

## The Effect of Smoke Cigarette on Immune Responses of Allergic Rhinitis Patients

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Allergic rhinitis (AR) is the most widely distributed diseases of upper respiratory tract. The disease is involved many immunological activities and any changes in this system can increase the risk of allergic rhinitis. The disease is also affected by some environmental agents such as dust house, mites, pollens, animal danders and cigarette smoking. The aim of this study was to investigate the effect of cigarette smoking on different immune system of patients suffered from allergic rhinitis divided in two groups as cigarette and non cigarette smokers to find whether these patients are more sensitive to cigarette smoke than others and this may aggravate allergies. This analytic descriptive study was conducted on 632 allergic rhinitis patients aged between 17 to 69 years olds referred to the hospitals of Zahedan city from 2005 to 2012. Complete blood cell count such as WBCs, RBCs, lymphocytes, Hb, the amount of serum IgA, IgG, IgM, C3, C4 levels and total serum IgE of patients were measured using a commercial SRID and nephelometry methods. The significant differences in obtained results were evaluated by  $\chi^2$  statistical test and SPSS software. The results indicated that low number of neutrophils, and low amount of IgA and IgM were found in smokers compared with nonsmokers. Increased number of WBCs, RBCs, lymphocytes and increased level of Hb, serum IgG, IgE, C3, C4, were found in smokers compared with nonsmokers. Significant correlation between all indices of smokers and nonsmokers individuals were observed (P value 0.01). Study results indicated that cigarette smoking is a risk factor for the development of allergic rhinitis and changing in variety immune responses, have a role in pathogenicity of disease.

**Key words:** IgE, IgA, cigarette and non cigarette smokers and allergic rhinitis.

Allergic rhinitis (AR) is one of the disease sensitivity of noise and upper respiratory tract that is widely distributed in human population around of world<sup>1</sup>. The disease is considered as manifestations of chronic airway inflammation as the major features of sinusitis, otitis and asthma<sup>2</sup>.

The disease is also affects people of all ages in industrialized countries suffer from this condition<sup>3</sup>. It is accompanied by frequent sneezing, runny nose and watery eyes<sup>4</sup>.

Seasonal symptoms of disease depends on exposing to outdoor allergens such as pollen, grasses, trees, and arriving of cold weather tend to decrease disease symptoms<sup>5</sup>, whereas the perennial allergic rhinitis induced by exposure of indoor irritants such as feather, dust house mite, mold and

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smoke cigarette leads to the symptoms of asthma and allergic rhinitis<sup>6,7</sup>.

It is now clear the disease is involved many immunological activities including cell types, T-lymphocytes, complement system and immunoglobulins<sup>8,9</sup>. Immunoglobulin's such as IgA and IgE are the major antibodies that act as a prevention of attaching microbe to the tissues<sup>6</sup>. C3 and C4 are a part of innate immunity that have inflammatory and anaphylaxis functions and have influence on susceptibility of host defenses to infectious diseases<sup>10</sup>. Any changes in amount of these molecules can increase the risk of diseases. Some environmental agents such as cigarette smoking may affect the disease and changes the level of these Igs and lead to increase the risk of allergic rhinitis.

Despite many efforts to prevent the spread of smoking, approximately one third over 15 years old of population around the world, were smokers. In Iran based on statistical reports of Ministry of Health and Medical Education in 2009, 15 percent of Iran's population (about 11 million people) were smokers and more than 75,000 people annually has died due to their smoking<sup>11</sup>.

Smoking as the first cause of death in the world, has been reported by WHO with different prevalence in modern societies and has predicted that by 2020 the death rate from its consumption, reach to 10 million<sup>12</sup>.

#### **It has been reported that smoking has effective role on the immune system of people**

Studies have shown that passive smoke exposure leads to changes in expression of genes controlling inflammatory responses and immune responses such as an increase in the number of neutrophils in the lung lymphocytosis and also increases the secretion of inflammatory mediators such as IL-8 increases in bronchial mucosa and increased expression of IL-10 and increase or decrease the level, such as TNF- $\alpha$  and IFN- $\gamma$ <sup>13,14,15</sup>.

It also reduces the body's resistance against biological and non biological pathogens and increases the incidence of allergic diseases including asthma and allergic rhinitis<sup>16</sup>. On the other hand smoke contains toxic chemicals, irritants and potent respiratory like sulfur, formaldehyde, carbon dioxide, akrolein and ammoniac and these materials have adverse effect on smooth muscle tone and inflammation of the bronchioles

airway and in adults cause more severe clinically and will intensify their pre-existing asthma<sup>17</sup>. The common symptoms of cigarette smoke are included as burning or watery eyes, nasal congestion, coughing and wheeze. The immediate and rapid effects of cigarette smoking on the respiratory, cardiovascular, gastrointestinal, metabolic systems and drug interactions have been interested of many investigators<sup>18</sup>.

