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ORIGINAL RESEARCH

STUDY OF THYROID DYSFUNCTION IN PATIENTS WITH CHRONIC KIDNEY DISEASES (CKD)

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ABSTRACT

Introduction: It has been observed that chronic kidney diseases(CKD) are often associated with thyroid dysfunction .Thyroid functional derangements in CKD are linked with excessive mortality from cardiovascular causes and death in CKD patients due to accelerated development of atherosclerosis. Keeping in view the cardiovascular mortality associated with the deranged thyroid profile there is need to understand the relationship between the thyroid and the kidney more thoroughly and verify the accuracy of earlier findings.

Aims & Objectives: The study aimed to assess the thyroid profile in patients with kidney disease and to correlate T3 and TSH with S Creatinine and Glomerular filteration rate (GFR) and to finally to study the C Reactive Protein (CRP) positivity in CKD patients with thyroid dysfunction .

Methods: The study group comprised of 70 patients with kidney diseases from 30 to 65years from Out Patient and Inpatient Departments of the a tertiary hospital.

Results: Out of the 70 patients in the study 38(54.29%) of patients were males and 32 (45.71%) patients were females. 44 patients (62.8%) had thyroid disorder .30% of patients had Hypothyroidism, 20% had Sub clinical Hypothyroidism and 7.14% had Low T3 syndrome, 4.2% had Low T4 , 1.4% patient had high T4 and 26 patients (37.2%) were euthyroid patients.The prevalence of thyroid dysfunction was higher in the group with GFR <15ml/min(Stage 5) (statistically insignificantly).Patients with higher TSH and low T3 were more prevalent in patients with lower GFR though statistically significant correlation could not be elicited. CRP positivity in CKD patients with thyroid dysfunction was significantly higher than those without any thyroid dysfunction .

Conclusion : Hence, it can be concluded that thyroid disorders are common in patients with chronic kidney diseases and the prevalence of thyroid dysfunction corresponds with severity of CKD.Therefore, it is essential that we screen the patients with CKD for thyroid dysfunction routinely, and manage accordingly in order to avoid excessive cardiac mortality and progression of CKD.

INTRODUCTION

Kidney diseases account for a large percentage of hospital admissions. It has been observed

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that kidney diseases are associated with thyroid dysfunction. Despite extensive research, the connection between kidney disease and hypothyroidism remains elusive.Hypothyroidism is thought to be due to impaired renal clearance of iodine which produces increased levels of inorganic iodide that blocks production of thyroid hormone resulting in "Wolff Chaikoff" effect. Patients with ESRD have some impairment in thyroid hormone function in the absence of coexisting thyroid disease. These include low free T3 and T4 and either normal or elevated basal TSH values. Low T3 levels are the most frequent laboratory finding followed by subclinical hypothyroidism in Chronic renal failure patients. Changes in T4 and T3 resemble those of other critical illnesses including infections and malignancies also termed as the "euthyroid sick syndrome" (ESS). In CKD, it is thought that this physiological compensation with a low T3/T4 causes decrease in protein catabolism which raises the nitrogen overload. Dialysis therapy minimally affects thyroid hormone metabolism. Thyroid hormone metabolism normalizes with renal transplantation. The reasons attributed to the low T3 levels in renal failure are

1. Due to displacement of T3 and T4 from their proteins by the uremic toxins.
2. The metabolic acidosis prevalent in CKD also decreases the protein binding ofT3 resulting in low levels.
3. Besides there is reduced clearance of inflammatory cytokines for instance TNF-alpha which inhibit the 1 5-deiodinase the enzyme that enables conversion of T4 toT3.

Most fatalities in CKD are due to cardiovascular causes and cannot be explained by traditional risk factors. Mounting data point to the thyroid derangements as the possible cause. Current data have found that hypothyroidism is associated with increased risk of heart disease and mortality in this population. In stage 3 and 4 CKD patients with ESS were associated with endothelial dysfunction, cardiomyopathy and higher risk of death. Some studies shows that low free T3 levels are an independent predictor of mortality in patients of hemodialysis and also correlated with higher levels of markers of inflammation. Low T3 is associated with atherosclerosis, vascular calcification, left ventricular hypertrophy, reduced systolic function and abnormal ventricular conduction.[1]They also had higher values of Carotid Intima Media Thickness (CIMT).One study is suggestive of the fact that treatment of "mild" subclinical hypothyroidism in CKD may reduce kidney disease progression.However, it is to be noted that levothyroxine has narrow toxic-to-therapeutic window and unnecessary treatment can increase protein catabolism, reduce bone mineral density and precipitate arrhythmia.

