Thyroid Functional Status in Chronic Kidney Disease

Md Mosharruf Hossain, Kabiruzzaman Shah, Nasrin Begum, Parvez Ahmed, A K M Monoarul Islam and Nurul Islam Chowdhury

Correspondence Address: Md Mosharruf Hossain, Senior Medical Officer, Institute of Nuclear Medicine & Allied Sciences Rajshahi, Rajshahi Medical College Hospital Campus, Email: mhossain.baec1@yahoo.com.

ABSTRACT

Objectives: **This study was done to find out the effect of chronic kidney disease on thyroid functional status. Kidneys normally play an important role in the metabolism, degradation and excretion of thyroid hormones. Therefore, impairment in kidney function leads to disturbed thyroid physiology. All levels of the hypothalamic-pituitary-thyroid axis may be involved, including alterations in hormone production, distribution, and excretion. As a result, abnormalities in thyroid function tests are common in chronic kidney disease (CKD).**

Materials And Methods: **A total of 100 patients suffering from different stages of chronic kidney disease were included for this study during the period of January 2010 to December 2010 at the Centre for Nuclear Medicine & Ultrasound, Rajshahi, Bangladesh.**

Results: **This study showed high prevalence of primary hypothyroidism (11%), low T3 syndrome (45%) and subclinical hypothyroidism (5%) in chronic kidney disease patients. Furthermore, there is an increasing trend of decreased thyroid functional status along with decrease of estimated GFR (eGFR).**

Conclusions: **Chronic kidney disease impairs thyroid functional status in different ways. Thyroid functional status evaluation is recommended in each and every patient of CKD. That can reduce the morbidity and mortality rate of CKD patients as well as reduce the social burden and health expenditure.**

Key words: **Chronic kidney disease (CKD), estimated GFR (eGFR), Primary hypothyroidism, Subclinical hypothyroidism, Low T3 syndrome.**

INTRODUCTION

Chronic kidney disease is an increasing health problem throughout the world including Bangladesh. It is a long-standing, progressive deterioration of renal function (1). The kidney normally plays an important role in the metabolism, degradation and excretion of several thyroid hormones. All levels of the hypothalamic-pituitary-thyroid axis may be involved, including alterations in hormone production, distribution, and excretion. As a result, abnormalities in thyroid function tests are frequently encountered in uremia (2,3). End-stage renal disease (ESRD) alters the hypothalamic-pituitary-thyroid hormone axis in addition to the peripheral thyroid hormone metabolism. Among thyroid hormones, triodothyronine (T3) is the most metabolically active thyroid hormone and can be reduced in ESRD patients even with a normal TSH level. In general, reduced T3 levels in ESRD patients are due to the decreased peripheral tissue conversion of T4 into T3, while thyroid gland production of T3 is normal and T3 clearance rates are normal or decreased, as in other non-thyroidal illnesses (4). Most patients with end-stage renal disease have decreased plasma levels of free triiodothyronine (FT3), which reflect diminished conversion of thyroxine (T4) to T3 in the periphery (5). This abnormality is not associated with increased conversion of T4 to the metabolically inactive reverse T3 (rT3), since plasma rT3 levels are typically normal. This finding differentiates the uremic patient from patients with chronic illness in which the conversion of T4 to T3 is similarly reduced, but the generation of rT3 from T4 is enhanced. In addition to decreased production, low levels of total T3 also may reflect reduced protein binding(6). 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 thyroidal iodide uptake. The ensuing marked increase in the intrathyroidal iodide pool results in diminished uptake of radiolabeled iodide by the thyroid in uremic patients. Increases in total body inorganic iodide can potentially block thyroid hormone production (the Wolff Chaikoff effect) (7,8). Chronic renal failure affects thyroid function in multiple ways, including low circulating thyroid hormone concentration, altered peripheral hormone metabolism, disturbed binding to carrier proteins, possible reduction in tissue thyroid hormone content, and increased iodine store in thyroid glands (9). The objective of the present study was to see the relationship between chronic kidney disease and thyroid functional status and also to see the effect of CKD on thyroid hormonal status and to stratify the severity of renal disease by eGFR and to correlate stages of CKD with serum FT3, FT4 and TSH level.

