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Original Article

Th1/Th2 cytokines profile in overweight/obese young adults and their correlation with airways inflammation

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الملخص

أهداف البحث: تهدف هذه الدراسة إلى مقارنة السيتوكينات للخلايا التائية المساعدة (1 و 2) بين الأشخاص المصابين بالسمنة العامة وسمنة البطن والأفراد غير البدينين، وربطها بالعلامات الحيوية لالتهاب الشعب الهوائية والتكوينات المختلفة للجسم.

طرق البحث: تم تقسيم ثمانين شخصًا إلى مجموعتين مجموعة الوزن الطبيعي وتشمل 37 شخصا (مؤشر كتلة الجسم أقل من 25) و43 مشاركا في مجموعة من الوزن الزائد / السمنة (مؤشر كتلة الجسم أكبر من أو يساوي 25). تم تصنيف جميع المشاركين أيضا وفقا لمحيط الخصر إلى مجموعة السمنة البطنية (32 شخصا) والمجموعة بدون سمنة بطنية (48 شخصا). تم قياس مستويات سيتوكينات الخلايا التائية المساعدة 1 وتشمل (إنترفيرون غاما، وعامل نخر الورم ألفا، وإنترلوكين-2)، وكذلك سيتوكينات الخلايا التائية المساعدة 2 وتشمل (إنترلوكين-4، وإنترلوكين-5، وإنترلوكين-13) في الدم باستخدام تقنية الأليزا المتعددة. تم تقييم التهاب الشعب الهوائية عن طريق قياس مستوى أكسيد النيتريك في هواء الزفير. وقد تم قياس تكوينات الجسم باستخدام محلل تكوين الجسم الكهربائي الحيوي.

النتائج: تم تسجيل ارتفاع في تركيز إنترلوكين-5 وعامل نخر الورم ألفا بشكل ملحوظ في الأشخاص المصابين بالسمنة العامة وسمنة البطن مقارنة بالأشخاص غير البدينين. كما أظهر إنترلوكين-5 علاقة إيجابية مع مؤشر التهاب الشعب الهوائية. كما ارتبط مؤشر كتلة الجسم ونسبة الدهون الكلية بشكل إيجابي مع إنترلوكين-5 وعامل نخر الورم ألفا، بينما ارتبط محيط الخصر ونسبة الدهون الحشوية مع مستوى إنترلوكين-5 وإنترلوكين-4.

الاستنتاجات: تؤكد هذه الدراسة ارتفاع بعض السيتوكينات الخاصة بالخلايا التائية المساعدة 1 و 2 في الأشخاص المصابين بالسمنة العامة وسمنة البطن. كما ارتبط إنترلوكين-5 ارتباطا إيجابيا مع مستوى أكسيد النيتريك في هواء الزفير، وهذا قد يربط السمنة مع التهاب الشعب الهوائية.

الكلمات المفتاحية: السيتوكينات؛ أكسيد النيتريك؛ الوزن؛ السمنة

Abstract

Objectives: This study aims to compare the Th1/Th2 cytokines of subjects with general/abdominal obesity and non-obese individuals, and to correlate them with the biomarker of airways inflammation and different body compositions.

Methods: Eighty subjects were divided into 37 normal weight (BMI >25) and 43 overweight/obese groups (BMI ≥25). All participants were further categorised by waist circumference (WC) into an abdominal obesity group (n = 32) and a group without abdominal obesity (n = 48). Serum levels of Th1 cytokines (INF-γ, TNF-α, IL-2,) and Th2 cytokines (IL-4, IL-5, IL-13) were measured using a multiplex ELISA technique. The fractional exhaled nitric oxide (FeNO) was used as a biomarker for airways inflammation. Different body compositions were assessed using a bioelectrical body composition analyser.

Results: Serum IL-5 and TNF-α were significantly increased in groups with general or abdominal obesity compared to control groups. IL-5 showed a significant positive correlation with FeNO. BMI and total fat percentage were positively correlated to IL-5 and TNF-α, whereas WC and visceral fat percentage were correlated with the levels of IL-5 and IL-4.

Conclusion: This study confirms the elevation of certain Th1 and Th2 cytokines in subjects with general and abdominal obesity. IL-5 was positively correlated with FeNO, which may link obesity to airways inflammation.