Disentangling hypothyroidism from functional changes present due to nonthyroidal illness and other thyroid hormone derangements observed in CKD poses a formidable challenge. Keeping in view the cardiovascular mortality associated with the deranged thyroid profile there is need to understand the relationship between the thyroid and the kidney more thoroughly and verify the accuracy of earlier findings.

AIMS AND OBJECTIVES

1. To determining the thyroid profile in patients with kidney disease
2. To correlate T3 and TSH with S Creatinine and GFR,
3. To study the prevalence of C Reactive Protein positivity in CKD patients with thyroid dysfunction.

METHODS- Study design

Present study was a prospective, cross sectional , hospital-based study comprised of 70 patients with kidney diseases with age group of 30 to 65years.

Inclusion criteria

Criteria includes, Patient with Chronic kidney disease:

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1. Uremic symptoms for the period of 3 months or more
2. Raised blood urea, serum creatinine and low creatinine clearance.
3. Ultrasound findings including: A. Kidneys Bilateral contracted - size less than 8 cm . B. Poor corticomedullary differentiation.
4. Supportive laboratory findings of CRF such as anemia, low specific gravity, variations in the serum electrolytes, etc.
5. Radiological findings of renal osteodystrophy

Exclusion criteria

1. Patient admitted in ICU with acute medical illness,
2. Patient with concomitant inflammatory disease.
3. Patient with hypothalamic-pituitary disorder.
4. Malignancy.
5. Phenytoin, Carbamazepine, Sertraline, Metformin and non-steroidal anti- inflammatory drugs.
6. Pregnancy given potential pregnancy-related changes in thyroid function
7. Patients with acute kidney injury
8. Known thyroid disease

RESULTS

70 CKD patients were studied. Their ages ranged from 30 to 65. 38 (54.29%) of patients were males and 32 (45.71%) patients were females.Out of 70 patients 44 CKD patients had thyroid dysfunction.26 were euthyroid.

Table 1-ANALYSIS OF THYROID DYSFUNCTION IN CKD PATIENTS

Thyroid dysfunction	No. of Patients	Percentage
Hypothyroidism	21	30%
Subclinical Hypothyroidism	14	20%
Low T3 Syndrome	5	7.14%
Low T4	3	4.28%
High T3	1	1.42%
Goiter	nil	0%
Hyperthyroidism	nil	0%
Euthyroid	26	37.10%

Table 2-DISTRIBUTION OF CKD PATIENTS WITH THYROID DYSFUNCTION IN DIFFERENT STAGES OF CKD.

GFR	Thyroid dysfunction	Euthyroid	Total
<15 (Stage 5)	37	22	59
>=15-30 (Stage 4)	7	4	11
Total	44	26	70

The prevalence of thyroid dysfunction was higher in the group with GFR <15ml/min (Stage 5) (statistically insignificantly) Thus the prevalence of Thyroid dysfunction corresponds with severity of CKD.(Table 2)

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Table 3-CORRELATION OF TSH WITH GFR

TSH	GFR		Total
	<15	15-30	
High	31	5	36
Normal	28	6	34
Low	NIL	NIL	NIL
Total	59	11	70

Patients with higher TSH were more prevalent in patients with lower GFR and severe renal disease though statistically significant correlation could not be elicited. (Table 3)

Table4 : CORRELATION OF TSH WITH S. CREATININE

TSH	Serum Creatinine (0.7 – 1.4)mg/dl					Total
	0-4	4-8	8-12	12-16	>16	
Normal	2	13	12	5	2	34
High	4	13	7	5	7	36
Total	6	26	19	10	9	70

Correlation between Serum TSH and S. Creatinine was statistical insignificant as p value was 0.318. (Table 4)

The Table 5 shows that Patients with Low T3 were more prevalent in patients with lower GFR and severe renal disease though statistically significant correlation could not be elicited.

Table no 5- CORRELATION OF T3 WITH GFR

T3	GFR		Total no. of Patients
	<15	15-30	
Normal	39	8	47
Low	19	3	22
High	1	NIL	1
Total	59	11	70

Table 6: CORRELATION OF CRP WITH THYROID DYSFUNCTION IN CKD PATIENTS

	CRP		Total
	Positive	**Negative**	
Thyroid Dysfunction	19	25	44
Euthyroid	4	22	26
Total	23	47	70

Table 6 shows that CRP positivity in CKD patients with thyroid dysfunction significantly higher than those without any Thyroid Dysfunction.

Discussion

The percentage patients with thyroid dysfunction in our CKD cases (70) was 62.7% as compared to Euthyroid (37.3%).