MATERIALS AND METHODS

It was a cross sectional study which was carried out at Institute of Nuclear Medicine & Allied Sciences INMAS, Rajshahi and Nephrology Department of Rajshahi Medical College Hospital during the period of January 2010 to December 2010. A total of 100 samples were taken for this study. Patients with all stages of CKD between age of 20 to 60 years were included and patients undergoing treatment for thyroid diseases, with chronic liver disease were excluded.

Estimation of GFR: GFR is estimated by serum creatinine based Modification of Diet in Renal Disease (MDRD) formula. Simplified MDRD equation: eGFR (ml/min/1.73m2) = 186.3 x (serum creatinine in mg/dl) -1.154 x (age in years)-0.203 x (0.742 if female) x (1.21 if African American). The MDRD equation was published in 1999 (10) and is widely used in clinical practice and epidemiologic studies (11) Serum FT3 and FT4 were estimated by radioimmunoassay (RIA) and Serum TSH was estimated by Immunoradiometric assey (IRMA).

RESULTS

A total of 100 patients of CKD of different age groups were enrolled for this study. Out of them 11% of the patients were between the age of 20-29 years, 20% between 30-39 years, 33% between 40-49 years and 36% between the ages of 50-60 years. Mean age of the patient was 44.42±12.42 years of age, 63% were male and 37% were female giving a male: female ratio of nearly 1.7: 1 (Table-1).

Table-1: Distribution of patients according to staging of CKD

Staging of CKD	Estimated GFR (eGFR ml/min/1.73 m2)	Total Number of patients	Percentage
Stage-I	≥ 90	2	2%
Stage-II	60-89	6	6%
Stage-III	30-59	13	13%
Stage-IV	15-29	31	31%
Stage-V	<15	48	48%
Total		100	100%

Table 2: Distribution of patients according to thyroid functional status

Thyroid status	Total Number of patients	Percentage (%)
Hypothyroidism	11	11%
Subclinical hypothyroidism	5	5%
Low FT3	45	45%
Normal Functioning	39	39%
Total	100	100%

Table 2: shows that out of 100 CKD patients of different stages II (11%) were suffering from primary hypothyroidism, 5 (5%) were from subclinical hypothyroidism and 45 (45%) were from low T3 syndrome and rest 39 (39 %) patients were free from any thyroid abnormality.

Table 3: Summary of the distribution of CKD patients of different stages suffering from different thyroid illnesses.

Stages	Hypothyroidism	Subclinical hypothyroidism	Low FT3	Normal	Total Pt
I	0(0%)	0(0%)	0(0%)	2(100%)	2(2%)
II	0(0%)	0(0%)	3(50%)	3(50%)	6(%)
III	3(23.1%)	1(7.7%)	4(30.8%)	5(38%)	13(13%)
IV	3(9.7%)	1(3.2%)	11(35.5%)	16(51.6%)	31(31%)
V	5(10.4%)	3(6.2%)	27(56.2%)	13(27.1%)	48(48%)
Total	11(11%)	5(5%)	45 (45%)	39(39%)	100(100%)

Among 100 CKD patients; 2 (2%) were of stage-I, 6 (6%) in stage-II, 13 (13%) were stage – III, 31 (31%) were stage –IV, and 48 (48%) were in stage –V. Highest incidence of thyroid abnormality was seen in stage –V but no thyroid illness was seen in stage-I. In stage – V, out of 48 patients 5 (10.4%) were suffering from hypothyroidism, 3 (6.2%) were subclinical hypothyroidism, 27 (56.2%) were low T3 syndrome. In stage – IV, out of 31 patients 3 (9.7%) were diagnosed as hypothyroidism, 1 (3.2%) were subclinical hypothyroidism and 11 (35.5%) were low T3 syndrome. In stage-III, out of 13 patients 3 (23.1%) were suffering from hypothyroidism, 1 (7.7%) were subclinical hypothyroidism and 4 (30.8%) were low T3 syndrome. In stage –II, out of 6 patients only 3 (50%) had low T3 syndrome (Table-III).