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Keywords: Cytokines; FeNO; Nitric oxide; Obesity; Weight

Introduction

Obesity has emerged as a global health problem affecting all ages and both genders, with large differences in the absolute prevalence across the world. A dramatic increase in the prevalence of overweight and obesity has been observed since 1980. Currently, overweight and obese subjects represent about 30% of the world's population. Both high income developed countries and low socioeconomic developing countries have been affected by the obesity pandemic.[1] In KSA, obesity showed a dramatic increase during the last decade. In a recent study, about 24.7% of the Saudi population was shown to have BMI >30. This was significantly associated with many obesity-related health problems, such us type 2 diabetes, hypercholesterolemia, and hypertension.[2] The adipose tissue had long been recognised as a storage site for excessive energy. However, recent advances in research have brought to light new functions of the adipose tissue involved in many metabolic, endocrine, and immune processes.[3] Obesity causes an abnormal fat deposition in the adipose tissue and liver, with chronic inflammation and abnormal production of different adipocytokines and T helper (Th) cytokines.[4] The inflammatory response associated with obesity is originated in the adipose tissue cells.[5] Adipose tissue contains other cells besides mature adipocytes called stromal-vascular cells, which play a role in obesity-induced inflammation, including: leukocytes, macrophages, fibroblasts, endothelial cells, and pre-adipocytes.[6] Obesity is associated with polarisation from normal resident type 2 macrophage (M2) to type 1 macrophage (M1), as well as a shift from Th2 cells to Th1, Th17, and cytotoxic T lymphocytes (CTL). This results in a state of chronic inflammation, with overproduction of inflammatory mediators, such as interferon-gamma (INF-γ), interleukin 6 (IL6), and tumour necrosis factor alpha (TNF-α), whereas interleukins (ILs) with anti-inflammatory properties (IL-4, IL-5, IL-10, IL- 13), as well as the activity of regulatory T cells, are reduced.[3]

The concentration of several inflammatory cytokines has been reported to be positively correlated with BMI.[7] In contrast, reducing body weight is associated with a reduction in the circulating inflammatory mediators.[8] It is believed that this cytokines network has crucial participation in the pathogenesis of obesity and its related health complications.[9] Furthermore, excessive visceral obesity (accumulation of fat in the abdominal cavity) is linked with the incidence of cardiovascular diseases, diabetes mellitus, metabolic syndrome, and cancer.[10] Many inflammatory cytokines and chemokines were found to be secreted by visceral fat into the blood, such as (IL-6 and TNF-α), which plays a major role in inducing a pro-inflammatory state and systemic inflammation associated with abdominal obesity.[11]

Many epidemiological studies have shown a dramatic increase in obesity-related asthma.[12] Two theories have been suggested as explaining the mechanism of obesity-related asthma, including the direct mechanical effect of increased body weight on airways function and an inflammatory pathway driven by obesity-related cytokines.[13] In a recent study, we demonstrated an increase fractional exhaled nitric oxide (FeNO) - a biomarker of airways inflammation - and a reduction in small airways function in obese/overweight subjects.[14] However, the mechanism that links obesity to airways dysfunction is not fully elucidated. There is paucity in the research investigating the underlying mechanism of obesity−related airways inflammation. This paper is one of the few studies to shed light on the possible key role of cytokines in the inflammatory mechanism relating airways inflammation to overweight and obesity.

A group of cytokines produced by T helper 1 (INF-γ, IL-2, TNF-α) and T helper 2 (IL-4, IL 5, IL 13) were selected based on a recent theory about inflammatory cytokines playing a key role in the pathogenesis of bronchial asthma.[15] Those cytokines were compared in the serum of overweight/obese subjects versus normal weight control. Additionally, the correlation of these cytokines with FeNO and body composition measurements was investigated. Fractional exhaled nitric oxide is a non-invasive biomarker that reflects the degree of airways inflammation, while FeNO measurement has been shown to be informative as the gold standard technique (bronchial biopsy and bronchoalveolar lavage) for determining ongoing airway inflammation.[16]

Materials and Methods

This study was a part of a research project evaluating the changes in lung functions and the biomarkers of airways inflammation induced by increasing body weight in healthy non-smoker students (18−25 years of age) recruited using the convenience sampling technique at Imam Abdulrahman Bin Faisal University.[14] Subjects were excluded if they had any illness or current medication that impacts the immune system, airways inflammation, or body composition, such as: asthma and allergic diseases, acute or chronic pulmonary diseases, acute or chronic infection, hypothyroidism, Cushing disease, usage of steroids or anti-inflammatory medicines. Written consent was obtained from all participants.

