Study of Thyroid Auto-Antibodies in Patients with Allergic Bronchial Asthma and Allergic Rhinitis

Thesis

Submitted For Partial Fulfillment of Master Degree
In Internal Medicine

By

Amira Ahmed Mohammed Mandour
M.B.B.ch. in
Misr University for Science and Technology

Under Supervision By

Prof. Dr. Mohmmed Fahmy Abd El-Aziz
Professor of Internal Medicine & Endocrinology
Faculty of Medicine - Ain Shams University

Prof.Dr. Maged Mohammed Refaat
Professor of Internal Medicine & Clinical Immunology
Faculty of Medicine - Ain Shams University

Dr. Inas Mohammed Sabry
Lecturer of Internal Medicine & Endocrinology
Faculty of Medicine - Ain Shams University

Faculty of Medicine
Ain Shams University

2008

Acknowledgment

I would like to thank ***Prof. Dr. Mohammed Fahmy Abd El-Aziz,*** *Professor of Internal medicine and Endocrinology, Head Endocrine Unit, Faculty of Medicine, Ain Shams University for his continuous support, guidance and help in the present work.*

I am very grateful to Prof. ***Dr. Maged Mohammed Refaat,*** *Professor of Internal Medicine and Clinical Immunology, Faculty of Medicine, Ain Shams University for his continuous assistance and advice during the course of this study*

My grateful acknowledgement is expressed to ***Dr. Inas Mohammed Sabry****, Lecturer of Interal Medicine and Endocrinology, Faculty of Medicine, Ain Shams University for her support and encouragement.*

I would like to thank Prof. ***Dr. Mohammed Yousef****, Professor of Clinical Pathology, Faculty of Medicine, Ain Shams University for his valuable help during this study.*

I would like to thank ***Dr. Hadeya El Sayed Abd El Fatah,*** *Assistant professor in Internal Medicine and Lecturer of Interal Medicine and Endocrinology, Faculty of Medicine, Ain Shams University for her support Endocrinology Departement, Ain Shams University for her support.*

I do not forget the help offered by ***my collegues in E.N.T*** *Departement, Faculty of Medicine, Ain Sham University.*

LIST OF ABBREVIATIONS

AMC	Antibody mediated cytotoxicity
AHT	Autoimmune hypothyroidism
AITD	Autoimmune thyroid disease
APC	Antigen-presenting cell
AR	Allergic rhinitis
cAMP	Cyclic adenosine mono phosphate
CTLA	Cytotoxic T-lymphocyte-associated antigen
CL Ts	Cysteinyl leukotrienes
DZ	Dizygotic
ECP	Eosinophilic cationic protein
ELISA	Enzym linked immunosorbant assay
EPR	Early-phase responses
FT3	Free triiodothyronin
FT4	Free thyroxin
GD	Graves' disease
H	Histamine
HT	Hashimoto's thyroiditids
IFN-γ	Interferon-γ
IgE	Immunoglobulin E
IL-4	Interleukin-4
LPR	Late-phase responses
LT	Leukotrienes
MBP	Major basic protein

LIST OF ABBREVIATIONS (CONT.)

MHC	Major histocompatibility complex
MZ	Monozygotic
NIS	$Na^{\pm}$/I-symporter
PAP	Perennial Allergic Rhinitis
PEFR	Peak expiratory flow rate
PEV_1	Peak erpiratory volume
PG	Prostaglandings
PTPN22	Protein typosine phosphatase non-receptor 22
SAR	Seasonal Allergic Rhinitis
SNPs	Single nucleotide polymorphisms
SPSS	Statistical program for social science version 12
T3	Thyroid hormones triiodothyronine
TG	Thyroglobulin
TH	T helper
TNF-α	Tumor necrosis factor
TPO	Thyroid peroxidase
TSAbs	Thyroid stimulating antibodies
TSH	Thyroid stimulating hormone
TSH-R	Thyroid stimulating hormone receptor
V	Variable
VCAM	Vascular cell adhesion molecule

List of Tables

Page

List of Tables (Cont.)