DISCUSSION

Chronic kidney disease is a worldwide public health problem. They are the 12th cause of death and 17th cause of disability respectively (WHO, 2004). CKD involves multiple systems of body. It affects thyroid function in multiple ways including peripheral hormone metabolism, decrease binding of thyroid hormones by transport proteins and impaired peripheral conversion of T4 to T3. Serum FT3, FT4 and TSH level were estimated among study population. It was a cross sectional study which was done at Institute of Nuclear Medicine Allied Sciences, Rajshahi and Nephrology department of Rajshahi Medical College Hospital, Rajshahi. All data were collected using standarad questionnaires which addressed all variables of interest.

In current study, mean age of the patients was 44.42 ± 12.42 yrs. Among them 11% were between the age of 20-29 yrs, 20% between 30-39 yrs, 33% were between 40-49 yrs and 36% between 50-60 yrs. Among all the patients 63% were male and 37% were female giving rise to a male:female ratio of nearly 1.7:1. In this study, mean ± SD of serum FT3 was 2.42 +/- 1.1 pmol/L, serum FT4 was 17.34+/-4.50 pmol/L and Serum TSH level was 3.50 ± 3.73 mIU/L, where normal range of FT3 = 2.80-9.50 pmol/L, FT4 = 9.50-25.50 pmol/L and TSH level = 0.30-5 mIU/L. In this study out of 100 patients of chronic kidney disease 2 (2%) were within stage-I, 6(6%) of stage-II, 13 (13%) were of stage – III, 31 (31%) of stage-IV and 48(48%) were of stage – V. A total of 61(61%) patients of CKD were suffering from different thyroid abnormalities. Among total patients of thyroid illness 61, 11 (11%) were suffering from primary hypothyroidism, 5(5%) were subclinical hypothyroidism and 45 (45%) were of low T3 syndrome.

Among 11(11%) of total hypothyroid patients 3(27.3%) were in stage –III, another 3 (27.3%) were in stage-IV and rest 5(45.4%) were of stage –V, but no patients of stage-I and stage-II were suffering from primary hypothyroidism. Among 5(5%) of subclinical hypothyroidism 1(20%) of stage-III, another 1(20%) were of stage-IV and rest 3 (60%) were stage-V but no patient of subclinical hypothyroidism was found in stage –I and II. Among 54 (54%) of Low T3 syndrome 3(5.5%) were of stage –II, 4(7.4%) were of stage-III, 11 (20.4%) were of stage-IV and rest 27 (66.7%) were of stage –V but not patient of stage-I was suffering from low T3 syndrome. This study recommends that prevalence of thyroid diseases were found to be increased according to the severity of CKD. In 1984 it was also reported that higher prevalence (5%) of hypothyroidism in patients with terminal renal failure in comparison with that in hospitalized patients with normal renal function (12). It was noticed that the prevalence of subclinical and clinical primary hypothyroidism increased progressively with lower levels of kidney function in a nationally representative cohort of US adults. Among these participants, more than 20% of those with an eGFR<60 mil/min/1.73m2 had clinical or subclinical hypothyroidism.

Song et al; hypothesized that the prevalence of low T3 syndrome would be increased according to the increase of CKD stage. There was an increasing trend form the population of low T3 according to the increase of CKD stage. This study showed that low T3 syndrome was highly prevalent in CKD and was a remarkable finding in early CKD. Furthermore, serum T3 levels were associated with severity of CKD in normal TSH level(13).