In this comparative cross-sectional study, 80 subjects who completed the cytokines profile analysis were included. Thirty seven were placed into a normal-weight group (BMI = 18.5−24.99) and 43 were placed into an overweight/obese group (BMI ≥25).[17] The sample size was determined based on previous studies investigating the effect of obesity on airways inflammation,[18−21] where the number of participants ranged between 35 and 117. To explore the effect of visceral fat, all participants were further categorised according to waist circumference (WC) into an abdominal obesity group (n = 32) and a group without

abdominal obesity (n = 48). Females with WC ≥ 80 cm and males with WC ≥ 94 cm were considered to have abdominal obesity.[22] The methods of anthropometrics, body composition, and FeNO measurement are described elsewhere.[14]

Serum cytokines assay

After drawing about 6 ml of blood, serum was extracted by centrifugation at 3000 rpm for 15 minutes, with serum then stored in 200 µl aliquots at − 80 C° for future measurements. A group of T helper 1 (INF-γ, IL-2, TNF-α) and T helper 2 (Interleukins 4,5 and 13) cytokines were assessed by high-sensitivity cytokines assay (Human High Sensitivity T cell Panel Premixed 13-plexed-Immunology Multiplex Assay − Merck-Millipore). The inter-assay and intra-assay CVs were <15% and <10%, respectively.

Statistical analysis

Data are presented as mean ± SEM. A Shapero-Wilk test was used to test the normality of the data; non-normally distributed variables were transformed to natural log (ln). Group differences for different variables were analysed using the Mann−Whitney U test or unpaired t-test. The association of different cytokine levels with FeNO, anthropometric measurements and body compositions were analysed using Pearson's correlation in the whole cohort. Data analyses were performed using SPSS software (version 16). A P-value <0.05 was considered statistically significant.

Results

The demographic characteristics and anthropometric and body compositions measurements are depicted in Table 1. There were no significant differences between groups in age, sex, and height (P > 0.0 5). All other variables showed a significant difference between groups (P < 0.001).

Comparisons of cytokine levels among groups

A panel of inflammatory cytokines, including T helper 1 (INF-γ, IL-2, TNF-α) and T helper 2 (Interleukins 4,5 and 13), were compared for normal-weight (n = 37) and overweight/obese (n = 43) groups based on BMI (Table 2−left side), and the whole cohort was further split based on WC into an abdominal obesity group (n = 32) and a group without abdominal obesity (n = 48) (Table 2-right side). Comparing cytokine levels for the normal-weight and overweight/obese groups revealed a significantly higher

Table 1: Demographic, anthropometrics, and body composition measurements of the participants.

Variables[a]	Normal weight (n = 37)	Overweight/obese (n = 43)	P value
Age (yrs)	20.3 ± 0.17	20.3 ± 0.29	0.997
Gender n (male/female)	(19/18)	(22/21)	0.987
Weight (kg)	58.31 ± 1.24	87.9 ± 2.95	<0.001
Height (cm)	165.4 ± 1.28	165.3 ± 1.48	0.957
BMI (kg/m^2)	21.38 ± 0.29	32 ± 0.81	<0.001
Waist circumference (cm)	73.1 ± 1	96.5 ± 2.54	<0.001
Hip circumference (cm)	92. 9 ± 0.79	115.5 ± 1.77	<0.001
Waist/hip ratio (WHR)	0.79 ± 0.01	0.83 ± 0.01	0.008
Body fat %	25.3 ± 0.02	42 ± 0.01	<0.001
Body Muscles %	33 ± 0.01	28 ± 0.02	0.02
Visceral fat %	4 ± 0.002	10 ± 0.007	<0.001

[a] Values given as mean ± SEM unless stated, group comparisons were performed using an independent t-test, except for gender where a Chi x^2 test was used.

Table 2: Comparisons of cytokine levels between normal-weight and overweight/obese groups (left) and between subjects with and without abdominal obesity (right).

