Evaluation the Role of IL-1β and TNFα with Asthma

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Abstract

Asthma is a heterogeneous disease that is characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time in intensity. Investigation the titer of IL-1β and TNF α in sample of asthmatic patients. Blood samples were taken from 50 serum of asthma patients whose age range 15-70 years, the samples were collected during December 2019 to May 2020 at AL-Zahra Center for Allergy and asthma in Baghdad city. In addition to control group included 30 apparently healthy individuals. The sera was separated from all and stored at -20°C, then TNFα and IL-1β were measured by ELISA (Indirect). The results indicated significant increase IL-1β serum level (P<0.00) of patients compared to control, while the level of TNFα elevated more than that control group without significant difference (P ≤ 0.1). The elevation level of IL-1β and TNF α as potential risk of asthma.

Keywords: IL-1β; Tumor Necrosis; health; Asthma

Introduction

Asthma is a heterogeneous disease that is characterized by chronic airway inflammation; it is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time in intensity, together with variable expiratory airflow limitation, affecting 1-18% of the population in different countries (Global Initiative for Asthma, 2019). Airway inflammation, together with bronchial hyper responsiveness and airway structural remodeling, is one of the prominent features of asthma (Pelaia et al., 2015). Respiratory tract infection, humidity, seasonal changes, indoor perfumes, spicy food diet, low dose of cortico steroid and dusty environments these all are common association with asthma symptoms in atopic individual (Mossa and Sherhan, 2018). Studies suggested
that about 325 million people worldwide are currently affected with asthma. This figure is predicted to increase to 425 million people in 2025 (Agache et al., 2012).

Interleukins (ILs) are a group of cytokines, secreted proteins and signal molecules that were expressed by white blood cells (Brocker et al., 2010). Interleukin-1 (IL-1) is a proinflammatory cytokine found in two forms (α and β). The IL-1α form is mainly cell-bound, whereas IL-1β is primarily secreted by macrophages in response to immune system stimulation (Sobkowiak et al., 2017). The interleukin-1 cluster on human chromosome 2 (q12-q14) harbors various promising candidate genes for asthma and other inflammatory diseases. The human genes for IL-1β and IL-1α, and their receptors and the IL-1 receptor antagonist are clustered on chromosome 2 (q14-q21) (Gohlke et al., 2004).

The IL-1β systemic inflammatory axis leading to future exacerbations in chronic obstructive pulmonary disease (COPD) and risk in asthma. Airway IL-1β and systemic inflammation are associated with frequent exacerbations and may mediate a vicious cycle between previous and future exacerbations in COPD and asthma (Fu et al., 2015). Tumor Necrosis Factor (TNF) is a pleiotropic cytokine and a master regulator of the immune system, most cells show at least some TNF responsiveness. Studies revealed two opposite functions of TNF in host defense. At low levels, it has beneficial homeostatic functions, such as for host defense mechanisms against for example intracellular pathogens (Mootoo et al., 2009). There are findings reveal that elevated serum levels of TNFα can be involved in the development and progression of Bronchial Asthma (Jiang et al., 2018). The gene encoding TNF reside in tightly loci within the major histocompatibility complex (MHC) on chromosome 6 in human and their receptors are linked on chromosome 12 (El-Tahan et al., 2016).

Materials and methods
This study was carried out during the period from 15 December 2019 to 15 May 2020. A total of 50 exacerbations asthmatic out-patients were included in the study, they are 29 male and 31 female with age ranged 15-70 who attended AL-Zahra Center for Allergy and asthma in Baghdad city. In addition to 30 apparently healthy individuals as control group. The participants have no any asthma sensitive or respiratory disease and any other Allergy. The exclusion criteria for both patients and control were any history of respiratory illness like chronic obstructive pulmonary disease, tuberculosis, pneumonia, other comorbid illness such as diabetes mellitus, hypertension and pregnant females. Description of the symptoms and many information from patients as name, age, gender, family history, job and treatment were obtained. Blood sample (3 ml) was collected from each individual and put into gel tubes to obtain sera for serological study by enzymelinked immune sorbent assay (ELISA), as following:

A- Fifty samples of blood were collected from patients with asthma. B- Thirty samples of blood will collected from apparently healthy individual as control.

Determinations the IL-1 β and TNF α serum level

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Investigation the level of IL-1β and TNF α in picogram per milliliter (pg/ml) by indirect ELISA through Elabscience Kit (Germany). The levels of IL-1β and TNF α were calculated from standard curve and expressed in pg/ml. Statistical analysis was performing.

