Diabetes & Metabolic Syndrome: Clinical Research & Reviews 13 (2019) 1369–1373

Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Original Article

# The association between dietary antioxidants and adipokines level among obese women

Elnaz Daneshzad [a], Alireza Farsad-Naeimi [b], Javad Heshmati [c], Khadijeh Mirzaei Associated Professor [a, *], Zhila Maghbooli [d], Seyed-Ali Keshavarz [e]

[a] Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences (TUMS), Tehran, 14155-6117, Iran
[b] Department of Nutrition, School of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran
[c] Department of Nutritional Science, School of Nutritional Science and Food Technology, Kermanshah University of Medical Sciences, Kermanshah, Iran
[d] Osteoporosis Research Center, Endocrine Diseases and Metabolism Research Institute, Tehran University of Medical Sciences, Tehran, Iran
[e] Department of Clinical Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences (TUMS), Tehran, Iran

ARTICLE INFO

*Article history:*
Received 30 January 2019
Accepted 12 February 2019

*Keywords:*
Antioxidants
ANGPTL6
Progranulin
Adipokines
Obesity

ABSTRACT

*Aim:* Adipokines are associated with several oxidative stress-related diseases and pathologic conditions. We aimed to assess the association between antioxidants and adipokines in obese adults.
*Methods and Materials:* In this cross-sectional study, a total of 160 obese women were included. Body composition and anthropometric characteristics were measured. Dietary intakes were assessed by 3-day, 24-h dietary recall. Blood samples were obtained following an overnight fasting. Serum concentrations of adipokines including progranulin, retinol binding protein 4 (RBP4) and Angiopoietin-related growth factor 6 (ANGPTL6) was measured using an enzyme-linked immunosorbent assay. ANCOVA and the linear regression model analysis was performed to assess the relationship between Progranulin, RBP4, AnGPTL6, and antioxidants.
*Results:* Mean age of included women was $39.31 \pm 12.10$. Mean and standard deviation for BMI was $35.05 \pm 4.26$ in this obese population. There was a positive significant association between ANGPTL6 and vitamin D intake ($p < 0.001$). Also, there was a marginal association between RBP4 and vitamin A ($p = 0.063$) intake, but after adjustment age, and fat mass, we found a significant association ($p = 0.008$). However, the associations between dietary antioxidants, progranulin, and ANGPTL6 were not statistically significant.
*Conclusions:* ANGPTL6 and RBP4 levels directly associated with dietary vitamins D and A intake, respectively. But, according to the results, the association between ANGPTL6 and vitamin D was bidirectional. The suggested associations probably can be useful in the development of interventional studies for management of chronic diseases.


## 1. Introduction

Adipose tissue, an endocrine and paracrine active organ produces a large number of cytokines and bioactive mediators [1]. Adipokines are proteins which also are secreted by adipose tissue [2]. These bioactive proteins have many physiological effects on brain, bones, reproductive organs, liver, skeletal muscles, blood vessels and immune cells [3] and regulate energy intake and energy expenditure [2]. These Substances not only can modulate fat metabolism and body weight homeostasis but also they have important effects on insulin resistance and inflammation process [1]. Most studies about adipokines have focused on the leptin, a determinant factor of oxidative stress and adiponectin, which has main role in insulin sensitivity and exerts anti-inflammatory and anti-atherogenic properties [4]. Limited studies conducted to assess other adipokines or proteins. Angiopoietin-related growth factor 6 (ANGPTL6), is a protein that can be useful in treatment of some ischemic diseases [5]. It seems that this hepatocyte derived protein antagonizes insulin resistance and obesity [6]. Progranulin is another regulatory protein and adipokine with anti-inflammatory properties and neuroprotective activities [7]. This protein expressed in many cells such as immune cells and epithelial cells as

* Corresponding author.
*E-mail address:* mina_mirzaei101@yahoo.com (K. Mirzaei).

https://doi.org/10.1016/j.dsx.2019.02.022
1871-4021/

**Abbreviation list**

| | |
|---|---|
| RBP4 | Retinol binding protein 4 |
| ANGPTL6 | Angiopoietin-related growth factor 6 |
| AGF | Angiopoietin-related growth factor |
| 3DR | 3-day, 24-h dietary recall |
| TFM | trunk fat mass |
| VFM | visceral fat mass |
| FFM | fat-free mass |
| TBW | total body water |

well as adipocytes and neurons [8]. Elevated levels of this adipokine have shown in obesity and obesity-associated insulin resistance. However, results from studies are inconsistent and they have shown that progranulin has both beneficial and detrimental effects [7]. Retinol binding protein 4 (RBP4), an adipocyte and hepatocyte derived adipokine, is responsible for retinol transportation in blood [9]. Previous studies have shown that RBP4 levels were increased in obese and type 2 diabetes humans [10–12]. Also, elevated RBP4 levels increased the risk of coronary heart disease. It seems that RBP4 promotes oxidative stress by deteriorating endothelial mitochondrial function [9].

