

Thyroid dysfunction in patients with chronic kidney disease undergoing maintenance hemodialysis

Vishal Kalasker^{1,*}, Arun Kumar², Srinivas Rao³, Harish Bhat⁴

¹Professor, ^{2,4}Assistant Professor, ³Associate Professor, Dept. of Biochemistry, Navodaya Medical College & Research Centre, Raichur

***Corresponding Author:**

Email: vishalkalasker83@gmail.com

Abstract

Background: A thyroid dysfunction is a medical condition impairing the function of the thyroid. Chronic Kidney Disease (CKD) is a clinical syndrome that resulting from progressive loss of renal functions. A number of studies have shown that serum thyroid hormones levels are frequently abnormal in patients on regular maintenance hemodialysis. The present study was planned to compare the status of serum total T3, T4 & TSH in CKD patients on regular maintenance hemodialysis(HD) with that of controls.

Materials and Methods: The present study was conducted in the department of biochemistry, Navodaya Medical College, Raichur. 40 cases that were on regular maintenance hemodialysis treatment were selected and 40 controls were taken for study.

Results: The mean serum TSH & T3 concentration was 5.30 ± 10.63 & 1.63 ± 0.60 in CKD patients which was significantly increased than in controls (3.13 ± 1.94 & 1.97 ± 0.99). Serum concentration of T4 was less in cases (79.58 ± 24.31) than in controls (100.51 ± 18.47) but the results was statistically not significant ($P=0.083$).

Conclusion: In our study, the mean levels of total T3 and T4 decreased and TSH increased significantly in study group. Prevalence of subclinical hypothyroidism in HD patients is 12.5% compared to 0% in controls. The diagnosis of hypothyroidism can be easily missed in HD patients. The patients of chronic kidney disease on HD should be routinely screened for thyroid disorders.

Keywords: Hemodialysis, Chronic Kidney Disease, Thyroid Stimulating Hormone (TSH), Subclinical hypothyroidism, Thyroxine (T4), Triiodothyronine (T3)

Introduction

A thyroid dysfunction is a medical condition impairing the function of the thyroid. The thyroid produces T3 & T4 hormones having actions on metabolism, development, protein synthesis and reproduction. Thyroid disease may be subtle and both signs and symptoms of thyroid disease are often very nonspecific, hence thyroid function testing is an important element in assessing the patients with possible thyroid disease. Chronic Kidney Disease (CKD) is a clinical syndrome that results from progressive loss of renal function. Symptoms of CKD results not only from simple excretory failure but also from the onset of regulatory failure. CKD is defined as either kidney damage or $GFR < 60 \text{ ml/min/1.73 m}^2$ for at least 3 months.⁽¹⁾ The kidney plays an important role in metabolism, degradation and excretion of thyroid hormones. Any impairment in kidney function leads to disturbed thyroid physiology.⁽²⁾

Hemodialysis (HD) is the removal of certain elements from the blood by virtue of the difference in the rates of their diffusion through a semi permeable membrane by means of a hemodialysis machine or filter. Hemodialysis is the most common method used to treat advanced and permanent kidney failure. Maintenance hemodialysis is hemodialysis carried out at regular intervals to treat chronic renal failure. A number of studies have shown that serum thyroid hormones levels are frequently abnormal in patients on regular maintenance hemodialysis.⁽³⁾ The prevalence of

primary hypothyroidism mainly in the subclinical form increases with decreasing glomerular filtration rate.⁽⁴⁾ The present study was planned to compare the status of thyroid hormones, serum total T3, T4 & TSH in CKD patients on regular maintenance hemodialysis irrespective of their stage with that of controls.