Result and discussion

Distribution of Human IL-1β serum level

The result of present study showed a highly significant elevation level of the IL-1β in the serum of asthma patients group when compared with control group, IL-1β level was 51.465 ± 35.793 pg/ml in patients, while in control individuals was 19.864 ± 6.636 pg/ml (Table 1).

Table (1): IL-1β level in asthma patients and control groups

<table>
<thead>
<tr>
<th>IL-1β (pg/ml)</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Std. Error Mean</th>
<th>T. test</th>
<th>P. value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>51.465</td>
<td>35.793</td>
<td>5.061</td>
<td>4.775</td>
<td>0.00</td>
</tr>
<tr>
<td>Control</td>
<td>19.864</td>
<td>6.636</td>
<td>1.211</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The outcome of IL-1β level in patients indicated positive relationship between the IL-1β and asthma. In addition, IL-1 stimulates the production of other cytokines such as tumor necrosis factor and granulocyte macrophage colony stimulating factor (GMSF) (Jooset et al., 2001); Mao et al. (2001) referred to, in certain disease and asthmatic sensitized state, there is an imbalance of production between IL-1β and IL-1α. Also the IL-1β and IL-1α are stored in platelets which can represent an additional source of this cytokine (Semple et al., 2011).

The results of this study going with previous studies as that conducted in Iraq by Mahdi and Al Saadi (2011) who investigated the serum levels of IL1β, TNF α and IL-6 and the severity of asthma, they recorded significant elevation (p<0.05) of these cytokines in bronchial asthma patients group with chronic obstructive pulmonary disease (COPD). Whereas this results disagree with the study by Hall et al. (1994) who found no significant differences between monocytes and macrophages groups in either TNF-α (p<0.06) and IL-1β (p<0.17). Also other study findings suggested that modulation at the level of the IL-1β and IgE to human Airway Smooth Muscle cells increase mRNA and protein expressions of both stimulatory and inhibitory IL-1 axis molecules (Whelan et al., 2004). Recently Ye et al. (2020) found that the inflammatory cytokines including TNF α (P < 0.001), and IL1β (P < 0.001) were higher in bronchial asthma at exacerbation patients and bronchial asthma at remission patients compared with control group.

Distribution of human TNF α serum level
The result of present study showed no significant elevation level of the TNF α in the serum of asthma patients group when compared with control group, TNF α level was $29.002 \pm 21.266$pg/ml in patients, while in control individuals was $22.325 \pm 6.802$pg/ml(Table 2).

| Table (2): TNF α level in asthma patients and control groups |
|-------------|----------|----------|----------|----------|---------|
|             | Mean     | Std. Deviation | Std. Error Mean | T. test | P. value |
| Patients    | $29.002$ | $21.266$   | $3.007$   | $1.666$ | $0.1$    |
| Control     | $22.325$ | $6.802$    | $1.241$   |          |          |

Onother hand it was found that the level of TNF α elevated significantly in 5 of patients (82.31 pg/ml) and that may be due to the previous other disease as that effect the lung function, increase the white blood cellsthat related to increase C Reactive Protein(CRP) or infected with microbial agents and elevated asproinflammatory cytokine which was generally more effective and the effect can be observed at early hours.

Also high levels of chemokines in asthmatic patients were observed suggesting an increased cellular infiltration (monocytes, neutrophils or eosinophils) at tissue level (Kallal and Lukacs, 2008). These results have agree with different previous studies such as, the study ofGoodi and ALSaadi (2019) whichfound thatthe levelof the TNF α have no significant differs between asthma patient and control. As well as Krogulska et al. (2009) reported there were no significant changes in the level of TNFα of children with atopy, compared to children without atopy whose disease was stable. While other study showed the contrary with present result as the study of Huang et al. (2016) who found the TNFα levels were significantly different among the control group, asthma group, Acute Exacerbation of Chronic Obstructive Pulmonary Disease (AECOPD) group, and Asthma-Chronic Obstructive Pulmonary disease Overlap Syndrome (ACOS) group (all P<0.05). When Halonen et al. (2009) measured the serum cytokines levels in parent with adult asthma and children, they noticed that among these cytokines were TNFα levels were rose in asthmatic adults and decreases in asthmatic children. There are many reasons to these differences may be related to age, immune response, smoking and infection with other systemic disease.

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