

Thyroid Dysfunction & Rheumatological Disease: is there a link or Association

Thesis

**Submitted for the Partial Fulfillment Of MD Degree in Internal
Medicine**

By

Nahla Emad el-Din Abdel-aziz

Assitant Lecturer of Internal Medicine, Cairo University

Supervised By

Prof. Dr. Hala Ibrahim El-Gendy

Professor of Internal Medicine
Cairo University

Prof. Dr. Khaled Al-Sayed Al-Hadidy

Professor of Internal Medicine
Beni Sweif University

Prof. Dr. Hala Gabr Metwaly

Professor of Clinical pathology
Cairo University

2014

*Thanks to Allah for blessing me with an able
body in the sight of so much illness;
for giving me the ability to learn and the
capability to apply my knowledge;
and for creating in me the desire to help people*

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

"وقل رب زدني علما"

صدق الله العظيم

(سورة طه، الآية ١١٤)

ACKNOWLEDGEMENT

First, and foremost, all thanks and gratitude to GOD, most gracious and most merciful.

I would like to express my deepest gratitude and sincere thanks to Prof. Dr. Hala el-Gendy, Professor of Internal medicine, Cairo University, for her continuous guidance and valuable advice for enriching this work.

I am extremely grateful to Dr. Khaled Al-Hadidy, Professor of Internal medicine, Beni Sweif University, for his continuous guidance and suggestions, saving no effort or time to make this work better.

I would like to express my highest appreciation to Dr. Hala Gabr, Professor of Clinical pathology, Cairo University, for her great cooperation, assistance and efforts during the whole work without which, it wouldn't have been a reality.

Dedications

*I dedicate this work to my family, especially to my dear **father** who gave me great support & advice, to my loving **mother** who always shows so much care ,aid and patience ,to my dear **husband** who gives me full support & help, to my dear **brother** & to my lovely **son**.*



Abstract

Autoimmune thyroid disease (ATD) is a multifactorial, genetic disease(ATD). Abnormalities in thyroid function and thyroid autoantibodies have been frequently described in patients with some rheumatological diseases as systemic lupus erythematosus (SLE). Autoimmune route is one of the links between thyroid dysfunction & rheumatological diseases. The recurrent study included 20 patientswith rheumatological diseases, 20 subjects with thyroid diseases & 20 subjects as a control group who were undergone measuring the levels of ANA, Ads NA, Anti thyroid peroxidase (TPO) & Anti thyroglobulin (TG) for evaluation the relation between autoimmune thyroid diseases & connective tissue diseases.

Key words:

- Autoimmune thyroid diseases (ATD).
- Anti thyroid peroxidase (TPO) & Anti thyroglobulin (TG).
- Connective tissue diseases.

Contents

List of abbreviations.....	I
List of tables.....	II
List of Figures.....	III
List of tables of statistics.....	IV
List of figures of statistics.....	V
Introduction and the aim of the work.....	1
Review of literature	
Chapter 1: Thyroid gland anatomy & physiology.	2
Chapter 2: Autoimmune thyroid dysfunction.	17
Chapter 3: Thyroid & rheumatological disorders.	42
Chapter 4: Thyroid autoantibodies.	56
Subjects and Methods.....	67
Results.....	74
Discussion.....	87
Summary and conclusion.....	95
Recommendations.....	98
References.....	99
Arabic summary.....	

List of abbreviations

AITD	Autoimmune thyroid disease
ACTH	Adrenocorticotrophic hormone
ADsNA	Antidouble strand nuclear antigen
ANA	Antinuclear antibodies
ANCA	Antineutrophilic cytoplasmic antibodies
ATMA	Thyroid microsomal antigen
AutoAbs	Auto-antibodies
BMR	Basal metabolic rate
CAD	Coronary heart disease
CAT	Chronic autoimmune thyroiditis
CBC	Complete blood count
CRP	C-reactive protein
CT	Computed tomography
CVS	Cardio-vascular system
DNA	Deoxyribonucleic acid
ELIZA	Enzyme linked immunosorbent assay
ESR	Erythrocyte sedimentation rate
FBS	Fasting blood sugar
FMS	Fibromyalgia syndrome
H& E	Heamatoxylin & euosin
GD	Graves' disease
GH	Growth hormone
hCG	Human Chorionic gonadotrophin
HLA	Human leukocyte antigens
HPT	Hypothalamic pituitary thyroid axis
HS	Highly significant
HT	Hashimoto's thyroiditis
IGF-I	Insulin-like growth factor-I
LDL	Low density lipoprotien
LH	Luteinizing hormone
LKFT	Liver kidney function tests
MCTD	Mixed connective tissue disease
MHC	Major histocompatibility
NS	Not significant
PMR	Polymyalgia rheumatica

