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

Thesis

Submitted for partial fulfillment
of the master degree of internal medicine

Presented by

Ahmed Yehia Saad Zaghloul

MBBCH of medicine
Ain Shams University

Under the supervision of

Prof. Dr. Khaled Hussein Abou Seif

Professor of internal medicine and Nephrology,
Faculty of Medicine-Ain Shams University

Dr. Waleed Anwar Abdel Mohsen

Associate professor of internal medicine and Nephrology,
Faculty of Medicine-Ain Shams University

Faculty of Medicine
Ain Shams University
2014

Acknowledgement

*Many thanks to **Allah**, who granted me the ability to perform this Review.*

*I have the greatest pleasure to express my deepest gratitude to **Prof. Dr., Khaled Hussein Abou Seif,** Professor of Internal Medicine & Nephrology , Faculty of Medicine, Ain Shams University, for suggesting, planning the point of research and providing research facilities. His generous encouragement, supervision, reading and critical discussions during the writing and preparation of the manuscript of this thesis.*

*I wish also to express my sincere thanks to **Assistant Prof Dr., Waleed Anwar Abdel Mohsen,** Assistant Professor of Internal Medicine & Nephrology , Faculty of Medicine, Ain shams University, for his supervision, continuous assistance, valuable support, unfailing interest in the progress of the work, his advice and critical review of the thesis.*

قَالُوا سُبْحَانَكَ لاَ عِلْمَ لَنَا
إِلاَّ مَا عَلَّمْتَنَا إِنَّكَ أَنتَ
الْعَلِيمُ الْحَكِيمُ

صدق الله العظيم

سورة البقرة الآية (32)

List of Contents

List of Abbreviations

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

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

List of Tables

List of Figures

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_4) and, sometimes, in total T_3 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. **(*Eknoyan 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^2 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^2. **(*Lamb et al; 2005)***