Cardiology in the Young

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Investigation of cardiovascular risk parameters in adolescents with metabolic syndrome

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Original Article

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Abstract

Background: Metabolic syndrome leading to type 2 diabetes mellitus and cardiovascular diseases is a chronic multifactorial syndrome, associated with low-grade inflammation status. In our study, we aimed at assessing the serum levels of follistatin (FST), pregnancy-associated plasma protein-A (PAPP-A), and platelet/endothelial cell adhesion molecule-1 (PECAM-1) in adolescent patients with metabolic syndrome. *Methods:* This study was performed in 43 (19 males, 24 females) metabolic syndrome adolescents and 37 lean controls matched for age and sex. The serum levels of FST, PECAM-1, and PAPP-A were measured by using ELISA method. *Results:* Serum FST and PAPP-A levels in metabolic syndrome were significantly higher than those of controls ($p < 0.005$ and $p < 0.05$). However, there was no difference in serum PECAM-1 levels between metabolic syndrome and control groups ($p = 0.927$). There was a significant positive correlation between serum FST and triglyceride ($r = 0.252$; $p < 0.05$), and PAPP-A and weight, ($r = 0.252$; $p < 0.05$) in metabolic syndrome groups. Follistatin was determined statistically significant in both univariate ($p = 0{,}008$) and multivariate ($p = 0{,}011$) logistic regression analysis. *Conclusions:* Our findings indicated a significant relationship between FST and PAPP-A levels and metabolic syndrome. These findings offer the possibility of using these markers in diagnosis of metabolic syndrome in adolescents as the prevention of the future complications.

Metabolic syndrome has become an important health problem in adolescents all over the world in recent years. Metabolic syndrome comprises glucose intolerance, insulin resistance, central obesity, vascular inflammation, prothrombotic state, dyslipidaemia, and hypertension and causes cardiovascular disease and diabetes.[1]

The basic approach is to lose weight and increase physical activity in metabolic syndrome. However, drug therapy may also be convenient to reduce the risk of complications. Diagnosis of metabolic syndrome and clarification of its pathology can reduce the risk of diabetes and cardiovascular disease through appropriate treatment.

A member of the TGF-beta superfamily, follistatin (FST), which is a glycosylated plasma protein, is produced in liver, ovary, pituitary, skeletal muscle, and white and brown adipose tissues. [2] FST inactivates activin associated with insulin production and insulin sensitivity.[3] Additionally, FST antagonising myostatin (Mst)/Smad3 signalling promotes browning of white adipocytes, increases mitochondrial biogenesis, and protects mice from diet-induced obesity with increasing insulin sensitivity and energy expenditure.[4] It is known that FST may induce classical brown adipose tissue mass by targeting Myf5 and promote browning in white adipose tissue by its target pp38 MAPK/pERK1/2/Cox-2 pathways.[4] Also, FST increases irisin secretion from subcutaneous fat via the AMPKPGC1 α-irisin signalling pathway to cause browning of white adipose tissue and regulates metabolism by activating the insulin pathway in beige fat.[5]

Pregnancy-associated plasma protein-A (PAPP-A) secreted from adipose tissue has been shown to cleavage of insulin-like growth factor (IGF)-binding protein-4 (IGFBP-4) and increase local IGF secretion which controls growth, visceral fat deposition, and longevity. It has been demonstrated that PAPP-A is highly secreted in preadipocytes of visceral origin than subcutaneous preadipocytes.[6] Further, PAPP-A has been found to be highly expressed in atherosclerotic plaques and in charge of the instability and rupture of atherosclerotic plaques.[7] It was indicated that PAPP-A, a high-molecular-weight and zinc-binding metallo proteinase, is an important regulatory protein in cell proliferation and development of atherosclerosis. PAPP-A secreted by vascular cells is thought to play an important role in cardiovascular disease.[8]

