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Correlation of Single Nucleotide Polymorphisms of IL4 Gene in Incidence and Progression of Asthma

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Abstract

Background: The chronic inflammatory condition known as asthma is characterized by inflammation of the airways, which is produced by a number of different cells and biological components. to investigate whether or not there is a correlation between the polymorphism of the IL-4, IL-6, and IL-18 genes with asthma in Iraqi patients. to determine whether or whether there is a correlation between the polymorphism of IL-4, IL-6, and IL-18 and the severity of asthma.

Method: Patients suffering from asthma were recruited for this study from the Asthma and Allergy Clinic at Al-Zahra Hospital, which is located in the region of Alkut. One hundred people who suffer from asthma were included in this study.

Results: For the purpose of this study, a total of one hundred people with asthma were recruited from the Al-Zahra hospital located in the Alkut province between the months of March 2021 and April 2022. At the same time, a hundred individuals who were considered to be healthy controls were also included in the study. In further study, there should be an increased focus on include a higher number of patients to guarantee a more precise assessment. It is probable that the conclusions of different studies will not align with one another owing to the heterogeneity of the illness, which is a consequence of the complexity of bronchial asthma as a disease. And the statistical power associated with a small sample, which is why there is a need for larger study to show any importance of this cytokine gene polymorphism in bronchial asthma and the involvement of cytokines in the severity of asthma.

Keywords: IL-4, Polymorphism, asthma, genetics, airway inflammation, inflammatory disorders.

Introduction

The patient body cells and other cell-related chemicals lead to airway inflammation. The many cell types that contribute to the development of asthma include mast cells, eosinophils, T lymphocytes, macrophages, neutrophils, and epithelial cells (1). Along with this inflammation, there are varying degrees of airflow obstruction, the majority of which may be treated naturally or with medicine (2). Most of these impediments may be removed naturally or with the use of medication. When a person

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is most susceptible, symptoms of asthma, such as recurrent coughing fits, dyspnea, tightness in the chest, and wheezing, most often develop at night or in the early hours of the morning (3). Inflammation and the airflow restriction it causes are mostly to blame for these symptoms (4,5). Inflammation, which may result from a variety of different reasons, is correlated with an increase in the bronchial reactivity to diverse stimuli. This increase in bronchial reactivity has also been associated with inflammation (6). The majority of medical professionals concur that the basic cause of asthma is the emergence of allergic inflammation, which leads to the manufacture of immunoglobulin E. (IgE). Antigen presentation cells, or APCs, are responsible for consuming allergens that have entered the airway. T helper type 2 cells, or TH2 cells, are produced when T cells activated by certain cytokines are exposed to particular allergens (7). Numerous cell types may be impacted by the cytokines that TH2 cells secrete. These cells include lymphocytes, mast cells, eosinophils, epithelial cells, smooth muscle cells, and others (8). The cytokines interleukin (IL)-4 and interleukin (IL)-13 are two that are released by TH2 cells. Activated B cells are the first cells in the body to begin producing IgE. The inflammation that results from all of these changes in the airways has the potential to impede airflow (9). This limitation of airflow causes the symptoms of asthma. More than 200 million people worldwide suffer from asthma, and it is the number one killer of over 0.2 million people year. Although asthma may affect persons of any age, young children and adults are disproportionately affected by the ailment because of its rising prevalence (10). The primary cytokine implicated in the development of allergy disorders may be identified as IL-4. One impact that is especially important for asthma is the stimulation of fibroblasts and mucus-producing cells. This demonstrates that the establishment of the airway remodeling involves IL-4 (11). Another function of interleukin-4 that may be significant in allergic inflammation is its ability to promote the expression of vascular cell adhesion molecule-1 on endothelial cells. Given that this capacity has been shown, it is more likely than not that interleukin-4 is to blame for allergic inflammation (11). As a consequence, the endothelium will have a larger potential for adhesion when T-cells, eosinophils, basophils, and monocytes-the many cell types involved during allergic reactions are present. IL-4 has long been discussed as a potential therapeutic target for allergic responses and asthma because of the aforementioned properties (12). It is commonly believed that the alveolar macrophages of asthmatic patients respond to allergen exposure by producing greater baseline levels of IL-6 than individuals without asthma. Those without asthma, however, suffer this. Eosinophil recruitment is boosted by IL-18 (IL-18) levels are higher in allergy sufferers; this suggests that IL-18 contributes to the development of chronic and progressing allergic inflammation. It is likely that IL-18 is a reflection of disease activity in moderate to severe asthma exacerbations since it has the potential to contribute to the activation of immune responses (11,13). The aim of this study is to investigate the Correlation Of Single Nucleotide Polymorphisms of IL4

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gene in the incidence and progression of asthma in Wasit province of Iraq.

