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Original Article

# Thyroid dysfunctions in patients with chronic renal failure

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ABSTRACT

The present study was conducted to estimate thyroid hormone levels i.e. T3, T4& TSH and to study the thyroid dysfunctions in patients with chronic renal failure. 30 male patients of aged between 40-70yrs with serum creatinine> 5.5mg/dl & urea > 55mg/dl and dipstick test positive for protein with symptoms of chronic renal failure are taken in the study.Serum levels of T3, T4& TSH were analysed by using CLIA method and the data obtained by these patient were compared with data from normal individuals of same age group using student t test. It was found that Mean of T3, T4 decreases TSH increases significantly($P<0.05$) in cases compare to controls and There is 10% of patients of CRF i.e cases are hypothyroid compare to 0% in controls. There is no hyperthyroidism both in cases & controls.



## 1. Introduction

Chronic renal failure (CRF) refers to an irreversible deterioration in renal function which classically develops over a period of years. Initially it manifests' only as a biochemical abnormality eventually loss of excretory, metabolic & endocrine functions of the kidney. This leads to the development of the clinical symptoms & signs, which are referred to as uremia. When death is likely without renal replacement therapy it is called as End stage renal failure.

Patients with CRF often have signs & symptoms suggestive of thyroid dysfunctions. Various Studies of thyroid functions in uremic patients have been carried out which have shown conflicting results. Hyperthyroidism, hypothyroidism &euthyroid state have all been reported by various Workers[1,2]

Serum Tri-iodothyronine(T3) level were consistently found to be low, serum total &free thyroxine(T4) concentration have been reported as low, normal or high. Serum thyroid stimulating hormone (TSH) levels were found to be normal in most of the patients of CRF even in those whose CRF is complicated by low T3 concentration[3].

Serum hormonal concentration may be altered by changes in the binding capacity of serum proteins. In CRF there is massive proteinuria mainly albuminuria. Globulin levels are not much altered. Hypothyroidism in CRF is mainly due to decreased level of albumin & thyroid binding pre-albumin[4].

In CRF Circulating thyroid binding inhibitors are increased, which inhibits the binding of thyroid hormones to carrier proteins, It may be additional cause for hypothyroidism[5].

Duration & Severity of renal failure affects the Serum thyroid hormone levels. Restoration of normal functions with renal transplant resulted in normalisation of all parameters of thyroid function with exception of blunted or absent TSH response to TRH. The latter may be a direct Consequence of glucocorticoid administration[6,7].

Because of these variability in previous studies, A definite change in the thyroid hormone levels in CRF is yet to be determined. So study of thyroid hormone levels in CRF is taken.

## MATERIALS AND METHODS

The present study was undertaken in Al-Ameen Medical college and Hospital, both inpatients & outpatients and patients attending to dialysis unit. The study subjects are divided in to 2 groups as cases & controls.Cases: - 30 Male patients aged between 40-70 years of having history of chronic kidney disease with serum creatinine > 5.5 mg/dl and urea > 55mg/dl and dipstick test positive for protein with symptoms of chronic renal failure.

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Controls: - 30 Healthy men aged between 40 -70 years. Patients with diabetic nephropathy, patients on treatment with estrogen, corticosteroids, sulphonylurea, phenobarbitones & β-blocker, Female & children's are excluded from the study.

All the subjects i.e. both cases & controls were subjected to medical examination as per a fixed proforma. Morning sample blood was drawn after 12 hrs fasting. The samples of blood were allowed to stand to clot. Serum was separated by centrifugation, and analyzed by the following methods. Serum Urea Estimated by Diacetyl Monoxide Method (DAM, Method), serum creatinine is estimated by Jaffe's method, and Estimation of T3, T4 & TSH by Chemiluminesence immunoassay (CLIA) method.

The T3,T4 assay employs a competitive test principle with polyclonal antibodies specially directed against T3,T4. Endogenous T3,T4 released by the action of 8 anilino-1- naphthalene sulphonic Acid (ANS), competes with the added biotinylated T3,T4 derivate for the binding sites on the antibodies labeled with the ruthenium complex. The TSH assay employs monoclonal antibody specifically directed against human TSH. The antibodies labeled with ruthenium complex consist of chimeric construct from human & mouse specific components. As a result, interfering effects due to HAMA (human anti-mouse antibodies) are largely eliminated.Results are determined via calibration curve which is instrument specifically generated by 2 point calibration and a master curve provided via the reagent barcode.

