Plant Archives Vol. 20, Suppliment q, 2020 pp. 875-880 **e-ISSN:2581-6063 (online), ISSN:0972-5210**

STUDY OF SOME IMMUNOLOGICAL PARAMETERS FOR EXPOSURE TO PARTICULATE MATTER IN THE POPULATION OF BAGHDAD

Suher A. Kadhem* and Adel M. Rabee

College of science, Baghdad University, Department of Biology, Baghdad, Iraq.

Abstract

Air pollution is the result of a complex interaction between natural and anthropogenic environmental conditions and considered a severe problem in major urban areas. PM (Particulate matter) is a widespread air pollutant, When the people are exposed to allergens (as PM) they can develop an immune reaction that leads to allergic inflammation. The aims of the study are determining some immunological aspects namely total IgE, Interleukin-6 (IL-6) and blood parameters in serum of exposed persons to particulate matter and apparently healthy control to determine their relationship to bronchial allergic disease. There is a major significant difference P≤0.01 in the level of total IgE between the exposed persons to particulate matter (bronchial allergic disease) and controls. The serum levels of IL-6 in the bronchial allergic patient was significantly high P d" 0.001 as compared to control. There was significantly increase P≤0.001 in some blood parameters as eosinophil, WBC, Neutrophil, and Monocyte in patient than control. And insignificantly difference in other blood parameters as Basophil, Lymphocyte and Hb in patient and control.

Key words : IL-6, bronchial allergic, particulate matter, air pollution, total IgE, asthmatic

Introduction

Air pollution is the result of a complex interaction between natural and anthropogenic environmental conditions and considered a severe problem in major urban areas (Silva *et al*., 2012). PM is a widespread air pollutant, consisting of a mixture of solid and liquid particles suspended in the air (WHO, 2013). The ambient air concentration of particulate matter is universally high in developing areas because of higher road dust loading contributed from ongoing construction/industrial activities (Yang *et al*., 2001). When the human inhalation Particles smaller than 10 mm can get into the large upper branches, just below the throat, where they are caught and removed (by coughing and spitting or swallowing). Particles smaller than 5 mm can get into the bronchial tubes at the top of the lungs, while particles smaller than 2.5 mm in diameter can penetrate the deepest (alveolar) portions of the lung. If these particles are soluble in water, they pass directly into the blood in the alveolar capillaries (Jang, 2012). The respiratory health effects have been documented in workers exposed to a variety of dusts in small and large-scale industries, which generate dust during their production process. The diseases of the respiratory system induced by occupational dusts are influenced by the type of dust, dose, duration of exposure and genetic factors (Subbarao, 2009; Meo, 2005).

Occupational diseases are caused by a pathologic response of the patients to their working environment (Imbus,1994). When someone is exposed to allergy causative agents (allergens) which trigger an immune response, this leads to allergic inflammation (Pawankar *et al*., 2013). Biomark*er* is a change in a biological system that can be related to an exposure to, or effects from, a specific xenobiotic or type of toxic material (Rogene *et al*., 1989). Inflammation is the first responder of immune response to infection or injury in the body. Inflammation is detected by an increased concentration of biomarkers in the human body. This inflammatory action is meant to take place in a short time. When the response proceeds for a longer period, it is probable to damage the body (Gallagher *et al*., 2010). Interleukin -6 (IL-6) is a pleiotropic cytokine secreted by many cells of the immune system, cardiovascular components and adipose tissue, and functions as a mediator of inflammatory response with both pro- and anti-inflammatory properties.

Author for correspondence : E-mail : suherali94@yahoo.com

Circulating levels of IL-6 differ greatly between individuals due to both genetic and environmental factors. Accumulated evidences have shown that IL-6 is involved in the development of asthma (Chen *et al*., 2011). The sequence of events in the allergic reaction consists of the production of IgE antibodies in response to an allergen, binding of IgE to Fc receptors of mast cells, cross-linking of the bound IgE by the allergen upon re-exposure, and release of mast cell mediators such as histamine, lipid mediators and cytokines. Some mast cell mediators cause rapid increase in vascular permeability and smooth muscle contraction, resulting in many of the symptoms (Kay, 2001; Holgate,1999). IgE also has an essential role in type I hypersensitivity, which manifests in various allergic diseases, such as allergic asthma, most types of sinusitis, allergic rhinitis, food allergies, and specific types of chronic urticaria and atopic dermatitis (Gould *et al*., 2003). The aims of the study are determining some immunological aspects namely total IgE, Interleukin-6 (IL-6) and blood parameters in serum of exposed persons to particulate matter and apparently healthy control to determine their relationship to bronchial allergic disease.

