

# **Thyroid Function Tests in relation to Glomerular Filtration Rate in patients with Chronic Kidney Disease**

**Thesis  
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of the master degree of internal medicine**

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قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا  
إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ  
الْعَلِيمُ الْحَكِيمُ

صدق الله العظيم

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## *List of Abbreviations*

<b>ACE</b>	Angiotensin converting enzyme
<b>ACR</b>	Albumin to clearance ratio
<b>AER</b>	Albumin excretion rate
<b>AVP</b>	Atrial vasoactive peptide
<b>BMI</b>	Body mass index
<b>BP</b>	Blood pressure
<b>CAD</b>	Coronary artery disease
<b>CAPD</b>	Chronic ambulatory peritoneal dialysis
<b>CBC</b>	Complete blood count
<b>Ccr</b>	Creatinine clearance
<b>CG</b>	Cockcroft-gault
<b>CGA</b>	Cause, GFR and Albuminuria categories
<b>C<sub>in</sub></b>	Inulin clearance
<b>CKD</b>	Chronic kidney disease
<b>CKD-EPI</b>	Chronic kidney disease epidemiology collaboration
<b>CNS</b>	Congenital nephrotic syndrome
<b>CVD</b>	Cardiovascular disease
<b>DI</b>	Diabetes insipidus
<b>DM</b>	Diabetes mellitus
<b>ESRD</b>	End stage renal disease
<b>FENA</b>	Fractional excretion of sodium
<b>FNB</b>	Fine needle biopsy
<b>FT3</b>	Free tri-iodothyronine
<b>FT4</b>	Free thyroxine
<b>GFR</b>	Glomerular filtration rate
<b>GN</b>	Glomerulonephritis
<b>Hb</b>	hemoglobin
<b>HD</b>	Hemodialysis
<b>HSCRP</b>	High sensitive c-reactive protein
<b>IGF-1</b>	Insulin growth factor 1
<b>IL-6</b>	Interleukin-6
<b>K/DOQI</b>	The kidney disease outcome quality initiative
<b>KDIGO</b>	Kidney disease improving global outcomes
<b>MDRD</b>	Modification of diet in renal disease
<b>NaS(i)-1</b>	Sodium sulfate cotransporter
<b>NG</b>	Nanogram
<b>NHANES III</b>	The third national health and nutrition examination survey
<b>NHE</b>	Sodium hydrogen exchange

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*List of Abbreviations*

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<b>NS</b>	Nephrotic syndrome
<b>PD</b>	Peritoneal dialysis
<b>PG</b>	Picogram
<b>PTH</b>	Parathyroid hormone
<b>RAAS</b>	Renin -angiotensin-aldosterone-system
<b>RAS</b>	Renal artery stenosis
<b>RPF</b>	Renal plasma flow
<b>SCH</b>	Subclinical hypothyroidism
<b>SIADH</b>	Syndrome of inappropriate antidiuretic hormone secretion
<b>SNGFR</b>	Single nephron glomerular filtration rate
<b>T3</b>	Tri-iodothyronine
<b>T4</b>	Thyroxine
<b>TBG</b>	Thyroxine binding globulin
<b>TFT</b>	Thyroid function tests
<b>TG</b>	Thyroglobulin
<b>TH</b>	Thyroid hormone
<b>THRT</b>	Thyroid hormone replacement therapy
<b>TPOAB</b>	Thyroid peroxidase antibody
<b>TRAB</b>	TSH receptor antibody
<b>TRH</b>	Thyrotropin-releasing hormone
<b>TSH</b>	Thyroid stimulating hormone
<b>TSI</b>	Thyroid stimulating immunoglobulin
<b>US</b>	United states
<b>VCAM-1</b>	Vascular adhesion molecule-1

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## Introduction

The concept of subclinical primary hypothyroidism has emerged over the past several decades, as our ability to detect subtle changes in thyroid function tests is progressively improved . (*Hamilton et al; 2008*)

Subclinical primary hypothyroidism is highly prevalent in the general population, especially in the elderly. However, the prevalence of subclinical primary hypothyroidism in persons with chronic kidney disease (CKD) not requiring chronic dialysis is not well defined. The presence of subclinical hypothyroidism in patients with CKD might be a risk factor for both cardiovascular disease and progressive kidney disease. (*Chonchol et al;2008*)

