EXPOSURE TO FUNGI AND COMBUSTION PARTICULATES AMONG CHILDHOOD ASTHMATICS IN RURAL ENVIRONMENT

Submitted By Maha El Sayed Hassan Selim M.B.,BCH, Faculty of Medicine, Alexandria University, 1979

> A thesis submitted in Partial Fulfillment of The requirement for the Master Degree in Environmental Science

Department of Environmental Medical Science Institute of Environmental Studies and Research Ain Shams University

2013

Approval Sheet

EXPOSURE TO FUNGI AND COMBUSTION PARTICULATES AMONG CHILDHOOD ASTHMATICS IN RURAL ENVIRONMENT

Submitted By

Maha El Sayed Hassan Selim

M.B., BCh, Faculty of Medicine, Alexandria University, 1979

This thesis towards a Master degree in Environmental Science has been approved by :

Name

Signature

1. Prof. Mahmoud Serry El Bukhary

Prof. & Head of Department of Environmental Medical Science Institute of Environmental Studies & Research Ain Shams University

2. Prof. Howayda Mohamed Kamal

Prof. of Clinical Pathology Faculty of Medicine Banha University

3. Prof. Dr. Talaat Abde El Aziz Arafa

Prof. of Chest Diseases Faculty of Medicine Al Azhar University

4. Prof. Dr. Rashwan Mohamed Farag

Prof. of Medical Biochemistry Faculty of Medicine Ain Shams University

2013

EXPOSURE TO FUNGI AND COMBUSTION PARTICULATES AMONG CHILDHOOD ASTHMATICS IN RURAL ENVIRONMENT

Submitted By Maha El Sayed Hassan Selim M.B.,BCh, Faculty of Medicine, Alexandria University, 1979

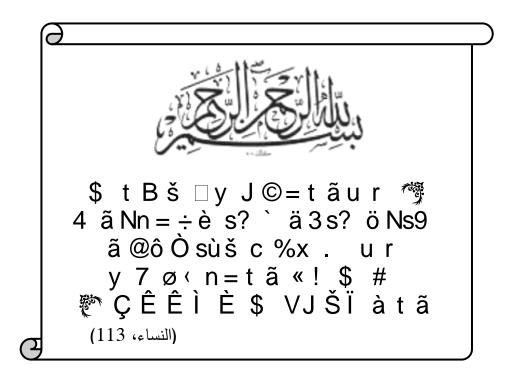
A thesis submitted in Partial Fulfillment of The requirement for the Master Degree in Environmental Science Department of Environmental Medical Sciences

Under the Supervision of :

1. Prof. Mahmoud Serry El Bukhary Prof. of Chest Diseases Chairman, Department of Environmental Health

2. Prof. Howayda Mohamed Kamal Professor of Clinical Pathology Banha University

2013



Acknowledgement

I want to express my appreciation and respect to the eminent **professor Mahmoud Serry El Bukhary,** professor of chest diseases, Ain Shams University, whom I am very fortunate to be one of his students. I am greatly indebted his generous support and constant advice.

My sincere gratitude and thanks is addressed to *professor Howayda Mohamed*, professor of heamatology, Banha University for her faithful suggestions, and critical review through this work.

I dedicate this work to the soul of *my Father, my Mother and my Grand father*, Prince / Moustafa Mounir Adham who dedicated all his life and money and properties to encourage the scientific research in (History, Art and Science) to put Egypt on top of the world. He was granted the Medal (Nishan El Nile) by King Ahmed Fouad at 1924 because of his great achievements.

I also dedicate this work to the soul of my grand grand father.

Al Sharif Dr. Mohammed Bey El Shafei one of twelve excellent medical scholars who were selected by Dr. Clute Bey to be the members of the fourth educational mission to France (The greater medical mission), they were sent by Mohammed Ali Pasha to France at 1832 for their Doctor degree in Medicine.

After his return back from France he was appointed by **Mohammed Ali Pasha** as one of the first Egyptian professors and directors of **The Medical School of Kasr EI-Einy** in Cairo, to be one of the celebrities of the Modern Egyptian Renaissance.

(He was the author and translator of four great works in Medicine).

Finally, and most importantly, I would like to thank my family especially my beloved nephews **Ismail, Ahmed El**

Sawy, Adham El Dafrawy and little Yassin Aiman Selim for their support, I want to plant in their mind that the value of education is priceless.