List of abbreviations

RA	Rheumatoid arthritis
RF	Rheumatoid factor
ROC	Reciever operator characteristic curve
S	Significant
SCHT	Subclinical hypothyroidism
SLE	Systemic lupus erythematosus
SS	Sjogren syndrome
TBAbs	Thyroid blocking antibodies
TBG	Thyroxine binding globin
Tg	Thyrogloglobin
THs	Thyroid hormones
TPO	Thyroid peroxidase
TSAbs	Thyroid stimulating antibodies
TSH	Thyroid stimulating hormone
TSHr	Thyroid stimulating hormone receptor
TRs	Thyroid hormone receptors
TRH	Thyroid releasing hormone
WAT	White adipose tissue

List of Tables

No.	Title	Page
1	Reagents for antithyroid peroxidase	69
2	Reagents for antithyroglobulin	71
3	Demographical, clinical features and laboratory results of the patients and the controls at the time of the study.	75
4	The clinical manifestations of group I at the present study.	76
5	The clinical presentation of group II at the current study	76
6	Comparison between group I and controls as regard ANA & AdsNA at the time of study.	77
7	Comparison between group II and controls as regard ANA & AdsNA at the time of study.	77
8	Comparison between group I and groupII as regard ANA & AdsNA at the time of study.	78
9	Comparison between group I and controls as regard Anti-TPO & Anti TG at the time of study.	81
10	Comparison between group II and controls as regard Anti-TPO & Anti TG at the time of study.	81
11	Comparison between group I and groupII as regard Anti-TPO & Anti TG at the time of study.	82
12	Validity of ANA and AdsNA as an emphasis of marker for autoimmune diseases in thyroid dysfunction patients.	85
13	Validity of Anti-TPO and Anti-TG as an emphasis of marker for autoimmune thyroid diseases in rheumatological patients.	86

List of Figures

Number	Title	Page
1	Gross anatomy of the thyroid and surrounding	2
2	Histology of thyroid gland	4
3	Blood & nerve supply of thyroid gland	5
4	Venous drainage of thyroid gland	6
5	Structure of thyroid hormones	11
6	Comparison between group I,II & controls as regard ANA.	79
7	Comparison between group I,II & controls as regard AdsNA.	80
8	Comparison between group I,II & controls as regard Anti-TPO.	83
9	Comparison between group I,II & controls as regard Anti-TG.	84
10	Validity of ANA and AdsNA as an emphasis of marker for autoimmune diseases in thyroid dysfunction patients.	85
11	Validity of Anti-TPO and Anti-TG as an emphasis of marker for autoimmune thyroid diseases in rheumatological patients.	86



INTRODUCTION

Abnormalities in thyroid function and thyroid autoantibodies have been frequently described in patients with some rheumatological diseases as systemic lupus erythematosus (SLE) (*Pyne et al., 2002*), rheumatoid arthritis (*Chan et al., 2001*) and sjogren syndrome (*Karsh et al., 1980*), mainly autoimmune thyroid diseases found to be mostly thyroiditis with end result hypothyroidism (*Miller et al., 1993*)

We believed that not only autoimmune route is the only link between thyroid dysfunction & rheumatological diseases.



THE THYROID GLAND

Anatomy Of The Thyroid Gland

The Germans call the thyroid the "shield gland" (Schilddrüse), and the English name, derived from the Greek, means the same thing. Such a term gives a most erroneous impression of its shape. It is interesting, however, that in the Minoan culture, a shield was used that had a shape somewhat like that of the mammalian thyroid gland (*Dumont et al., 2005*).