Cytokines[a] (pg/ml)	General obesity			Abdominal obesity		
	Normal weight (n = 37)	overweight/obese (n = 43)	P value	No abdominal obesity (n = 48)	Abdominal obesity (n = 32)	P value
INF-γ[b]	1.53 ± 0.08	1.65 ± 0.08	0.275	1.53 ± 0.08	1.68 ± 0.05	0.157
TNF-α[c]	2.54 ± 0.20	3.48 ± 0.24	**0.004**	2.67 ± 0.18	3.61 ± 0.29	**0.005**
IL-2[b]	3.57 ± 0.23	3.72 ± 0.18	0.602	3.59 ± 0.19	3.75 ± 0.21	0.584
IL-4[b]	1.79 ± 0.20	1.89 ± 0.21	0.741	1.81 ± 0.18	1.90 ± 0.24	0.756
IL-5[b]	0.14 ± 0.12	0.74 ± 08	**< 0.001**	0.32 ± 0.11	0.68 ± 0.09	**0.027**
IL-13[b]	0.46 ± 0.17	0.73 ± 0.12	0.202	0.58 ± 0.14	0.64 ± 0.15	0.791

TNF-α: Tumour necrosis factor alpha, IL-2: Interleukin 2, IL-4: Interleukin 4, IL-5: Interleukin 5, IL-13: Interleukin 13, INF -γ: interferon gamma.

[a] Cytokine levels were log transformed using formula LN (X) and displayed as mean ± SEM.

[b] Between groups comparison using the Mann−Whitney test.

[c] Between groups comparison using an independent t-test. Values in bold indicate statistical significance.

Table 3: Correlation of cytokine levels with FeNO, anthropometrics, and body composition measurements.

cytokines[a]	FeNO[a]		BMI		WC		Total fat%		Visceral fat%		Muscle mass%	
	r	P value	r	P value	r	P value	r	P value	r	P value	r	P value
INF-γ	0.02	0.852	0.18	0.104	0.12	0.275	0.18	0.121	0.11	0.331	−0.09	0.416
TNF-α	0.18	0.116	0.27	**0.013**	0.16	0.161	0.29	**0.008**	0.14	0.224	−0.19	0.093
IL-2	−0.16	0.168	0.06	0.604	−0.1	0.392	0.23	**0.042**	−0.016	0.885	−0.16	0.155
IL-4	0.19	0.103	0.13	0.235	0.12	**0.035**	−0.21	0.06	0.27	**0.02**	0.33	**0.003**
IL-5	0.23	**0.04**	0.35	**0.001**	0.25	**0.027**	0.35	**0.002**	0.32	**0.004**	−0.09	0.38
IL-13	−0.06	0.597	0.02	0.889	−0.01	0.932	0.07	0.566	−0.04	0.703	0.01	0.939

r: Pearson's correlation coefficient.
TNF-α: Tumour necrosis factor alpha, IL-2: Interleukin 2, IL-4: Interleukin 4, IL-5: Interleukin 5, IL-13: Interleukin 13, INF -γ: interferon gamma, FeNO; Fractional exhaled nitric oxide; WC: Waist circumference, BMI: Body mass index.
[a] Data was log-transformed. Values in bold indicate statistical significance.

concentration of interleukin-5 and TNF-α in overweight/obese subjects compared to normal-weight individuals (IL-5 = 0.74 ± 08 vs 0.14 ± 0.12, respectively, $p < 0.001$; TNF-α = 3.48 ± 0.24 vs 2.54 ± 0.20, respectively, $p = 0.004$). Similarly, both IL-5 and TNF-α showed elevated serum concentration in the abdominal obesity group compared to the group without abdominal obesity (IL-5 = 0.68 ± 0.09 vs 0.32 ± 0.11, respectively, $p = 0.027$; IL-6 = 3.61 ± 0.29 vs 2.6727 ± 0.18, respectively, $p = 0.005$). Other interleukins seemed to be elevated in both the overweight/obese and abdominal obesity groups compared to the control but failed to reach statistical significance (Table 2).

Associations of cytokine levels with FeNO, anthropometrics, and body composition measurements in the whole cohort

Among the studied cytokines, only IL-5 showed positive correlation with the levels of FeNO measurement. In addition, significant positive correlation was found between IL-5 and the general obesity indicators (BMI and total body fat %), as well as indicators of central obesity (WC and visceral fat %). In contrast, TNF-α was only correlated with BMI and total body fat %, whereas IL-4 showed a positive correlation with WC, visceral fat %, and muscle mass %. Other cytokines (IL-2, INF-γ, IL-13) did not show any correlation with FeNO, anthropometrics, or body composition measurements (Table 3).

