



Biochemical Assessments of Thyroid Profile and Renal Function Test in Chronic Kidney Disease

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ABSTARCT

Introduction: CKD is a clinical syndrome which occurs due to irreversible loss of renal function leading to metabolic, endocrine, excretory and synthetic function resulting in accumulation of non – protein nitrogenous substances which leads to metabolic derangements and ends up with distinct clinical manifestations.

Aim: To study thyroid function abnormalities in patients with chronic kidney disease. To correlate the thyroid function abnormalities with severity of renal failure. To differentiate primary hypothyroidism from thyroid dysfunction due to chronic kidney disease.

Methodology: After selection of patients, fulfilling the above criteria, about 5 ml of blood sample is collected in non-heparinised serum bottle and sent for thyroid profile test. Components of thyroid profile included in our study and Quantitative determination of T3, T4 and TSH is done by Enzyme Linked Immunosorbent Assay.

Result: In our study out of 50 patients, 33 patients had low serum T3 levels . 4 patients among low serum T3 value, they also had low T4 and high TSH suggesting primary hypothyroidism. So excluding 4 patients of hypothyroidism 29 patients had low T3 syndrome in our study. Low T4 levels in our study, out of which 4 patients had low T3 and high TSH suggesting primary hypothyroidism.

Conclusion: In my study population, 50 CKD patients who were on conservative management were studied. Among them 66% of the patients had low T3 values. The change in the serum levels of T3 and T4 in patients with CKD can be considered as being protective, promoting conservation of protein. There is increase in incidence of hypothyroidism in patients with chronic kidney disease.

KEYWORDS: Chronic Kidney Disease, Glomerular Filtration Rate, Thyroid Stimulating Hormone

INTRODUCTION

Chronic kidney disease includes a spectrum of distinct pathophysiological processes which is associated with abnormal kidney function and a progressive reduction in glomerular filtration rate^{1, 2}.

CKD is a clinical syndrome which occurs due to irreversible loss of renal function leading to metabolic, endocrine, excretory and synthetic function resulting in accumulation of non – protein nitrogenous substances which leads to metabolic derangements and ends up with distinct clinical manifestations.

End stage renal disease is described as a terminal stage of chronic kidney disease that without any replacement therapy patients could not survive would result in death.

In spite of diverse etiologies, CKD is the final common pathway of irreversible loss of nephrons finally resulting in alteration of “milieu interior” affecting every system in the body including thyroid hormonal system.

The functions of thyroid and kidney are interrelated³⁻⁶. The thyroid hormones are essential for growth and development of the kidney and for maintaining electrolyte and water homeostasis. On the other hand, kidney has its vital role in metabolism and elimination of thyroid hormones.

In CKD patients reduction of renal function leads to change in the synthesis, secretion, metabolism and elimination of thyroid hormone. And also treatment strategies of one organ affect the other organ.

The kidney helps in the clearance of iodine mainly by glomerular filtration. So excretion of iodine is reduced in advanced renal failure. Impaired renal clearance of iodine leads to elevated serum levels of inorganic iodide that potentially blocks thyroid hormone



production resulting in “Wolff Chaikoff” effect.

Chronic kidney disease is associated with thyroid function abnormalities leading to low levels of serum total and free T3 concentration and normal reverse T3 and free T4 levels. The TSH levels are almost normal in most patients and found to be in euthyroid state.

CKD patients may have various symptoms and signs suggestive of hypothyroidism like cold intolerance, dry coarse skin, sallow complexion, lethargy, fatigue, edema, reduced basal metabolic rate, alopecia, hyporeflexia and asthenia. So it is difficult to exclude thyroid function abnormality in patients with chronic kidney disease merely on clinical background.

Various studies have been conducted to study thyroid function abnormalities in chronic kidney disease patients. All abnormalities like hypothyroidism, hyperthyroidism and euthyroid state have been reported in the studies done previously.

The relation between severity of renal failure and thyroid dysfunction is not clear. The estimated problem of hypothyroidism is between 0-9 percent in end stage renal disease. In ESRD increased prevalence of thyroid swelling (goitre) has also been noted.

AIM AND OBJECTIVES

1. To study thyroid function abnormalities in patients with chronic kidney disease.
2. To correlate the thyroid function abnormalities with severity of renal failure.
3. To differentiate primary hypothyroidism from thyroid dysfunction due to chronic kidney disease.

REVIEW OF LITERATURE

Chronic kidney disease (CKD)¹ encompasses a spectrum of different pathophysiologic processes associated with abnormal kidney function, and a progressive decline in glomerular filtration rate (GFR).