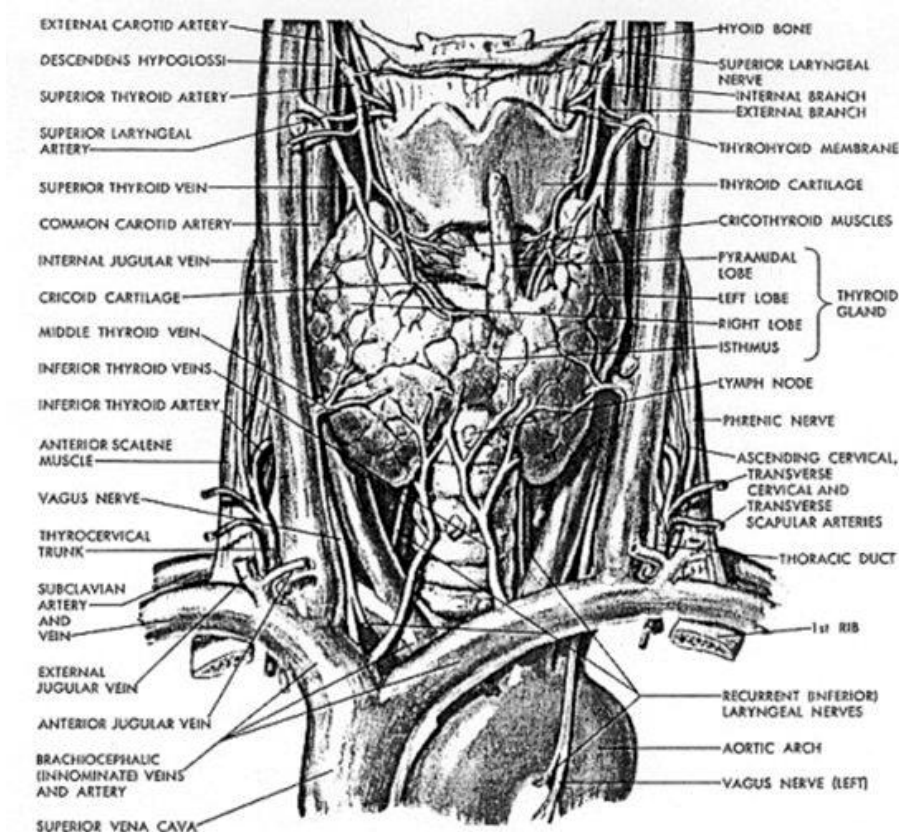


Fig. (1): Gross anatomy of the thyroid and surroundings(From: Netter FH, 1965)



The thyroid is a brownish-red and highly vascular gland located anteriorly in the lower neck, extending from the level of the fifth cervical vertebra down to the first thoracic. The gland varies from an H to a U shape and is formed by 2 elongated lateral lobes with superior and inferior poles connected by a median isthmus (with an average height of 12-15mm) overlying the second to fourth tracheal rings.

Each lobe is 50-60mm long, with the superior poles diverging laterally at the level of the oblique lines on the laminae of the thyroid cartilage. The lower poles diverge laterally at the level of the fifth tracheal cartilage. Thyroid weight varies but averages 25-30g in adults (slightly heavier in women).(*Braun et al.,2007*). Usually, 2 pairs of parathyroid glands lie in proximity to the thyroid gland .

Histology:

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 (pink on hematoxylin and eosin [H&E] stain) contains an iodinated glycoprotein, iodothyroglobulin, a precursor of thyroid hormones. The 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 (*David, 2005*).

Epithelial cells are of 2 types: principal cells (ie, follicular) and parafollicular cells (ie, C, clear, light cells). Principal cells are responsible for formation of the colloid (iodothyroglobulin), whereas



parafollicular cells produce the hormone calcitonin. Parafollicular cells lie adjacent to the follicles within the basal lamina (**Hollenberg, et al.,2005**).

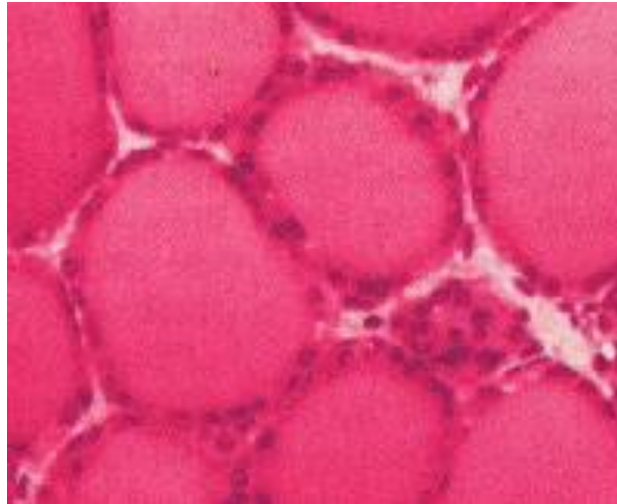


Fig. (2): Histology of the thyroid gland shows the structural units of the gland and the follicles, consisting of a layer of simple epithelium enclosing a colloid-filled cavity.

The arterial supply Comes from the superior and inferior thyroid arteries and, occasionally, the thyroidea ima artery. These arteries have abundant collateral anastomoses with each other, both ipsilaterally and contralaterally. The thyroid ima artery is a single vessel, which originates, when present, from the aortic arch or the innominate artery and enters the thyroid gland at the inferior border of the isthmus (**David, 2005**).