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Evaluation of the effect of cigarette smoking on interleukin-4

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Abstract:

Background*: Cigarette smoke have adverse effects on the control of allergic sensitization and Bronchitis. Also, numerous Studies related to IL-4 have been revealed a huge of information on the different roles for this cytokine in homeostatic regulation and disease pathogenesis.*

Methods*: 100 is the total number of subjects who were participated in our study and suffering bronchitis, 50 of them were smokers, other 50 subjects were non-smoker as controls. Our study lasted for four months Between November 2019 and the end of February 2020; smokers consumed 30-60 cigarettes a day regularly for at least five years. Also, Smokers have had respiratory allergies. The ethical guidelines accepting forma were taken and signed by each volunteer Blood samples were collected via GEL & Clot Activator 3-5ml blood tubes to separate the IL-4 serum*

Results*: The total amounts of IL-4 were significantly elevated in bronchitis diseased for smokers subjects compared to non-smoker subjects, whereas IL-4 showed a positive relationship to the bronchitis smokers' status, and low amounts were found in the non-smoker's group.*

Conclusion*: Our present outcome concluded that IL-4 shows a correlation to expulsion. That promotes the production of inflammatory cytokines together in the presence of smoking as stress and the illness.*

Keywords: *Cigarette smoke, IL-4, cytokine*

I. Introduction:

The increasing number of smokers has become a matter of concern that should be taken care of. Especially, In the era of civilized development, people start focusing on their health and thinking about how to avoid diseases. Because of cigarette smoking,each year four million people die (1). According to WHO statistics (2),This number of deaths can be doubled or increased every year. Numerous studies have demonstrated that tobacco smoking is the principal cause of an irregular rise in hematological parameters contributing to early atherosclerosis, coronary

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disorders, polycythemia vera, and chronic obstructive pulmonary disorder (3). Additionally, smoke use causes cancer (4), pancreatitis (5), periodontal disease (6), stomach diseases (7).

Interleukin (IL)-4 plays a vital role in the development of allergic inflammation by stimulating and associating with IgE secretion by B lymphocytes in the π isotype switch (8).Studies have explained that IgE-mediated immune responses are further enhanced by IL-4 's ability to upregulate existing IgE receptors on the cell surface:(FcεRII; CD23)Low-affinity IgE receptors are present in B lymphocytes and mononuclear phagocytic cells, while high-affinity IgE receptors are present in mast cells and basophils (9). In the spread of immediate allergic reactions, IgE-dependent activation of IL-4-stimulated mast cells plays a critical role.

Studies concluded that there is another mechanism by which IL-4 participates in asthma obstruction of the airway through stimulation of the expression of the mucin gene, also through mucous hypersecretion (10). Researchers have suggested that IL-4 increases the expression of fibroblast inflammatory cytokines which can contribute to chronic asthma inflammation and lung remodeling (11).

One of the vital activities of IL-4 is the promotion of asthmatic lung cellular inflammation by inducing a vascular cell adhesion molecule called (VCAM)-1 on vascular endothelium (12).

This VCAM-1 interacts with IL-4 and contributes to the migration to an inflammatory site of T-lymphocytes, basophils, monocytes, and eosinophils.

Also, IL-4 can inhibit eosinophilic apoptosis and elevate eosinophilic inflammation by inducing and activating eosinophilic chemotaxis by increasing eotaxin expression (13). During the production of allergic inflammation, the main biological activity of IL-4 identifiedCapacity to induce naive T-helper type 0 (TH0) lymphocyte conversion into TH2 lymphocytes (14,15). TH2 cells that secrete IL-4, IL-5, IL-9, and IL-13 but cannot produce interferon-ÿ (16). Recent studies have shown that IL-4 administration can produce TH2-like lymphocyte clones whereas the anti-IL-4 incubation blocks this differentiation. TH2-like lymphocyte stimulation to the IL-4 receptors(17),Is a special biological feature of IL-4. Given its ability to inhibit T-lymphocyte apoptosis, IL-4 plays a key role in allergic immune responses. These cell activation also enables the release of cytokines to spread rapidly.

Since smoking cigarettes have a negative impact, especially its negative effects on the respiratory system, as well as the extreme importance of interleukins of the respiratory system, our current study aimed to estimate the harmful effects of cigarette smoking on one type of interleukins which is IL-4.

II. Materials and Methods:

In a clinically smokers and non-smokers group of subjects, both groups have bronchitis, our current research was conducted to scrutinize the associated effects of cigarette smoking on IL-4 as a monitor. The research included a total of 100 subjects;Fifty were smokers, and fifty were 12–62 non-smokers. All those volunteers were male. The volunteers were recruited from the Diyala Governorate / Iraq Teaching Hospital in Baquba.

For at least 5 years the smokers have been consuming 30-60 cigarettes per day regularly. Additionally, acceptance of the research It was taken from each individual; it was confirmed by the Diyala University / Science College Ethical Review Committee. For each volunteer, a questionnaire was completed including name, age, number of smoked cigarettes per day, smoking time, and chronic illnesses. This removed patients with acute side effects such as influenza, nervous system, asthma, diabetes, and hypertension.