Oxidative stress which results from an increase in reactive oxygen species (ROS) levels, can lead to obesity, diabetes and other metabolic and chronic diseases. Moreover, oxidative stress plays out a significant role in the production of adipokines [13]. Specially, due to high fat mass, the obese individuals are more prone to systemic inflammation, high levels of ROS and weak antioxidant defense system [14,15]. Nowadays, due to the potential anti-inflammatory properties of dietary antioxidants, they are more often consumed by obese and inactive people to reduce the risk of cardiovascular disease [16]. In high oxidative stress conditions, the raised levels of serum pro-inflammatory cytokines and decreased adiponectin levels, can adversely affect the insulin sensitivity. On the other hand, reductions in antioxidant defense, can change the production of inflammatory factors and cause an imbalanced situation in adipose tissue and further insulin resistance [17]. Activation of antioxidant defense mechanisms reduces the progression of atherosclerosis and endothelial dysfunction [18].

Therefore, higher antioxidant intakes can be considered as an effective approach in modulating of the process. In this regard, rising the serum adiponectin levels has observed in response to certain foods containing antioxidants [19]. However, some studies failed to find any significant effect of antioxidants on concentrations of adipokines [20,21]. Considering the limited studies with contradicted results regarding the possible relationship between antioxidants and adipokines, particularly, ANGPTL6, RBP4, and progranulin, this study aimed to investigate the association between antioxidants levels and adipokines in obese adults.

## 2. Methods and materials

### 2.1. Study population

This cross-sectional study was conducted among 160 obese women, in Iran, Tehran between November 2013 and December 2014. All participants were recruited from the Nutrition Department in outpatient clinic of the Shariati Hospital which covered all urban residency regions in Tehran. All participants were signed a written informed consent prior to the study. Subjects were chosen according to the inclusion and exclusion criteria as follows: subjects had a BMI of 30 or more with an age between 19 and 69 years old. The exclusion criteria were: pregnancy, alcohol or drug abuse, current smoking, suffering from hypertension, diabetes mellitus or cardiovascular diseases, having thyroid, hepatic or renal disorders, malignancies, being in any acute or chronic inflammatory condition or infection.

This study was supported and got ethical approve by “blinded for reviewing”.

### 2.2. Dietary intake assessment

We asked the participants to follow their usual diet. Dietary intakes was assessed by 3-day, 24-h dietary recall (3DR), which two days were on the weekend. All consumed foods and drinks on the previous day were requested. Data from dietary intakes were recorded by common household servings and after conversion into grams and milliliters, were analyzed using the NUTRITIONIST 4 (First Data Bank, San Bruno, CA) food analyzer.

### 2.3. Circulating adipokines measurements

Blood samples were obtained following an overnight fasting from all subjects. Serum concentrations of all adipokines were measured in triplicate while, 10 replicates per enzyme-linked immunosorbent assay (ELISA) plate were used as internal quality controls. RBP4 in serum samples was measured by competitive ELISA (AdipoGen, Seoul, Korea) and inter- and intra-assay variability was 4.2% and 4.5%, respectively (Cat. No. R0822EK). Serum ANGPTL6 (AdipoGen Inc., Incheon, Korea) and progranulin (AdipoGen; Seoul, Korea) (Cat. No. AG-45A-0018 EK-KI01) were measured using ELISA kits.

### 2.4. Complete body composition analysis

Height measured to the nearest 1 mm using a stadiometer (SECA 206, Germany). Weight measured using by the body composition analyzer. Following height and weight measurements, BMI was calculated as weight (kg)/height ($m^2$). For all subjects total body composition were assessed using a BC-418MA body composition analyzer (Tanita, UK). To prevent any possible bias in measured values, the participants were refrained from vigorous exercise for 2 days prior to the study. The body composition analyzer calculated variables were as follows: weight, body fat percentage, body fat mass (FM), trunk fat mass (TFM), visceral fat mass (VFM), abdominal fat mass, fat-free mass (FFM), estimated muscle mass, and total body water (TBW). Muscle mass was predicted on the basis of data which obtained from dual-energy X-ray absorptiometry (DXA) using bioelectrical impedance analysis (BIA). Measurements were performed on all subjects by professional nutritionists using a standard protocol that described in details previously [22].