In this study only FT3 and FT4 levels were measured but total T3 and T4 levels were not measured. In future total T3 and T4 level should be measured to assess the peripheral conversion of T4 to T3. This is a small scale study, however this study provides a guideline for the diagnosis and management of the patients of CKD associated with thyroidal illness.

CONCLUSION

This study showed that high prevalence (11%) of primary hypothyroidism, low T3 syndrome (45%) and subclinical hypothyroidism (5%) in CKD and was a remarkable finding in CKD. Furthermore, there is an increasing trend of low serum FT3 levels (low T3 syndrome), Subclinical hypothyroidism and primary hypothyroidism according to the severity of CKD. So thyroid functional status should be evaluated in each and every patient of CKD especially of stage-III, IV and V that can reduce the morbidity and mortality rate of CKD patients as well as reduce the social burden and health expenditure.

REFERENCES

1. Levey As, Coresh J, Balk E, Kausz AT, Levin A, Steffes MW, Hogg RJ, Perrone RD, Lau J, Eknoyan G. National Kidney Foundation Practice Guidelines For Chronic Kidney Disease: Evaluation, Classification, and Stratification. Ann Intern Med.2003;139:137-47.
2. Lo JC, Chertow GM, Go AS, Hsu CY. Increased Prevalence of Subclinical and Clinical Hypothyroidism in Persons with Chronic Kidney Disease. Kidney Int 2005;67:1047.
3. Chonchol M, Lippi G, Salvagno G et al. Prevalence of Subclinical Hypothyroidism in Patients with Chronic Kidney Disease. Clin J Am Soc Nephrol 2008;3:1296.
4. Kaptein EM. Thyroid Hormone Metabolism and Thyroid Diseases in Chronic Renal Failure. Endocrine Reviews 1996 Feb;17(1):45-63.
5. Wartofsky L, Burman KD. Alterations in Thyroid Function in Patients with Systemic Illness: The “Euthyroid Sick Syndrome”. Endocr Rev 1982;3:164-217.
6. Palmer BF. Metabolic Disturbances in Chronic Renal Failure. Saudi J Kidney Dis Transpl 2002;13:273-80.
7. Lin CC, Chen TW, Ng YY, Chow YH, Yang WC. Thyroid Dysfunction and Nodular Goiter in Hemodialysis and Peritoneal Dialysis Patients. Perit Dial Int 1998;18:516-21.
8. Ramiraz G. Abnormalities in the Hypothalamic-Hypophyseal Axes in Patients with Chronic Renal Failure. Semin Dial 1994;7:138-42.
9. Hoek IV and Daminet S. Interactions Between Thyroid and Kidney Function in Pathological Conditions of These Organ Systems: A Review. General and Comparative Endocrinology 2009; 160(3):205-15.
10. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A More Accurate Method to Estimate Glomerular Filtration Rate From Serum Creatinine: A New Prediction Equation. Modification of Diet in Renal Disease Study Group. Ann Intern Med 1999;130:461-70.
11. Coresh J, Astor BC, Greene T, Eknoyan G, Levey AS. Prevalence of Chronic Kidney Disease and Decreased Kidney Function in the Adult US Population: Third National Health and Nutrition Examination Survey. Am J Kidney Dis. 2003;41:1-12.
12. Quin-Verde H, Kaptein EM, Chooljian CJ, Rodriquez HJ, Massary SG. Prevalence of Thyroid Disease in Chronic Renal Failure (CRF) and Dialysis Patients. Los Angels: IX th Int Congr of Nephrol; Abstract No:120,1984.
13. Song SH, Kwak AS, Lee DW, Kang YH, Seong EY and Park JS. The Prevalence of Low Triiodothyronine According to the Stage of Chronic Kidney Disease in Subjects With a Normal Thyroid Stimulating Hormone. Nephrol Dial Transplant 2009;24(5):1534-38.