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Research Article

Association between Immune System Response, Inflammatory Cytokines and Obesity among Asthmatic Saudi Patients

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Abstract

Background: Currently, the global prevalence of asthma and obesity is progressively rising. However, obesity is linked with systemic inflammation and altered immune system parameters. There is limited studies investigated the immuno-competence among asthmatic obese patients.

Objective: This study designed to detect the association between immune system response, inflammatory cytokines and body mass index among asthmatic Saudi patients.

Subjects and Methods: One hundred asthmatic obese Saudi patients of both sex; their age mean was 42.63 ± 9.15 year and their body mass index (BMI) mean was 32.42 ± 2.96 Kg/m2 known as group (A), in addition to one hundred non-obese asthmatic, who were gender, age and BMI matched with study group, were enrolled in the study. Results: There was higher levels of high-sensitivity C-reactive protein (hsCRP), Interleukin-6 (IL-6), Tumor necrotic factor-alpha (TNF-α), serum IgE, white blood cells count, Total leukocytes count, Neutrophils count, Monocytes, lymphocytes count, T lymphocytes (CD3) count and B lymphocytes (CD19) count among obese asthmatics(group A) than lean asthmatic (group (B), in addition to a strong association between these parameters and body mass index in both groups.

Conclusion: There is a strong association between inflammatory cytokines, immune system response and BMI among obese asthmatic patients; therefore future studies are essential to explore impact of life style modification intervention on immune system and systemic inflammation modulation.

Keywords: Immune system; Systemic inflammation; Obesity; Bronchial asthma; Body mass index

Introduction

Asthma is a common medical problem as there is about 300 million patients with bronchial asthma all over the world [1,2]. However, asthma is more common among obese than no-obese individuals [3-5]. In addition, severity of asthma positively correlated with body mass index [6], where obesity reduces the effects of asthma medications [7-9]. There is association asthma and obesity [10-11].

Immune system insufficiency is one of the possible links between high risks of asthma among obese subjects [12] as adipose tissue is the site for immune cells accumulation [13], which is evident with improvement of immune system parameters after weight reduction [14-17].

Obesity is a pro-inflammatory state [18-20]. Systemic low-grade inflammatory status that is associated with obesity adversely affect immune system performance [21] and worsen the airway inflammation among patients with bronchial asthma [22,23]. Impaired immune system performance led to increased rate and severity of infections among obese subjects [24,25].

The purpose of this study was to determine the relationship between Body Mass Index (BMI), immune system and inflammatory cytokines in asthmatic Saudi patients.

Subjects and Methods

One hundred asthmatic obese Saudi patients; their age mean was 42.63 ± 9.15year and their BMI mean was 32.42 ± 2.96 Kg/m^2 known as group (A), in addition to one hundred non-obese asthmatic, who were gender, age and BMI matched with study group, were enrolled in the study upon referral to Internal Medicine Department, King Abdulaziz University Hospital, Jeddah, Saudi Arabia Known as group (B). Exclusion criteria included diabetes, liver, kidney, neurological and other respiratory disorders rather than bronchial asthma. All participants signed the consent and the Scientific Research Ethical Committee, Faculty of Applied Medical Sciences at King Abdulaziz University approved this study.

Methods

Evaluated Parameters: Blood samples were collected in two different vacutainer tubes (BD vacutainer). One tube was a red top for hsCRP level, IL-6, TNF-α and for the total IgE measurement. The second tube contains EDTA K2, EDTA K3 for measuring Complete Blood Count (CBC) and flow cytometry. Whole blood Samples were

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Table 1: Demographic and clinical characteristics of all participants.

	Obese asthmatics	Non-obese asthmatics
Age (year)	42.63 ± 9.11	41.14 ± 8.42
Body mass index(kg/m^2)	32.42 ± 3.16*	21.48 ± 2.91
Hip circumference (cm)	125.73±14.17*	102.38±9.15
Waist hip ratio	0.89 ± 0.28*	0.80 ± 0.24
Waist circumference (cm)	95.24 ± 7.23*	70.32 ± 5.19
Hemoglobin (gm/dl)	13.10 ± 1.78	13.51 ± 1.93
Erythrocyte sedimentation rate (ESR) (mm/h)	28.12 ± 10.64*	17.96 ± 7.18
FVC (L)	2.91± 1.02*	3.72 ± 1.31
FEV_1(L)	1.62 ± 0.97*	2.92 ± 1.25
FEV_1/FVC (%)	58.27 ± 12.83*	85.45 ± 11.70
$FEF_{25-75\%}$(L/s)	1.16 ± 1.15*	2.94 ± 1.42

FVC: Forced Vital Capacity; FEV1: Forced Expiratory Volume in the First Second; FEV1/FVC: Ratio between Forced Expiratory Volume in the First Second and Forced Vital Capacity; FEF25-75: Forced Expiratory Flow during the middle half of the FVC maneuver; (*) indicates a significant difference between the two groups, P < 0.05.

centrifuged (at 3500 rpm for five minutes), to separate the serum and plasma. Samples were stored at -80°C until time of processing.

