

A Prospective Study of Pattern of Hypothyroidism in Patients of Chronic Kidney Disease in a Tertiary Care Center in North India

Kusum Bali¹, Jaswinder Kaur^{2*}, Amarjit Vij³, H.L.Kazal⁴, Uma Arora⁵, Davinder Kumar⁶, Satyam Krishan⁷¹Associate Professor, Dept. of Medicine, Punjab Institute of Medical Sciences, Jalandhar, Punjab, India²Assistant Professor, Dept. of Medicine, Punjab Institute of Medical Sciences, Jalandhar, Punjab, India³Professor, Dept. of Medicine, Punjab Institute of Medical Sciences, Jalandhar, Punjab, India⁴Professor and HOD, Dept. of Medicine, Punjab Institute of Medical Sciences, Jalandhar, Punjab, India⁵Professor, Dept. of Biochemistry, Punjab Institute of Medical Sciences, Jalandhar, Punjab, India⁶Senior Resident, Dept. of Medicine, Punjab Institute of Medical Sciences, Jalandhar, Punjab, India⁷Intern, Dept. of Medicine, Punjab Institute of Medical Sciences, Jalandhar, Punjab, India

*Corresponding author: Jaswinder Kaur

| Received: 01.02.2019 | Accepted: 10.02.2019 | Published: 20.02.2019

DOI: [10.21276/sjams.2019.7.2.32](https://doi.org/10.21276/sjams.2019.7.2.32)

Abstract

Original Research Article

Background: Thyroid hormones T3 and T4 play a very important role in regulating metabolism, development, protein synthesis and also influence other hormone functions. These hormones also tend to have a significant impact on Chronic Kidney Disease. CKD also affects the pituitary thyroid axis. Low T3 levels is one of the most common finding along with subclinical hypothyroidism in CKD patients. **Methods:** This prospective study recruited 105 consecutive patients with Chronic Kidney Disease presenting to medicine OPD in our institute over a period of 6 months. For all these patients FT3, FT4 and TSH levels were measured. **Results:** Out of 105 CKD patients 38 patients had low FT3 levels and 35 had low FT4 levels. 31 patients were found to have either Subclinical Hypothyroidism or Hypothyroidism. **Conclusion:** In this study we observed a high prevalence of Subclinical Hypothyroidism in CKD patients. Subclinical Hypothyroidism is a relatively common condition in CKD patients. The prevalence of hypothyroidism increased with the increasing severity of CKD.

Keywords: Thyroid, hormones T3, T4.

Copyright © 2019: This is an open-access article distributed under the terms of the Creative Commons Attribution license which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use (NonCommercial, or CC-BY-NC) provided the original author and source are credited.

INTRODUCTION

The Thyroid gland produces hormones – Triiodothyronine T3 and Thyroxine T4 that regulate the metabolism, development, protein synthesis and other important hormones. Thyroid hormone levels also affect the prognosis of CKD. Disorders in thyroid hormones have been seen to coexist with disorders in renal function.

TSH is a 28 to 30 kDa glycoprotein subunit, produced by the basophilic cells of anterior pituitary gland [1]. It travels to the thyroid gland to bind with TSH receptors. This activates the second messenger pathway thereby causing thyroid gene expression and release of T3 and T4. The prevalence of subclinical hypothyroidism increases with reduction in GFR

METHODS

This prospective study was conducted in a tertiary care hospital in North India. 105 patients of Chronic Kidney disease coming to OPDs or Emergency department or Dialysis unit were enrolled

Inclusion criteria

All patients with Chronic Kidney Disease above 18 years of age were considered for the study. These patients were either on regular haemodialysis or on conservative management. Patients were asked about the duration of Diabetes or Hypertension or any other underlying disease leading to CKD. Patients were enquired about any anti-thyroid drugs or any drug which can cause thyroid dysfunction like Amiodarone, Rifampicin, Interferon, Lithium etc. Serum free T3, free T4 and TSH levels were quantified by Chemiluminescence method and the eGFR (estimated GFR) was also calculated.

