean 95.05±29.1). Most of the study patients 84 (84%) had Thyroxine (T4) level in the normal reference range (66-181 µg/ml) and 16 (16%) patients had low T4 (<66 µg/ml). Maximum patients 85 (50%) of CGN had low T4 followed by 6 (37.5%) patients of Diabetic nephropathy and 2 (12.5%) patient of obstructive uropathy. Jasso et al 44 found that uremic patients had low serum TT3 and elevated T3 resin uptake suggesting a decrease in TBG. However actual measurement of TBG was normal. They postulated that uremic toxin might have displaced T4 from TBG. Anima X et al 45 evaluated the level of TT4, T3 and TSH in 96 clinically euthyroid patients with chronic renal failure and 25 healthy individual as control and they found that there was significant decrease in total T4 in 26 (42%) patients. In our study 16 (16%) patients had T4 level below normal which is comparable with previous studies. The different studies mentioned various reasons for decreased level of T4. The decreased level of T4 may be secondary to the protein loss which occurs in CKD. Serum albumin and thyroid binding Pre-albumin level are decreased in patients of CKD. Decrease in T4 is also attributed to the presence of the circulating inhibitors which impairs binding of T4 to thyroxin binding globin.

In our study, out of 100 Chronic kidney disease patients, 18 (18%) had Hypothyroidism, 4 (4%) had sub-clinical hypothyroidism and 78 (78%) were in Euthyroid state. None of them had Hyperthyroidism. ChonchoM et al 46 in their study of 3089 patients found that most participants (84.6%) had serum thyroid function test results within the reference range whereas 9.5% had subclinical biochemical hypothyroidism and 5.9% had subclinical biochemical hyperthyroidism. Lo JC et al 47 in their study found that the prevalence of hypothyroidism was 8.62%. Among the 18 hypothyroid patients maximum number of hypothyroid patients i.e.
13(72.2%) were in CKD stage V followed by 3(16.6%) patients in CKD stage IV and 2(11.2%) patients in CKD stage III. Among the 4 Subclinical hypothyroid patients, maximum 3 (75%) patients of Sub-clinical Hypothyroidism occurred in CKD stage V and 1(25%) patients in CKD stage IV. In our study that the prevalence of hypothyroidism was increased in patients with reduced GFR, ranging from 14.2% for patients with estimated GFR 30-59 ml/min/1.73m² (CKD stage III) to 21.3% in patients with estimated GFR <15 ml/min/1.73m² (CKD stage V). However this findings was not statistically significant.

In our study, among the etiology of CKD the prevalence of hypothyroid is maximum in Lupus Nephritis (33.3%) The prevalence of Sub-clinical hypothyroidism is maximum (5.7%) in Diabetes mellitus followed by Obstructive Uropathy (4.3%) and Chronic glomerulonephritis 2.8%, though not reaching statistical significance.

Mean TSH is higher in CKD stage V as compared to stage IV and III showing that the mean TSH level increases along with decrease in GFR. Mean T3,T4 were found to be higher in CKD stage III as compared to CKD Stage IV and V, which also shows that mean T3 and T4 level were found to be higher in patients with higher GFR. Lo JC et al 37 in their study found that prevalence of hypothyroidism progressively increases from patients with higher GFR to patients with low GFR. Chonchol M et al 36 studied 3089 patient of CKD and they found that the prevalence of subclinical hypothyroid increases progressively from 7.6% in patients with GFR ≥90 ml/min/1.73m² to 21% in patients with GFR <60 ml/min/1.73m². The findings in our study are comparable with others previous studies showing that there is an increase prevalence of hypothyroidism in patients with low GFR.

V.Conclusion

The most common cause of CKD was Diabetic Nephropathy (35%) and Chronic Glomerulonephritis (35%). The mean age of the patients ranged from 21 to 77 years (mean age 50.38±14.91 yrs). The body mass index ranged from 13.04 to 30.50 kg/m² (mean of 21.68 ± 3.34). Mean TSH level was 4.11±3.5 µIU/ml. 79% patients had TSH level in the normal range (0.25-5 µIU/ml) and 21 patients had TSH level above normal range (>5 µIU/ml). Mean T3 level was 1.63±0.63. 81% Patients had T3 level in normal range (1.3-3.1 ng/ml) and 19% patients had low T3 (<1.3 ng/ml) and of these patients with low T3, CGN had maximum patients (52.6%) Mean T4 was 95.05±29.1. Maximum 84% patients had T4 level in the normal reference range (66-181 µg/ml) and 16% patients had low T4 (<66 µg/ml). The prevalence Hypothyroidism was 18%. 4% had sub-clinical hypothyroidism and 78% were in Euthyroid state. There was no Hyperthyroid patients. The prevalence of hypothyroidism was found to be increased in patients with reduced GFR. The prevalence of hypothyroid was maximum in Lupus Nephritis (33.3%). The prevalence of Sub-clinical hypothyroidism was 5.7% in Diabetes mellitus followed by 4.3% in Obstructive Uropathy and 2.8% in Chronic glomerulonephritis. Mean TSH level increased along with decline in GFR. Mean T3, T4 were found to be higher in CKD stage III as compared to CKD Stage V showing that mean T3 and T4 level were higher in patients with higher GFR.

References


DOI: 10.9790/0853-1812106268 www.iosrjournals.org 67 | Page
Thyroid Profile in Chronic Kidney Disease Patients: A Study in Rims Hospital

27. Third annual report of CKD registry of India. Indian society of nephrology.
32. Ramírez G Ramírez g, O’Neill W, Jr, Jubiz W and Bloomer HA. Thyroid dysfunction in uraemia, evidence for thyroid and hypophyseal abnormalities. Annals of internal Medicine. 1976; 84: 672-676.