### 2.5. Statistical analysis

Statistical analysis was performed using SPSS 16 (SPSS Inc., Chicago, IL). The Kolmogorov-Smirnov test was used to check data normality. The values are expressed as mean and standard deviation for anthropometric characteristics. Dietary antioxidant intakes were adjusted for total energy intake using the residual model [23]. The levels of dietary antioxidant intakes compared between tertiles of adipokines (ANGPTL6, progranulin, RBP4) by one-way ANOVA, and ANCOVA used to adjust the confounder's effect. The linear regression model (LRM) analysis was performed to assess the relationship between Progranulin, RBP4, AnGPTL6, and antioxidants. The statistically significant level considered as p-value $\leq 0.05$ for all analyses.

## 3. Results

Mean age of included women was 39.31 ± 12.10 in the present study. Baseline characteristics and biochemical measurements of participants are demonstrated in Table 1. According to this table mean and SD for BMI was 35.05 ± 4.26. In order to examine the association of dietary antioxidants intake with adipokine levels, the participants were grouped based on tertiles of adipokoines level (Table 2). As shown in this table, vitamin D ($P < 0.0001$), E, and α-tocopherol intake ($P > 0.05$) was higher in the last tertile of ANGPTL6. Also vitamin A, E, β-carotene and α-tocopherol intake ($P < 0.05$) was higher in the last tertile of RBP4. β-carotene intake was lower in the last tertile of Progranulin ($P = 0.02$). As shown in Table 3, we found a significant association between ANGPTL6 and vitamin D intake before and after confounders adjustment, ($P < 0.001$) and ($P = 0.001$), respectively. A significant association was shown between RBP4 and vitamin A intake after confounders adjustment ($P = 0.008$), however, it was marginally significant before adjustment ($P = 0.063$). Also, there was a marginally significant association between RBP4 and β-carotene intake after adjustment ($P = 0.051$). There was a marginally significant inverse association between progranulin and β-carotene intake before and after adjustment ($P = 0.06$). Our results demonstrated no significant association between other adipokines and dietary antioxidant.

**Table 1**
Demographic and biochemical characteristics among 160 participants.

| Variables | Mean ± SD |
|---|---|
| Age (years) | 39.31 ± 12.10 |
| Height (cm) | 160.75 ± 7.85 |
| Weight (kg) | 90.31 ± 13.49 |
| BMI (kg/m$^2$) | 35.05 ± 4.26 |
| Body fat percentage (%) | 41.23 ± 6.23 |
| FAT Mass | 37.39 ± 8.91 |
| FFM | 52.93 ± 9.05 |
| TBW | 38.74 ± 6.62 |
| Visceral fat mass | 10.13 ± 2.85 |
| Trunk fat mass | 18.54 ± 4.88 |
| Energy intake (Kcal) | 1918.30 ± 600.64 |
| Vitamin A | 552.27 ± 510.47 |
| Vitamin C (mg) | 109.41 ± 72.01 |
| Vitamin E (mg) | 23.45 ± 10.64 |
| Vitamin D (mcg) | 0.54 ± 0.48 |
| Beta-Carotene (mcg) | 733.31 ± 530.68 |
| Alpha-Tocopherol (mcg) | 16.01.31 ± 6.72 |

BMI: Body Mass Index, FBS: Fasting Blood Sugar, TG: Triglyceride, HDL-C: High-Density Lipoprotein cholesterol, LDL-C: Low-Density Lipoprotein cholesterol, hs-CRP: high sensitive C Reactive Protein, FFM: Fat-Free Mass, TBW: Total Body Water, RMR: Resting Metabolic Rate.

## 4. Discussion

This cross-sectional study evaluated the relationship between antioxidant intake and adipokines in a population of obese individuals. We found a significant direct association between ANGPTL6 and dietary vitamin D intake. Additionally, there was a significant direct association between RBP4 and vitamin A intake from food sources. ANGPTL6 is one of the angiopoietin-like proteins which expressed in the liver and it can regulate angiogenesis. This protein plays a role in promoting proliferation of keratinocytes, cancer cell invasion and hematopoietic stem cell activity. It also can affect lipid, glucose and energy metabolism and decrease energy expenditure, modulate body weight and has an antagonizing effect on obesity and insulin resistance [24]. The higher levels of ANGPTL6 are related to alleviation of insulin resistance, while it is well-known that insulin resistance is common in obese individuals. Furthermore, several studies have indicated that ANGPTL6 was increased in chronic diseases such as metabolic syndrome and diabetes [6,25,26]. However, regulation of adipokines and their levels depend on various factors such as amount of adiposity in tissues, maturity of adipocytes, age, genetic factors and pathological conditions, while, diet and dietary ingredients may have effect on them as well [27,28].