Materials and Methods

The present study was conducted in the department of biochemistry, Navodaya Medical College, Raichur. The study was carried out for a period of 8 months from Nov 2015 to June 2016, ethical clearance was approved before the study. 40 cases that were on regular maintenance hemodialysis treatment were selected and 40 controls were taken for study. Age & sex matched controls with normal renal function and no previous H/O thyroid dysfunction were included in the study as controls. After taking the consent from cases and controls under strict aseptic precaution venipuncture was done and 3 ml blood was drawn into plain vacutainer and blood was allowed to clot and then centrifuged at 3000 rpm for 3 min to separate the serum, the sample was analyzed within 6 hours. The quantitative determination of serum T3, T4 & TSH was done by Enzyme linked immuno fluorescent assay (Minividas, Biomerieux, Germany). The assay principle combines a one step enzyme immunoassay sandwich method with a final fluorescent detection (ELFA). Serum urea and creatinine was estimated by urease/ glutamate dehydrogenase method

and modified Jaffe's alkaline picrate method A-15.^(5,6) respectively in fully automate analyzer Bio-systems

Statistical analysis: All continuous variables are expressed as mean± Standard Deviation. We compared the data of the controls with the study group using unpaired student t-test, the data generated from the study was analyzed by statistician, and we considered the $P \leq 0.05$ as significant.

Results

Comparison of measured parameters in healthy controls and CKD patients undergoing maintenance hemodialysis.

Parameters	Controls (n=40)	Cases(n=40)	P value
Triiodothyronine(T3) nmol/L	1.97±0.99	1.63±0.61	0.000*
Thyroxine (T4) nmol/L	100.51±18.47	79.58±24.31	0.083(statistically not significant)
Thyroid stimulating hormone (TSH) mIU /ml	3.13±1.94	5.30±10.63	0.010
Urea mg/dl	18.20±9.7	82.20±38.60	0.000*
Creatinine mg/dl	0.62±0.4	5.32±1.46	0.000*

*= Highly significant

There was a significant difference between the control and study group with respect to serum TSH & T3 levels, serum T4 levels were found to be not statistically significant. The serum TSH level was increased in 5 patients (12.5%) among those with CKD; the mean serum TSH concentration was 5.30 ± 10.63 in CKD patients which was significantly increased than in controls (3.13 ± 1.94). Serum T3 concentration was less than normal range in 7 of the 40 (17.5%) CKD patients, the mean serum total T3 concentration was 1.63 ± 0.60 in CKD patients was significantly lower than that in the control subjects (1.97 ± 0.99). Serum concentration of T4 was less in cases (79.58 ± 24.31) than in controls (100.51 ± 18.47) but the results was statistically not significant ($P=0.083$).

Discussions

Mean TSH levels are high compared to controls, even though in majority of cases TSH level still remains within the normal range. Our study shows increased TSH in patients who had low T3 and T4 suggesting maintenance of pituitary axis. This is in accordance with the studies conducted by G Avasthi et al & Joseph et al.^(7,8) In our study serum TSH concentration was significantly increased in 5 (12.5%) of CKD patients, similar findings were observed by Gilles R et al.⁽⁹⁾ Any impairment in kidney function leads to disturbed thyroid physiology; all levels of hypothalamic pituitary thyroid axis are involved including alterations in hormone production, distribution and excretion.⁽¹⁰⁾ There was more frequent subclinical hypothyroidism in patients on maintenance hemodialysis compared to control group (12.5% Vs 0%). In some studies there was no significant difference in mean TSH levels in patients on maintenance hemodialysis and healthy controls.⁽¹¹⁾ In uraemia the

mean values of both serum T3 and T4 were low, this is comparable to various studies done earlier.⁽¹²⁾ There are many factors leading to low T3 and T4 in patients undergoing Hemodialysis. Due to reduced deiodinase activity, reduced renal excretion and inorganic iodide generated by residual deiodinase activity accumulates in CKD, which reduces thyroid hormone synthesis.⁽¹³⁾ Increase in total body inorganic iodide can potentially block thyroid hormone production (Wolff-chaikoff effect). In addition, inflammatory cytokines such as TNF- α , IL-1 inhibits the expression of type-15' deiodinase which is responsible for the peripheral conversion of T4 to T3.

