STUDY OF CANDIDA ALBICANS AND ASPERGILLUS FUMIGATUS AMONG EGYPTIAN POPULATION WITH ALLERGIC BRONCHIAL ASTHMA

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Study of *Candida Albicans* & *Aspergillus fumigatus* sensitization among Egyptian patients with allergic bronchial asthma

Thesis

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دراسة التحسس لفطر الكنديدا البيضاء والأسبرجلس فيوميجاتس بين المرضى المصريين اللذين يعانون من الربو الشعبى التحسسي

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للحصول على درجة الماجستير

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List of Abbreviations

AAFS	Asthma associated with fungal sensitization
AAS	Allergic Aspergillus Sinusitis
ABPA	Allergic BronchoPulmonary Aspergillosis
ABPA-CB	Allergic bronchopulmonary aspergillosis with central bronchiectasis
ABPA-S	Seropositive allergic bronchopulmonary aspergillosis
ABPM	Allergic bronchopulmonary mycosis
ACE	Angiotensin converting enzyme
ACOS	Asthma–COPD overlap syndrome
ACQ	Asthma Control Questionnaire
ACT	Asthma control test
AERD	Aspirin-exacerbated respiratory disease
AH	Aspergillus hypersensitivity
ASMCs	Airway smooth muscle cells
BD	Bronchodilator
BPT	Bronchial provocation test
CD	Cluster of differentiation
CF	Cystic fibrosis
COPD	Chronic obstructive pulmonary disease
COX	Cyclooxygenase
CP3A4	Cytochrome P3A4
DCs	Dendritic cells
DNA	Deoxyribonucleic acid
ECRHS	European Community Respiratory Health Survey
EIB	Exercise induced bronchoconstriction
ELF	Extra-cellular lung fluid
ELISA	Enzyme-linked immunosorbent assay
FeNO	Fractional exhaled nitric oxide
FEV1	Forced Expiratory Volume in first second
FVC	Forced vital capacity
GINA	Global initiative for asthma

GM-CSF	Granulocyte-macrophage colony-stimulating factor
GOLD	Global Strategy for Management of Chronic Obstructive Lung Disease
GR-β	Glucocorticoid receptor beta
GWAS	genome-wide association study
HCV	Hepatitis C virus
HDM	House dust mite
HLA	The human leukocyte antigen
ICS	Inhaled corticosteroids
IgE	Immunoglobulin E
IL	Interleukin
IL-1β	Interleukin 1 beta
INF	Interferon
KIU/l	Kilo international unit per litre
LABA	Long-acting beta2-agonist
LR	Likelihood ratio
LTRA	Leukotriene receptor antagonists
MCP-1	Macrophage chemoattractant protein-1
MHC	Major histocompatibility complex
MMP-9	Neutrophils release matrix metalloproteinase 9
MnSOD	Manganese superoxide dismutase
NSAIDs	Non-steroidal anti-inflammatory drugs
OCS	Oral Corticosteroids
PAF	Platelet-activating factor
PEF	Peak expiratory flow
PFT	Pulmonary function test
PPV	Positive predictive value
RANTES	Regulated on Activation, Normal T Cell Expressed and Secreted
RAST	Radioallergosorbent test
RCP	Royal College of Physicians
SABA	Short-acting beta2-agonist
SAFS	Severe asthma with fungal sensitization
SARP	Severe Asthma Research Program

SCF	Stem cell factor
SCIT or	Sub-cutaneous immunotherapy
sIgE	specific immunoglobulin E
SLIT	Sub-lingual immunotherapy
SNPs	single nucleotide polymorphisms
SPT	Skin Prick Test
TH0	Naïve T-helper cell (undifferentiated)
Th2	T-helper type 2
TLR	Toll-like receptor
TMB	Tetramethylbenzidine
TNF-α	Tumor necrosis factor alpha
TSLP	Thymic stromal lymphopoietin
TSLPR	Thymic stromal lymphopoietin receptor
UK	United kingdom
USA	United states of America
VOCs	Volatile organic compounds
WHO	World health organization

Introduction

The word asthma is a derivation from the ancient Greek, *aazein*, meaning "gasping" or "panting". **(Marketos *et al,* 1982)** Asthma is a common and potentially serious chronic disease that imposes a substantial burden on patients, their families and the community. It causes respiratory symptoms, limitation of activity, and flare-ups (attacks) that sometimes require urgent healthcare and may be fatal**.** Fortunately, asthma can be effectively treated, and most patients can achieve good control of their asthma. **(Reddel *et al,* 2015)**

Sensitization to fungi is an important factor in patients with allergic respiratory tract diseases, playing a major role in the development, persistence, and severity of lower airway disease, particularly asthma. Direct associations between increased fungal exposure and loss of asthma control are numerous, but only recently have direct causal associations with the development of asthma become apparent. **(Denning *et al,* 2006)**

Various studies report that 12% to 42% of atopic patients are mould sensitive. **(Bartra *et al,* 2009; Hedayati *et al,* 2009; Almogren *et al,* 2009)** It is reported that Sixty-six percent of mould sensitized patients were sensitive to one or more fungi based on SPT and/or specific serum IgE results. Positivity to SPT and/or specific serum IgE was 45%

for *A. fumigatus* & 36% for *C. albicans*. **(O'Driscoll *et al*, 2009)**

Aspergillus, a genus of spore-forming fungi found worldwide, is linked to asthma in more ways than one. This generally develops in atopic subjects and is sustained by continuous inhalation of *Aspergillus* antigens, triggering asthma. The clinical spectrum of *Aspergillus*-associated hypersensitivity respiratory disorders includes *Aspergillus*induced asthma, allergic bronchopulmonary *aspergillosis* (ABPA) and allergic *Aspergillus* sinusitis (AAS). **(Shah, 1998)**

The reported frequency of *Aspergillus* sensitization in patients with asthma has varied from 16-38% in different parts of the world. **(Longbottom and Pepys, 1964; Hendrick *et al*, 1975; Schwartz *et al*, 1978; Maurya *et al*, 2005)**

In Delhi, they found that (28.5%) of patients with asthma had a positive skin test to *Aspergillus* antigens. In Cleveland and London, they found that 28% and 23% of patients respectively had immediate skin reactivity to *Aspergillus* antigens. **(Maurya *et al*, 2005; Schwartz *et al*, 1978)**

While the role of several moulds as aero-allergens has been studied, the significance of the yeast *Candida albicans* in allergic diseases is still unclear. Studies of *Candida* as a potential allergen are rather few. Earlier studies found that

sensitization to this yeast is associated with chronic asthma and rhinitis both in children and adults **(Asero and Bottazzi, 2004; Shah, 2004)**

In a study of fungal allergy Positive SPT with mould allergens were found among 10.8% farmers and 6.8% bakers with occupational allergy. The fungi allergens giving positive SPT results most frequently were *Candida albicans, Levures mélanges, Aspergillus mix*. and *Charbons cerealiers* in both groups. **(Wiszniewska *et al*, 2013)**