Platelet/endothelial cell adhesion molecule-1 (PECAM-1, CD31), a member of the immunoglobulin gene superfamily and a 130-kDa integral membrane glycoprotein, is expressed on the surface of circulating leucocytes and platelets and endothelial cell-to-cell junctions. PECAM-1 concerning the formation of the vascular bed upregulates integrin function on leucocytes.[9] In response to inflammatory mediators, PECAM-1 induces the extravasation of leucocytes from the vessel wall.[10] Endothelial activation in the development and progression of

inflammation includes upregulation of endothelial cellular adhesion molecules like E-selectin, ICAM-1, VCAM-1, and PECAM-1 via proinflammatory cytokines such as interleukin-1 (IL-1) and tumour necrosis factor-alpha.[11]

Prevention, diagnosis, and treatment of metabolic syndrome and clarification of its pathology can diminish the risk of diabetes and cardiovascular disease.

Thus, the aim of this study was to evaluate the serum levels of FST, PECAM-1, and PAPP-A in metabolic syndrome of adolescents compared to control groups. However, little is known about their dysregulation during the course of metabolic syndrome patients in the literature. Another aim was to reveal the relationships among FST, PECAM-1, and PAPP-A levels, body mass index, and the homeostasis model assessment of insulin resistance (HOMA-IR) in adolescent metabolic syndrome.

Materials and methods

Participants

This study was performed in randomly selected 43 metabolic syndrome adolescents from the outpatient clinic of Pediatric Endocrinology Department in Konya City Hospital and in 37 control patients matched by age and gender. Controls are composed of adolescents with body mass index between 25th and 74th percentiles according to body mass index reference curves for Turkish adolescents.[12,13] The height and weight scores of controls were between 3rd and 97th percentiles.[12,13] The controls were selected from the adolescents of hospital staff.

Metabolic syndrome in children was defined by using the International Diabetes Federation criteria (waist circumference > 90th percentile with any two of the parameters triglyceride ≥ 150 mg/dL, high-density lipoprotein cholesterol < 40 mg/dL, fasting plasma glucose > 100 mg/dL, and blood pressure > 130/85 mmHg).[14] Pubertal stage was determined in both metabolic syndrome and control groups according to the Tanner criteria and validated by plasma sex hormone concentrations.[14,15]

The exclusion criteria were the presence of any genetic or endocrine disorder, systemic or chronic disease, and smoking. Any patient receiving pharmacological treatment such as supplement vitamin and antihypertensive drugs was also excluded. The study was approved by the Local Ethics Committee of Meram Faculty of Medicine at Necmettin Erbakan University. All parents were informed about the study design, and written consents were obtained.

Anthropometric measurements

The weight of the each patient was measured by a weight scale sensitive to ± 0.1 kg while the patient was wearing light clothes and standing in bare feet. The height of each patient was recorded in the Frankfort plane position. Body mass index was measured in all patients and calculated as weight (in kilograms) divided by height (in metres) squared. Adolescents with waist circumference > 90th percentile for age and sex were evaluated as obese according to normal values for waist circumference of Turkish adolescents.[16] Systolic blood pressure and diastolic blood pressure were measured after 20 min rest in the supine position. The average of two measurements taken in the right arm was recorded. Patients with age- and sex-adjusted systolic and/or diastolic blood pressures > 95th percentile were considered hypertensive.[17]

Analytical methods

HOMA-IR was calculated by using the following formula: [fasting plasma insulin (μU/mL) × fasting plasma glucose (mmol/L)] /22.5. HOMA-IR scores of higher than 3.16 shows IR.[18]

Blood samples were obtained after an overnight (12 hours) fasting between 8 and 9 a.m. into empty vacuum tubes. Serum samples were obtained after centrifugation and stored frozen at -80 °C until the day of analysis. Serum biochemical analyte levels were immediately measured. Detailed characteristics of the study population are presented in Table 1.

Analyses of other analytes

Serum biochemical analyte levels were measured by commercially available kits based on routine methods on the Architect C 8000 System (Abbott Laboratories, Abbott Park, Illinois, USA). Serum insulin was determined by routine chemiluminescence method on E170 analyzer (Roche Diagnostics, Mannheim Germany).

