



# HIGH SENSITIVITY C-REACTIVE **PROTEIN IN ASTHMA**

Thesis Submitted in Partial Fulfillment of the Master Degree

In

**Chest Diseases** 

Bv

Gamalat Mohamed awad

(M.B.B.CH.,)

# Supervisors

Prof. Dr.

### HODA ALI ABU YOUSSEF

Professor of chest diseases –Chest **Department Faculty of Medicine** Cairo University

Prof. Dr.

### **SHERIF NASEH AMEN**

**Professor of Clinical Pathology Faculty of Medicine Cairo University** 

Dr.

### **IRENE MOHAMED SABRY**

Lecturer of chest diseases – Chest Department **Faculty of Medicine** Cairo University

> **FACULTY OF MEDICINE CAIRO UNIVERSITY** 2010



# دراسة مستوى بروتين (ج) التفاعلي عالى الحساسية في مرضى الربو الشعبي

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ف*ي* الأهراض الصدرية

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# لِهُ فِي اللَّهِ مِنْ اللَّهِ مِلَّالِمِي مِنْ اللَّهِ مِ

الاستاذ السدكتور

شريف ناصح أمين

أَسْتَاذَ الباثولوجيا الإكلينيكيّةُ كلية الطب — جامعة القاهرة

الاستاذاك دكتور

هدى علي أبو يوسف

أُستاذ الأُمراض الصدرية كلية الطب – جامعة القاهرة

الحكتور

إيرين محمد صبرى

مدرس الأمراض الصدرية كلية الطب — جامعة القاهرة

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#### LIST OF ABBREVATIONS

A1AT : Alpha -1 antithypsin

A1P1 : Alpha-1 proteinase in hibitar BAL : Bronchoalvealar lavage

BMI : Body mass index CCR-3 : Chemokin receptar-3

COPD : Chronic obstructive pulmonary disease

COX-2 : Cyclo oxygenase 2
CRP : C-Reactive protein
Cyst T1 : Cysteinyl- leukotriene-1

DIC : Disseminated intravascular coagulation

DVT : Deep venaus thrombosis
 ECP : Eosinophil cationic protien
 ESR : Erythrocyte sedimentation rate
 FCγ : Crystellisable fragments gamma
 FDA : Food and drug adminstration

Fe Co : Fraction of exhaled carbon monoxide FEF 25% : Forced expiratory flow at 25% of FVC FEF 75% : Forced expiratory flow at 75% of FVC FEV1 : Forced expiratory volume in 1st second

FeNO : Fraction of exhaled nitric oxide

FVC : Forced vital capacity

GERD : Gastro-esophageal reflux disease

GM-CSF : Granulocyte- macro phage colony-stimulating factor

HS-CRP : High-sensitivity C-reactive protein ICAM-1 : Intracellular adhesion molecule-1

**ICS** Inhaled corticosteraids IFN-γ Interferon gamma Ig-E Immunoglobulin E IL-10 interleukin 10 IL-3 interleukin 3 IL-4 interleukin 4 IL-5 Interleukin 5 Interleukin 6 IL-6 IL-8 interleukin 8

IL-1° : Interleukin-1 alpha IL-1B : Interleukin-1 beta

LABA; Long acting beta-2 agonists LDL: Low-density lipprotein

LTC4 : Leukotriene C4
LTD4 : Leukotriene D4
LTE4 : Leukotrine E4
MB : Mannose-binding
MBL : Mannose-binding lectin
MBP : Mannan-binding protein

MCP-4 : Macrophage chemoattractant protein 4

MDI : Metered dose inheler NGF : Nerve growth factor

NSAID : Non steroidal anti-inflammatory drugs

PAF : Platelet activating factor

PaCo<sub>2</sub> : Arterial tension of carbon dioxide

PaO<sub>2</sub> : Arterial oxygen tension

PDGF : Prostaglandin derived grawth factor

PE : Pulmonary embolism
PEF : Peak expiratory flow
PGD2 : Prostaglandin D2

RSV : Respiratory syncytial virus
SAA : Serum amyloid A protein
SAP : Serum amyloid P component
SaO2% : Arterial oxygen saturation percent
TGF-β : Trans forming growth factor –beta
TH1 : T-helper cell type I lymphocyte
TH2 : T-helper cell type 2 lymphocyte

TLR-2 : Toll-like receptor

TNF-α : Tumour necrosis factor-alpha US : United states of America.

