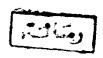
## SERUM E-SELECTINS AS ADHESION MOLECULES IN CHILDREN WITH BRONCHIAL ASTHMA



53396

Acha I.A Ch

Thesis Submitted for the Partial Fulfillment for the M.S. Degree in Clinical Pathology Presented By

Dr. Kawther Mohammed Abdou

616.07 K.17

Under the Supervision of

Prof. Dr. Laila El-Shawarby

Prof. of Clinical Pathology Faculty of Medicine

Dr. Elham Mohammad Hossny

Ass. Prof. of Pediatrics Faculty of Medicine

Dr. Randa Reda Mabrouk

Lecturer of Clinical Pathology Faculty of Medicine

> Ain Shams University 1995/1996



### **ACKNOWLEDGEMENT**

First, I thank "GOD" for granting me the power to proceed and to accomplish this work.

I would like to express my endless gratitude and appreciation to Prof. Dr. Laila EL-SHAWARBY, Professor of Clinical Pathology, Ain Shams University, for giving me the honour of working under her supervision and for providing me with a lot of encouragement and support throughout this work and always.

I do appreciate the kind and active participation of Dr.Elham Mohammad HOSSNY, Assistant Professor of Pediatrics, Ain Shams University, in the clinical part of this work.

Thanks are due to Dr. Randa REDA, Lecturer of Clinical Pathology, Ain Shams University for her encouragement, and honest assistance in every step of this work. Truly she gave me a lot of guidance, and support to accomplish this work in the appropriate way.

### **CONTENTS**

List of Abbreviations.	i
List of Tables.	ii
List of Figures.	iii
Introduction and Aim of the Work .	1
Review of Literature .	2
Bronchial Asthma.	2-23
* Classification of Bronchial Asthma	3
A- Extrinsic Asthma.	3
B- Intrinsic Asthma.	4
* Genetic Basis of Asthma.	5
* Immunologic concept of asthma.	7
- Cells involved in asthma.	8
- Important mediators in asthma.	19
- Role of cytokines in the regulation of allerg	ic
inflammation.	22
Adhesion Molecules.	24-52
* Introduction.	24
* Families of adhesion molecules.	25
- Selectins.	25
<ul> <li>Immunoglobulin Supergene Family.</li> </ul>	38
- Integrins.	41
- Others.	44
* Regulation of adhesion molecules.	49
Pathophysiological Role of Adhesion molecular	ules in
Pulmonary Tissue.	53-64
* Adhesion molecules in normal lung structure.	53
* Adhesion molecules in pulmonary inflammation.	54
* Adhesion molecule in allergic inflammation and ast	hma 58
* Adhesion molecules antagonists in treatment of asth	ma. 63
Subjects and Methods.	65-68
Results.	69-82
Discussion.	83-87
Summary & Conclusion.	88-90
Recommendations.	91
References.	92-121
Arabic Summary.	101

### **ABREVIATIONS**

 $\alpha$  : Alpha  $\beta$  : Beta

BAL : Bronchoalveolar lavage .

CD : Cluster of differentiation antigen.

CTMCs : Connective tissue mast cells.

ECF-A : Eosinophil chemotactic factor-A.

ECP : Eosinophil cationic protein.EDTA : Ethylene diamine tetracetate.EGF : Epidermal growth factor.

ELAM-1 : Endothelial leukocyte adhesion molecule-1.

Fc<sub>E</sub> RI : IgE Fc receptor-1 Fc<sub>E</sub> RII : IgE Fc receptor-II

Y : Gamma

GM-CSF: granulocyte macrophage-colony stimulating

factor.

HLA : Human leukocyte antigenHRF : Histamine releasing factor.

HRIF : Histamine release inhibitory factor

HUVEC: Human umbilical vein endothelial cells.

ICAM : Intercellular adhession molecule.

IFN-γ : Interferon gamma
 IgE : Immunoglobulin E
 IgE-BF : IgE - binding factor
 IgER : IgE responsiveness
 Igs : Immunoglobulins

IGSF : Immunoglobulin supergene family.

IL-2R : IL-2 receptor ILs : Interleukins

kD : Kilo dalton.

LEC CAM: Lectin cellular adhesion molecules.

LFA: Lymphocyte functioning antigen.

LPR: Late phase response.

LPR: Late phase response.

LPS: Lipopolysaccharide

LT : Leukotrienes.

mAb : Monoclonal antibody

MAd CAM: Mucosal addressin cell adhesion molecules

MBP : Major Basic Protein.MMCs : Mucosal mast cells.

NCAM : Neural cell adhesion molecules.

PAF : Platelet activating Factor

PECAM : Platelet and endothelial cell adhesion molecule.

PGs : Prostaglandins

PMN : Polymorph Nuclear Leukocytes.

SCR : Short concencus repeat.

sE-selectin: Soluble E-selectin.

SLe<sup>x</sup>: Sialyl-Lewis x

SRS-A : Slow reacting substance of anaphylaxis

TH: T-helper.

TNF : Tumour necrosis factor.

VCAM : Vascular cell adhesion molecule

VLA : Very late antigen.

# LIST OF TABLES

	Page
Table of Review of Literature :	_
Table (1): Molecules and pathways involved in adhesion/signalling.	26
Table (2): Slectins: Nomenclature and Expression.	28
Table (3): Regulation of adhesion receptors.	50
Table of Results :	
Table (4): Clinical and laboratory data of the patients' group.	72
Table (5): Descriptive data of the control group.	73
Table (6): Statistical comparison of laboratory data of the patient's	7.5
group versus control group.	73
Table (7): Statistical comparison of laboratory data of the patients'	
group versus each other.	74
Fable (8): Correlation table.	75

# **List of Figures**

Figures of Review of Literature	
Fig. (1): As cheme to explain the relationship between early, late	e phase
and ongoing chronic asthma.	9
Fig. (2): Inflammatory response in asthmatic lung.	1:
Fig. (3): Phusiological effect of mast cell derived mediators.	13
Fig. (4): Domain composition of the three known human selectins	. 28
Fig. (5): Expression and induction of endothelial cell ac	
molecules.	31
Fig. (6): Modulation of leukocyte adhesion.	50
Fig. (7): Role of adhesion molecules in inflammation. 56	
Fig. (8): Proposed steps in the development of airway inflammati	ion. 60
Fig. (9): sE-selectin concentration in the sera of asthmatic particles during and inbetween the attacks in comparison to the sera of asthmatic particles.	oatients
controls.	76
Fig. (10): Comparison of IgE percentage values in the sera of p during and inbetween the attacks.	77
Fig. (11): sE-selectin concentration in the sera of asthmatic p	atients
during and inbetween the attacks in relation to the presence that X-ray infiltrates.	ence of
Fig. (12 & 13): Comparison between sensitivities of IgE perc	
values and sE-selectin levels alone and in combinat	ion as
parameters for diagnosis of asthma during and inbetwe	en the
attacks.	79 - 80
Fig. (14 & 15): Correlation between IgE% and sE-selectin in the	
patients during and inbetween the attacks.	81-82

# Introduction and Aim of The Work