Discussion

Six different cytokines were investigated in the present study in 80 participants. Significant elevation of serum IL-5 and TNF-α were observed in overweight/obese subjects compared to those of normal weight. Only serum IL-5 showed a significant positive correlation with the level of FeNO. The indicators of general obesity (BMI and total body fat %) both showed positive correlation with the levels of interleukin-5 and TNF-α, whereas WC and the visceral fat %, which indicate abdominal obesity, were correlated with IL-5 and IL-4 levels. These observations point to the role of Th1 and Th2 cytokines in the subclinical low-grade inflammation that could be detected early in apparently healthy overweight/obese young adults. In addition, these findings shed light on the role of the less commonly described cytokine IL-5 in obesity-related inflammation and its relation to airways inflammation.

Many inflammatory cells and mediators play central roles in the pathogenesis of the inflammatory response induced by increasing body weight. In obesity, the hypertrophied and hyperplastic adipocytes secrete chemo-attractants and pro-inflammatory cytokines causing migration of macrophages into adipose tissue with polarisation of the normal resident M2 macrophage to M1 macrophages.[5] Similarly, there is an increase in Th1 activity, with a reduction in Th2 and T-regulatory activity, and the overall effect of obesity is to shift the immune cells and cytokines from those with anti-inflammatory activity to a pro-inflammatory profile.[3,4]

However, the current study showed that serum concentration of certain pro-inflammatory Th1 cytokines and anti-inflammatory Th2 cytokines could be up-regulated by obesity; both TNF-α and IL-5 showed higher concentrations in the overweight/obese group and the abdominal obesity group compared to control groups. Similar findings have been observed in other studies where both pro-inflammatory cytokine and ant-inflammatory cytokine had increased in patients with obesity. In one study investigating the inflammatory cytokines profile in patients with metabolic syndrome (MetS), the pro-inflammatory cytokines INF-γ, IL-13, as well as the anti-inflammatory IL-4 and IL-5 showed significant increase in MetS patients compared to the normal healthy control.[23] In another study comparing the cytokine profile in general and central obesity participants, significant increases in INF-γ and interleukins 5, 10, 12, and 13 were reported in general, as well as in abdominal obesity, while increased TNF-α was associated with abdominal obesity.[24]

TNF-α is a commonly described cytokine in the pathogenesis of obesity-induced inflammation.[3] The present results are in agreement with previous studies showing significant elevation of TNF-α in participants with obesity.[24,25] In addition, several studies reported a similar pattern of association, where TNF-α showed positive correlation with BMI but not with any index of abdominal obesity. A study on overweight/obese postmenopausal women showed positive correlation between blood TNF-α and BMI; however, no association was observed for WC and visceral fat layer thickness determined by abdominal ultrasound.[26] Another study by Cartier et al. found an association between TNF-α and indices of total body fat rather than visceral fat.[27] However, different phenotypes of fat deposition (generalised vs visceral) involve different pathogenic mechanisms, such as altered lipid metabolism,

hormonal secretion, and inflammatory cytokines production. For example, in contrast to subcutaneous, visceral fat showed an increased production of certain adipocytokines (e.g. adiponectin and resistin) and inflammatory cytokines (e.g. IL 6).[28]

In contrast, IL-5 is a less commonly described cytokine in relation to the inflammatory milieu induced by hypertrophied adipose tissue; its role in obesity-related inflammation has not been fully elucidated. A few studies have investigated the level of IL-5 in relation to general and central obesity. In agreement with the current study, Schmidt et al. showed a significant increase in IL-5 in general and central obesity, as well as reporting a positive correlation for IL-5 with BMI, WC, and hip circumference.[24] Furthermore, IL-5 has been found to be elevated in girl students with abdominal obesity and was positively correlated with waist/hip ratio.[29] No significant differences have been detected by the present study for INF-γ, L-2, IL-4, and IL-13; this is consistent with other studies that did not find any differences in the levels of IL-2 and IL-4.[30]