Sampling and methods

The research protocol was ethically accepted by the Alkut College University council. According to the Iraqi Community Respiratory Health Survey, which defined someone as having asthma if they had an attack during the preceding 12 months or often used asthma medications, all of the asthmatic individuals had been diagnosed with the condition by a specialised physician. Randomly chosen from the general community, the control group consisted of unrelated individuals without a history of atopy or asthma who were age and sex matched with asthmatic patients.

Ethical approval

The Alkut College University council approved the study process in terms of ethics. The Iraqi Community Respiratory Health Survey determined that someone had asthma if they had had an attack during the previous 12 months or often used asthma medications. The study's asthmatic participants were all diagnosed with the condition by a qualified medical professional. The participants in the control group were picked at random from the general population. These volunteers were matched in age and gender to asthmatic patients and did not have a history of asthma or atopy.

Patients and examination

On the basis of a questionnaire that had been designed expressly for the aim of assessing the severity of the asthma and the symptoms that are linked with it, a detailed history was gathered. According to the agreement reached in Canada, a patient's asthma is considered to be very mild if the person only has moderate symptoms on a very seldom basis and if the individual only sometimes needs to take a drug that has a short-acting beta agonist in it. Mild to moderate if signs and symptoms are well-controlled and if moderate doses of inhaled corticosteroids are used seldom in conjunction with short-acting beta agonists. If these conditions are met, the severity of the condition is likely to be low. When used in conjunction with beta agonists that have a rapid onset of action, inhaled corticosteroids are administered in dosages that range from low to moderate, but the end effect is that symptoms are only partially controlled. High dosages of inhaled corticosteroids are often used in conjunction with severe symptoms that the patient is able to control on their own as well as the usage of short-acting beta agonists. Extremely hazardous in the case that the symptoms are not well treated despite the treatment of oral corticosteroids, significant doses of inhaled corticosteroids, and short-acting beta agonists. Patients had a history of smoking or other lung-related disorders, such as chronic bronchitis, emphysema, TB, pneumonia, and so on, were not

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included in this research. Patients who had a history of lung cancer were also not included in this investigation. Asthma-like symptoms, a history of smoking, known allergies, asthma-like symptoms, and a positive family history of allergies and asthma were all characteristics that disqualified prospective volunteers from the control group.

Results

In the study, which took place between March 2021 and April 2022, 100 asthmatics from the Al-Zahra hospital in the Alkut province participated. The calendars for the years 2021 and 2022 featured these months. The planet's Alkut area is home to the station at the center of this controversy. Those who received their diagnosis of asthma from a specialized clinic are candidates for this therapy. The clinic had to have had patients. According to the agreement made in Iraq, patients were divided into three categories based on the severity of their conditions: mild, moderate, or severe symptoms. The primary objective of the research was to investigate the relationship between the levels of polymorphism in IL-4, IL-6, and IL-18 and the severity of asthma in Iraqi patients. In order to direct future research, this was done. Asthma in Iraqi patients was investigated, as well as any potential associations between IL-4, IL-6, and IL-18 polymorphisms. To determine whether or not there is a relationship of this kind, this was done (Table 1) (figure 1, 2, 3).

Samples demographics

Data of this study showed that asthmatic patients had positive family history more than control which is statistically significant. Regarding age and sex there was no statistical difference between asthmatic patients and control group (figure 1, 2, 3) (Table 1).

Table 1: demographics of study

Type of data		**Cases**	**Healthy**	**Significancy (P)**
Age	**Average**	20-65	20-65	0.07
	Mean ±SD	45.2±5.2	42.3±6.6	
Gender	**M**	55%	56%	0.05
	F	45%	44%	0.06
History Prescence/absence of disease	**+**	35%	0	0.008
	-	65%	100%	0.002

M: male, F: female, +: positive, -: negative, P: P. value, SD: standard deviation.

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Atopy and asthma have numerous similarities. The prevalence of atopic diseases such allergic rhinitis and allergic dermatitis was studied in relation to asthma. The incidence of hepatitis C, diabetes mellitus (DM), and hypertension were investigated in relation to asthma in Iraq. It was discovered that patients with asthma had hypertension 11% of the time, diabetes 9% of the time, allergic rhinitis 7% of the time, HCV 6% of the time, and hypertension + DM 3.5% of the time (Table 1) (figure 1, 2, 3).