Many studies demonstrated a low T4 in CKD patients primarily because of an impaired protein Binding of T4. The accumulation of toxic uremic solutes alters the hypothalamic control of the pituitary gland and the TSH response to thyrotropin releasing hormone is subnormal in these patients. In recent studies it was shown that, the systemic inflammation and metabolic acidosis might alter the thyroid function in CKD patients.⁽¹⁴⁾ The minor increase in TSH levels (5 to 20 mU/l) observed in about 20% of uremic patients are usually not considered to be reflecting hypothyroidism. Thyroid hormone supplementation should not be initiated without substantial elevation in TSH levels and careful consideration.⁽¹⁵⁾ The clinical features of hypothyroidism are often masked with uremic state; hence it is necessary to conduct periodic screening of thyroid function in all hemodialysis patients. The early diagnosis and treatment of thyroid disease significantly reduce morbidity and mortality.

Conclusion

In our study, the mean levels of total T3 and T4 decreased and TSH increased significantly in study

group. Prevalence of subclinical hypothyroidism in HD patients is 12.5% compared to 0% in controls. The diagnosis of hypothyroidism can be easily missed in HD patients. Timely diagnosis and treatment of hypothyroidism may prevent deterioration of patient's condition and prolong survival. The thyroid disorders on HD patients are known to be strong risk factor for cardiovascular disease and predictor for all cause mortality. The patients of CKD on HD should be routinely screened for thyroid disorders.

References

1. National kidney foundation k/DOQI, clinical practice guidelines for chronic kidney disease; evaluation, classification and stratification, Am j. Kidney Dis 2002; 39 (suppl 1) S 1-266.
2. Lo JC, Chertow GM, Go AS and Hsu CY. Increase prevalence of subclinical and clinical hypothyroidism in persons chronic kidney disease. *Kidney Int*, 2005 Mar; 67(3):1047-52.
3. Lukinac L, Kusic Z, Kes P, Nothing-Hus D. effect of chronic hemodialysis on thyroid function tests in patients with end-stage renal disease. *Acta Med Croatica* 1996;50(2):65-8.
4. Chonchol M, Lippi G, Salvagno G, Zoppini G, Michele M, Giovanni T, prevalence of subclinical hypothyroidism in patients with chronic kidney disease. *Clin J Am Soc Nephrol* 2008;3(5):1296-1300.
5. Glutmann L, Bergmeyer HU. Methods of enzymatic analysis, ed Bergmeyer HU, Academic Press, NY, 1974;4:1794-98.
6. Peak M, Whitting M. Measurement of serum creatinine – current status and future goals. *Clin Biochem* 2006;27:173-84.
7. G Avasthi, S Malhotra, A P S Narang, S Sengupta. Study of thyroid function on patients of chronic renal failure. *Indian J Nephro*, 2001;11;165-9.
8. Joseph L J, Desai K B, Mehta H J, Mehta M N. Measurement of thyrotropin levels using sensitive immuno radiometric assays in patients with chronic renal failure. *Thyroidology* 1993;5:35-9.
9. Gilles R, Den Heijer M, Ross AH, Sweep FC, Hermus AR, Wetzels JF. Thyroid function in patients with proteinuria. *Neth J Med* 2008;66:483-5.
10. Lo JC, Chertow GM, Go As, Hsu CY. Increased prevalence of subclinical and clinical hypothyroidism in persons with chronic renal disease. *Kidney Int* 2005;67(3):1047-52.
11. Hegedus L, clinical practice; the thyroid nodule. *N Eng J Med*. 2004;351:1764-71.
12. Paqualini T, Zantieifer D, Balzaretto H, Granillo E, Patricia FD, Ramierz ZJ et al. evidence of hypothalamus pituitary thyroid abnormalities in children with end stage renal disease. *J Paed*. 1991;118:873-78.
13. Kaptein EM, thyroid hormone metabolism and thyroid diseases in in chronic renal failure. *Endocrine reviews*. 1996; 17(1):45-63.Epub 1996/02/01.
14. Zoccali C, Tripepi G, Cutrupi S, Pizzini P, Mallamaci F, Low triiodothyronine: a new facet of inflammation in end stage renal disease. *Journal of the American society of nephrology: JASN*. 2005;16(9):2789.Epub 2005/07/22.
15. Rodrigues MC, Santos GM, da silva CA, Baxter JD, Webb P, Lomri N et al. thyroid hormone transport is disturbed in erythrocytes from patients with chronic renal failure on hemodialysis. *Ren fail*. 2004;26:461-6.