There is a huge body of evidence pointing to the role of different immune cells and interleukins in the pathogenesis of obesity and its immunological complications, such as diabetes mellitus, arthritis, and asthma.[6] Obesity is considered a risk factor for asthma development,[12] but the mechanistic basis for this relationship is still an area of controversy. One theory attributes the airways dysfunction associated with obesity to a mechanical reduction in lung compliance from excess body weight, leading to reduced lung volume.[31] Meanwhile, other studies have showed that inflammation in adipose tissue could provoke true airways inflammation and hyperresponsiveness.[32] It has been documented that TNF-α could elicit an airways hyperresponsiveness by direct action on the airways.[33] Furthermore, an increase in the number of inflammatory cells and elevation of INF-γ, TNF-α, IL- 6, and other pro-inflammatory cytokines in the lungs tissue, sputum, and bronchoalveolar lavage fluid have been reported in a number of animal models of obesity[34] and human studies on obese individuals.[35] Possible spread of inflammatory mediators from adipose tissue into the bloodstream to the lungs could explain the obesity-induced airways inflammation and hyperresponsiveness, a mechanism that needs further investigation and proof. Obesity-related asthma is characterised by enhancement of Th1 immune response with neutrophilic airways inflammation but paucity in Th2 mediated eosinophilic airways inflammation.[36] In contrast and in agreement with the present study findings for increased IL-5, Th2 role in obesity-related asthma have been described, and more than one phenotype with subgroups exhibiting Th2 inflammation have been reported with increased IL-5 and eosinophilic inflammation.[32] In addition, a concurrent airway eosinophilia has been reported in animal models of obese leptin-deficient ob/ob mice[37] and in clinical studies of obese asthmatic patients.[38]

Fractional exhaled nitric oxide is a non-invasive biomarker of eosinophilic airway inflammation characterising the Th2 inflammatory response.[39] The effect of being overweight on FeNO is still an area of controversy; some studies did not report any changes in FeNO associated with increasing body weight,[19] while others showed low levels[21] or demonstrated overproduction of FeNO in individuals with obesity.[40,41] In a very recent study, we have demonstrated an elevation in FeNO level in overweight/obese subjects;[14] however, the underlying mechanism needs further investigation. The observation of increased IL-5 levels associated with obesity by the current study and its positive correlation with FeNO are rather interesting; IL-5 is a Th2 cytokine that plays a central role in the maturation, migration, and function of blood and airways eosinophils. IL-5, together with other Th2 cytokines (IL-4, IL-13), promotes airways eosinophilia, mucous secretion, immunoglobulin E (IgE) production, and airways hyperresponsiveness, a characteristic feature of type-2 high asthma.[15] This could be a plausible explanation for the mechanism of obesity-related asthma subtypes showing markers of Th2 inflammatory response and increased FeNO production.

One limitation of the current study is the cross-sectional design. Only a simple correlation between different cytokine levels and being overweight could be concluded without any causal relationship.

Conclusion

An elevation of certain Th1 and Th2 cytokines in participants with general and abdominal obesity was reported from this study. This highlights the importance of Th1/Th2 cytokines in the process of the inflammation associated with obesity; it also reveals a positive correlation between IL-5 and the airways inflammation biomarker (FeNO).

Recommendations

This study warrants further investigation into the susceptibility of obese subjects to airways inflammation and allergic bronchial asthma.

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Conflicts of interest

The author has no conflict of interest to declare.

Ethical approval

This study followed the principles of the Helsinki Declaration and was approved by the ethical committee at Imam Abdulrahman Bin Faisal University (IRB-2019-03-032 dated on 29/1/2019).

