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

صدق الله العظيم
سورة البقرة الآية (٣٢)

Study of Subclinical Hypothyroidism in Type 2 Diabetes Mellitus among Egyptian Women

Thesis

Submitted for Partial Fulfillment of the M.D. Degree in Internal Medicine

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دراســة نقص إفـراز الغدة الـدرقيـة الـتحـت إكلينيكى فى مرضى السكر من النوع الثانى فى الإناث بمصر

رسالة

توطئة للحصول على درجة الدكتوراة

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List of Abbreviations

AACE	American association of clinical endocrinologists
2h	2 hour
2h PG	2 hours plasma glucose
ADA	American diabetic association
ATA	American thyroid association
ATP	Adenosine triphosplate
BMI	Body mass index
c- DNA	C- form DNA
Ca+2	Calcium
CHD	Cornary heart disease
CNS	Centeral nervous system
Co2	Corbar dioxide
CRP	C- reactive protein
D	Day
DCCT	Diabetes control and complication trial
DM	Diabetes mellitus
DNA	deoxyribonucleic acid
ELISA	Enzyme linked immuno- sorbent assay
FFA	Free fatty acid
FMV	First morning viod
FPG	Fasting plasma glucose
FT4	Free thyoxine
G	Grams
G6PD	Glucose 6 phosphate dehydrogenase
GCT	Glucose challenge test
GDM	Gestational diabetes mellitus
GFR	Glomerare fitteration rate
GH	Growth harmone
GIT	Gastrointeslinal tract
GLUT2	Glucose Transport 2
HbA1C	Hemoglobin A1C (Glycosylated hemoglobin)
HDL	High density lipoprotein cholesterol

HNF-1	Hepatocyte nuclear factor 1
HPA	Hypothalamic pituitary adrenal axis
HPTA	Hypothalamic Pituitary thyroid axis
IDDM	Insulin dependent diabetes mellitus
IFG	Impaired fastirg glucose
IgG	Immunoglobulin –G
IGT	Impaired glucose tolerance
IL-1	Interleukin-1
K+	Potassium
LDL	Low density lipoprotein cholesterol
L-T4	Levothyroxine
Mg	Milligram
Mg/dl	Milligram/ deciliter
MIu/L	Mili- international unit/liter
Mmol/l	Millimol/ liter
MODY	Maturity onset diabetes of the young
mRNA	Messanger ribonucleic acid
Na+	Sodium
NE	Norepinephrine
NGSP	National glycohemeglobin standardization program
NHANES	National health and nutrition examination nutrition
NIDDM	Non-insulin dependent diabetes mellitus
NIS	Sodium/iodide syntransporter
NPY	Neuropeptide Y
NTI	Non- thyroidal illness
O2	Oxygen
OGTT	Oral glucose tolerance test
PTU	Proply-thiouracil
PVN	Paraventicular nucleus
rT_3	Reverse T_3
SPSS	Program for special science
SS	Somatostatin
STZ	Streptozotocin

T_3	Triodothyronine
T_4	Thyroxine
TBG	Thyroxine binding globuline
Tg	Thyroglobulin
TH	Thyroid hormone
TMAB	Thyroid microsomel Antibodes
TNF	Tissue necrosis factor
TPO	Thyroid poroxidase
TRE	Thyroid hormone responsive element
TRH	Thyrotropin releasing hormone
TSH	Thyroid stimulating hormone
TSI	Thyroid stimulating immunoglobulin
US	United states
VIP	Vasoactive intestinal peptide
WHO	World health organization
Yrs	Years

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INTRODUCTION

Thyroid disease is common in the general population, and the prevalence increases with age. The assessment of thyroid function by modern assays is both reliable and inexpensive. Screening for thyroid dysfunction is indicated in certain high-risk groups, such as neonates and the elderly ***(Radaideh et al., 2004).***

Hypothyroidism is by far the most common thyroid disorder in the adult population and is more common in older women. It is usually autoimmune in origin ***(Gopinath et al., 2008)***.

Subclinical hypothyroidism is defined as an asymptomatic state characterized by a normal serum free-thyroxine level and elevated serum concentration of thyrotropin ***(Helfand and Redfern, 1998)***. Generally, subclinical hypothyroidism is more common in females and is associated with anti-thyroid antibodies ***(Cooper, 2001)***. Several epidemiological studies have shown that subclinical hypothyroidism may be an independent risk for cardiovascular disease ***(Biondi et al., 2002 and Walsh et al., 2005)***.

Patients with Type 2 diabetes have a risk of death from cardiovascular causes that is two to six times greater than that of persons without diabetes ***(Gu et al, 1999)***.

A number of reports have indicated a higher than normal prevalence of thyroid disorders in type 2 diabetic patients compared with the normal population, with hypothyroidism being the most common disorder ***(Smithson, 1998 and Radaideh et al., 2004)***.

Subclinical thyroid dysfunction is associated with a poor lipid profile and cardiac dysfunction. Patients with Type 2 diabetes suffer from a greater risk of vascular disease, often in association with dyslipidemia. Thyroid dysfunction might either contribute to these factors or make them worse ***(El-Nobre et al., 2002)***. Subclinical hypothyroidism may be an independent risk factor of cardiovascular events in Type 2 diabetic patients ***(Chen et al., 2007)***.

Although there is a recognized association between thyroid disease and diabetes mellitus, there is no definite answer as to whether screening for subclinical hypothyroidism is necessary in patients with type 2 diabetes.

AIM OF THE WORK

To estimate the prevalence of subclinical hypothyroidism and thyroid antibodies in Type 2 diabetic Egyptian women in comparison to normal Egyptian women.

THE THYROID GLAND

The thyroid gland is the largest organ specialized for endocrine function in the human body. The major function of the thyroid follicular cells is to secrete a sufficient amount of thyroid hormones; primarily tetraiodothyronine (T_4), and a lesser quantity of triiodothyronine (T_3). Thyroid hormones promote normal growth and development and regulate a number of homeostatic functions, including energy and heat production. In addition, the parafollicular cells of the human thyroid gland secrete calcitonin, which is important in calcium homeostasis ***(Greenspan, 2004)*.**

The Secretory Unit - The Follicle

Under the middle layer of deep cervical fascia, the thyroid has an inner true capsule, which is thin and adheres closely to the gland. Extensions of this capsule within the substance of the gland form numerous septae, which divide it into lobes and lobules. The lobules are composed of follicles, the structural units of the gland, consisting of a layer of simple epithelium enclosing a colloid-filled cavity. This colloid contains an iodinated glycoprotein, iodothyroglobulin, a precursor of thyroid hormones. Follicles vary in size, depending upon the degree of distention, and they are surrounded by dense plexuses of fenestrated capillaries, lymphatic vessels and sympathetic nerves ***(Oertel and Oertel, 2000)*.**