The analyses of serum FST, PECAM-1, and PAPP-A levels were performed using an enzyme immunoassay method using commercial kits (BT Lab Bioassay Technology Laboratory Human Elisa Kits, Shanghai Korain Biotech, China) in accordance with the manufacturer's guidelines. Absorbance was measured at 450 nm on an ELx800 Absorbance Microplate Reader (Biotek, Winooski, VT, USA). Concentration values were reported in ng/mL for FST, PECAM-1and PAPP-A.

Statistical analysis

Statistical analyses were done using SPSS v. 22.0 (SPSS Inc., IL, USA). To compare the ratio of categorical variables, we used the chi-squared test [gender (male/female)]. The normality of the variables was evaluated using the one-sample Kolmogorov–Smirnov test.

Differences in the means of variables were tested using both parametric and non-parametric tests depending on the distribution of the variables. For the independent samples, the Student's t-test and Mann–Whitney U-tests were used for comparing mean and median values, respectively. The correlations between variables were performed by Spearman's correlation test. Binary logistic regression analysis was used to examine the risk factors affecting metabolic syndrome (MS). While age, gender, follist, and PAPP-A were modelled individually in the univariate analysis, these four variables were included in the model together in the multivariate analysis and risk factors were examined. Differences were considered significant at a probability level of $p < 0.05$.

Results

This study was performed on 43 (19 males, 24 females) metabolic syndrome adolescents between the ages of 11 and 19 years (14.6) and 37 (14 males, 23 females) controls between the ages of 10 and 18 years (14.7). Anthropometric and analytical characteristics of the metabolic syndrome individuals and controls are shown in Table 1. Body mass index, HOMA-IR, triglyceride, systolic blood pressure, diastolic blood pressure, and fasting insulin values were higher, compared with those of controls ($p < 0.001$), while weight ($p < 0.005$) were significantly higher than those of the group. High-density lipoprotein-cholesterol levels of the metabolic syndrome were lower than those of controls ($p < 0.001$). No difference was found in terms of height and fasting glucose between the metabolic syndrome and control groups (Table 1).

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Table 1. Clinical and demographic characteristics of control and metabolic syndrome adolescents.

	MetS patients n = 43	Controls n = 37	p-Value
Age (years)	14.6 (11–19)	14.7 (10–18)	0.785
Female/male	24/19	23/14	0.565
Weight, kg	88 (54–139)	46 (31–61)	< 0.005
Height, cm	163.0 ± 10.0	158.7 ± 10.9	0.07
Waist circumferance, cm	100.12 ± 10.15	8O.15 ± 6.13	< 0.001
Systolic BP, mmHg	127.1 (100–170)	101.1 (80–120)	< 0.001
Diastolic BP, mmHg	76.5 (58–110)	61.4 (50–70)	< 0.001
Fasting insulin, µIU/mL	28.8 (7.3–92.2)	8.4 (2.4–17.8)	< 0.001
Fasting glucose, mg/dL	91.8 (76–400)	89.6 (78–110)	0.437
Triglycerides, mg/dL	183 (55–474)	68.7 (33–204)	< 0.001
HDL-C, mg/dL	36.1 (25–51)	50 (38–75)	< 0.001
BMI, kg/m2	33.9 (27–44)	18.4 (15–22)	< 0.001
HOMA-IR	7.3 (2–33)	2 (1–5)	< 0.001
FST, ng/ml	4.3 (2–13)	3.7 (1–7)	< 0.005
PAPP-A, ng/ml	2.0 (1.2–12.8)	1.8 (1–5)	< 0.05
PECAM-1, ng/ml	1.0 (0.5–6.6)	1.1 (0.2–3.2)	0.927

BMI = body mass index; BP = blood pressure; HDL-C = high-density lipoprotein-cholesterol; HOMA-IR = homeostasis model assessment of insulin resistance; FST = follistatin; Mets = metabolic syndrome; PAPP-A = pregnancy-associated plasma protein-A; PECAM-1 = platelet/endothelial cell adhesion molecule-1.