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References

1. Chooi YC, Ding C, Magkos F. The epidemiology of obesity. **Metab Clin Exp 2019**; 92: 6–10.
2. Althumiri NA, Basyouni MH, AlMousa N, AlJuwaysim MF, Almubark RA, BinDhim NF, et al. Obesity in Saudi Arabia in 2020: prevalence, distribution, and its current association with various health conditions. **Healthcare (Basel) 2021**; 9(3): 311.
3. Ignacio RM, Kim CS, Kim SK. Immunological profiling of obesity. **J Lifestyle Med 2014**; 4(1): 1–7.
4. Ellulu MS, Patimah I, Khaza'ai H, Rahmat A, Abed Y. Obesity and inflammation: the linking mechanism and the complications. **Arch Med Sci 2017**; 13(4): 851–863.
5. Wellen KE, Hotamisligil GS. Obesity-induced inflammatory changes in adipose tissue. **J Clin Invest 2003**; 112(12): 1785–1788.
6. Kanneganti T-D, Dixit VD. Immunological complications of obesity. **Nat Immunol 2012**; 13(8): 707–712.
7. Himmerich H, Fulda S, Linseisen J, Seiler H, Wolfram G, Himmerich S, et al. TNF-alpha, soluble TNF receptor and interleukin-6 plasma levels in the general population. **Eur Cytokine Netw 2006**; 17(3): 196–201.
8. Sideleva O, Black K, Dixon AE. Effects of obesity and weight loss on airway physiology and inflammation in asthma. **Pulm Pharmacol Therapeut 2013**; 26(4): 455–458.
9. Emanuela F, Grazia M, Marco de R, Maria Paola L, Giorgio F, Marco B. Inflammation as a link between obesity and metabolic syndrome. **J Nutr Metab 2012**; 476380(10): 1.
10. Zhang C, Rexrode KM, Dam RMv, Li TY, Hu FB. Abdominal obesity and the risk of all-cause, cardiovascular, and cancer mortality. **Circulation 2008**; 117(13): 1658–1667.
11. Fontana L, Eagon JC, Trujillo ME, Scherer PE, Klein S. Visceral fat adipokine secretion is associated with systemic inflammation in obese humans. **Diabetes 2007**; 56(4): 1010–1013.
12. Wood LG. Asthma in the obese: a big and growing problem. **Am J Respir Crit Care Med 2016**; 195(1): 4–5.
13. Rasmussen F, Hancox RJ. Mechanisms of obesity in asthma. **Curr Opin Allergy Clin Immunol 2014**; 14(1): 35–43.
14. Al Khathlan N, Salem AM. The effect of adiposity markers on fractional exhaled nitric oxide (FeNO) and pulmonary function measurements. **Int J Gen Med 2020**; 13: 955–962.
15. Lambrecht BN, Hammad H, Fahy JV. The cytokines of asthma. **Immunity 2019**; 50(4): 975–991.
16. Barnes PJ, Dweik RA, Gelb AF, Gibson PG, George SC, Grasemann H, et al. Exhaled nitric oxide in pulmonary diseases: a comprehensive review. **Chest 2010**; 138(3): 682–692. Epub 2010/09/09.
17. Nuttall FQ. Body mass index: obesity, BMI, and health: a critical review. **Nutr Today 2015**; 50(3): 117–128. Epub 2015/04/07.
18. Kim SH, Kim TH, Lee JS, Koo TY, Lee CB, Yoon HJ, et al. Adiposity, adipokines, and exhaled nitric oxide in healthy adults without asthma. **J Asthma : Off J Assoc Care Asthma 2011**; 48(2): 177–182. Epub 2011/01/13.
19. van de Kant KD, Paredi P, Meah S, Kalsi HS, Barnes PJ, Usmani OS. The effect of body weight on distal airway function and airway inflammation. **Obes Res Clin Pract 2016**; 10(5): 564–573. Epub 2015/12/02.
20. Zerah F, Harf A, Perlemuter L, Lorino H, Lorino AM, Atlan G. Effects of obesity on respiratory resistance. **Chest 1993**; 103(5): 1470–1476. Epub 1993/05/01.
21. Maniscalco M, Zedda A, Faraone S, Cristiano S, Sofia M, Motta A. Low alveolar and bronchial nitric oxide in severe uncomplicated obesity. **Obes Res Clin Pract 2015**; 9(6): 603–608. Epub 2015/04/13.
22. World Health Organization. *Waist circumference and waist–hip ratio, Report of a WHO expert consultation, Geneva, 8-11 December 2008*; 2011 [cited 2020 June 9]; Available from: https://www.who.int/nutrition/publications/obesity/WHO_report_waistcircumference_and_waisthip_ratio/en/.
23. Surendar J, Mohan V, Rao MM, Babu S, Aravindhan V. Increased levels of both Th1 and Th2 cytokines in subjects with metabolic syndrome (CURES-103). **Diabetes Technol Therapeut 2011**; 13(4): 477–482.