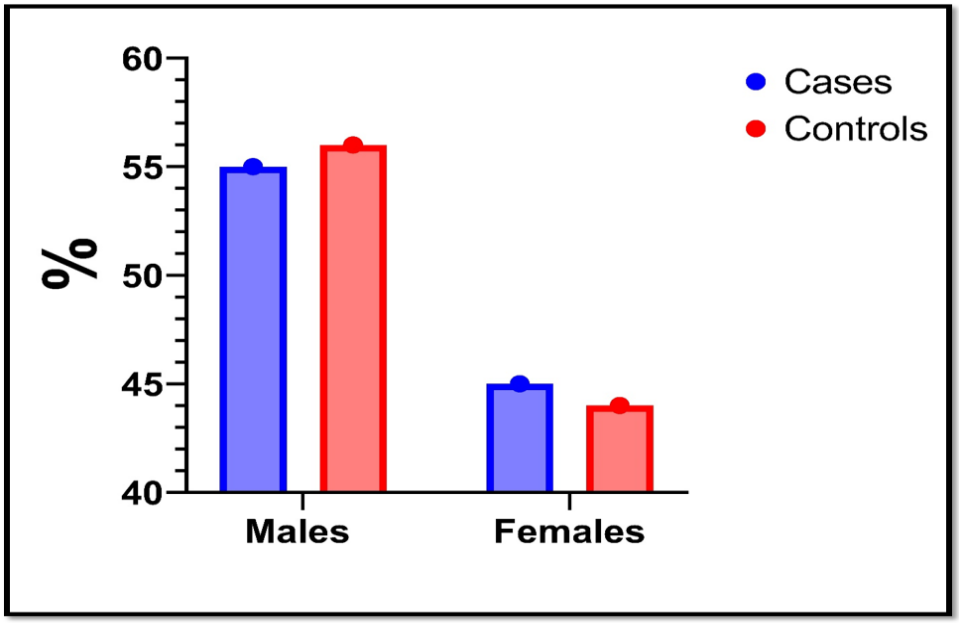

Figure 1: distribution of cases according to the gender

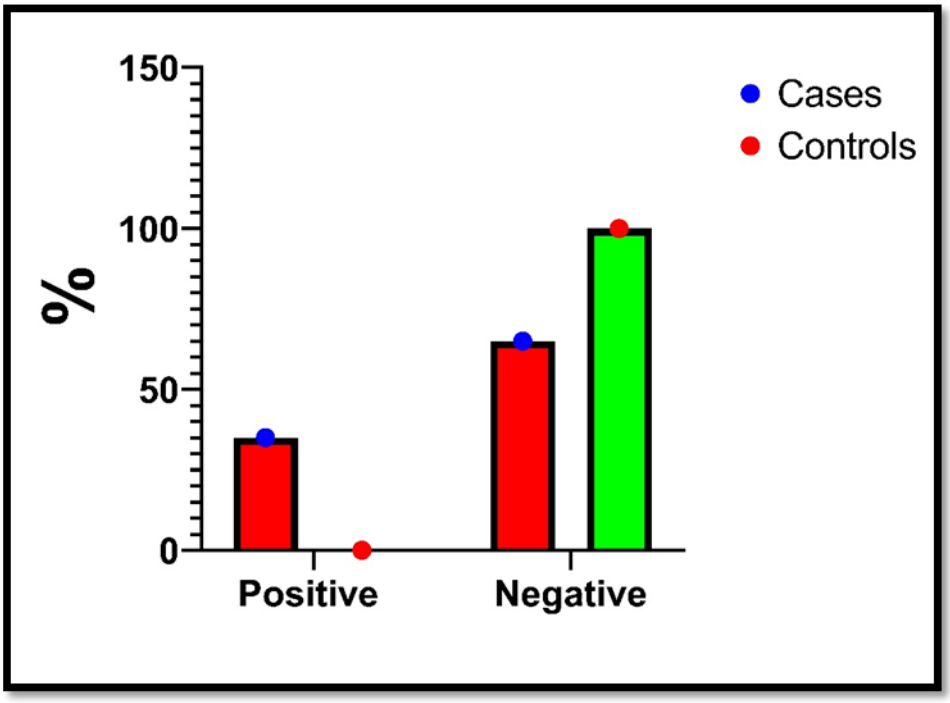

Figure 2: Asthma family history of patients and controls.

