High-Sensitivity C - reactive protein Level: A Measure for Asthma Severity and Control in Egyptian Asthmatic Children

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بسم الله الرحمن الرحيم

(قالُوا سُبْحَانَكَ لا عِلْمَ لَنَا إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ الْعَلِيمُ الْحَكِيمُ)

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`ABSTRACT

Asthma is the most common chronic inflammatory disease in childhood and some reports have demonstrated systemic inflammation. The relevance of high sensitivity assays for C-reactive protein (Hs-CRP), which are known to be a sensitive marker of low-grade systemic inflammation, has not been fully studied in childhood asthma.

This cross sectional case–control study aimed at evaluating serum Hs-CRP in two groups of asthmatic children, steroid inhaling and steroid naive patients with special emphasis on the relation of measured parameter to different clinical (severity, smoking, family history, other atopic manifestations) and laboratory data (IgE-peripheral blood eosinophil count) and pulmonary function tests. Ninety eight asthmatic Children aged 2yr to 12yr and matched control group of 38 children were recruited for the present study.

The Serum Hs-CRP analysis of patients and controls revealed a non significant statistical difference. The relation between the serum analysis of Hs-CRP in the two asthmatic groups was statistically insignificant.

A statistical significant difference was found between the HsCRP and the result of the pulmonary function tests, but no statistical significant difference was found between HsCRP and asthma severity.

In conclusion HsCRP can be used for indirect detection of airway inflammation, and may be also used to assess response to steroid treatment in asthmatic children but cannot be used as a marker for assessment of different grades of asthma severity.

Key Words: Asthma -HsCRP- Severity.

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Arabic Summary

Abbreviations

ACE	Angiotensin-converting enzyme
ACT	Asthma control test
ADRB2	β2 adrenergic receptor
AEC	Absolute Eosinophilic Count
AHR	Airway hyperresponsivness
ALOX5	5-lipoxygenase5-lipoxygenase
ANOVA	One way analysis of variance
API	Asthma predictive index
ASM	Airway smooth muscle
BA	Bronchial asthma
BHR	Bronchial hyperresponsiveness
BMI	Body mass index
BTPS	Body temperature, barometric pressure and saturated with water vapour conditions
BTS	British Thoracic Society
COPD	Chronic obsrtructive lung disease
CRP	C-reactive protein
C_{rs}	Respiratory system compliance
CXR	Chest X-ray
CysLT1	Cysteinyl leukotriene type 1
Da	Dalton : is the standard unit that is used for indicating mass on an atomic or molecular scale (atomic mass)
ECM	Extra cellular matrix
ED	Emergency department
EEL	End expiratory level
EGF	Epidermal growth factor
EIA	Exercise-induced asthma
EPR-3-NAEPP	Expert Panel Report 3 of the National Asthma Education and Prevention Program
ERS	The European Respiratory Society
ETS	Enviromental tobacco smoke
FcεRI	High-affinity receptor
FcγR	Immunoglobulin receptors
FEF25-75	Forced expiratory flow between 25% and 75% expired volume
FeNO	Fractional exhaled NO
FEV1	Forced expiratory volume at 1 second
FRC	Functional residual capacity
FRCp	Plethysmographic Functional Residual Capacity
FVC	Forced vital capacity
GERD	Gastroesophageal reflux disease
GINA	Global Initiative for Asthma
GM-CSF	Granulocyte–macrophage colony-stimulating factor
H2O2	Hydrogen peroxide
HRVC	Human rhinovirus C
Hs-CRP	High- sensitive CRP
IC	Immobilized complex
ICAM-1	Intercellular adhesion molecule 1