It is to be noted that the prevalence of hypothyroidism in India in normal population is 10.95%.[2]The prevalence of hypothyroidism in CKD documented in different studies is

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variable ranging 9.9 % to 35%. In a study by Rhee et al[3] in 2015 the prevalence was found to be 25%. In a study by Faisal Alshammariet al.[4]the percentage of hypothyroidism among CKD patients was 34.9% including dialysis patients and 17.66% after exclusion.These results of these studies are in conformity with our study.

Epidemiological studies in India have shown a prevalence rate of SCH in normal population varying between 9% and 12.8%. In our study 20% (14 patients) of CKD patients had Subclinical Hypothyroidism. Abhishek Gupta et al[5] in 2017 found it to be 25% and 24.8% in a study by Shantha GP et al[6] in 2011. Thus, the results of our study almost similar to the above studies.The variable results pertaining to the prevalence of hypothyroidism and SCH could be due to the different geographical locations, different populations with varied iodine intake, different lab methodology and the sample size.

In our study 7.14% (5 patients) of CKD patients had Low T3 Syndrome. Drechsler C et al[7] in 2014found it to be 5.4% of patients.

It was observed that the percentage of patients with thyroid dysfunction increased with the severity of renal failure.In our study 84 % subjects had eGFR <15ml/min (Stage 5) as compared to 16% with GFR above 15 ml / min(Stage 4) though the difference was not statistically significant. This is in conformity with other studies .Woodward et al[8] in 2008 showed thyroid dysfunctionwas associated with significant alterations in eGFR and actual GFR.

The percentage of Low T3 syndrome was also higher in patients with severer disease. Out of 5 patients with Low T3 syndrome 4 had GFR <15 ml/min/1.73m^2 (Stage 5) .This observation was concurrent with the study of Song SH et al in 2009[9], and Yilmaz et al[10] in 2011 studied that prevalence of low T3 would be increased according to the increase in CKD stage.

In our study patients with higher TSH were more prevalent in patients with lower GFR and severer renal disease though statistically significant corelation could not be elicited. Out of 36 patients with high TSH level 31 (86%) patients had eGFR less than 15ml/min/1.73m^2 Some other studies found no significant correlation between TSH and severity of chronic renal failure as in our study and corroborated the findings of our study. These studies include the ones by Ahmed MM et al[11] in 2014, Huang X et al[12] in 2016.

In our study the prevalence of hypothyroidism was more in cases with GFR less than 15 ml/min (32.20%) as compared to the cases with GFR higher than 15ml/min (18.10%) . Other studies also showed higher prevalence of hypothyroidism with increasing severity of kidney dysfunction. These include studies by Klara Paudel et al[13] in 2014, Chuang MH et al[14] in 2016,

The prevalence of SCH was 18% in patients with GFR less than 15 ml/min as compared to 27% in the cases with GFR higher than 15ml/min However in contrast some studies Shantha GP et al[15] in 2011.

No correlation was found between thyroid dysfunction and s creatinine levels . The reason may be that S creatinine levels are not constant but variable at different times due to many factors such as duration of last dialysis and prerenal factors .

CKD patients with thyroid dysfunction correlated with higher levels of markers of inflammation including highly sensitive C-reactive protein (hsCRP). Out of 23 CRP positive (out of total of 70 CKD patients 19 (82.6%) patients had thyroid dysfunction in and 4 were Euthyroid. Thus, CRP positivity was significantly higher in patients with Thyroid dysfunction in CKD patients.

Out of 23 CRP Positive patients in CKD, 10 patients (43.5%) had hypothyroidism, 5 (21.7%) had hypothyroidism only 1 (4.3%) patients had Low T3 Syndrome .

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The percentage of thyroid dysfunction corresponded with the severity of renal disease. CRP which has a role in atherosclerosis and is a predictor of future cardiovascular was significantly higher in patients with thyroid dysfunction in our study.

Conclusion

The thyroid-kidney link is bidirectional and needs to be fully elucidated. CKD patients have a disproportionately higher prevalence of hypothyroidism. The prevalence of thyroid dysfunction in our study is 62.8% out of which 30% had hypothyroidism 20% SCH and 7.14% with Low T3 syndrome. Also, the prevalence increased with severity of CKD. Thyroid functional derangements, including hypothyroidism in CKD are linked with mortality from cardiovascular causes and death in CKD patients. We must consider the dangers of thyroid disease and its treatment in conjunction to treating CKD. Some studies have shown that treatment decreased the chance of exacerbating renal dysfunction and was associated with decreased CKD progression. However, the safety and effectiveness of exogenous thyroid hormone replacement in hypothyroid CKD patients needs to be studied further. Therefore, it is essential that we screen the patients with CKD for thyroid dysfunction routinely, so as to recognize these dysfunctions at the earliest to and take appropriate steps.

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