FST ($p < 0.005$) and PAPP-A ($p < 0.05$) values of the metabolic syndrome individuals were significantly higher than those of the controls. No difference was found in terms of PECAM-1 values between the metabolic syndrome and control groups (Table 1).

Spearman's Rho correlation analysis was performed to investigate the association between measures of serum FST, PAPP-A, and PECAM-1 values, and body mass index, HOMA-IR, triglyceride, fasting glucose and insulin, high-density lipoprotein-cholesterol, weight, and systolic blood pressure and diastolic blood pressure in metabolic syndrome groups (Table 2). In metabolic syndrome group, the levels of FST were positively correlated with triglyceride ($p < 0.05$; $r = 0.252$) and the levels of PAPP-A were positively correlated with weight ($p < 0.05$; $r = 0.228$).

According to logistic regression analysis, in the univariate analysis, age ($p = 0.822$) gender ($p = 0.566$) follistatin ($p = 0.008$), and PAPP-A ($p = 0.077$) were modelled individually; in the multivariate analysis, using the enter method, age ($p = 0.809$), gender ($p = 0.695$), follistatin ($p = 0.011$), and PAPP-A ($p = 0.064$) were added to the model and corrected OR values were obtained. Follistatin was determined to be statistically significant in both univariate and multivariate analysis. In the multivariate analysis, the accuracy rate was 53.8%. (Table 3).

Discussion

In this study, higher FST and PAPP-A levels were observed in the group of metabolic syndrome adolescents than in the control patients. On the other hand, PECAM-1 levels did not show any significant difference between two groups. There was a significant positive correlation between serum FST and triglyceride, and PAPP-A and weight in metabolic syndrome group. In our knowledge, this is the first study to investigate the relation between circulating FST, PECAM-1, and PAPP-A levels of the metabolic syndrome in adolescents.

Metabolic syndrome is associated with diverse cardiovascular risk factors like IR, obesity, atherogenic dyslipidemia, prothrombotic state, and hypertension. Several biomarkers, such as FST, PECAM-1, and PAPP-A may be linked to increased cardiovascular diseases.[19]

FSTs are involved in reproductive function, muscle and liver metabolism, as well as glucose and lipid homeostasis.[20] In morbid obesity, IR, glycaemia and circulating FST are all reduced (by 22–33%) after Roux-en-Y gastric bypass and/or vertical sleeve gastrectomy. Circulating FST concentrations were positively correlated with body mass index, insulin, HOMA-IR, HbA1c, and epicardial fat thickness.[20] In a mouse model of diet-induced obesity and type 2 diabetes mellitus, it was shown that intravascular FST gene delivery can reduce serum activin concentrations and ameliorate metabolic dysfunction, glycaemia, insulin increase, and the diabetic progression.[21] Exercise plays an important role in the prevention of metabolic syndrome. Studies examining the effect of exercise on FST, Silva et al[3] noted that FST liver mRNA expression was significantly lower in control (C) rats-swimming exercise (Swim) and high-fat diet (HFD) fed rats-(Swim) than in either C-sedentary group (Sed) or HFD-Sed animals. In humans, blood FST level is positively correlated with serum cholesterol and low-density lipoprotein-cholesterol (LDL-C), body mass index, and body fat percentage in physically active patients[22] In epi adipose tissues from FST-transgenic (Tg) mice, Singh et al[23] found significant decrease in several lipid metabolites, including triglyceride, free fatty acid, phosphotidylcholine, and phosphotidylethanolamine and several amino acids including branched chain amino acid, lactate levels, and betahydroxybutyric acid, associated with metabolic syndrome. In line with these results, they suggested that FST may favourably regulate overall carbohydrate metabolism and protect against these diseases. In the HFD group, overexpression of FST significantly diminished serum levels of several adipokines, including leptin, resistin, IL-1β, and C-peptide as well as serum insulin, glucose, triglyceride, cholesterol, and free fatty acids. FST gene delivery also significantly increased blood levels of vascular endothelial growth factor.[24] It was identified that knockdown of FST in HFD obese mice ameliorated glucose tolerance by elevating white adipose tissue insulin sensitivity and diminishing hepatic glucose output.[25] Targets of MyomiRs (miR-1, miR-133a, and miR-206) concerning in IGF-1 pathway related to insulin response such as Irs-1 and FST, decreased after 12 weeks in HFD compared to the control or HFD for 4 or 8 weeks.[26]