To the best of our knowledge, there was not any publication regarding the association of dietary ingredients and adipokines regulation. Cinkajzlova et al.'s study [24] had shown that very low calorie diet (VLCD) can increase ANGPTL6 mRNA expression in

**Table 2**
Antioxidants intake among tertiles of Adipokines level (N = 160).

| Variables | T1 N = 53 | T2 N = 53 | T3 N = 54 | P* | P** |
|---|---|---|---|---|---|
| AnGPTL6 | | | | | |
| Vitamin A | 860.42 ± 525.64$^a$ | 613.07 ± 336.95$^{a,b}$ | 851.61 ± 438.98$^b$ | **0.005** | 0.12 |
| Vitamin D | 0.41 ± 0.41$^a$ | 0.48 ± 0.30$^b$ | 0.87 ± 0.82$^{a,b}$ | **<0.0001** | **0.02** |
| Vitamin E | 23.66 ± 10.98 | 22.47 ± 11.19 | 25.38 ± 98.67 | 0.96 | 0.56 |
| Vitamin C | 134.75 ± 99.40$^{a,b}$ | 97.58 ± 66.67$^a$ | 79.15 ± 64.68$^b$ | **0.001** | 0.26 |
| Beta-Carotene | 851.71 ± 686.77 | 645.87 ± 482.08 | 782.32 ± 436.25 | 0.14 | 0.73 |
| Alpha-Tocopherol | 16.46 ± 8.91 | 15.04 ± 4.84 | 17.62 ± 7.72 | 0.19 | 0.83 |
| RBP4 | | | | | |
| Vitamin A | 655.49 ± 263.47 | 676.07 ± 333.20 | 898.19 ± 435.89 | **<0.001** | **0.03** |
| Vitamin D | 0.26 ± 0.22 | 0.60 ± 0.32 | 0.24 ± 0.18 | **<0.001** | **0.04** |
| Vitamin E | 21.49 ± 13.14 | 19.17 ± 12.10 | 27.10 ± 9.69 | **0.002** | 0.54 |
| Vitamin C | 161.70 ± 63.45 | 133.24 ± 96.67 | 55.39 ± 43.06 | **<0.001** | 0.12 |
| Beta-Carotene | 662.81 ± 427.76 | 386.48 ± 679.46 | 963.35 ± 837.28 | **<0.001** | 0.34 |
| Alpha-Tocopherol | 13.92 ± 5.81 | 13.74 ± 6.25 | 18.03 ± 8.09 | **0.0014** | 0.21 |
| Progranulin | | | | | |
| Vitamin A | 952.49 ± 557.58 | 584.37 ± 416.15 | 782.39 ± 301.47 | **0.0001** | 0.49 |
| Vitamin D | 0.38 ± 0.49 | 0.63 ± 0.53 | 0.51 ± 0.48 | **0.03** | 0.72 |
| Vitamin E | 20.55 ± 11.84 | 26.13 ± 11.59 | 21.39 ± 10.08 | **0.02** | 0.81 |
| Vitamin C | 84.60 ± 41.62 | 88.56 ± 57.97 | 143.57 ± 89.28 | **<0.001** | 0.13 |
| Beta-Carotene | 793.14 ± 649.37 | 877.77 ± 645.03 | 517.67 ± 189.22 | **0.001** | **0.02** |
| Alpha-Tocopherol | 14.42 ± 7.59 | 17.74 ± 6.06 | 14.51 ± 7.52 | **0.02** | 0.32 |

Data presented as Mean ± SD.
*P value resulted from one-way ANOVA test-the same letter demonstrated the significant difference between two groups in Turkey's procedure of Post-hoc analysis. The bolded P values are significant.
**P values are adjusted for Energy intake and Fat Mass in General Linear model.
RBP4: Retinol-binding protein 4.
¥ All variables adjusted to energy intake by Residual model.

