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Relationship Between C-Reactive Protein, Uric Acid and Fibrinogen Levels and Insulin Resistance in Different Body Mass Indexes: Descriptive Research

Farklı Beden Kitle İndekslerinde C-Reaktif Protein, Ürik Asit ve Fibrinojen Düzeyleri ile İnsülin Direnci Arasındaki İlişki: Tanımlayıcı Araştırma

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ABSTRACT Objective: Chronic inflammation in obesity is the main factor that increases insulin resistance by causing changes in insulin sensitivity. Our study aimed to investigate the relationship between insulin resistance and C-reactive protein (CRP), uric acid, and fibrinogen levels in different body mass indexes (BMI). **Material and Methods:** In our study, patients who applied to our hospital with the complaint of overweight in 2021-2022 were retrospectively analyzed, and 149 women aged 20 and over were included in the study. Glucose, uric acid, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglyceride (TG), CRP, insulin, fibrinogen results, which were measured simultaneously with the height and weight measurements of the patients, were obtained from the laboratory information system. **Results:** The patients included in the study were 25 normal weight, 56 overweight, 53 obese and 15 morbidly obese according to BMI. The uric acid and TG levels of the overweight group were found to be significantly higher than the normal group (respectively; p=0.012, p=0.031), the CRP level of the morbidly obese group was found to be significantly higher than the normal, overweight, and obese groups (respectively; p<0.001, p<0.001, p=0.006). A significant positive correlation was found between Homeostatic Model Assessment for Insulin Resistance and CRP and uric acid (respectively; r=0.219, p=0.009; r=0.353, p<0,001). **Conclusion:** We think that uric acid levels in the early stage of obesity and CRP levels in the advanced stage may be a guide for insulin resistance and obesity-related diseases.

Keywords: Fibrinogen; uric acid; C-reaktive protein; obesity; insulin resistance

ÖZET Amaç: Obezitede görülen kronik inflamasyon, insülin duyarlılığında değişikliğe neden olarak insülin direncini artıran temel faktördür. Çalışmamızda, farklı beden kitle indekslerinde (BKİ) insülin direnci ile C-reaktif protein (CRP), ürik asit ve fibrinojen düzeyleri arasındaki ilişkiyi araştırmayı amaçladık. **Gereç ve Yöntemler:** Çalışmamızda, 2021-2022 yıllarında fazla kilo şikâyeti ile hastanemize başvuran hastalar retrospektif olarak incelendi ve 20 yaş ve üzeri 149 kadın çalışmaya dâhil edildi. Hastaların boy ve kilo ölçümleri ile eş zamanlı olarak ölçülen glukoz, ürik asit, total kolesterol, yüksek dansiteli lipoprotein kolesterol, düşük dansiteli lipoprotein kolesterol, trigliserid (TG), CRP, insülin ve fibrinojen sonuçları laboratuvar bilgi sisteminden alındı. **Bulgular:** Çalışmaya dâhil edilen hastalar BKİ'ye göre 25 normal kilolu, 56 kilolu, 53 obez ve 15 morbid obezdi. Aşırı kilolu grubun ürik asit ve TG düzeyleri normal kilolu gruba göre anlamlı olarak yüksek (sırasıyla; p=0,012, p=0,031), morbid obez grubun CRP düzeyi normal, fazla kilolu ve obez gruplara göre anlamlı yüksek bulundu (sırasıyla p<0,001, p<0,001, p=0,006). İnsülin Direncinin Homeostatik Modeli Değerlendirmesi ile CRP ve ürik asit arasında anlamlı pozitif korelasyon saptandı (sırasıyla; r=0,219, p=0,009; r=0,353, p<0,001). **Sonuç:** Obezitenin erken evresinde ürik asit, ileri evresinde ise CRP düzeylerinin, insülin direnci ve obezite ile ilişkili hastalıklar için yol gösterici olabileceğini düşünüyoruz.