The levels of FST, detected in our metabolic syndrome adolescents, were consistent with the findings reported in studies by other investigators.

Previous studies showed that PAPP-A regulates circulating and potentially local IGF-1 concentrations, leading to proliferation of vascular smooth muscle cells and modulation of local inflammatory processes, thereby putatively acting pro-atherogenic.[27] In adult patients with type 2 diabetes mellitus, it was shown a significant correlation between serum PAPP-A concentrations and intima-media thickness of the carotid artery; this was suggested as a non-invasive indicator of early atherosclerosis. Also serum cholesterol was found as an independent predictor of serum PAPP-A concentrations.[28] In obese patients, PAPP-A (4.4-fold) and PAPP-A-generated IGFBP-4 fragments (1.5-fold), IGF-II (1.4-fold) concentrations increased more in VAT media than SAT at

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Table 2. Spearman's correlation analyses were performed to investigate the association of biomarkers levels in the MetS adolescents.

		FST	PAPP-A	PECAM-1	Insulin	Systolic BP	Diastolic BP	Glucose	Triglycerides	HDL-C	BMI	HOMA-IR
Weight	r	0.191	0.228*	−0.049	0.679**	0.791**	0.698**	0.067	0.597**	−0.759**	0.833**	0.630**
	p	0.089	< **0.05**	0.663	0.000	**0.000**	0.000	0.553	0.000	0.000	0.000	0.000
Insulin	r	0.105	0.101	−0.041	1.000	0.640**	0.508**	0.009	0.591**	−0.615**	0.623**	0.716**
	p	0.352	0.373	0.721		**0.000**	0.000	0.937	0.000	0.000	0.000	0.000
Systolic BP	r	0.056	0.164	−0.004	0.640**	1.000	0.812**	0.058	0.574**	−0.695**	0.688**	0.640**
	p	0.624	0.147	0.973	0.000		0.000	0.609	0.000	0.000	0.000	0.000
Diastolic BP	r	0.165	0.192	0.104	0.508**	0.812**	1.000	0.046	0.554**	−0.664**	0.596**	0.523**
	p	0.144	0.087	0.359	0.000	**0.000**		0.687	0.000	0.000	0.000	0.000
Glucose	r	−0.050	0.041	0.001	0.009	0.058	0.046	1.000	0.123	-0.061	0.091	0.227*
	p	0.657	0.720	0.993	0.937	0.609	0.687		0.277	0.592	0.423	0.043
Triglycerides	r	0.252*	0.190	0.178	0.591**	0.574**	0.554**	0.123	1.000	−0.679**	0.602**	0.581**
	p	< **0.05**	0.091	0.114	0.000	0.000	0.000	0.277		0.000	0.000	0.000
HDL-C	r	−0.214	−0.150	0.015	−0.615**	−0.695**	−0.664**	−0.061	−0.679**	1.000	−0.702**	−0.680**
	p	0.057	0.185	0.897	0.000	0.000	0.000	0.592	0.000		0.000	0.000
BMI	r	0.195	0.211	−0.036	0.623**	0.688**	0.596**	0.091	0.602**	−0.702**	1.000	0.638**
	p	0.083	0.060	0.752	0.000	0.000	0.000	0.423	0.000	0.000		0.000
HOMA-IR	r	0.052	0.026	−0.125	0.716**	0.640**	0.523**	0.227*	0.581**	−0.680**	0.638**	1.000
	p	0.649	0.819	0.269	0.000	0.000	0.000	0.043	0.000	0.000	0.000	