Previous studies have suggested a higher prevalence of thyroid abnormalities in persons with end-stage renal disease. However, little is known regarding the epidemiology of thyroid disorders in persons with less severe kidney dysfunction. (*Lo et al; 2005*)

CKD affects both hypothalamus–pituitary–thyroid axis and thyroid hormone TH peripheral metabolism (*Singh et al ;2006*)

Uremia influences the function and size of the thyroid; Uraemic patients have an increased thyroid volume compared with subjects with normal renal function and a

higher prevalence of goiter, mainly in women. (*Kutlay et al ;2005*)

The different types of kidney diseases can be associated with various disorders of thyroid function; Thyroid disease may be linked to different forms of glomerulonephritis , Both hypothyroidism and hyperthyroidism can coincide with different forms of glomerular disease, The more frequent form is membranous glomerulopathy associated with nephrotic syndrome. (*Gurkan et al ;2009*)

Thyroid dysfunction has been reported to be associated with IgA glomerulonephritis, mesangiocapillary or membranoproliferative glomerulonephritis , and minimal change glomerulonephritis. (*Enriquez et al ;2002*)

Although less frequently than glomerular disease, tubular or tubulointerstitial damage has also been reported to be associated with thyroid dysfunction.

Isolated cases of hyperthyroidism have been reported in association with tubulointerstitial nephritis and uveitis. (*Hudde et al ;2007*)

Nephrotic syndrome is associated with changes in serum TH levels ,Urinary losses of binding proteins, such as thyroxine binding globulin (TBG), transthyretin or pre-albumin, albumin, and TH binded to them, result in a reduction in serum total thyroxine (T<sub>4</sub>) and, sometimes, in total T<sub>3</sub> levels. (*Junglee et al ; 2006*)

Plasma triiodothyronine (fT3) is a strong predictor of adverse clinical outcomes in various clinical conditions. Since fT3 in patients with end-stage renal diseases (ESRD) is frequently reduced and is associated with inflammation and cardiovascular damage. (*Cutrupi et al ;2006*)

## **Aim of the work**

The aim of the work is to study the correlation between the thyroid functions and the glomerular filtration rate in patients with chronic kidney disease.

## **Chronic Kidney Disease Overview**

Kidney disease is a worldwide public health problem, with increasing incidence and prevalence, high costs, and poor outcomes. There is even a substantially higher prevalence of the earlier stages of chronic kidney disease (CKD), with adverse outcomes, including loss of kidney function, cardiovascular disease (CVD), and premature death. Strategies to improve outcomes will require a global effort directed at the earlier stages of CKD. (*Eknayan et al; 2004*)

The rationale for a global initiative to address this problem is simple and self-evident. The epidemic of CKD is global. The adverse outcomes of CKD are universal, as are the underlying science and evidence-based strategies for prevention, detection, evaluation, and treatment. Although risk factors and resources for care vary locally, it is important to increase the efficiency of utilizing available expertise and resources in improving the care and outcomes of CKD worldwide. (*Andrew et al; 2005*)

Progression of kidney disease to ESRD can be slowed if kidney disease is recognized and treated in its earlier stages. Socioeconomic benefits of early CKD identification are potentially enormous because kidney failure is accompanied by poor outcomes and much higher

financial costs than those for earlier stages of CKD. (*Collins et al; 2005*)

### **Definition:**

In 2002 the Kidney Disease Outcomes Quality Initiative (K/DOQI) of the National Kidney Foundation (NKF) developed a practice guideline for CKD. (*Andrew et al; 2002*)

According to this guideline, CKD is defined as either kidney damage or glomerular filtration rate (GFR) below 60 ml/min/1.73 m<sup>2</sup> for three or more months with or without evidence of kidney damage, irrespective of the cause. (*Levey et al; 2003*)

GFR is estimated by serum creatinine based on equations rather than on direct measurements. Several equations have been developed and the most frequently used ones are the Cockcroft-Gault (CG) equation and the Modification of Diet in Renal Disease Study (MDRD) equation. Both equations are currently considered to be the best methods to estimate GFR for adults in epidemiologic studies. (*Verhave et al; 2003*)

The MDRD equation provides a more accurate and clinical acceptable estimation of GFR than the CG equation in patients with GFR less than 60 ml/min/1.73 m<sup>2</sup>. (*Lamb et al; 2005*)