A. Biochemical Parameters: Biochemical parameters including serum hsCRP, total IgE and CBC were measured at the same time after collection. Serum for hsCRP was quantified by enzymatic-colorimetric methods using commercially available kits (Roche Diagnostics, Mannheim, Germany). Beckman Coulter Ac·T 5diff hematology analyzer at king Abdul-Aziz University Hospital used for peripheral blood cells analysis.

B. Measurement of Biomarkers of Inflammatory Cytokines: Biomarkers of inflammatory cytokines including tumor necrosis factor-alpha (TNF-α), and Interleukin-6 (IL-6) levels were measured from frozen plasma samples stored at −80°C. Enzyme-linked Immunosorbent Assays Kits (ELISAs) used to measure soluble levels of (TNF-α), and IL-6 (GE Healthcare Amersham, Biotrak Easy ELISA), which utilized the quantitative sandwich enzyme immunoassay technique.

C. Flow cytometric analysis: The human leukocyte differentiation antigens CD3, and CD19 (Beckman Coulter, Marseille, France) were analyzed by flow cytometry using Cytomics FC500 and CXP software (Beckman Coulter).

D. Analysis of serum IgE: Blood was collected into red top tubes (BD vacutainer, USA) and UniCAP Total IgE fluoro enzyme immunoassay was used to determine serum IgE levels (Pharmacia and Upjohn Diagnostics, Freiburg, Germany).

E. Body Mass Index (BMI): Body weight of participants in both groups was measured (HC4211, South Korea) while wearing hospital gowns and undergarments. Where the height was measured using digital stadiometer (JENIX DS 102, Dongsang). Body Mass Index (BMI) was computed as BMI= Body weight/Height.

Statistical analysis

Independent t-test was used to compare mean differences between measured parameters between both groups. Statistical analysis of data was performed using SPSS (Chicago, IL, USA) version 23. The degree of correlation between immune system & inflammatory cytokines and BMI was detected by Pearson's product moment correlation coefficients (r) (P> 0.05).

Table 2: Mean value and significance of hsCRP, IL-6, TNF-α, IgE, white blood cells count, Total leukocytes count, Neutrophils count, Monocytes, lymphocytes count, T lymphocytes (CD3) count and B lymphocytes (CD19) count of group (A) and group (B).

	Obese asthmatics	Non-obese asthmatics
hsCRP (mg/dl)	17.36 ± 4.81*	13.15 ± 3.93
TNF-α (pg/ml)	13.10 ± 3.12*	11.08 ± 2.15
IL-6 (pg/ml)	5.82 ±1.21*	4.17 ±1.13
Serum IgE(IU/mL)	317.31 ± 47.11*	188.26 ± 35.82
white blood cells count (10^9/μL)	8.95±1.97*	6.32 ±1.64
Total leukocytes count (10^9/μL)	6.87 ±1.67*	4.63 ±1.23
Neutrophils count (10^9/μL)	3.41 ±1.30*	2.42 ±0.92
Monocytes (10^9/μL)	0.54 ±0.16*	0.37 ±0.18
lymphocytes count (10^9/μL)	2.07 ±0.48*	1.73 ±0.36
T lymphocytes (CD3) count (10^9/μL)	1.91 ±0.74*	1.40 ±0.53
B lymphocytes (CD19) count (10^9/μL)	1.20 ±0.69*	0.92 ±0.81

hsCRP: high-sensitivity C-Reactive Protein; IL-6: Interleukin-6; TNF-α: Tumor necrotic factor-alpha; (*) indicates a significant difference between the two groups, P < 0.05

Results

The demographic and clinical characteristics of the subjects shown in (Table 1). There was no significant age and hemoglobin difference between the obese asthmatics (group A) and lean asthmatic (group (B). However BMI, hip circumference, waist hip ratio, waist circumference, Erythrocyte sedimentation rate, forced vital capacity (FVC), forced expiratory volume in the first second (FEV1), ratio between forced expiratory volume in the first second and forced vital capacity (FEV1/FVC) and forced expiratory flow during the middle half of the FVC maneuver (FEF25-75%) were significantly different between obese asthmatics (group A) and lean asthmatic (group (B).

The number of high-sensitivity C-reactive protein (hsCRP), Interleukin-6 (IL-6), IgE, tumor necrotic factor-alpha (TNF-α), white blood cells count, total leukocytes count, neutrophils count, monocytes, lymphocytes count, T lymphocytes (CD3) count and B lymphocytes (CD19) count were significantly elevated in among obese asthmatics(group A)when compared with lean asthmatic (group (B) (Table 2). The Pearson's correlation coefficients test for the relationship between body mass index and high-sensitivity C-reactive protein (hsCRP), interleukin-6 (IL-6), tumor necrotic factor-alpha (TNF-α), IgE, white blood cells count, total leukocytes count, neutrophils count, monocytes, lymphocytes count, T lymphocytes (CD3) count and B lymphocytes (CD19) count showed a strong direct relationship in both groups (Table 2 and 3).