**Table 3**
Association between Antioxidants intake and adipokines level (N = 160).

| Variables | Crude Model | P (T value) | Adjusted Model[a] | P (T value) |
|---|---|---|---|---|
| | Beta (95%CI) | | Beta (95%CI) | |
| AnGPTL6 | | | | |
| Vitamin A | 0.030 (−0.006–0.008) | 0.851 (0.18) | 0.013 (−0.008–0.008) | 0.944 (0.07) |
| Vitamin D | 0.623 (6.504–18.372) | **<0.0001** (4.28) | 0.596 (5.521–18.267) | **0.001** (3.83) |
| Vitamin E | 0.191 (−0.113–0.454) | 0.231 (1.21) | 0.227 (−0.094–0.499) | 0.175 (1.38) |
| Vitamin C | −0.213 (−0.068–0.013) | 0.181 (−1.36) | −0.249 (−0.075–0.011) | 0.137 (−1.52) |
| Beta-Carotene | 0.125 (−0.003–0.008) | 0.437 (0.78) | 0.118 (−0.004–0.008) | 0.485 (0.70) |
| Alpha-Tocopherol | 0.167 (−0.215–0.686) | 0.296 (1.05) | 0.185 (−0.208–0.728) | 0.267 (1.12) |
| RBP4 | | | | |
| Vitamin A | 0.363 (0.00–0.005) | **0.063** (1.94) | 0.461 (0.001–0.005) | **0.008** (2.89) |
| Vitamin D | −0.028 (−4.514–4.038) | 0.908 (−0.11) | 0.094 (−4.198–5.818) | 0.735 (0.34) |
| Vitamin E | 0.122 (−0.066–0.122) | 0.546 (0.61) | 0.001 (−0.086–0.087) | 0.995 (0.007) |
| Vitamin C | −0.285 (−0.022–0.004) | 0.149 (−1.48) | −0.163 (−0.017–0.007) | 0.375 (−0.90) |
| Beta-Carotene | 0.298 (0.00–0.003) | 0.132 (1.55) | 0.348 (0.00–0.003) | **0.051** (2.06) |
| Alpha-Tocopherol | 0.147 (−0.105–0.224) | 0.465 (0.74) | 0.087 (−0.113–0.183) | 0.630 (0.48) |
| Progranulin | | | | |
| Vitamin A | −0.088 (−0.043–0.025) | 0.594 (−0.53) | −0.90 (−0.048–0.029) | 0.627 (−0.49) |
| Vitamin D | −0.144 (−43.849–20.649) | 0.466 (−0.73) | −0.153 (−47.612–22.862) | 0.475 (−0.72) |
| Vitamin E | −0.122 (−1.779–0.821) | 0.460 (−0.74) | −0.067 (−1.652–1.125) | 0.702 (−0.38) |
| Vitamin C | 0.255 (−0.039–0.339) | 0.117 (1.60) | 0.243 (−0.054–0.340) | 0.149 (1.47) |
| Beta-Carotene | −0.298 (−0.050–0.002) | **0.066** (−0.18) | −0.312 (−0.051–0.001) | **0.060** (−1.94) |
| Alpha-Tocopherol | −0.165 (−3.111–1.029) | 0.315 (−1.01) | −0.127 (−2.982–1.381) | 0.461 (−0.74) |

- Linear regression.
[a] Adjusted for age, and fat mass.

obese individuals. But the ingredients of this diet was not clear whether low calorie led to increased expression of ANGPTL6 mRNA or other ingredients of VLCD such as vegetables which contained antioxidants. Regarding the observed association between vitamin D and ANGPTL6 in our study, the possible role of vitamin D ANGPTL6 regulation is unknown yet. But, this nutrient previously was associated with regulation of other adipokines, such as Resistin [29] and adiponectin [30,31], similar to our finding. Vitamin D has an alleviating effect on insulin resistance which can decrease severity of insulin resistance and also can prevent diabetes by improving insulin sensitivity which again support the probably of mentioned relationship for this vitamin with ANGPTL6 [32]. According to a meta-analysis, vitamin D supplementation can be effective on decreasing LDL-cholesterol levels. Similarly, ANGPTL6 can have impact on lipids metabolism [33]. In facts, there is a report that ANGPTL6 improved lipid profile significantly [34].