BMI = body mass index; BP = blood pressure; HDL-C = high-density lipoprotein-cholesterol; HOMA-IR = homeostasis model assessment of insulin resistance; FST = follistatin; Mets = metabolic syndrome; PAPP-A = pregnancy-associated plasma protein-A; PECAM-1 = platelet/endothelial cell adhesion molecule-1.
*p<0.05; **p=0.000.

Table 3. Logistic regression analysis for metabolic syndrome.

	Group		Univariate		Multivariate (enter)*	
	Controls	MetS patients	OR (%95 CI)	p	OR (%95 CI)	p
Age. mean (SD)	14.7 (2.1)	14.6 (1.9)	0.98 (0.784–1.213)	0.822	0.97 (0.76–1.239)	0.809
Gender. n (%)						
Female	23 (62.2)	24 (55.8)	Reference			
Male	14 (37.8)	19 (44.2)	1.301 (0.531–3.188)	0.566	1.219 (0.454–3.271)	0.695
Follistatin. mean (SD)	3.2 (1.5)	4.5 (2.3)	1.5 (1.110–2.026)	**0.008**	1.503 (1.1–2.054)	**0.011**
PAPP-A. mean (SD)	2.0 (1.0)	3.0 (2.8)	1.381 (0.966–1.975)	0.077	1.413 (0.980–2.038)	0.064

Mets = metabolic syndrome; SD = standard deviation.
*Accuracy= %53,8; R^2=%22,4.

baseline The most notable differences included IGFBP-4 and PAPP-A, which at baseline were 2.0-fold and 1.8-fold higher, respectively, in SAT media from obese than those from lean women.[29] In another study, PAPPA levels decreased in obese patients participating in an intervention programme based on physical exercise, nutrition education, and behaviour therapy.[27] PAPP-A was related to higher rates of cardiovascular death or myocardial infarction at 30 days and at 1 year, and it was independently associated with recurrent cardiovascular events in patients with non–ST-segment elevation acute coronary syndrome (NSTE-ACS). PAPP-A was offered as a prognostic marker in patients with acute coronary syndrome and may be therapeutic target.[30] In acute coronary syndrome, high blood PAPP-A level is present in vulnerable coronary plaque but not in stable plaques.[31] PAPP-A increased in acute coronary syndrome patients with type 2 diabetes mellitus and higher levels of its were significantly related to increased risk of cardiovascular disease events during 2-year follow-up in type 2 diabetes mellitus.[8] High PAPP-A acute myocardial infarction (AMI) expression was significantly found in omental preadipocytes compared to mesenteric and subcutaneous preadipocytes. PAPP-A expression elevated significantly in the treatment of cultured primary human preadipocytes with tumour necrosis factor-alpha and IL 1-β, associated with intracellular pathways, including the nuclear factor (NF) κB pathway and the mitogen-activated protein kinase (MAPK) family, particularly c-Jun NH2-terminal kinase (JNK) and p38 mitogen-activated kinase. Resveratrol, a polyphenol with beneficial cardiometabolic effects, significantly suppressed IL1-β and tumour necrosis factor-alpha

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stimulated by PAPP-A mRNA expression.[32] A recent study by Hill et al[33] showed that PAPP-A KO mice fed high-fat, high sucrose diet were more glucose tolerant and had increased insulin sensitivity and anti-inflammatory cytokine levels (IL-4 and adiponectin) and lower levels of pro-inflammatory cytokines (IL-2, IL-6, and tumour necrosis factor-alpha). PAPP-A KO mice are resistant to the high-fat, high sucrose diet induction of metabolic dysfunction, associated with higher levels of anti-inflammatory cytokines. Some harmful effects of high-fat, high sucrose diet in normal animals may be due to increased levels of PAPP-A.