Anahtar Kelimeler: Fibrinojen; ürik asit; C-reaktif protein; obezite; insülin direnci

Obesity is a common public fitness hassle with important clinical (Type 2 diabetes mellitus, cardiovascular and cerebrovascular sicknesses, digestive and respiration issues, cancer), psychosocial and monetary outcomes inside the global.[1] In the European Cardiovascular Disease Statistics study published in 2018, the reported obesity rates for Turkish men and women were 35.8% and 22.9%, respectively.[2]

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Many factors have an important effect on the pathogenesis of obesity. Inflammation, characterized by the infiltration of adipose tissue by macrophages and abnormal cytokine production, is one of the factors leading to insulin resistance, impaired glucose intolerance, and diabetes.[3,4] With the increase in body mass index (BMI), the release of inflammatory mediators increases. Developing chronic inflammation is the main factor that increases insulin resistance by causing changes in insulin sensitivity as a result of pathological changes in β cells and insulin-sensitive tissues.[5]

C-reactive protein (CRP) is a non-particular acute phase reactant produced through the liver beneath the manipulation of cytokines, especially interleukin-6.[6] CRP has been reported to be a diagnostic and prognostic biomarker for acute infections as well as for various chronic diseases. It has been suggested that CRP is an inflammatory marker with an important role in energy balance, body weight, insulin sensitivity, and glucose homeostasis.[7]

Uric acid, the final made from purine metabolism in human beings, acts as an antioxidant and constitutes 55% of the entire antioxidant ability of biological fluids.[8] Although uric acid is an important antioxidant in the plasma, it exerts a potent pro-oxidant activity once inside the cell. The mechanism underlying the dual role of uric acid as an antioxidant and prooxidant is largely unknown.[9] It is accepted that the main cause of insulin resistance is oxidative stress in adipose tissue. Hyperuricemia-induced changes in the oxidative homeostasis of adipose tissue have suggested the potential role of uric acid as a cause of insulin resistance.[10] In epidemiological studies, it has been suggested that there is a positive correlation between insulin resistance, diabetes, metabolic syndrome, and high uric acid levels.[11,12]

Fibrinogen, which has been suggested to be one of the main factors responsible for blood viscosity, is a plasma protein that plays an important role in blood coagulation. Fibrinogen levels, one of the subclinical inflammation biomarkers, are acutely elevated in inflammatory conditions. It has been suggested that insulin resistance and hyperinsulinemia stimulate fibrinogen synthesis, and an increase in fibrinogen levels is observed before the development of diabetes.[13,14]

Although there are various publications in the literature investigating the levels of CRP, uric acid, and fibrinogen in obesity, we could not find a study in which these parameters were evaluated simultaneously in different BMI. Therefore, our study aimed to investigate the effects of CRP, uric acid, and fibrinogen levels on insulin resistance in different BMI.

MATERIAL AND METHODS

The study was initiated with 293 (42 males, 251 females) cases who applied to the general surgery and endocrinology clinics of our hospital with the complaint of being overweight in 2021-2022. 102 cases in women and 33 cases in men were excluded from the study. While 149 female cases aged 20 years and over were included in the study, 9 male cases were excluded due to the small number of cases. All data on women were obtained retrospectively from the Hospital Information Management System. Those using drugs for hypertension, hyperuricemia, and dyslipidemia, those with cardiovascular disease, diabetes mellitus, rheumatoid arthritis, collagen tissue disease, liver and kidney failure, and pregnancy and acute infection diagnosis codes were excluded from the study. Helsinki Declaration principles were considered and applied during our study. The written informed consent form was not obtained from the participants because our study was planned retrospectively. Tepecik Training and Research Hospital Ethics Committee approval were received for our study (date: August 15, 2022, no: 2022/08-04).

BMI= weight(kg)/[height(m)]^2 was calculated with the formula. Individuals, according to BMI; were divided into 4 groups morbidly obese (≥40.00 kg/m^2), obese (BMI 30.00-39.99 kg/m^2), overweight (BMI 25.00-29.99 kg/m^2), and normal weight (BMI 18.50-24.99 kg/m^2).[15]

Glucose, uric acid, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglyceride (TG), CRP, insülin, and fibrinogen results, which were measured simultaneously with the height and weight measurements of the patients, were obtained from the laboratory information system.