In this study, there was a positive relationship between vitamin A intake and RBP4 levels. In fact, dietary vitamin A may effect adipogenesis and decrease adiposity. RBP4 is synthesized and secreted in adipose tissue except the amounts which is secreted by liver. RBP4 can modulate the effect of vitamin A on adiposity reduction, because it can attune cellular uptake of vitamin A (retinol) in adipose tissue [35]. Therefore retinol and its metabolites such as retinaldehyde and retinoic acid involved in fat metabolism and anti-adipogenic effects [36]. In line with current study, a research has shown a positive and significant association between total vitamin A intake and RBP4. Also, there was a significant indirect association between RBP4 concentration and selenium as an antioxidant dietary ingredient [37]. According to this findings, higher vitamin A intake could elevate the expression of RBP4 probably due to necessity for transportation and metabolizing of this vitamin [38]. Since, the observed significant association between dietary vitamin A and RBP4, was marginally significant prior to adjustments for cofounding variables, therefore probably the confounding factors including age, gender and fat mass affect dietary intakes of vitamin A.

The most important limitation of current study was its cross-sectional nature that cannot may not reveal the causality relationship. The relatively small sample size was another limitation of this study. The broad age range could be an important confounder for data analyses of this study, however we adjusted this variable in our analysis. To the best of our knowledge, this was the first study that examined the association between adipokines and vitamin intakes which as a strength it can open a new window for further researches.

## 5. Conclusion

There were direct associations between dietary vitamin D with ANGPTL6 and vitamin A intake with RBP4 levels. Apparently, the association of vitamin D and ANGPTL6 is bidirectional. Future longitudinal studies can be helpful to better clarify the reported associations.

## Ethical standards disclosure

Written informed consent was obtained from all subjects.

## Financial support

This study was supported by research grants from Tehran University of Medical Sciences (Grant IDs 34479 and 33893).

## Authorship

KhM and ZhM designed the study. KhM and MK supervised the study. ED and AF conducted the study. KhM and ED analyzed the data. ED and AF wrote the manuscript. KhM and MK finalized the manuscript.

## Conflicts of interest

None.

## Acknowledgements

The authors thank the directors of Tehran University of Medical Sciences, for allowing us to conduct this cross-sectional study.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dsx.2019.02.022.