**Statistical Methods**[8,9]Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. Student t- test is used to find out the correlation

co-efficient.Significant figures are,

+ Suggestive significance (P value: 0.05<P<0.10)

* Moderately significant (P value: 0.01<P 0.05)

** Strongly significant (P value: P0.01)

**RESULTS AND DISCUSSION**

Mean of blood urea levels in cases are 96.23±12.24 mg/dl and in controls are 28.47±8.40 mg/dl. The mean of serum creatinine in cases are 5.83±0.69 mg/dl and in controls are 1.07±0.17 mg/dl. The mean of blood urea and serum creatinine is high when compared to the controls. p value is <0.001 which is statistically significant.

Mean of $T_3$ levels in cases are 81.67±15.07 ng/dl and in controls are 111.96±10.17 ng/dl. The mean of T3 in all 30 cases is decreased when compared to controls even though most of them are within the normal range. p value is <0.001 which is statistically significant.

Ramirez Get alconductedThyroid function studies in clinically euthyroid uremic dialysis patients found decrease levels of tri-iodothyronine,[10].Lim VS et al studied the Thyroid function in chronic renal disease also found that decrease levels of serum tri-iodothyronine levels [11]. This reduction in $T_3$ concentration has been linked to the decrease in the peripheral synthesis of $T_3$ from $T_4$,[12]. Recent studies have demonstrated a reduction in serum concentration of total tri-iodothyronine ($T_3$) in uremic patients, since more than half of circulating $T_3$ is derived from conversion of thyroxine $T_4$ To $T_3$ in periphery[13,14].

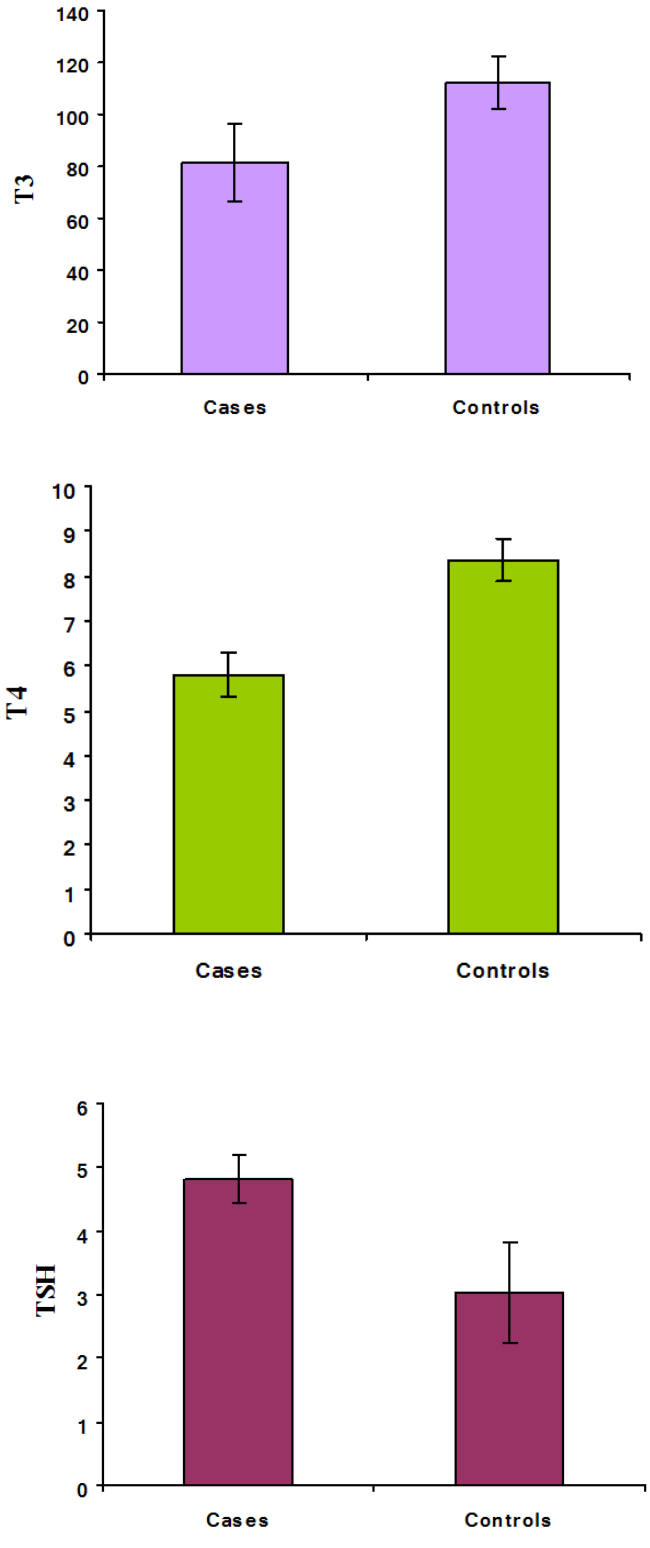
The mean of T4 level in cases are 5.80±0.50µg/dl and in controls is 8.36±0.46µg/dl. The mean of $T_4$ in all 30 cases is decreased when compared to the controls, p value is <0.001 which is statistically significant. Neuhaus et al. have reported low T4 values, when found in renal insufficiency, may be secondary to low serum albumin & pre-albumin[4].Joasso et.al. Found that uremic patients had low serum $TT_4$& elevated $T_3$ resin uptake suggesting a decrease in TBG. However actual measurement of TBG was normal. They postulated that uremic toxins might have displaced T4 from TBG[15].Study conducted by Victoria Sy Lim et. Al[16].patients whose TBG capacity was decreased, their $TT_4$ was always low, but low $TT_4$ was not necessarily accompanied by a reduction in TBG capacity, suggesting that factor other than decreased binding might, in part, be responsible for the slightly decreased serum $TT_4$ concentration. The reduction in $T_4$ is attributed to the presence of circulating inhibitors, which impairs binding of $T_4$ to thyroxine binding globulin[5].