Materials and Methods

Study groups

A total of 50 blood samples from exposed persons to particulate matter diagnosed with bronchial allergic patients and 40 blood samples that were collected from apparently normal people and were considered as controls.

Serological tests

Total serum IgE was determined by Immunoenzymetric Assay by the uses of the total IgE ELISA Kit (Calbiotech/USA). The level of IL-6 in serum was estimated by serum level of IL-6 Kit (Elabscience/ USA). Blood parameters determined from complete blood count that was performed by Beckman Coulter analyzer instrument.

Statistical analysis

SPSS program (version 22) was used to elucidate the difference in parameters. Chi-square and T tests were used to compare between means of parameters of patients and apparently healthy control.

Results

Immunological results

The blood parameters

The means of Hemoglobin in exposed persons was (14.4 ± 1.7) and in controls (13.3 ± 1.8), lymphocyte in exposed persons was (29.7±10.7) and in controls was (28.3± 6.96), and basophils count in exposed persons was (0.16 ± 0.08) while in controls was (0.11 ± 0.1). These results indicated that the values of previous parameters within normal range with insignificant differences between exposed persons to particulate matters and controls.

However, eosinophil count in patients was (2.5 ± 0.8) and in controls was (0.46 ± 0.2), WBC in exposed persons was (8.3± 3.0) and in controls was (6.8 ± 1.6), Neutrophil in exposed persons was (60.02± 12.8) and in controls was (50.23 ± 7.85), Monocyte in exposed persons was (7.2± 2.2) and in controls was (6.8± 2.2). All the previous results showed significant increase in exposed persons compare to control, as shown in (Table 1).

Table 1: Mean and standard deviation of the blood parameters.

Parameters	Patients (mean ± SD)	Controls (mean ± SD)	P value
HB (g/dl)	14.4 ± 1.7	13.3 ± 1.8	NS
WBC (x 10^9/L)	8.3± 3.0	6.8 ± 1.6	S
Neutrophils (x 10^9/L)	60.02± 12.8	50.23 ± 7.85	S
Lymphocytes (x 10^9/L)	29.7±10.7	28.3± 6.96	NS
Monocytes (x 10^9/L)	7.2± 2.2	6.8± 2.2	S
Basophile (x 10^9/L)	0.16 ± 0.08	0.11 ± 0.1	NS
Eosinophil (x 10^9/L)	2.5 ± 0.8	0.46 ± 0.2	P≤0.001 S

S: significant, NS: non-significant

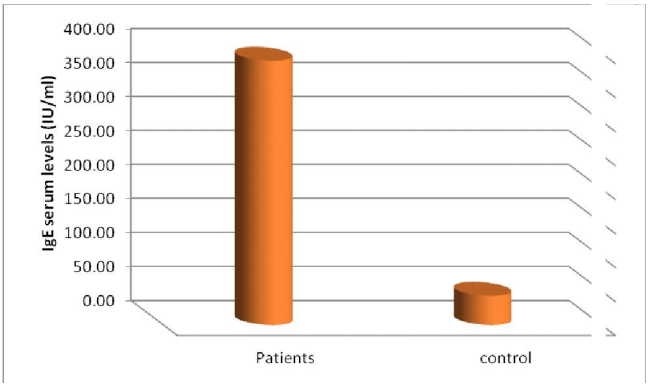

Fig. 1: Serum level of IgE in patients and controls groups.

Serum levels of total IgE

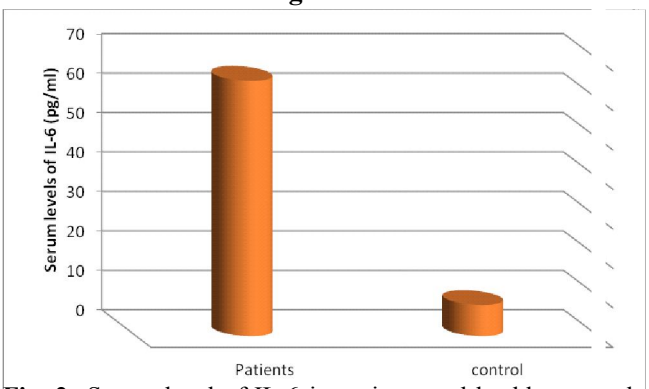

Fig. 2: Serum level of IL-6 in patients and healthy controls (P≤0.001).