In our laboratory, AU 5800 (Beckman Coulter Inc., CA, USA) device is used for the analysis of uric acid, glucose, TG, TC, LDL-C, HDL-C, and CRP tests. DXI-800 (Beckman Coulter, Fullerton CA, USA) immunoassay device is used for the analysis of insulin parameter, and Sysmex CS-2500 (Sysmex

Corporation, Kobe, Japan) analyzer is used for the analysis of fibrinogen levels. Insulin resistance was calculated by the usage of the "Homeostasis Model Assessment of Insulin Resistance (HOMA-IR)" formula (Insulin (U/L)xGlucose (mg/dL)/405).[16]

The acquired data had analyzed using the "SPSS 24.0 (SPSS Inc., Chicago, USA)" software. The compatibility of the variables with normal distribution turned into tested with the Kolmogorov-Smirnov test, and Kruskal-Wallis and Mann-Whitney U statistics were used for intergroup comparisons since they did not fit the normal distribution. The correlation between anthropometric measurements and biochemical parameters was analyzed by Spearman correlation. Data were expressed as median (interquartile range). $p<0.05$ level was considered statistically significant.

RESULTS

According to the participants' BMI; 25 (16.8%) were normal weight, 56 (37.6%) were overweight, 53 (35.5%) were obese and 15 (10.1%) were morbidly obese. A statistically significant difference was found between normal-obese, normal-morbidly obese, overweight-obese, and overweight-morbidly obese groups in insulin (respectively; $p<0.001$, $p=0.001$, $p<0.001$, $p=0.005$), HOMA-IR (respectively; $p<0.001$, $p<0.001$, $p<0.001$, $p=0.004$), TG (respectively; $p=0.002$, $p=0.005$, $p=0.048$, $p=0.029$), HDL-C (respectively; $p=0.001$, $p=0.004$, $p=0.001$, $p=0.017$), CRP (respectively; $p<0.001$, $p<0.001$, $p=0.003$, $p<0.001$), uric acid (respectively; $p<0.001$, $p<0.001$, $p<0.001$, $p<0.001$), and fibrinogen levels (respectively; $p=0.004$, $p=0.002$, $p=0.047$, $p=0.027$). In addition, the uric acid and TG levels of the overweight group were found to be significantly higher than the normal group (respectively; $p=0.012$, $p=0.031$), and the CRP level of the morbidly obese group was significantly higher than the obese group ($p=0.006$). There was no statistically significant difference between the groups in age, glucose, TC, and LDL-C values (Table 1). There was a moderate positive correlation between BMI and insulin, HOMA-IR, CRP, and uric acid (respectively; $r=0.475$, $r=0.484$, $r=0.533$, $r=0.521$) ($p<0.001$), and a weak correlation between BMI and fibrinogen ($r=0.327$) ($p<0.001$) (Table 2).

DISCUSSION

In studies, it has been found that adipose tissue in obese individuals produces increased amounts of inflammatory mediators and that inflammatory cells are more numerous when compared to adipose tissue of non-obese individuals.[17,18] In our study comparing CRP, uric acid and fibrinogen levels between BMI groups, a significant difference was observed in uric acid levels in the normal and overweight groups, and in CRP levels in the obese and morbidly obese groups. In addition, a significant positive correlation

TABLE 1: The comparison of biochemical and anthropometric parameters of groups.

					p-values of statistical tests	
	Normal n=25	**Overweight n=56**	**Obese n= 53**	**Morbidly obese n=15**	**Kruskal-Wallis**	**Mann-Whitney U**
Age (year)	32 (26-37)	32 (26-38)	31.5 (27-40)	35 (30-43)	0.460	NS
BMI (kg/m^2)	23.1 (22.1-24.4)	27.5 (26.2-28.7)	33.8 (31.5-36.9)	43.4 (40.7-49.2)	**<0.001**	**<0.001**^{a,b,c,d,e,f}
Glucose (mg/dL)	88.0 (82.5-96.5)	89.0 (85.3-95.7)	90.0 (85.0-95.5)	92.0 (86.0-98.0)	0.521	NS
Insulin (µIU/mL)	7.1 (4.9-8.8)	7.9 (5.7-10.2)	10.3 (8.6-14.3)	12.8 (6.7-19.3)	**<0.001**	**<0.001**^{b,d}, **0.001**^{c}, **0.005**^{e}
HOMA-IR	1.5 (1.2-1.9)	1.8 (1.3-2.3)	2.3 (1.9-3.3)	3.1 (1.6-4.4)	**<0.001**	**<0.001**^{b,c,d}, **0.004**^{e}
TC (mg/dL)	171 (139-190)	183 (162-203)	181 (162-211)	170 (158-208)	0.314	NS
TG (mg/dL)	67 (61-90)	88 (69-119)	106 (76-156)	131 (76-210)	**0.001**	**0.031**^{a}, **0.002**^{b},**0.005**^{c},**0.048**^{d},**0.029**^{e}
LDL-C (mg/dL)	92 (71-120)	111 (94-126)	112 (93-136)	103 (91-135)	0.078	NS
HDL-C (mg/dL)	59 (50-73)	54 (49-63)	47 (44-54)	48 (41-56)	**<0.001**	**0.001**^{b,d}**0.004**^{c},**0.017**^{e}
CRP (mg/dL)	0.33 (0.33-0.33)	0.33 (0.33-0.33)	0.33 (0.33-0.76)	0.86 (0.34-1.35)	**<0.001**	**<0.001**^{b,c,e},**0.003**^{d},**0.006**^{f}
Uric Acid (mg/dL)	3.5 (2.9-3.9)	3.8 (3.4-4.3)	4.5 (3.8-4.9)	4.9 (4.2-5.5)	**<0.001**	**0.012**^{a},**<0.001**^{b,c,d,e}
Fibrinogen (mg/dL)	301 (273-355)	321 (295-363)	356 (313-394)	384 (327-415)	**0.003**	**0.004**^{b},**0.002**^{c},**0.047**^{d},**0.027**^{e}