The mean of TSH level in cases are 4.81±0.38µIU /mland in controls is 3.02±0.79µIU /ml.Mean of TSH in cases increases compare to controls. P value is <0.001. which is statistically significant. Studies conducted by G. Avasthi-et.al,[3] Joseph et.al[17]shows increased TSH in those patients who had low $T_3$, $T_4$& $FT_4$ suggesting maintenance of pituitary thyroid axis. The absence of TSH elevation is generally regarded as evidence against hypothyroidism, yet hypothalamo-pituitary dysfunction may also present suggested by the subnormal TSH response to TRH. Blunted TSH after TRH administration was also reported by Alvarez-ude-et.al[18],Czernichow et.al[19].

**Table - 1Comparison of study parameters in cases and controls (mean ±SD)**

| Study variables | Cases | Controls | P value |
|---|---|---|---|
| Blood urea (mg/dl) | 96.23±12.24 | 28.47±8.40 | <0.001** |
| S. creatinine (mg/dl) | 5.83±0.69 | 1.09±0.17 | <0.001** |
| $T_3$ | 81.67±15.07 | 111.96±10.17 | <0.001** |
| $T_4$ | 5.80±0.50 | 8.36±0.46 | <0.001** |
| TSH | 4.81±0.38 | 3.02±0.79 | <0.001** |

**Figure:**
**Graph - 1**
**Comparison of study parameters in cases and control**

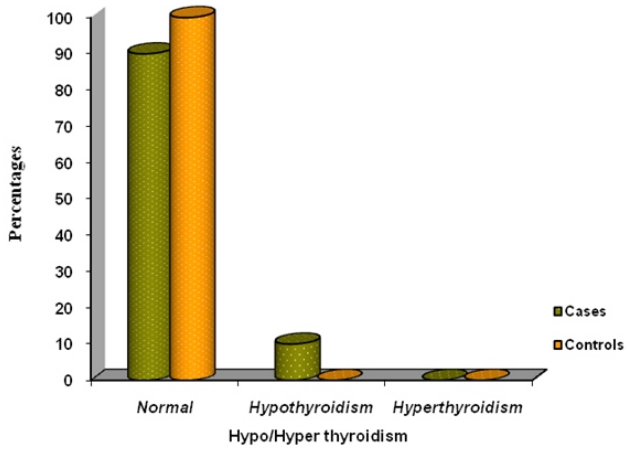



In this study 3 patients (i.e 10% of cases) among 30 cases have T3, T4 levels below normal range and TSH above the normal range. These 3 patients are hypothyroid, compared to none among control groups. The remaining 27 patients that is 90% of cases are euthyroid. There is no hyperthyroid in both cases and controls. In this study, findings are comparable with previous studies. Prevalence of hypothyroidism in patients with terminal renal failure is 5%, in comparison with that in hospitalized patients with normal renal function [20].CKD is associated with higher prevalence of hypothyroidism, both overt and subclinical, but not with hyperthyroidismI[21]. In fact, the prevalence of primary hypothyroidism is mainly in the subclinical form, which increases as GFR decreases[12].