## References


[1] Alivand M. Association between adipokines and cardiovascular disease with obesity syndrome in normal weight women. Veterinary Faculty; 2012.
[2] Fain JN, Tagele BM, Cheema P, Madan AK, Tichansky DS. Release of 12 adipokines by adipose tissue, nonfat cells, and fat cells from obese women. Obesity 2010 May;18(5):890–6. PubMed PMID: 19834460. Epub 2009/10/17. eng.
[3] Drevon CA. Fatty acids and expression of adipokines. Biochim Biophys Acta 2005 May 30;1740(2):287–92. PubMed PMID: 15949695. Epub 2005/06/14. eng.
[4] Adya R, Tan BK, Randeva HS. Differential effects of leptin and adiponectin in endothelial angiogenesis. J Diabetes Res 2015;2015:648239. PubMed PMID: 25650072. Pubmed Central PMCID: Pmc4310451. Epub 2015/02/05. eng.
[5] Urano T, Ito Y Fau - Akao M, Akao M Fau - Sawa T, Sawa T Fau - Miyata K, Miyata K Fau - Tabata M, Tabata M Fau - Morisada T, et al. Angiopoietin-related growth factor enhances blood flow via activation of the ERK1/2-eNOS-NO pathway in a mouse hind-limb ischemia model. (1524-4636 (Electronic)). eng.
[6] Ebert TKS, Loessner U, Jessnitzer B, Stumvoll M, Fasshauer M, et al. Relationship between serum levels of angiopoietin-related growth factor and metabolic risk factors. Horm Metabolic Res = Hormon- und Stoffwechselforschung = Hormones et metabolisme 2014;46(10):685–90.
[7] Korolczuk A, Beltowski J. Progranulin, a new adipokine at the crossroads of metabolic syndrome, diabetes, dyslipidemia and hypertension. Curr Pharmaceut Des 2017;23(10):1533–9. PubMed PMID: 28120721. Epub 2017/01/26. eng.
[8] Nicoletto BB, Canani LH. The role of progranulin in diabetes and kidney disease. Diabetol Metab Syndrome 2015;7:117. PubMed PMID: 26697121. Pubmed Central PMCID: PMC4687133. Epub 2015/12/24. eng.
[9] Wang J, Chen H, Liu Y, Zhou W, Sun R, Xia M. Retinol binding protein 4 induces mitochondrial dysfunction and vascular oxidative damage. Atherosclerosis 2015 Jun;240(2):335–44. PubMed PMID: 25875385. Epub 2015/04/16. eng.
[10] Yang Q, Graham TE, Mody N, Preitner F, Peroni OD, Zabolotny JM, et al. Serum retinol binding protein 4 contributes to insulin resistance in obesity and type 2 diabetes. Nature 2005 Jul 21;436(7049):356–62. PubMed PMID: 16034410. Epub 2005/07/22. eng.
[11] Graham TE, Yang Q, Blüher M, Hammarstedt A, Ciaraldi TP, Henry RR, et al. Retinol-binding protein 4 and insulin resistance in lean, obese, and diabetic subjects. N Engl J Med 2006;354(24):2552–63. PubMed PMID: 16775236.
[12] Sun Q, Kiernan UA, Shi L, Phillips DA, Kahn BB, Hu FB, et al. Plasma retinol-binding protein 4 (RBP4) levels and risk of coronary heart disease: a prospective analysis among women in the nurses' health study. Circulation 2013 May 14;127(19):1938–47. PubMed PMID: 23584360. Pubmed Central PMCID: PMC3741657. Epub 2013/04/16. eng.
[13] Agyemang-Yeboah F. Oxidative stress and adipokines and their health implications. Top Ser in Health Sci 2013:1–8.
[14] Davi G, Guagnano MT, Ciabattoni G, Basili S, Falco A, Marinopiccoli M, et al. Platelet activation in obese women: role of inflammation and oxidant stress. Jama 2002 Oct 23-30;288(16):2008–14. PubMed PMID: 12387653. Epub 2002/10/26. eng.
[15] Tofighi AZM, Najafi ES, Asemi A. The effect of short-term aerobic exercise and vitamin E+C supplementation on CRP, IL-6 and stress oxidative in obese unactive women. Urmia Med J 2011;21(3):228–36 [Persian].
[16] Haghighi AYH, Ildarabadi A. The effect of green tea and aerobic sport on serum adiponectin and gerlin. Med J Mashhad 2015;57:904–12 [In Persian].
[17] D'Alessandro ME, Selenscig D, Illesca P, Chicco A, Lombardo YB. Time course of adipose tissue dysfunction associated with antioxidant defense, inflammatory cytokines and oxidative stress in dyslipemic insulin resistant rats. Food & Funct 2015 Apr;6(4):1299–309. PubMed PMID: 25765549. Epub 2015/03/15. eng.
[18] Fulop P, Seres I, Lorincz H, Harangi M, Somodi S, Paragh G. Association of chemerin with oxidative stress, inflammation and classical adipokines in non-diabetic obese patients. J Cell Mol Med 2014 Jul;18(7):1313–20. PubMed PMID: 24702860. Pubmed Central PMCID: Pmc4124016. Epub 2014/04/08. eng.
[19] Nakagawa K, Ninomiya M, Okubo T, Aoi N, Juneja LR, Kim M, et al. Tea catechin supplementation increases antioxidant capacity and prevents phospholipid hydroperoxidation in plasma of humans. J Agric Food Chem 1999 Oct;47(10):3967–73. PubMed PMID: 10552751. Epub 1999/12/10. eng.
[20] Johnston CS, Beezhold BL, Mostow B, Swan PD. Plasma vitamin C is inversely related to body mass index and waist circumference but not to plasma adiponectin in nonsmoking adults. J Nutr 2007 Jul;137(7):1757–62. PubMed PMID: 17585027. Epub 2007/06/23. eng.