The various risk factors leading to CKD were noted like history of Diabetes Mellitus, Hypertension, Obstruction Uropathy, Polycystic kidney Disease, Chronic Glomerulonephritis etc.

Exclusion criteria

- Subjects younger than 18 years.
- Pregnant women.
- Subjects receiving any drug that can contribute to

thyroid dysfunction.

- Patients receiving any anti-thyroid drugs for hyperthyroidism.

CKD not only affects the pituitary – thyroid axis but also the peripheral metabolism of thyroid hormones [2].

Low T3 syndrome is the commonest thyroid function disorder in CKD patients. Low T3 syndrome occurs as Metabolic Acidosis and Protein Malnutrition. It affects Iodothyronine deiodination, reducing the peripheral conversion of T4 to T3 and protein binding. The free T4 levels may vary from being low to normal as there is impaired protein binding of T4. CKD patients have low T3, normal to reduced T4 levels and elevated TSH levels [3]. They also have an increase in thyroid gland volume [3].

Thyroid hormones affect renal clearance of water load by affecting the glomerular filtration rate. They increase the activity of Na /k ATP ase and influence Na + re-absorption in the Proximal Convulated Tubule and also Tubular potassium permeability [4]. They also affect the renin – angiotensin- aldosterone axis and regulate the adrenergic receptors and dopaminergic activation of Renal tubular cells [5].

RESULTS

Out of 105 chronic kidney disease patients, 67 (63.8%) were males and 38 (36.2 %) were females. Age range was 18 to 85 years with mean of 55.8 +- 12.79 years. The distribution of the patients according to gender and age is presented in Table 1.

Tabel-1: Distribution of chronic kidney disease patients according to gender and age

Age (years)	Female		Male		Total	
	N	%	N	%	n	%
18-30	1	1	3	2.9	4	3.8
30-45	5	4.8	14	13.3	19	18.1
45-60	20	19	28	26.7	48	45.7
60-75	9	8.6	20	19	29	27.6
> 75	3	2.9	2	1.9	5	4.8
Total	38	36.2	67	63.8	105	100

Diabetes mellitus was the leading cause of CKD found in 55 (52.4 %) patients followed by hypertension in 35 (33.3%). Other causes of CKD were polycystic kidney disease 1 (1.0%), chronic glomerulonephritis 3 (2.9 %), NSAID misuse 1 (1.0%),

obstructive uropathy 3 (2.9%) and 7 (6.7%) unknown (Table2).

Eighty four (80.0%) CKD patients belonged to stage 5 followed by 17 (16.2%) to stage 4 and 4 (3.8%) to stage 3a (Table 3).

Table-2: Spectrum of chronic kidney disease according to cause

Causes	Frequency (n)	Percentage (%)
Polycystic kidney disease	1	1.0
Chronic glomerulonephritis	3	2.9
Diabetes Mellitus	55	52.4
Hypertension	35	33.3
NSAID misuse	1	1
Obstructive uropathy	3	2.9
Unknown	7	6.7

Table-3: Distribution of patients according to CKD stages

CKD Stage	Frequency (n)	Percentage (%)
1	0	0.0
2	0	0.0
3a	0	0.0
3b	4	3.8
4	17	16.2
5	84	80.0
Total	105	100

Thirty eight (36.2%) CKD patients had low FT3 values (3 from stage 4 and 35 from stage 5) and 35 (33.3%) had low FT4 (1 from stage 3a, 12 from stage 4

and 22 from stage 5). Seventy two (68.6%) CKD patients had normal TSH values, 31 (29.5%) had

increased and 2 (1.9%) had decreased TSH values (Table 4).

Table-4: Distribution of patients having normal and deranged FT3, FT4 and TSH

Thyroid Profile	Normal		Increased		Decreased	
	n	%	N	%	N	%
FT3 (3.1-6.8pg/ml)	65	61.9	2	1.9	38	36.2
FT4 (12-22 ng/dl)	68	64.8	2	1.9	35	33.3
TSH (0.27-4.2 uIU/ml)	72	68.6	31	29.5	2	1.9

DISCUSSION

Hypothyroidism is sometimes overlooked and remains undiagnosed due to its non-specific symptoms. In the third National Health And Nutrition Examination Survey (NHANES III) in United States the data of 14623 adult participants revealed that the prevalence of hypothyroidism increased with reduced GFR, 10.9% occurrence in stage 2 CKD, 21% in stage 3 and 23.1% in stage 4 or 5 CKD. There was an independently high risk of hypothyroidism in stage 2-5 CKD patients [6].