**Table - 2. Incidence of hypothyroidism and hyperthyroidism**

| Hypo/Hyper thyroidism | Cases | Controls |
|---|---|---|
| Normal | 27 (90.0%) | 30(100.0%) |
| Hypothyroidism | 3 (10.0%) | 0 |
| Hyperthyroidism | 0 | 0 |
| Total | 30(100.0%) | 30(100.0%) |

**Graph - 2**
**Incidence of hypothyroidism and hyperthyroidism**




## CONCLUSION

From the above study we finally concluded that Mean of $T_3$, $T_4$ decreases TSH increases significantly in cases compare to controls. There is 10% of patients of CRF i.e cases are hypothyroid compare to 0% in controls. There is no hyperthyroidism both in cases & controls.

## REFERENCES

[1] Yashpal et al. Thyroid function in uremia. Ind J Nephrol (New Series) 1991: 1; 2 vol. 1, no. 2. April June, 1991.

[2] Spector DA, Davis PJ, Helderman JH et al. Thyroid function and metabolic state in chronic renal failure. Ann Int Med 1976: 85; 724-30.

[3] G Avasthi, S Malhotra, APS Narang, S Sengupta. Study of thyroid function on patients of chronic renal failure. Indian J Nephro, 2001: 11; 165-169.

[4] K Neuhaus, G Baumann, A Walter and H Tholen Serum thyroxine and thyroid binding proteins chronic renal failure. J of Clinical endocrinology and metabolism, 1975: 41; 395-398.

[5] Nephrology division. Dept of Internal Medicine, University Lowa, Lowa city, IA, USA. Thyroid function in patients with chronic renal failure. Amj kidney dis, oct, 2001: 38,4 (supp 1): 580-4 links.

[6] Kohli HJ, Mahajan SK Karla OP. Malhotra KC. Thyroid status in chronic renal failure. Indian J Nephrology.1993:vol 3(2); 32-36.

[7] Mehta HJ et al. Total free thyroid hormone levels in chronic renal failure. Journal postgraduate Medicine. 1991: vol 37; issue 2,79-83.

[8] Bernard Rosner (2000), Fundamentals of Biostatistics, 5th Edition, Duxbury, page 80-240.

[9] Sunder Rao P S S, Richard J (2006): An Introduction to Biostatistics, A manual for students in health sciences, New Delhi: Prentice hall of India. 86-160.

[10] Ramirez G,O Neill WM, Jubiz w, Bloomer HA. Thyroid dysfunction in uremia; Evidence with thyroid and hypophyseal abnormalities. Ann Int Med 1976: 84; 672.

[11] Lim VS, Fang VS, Katz AI.Thyroid function in chronic renal disease. journal of clinical investigation 1977: 60; 522-34.

[12] Lo JC, Chertow GM, Go AS and Hsu CY. Increased prevalence of subclinical and clinical hypothyroidism in persons with chronic kidney disease.Kidney international 2005: 67; 1047-52.

[13] Braverman L.E., S.H.Ingbar and K.Sterling 1970. Conversion of T4 to T3 in athyrotic human subjects.J.Clin.Invest. 49; 855-64.

[14] Pittman CS , JB Chambers jr, VH Read 1971. The extrathyroidal conversion rate of Thyroxine and tri-iodothyronine in normal man. J.Clin.Invest. 50; 1187-96.

[15] Jasso AI, PC Murray, J Parkin, MR Robertson 1974, Abnormalities of in vitro thyroid function tests in renal failure. QJ Med 43; 245-61.

[16] Lim VS, Fang VS, Katz AL, Refetoffs. Thyroid dysfunction in chronic renal failure. J Clin Invest. Sept, 1977: 66(3); 522-534.

[17] Joseph L.J, Desai K.B, Mehta H.J, Mehta M.N et al. Measurement of thyrotrophin levels using sensitive immunoradiometric assays in patients with chronic renal failure.Thyroidology 1993: 5; 35-39.

[18] Alvarez Ude, F.A Gomez D.C. Evered.1975 Pituitary response to thyrotrophin releasing hormone in patients with chronic renal failure. Int Cong Nephrl 6th 883.

[19] Czernichow, P M S Dautez, M.Broyer and R.Rappaport 1976. Abnormal TSH PRL GH response to TSH releasing factor in chronic renal failure J.ClinEndocrinolMetab 43; 630-637.

[20] Quion-Verde H, Kaptein EM, Choolijan CJ, Radriquez HJ, Massary SG, Prevalence of thyroid disease in chronic renal failure(CRF) and dialysis patients. Los Angeles: 9th IntCongr of Nephrol Abstract 1984: 120.

[21] Kaptein EM, Thyroid hormone metabolism and thyroid disease in chronic renal failure. Endocrine reviews 1996: 17; 45-63.