a: Normal vs overweight, **b:** Normal vs obese, **c:** Normal vs morbidly obese, **d:** Overweightvs obese, **e:** Overweight vs morbidly obese, **f:** Obese vs morbidly obese; Data were expressed as median (interquartile range); NS: Non-significant ($p>0.05$); BMI: Body mass index; HOMA-IR: Homeostasis Model Assessment of Insulin Resistance; TC: Total cholesterol; TG: Triglyceride; LDL-C: Low-density lipoprotein cholesterol; HDL-C: High-density lipoprotein cholesterol.

TABLE 2: Correlation analysis between parameters.

		Age	BMI	Glukoz	Insulin	HOMA-IR	TC	TG	LDL-C	HDL-C	CRP	Uric acid
BMI	r value	0.125										
	p value	0.130										
Glucose	r value	0.144	0.068									
	p value	0.080	0.413									
Insulin	r value	-0.206*	0.475**	0.067								
	p value	0.012	<0.001	0.415								
HOMA-IR	r value	-0.167*	0.484**	0.254**	0.974**							
	p value	0.042	<0.001	0.002	<0.001							
TC	r value	0.269**	0.052	0.205*	0.010	0.051						
	p value	0.001	0.526	0.012	0.905	0.537						
TG	r value	0.083	0.353**	0.124	0.397**	0.406**	0.404**					
	p value	0.318	<0.001	0.133	<0.001	<0.001	<0.001					
LDL-C	r value	0.223**	0.117	0.202*	0.074	0.107	0.923**	0.463**				
	p value	0.006	0.155	0.014	0.372	0.193	<0.001	<0.001				
HDL-C	r value	0.179*	-0.372**	-0.028	-0.297**	-0.292**	0.228**	-0.456**	-0.036			
	p value	0.029	<0.001	0.733	<0.001	<0.001	0.005	<0.001	0.663			
CRP	r value	-0.096	0.533**	0.049	0.214*	0.219**	-0.048	0.275**	0.012	-0.386**		
	p value	0.255	<0.001	0.561	0.010	0.009	0.571	0.001	0.889	<0.001		
Uric acid	r value	0.011	0.521**	0.127	0.314**	0.353**	0.100	0.319**	0.124	-0.264**	0.268**	
	p value	0.891	<0.001	0.122	<0.001	<0.001	0.226	<0.001	0.132	0.001	0.001	
Fibrinogen	r value	-0.078	0.327**	0.014	0.241**	0.234**	0.201*	0.272**	0.264**	-0.256**	0.498**	0.218**
	p value	0.345	<0.001	0.868	0.003	0.004	0.014	0.001	0.001	0.002	<0.001	<0.001

*Correlation is significant at the 0.005 level; **Correlation is significant at the 0.001 level; BMI: Body mass index; HOMA-IR: Homeostasis Model Assessment of Insulin Resistance; TC: Total cholesterol; TG: Triglyceride; LDL-C: Low-density lipoprotein cholesterol; HDL-C: High-density lipoprotein cholesterol.

was found between HOMA-IR and CRP, uric acid and fibrinogen levels.