ICS	Inhaled corticosteroids
IFN-α	interferon α
IgE	Immunoglobulin E
IgG	Immunoglobulin G
IL	Inteleukin
IL-2	Interleukin -2
IOM	Institute of medicine in Washington
IOS	Impulse oscillometry
ITAM	Immunoreceptor tyrosine-based activation motif
ITIM	Immunoreceptor tyrosine-based inhibition motif
kPa	Kilo Pascal
LABA	Long-acting β2-agonist
LRTIs	Lower respiratory tract infections
LTA4	Leukotriene epoxide hydrolase
LTB4	Leukotriene B4
LTC	Cysteinyl-leukotrienes
LTC4	Cysteinyl leukotrienes C4
MDCs	Macrophage-derived chemokines
NO	Nitric oxide
PC	Phosphatidylcholine
PDGF	Platelet derived growth factor
PEF	Peak expiratory flow
PEFR	Peak expiratory flow rate
PFT	Pulmonary function tests
PGD2	Prostaglandin D2
P_j	Jacket pressure
PNT	Pneumotachograph
PT	Pneumotach
PUFAs	Polyunsaturated fatty acids
R_{rs}	Respiratory system resistance
RSV	Respiratory syncitial virus
RTC	The tidal rapid thoracoabdominal compression
RV	Residual volume
RV/TLC	Residual volume to total lung capacity
SAA	Serum amyloid A
SABA	Short acting b2 agonist
SAP	Serum amyloid P component
sm- 22	Transgelin
sm-MHC	Smooth muscle myosin heavy chain
sm-MLCK	Smooth muscle myosin light chain kinase
SPSS	Statistical Package for the Social Science
SPT	Skin-prick test
sRaw	Specific airways resistance
sRaw	Specifc Airway Resistance
TARCs	Thymus and activation-regulated chemokines and
TGF-b	Transforming growth factor-b
Th1	T helper 1
Th2	T-helper 2
TMB	Tetramethylbenzidine
TNF-α	Tumour necrosis factor alpha

$\mathbf{T_{rs}}$	Time constant of the respiratory system
$\mathbf{V'_{maxFRC}}$	Maximal flow at functional residual capacity
VB	Box volume
VCAM-1	Vascular-cell adhesion molecule 1
VEGF	Vascular endothelial growth factor
VOCs	Volatile organic compounds
WHO	World Health Organization

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Introduction

Asthma is a heterogeneous and multifactorial disease manifested as episodes of wheezing, coughing, and shortness of breath particularly at night. Both family-based and twin studies indicate that asthma is a complex genetic disorder. Multiple genetic and environmental factors are also known to modulate the clinical expression of the disease and its associated phenotype bronchial hyperresponsiveness, atopy, and elevated IgE ***(Patrick et al., 2010)***

Bronchial asthma is prevalent worldwide, especially in developed countries where its prevalence is increasing to epidemic proportions ***(Chen and Shi, 2006).***

Asthma comprises a range of heterogeneous phenotypes that differ in presentation, etiology and pathophysiology. The risk factors for each recognized phenotype of asthma include genetic, environmental and host factors. Although a family history of asthma is common, it is neither sufficient nor necessary for the development of asthma ***(Burke et al., 2003).***

Asthma is characterised by airway hyperresponsiveness and inflammation, in which various cells (such as eosinophils, neutrophils, macrophages and T-lymphocytes), cytokines and mediators play a role. Beside local inflammation, systemic inflammation is present in asthma, as shown by increased levels of plasma fibrinogen and serum amyloid A ***(Jousilahti et al., 2002)***. 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 ***(Sa¨vykoski et al., 2004).***

Increased Hs-CRP levels may be associated with allergic inflammation, particularly eosinophilic inflammation, and the degree of

airway obstruction in asthmatic patients. It is an important new marker that can help physicians care for asthmatic patients ***(Fujita et al., 2007).***

Also, low-level inflammation, as indicated by increased Hs-CRP serum concentrations, has been described in both chronic obstructive pulmonary lung diseases (COPD) and asthma ***(Tilemanna et al, 2011).***

In asthma, serum Hs-CRP measurement is noninvasive and easier than measurement in induced sputum or bronchoalveolar lavage fluid. Therefore, Hs-CRP might be a useful clinical marker of eosinophilic airway inflammation in asthma and might assist in the clinical management of the disease ***(Fujita et al., 2007)***.

Aim of work

The aim of the present study is to evaluate the serum HsCRP levels in two of asthmatic children (group A=steroid inhaling patients; group B=steroid naive asthmatic patients) through a case–controlled study and to assess its correlation to clinical (age, age of onset, sex, duration, severity, asthma control), laboratory (total serum IgE, absolute eosinophilic count) and pulmonary function parameters