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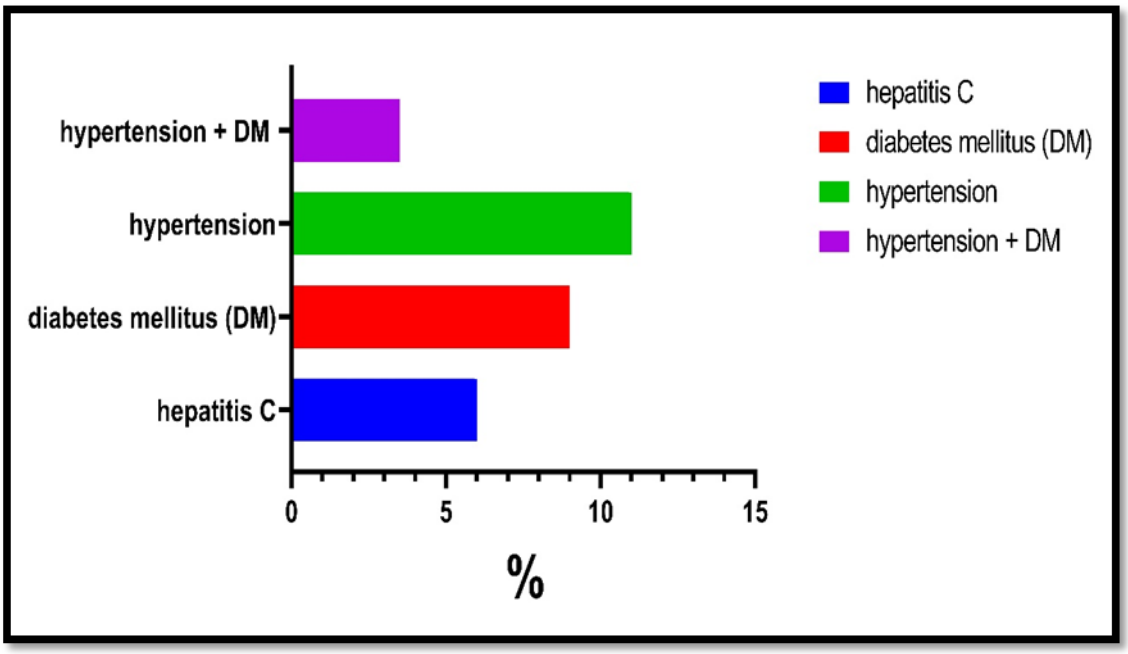

Figure 3: history of other diseases in patients.

Discussion

Asthma and other atopic diseases are caused by a confluence of environmental and genetic risk factors, according to a broad agreement among medical specialists. It is also widely known that both types of factors contribute to the manifestation and course of the disease. This holds true for each of these illness features. This study was conducted due to a lack of understanding about the association between IL-4, IL-6, and IL-18 polymorphisms and asthma in the adult population of Egypt, which inspired the researchers to examine the problem (14). This study was conducted due to a dearth of information on the association between IL-4, IL-6, and IL-18 polymorphisms and asthma in the adult population (1, 2). Due to the paucity of information on their relationship, this inquiry was conducted to fill in the blanks (15). The participants in this trial were randomly recruited from a pool of asthmatic patients already receiving therapy at a clinic specialising in the treatment of asthma (2). These patients have been frequenting this clinic for an extended period of time. The clinic was formally recognised as an asthma treatment centre. This assessment was completely voluntary on the side of the participant (16–18). In accordance with the severity of their symptoms, asthmatic patients were categorised as mild, moderate, or severe (3,6). These categories were designated as mild, moderate, and severe (19). Asthma severity was used as the criteria for classifying individuals into these groups (20). Patients stated that someone in their family had asthma, either in conjunction with or apart from other allergy illnesses (21–23). A significant proportion of patients brought this up in dialogue with their doctors (8,9). IL-4, which plays a well-