From the University of Ain Shams where one of their Grand fathers "Abd EI Rehim Pasha EI Demerdash" dedicated a part of his properties to build this university in order to share in lighting the way of all students who seek a decent education in Egypt. I would like to deliver them the Torch of Nobility, Science, and Success.

ABSTRACT

Background: Children growing up in rural environments that afford them a wide variety of microbial exposures are protected from childhood asthma and atopy. Conversely, urban air pollution may trigger asthma symptoms in sensitive children.

Subjects and Methods: Out of 1100 questionnaires completed 103 childhood asthmatics were diagnosed from an urban (Shoubra El Khema) and rural Kaliope areas (The study duration was 3 years).

Objective : To determine the prevalence of childhood asthma and atopy in rural versus urban environments and to compare dust microbiological contamination and endotoxin levels in rural and urban areas.

Results : It was found that out of 500 children in Shoubra El Khema region, 55 (11%) had asthma, while out of 600 children from Kaliope region, 48 (8%) were asthmatics, (p < 0.05).

Air pollutant, (nitrogen dioxide NO_2 , sulfur dioxide, SO_2 , Ozone, O_3 and particulate matter less than 10Mm in aerodynamic diameter, PM10) were higher in Shoubra El Khema compared to Kaliope.

Severe asthma was more prevalent in Shoubra El Khema, (18%) compared to Kaliope, (10.4%), P < 0.05.

Skin test reactivity to fungal spores were higher in Shoubra El Khema, (23.6%) compared to Kaliope (14.6%). Among patients sensitized to fungal allergens, aspergillus is in both urban and rural areas.

Skin test reactivity to house dust mite (HDM) was higher also,, in Shoubra El Khema, (16.36%) compared to (6.25%) in Kaliope, (P < 0.05).

Microbial contamination of dust, differed greatly in rural and urban areas, where mean values of contamination by total bacteria were significantly higher in Kaliope, 5.15 (CFU/m³), P < 0.05. Also, mean values of Gram negative (G-ve) bacterial contamination were significantly higher, 3.51 (CFU/m³) in Kaliope area compared to G-ve bacteria in Shoubra El Khema, 1.89 (FU) (P < 0.05).

Although/moulds concentrations in dust samples were higher in Kaliope, (1.97 CFU/m^3) compared to Shoubra El Khema, (1.88 CFU/m^3) , the values were insignificant.

Endotoxin levels above 100 endotoxin unit (EU) were found in 11 out of 12 dust samples from Kaliope, (91.7%) compared to one out of 12 (8.3%) (P < 0.000).

Conclusion: Children living in rural areas had a wide range of microbial exposure and endotoxin, which might have protective effect against atopy and asthma.

Key words: Indoor air pollution, house dust, house dust mites, fungi, moulds, combustion particulates, endotoxins, aeroallergen, air pollution, atopy, asthmatic school children, rural environment, innate immunity.

TABLE OF CONTENTS

	Page
Abbreviation list.	
Tables list.	
Introduction.	1
Aim of the study.	
Review of literature :	10
- Chapter I: Asthma.	11
I.1 History of Asthma.	11
I.2 Definition.	11
I.3 Epidemiology.	12
I.4 Etiology.	15
I.5 Pathophysiology.	17
I.6 Acute inflammation.	18
I.7 Chronic inflammation	19
a. Epithelial cells.	20
b. Eosinophil.	20
c. Lymphocytes.	21
d. TH1 and TH2 cell imbalance.	21
e. Mast cells.	22
f. Alveolar macrophage.	23
g. Neutrophils.	24
h. Fibroblast - myofibroblast.	24
I.8. Inflammatory mediators.	25
I.9 Clinical Consequences of chronic Inflammatic	on. 27
- Chapter II: Indoor risk factors.	29
II.1 What are allergens.	30
II.2 Causes.	31
II.3 Dust mites.	32
II.4 How can mites causes allergy?	32