24. Schmidt FM, Weschenfelder J, Sander C, Minkwitz J, Thormann J, Chittka T, et al. Inflammatory cytokines in general and central obesity and modulating effects of physical activity. **PloS One 2015**; 10(3):e0121971. Epub 2015/03/18.
25. Borges MD, Franca EL, Fujimori M, Silva SMC, de Marchi PGF, Deluque AL, et al. Relationship between proinflammatory cytokines/chemokines and adipokines in serum of young adults with obesity. **Endocr Metab Immune Disord - Drug Targets 2018**; 18(3): 260–267. Epub 2018/02/01.
26. Fenkci S, Rota S, Sabir N, Sermez Y, Guclu A, Akdag B. Relationship of serum interleukin-6 and tumor necrosis factor alpha levels with abdominal fat distribution evaluated by ultrasonography in overweight or obese postmenopausal women. **J Invest Med : Off Publ Am Fed Clin Res 2006**; 54(8): 455–460. Epub 2006/12/16.
27. Cartier A, Lemieux I, Almeras N, Tremblay A, Bergeron J, Despres JP. Visceral obesity and plasma glucose-insulin homeostasis: contributions of interleukin-6 and tumor necrosis factor-alpha in men. **J Clin Endocrinol Metabol 2008**; 93(5): 1931–1938. Epub 2008/03/06.
28. Hansen E, Hajri T, Abumrad NN. Is all fat the same? The role of fat in the pathogenesis of the metabolic syndrome and type 2 diabetes mellitus. **Surgery 2006**; 139(6): 711–716.
29. El-Wakkad A, Hassan Nel M, Sibaii H, El-Zayat SR. Proinflammatory, anti-inflammatory cytokines and adiponkines in students with central obesity. **Cytokine 2013**; 61(2): 682–687. Epub 2013/01/12.
30. Azizian M, Mahdipour E, Mirhafez SR, Shoeibi S, Nematy M, Esmaily H, et al. Cytokine profiles in overweight and obese subjects and normal weight individuals matched for age and gender. **Ann Clin Biochem 2016**; 53(6): 663–668. Epub 2016/01/21.
31. Littleton SW. Impact of obesity on respiratory function. **Respirology (Carlton, Vic). 2012**; 17(1): 43–49. Epub 2011/11/02.
32. Peters MC, Fahy JV. Type 2 immune responses in obese individuals with asthma. **Am J Respir Crit Care Med 2013**; 188(6): 633–634.
33. Brightling C, Berry M, Amrani Y. Targeting TNF-alpha: a novel therapeutic approach for asthma. **J Allergy Clin Immunol 2008**; 121(1): 5–10.
34. Yu G, Zhu L, Li H, Shao Y, Chong L, Zhang H, et al. Influence of gender on OVA-induced airway inflammation in C57/B6J mice on a high-fat diet. **Eur J Inflamm 2018**; 16. 2058739218760946.
35. Telenga ED, Tideman SW, Kerstjens HA, Hacken NH, Timens W, Postma DS, et al. Obesity in asthma: more neutrophilic inflammation as a possible explanation for a reduced treatment response. **Allergy 2012**; 67(8): 1060–1068.
36. Fahy JV. Type 2 inflammation in asthma–present in most, absent in many. **Nat Rev Immunol 2015**; 15(1): 57–65. Epub 2014/12/24.
37. Lintomen L, Calixto MC, Schenka A, Antunes E. Allergen-induced bone marrow eosinophilopoiesis and airways eosinophilic inflammation in leptin-deficient ob/ob mice. **Obesity 2012**; 20(10): 1959–1965.
38. Grotta MB, Squebola-Cola DM, Toro AA, Ribeiro MA, Mazon SB, Ribeiro JD, et al. Obesity increases eosinophil activity in asthmatic children and adolescents. **BMC Pulm Med 2013**; 13: 39. Epub 2013/06/19.

39. Dweik RA, Boggs PB, Erzurum SC, Irvin CG, Leigh MW, Lundberg JO, et al. An official ATS clinical practice guideline: interpretation of exhaled nitric oxide levels (FENO) for clinical applications. **Am J Respir Crit Care Med 2011**; 184(5): 602–615. Epub 2011/09/03.
40. Erkocoglu M, Kaya A, Ozcan C, Akan A, Vezir E, Azkur D, et al. The effect of obesity on the level of fractional exhaled nitric oxide in children with asthma. **Int Arch Allergy Immunol 2013**; 162(2): 156–162. Epub 2013/08/08.
41. Uppalapati A, Gogineni S, Espiritu JR. Association between body mass index (BMI) and fraction of exhaled nitric oxide (FeNO) levels in the national health and nutrition examination survey (NHANES) 2007-2010. **Obes Res Clin Pract 2016**; 10(6): 652–658. Epub 2016/01/18.

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