Discussion

Obesity increases the risk of many medical problems and asthma is characterized by altered immune system response and systemic inflammation. As the impact of obesity on the immune system in the asthmatic patients is not well known, our study was conducted

Table 3: Shows the Pearson's correlation coefficients test value and the relationship between the BMI and hsCRP, IL-6, TNF-α, IgE, white blood cells count, Total leukocytes count, Neutrophils count, Monocytes, lymphocytes count, T lymphocytes (CD3) count and B lymphocytes (CD19) countof group (A) and group(B).

	Pearson's value *(r)*	
hsCRP (mg/dl)	**Obese asthmatics** 0.629*	**Non-obese asthmatics** 0.592*
TNF-α (pg/ml)	0.617*	0.721*
IL-6 (pg/ml)	0.598*	0.618*
Serum IgE(IU/mL)	0.582*	0.625*
white blood cells count (10^9/μL)	0.564*	0.568*
Total leukocytes count (10^9/μL)	0.713*	0.672*
Neutrophils count (10^9/μL)	0.642*	0.526*
Monocytes (10^9/μL)	0.681*	0.714*
lymphocytes count (10^9/L)	0.611*	0.559*
T lymphocytes (CD3) count (10^9/L)	0.710*	0.645*
B lymphocytes (CD19) count (10^9/L)	0.587*	0.623*

hsCRP: high-sensitivity C-Reactive Protein; IL-6: Interleukin-6; TNF-α: Tumor necrotic factor-alpha; Significance was calculated by Spearman or Pearson correlation (2-tailed),*p < 0.05; *r*: correlation coefficient.

to explore the association between immune system, inflammatory cytokines and body mass index among obese asthmatic Saudi patients.

In our study, obese asthmatic Saudi patients showed increased values of high-sensitivity C-reactive protein (hsCRP); interleukin-6 (IL-6), tumor necrotic factor-alpha (TNF-α), IgE, white blood cells count, total leukocytes count, neutrophils count, monocytes, lymphocytes count, T lymphocytes (CD3) count and B lymphocytes (CD19) count among obese asthmatics than among lean asthmatic, in addition to a strong direct relationship between these parameters and body mass index. Our findings are in line with the results of many previous studies as Moulin etal. who showed in his study that obesity is associated with the modulation of immune parameters [26], increased numbers of circulating immune cellsas neutrophil, monocyte, leukocyte and total WBC [27,28], as well as altered immune cell function [29] in addition to low grade of systemic inflammation [30-33]. However, Mahassni and Sebaastated that circulating immune cells and total WBCs counts significantly increased among obese and overweight adolescent Saudi female [34]. Moreover, O'Rourke et al. found high $CD4^+$ T cells frequency among obese individuals [35].

In our study we found that hsCRP levels in obese asthmatics were significantly higher than that in non-obese asthmatics, these results agree with Christina et al. who hsCRP concentration was higher among obese subjects [36], also Yue and Robert & Ólafsdittir et al. concluded in their studies that higher level of hsCRP exacerbate respiratory symptoms among subjects with non-allergicasthma [37,38]. The results of the current study showed that IL-6 levels in obese asthmatics were significantly higher than that in lean asthmatics; this also goes with leonidet al. found increased level of IL-6 in obese persons [39]. In addition, Rachel and Takemura sought that airway inflammation up regulated by obesity in asthma [40,41] as inflammatory markers were higher in obese asthmatic subjects [42-45]. In addition, Han et al. and Shore & Johnston reported that serum levels of IL-2, IL-4,IL-6, TNF- α and hsCRP and leptin were significantly higher (P<.001) in the obese than non-obese individuals [46,47].

Our results also revealed significant positive correlations between BMI and inflammatory markers included IL-6, TNF- α and hsCRP of obese asthmatics, these findings agreed with Marjolien et al. reported that human adipose tissue expresses supported this and release the pro-inflammatory cytokines included IL-6 and hsCRP correlated with body fat [48]. In addition, another positive correlation between BMI and white blood cells count, total leukocytes count, neutrophils count, monocytes, lymphocytes count, CD3 & CD19, these results agreed with Kintscher et al. found correlation between BMI and CD3 and CD4 in obese women [49] and Antuna-Puente et al. reported that number of macrophages positively correlated with BMI [50].

Conclusion

There is a strong association between inflammatory cytokines, immune system response and BMI among obese asthmatic patients; therefore future studies are essential to explore impact of life style modification intervention on immune system and systemic inflammation modulation.

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