In the our study, PAPP-A levels elevated in metabolic syndrome adolescents, which is in agreement with previous works.

Platelet-bound PECAM-1 expression increased in acute myocardial infarction patients, while soluble PECAM-1 plasma levels were unchanged. Three hours after thrombolysis, a platelet PECAM-1 significantly decreased and a soluble PECAM-1 expression significantly increased.[9] PECAM-1 has been related to platelet aggregation and is an important modulator of platelet function in mice.[34] It was divulged that the natural stilbenoid, resveratrol and resveratrol-linoleic acid decreased the in vitro endothelial permeability and precluded the dissociation of the intercellular adherent junctions including PECAM-1 by inhibiting matrix metalloproteinases (MMP-9) activity.[35] As described previously, Ilan et al[36] PECAM-1 cleaving during endothelial cell apoptosis ultimately results in the generation of two fragments: a secreted ectodomain (100 kDa) and a truncated molecule comprised of the transmembrane and the cytoplasmic domains. Beta-catenin and SHP-2 proteins recruited by PECAM-1 were associated with the truncated PECAM-1 fragment leading to attenuation of cell growth due to an increase in apoptosis. In contrast, the full-length PECAM-1 protein was shown to inhibit cell death. The presence of the truncated PECAM-1 protein enhances signalling cascades leading to p38/JNK activation, β-catenin dephosphorylation, and STAT5 phosphorylation. Thus, PECAM-1 shows diverse functions: mediating adhesion between neighbouring endothelial cells and the interaction between endothelial cells and cells of the immune system.[36] PECAM-1 is involved in the monocyte-mediated inhibition of collagen-induced platelet activation. Blood PECAM-1 was shown to restrict thrombus formation by regulating platelet responses in low activation conditions.[37] The total cellular PECAM-1, upregulated by statins, reduced endothelial permeability and the inhibitory effect on leucocyte trans-endothelial migration including altered cellular distribution of PECAM-1 through inhibition of Rho A GTPase. Also, it was found that the total cellular PECAM-1 was downregulated by tumour necrosis factor-alpha.[38] PECAM-1 and MMP-9 are coexpressed at sites of inflammation. Interferon-β significantly increased the expression of PECAM-1 in human umbilical vein endothelial cells and reduced MMP-9 secretion human peripheral blood mononuclear cells.[39] Plasma PECAM-1 concentration was higher on admission in patients with AMI and unstable angina pectoris than in the stable angina pectoris and control. In patients with acute coronary syndromes including AMI and unstable angina, there were no differences in plasma PECAM-1 concentrations between patients with and without hypertension or diabetes mellitus. They concluded that an increase in PECAM-1, which mediates both migration of leucocytes and platelet–endothelium interactions, plays a significant role in thrombus formation in patients with acute coronary syndromes.[40]

In the present study, we also did not find any significant difference in serum PECAM-1 levels in metabolic syndrome adolescents compared to the control patients. The use of serum FST and PAPP-A levels before the development of metabolic syndrome complications together with other metabolic syndrome and cardiovascular tests will make a great contribution to the clinic.

According to our knowledge, this is the first study to investigate the relation between circulating FST, PECAM-1, and PAPP-A levels, and the metabolic syndrome in adolescents. In the present study, FST and PAPP-A levels were higher in metabolic syndrome, suggesting that the rise in these markers may be a result of the inflammatory atherogenic and prothrombotic status in metabolic syndrome. Overall, these markers may be prominent indicators in diagnosis of metabolic syndrome in adolescents to prevent future complications and be a novel drug target without a need for dietary restriction.

There is a need for the large population to study extensively in adolescents with metabolic syndrome. Moreover, the subgroup analysis according to the body mass index class provides important new data and may be considered as a strength of the study.

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Competing interests. None.

Ethical standard. The study was approved by the Local Ethics Committee of Meram Faculty of Medicine at Necmettin Erbakan University. All parents were informed about the study design, and written consents were obtained.

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