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established function in the pathophysiology of asthma and has been linked to asthma severity, has also been linked to the severity of dermatitis and allergic rhinitis. IL-4 is associated with the severity of asthma and other atopic diseases (24). Some data suggests that IL-4 is associated with the severity of asthma and other atopic illnesses (9). It has been shown that the IL-4 gene has several polymorphisms, each of which has been linked to an increased risk of getting asthma (25). In this study, the 620 C T polymorphism of the IL-4 gene was evaluated to discover whether it is linked with bronchial asthma in Iraqi patients (7). This study was conducted to evaluate whether or not a link exists between the polymorphism and bronchial asthma (12). To qualify for participation in the control group, prospective patients were required to show that they had no history of asthma (26). Our study indicates that the IL-4 620 C T polymorphism seems to have no significant association with the development of asthma (27). In asthma patients, the probability of having the CC genotype was 29%, the frequency of having the TC genotype was 44.2%, and the frequency of having the TT genotype was 27.5% (28). In contrast, the frequency of these genotypes in the control group was 41.11 percent, 43.22 percent, and 22.12 percent, respectively (29). Compared to the frequency of the "C" allele in the control group, which was found to be 60.21 percent, the frequency of the "C" allele among persons with asthma was found to be 49.2 percent (30). The frequency of the "T" allele was higher in the asthmatic population than in the control group, coming in at 45.7% compared to 38.1% in the control group (31). In contrast, the frequency of the allele containing the letter "A" was much lower than in the control group (32-34).

Concluding Remarks and Summation

Bronchial asthma is one of the most common chronic disorders seen across the globe, and it is a substantial contribution to the costs that are borne by the health care system. It is a significant problem that has an effect on the health of individuals all around the globe. Cytokines have a role in the control of the immune response, as well as a variety of other components of the immunological response. There are variations in the production of cytokines that are caused by individuals, and it is possible that these variations might be ascribed to SNPs that are present in the DNA of the cytokines in question. These changes disturb the balance between pro-inflammatory and anti-inflammatory cytokines and may have an influence, not only on the severity of bronchial asthma, but also on how effectively patients respond to treatment for the illness. There is substantial evidence that the cytokines IL-4, IL-6, and IL-18 all have a role in the development of bronchial asthma. One hundred individuals who were diagnosed with asthma were used as participants in this study, while a control group consisting of seventy-five individuals who were in good health served as volunteers. Patients were categorised into one of three different categories depending on the degree to which they were impacted by the condition: mild, moderate, or severe. All of the patients

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and the healthy controls had their veins pricked in order to collect blood samples for analysis. The veinous blood samples that the participants in the study submitted were used to extract the individuals' genomic DNA. Researchers genotyped SNPs that were located in IL-4 and IL-18 in their study (PCR-ssp). The genotyping of IL-6 SNPs was carried out by (RFLP -PCR). Everyone who took part in the study was more than 20 years old. The patients' ages varied from 20 to 65 years old, with a mean of 42.3%, while the healthy controls' ages were 45.2%. There was no significant difference in the genotype distribution for the IL-4 polymorphism (620 C T) between asthmatic patients and healthy control persons. This is due to the fact that the frequency of the CC, TC, and TT among patients was, respectively, 35 percent, 65 percent, and 24.5 percent, while the frequency among healthy control individuals was, respectively, 36 percent, 42.7 percent, and 21.3 percent. There was no discernible difference in the distribution of genotypes for the IL-6 (620 G C) polymorphism between the asthmatic group and the control group. The frequency of the alleles CC, GC, and GG was 1.5 percent, 34.2 percent, and 66.5 percent, respectively, among patients, while the frequency of these alleles was 0 percent, 28.7 percent, and 77.3 percent, respectively, among control individuals. The frequencies of the genotypes CC, GC, and GG were respectively 4%, 0%, and 96 % in healthy participants, while in control subjects, those rates were respectively 0%, 11.7 %, and 90.3 %. This suggests that the distributions of genotypes for the IL-18 (134 G C) polymorphism were substantially different in healthy individuals compared to control participants. In the IL-4 (622 C T), IL-6 (620 G C), or IL-18 (137 G C) SNPs, there was not a significant difference seen between the genotype distributions of the three various severity levels of asthma. In conclusion, neither the IL-4 (620C T) SNP nor the IL-6 (620G C) SNP had any effect on the severity of bronchial asthma in the Iraqi patients who took part in our experiment. Patients hailing from Iraq who have the IL-18 (134 G C) SNP are at an increased risk of experiencing asthma symptoms. In further study, there should be an increased focus on include a higher number of patients to guarantee a more precise assessment. Because bronchial asthma is a difficult disease, it is likely that the heterogeneity of the condition may lead to conflicting results in research. This possibility arises in light of the fact that bronchial asthma is a complicated sickness. And the statistical power that comes with a tiny sample, which is why there is a need for more extensive study in order to determine whether or not this has any impact. cytokine gene polymorphism in bronchial asthma and the role of cytokines in the severity of asthma.

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