

To Study the Prevalance of Proteinuria in Severe Hypothyroidism

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Abstract

Background and Aim:

Hypothyroidism is common medical condition with elevated TSH level. It may associate with reversible reduction in estimated glomerular filtration rate which results in decline in renal function. Many experimental studies assessed association of hypothyroidism with proteinuria and impact of its treatment on proteinuria.

Materials and methods: A Hospital based study was done on patients of severe hypothyroidism fitting in inclusion and exclusion criteria attending the OPD/IPD of Mahatma Gandhi Hospital, Jaipur, Rajasthan, India.

Results: On comparison of urine protein at baseline and follow up using t test, statistically significant difference was found and eGFR also improved at baseline and follow up comparison.

Conclusion: We came to the conclusion that primary hypothyroidism is linked to higher protein excretion in the urine. This observation indirectly points to a considerable effect of thyroid hormones on renal protein processing and metabolism. It is conceivable that severe hypothyroidism may be a potentially modifiable component in a variety of proteinuric renal disorders given that proteinuria considerably decreased with medication.

Key words: proteinuria, severe primary hypothyroidism, glomerular filtration rate, 24 hours urine protein, thyroid function test,

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I. Introduction:

Thyroid hormones are essential for growth, development, and metabolic homeostasis.[1].

Hypothyroidism is a common medical disorder in which serum T3, T4 level decreased and serum TSH level increase due to negative feed-back mechanism. Hypothyroidism has many metabolic effects like heart dysfunction [2] due to reduced myocardial contractility, which leads to reduced stroke volume and bradycardia; dyslipidemia, accelerated atherosclerosis, hypertension (diastolic) due to increase peripheral resistance [5], insulin resistance which ultimately increase the risk of heart failure, cardiovascular disease and mortality [3,4]

In many cases muscular symptoms with creatine phosphokinase (CPK) was found. Myopathy might play some degree of role in hypothyroidism induced renal dysfunction (reduced GFR). There might be reduction in glycolysis oxidative phosphorylation which leads to reduction in adenosine triphosphate concentration. This impaired muscle energy metabolism leads to elevation of CPK and myoglobin level, which could cause renal tubule obstruction. Due to decreased activity of Na/K ATPase these is net reduction in sodium and bicarbonate reabsorption which results in defective urinary acidification. It's association with renal dysfunction may be due to reduced GFR (reversible) [5] because of decreased cardiac output (negative inotropic and chronotropic effect) [6], intrarenal vasoconstriction, reduced renal response to vasodilators like vascular endothelial growth factor (VEGF) and insulin likegrowth factor-1 (IGF-1)

Serum creatinine level elevate in short period of hypothyroidism and renal function improves

significantly shortly after initiation of treatment.

Hypothyroidism also results in increased glomerular capillary permeability to proteins. Thesequent proteinuria precedes the reduction in GFR in hypothyroidism.

In this study, we will prospectively analyse the changes of renal function after short- term thyroid replacement therapy in hypothyroid patients and correlation between renal and thyroid function.

II. Materials And Methods

This is a hospital based observational study. It was conducted in Department of General Medicine, Mahatma Gandhi Medical College & Hospital, Jaipur, Rajasthan, India. A total of 51 cases of severe hypothyroidism were considered as sample size.

Inclusion Criteria: Diagnosed cases of severe primary hypothyroidism irrespective of etiology, age 18 years and above and serum thyrotropin (TSH) greater than 50 uIU/mL and given written consent for the study.

Exclusion Criteria: Patients who have not given written consent, Patients with pre-existing CKD, history of AKI, Patients with diabetes mellitus, hypertension, drug allergy, Patients with malignancy, having undergone organ transplantation, Patients with renal or urinary tract stones or surgery, Patients with pregnancy, lactation.

III. Results

Table 1: Gender distribution among the study subjects

Gender	N	%
Male	18	35.29
Female	33	64.71
Total	51	100

Table 2: Age distribution among the study subjects

Age Group (in years)	N	%
18-30	16	31.37
31-45	10	19.61
46-60	12	23.53
>60	13	25.49
Total	51	100

Table 3: Descriptive analysis of thyroid profile

Variables	Minimum	Maximum	Mean	SD
T3	.21	1.80	.74	.31
T4	.10	9.40	1.37	1.85
TSH	49.8	762.0	222.74	185.52

Table 4: Prevalence of proteinuria among the study subjects

Proteinuria	N	%
Present	10	19.61
Absent	41	80.39

Table 5: Comparison of 24-h urine protein (mg/d) at baseline and follow up

Urine Protein (mg/d)	Mean	SD	t test	p value
Baseline	221.52	137.63	7.01	<0.01*
Followup	108.21	106.44		

*: statistically significant

Table 6: Comparison of eGFR, mL/min/1.73 m² at baseline and follow up

eGFR	Mean	SD	t test	p value
Baseline	82.55	26.17	6.83	<0.01*
Followup	106.29	21.08		

Table 7: Comparison of total cholesterol, mg/dL at baseline and follow up

eGFR	Mean	SD	t test	p value
Baseline	237.61	68.63	6.79	0.006*
Followup	183.76	61.25		

IV. Discussion:

The association of hypothyroidism with reversible change in GFR has been well documented in the literature. A gradual fall in estimated GFR (eGFR) and reversibility with thyroid hormone replacement therapy in hypothyroidism means the majority of patients with hypothyroidism and reduced eGFR would qualify for a diagnosis of kidney disease. Increased urinary excretion of protein is not only used for diagnosis of kidney disease but is also associated with a higher risk of progression of disease. Proteinuria is usually due to functional alterations in protein handling at the glomerular filtration and/or tubular levels. Recently, hypothyroidism has been shown to be associated with excess proteinuria, an important clinical manifestation of kidney disease, in cross-sectional data. Though a few case reports have documented reversible proteinuria in hypothyroidism, it has not been studied systematically.