VCAM-1 : vascular cell adhesion molecule-1 VEGF : vascular endothelial grawth facto

VLA : Very late antigen

VLDL : Very-low –density lipoproteins WHO : World Health ovganization



### INTRODUCTION

Asthma is a chronic inflammatory disorder of the airways in which many cells and molecular elements play a role. The chronic inflammation causes an associated increase in airway 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 that is often reversible either spontaneously or with treatment. (GINA 2008).

Asthma is characterized by airway hyper responsiveness and inflammation in which various cells (such as eosinophils, neutrophils, macrophages and T lymphocytes predominantly of the CD4+ type), cytokines and mediators play a role.

Besides local inflammation, systemic inflammation is present in asthma as shown by increased levels of plasma fibrinogen and serum  $\alpha$  a myloid A *(Jousilahti et al., 2002)*.

Serum levels of the well known inflammatory marker C- reactive protein (CRP) can be simply and inexpensively measured in order to assess systemic inflammation. However, standard assays for CRP, with a lower detection limit of 3-8 mg L<sup>-1</sup>, lack the sensitivity required to determine levels of inflammation within the normal range (*Rider*, 2001).

Recently, high- sensitivity assays for CRP (hs-CRP) have become available in clinical laboratories.

Measurement of hs. CRP levels has suggested the involvement of low- grade systemic inflammation in several disorders, such as cardiovascular disease and diabetes mellitus Serum hs-CRP levels can be a prognostic marker for the development of diabetes mellitus *Pradhan et al 2001* or future cardiovascular events. (*Ridker et al 1997*).

Furthermore, a population based study showed associations of increased levels of serum hs-CRP with a high frequency of airway hyper responsiveness and low forced expiratory volume in one second (FEV1) among subjects without heart disease suggesting that systemic inflammation may be associated with respiratory impairment, (Kony et al 2004.

Another epidemiological study showed that elevated levels of hs-CRP correlate significantly with respiratory symptoms and with prevalence of non allergic asthma. *(Olafsdottir et al 2005)* 

Thus, hs-CRP could theoretically also be a useful tool for detecting systemic inflammation in asthma, indeed an association between serum hs-CRP level and severity of asthma has been suggested. (Savykoski et al 2004).

# AIM OF THE WORK

o measures the serum levels of hs-CRP of asthmatic patients with and without inhaled corticosteroid treatment compared to those of healthy controls.

### **ASTHMA**

#### **Definition of asthma**

Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role, in particular mast cells, eosinophils, T-lymphocytes, macrophages, neutrophils, and epithelial cells. 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,2008).

#### THE BURDEN OF ASTHMA

#### Prevalence, Morbidity, and Mortality

Asthma is a problem worldwide, with an estimated 300 million affected individuals. Despite hundreds of reports on the prevalence of asthma in widely differing populations, the lack of a precise and universally accepted definition of asthma makes reliable comparison of reported prevalence from different parts of the world problematic, (Masoli *et al.*, 2004).

Nonetheless, based on the application of standardized methods to measure the prevalence of asthma and wheezing illness in children and adults, it appears that the global prevalence of asthma ranges from 1% to 18% of the population in different countries, (Yan *et al.*,2005).

There is good evidence that asthma prevalence has been increasing in some countries and has recently increased but now may have stabilized in others. (Garcia-Marcos et al., 2004).

The World Health Organization has estimated that 15 million disability-adjusted life years (DALYs) are lost annually due to asthma, representing 1% of the total global disease burden. Annual worldwide deaths from asthma have been estimated at 250,000 and mortality does not appear to correlate well with prevalence, (Beasley, 2004)

#### Social and Economic Burden.

Absence from school and days lost from work are reported as substantial social and economic consequences of asthma. analyses of economic burden of asthma, attention needs to be paid to both direct medical costs (hospital admissions and cost of medications) and indirect, non medical costs (time lost from work, premature death)

• The costs of asthma depend on the individual patient's level of control and the extent to which exacerbations are avoided. (GINA,2008).