Serum levels of IL-6

Discussion

Air pollution is the source of many substances that may enter the human bloodstream through the nose, mouth, skin, and the digestive tract. Most air pollutants reach the blood quickly without previous bio-transformation and have been shown to produce harmful effects on the blood, bone marrow, spleen, and lymph nodes (Seaton *et al*.,1999; Pope *et al*.,1999)**,** making the blood system highly sensitive to environmental poisoning. Epidemiological studies report associations between particulate air pollution and increased mortality from pulmonary diseases. The exposure to ambient gaseous and particulate air pollution leads to an alteration of the differential white blood cell count in patients with chronic pulmonary diseases like chronic bronchitis, chronic obstructive pulmonary disease, and asthma (Brüske *et al.,* 2010).

The current study showed that the mean level of white blood cell count was (8.3± 3.0), (6.8 ± 1.6) in exposed persons and controls respectively with significant difference between them. Air pollutant such as particulate matter and nitrogen dioxide ($NO_{2)}$ enhances the airway reaction in humans to allergen, measured as decreased pulmonary function this case agreed with (Barck *et al*., 2005).

The mean of neutrophils was (60.02± 12.8) in patients and (50.23 ± 7.85) in controls there is significant difference between exposed persons and controls.

Neutrophils are polymorphonuclear leukocytes that play an essential role in the immune system, acting as the first line of defense against bacterial and fungal infections. Their role in the inflammatory process was once thought to be restricted to phagocytosis and the release of enzymes and other cytotoxic agents, but it is now known that these cells can release diverse mediators that have profound effects on the airways of asthmatic individuals. There is increasing evidence of the participation of neutrophils in allergic processes in general, and in asthma in particular. (Monteseirín, 2009).

The present result in agreement with Gungen and Aydemir (2017) who concluded that blood neutrophil was higher in patients with high allergic and asthma compared to control group.

The mean of eosinophil cells was (0.46 ± 0.2), in controls. The means of cells were in allergic asthma patients was (2.5 ± 0.8). The mean of patients is significantly high as compared to control (P<0.001).

This results in agreement with Previous studies (Bel *et al.,* 2014; Ortega *et al.,* 2014; Brakhas *et al.,* 2015; Èelakovská and Bukaè, 2016; Rasheed, 2016; Celakovská *et al.*, 2019) who concluded that blood eosinophilia was detected in patients with asthmatics, and other disease as allergic rhinitis and atopic dermatitis. Allergen irritation of the airways can produce blood eosinophilia within hours (Klion, 2015). The pathophysiology of allergy and asthma involves a variety of changes at the cellular level, due to the activity of eosinophils, mast cells, neutrophils, and T lymphocytes (Adkinson *et al*., 2009). Mast cells contribute to the release of acute phase mediators and cytokines, which promote deleterious effects to healthy tissue. Eosinophils release cytokines, growth factors, and leukotrienes which cause further inflammation and produce the characteristic and recurrent symptoms of the disorder, including hyperreactivity in response to various provocative factors. With time, swelling and deposition of inflammatory cells, mucus, and debris ultimately denude the epithelium of the airway. Smooth muscle hypertrophy and neovascularization occur as a form of remodeling, mostly to detrimental effects as they because airway wall thickening. Additionally, deposits of collagen promote constriction and obstruction (Adkinson *et al*., 2009; Lemanske and Busse, 2010; Keglowich *et al*., 2013).

Moreover, the means of monocyte was in exposed persons was (7.2± 2.2). The mean of exposed persons is significantly high as compared to control (6.8± 2.2). The present result in agreement with (Tomita *et al.,* 1995).

Asthmatic syndrome is characterized by airway inflammation with different cell types, including neutrophils, eosinophils, mast cells, monocytes, and macrophages (Gin and Kay, 1985; Corrigan *et al*., 1988) Recent research has shown that monocytes and macrophages may play important roles in the pathogenesis of asthma and bronchial allergy. (Kay *et al.,* 1981; Melewicz *et al*., 1981; Rankin *et al*.,1982; Carrol *et al*.,1985; Cluzel *et al*.,1987 Wilkinson *et al*., 1989; Howell *et al*.,1989). Monocytes, whose numbers were also found to be increased in the airway mucosa, are known to be capable of migrating from the blood to the lung, where they mature and acquire more stimulatory activity. Monocytes are also present in the lung and, indeed, most alveolar macrophages and dendritic cells originate from monocytes (Bluase *et al*.,1979; Bowden and Adamson,1980).

