Assessment of resistin in asthmatic children

Protocol of Thesis

Submitted for partial fulfillment
of master degree in paediatrics

By

Mohamed Abdelaziz Khalaf Allah Ghaleb
M. B., B. Ch. (2007)

Under Supervision Of

Prof. Malak Ali Shaheen
Professor of Paediatrics
Faculty of medicine – Ain Shams University

Doctor / Asmaa El-Hussieny Ahmed
Assistant professor of Paediatrics
Faculty of medicine – Ain Shams University

Doctor / Enas Samir Nabih
Assistant professor of Biochemistry and Molecular Biology
Faculty of medicine – Ain Shams University

Faculty of Medicine
Ain Shams University
Cairo – 2014

بسم الله الرحمن الرحيم

"الحَمْدُ لِلَّهِ الَّذِي هَدَانَا لِهَذَا وَمَا كُنَّا لِنَهْتَدِيَ لَوْلا أَنْ هَدَانَا اللَّه"

صدق الله العظيم

سورة الأعراف :أية 43

Acknowledgment

First of all, ultimate thanks are to ALLAH. Without your power and mercy one could do nothing. Please help us to fulfill our greatest hope of gaining your acceptance.

Words will never express my deepest gratitude to all those who helped me during preparation of this study.

I gratefully acknowledge the sincere advices and guidance of ***Dr. Malak Ali Shaheen****,Professor of Pediatrics, Faculty of medicine, Ain Shams University, for her constructive guidance, continuous support and thorough revision of this work till it reached this picture .I owe her the bulk of work she had offered me with a lot of patience and kindness; I shall always appreciate and remember her help.*

I'm very grateful to ***Dr.Asmaa El-Husseiny Ahmed****.Assistant prof. of Pediatrics, Faculty of medicine, Ain Shams University,for her kind supervision, creative ideas and stimulating suggestions throughout this work. It is a great honor to work under her supervision.*

My sincere appreciation and deep thanks goes to ***Dr. Enas Samir Nabeeh,*** *Assistant prof. of Bio chemistry, Faculty of medicine, Ain Shams University, for her guidance, support and patience.*

Nevertheless, I would like to thank all those who made this work possible, those who helped me in carrying

out the investigation necessary for completion of this work as well as my friends and colleagues for their support and help when needed.

I am deeply thankful to the Ain Shams University for providing the laboratory facilities without which this work could not be accomplished.

I would also like to thank Ghamra military hospital and ***Dr. Mourad Alfy Ramzy*** *for his great support towards me.*

And at last but not least, I want to mention my beloved ones, nothing would describe my feelings towards them all. I would like to thank my father for being my guide, my mother and all my family members for believing in me and supporting me.

Mohamed Abdelaziz Khalaf ALLAH

Table of contents

List of Figures

List of Abbreviations

ATPIII	Adult Treatment Panel III
BHR	Bronchial hyperresponsiveness
BMI	Body mass index
BP	Blood pressure
CDC	Child Development Center
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
DCs	Dendritic cells
ELISA	Enzyme-linked immunosorbent assay
FBG	Fasting blood glucose
FIZZ	Found in inflammatory zone
FIZZ1	Found in inflammatory zone 1
FIZZ2	Found in inflammatory zone 2
GINA	Global Strategy for Asthma Management and Prevention
GM-CSF	Granulocyte-macrophage colony-stimulating factor
GR	Glucocorticoid receptor
HDL	High-density lipoprotein
HOMA	Homeostasis model assessment
ICAM-1	Intercellular adhesion molecule-1
ICS	Inhaled corticosteroids
IDF	International Diabetes Federation
IgE	Immunoglobulin E
IL-1β	Interleukin 1 beta
IL-10	Interleukin-10
IL-12	Interleukin-12
IL-4	Interleukin-4
IL-5	Interleukin-5
IL-6	Interleukin-6
LABA	Long acting beta 2 agonist
LDL	Low-density lipoprotein
mRNA	messenger RNA
MAP	Mean arterial pressure
MetS	Metabolic syndrome
MMPs	Matrix metalloproteinases
NK1	Neurokinin-1
NK2R	Neurokinin-2 receptor
OGTT	Oral glucose tolerance test

oxLDL	Oxidized low-density lipoprotein
PBMCs	Peripheral blood mononuclear cells
RANKL	Receptor activator of NF-κB ligand
RBM	Reticular basement membrane
RELMα	Resistin-like molecule alpha
Relm-β	Resistin-like molecule beta
Relm-γ	Resistin-like molecule gamma
RELMs	Resistin-like molecules
RETN	Resistin gene
NIDDM	Short acting beta 2 agonist
SBP	Systolic blood pressure
SNPs	Single-nucleotide polymorphisms
SREBP1c	SRE-binding protein 1c
TC	Total cholesterol
TG	Triglycerides
Th1	T helper 1 cells
Th2	T helper 2 cells
Th17	T helper 17 cells
TNFα	Tumour necrosis factor alpha
TRAF3	TNF receptor-associated factor-3
TZD	Thiazolidinediones
USA	United states of America
VCAM-1	vascular cell adhesion molecule 1
VEGFR	vascular endothelial growth factor receptor
VLDL	Very low density lipoproteins
WC	waist circumference
Wt	Weight
WHO	World Health Organization

List of Tables

INTRODUCTION

Bronchial asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation is associated with airway hyper responsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning. These episodes are usually associated with widespread, but variable, airflow obstruction within the lung that is often reversible either spontaneously or with treatment ***(Gina, 2007).***

Scientists have long suspected an association between overweight and asthma to be likely. The common assumption is that weight gain occurs because many asthmatic patients avoid exercise since physical activity can trigger their symptoms. ***(Redd et al., 2002).*** While obesity can lead to asthma through some theories including dietary components containing high fats ***(Flaherman and Rutherford et al., 2006*)**. Presence of gastroesophageal reflux (which is prevalent in both conditions), hormonal influences , atopy , chronic systemic inflammation , mechanical effects of obesity and a more detailed theory is that some cytokines increased in obese humans are promoters of inflammation ***(Beuther et al., 2006***).

In recent years metabolic syndrome has aroused universal interest from the scientific community as well as healthcare managers, this condition is highly prevalent in both developed and developing countries ***(Ford et al., 2004).*** It involves all ages and is associated with an increased risk of diabetes, cardiovascular morbidity and mortality ***(Lorenzo et al., 2007).***The metabolic syndrome is characterized by a group of metabolic risk factors in one person. They include abdominal obesity, atherogenic dyslipidaemia, elevated blood pressure ***(Sorof et al., 2002)***, insulin resistance or glucose intolerance ***(Sinha et al., 2002).***

Many adipocytes hormones, such as tumor necrosis factor (TNF)-α, leptin, adiponectin, retinol binding protein 4, resistin, adipsin, Vaspin, Visfatin and interleukin (IE)-6, collectively called adipokines, play important roles in the inflammatory diseases like bronchial asthma ***(Lyon et al., 2003).***

AIM OF THE WORK

The aim of this study is to assess the level of resistin in asthmatic children together with other parameters of metabolic syndrome.