Several studies examined the impact of smoking on incident of allergic rhinitis diseases<sup>19</sup>. They showed that cigarette smoking is common in these patients. These findings offered the different effect of cigarette smoking on immune responses. But how cigarette smoking has pathological effect on different immune system of allergic rhinitis patients is not well understood. The aim of this study was to investigate the effect of cigarette smoking on different immune responses of allergic rhinitis patients during the process of their disease with and without cigarette smoking.

## **MATERIAL AND METHODS**

The method of study was cross sectional analytic descriptive in which, 632 allergic rhinitis patients who have admitted to the Ali Ebne Abi Taleb and Ali Asghar hospitals of Zahedan city from 2005 to 2012 with included criteria such as history, symptoms of nasal obstruction, rhinorrhoea and nasal itching.

After gathering profile and questionnaire completion, 5ml peripheral blood was taken from patients and after clotting, serum was separated. Complete blood cell count such as WBCs, RBCs, lymphocytes, Hb, the amount of serum IgA, IgG, IgM, C3, C4 levels and total serum IgE of patients were measured with regards to correlation between these molecules and cigarette smoking. The significant differences in obtained results of allergic rhinitis patients with cigarette and non-cigarette smokers were evaluated by  $\chi^2$  statistical test and SPSS software and P value of less than 0.05 was considered significant.

## **RESULTS**

The study population included 632 allergic rhinitis patients, who 466 (73.7%) were male and 166 female (26.3%) aged between 17 to

69 years old. The results of measuring amount of different immunological and non immunological parameters showed that the concentration of some of them were increased and decreased regarding to the sex and smoking and non smoking status (Table 1).

Based on these results, all studied parameters were changed based on gender and smoking and non smoking statuses. Comparing the mean and standard deviation of these parameters, showed significant differences between all examined indices in smokers and nonsmokers patients, were obtained (P value 0.01) (table 2).

These results indicated the effect of cigarette smoker in allergic rhinitis patients compared in non cigarette smoker

We investigated the effect of cigarette smoking on different immune systems of patients suffered from allergic rhinitis during the process of disease. These patients have been divided in two groups as cigarette and non cigarette smokers. The results indicated that significant differences between all examined indices in smokers and non smokers patients, were obtained (P value 0.01).

Only one search of the available literature revealed results of some immunological parameters determination in healthy smoker individuals. They

**Table 1.** Differential percentage of immunological and non immunological parameters regarding to the gender and smoking and non smoking statuses of allergic rhinitis patients (see the text)

Patient and sex Parameters	Decreased concentration					
	Smoker			Non smoker		
	Male	Female	Total	Male	Female	Total
WBC	56.5%	43.5%	52.4%	58.7%	41.3%	11.8%
Lymphocytes	46.7%	53.3%	58.7%	45.1%	54.9%	9.6%
Neutrophils	59.5%	40.5%	62.8%	43.6%	56.4%	21.4%
IgA	83%	17%	61.1%	56.3%	43.7%	11.8%
IgM	41.7%	58.3%	20.7.2%	34.6%	65.4%	6.3%
Increased concentration						
IgG	43.1%	56.9%	23.4%	44.2%	55.8%	12.6%
IgE Total	56.7%	43.3%	68.6%	64.8%	35.2%	57.9%
C3	62.7	37.3%	34.4%	54.1%	45.9%	26.8%
C4	58.3%	41.7%	28.7%	67%	33%	11.7%
RBCs	73.2%	26.8%	73.6%	64.6%	35.4%	12.8%
Hb	61.4%	38.6%	52.3%	49.6%	50.4%	11.8%

**Table 2.** Mean and standard deviation of parameters between smokers and non smokers patients

Patient Parameters	Smokers Mean $\pm$ SD	Non smokers Mean $\pm$ SD	P value
WBC	7.97 $\pm$ 1.80	5.56 $\pm$ 1.64	0.01
Lymphocytes	35.9932	26.3467	0.01
Neutrophils	59.7561	42.4532	0.01
IgG	1045.7634	1167.9080	0.01
IgA	97.9756	87.5678	0.01
IgM	56.9324	67.6721	0.01
IgE Total	358.8932	174.5463	0.01
C3	60.4523	49.6743	0.01
C4	14.8532	13.5643	0.01
RBCs	5.6765	3.4523	0.01
Hb	15.6582	12.6754	0.01

compared immunological and hematological parameters concentration in healthy smokers and non smokers individuals and found IgG, IgM and IgA were decreased in smokers and the amount of IgE, and WBCs, PMNs and lymphocytes counts were significantly higher in smokers as compared with non smokers. They also reported no correlation between concentration of C3 and C4 and smoking<sup>20</sup>.