[21] Jamka M, Małgorzata W, Walkowiak Jarosław, Bogdański Paweł, Jeszka Jan, Stelmach-Mardas Marta. The effect of vitamin D supplementation on selected inflammatory biomarkers in obese and overweight subjects: a systematic review with meta-analysis. Eur J Nutr 2016;55(6):2163–76.
[22] Moradi S, Mirzaei K, Abdurahman AA, Keshavarz SA. Adipokines may mediate the relationship between resting metabolic rates and bone mineral densities in obese women. Osteoporosis International: a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA 2017 May;28(5):1619–29. PubMed PMID: 28116469. Epub 2017/01/25. eng.
[23] Willett WCHG, Kushi LH. Adjustment for total energy intake in epidemiologic studies. Am J Clin Nutr 1997;65. 1220S-8S. Discussion 9S-31S.
[24] Cinkajzlova ALZ, Klouckova J, Kavalkova P, Trachta P, Kosak M, et al. Angiopoietin-like protein 6 in patients with obesity, type 2 diabetes mellitus, and anorexia nervosa: the influence of very low-calorie diet, bariatric surgery, and partial realimentation. Endocr Res 2017;42(1):22–30.
[25] Tuuri AL, Jauhiainen MS, Ehnholm CP, Tikkanen MJ, Nicholls MG, Kaaja RJ. Elevated serum angiopoietin-like protein 6 in women with subsequent pregnancy-induced hypertension: a preliminary study. Hypertens Pregnancy 2013 Aug;32(3):203–13. PubMed PMID: 23905605. Epub 2013/08/03. eng.
[26] Namkung J, Koh SB, Kong ID, Choi JW, Yeh BI. Serum levels of angiopoietin-related growth factor are increased in metabolic syndrome. Metab Clin Exp 2011 Apr;60(4):564–8. PubMed PMID: 20673930. Epub 2010/08/03. eng.
[27] Kratzsch J, Deimel A, Galler A, Kapellen T, Klinghammer A, Kiess W. Increased serum soluble leptin receptor levels in children and adolescents with type 1 diabetes mellitus. Eur J Endocrinol 2004 Oct;151(4):475–81. PubMed PMID: 15476448. Epub 2004/10/13. eng.
[28] Majewska KA, Majewski D, Skowronska B, Fichna P. Serum resistin concentrations in children with type 1 diabetes mellitus–negative relation to body fat mass. Endokrynol Pol 2014;65(5):342–7. PubMed PMID: 25301483. Epub 2014/10/11. eng.
[29] Ismail MM, Abdel Hamid TA, Ibrahim AA, Marzouk H. Serum adipokines and vitamin D levels in patients with type 1 diabetes mellitus. Arch Med Sci : AMS 2017 Jun;13(4):738–44. PubMed PMID: 28721140. Pubmed Central PMCID: Pmc5510519. Epub 2017/07/20. eng.
[30] Nunlee-Bland G, Gambhir K, Abrams C, Abdul M, Vahedi M, Odonkor W. Vitamin D deficiency and insulin resistance in obese African-American adolescents. J Pediatr Endocrinol Metab: JPEM (J Pediatr Endocrinol Metab) 2011;24(1–2):29–33. PubMed PMID: 21528812. Pubmed Central PMCID: Pmc5477057. Epub 2011/05/03. eng.
[31] Vaidya A, Forman JP, Underwood PC, Hopkins PN, Williams GH, Pojoga LH, et al. The influence of body mass index and renin-angiotensin-aldosterone system activity on the relationship between 25-hydroxyvitamin D and adiponectin in Caucasian men. Eur J Endocrinol 2011 Jun;164(6):995–1002. PubMed PMID: 21402748. Pubmed Central PMCID: Pmc3104074. Epub 2011/03/16. eng.
[32] Gupta T, Rawat M, Gupta N, Arora S. Study of effect of vitamin D supplementation on the clinical, hormonal and metabolic profile of the PCOS women. J Obstet Gynaecol India 2017 Oct;67(5):349–55. PubMed PMID: 28867886. Pubmed Central PMCID: Pmc5561752. Epub 2017/09/05. eng.
[33] Akbari MMM, Lankarani KB, Tabrizi R, Samimi M, Karamali M, et al. The effects of vitamin D supplementation on glucose metabolism and lipid profiles in patients with gestational diabetes: a systematic review and meta-analysis of randomized controlled trials. Horm Metab Res 2017;49(9):647–53.
[34] Mirzaei K, Hossein-Nezhad A, Chamari M, Shahbazi S. Evidence of a role of ANGPTL6 in resting metabolic rate and its potential application in treatment of obesity. Minerva Endocrinol 2011 Mar;36(1):13–21. PubMed PMID: 21460784. Epub 2011/04/05. eng.
[35] Goodwin KAM, Leonard G, Perron M, Richer L, Veillette S, et al. Dietary vitamin A and visceral adiposity: a modulating role of the retinol-binding protein 4 gene. J Nutrigenetics Nutrigenomics 2015;8:164–73.
[36] Yasmeen R, Jeyakumar SM, Reichert B, Yang F, Ziouzenkova O. The contribution of vitamin A to autocrine regulation of fat depots. Biochim Biophys Acta 2012 Jan;1821(1):190–7. PubMed PMID: 21704731. Pubmed Central PMCID: Pmc3196743. Epub 2011/06/28. eng.
[37] Hermsdorff HH1 ZM, Puchau B, Bressan J, Martínez JA. Association of retinol-binding protein-4 with dietary selenium intake and other lifestyle features in young healthy women. Nutrition 2009;25(4):392–9.
[38] Quadro WSB L, Salchow DJ, Vogel S, Piantedosi R, Gouras P, et al. Impaired retinal function and vitamin A availability in mice lacking retinol-binding protein. EMBO J 1999;18:4633–44.