II.5 What is difference dust mites and house dust.	32
II.6 Pet dander	33
II.7 An allergic reaction may triggered by any of the	
following.	34
II.8 Molds.	35
II.9 Cockroaches.	36
II.10 Indoor pollens and housplants.	37
II.11 Tobacco smoke.	37
II.12 Indoor allergies symptoms.	38
- Chapter III: Indoor air pollution and asthma.	39
III.1 Biomass fuels.	39
III.2 Respiratory illness.	44
- Chapter IV: Clinical presentation.	47
IV.1 Chronic asthma.	47
IV.2 Chronic ambulatory asthma.	47
a. General.	47
b. Symptoms	47
c. Signs.	48
d. Laboratory	48
IV.3 Other diagnostic tests.	48
IV.4 Severe acute asthma.	49
- Chapter V: Environmental exposure to endotoxin and	
its relation to asthma in School-age children.	51
V.1 Definition.	51
V.2 Genetic.	51
V.3 Hygiene hypothesis.	52
- Chapter VI: The interaction between host genetics	
and environmental exposures.	57
Patients and methods.	64
• Results.	71
• Discussion.	82

•	Conclusions.	126
٠	Recommendation.	128
٠	Summary.	130
•	References.	136
•	Arabic summary.	178

LIST OF TABLES

Table	Title	Page
Table (1) :	Age and sex distribution of childhood	
	asthmatics in rural and urban areas.	75
Table (2) :	Childhood asthmatics in Shoubra El Khema	
	versus Kaliope.	76
Table (3) :	Asthma severity in childhood asthmatics from	
	Shoubra El Khema versus Kaliope.	77
Table (4) :	Aeroallergen sensitization among childhood	
	asthmatics from Shoubra El Khema versus	
	Kaliope.	78
Table (5) :	Air pollutant levels in Shoubra El Khema versus	
	Kaliope.	79
Table (6) :	Microbiological air contamination in dust	
	samples from Shoubra El Khema versus	
	Kaliope.	80
Table (7) :	Endotoxin levels in dust samples from Shoubra	
	El Khema versus Kaliope.	81

ABBREVIATIONS LIST

ABPA	Allergic bronchopulmonary aspergillosis
ADAM ₃₃	A disintegrin and metalloprotease
AF	Aspergillus fumigates
AHR	Airway hypersponsiveness.
Alex. Study	Allergen and Endotoxin.
ANOVA	Analysis of variance.
BAL	Broncho-alveolar lavage.
BHR	Bronchial hyper-responsiveness.
CD	Cluster of differentiation.
CFU	Colony forming unit.
CI	Confidence interval.
DCs	Dendritic cells.
DEPs	Diesel exhaust particles
EIB	Exercise induced bronchospasm.
ELF	Epithelial lining fluid.
ETs	Environmental tobacco smoke.
EU	Endotoxin unit.
FeNO	Fraction of exhaled nitric oxide.
FEV ₁	Forced expiratory volume in 1 second.
FVC	Force vital capacity.
GM-CSF	Granulocyte macrophage colony stimulating factor.
GSTP1	Glutathione S-transferase P1.
HDM	House dust mite.
ICAM-1	ICAM-1 Intercellular adhesion molecule-1
ICAS	Inner city asthma study
IgE	IgE Immunoglobulin E.
IL	Interleukin.
INF-γ	Interferon γ.
ISAAC	International study of asthma and Allergy in childhood

LAL	Limulus Amoebocyte lysate.
LISA	Life style-Immune System Allergy.
LPS	Lipopolysaccharides.
LTD ₄	Leukotrienes D ₄ .
LTs	Leukotrienes.
MiRNA	Micro ribonucleic acid.
MRC	Modified medical research council
MSD	Maximum Symptom day
NAEPP	National asthma education and prevention program.
NHLBI	National Heart, Lung, and blood institute.
NO	Nitric oxide
NO ₂	Nitrogen dioxide.
NST	Negative skin test
03	Ozone.
OR	Odd ration (probability of having or not having).
Р	Probability of obtaining the value of the observed
	statistic.
PAF	PAF Platelet activating factor.
PAMPS	Pathogen associated molecular patterns
PCR	Polymerase chain reaction.
PM ₁₀	Particulate matter (particles with diameter smaller or
	equal to 10 microns.
PST	Positive skin test
RSV	Respiratory syncytial virus
SAFS	Severe asthma associated with fungal sensitization
SO ₂	Sulfur dioxide.
SPSS	Statistical Package for the Social Science.
SRS-A	Slow reacting substances of anaphylaxis.
TH ₁	T helper lymphocytes type 1.
TH ₂	T helper lymphocytes type 2.
TLR	Toll like receptor.