In our study, both smokers and non smokers with allergic rhinitis had the mean and standard deviation differently in all examined indices.

According to thereports of some authors, immune responses to the variety agents such as cigarette smoking could be verified in allergic

rhinitis patients, since these patients had variation of concentration of some proteins. Our study revealed that patients with cigarette smoking have a low number of neutrophils, and low amount of IgA and IgM and high WBCs, RBCs, lymphocytes count and increased concentration of Hb, serum IgG, IgE, C3, C4 than nonsmokers, supporting the existence of different immune responses to cigarette smoking in allergic rhinitis patients.

On the other hand it may be stated that smoking causes impairment of variety proteins synthesis, which may affect natural defense or homeostasis in the immune system of allergic rhinitis<sup>21,22</sup>.

So our result examined this and therefore demonstrated that complement system plays a role in combination with cigarette smoking, as the C3 and C4 levels changed significantly in smokers patients than in non smokers. Interestingly as the action of these two proteins is well documented to have inflammatory and anaphylaxis functions and have influence on susceptibility of host to infectious diseases and immunopathologic reactions to several diseases such as allergic rhinitis<sup>10, 23</sup>. Thus our results showed patients with cigarette smoking are more susceptible to getting infectious diseases and immunopathologic reactions. Furthermore change in IgG and IgM concentration in these patients are known to be able to activate classical complement components since their biological actions with combination agents as a complex could activate more C3 and C4 components<sup>24</sup>.

The reason for these phenomena is not well understood and needs to be clarified in future. It is also reported that RBCs and hemoglobin was also increased in patients with smokers but not in those with non smokers allergic rhinitis. So the reason for this is due to this fact in which RBCs itself and all its indices, may have a varying role in allergic rhinitis patients<sup>25</sup>, suggesting future studies are needed to be done to investigate the causes of this differences between smokers and non smokers.

On the hand it is not clear whether determination of RBCs count and all its indices concentration can be useful in diagnostic monitoring of patients suffered from allergic rhinitis who are encountered with cigarette smoking,

Our results also revealed that immunity of male patients in some parts have more affected by smoking than female. Similar findings have reported by Hakim IA, et al and Okayasu I, et al in which some biomarkers were significantly higher in males than in females<sup>26,27</sup>.

Therefore our results showed that cigarette smoking is independently risk factor for the development of allergic rhinitis associated with increased airway responsiveness to the allergens such as cigarette and any other allergens.

However in previous study that has been reported by Moszczynski, P *et al.*,<sup>28</sup>, linked separately with our study showed the effect of cigarette smoking as a serious public health problem, posed by diseases such as respiratory and cardiovascular diseases and increases asthma and acts on inflammation of the middle ear (otitis media), sinus inflammation (sinusitis), inflammation of the inner lining of the nasal passages (rhinitis) and inflammation of the lining of the lungs (pneumonia), therefore our results has consistency with this study. Furthermore another action of cigarette smoking has reported by Vassallo, R and Luppi, P<sup>29, 14</sup>. They showed that suppression of human dendritic cell functions leading to preferential induction of Th-2 priming and circulating maternal leukocytes during pregnancy. Even if increased risk of bronchiolitis during infancy has been associated with maternal smoking and maternal asthma<sup>30</sup>.

On the other hand Petersen and his colleague reported on 2007 the effect of cigarette smoking on impairs muscle protein synthesis through increases the expression of myostatin in muscle<sup>31</sup>. So these studies offer different effect of cigarette smoking on many organs. But we could not investigate these relations linked by allergic rhinitis and cigarette smoking that needs to be investigated in future.

Despite of fact, we were aware of the limitations of the present study due to the lack of information on the role of number of cigarette, duration time of smoking and effect of cigarette smoking on immune responses of those around smokers such as children and spouses of smokers. According to reports of Eisner MD and Nieman CL *et al*, cigarette smoking tend to have more effect on respiratory infections and asthma and allergic complications such as sinusitis and

bronchitis on those especially children and spouses and all others who lives around the smokers than those of non-smokers<sup>32,33</sup>, therefore we are suggesting further study to clarify this relation.

## CONCLUSION

In the present study, that was one of the first in this area, and performed on allergic rhinitis patients, cigarette smoking had significant immunological and non immunological alterations on immune responses of allergic rhinitis patients. This study also revealed that smoking may have a role in the pathogenesis of diseases and increase the risk of allergic complications such as sinusitis and bronchitis.

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