In addition, some studies suggest that abnormal thyroid hormone levels that are low T3 syndrome in patients on chronic hemodialysis are also independent predictors of cardiovascular as well as all-cause mortality, possibly due to chronic inflammation [7].

Although some studies have demonstrated that restoration of euthyroidism has a beneficial effect on cardiac function in patients with subclinical hypothyroidism, whether to treat Subclinical Hypothyroidism or not is an issue of debate.

In Primary Hypothyroidism patients reduction in RPF and GFR, increase in serum creatinine concentration and hyponatremia are frequently observed [9, 10] and these are normalized by replacement of thyroid hormone [11, 12].

Our study showed that the prevalence of hypothyroidism was 29.5 %. A similar study conducted by Gupta *et al.* showed the prevalence of thyroid dysfunction as 25% [13]. Our findings suggest that regular screening of thyroid function tests needs to be done in patients with CKD, which may further help to prevent CVD risk.

REFERENCES

- Szkudlinski MW, Fremont V, Ronin C, Weintraub BD. Thyroid-stimulating hormone and thyroid-stimulating hormone receptor structure-function relationships. *Physiological reviews*. 2002 Apr 1;82(2):473-502.
- Kaptein EM. Thyroid function in renal failure. *Contrib nephrol*. 1986;50:64-72.
- Basu G, Mohapatra A. Interactions between thyroid disorders and kidney disease. *Indian journal of endocrinology and metabolism*. 2012 Mar;16(2):204.
- Katz AI, Lindheimer MD. Renal sodium and potassium activated adenosine triphosphatase and sodium reabsorption in the hypothyroid rat. *J Clin Invest*. 1973;52:796-804.
- Del Compare JA, Aguirre JA, Ibarra FR, Barontini M, Armando I. Effects of thyroid hormone on the renal dopaminergic system. *Endocrine*. 2001 Aug 1;15(3):297-303.
- Lo JC, Chertow GM, Go AS, Hsu CY. Increased prevalence of subclinical and clinical hypothyroidism in persons with chronic kidney disease. *Kidney international*. 2005 Mar 1;67(3):1047-52.
- Carrero JJ, Qureshi AR, Axelsson J, Yilmaz MI, Rehnmark S, Witt MR, Bárány P, Heimbürger O, Suliman ME, Alvestrand A, Lindholm B. Clinical and biochemical implications of low thyroid hormone levels (total and free forms) in euthyroid patients with chronic kidney disease. *Journal of internal medicine*. 2007 Dec;262(6):690-701.
- Biondi B, Palmieri EA, Lombardi G, Fazio S. Effects of subclinical thyroid dysfunction on the heart. *Annals of internal medicine*. 2002 Dec 3;137(11):904-14.
- Iglesias P, Diez JJ. Thyroid dysfunction and kidney disease. *European journal of endocrinology*. 2009 Apr 1;160(4):503-15.
- Mariani LH, Berns JS. The renal manifestations of thyroid disease. *Journal of the American Society of Nephrology*. 2012 Jan 1;23(1):22-6.
- Den Hollander JG, Wulkan RW, Mantel MJ, Berghout A. Correlation between severity of thyroid dysfunction and renal function. *Clinical endocrinology*. 2005 Apr;62(4):423-7.
- Villabona C, Sahun M, Gómez N, Gómez JM, Soler J, Roca M, Mora J, Puchal R. Blood volumes and renal function in overt and subclinical primary hypothyroidism. *The American journal of the medical sciences*. 1999 Oct 1;318(4):277-80.
- Gupta AK, Kuldeep K, Virmani SK, Arora Mayank. Thyroid dysfunction in patients of Chronic Kidney disease. *Int J Adv Med*. 2017. Oct ;4 (5) :1333-1337.