Hence the present hospital based observational study was conducted from January 2021 to December 2022 in the Department of General Medicine, Mahatma Gandhi Medical College & Hospital, Jaipur among 51 patients of severe hypothyroidism outpatients and inpatients attending our institute. The aim of the study was to find the prevalence of proteinuria in patients of severe hypothyroidism and to analyze effect of thyroxine hormone therapy on 24hour urine protein excretion and eGFR change in severe hypothyroid patients.

Gender: Out of 51 subjects, 64.71% were females and 35.29% were males. Hence there was female dominancy in this study.

Age: Maximum subjects in this study were from age group of 18-30 years (31.37%) followed by >60 years (25.49%) and 46-60 years (23.53%). Minimum subjects were from age group of 31-45 years (19.61%) in this study.

Investigative Profile: Mean±SD T3, T4, TSH was .74±.31, 1.37±1.85 and 222.74±185.52 respectively in this study.

eGFR: Mean eGFR, mL/min/1.73 m² at baseline was 82.55±26.17 and it increased to 106.29±21.08 at followup. When eGFR, mL/min/1.73 m² was compared at baseline and follow up using t test, statistically significant difference was found in this study.

It has been shown that measured GFR decreases in patients with hypothyroidism and increases with thyroid replacement. This is due to decreased renal blood flow in hypothyroidism that leads to a fall in GFR. Thyroid replacement increases intravascular volume, which in turn leads to an increase in cardiac output, renal blood flow, and subsequently GFR.

Total Cholesterol: Mean total cholesterol, mg/dL at baseline was 237.61±68.63 and it decreased to 183.76±61.25 at followup. When total cholesterol, mg/dL was compared at baseline and follow up using t test, statistically significant difference was found in this study.

Proteinuria: In this study, prevalence of proteinuria was reported among 19.61% of the subjects.

Urine Protein: Mean urine protein (mg/dl) at baseline was 221.52 ± 137.63 and it decreased to 108.21 ± 106.44 at followup. When urine protein was compared at baseline and follow up using t test, statistically significant difference was found in this study.

Except for the diagnosis of severe primary hypothyroidism, the selected study population seemed to be otherwise healthy and young. Therefore, the likelihood of study results being confounded by participant selection or background kidney disease is very low in our study.

The current data set is small and includes patients with very high circulating TSH levels. Whether the same observations would be present in individuals with relatively milder degrees of hypothyroidism is not known. There is a possibility that changes, even if present, may not be clinically significant. However, it is important to explore these observations to advance understanding of thyroid hormone action and physiology.

V. Conclusion:

The conclusion of this study was that primary hypothyroidism is linked to higher protein excretion in the urine. This observation indirectly points to a considerable effect of thyroid hormones on renal protein processing and metabolism. It is conceivable that severe hypothyroidism may be a potentially modifiable component in a variety of proteinuric renal disorders given that proteinuria considerably decreased with medication.

This study showed that levels and incidence of hypothyroidism were considerably higher in persons with proteinuria.

Future research should concentrate on how proteinuria and renal dysfunction are improved by hypothyroidism treatment, and vice versa. In addition, clinical practice needs to acknowledge the link between hypothyroidism and proteinuria. Thyroid function should be assessed in patients with newly developed proteinuria, and if increased TSH is found, hormonal supplementation should be begun. Conversely, when dealing with patients who have significant proteinuria, practitioners should interpret thyroid function tests cautiously.

References

- [1]. Iglesias P, Bajo MA, Segas R, diez JJ. Thyroid dysfunction and kidney disease: an update. *Rev Endocr Metab Disord.* 2017 Mar; 18(1): 133-44.
- [2]. Brenta G, Mutti LA, Schnitman M, Fretes O, Perrone A, Matute ML. Assessment of left ventricular diastolic function by radionuclide ventriculography at rest and exercise in subclinical hypothyroidism, and its response to L-thyroxine therapy. *Am J Cardiol.* 2003 Jun;91(11):1327-30.
- [3]. Razvi S, Weaver JU, Vanderpump MP, Pearce SH. The incidence of ischemic heart disease and mortality in people with subclinical hypothyroidism: reanalysis of the Whickham Survey cohort. *J Clin Endocrinol Metab.* 2010 Apr;95(4):1734-40.
- [4]. Walsh JP, Bremner AP, Bulsara MK, O'Leary P, Leedman PJ, Feddema P, et al. Subclinical thyroid dysfunction as a risk factor for cardiovascular disease. *Arch Intern Med.* 2005 Nov;165(21):2467-72.
- [5]. Falk SA, Buric V, Hammond WS, Conger JD. Serial glomerular and tubular dynamics in thyroidectomized rats with remnant kidneys. *Am J Kidney Dis.* 1991 Feb;17(2):218-27.
- [6]. Vargas F, Moreno JM, Rodriguez-Gomez I, et al: Vascular and renal function in experimental thyroid disorders. *Eur J Endocrinol* 2006; 154: 197-212.

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