When individuals inhaled allergens they have a genetic propensity to produce IgE antibodies against inhaled allergens. Allergic diseases are characterized by the development of IgE antibodies that react with the allergens. These IgE antibodies bind firmly to high affinity

IgE Fc receptors on mast cells in the tissues and upon exposure to the allergen that induced the IgE synthesis, the mast cells release mediators from their granules. The mediators (histamine, bradykinin, eosinophil chemotactic factors, etc.) cause the resultant clinical signs, such as lacrimation, nasal discharge, itching, and sneezing. In the asthmatic patient, additional effects include bronchial smooth muscle contraction, leading to a decrease in expiratory volume (Gershwin, 2003). Serum level of IgE high significantly ($P \leq 0.01$) increased in exposed persons to particulate matter (patients group) with the median of (388.72 IU/ml) and rang from 212.96 to 433.73 IU/ml as compared to healthy control group median (42.96 IU/ml) and rang from 0.72 to 170.79 IU/ml, as shown in figure 1. The present results in agreement with other studies (Pien and Orange, 2008; Smith and Ownby, 2009; Hussein *et al.,* 2009; Rasheed *et al.,* 2018; Jo *et al.,* 2018; Celakovská *et al.,* 2019). All these studies concluded that total IgE increase in most patients with asthma and allergic rhinitis.

Brakhas *et al.,* (2015) concluded that allergic patients with any age have significant increased level of total IgE compared to healthy controls and explained that immune response to allergens mediated by IgE antibody specific to the allergen, after IgE bindings, mast cells and basophils are activated, starting a series of cellular and molecular events that results in the clinical manifestation of allergic diseases.

Serum level of IL-6 high significantly ($P \leq 0.001$) increased in exposed persons (patients) group with serum median levels (64.67 pg/ml) and it ranged from 11.08 to 456.08 pg/ml as compared to apparently healthy control group serum median levels (7.84 pg/ml) with rang of 0.24 to 61.96 pg/ml, as shown in fig.2. The present results in agreement with (Yokoyama *et al*.,1997; Song *et al*., 2001; Stankiewicz *et al*., 2002; Neveu *et al*., 2010; Alwakil *et al*., 2011; Rincon and Irvin, 2012; Poynter and Irvin, 2016) who found increased serum levels of IL-6 in asthmatic exposed persons compared with normal subjects.

Lacy *et al*., (1998) concluded that elevated levels of circulating IL-6 were observed in asthmatic subjects (both symptomatic and asymptomatic) compared to normal controls with further increase during natural exacerbation of asthma compared to asymptomatic periods.

Particulate matter (PM) in ambient air is a risk factor for human respiratory and cardiovascular diseases. The delivery of PM to airway epithelial cells has been linked to release of proinflammatory cytokines (Zhao *et al*., 2009). Inflammation seems to result from elevated cytokines/chemokines production in airway epithelial, endothelial, and Th1/Th2 lymphocytes. secretion of IL-6 from the lung is significantly higher in response to environmental toxins and stimuli, including PM (Yu *et al*., 2002; Becker *et al*., 2005; Mutlu *et al*., 2007).

Although most cytokines initiate or amplify inflammation, some cytokines appear to have an inhibitory or anti-inflammatory effect on allergic inflammation. There is increasing evidence that certain cytokines do have both anti-inflammatory and modulatory effects and their secretion may be defective in asthmatic patients (Yssel and Groux, 2000). IL-6 is a representative pro-inflammatory cytokine that has been shown to be connected to various inflammatory states or diseases. Various cells were found to be capable of producing it as T-cells and airway epithelial cells (Peter *et al*., 2006).

Conclusions

As a conclusion, Inhalation of air pollutants (allergens) as particulate matter they can develop an immune reaction that leads to allergic inflammation. Based on current results, a significant increase of serum IgE levels and serum IL-6 levels in the exposed person to particulate matter than controls. The blood parameters such as eosinophil, WBC, Monocyte, and Neutrophil considered a good biomarkers of exposure to particulate matter.

Recommendations

We need other studies from other regions of Iraq to confirm the results of the current study. Promote environmental awareness among people to stay away from exposure to particulate matter because of its severe risks to human health. Other studies are needed to find out about other diseases associated with particulate matter.

Acknowledgements

The authors thank the Iraqi Ministry of higher Education and the University of Baghdad (College of Science) for the support for this research.

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