GEL & Clot Activator tubes collected the samples, and 3-5ml of venous blood was drawn, after which serum was isolated by centrifugation (Nuve-NF200). Serum samples were investigated by using ELISA Human Reader HS, also the Elisa kit was used to measuring IL-4 is the Shanghai/china kit which method of diagnosis depends on the Sandwich Elisa test principle. The inspection steps have been followed according to the instructions of the kit which is recommended by the producing company.

III. Statistical analyses

Current study data were analyzed by comparing percentages using the Chi-square (X^2) test. Also, the sensitivity and specificity of the mean volume of platelets (MPV) measured. It described numeric data (Mean ± SD).T-test used to compare two numerical variables whereas F test (ANOVA) used to compare three or more numerical variables. For testing a meaning level of α=0.05 has been applied. Program (SPSS v.22 and Excel 2013) used for the analysis of current data.

IV. Result:

This study included 100 volunteers who were divided into two groups 50 cases who were smokers and 50 cases were non-smokers as a control both of them suffering Bronchitis. Table 1 displays the features of 100 cases. Depending on age, the mean ± SD was 34.3±1.34 years for non-smokers (P-value=0.001), while the mean ± SD age was 43.93±12.99 (P-value=0.001) for smokers.

Table (1) Comparison of anthropometric characters among research groups

Age	Smokers		Non-smokers	
	No.	%	No.	%
12-22	13	26	5	10
22-32	23	46	19	38
32-42	3	6	15	30

42-52	7	14	6	12
52-62	4	8	5	10
Total	**50**	**100 %**	**50**	**100 %**

According to a questionnaire that was collected from volunteers, a question was asked about the severity of their bronchial allergies. We found that through their answers, the severity of the disease in smokers is significantly stronger than non-smoking volunteers, where the percentage was 80% for the smokers and 20% in non-smokers (p-value=0.01) as in theTable2.

Table (2) Severity of bronchitis effect

Groups	**Severity of bronchitis**		**otal**
Smokers	**40**	**0**	**0**
Non-smokers	**10**	**0**	**0**
P-value=0.01			

After separating the serum from the blood, The ELISA device Human Reader HS measured the concentration of interleukin-4 by the procedure recommended by the company for all models and after statistical analysis.Our results showed that there are significant increases of IL-4 concentration the smokers comparing with non-smokers who are suffering from bronchitis (p-value=0.01) as shown in Table 3.

Table 3 IL-4 Concentrations in smokers and non-smokers

Groups	**IL-4 concentration**	**Total**
	Mean±SD	
Smokers	390±500	50
Non-smokers	230±312	50

P-value=0.001*

V. Discussion:

The latest findings have demonstrated that smoking tobacco hurts the human body. In specific, the effect on the immune system, Mustafa abdulkareem SALMAN et al.mentioned in their study the severity effect of smoking on one barrier of the immune system, where the effect was significantly on white blood cells also they concluded that the Excessive smoking may cause chronic obstructive pulmonary diseases (3).

Despite huge epidemiological data associated with cigarette smoke exposure to the development of respiratory diseases, in particular, it remains to be established the role of cigarette smoke effects in some respiratory diseases.Recent studies have begun describing the association between cigarette smoke and the previous effects on host anti-mycobacterial immunity (18,19).

In vivo studies have found that the continuous smoke of cigarettes has a profound effect on local Immunity in the lungs They also did not find any modification in peripheral lymphoid organs to the generation of CD4+IFN-Δ+ T cells. Also, another study observed that tobacco smoke dramatically inhibited T-cell entry into the lung, these T-cells that received enhanced Th2 reactions, facilitated an increase in Th2 CD4 + IL-4 + T cells, and decreased IL-4 levels (20).

Our study, therefore, aimed to assess the level of IL-4 concentrations in patients suffering from bronchitis in two groups that are smokers and to compare them with patients who are non-smokers.

First, our results showed that the age group that was significantly susceptible to bronchitis was between the ages of 22-32, mean ± SD was 34.3±1.34 yearsAmong non-smokers (P-value = 0.001), the median ± SD age among smokers was 43.93±12.99 (P-value = 0.001).the intensity of bronchitis among smokers could be due to people experiencing two types of stress which were cigarette smoking and the disease. This is an explanation about the severity of bronchitis also the most of individuals who felt the severity of bronchitis were ages 22-32 and 32-42 years.

The results above indicate a significant increase of IL-4 concentrations in smokers with bronchitis, which in turn indicates an increase in inflammation due to the induction of T cells which is lead to increase the production of IL-4. This Increasing IL-4 production could be a natural response to suppress inflammation.

Interestingly we have noticed that there is an excessive increase in IL-4 levels for smokers, which could be a natural response to suppressing the stress caused by smoking and at the same time in response to bronchitis.

VI. Conclusion:

Our current study results showed that bronchitis affects the 22-32 age groups significantly, while the elder year groups are the least susceptible to this disease. Additionally, the severity of the disease was greater in smokers than in non-smokers.

Moreover, IL-4 levels were significantly higher in smokers, which was directly participated in inflammatory processes also IL-4 was vitally responsible for the serial activation of inflammation, this could be an excessive response or a natural response as a result of smoking and illness at the same time

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