Page

List of Figures

Page

List of contents

INTRODUCTION

Allergic disorders are diseases where the immune system reacts inappropriately to exogenous antigens, whereas in autoimmune diseases, reactions are directed against auto-antigens, resulting in different kinds of diseases depending on which organ is affected. The auto-antibodies in allergic patients, react against exogenous antigens may also react more readily to endogenous antigens *(Lindberg et al., 1998)*

The prevalence of allergic disease is increasing allover the world, but its influence on the clinical course of autoimmune disease in unknown *(Takeoka et al., 2003).* Little is known about relation between thyroid disease and allergic diseases *Jenkins and Weetman,(2002). Izum and Coworkers (1998)* reported that auto immunity in patients with allergic rhinitis have increased frequency of Grave's disease. Moreover, it has recently been clarified that the association of seasonal allergic rhinitis was frequent in Grave's disease and rare in painless thyroiditis *(Amino et al., 2003)*. However, little is known about the influence of allergic rhinitis and the clinical course of autoimmune disease and production of autoantibodies *(Takeoka and colleagues, 2003).* Takeoka and coworkers (2003) Concluded that seasonal allergic rhinitis aggravated the clinical course of Grave's disease and induce an

increase in serum antithyroid autoantibody concentration as well as an increase in pollen-specific IGE concentration. *Hidaka and co-workers (1996)* observed that Grave's thyrotoxicosis frequently replased or was aggravated after attacks of seasonal allergic rhinitis. *Lindberg and Coworkers (1998)* found higher thyroid peroxidase antibodies in children with allergic asthma.

Knowledge of the presence of thyroid disease in patients with bronchial asthma is of importance since hypothyroidism may ameliorate coexistent asthma, whereas hyperthyroidism has been reported to have opposite effect *(Rowe, 1991).* This finding may be useful to alert clinician that thyroid disease may be super imposed on allergic diseases *(Lindberg et al., 1998).*

AIM OF THE WORK

The aim of this work is to study the co-existence of thyroid auto-antibodies in patients with bronchial asthma and allergic rhinitis.

BRONCHIAL ASTHMA

I – Definition:

Asthma is a disorder defined by its clinical, physiological, and pathological characteristics. The predominant feature of the clinical history is episodic shortness of breath, particularly at night, often accompanied by cough. Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role *(Cohn et al., 2004)*.

.

The chronic inflammation causes increasing in airway hyper responsiveness that leads to recurrent episodes of wheezing, shortening of breath, and coughing, particularly at night or the early morning*(Black, 2004)*. .

These episodes may be triggered by such things as exposure to an environmental stimulant (allergen) – cold air – exercise or exertion or emotional stress, are usually associated with widespread but variable airflow obstruction that is often reversible either spontaneously or with treatment *(Vincent et al., 2006)*.

II – Classification:

A. <u>Classification of asthma severity by clinical features before treatment according to Gian (2006) and Egyptian society of chest diseases and tuberculosis:</u>

⊙ *Step (1): Intermittent:*

- Symptoms less than once a week.
- Brief exacerbations.
- Nocturnal symptoms not more than twice a month:
  - FEV1 or PEF Γ 80% predicted.
  - PEF or FEV1 variability <20%.

⊙ *Step (2): Mild persistent:*

- Symptoms more than once a week but less than once a day.
- Exacerbations may affect activity and sleep.
- Nocturnal symptoms more than twice a month:
  - FEV1 or PEF Γ 80% predicted.
  - PEF or FEV1 variability <20-30%.

⊙ *Step (3): Moderate persistent:*

- Symptoms daily.
- Exacerbations may affect activity and sleep.

- Nocturnal symptoms more than once a week.
- Daily use of inhaled short-acting B_2-agonist:
  - FEV1 or PEF 60-80% predicted.
  - PEF or FEV1 variability > 30%.

⊙ *Step (4): Severe persistent:*

- Symptoms daily (wheezing, dyspnea, tachypnea and indrawing of tissues and muscles between the ribs).
- Frequent exacerbations.
- Frequent nocturnal asthma symptoms.
- Limitation of physical activities:
  - FEV1 or PEF Φ 60% predicted.
  - PEF or FEV1 variability > 30%.

(Tarlo and Liss, 2003)

B. Classification according to special types:

⊙ Occupational asthma.
⊙ Aspirin induced asthma.
⊙ Cough variant asthma.
⊙ Exercise-induced asthma.

III – Risk factors:

A. Exposures to (Environmental factors):

Many allergens are soluble proteins that function in their natural states as enzymes e.g. proteolysis.