In our study, as BMI increased, TG levels increased and HDL-C levels decreased. There was no statistically difference in TG only between the obese and morbidly obese groups, and HDL-C between both normal and overweight and obese and morbidly obese groups, while a significant difference was found between the other groups. There was no significant difference between LDL-C and TC levels and BMI. In the study conducted by Abbasi et al., high TC, TG, and LDL-C levels and low HDL-C levels were found in obesity.[19] In another study conducted by Baskın et al., it was reported that HDL-C levels were lower and TG levels were higher in obese compared to the control group, and no significant difference was observed in terms of TC and LDL-C levels.[20]

In our study, it was determined that there was a significant relationship between obesity and HOMA-IR and insulin, and HOMA-IR and insulin values increased with weight gain. In the study of Hancı et al., it was found that there was a significant difference between the groups made according to BMI in terms of insulin and HOMA-IR and a positive relationship in the whole group.[21] In another study, insulin and HOMA-IR levels were higher in obese patients compared to the control group.[20]

In our study, there was a statistically difference in CRP levels between the groups with the exception of the normal weight and overweight groups. It was found that BMI and CRP levels were significantly related, and there was an increase in CRP levels with weight gain. In the study of Visser et al., it was determined that the CRP values of both overweight and obese individuals were higher than those of normal weight.[22] In the study of Bastard et al., serum CRP levels were found to be higher in both diabetic and non-diabetic obese patients compared to healthy normal-weight individuals.[23] In the study by Missel et al., it was found that high fasting insulin levels were associated with high CRP levels. It has been suggested that therapeutic approaches that reduce insulin levels may provide additional anti-inflammatory effects.[24]

In our study, we observed that as BMI increased, plasma uric acid levels increased and were statistically significantly associated with BMI. Similarly, in the study of Çarlıoğlu et al., uric acid levels were found to be significantly higher in obese compared to control and overweight groups.[25] In a study including 130 male patients, the uric acid levels of the group with BMI≥25 kg/m^2 were found to be significantly higher than those with BMI<25 kg/m^2.[26] In the study of Lippi et al. in which they compared the hyperuricemic and normouricemic groups, they stated that HDL-C, TG, and TC/HDL-C levels were significantly higher in hyperuricemics.[27] In a study of 6,027 individuals, uric acid levels were positively correlated with fasting glucose, fasting insulin, and HOMA-IR. It has been reported that uric acid levels are independently associated with insulin resistance and individuals with hyperuricemia are at high risk for diabetes.[28] Studies have suggested that high uric acid levels are an independent risk factor for obesity, and increased uric acid may be an additional component of metabolic syndrome.[29,30]

In our study, it was observed that fibrinogen values increased with the increase in BMI and there was a relationship between obesity and fibrinogen. Koçak et al. found that the plasma fibrinogen level in obese individuals was higher than in the control group.[31] In the study of Keskin et al., similar to our results, plasma fibrinogen levels of obese subjects were found to be statistically higher than non-obese subjects.[32] In the study of Gómez-Ambrosi et al., higher fibrinogen concentrations were found in obese patients compared to non-obese subjects, and a strong correlation was observed between HOMA values and fibrinogen.[33]

The limitations of our study are that it was single-centre, normal CRP levels were evaluated instead of high-sensitivity CRP, only women were included in the study, and it was insufficient to reflect the characteristics of the general population.

CONCLUSION

CRP, uric acid, and fibrinogen parameters are associated with BMI and HOMA-IR and play a role in the development of obesity-related diseases. We think that uric acid levels in the early stage of obesity and CRP levels in the advanced stage may be a guide for insulin resistance and obesity-related diseases. For this reason, close weight monitoring, follow-up, and treatment in terms of hyperinsulinemia and insulin

resistance may be beneficial in individuals with high uric acid levels. We think that clinical studies evaluating the effects of agents used to improve glycemic control on uric acid, CRP, and fibrinogen, which appear to be related to HOMA-IR, are necessary.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Murat Akşit;* ***Design:*** *Murat Akşit;* ***Control/Supervision:*** *Murat Akşit;* ***Data Collection and/or Processing:*** *Murat Akşit;* ***Analysis and/or Interpretation:*** *Murat Akşit, Merve Zeytinli Akşit;* ***Literature Review:*** *Murat Akşit, Merve Zeytinli Akşit;* ***Writing the Article:*** *Murat Akşit, Merve Zeytinli Akşit;* ***Critical Review:*** *Murat Akşit.*

