شبكة المعلومات الجامعية

التوثيق الإلكتروني والميكروفيلم

بسم الله الرحمن الرحيم

HANAA ALY

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جامعة عين شمس

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قسم

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HANAA ALY

Detection of TNF-α as a Cofactor in the Pathogenesis of Nasal Polypi

Thesis

Submitted for partial fulfillment of master degree in ***Science of Otorhinolaryngeology***

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Zeinab Rezk Abd_elnazer Ali

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List of Abbreviations

Abb.	Full term

A .....Allele

AA .....Homozygote mutant

AFRS .....Allergic fungal rhino sinusitis

AFS .....Allergic Fungal Sinusitis

ASA .....Acetylsalicylic acid

CF .....Cystic fibrosis

CRS .....Chronic rhinosinositis

ECP .....Eosinophil cationic protein

G .....Genotype

GA .....Heterozygote

GG .....Homozygote wild

HLA .....Human lecuocyte antigine

ICAM-1.....Intercellular adhesion molecule-1

IL-5 .....Interleukine 5

MAPK .....Mitogen-activated protein kinases

MHC .....Major histocompatibility complex

NARES..... Nonallergic rhinitis with eosinophilia syndrome

NF- B.....Nasal fibroblasts binding receptors

NP .....Nasal polypi

PGE2 .....Prosta gladin E2

SAE .....Staphylococcus aureus enterotoxin

SNP.....Single neculiotide polymorphism

TACE .....TNFα converting enzyme

List of Abbreviations

Abb.	Full term
TNFR-I	*Type I TNF-a receptor*
TNFRII	*Type II TNF-a receptor*
TNF-α	*Tumour necrosis factor-α*
TNF-α 308G	*Tumor necrosis factor alpha*
VCAM-1	*Vascular cell adhesion molecule-1*

ABSTRACT

Background: Nasal Polyposis (NP) is a complex multi-factorial disease; associated with several environmental, genetic and inflammatory factors. TNF-alpha is one of the major pro-inflammatory cytokines involved in NP pathogenesis. Some of the polymorphisms of this gene affect its expression.

Aim of the Work: To evaluate the polymorphism of TNF-alpha G/A308 gene and its association with nasal polyposis in Egypt.

Patients and Methods: In this case-control study, 25 patients with NP and 25 healthy individuals referred to Ain Shams University hospital were evaluated. After DNA extraction, RFLP-PCR was used to determine polymorphism. Chi-square test was used to compare the frequency distribution of genotype and alleles of TNFalpha gene with NP. The frequency of genotype G/G, A/A and G/A in the NP group was 8, 40 and 52%, and in the control group was 76, 1 and 5 %, respectively.

Results: There was a statistically significant difference between genotype G/G in two groups (P = 0.0001). In addition, the frequency of allele A in patients and controls was 10 and 1%, respectively; and this difference was statistically significant (p = 0.0001). The findings of this study demonstrated that polymorphism in TNF-alpha gene might be a risk factor for NP in Egypt and the minor frequency of TNF-alpha G308A allele in the current study is slightly more than other major populations. However, more investigations with high number of population are necessary in future.

Conclusion: According to scientific evidence on TNF-α gene promoter G/A 308 polymorphism in Egypt, it seems that the pattern of genotypic distribution in all areas is the same. However, we found the greater amount of allele A in this study compared with the control group, and the occurrence of G/A genotype related to NP but for more valid results, a larger sample size is necessary. However on our results this polymorphism might be considered as a risk factor of susceptibility of NP in Egyptian people.

Keywords: *Nasal Polypi, Chronic rhinosinositis, Eosinophil cationic protein, Intercellular adhesion molecule-1*

INTRODUCTION

Nasal polyposis is one of the most common chronic inflammatory diseases of mucosa of nose and paranasal sinus causing stuffy nose. Most of the Patients are complaining of nasal obstruction, difficulty of breathing, nasal discharge, post nasal drip, nasal congestion, sinus pain, anosmia and hyposmia. It is not clear why some people develop the chronic inflammation that tends to lead to nasal polyps, or why this chronic inflammation causes polyps in some people and not in others. People with chronic sinus infections, allergic rhinitis, asthma, and cystic fibrosis are more likely to have nasal polyps ***(Bachert et al., 2014).***

During the past 10 to 20 years, many studies have been performed to identify susceptible genes that are associated with nasal polypi-related traits. Despite achievement in the identification of candidate genes and their association with formation of nasal polypi. The large challenges remain as the genetic and molecular alterations required for its development and progression are still unclear ***(Wang, 2008).***

Although many inflammatory cytokines have been identified in nasal polypi tissue, the initial trigger that causes