PHYSIOLOGY OF THYROID HORMONES

The principal hormones secreted by thyroid gland are T3 (Triiodothyronine) and T4 (Thyroxine). Thyroid hormones play a vital role in cell differentiation during development and maintain metabolic homeostasis in adults⁵. The secretion of T3 and T4 are mainly controlled by Thyroid Stimulating Hormone. Thyrotropin releasing hormone (TRH) stimulates the secretion of T3 and T4. The hypothalamic secretion TSH and pituitary secretion of TRH are under negative feedback control of free T4 and free T3.⁶

Once the thyroid hormones are secreted into the blood, most of T3 and T4 binds with plasma proteins namely, thyroxine – binding globulin and thyroxine – binding prealbumin and albumin. T4 mainly binds with thyroxine – binding globulin whereas T3 binds mainly with albumin. The plasma binding proteins delays hormonal clearance, increases the circulating pool and helps in regulating hormonal delivery to selected tissue sites. The rest of the thyroid hormones are transported in unbound form as free T3 and free T4. In circulation bound forms are in equilibrium with free forms.^{6,7}

In non thyroid illness, fall in serum T3 level (both total and free T3) along with raise in reverse T3 is seen. As disease progresses, fall in serum total T4 is also seen, a condition called ‘low T3 T4 State’. Free T4 remains normal or reduced. Although there is fall in T3 and T4, serum TSH remains either normal or reduced which differentiates it from primary hypothyroidism. Many studies have shown that there is mild elevation of TSH in absence of hypothyroidism in non-thyroidal illness⁸

HYPOTHYROIDISM

Hypothyroidism is caused by reduced secretion of thyroid hormones. It leads to cretinism in children and myxedema in adults. Hypothyroidism can be either primary or secondary. There is intrinsic defect in thyroid gland in primary hypothyroidism whereas it is secondary to hypothalamic or pituitary defect in secondary hypothyroidism.⁹

Non Thyroidal Illness:¹⁰⁻¹¹

Various conditions predominantly affect serum T3 level, with no intrinsic disease of Thyroid gland. This is termed as ‘Low T3 Syndrome’, ‘Non Thyroid Illness syndrome’, ‘Sick euthyroid syndrome’

NORMAL KIDNEY:^{12,13}

The kidneys are bean shaped paired retroperitoneal organs located in the lumbar region in the posterior part of the abdomen on either side of the vertebral column. The upper pole of each kidney lies opposite the 12th thoracic Vertebra¹⁶ and the lower



pole of each kidney lie opposite .The third lumbar vertebra. The weight of each kidney is about 125 to 170 grams in male 115 to 155 grams in females¹⁴. The length of each kidney is about 11 to 12 cms, breadth is about 5.0 to 7.5 cms, and thickness is about 2.5 to 3.0 cms.

CHRONIC KIDNEY DISEASE¹⁵

Definition

➤ Evidence of kidney damage for more than or equal to three months as described by anatomical or physiological abnormalities of the kidney, with or without reduced GFR.GFR less than 60 ml/min/1.33m² for more than or equal to three months with or without other signs of kidney damage.

Stages of CKD^{15,16}

Stage	Description	GFR (mL/min/1.73 m ²)
1	Kidney damage With normal or ↑ GFR	≥90
2	Kidney damage With mild ↓ GFR	60–89
3	Moderate ↓ GFR	30–59
4	Severe ↓ GFR	15–29
	Kidney failure	<15 (or dialysis)

Chronic kidney disease is defined as either kidney damage or GFR <60 mL/min/1.73 m² for ≥3 months. Kidney damage is defined as pathologic abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies.

KDIGO: The Kidney Disease Improving Global Outcomes, CKD: Chronic kidney disease, GFR: Glomerular filtration rate

THYROID AND KIDNEY

Thyroid hormones play a vital role in renal development and physiology^{17,18,19,20,21}. On the other hand kidney disease can lead to thyroid dysfunction.

Effects of thyroid hormone on renal development:

It helps in protein synthesis and cell growth. The functioning renal mass (kidney to body mass ratio) is affected by thyroid hormone. In hypothyroidism the ratio is reduced, increased in hyperthyroidism whereas protein breakdown and ultimately renal atrophy occurs in severe hyperthyroidism²². Thyroid hormone increases the activity of Na-P co-transporter, Na-H exchanger⁵⁰ and Na/K ATPase in the proximal convoluted tubule.

Effect of thyroid hormone on renal physiology:

Thyroid hormones have both direct and indirect effects on renal function. The indirect effect is mediated on cardiovascular system and renal blood flow. The direct effects are mediated on glomerular filtration rate, tubular secretory and reabsorptive function and hormonal influences.

The thyroid hormone increases the activity of Na/K/ATPase on proximal convoluted tubule and also increases sodium reabsorption. Thyroid hormones also influences on tubular potassium permeability and tubular calcium reabsorption²³. By adrenergic regulation²⁴ thyroid hormones also affect the renin angiotensin aldosterone axis and helps in renin release.²

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