REFERENCES

1. Raza Q, Doak CM, Khan A, Nicolaou M, Seidell JC. Obesity and cardiovascular disease risk factors among the indigenous and immigrant Pakistani population: a systematic review. Obes Facts. 2013;6(6):523-35. [Crossref] [PubMed] [PMC]
2. Timmis A, Townsend N, Gale C, Grobbee R, Maniadakis N, Flather M, et al; ESC Scientific Document Group. European Society of Cardiology: Cardiovascular Disease Statistics 2017. Eur Heart J. 2018;39(7):508-79. [PubMed]
3. Nomiyama T, Perez-Tilve D, Ogawa D, Gizard F, Zhao Y, Heywood EB, et al. Osteopontin mediates obesity-induced adipose tissue macrophage infiltration and insulin resistance in mice. J Clin Invest. 2007;117(10):2877-88. [Crossref] [PubMed] [PMC]
4. Patel PS, Buras ED, Balasubramanyam A. The role of the immune system in obesity and insulin resistance. J Obes. 2013;2013:616193. [Crossref] [PubMed] [PMC]
5. Kim J, Lee J. Role of obesity-induced inflammation in the development of insulin resistance and type 2 diabetes: history of the research and remaining questions. Ann Pediatr Endocrinol Metab. 2021;26(1):1-13. [Crossref] [PubMed] [PMC]
6. Hortin GL. Amino acids, peptides, and proteins. In: Burtis CA, Ashwood ER, Bruns DE, eds. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics. 5th ed. St. Louis, USA: Elsevier Saunders; 2012. p.509-62. [Crossref]
7. Stanimirovic J, Radovanovic J, Banjac K, Obradovic M, Essack M, Zafirovic S, et al. role of C-reactive protein in diabetic inflammation. Mediators Inflamm. 2022;2022:3706508. [Crossref] [PubMed] [PMC]
8. Gherghina ME, Peride I, Tiglis M, Neagu TP, Niculae A, Checherita IA. Uric acid and oxidative stress-relationship with cardiovascular, metabolic, and renal impairment. Int J Mol Sci. 2022;23(6):3188. [Crossref] [PubMed] [PMC]
9. Varesi A, Chirumbolo S, Campagnoli LIM, Pierella E, Piccini GB, Carrara A, et al. The role of antioxidants in the interplay between oxidative stress and senescence. Antioxidants (Basel). 2022;11(7):1224. [Crossref] [PubMed] [PMC]
10. Kang DH, Ha SK. Uric acid puzzle: dual role as anti-oxidantand pro-oxidant. Electrolyte Blood Press. 2014;12(1):1-6. [Crossref] [PubMed] [PMC]
11. Kim HK, Lee M, Lee YH, Lee BW, Cha BS, Kang ES. Uric acid variability as a predictive marker of newly developed cardiovascular events in type 2 diabetes. Front Cardiovasc Med. 2021;8:775753. [Crossref] [PubMed] [PMC]
12. Ciarla S, Struglia M, Giorgini P, Striuli R, Necozione S, Properzi G, et al. Serum uric acid levels and metabolic syndrome. Arch Physiol Biochem. 2014;120(3):119-22. [Crossref] [PubMed]
13. Liu SL, Wu NQ, Shi HW, Dong Q, Dong QT, Gao Y, et al. Fibrinogen is associated with glucose metabolism and cardiovascular outcomes in patients with coronary artery disease. Cardiovasc Diabetol. 2020;19(1):36. [Crossref] [PubMed] [PMC]
14. Mahjabeen S, Selim S, Mustari M, Rajib MH, Rahman AK, Fariduddin M, et al. Association of plasma fibrinogen and insulin resistance in women with gestational diabetes mellitus. Archives of Clinical and Biomedical Research. 2022;6(3):492-502. [Crossref]
15. Türkiye Endokrinoloji ve Metabolizma Derneği. Obezite Tanı ve Tedavi Kılavuzu. 3. Baskı. Ankara: Miki Matbaacılık San ve Tic Ltd Şti; 2016. p.12-24.
16. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia. 1985;28(7):412-9. [Crossref] [PubMed]
17. Rocha VZ, Libby P. Obesity, inflammation, and atherosclerosis. Nat Rev Cardiol. 2009;6(6):399-409. [Crossref] [PubMed]
18. Gregor MF, Hotamisligil GS. Inflammatory mechanisms in obesity. Annu Rev Immunol. 2011;29:415-45. [Crossref] [PubMed]
19. Abbasi F, Brown BW Jr, Lamendola C, McLaughlin T, Reaven GM. Relationship between obesity, insulin resistance, and coronary heart disease risk. J Am Coll Cardiol. 2002;40(5):937-43. [Crossref] [PubMed]
20. Baskın Y, Yiğitbaşı T, Afacan G, Bağbozan Ş. İnsülin direnci olan erişkin kilolu ve obezlerde lipoprotein (a) ile lipid parametreleri [Lipoprotein (a) and lipid parameters in overweight and obese adults with insulin resistance]. Türk Klinik Biyokimya Derg. 2008;6(2):65-71. [Link]
21. Hancı T, Türkön H, Çolak Aydoğdu A, Yıldız Ö, Karademirci İ, Çoker I. Yüksek duyarlıklı C-reaktif protein (HSCRP) ve obezite ilişkisi [Association of high sensitivity C-reactive protein (HSCRP) and obesity]. Türk Klinik Biyokimya Derg. 2012;10(1):1-7. [Link]
22. Visser M, Bouter LM, McQuillan GM, Wener MH, Harris TB. Elevated C-reactive protein levels in overweight and obese adults. JAMA. 1999;282(22):2131-5. [Crossref] [PubMed]
23. Bastard JP, Jardel C, Bruckert E, Blondy P, Capeau J, Laville M, et al. Elevated levels of interleukin 6 are reduced in serum and subcutaneous adipose tissue of obese women after weight loss. J Clin Endocrinol Metab. 2000;85(9):3338-42. [Crossref] [PubMed]
24. Missel AL, Saslow LR, Griauzde DH, Marvicsin D, Sen A, Richardson CR, et al. Association between fasting insulin and C-reactive protein among adults without diabetes using a two-part model: NHANES 2005-2010. Diabetol Metab Syndr. 2021;13(1):29. [Crossref] [PubMed] [PMC]
25. Çarlıoğlu A, Karakurt F, Maral S, Kasapoğlu B, Darcın T. Serum uric acid levels in obese women. The New Journal of Medicine. 2011;28:34-7. [Link]
26. de Carvalho Vidigal F, de Lima Rosado LE, Paixão Rosado G, Lanes Ribeiro Rde C, Castro Franceschini Sdo C. Serum uric acid can predict higher C-reactive protein levels in apparently healthy men. Nutr Hosp. 2014;29(4):935-40. [PubMed]
27. Lippi G, Montagnana M, Luca Salvagno G, Targher G, Cesare Guidi G. Epidemiological association between uric acid concentration in plasma, lipoprotein(a), and the traditional lipid profile. Clin Cardiol. 2010;33(2):E76-80. [Crossref] [PubMed] [PMC]
28. Yu P, Huang L, Wang Z, Meng X, Yu X. The association of serum uric acid with beta-cell function and insulin resistance in nondiabetic individuals: a cross-sectional study. Diabetes Metab Syndr Obes. 2021;14:2673-82. [Crossref] [PubMed] [PMC]
29. Li F, Chen S, Qiu X, Wu J, Tan M, Wang M. Serum uric acid levels and metabolic ındices in an obese population: a cross-sectional study. Diabetes Metab Syndr Obes. 2021;14:627-35. [Crossref] [PubMed] [PMC]
30. Adnan E, Rahman IA, Faridin HP. Relationship between insulin resistance, metabolic syndrome components and serum uric acid. Diabetes Metab Syndr. 2019;13(3):2158-62. [Crossref] [PubMed]
31. Koçak A, Kutlu R, Çivi S, Kılınç İ. Obezitede insülin direnci ile leptin, interlökin-6, hs-CRP ve fibrinojen ilişkisi [Relationship between insulin resistance and leptin, interleukin-6, hs-CRP and fibrinogen in obesity]. Turk J Biochem. 2014;39(3):373-82. [Link]
32. Keskin S, Sayalı E, Temeloglu E, Ekizoglu E. Obezite ve inflamasyon [Obesity and inflammation]. Turkiye Klinikleri J Med Sci. 2005;25(2):636-41.
33. Gómez-Ambrosi J, Salvador J, Silva C, Pastor C, Rotellar F, Gil MJ, et al. Increased cardiovascular risk markers in obesity are associated with body adiposity: role of leptin. Thromb Haemost. 2006;95(6):991-6. [Crossref] [PubMed]