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ARAŞTIRMA / RESEARCH

Relationship between obesity and platelet indices in children

Çocuklarda trombosit indeksleri ve obesite arasındaki ilişki

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Abstract

Purpose: The aim of this study was to assess platelet count, MPV and PDW as metabolic indicator in obese children with or without insuline resistances.

Materials and Methods: Two hundered sixtyseven obese patients (160 female) and 50 (25 female) controls were enrolled. Anthropometric measurements, triglyceride, total cholesterol, high-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol (LDL), alanine aminotransferase (ALT), aspartate aminotransferase (AST), uric acid, hemoglobin, platelet count, MPV, PDW and insulin resistance by using homeostasis model of assessment of insulin resistance (HOMA-IR) and oral glucose tolerance test were investigated.

Results: Uric acid level were significantly higher in the obese group while there was no statistically significantly differences in platelet indices between in the two groups. Platelet counts, MPV and PDW levels were not significantly different between in three groups. However MPV inversely correlated with HOMA-IR, platelet counts, ALT and LDL levels and positively correlated with PDW.

Conclusion: The relationship between platelets, MPV, PDW has previously been demonstrated. However platelet indices may not to be related to degree of obesity as currently thought. Uric acid may be a more useful marker for selected patients with insulin resistance.

Key words: Childhood, obesity, platelet,mean platelet volume, platelet distribution with

Öz

Amaç: Bu çalışmada insulin direnci olan ve olmayan obez çocuklarda trombosit sayısı, ortalama trombosit volümü (MPV) ve trombosit dağılım genişliği (PDW) parametrelerinin metabolik bir belirleyici olarak kullanılıp kullanılamayacağını göstermeyi amaçladık.

Gereç ve Yöntem: Çalışmaya 267 obez çocuk (160 kız) ve 50 (25 kız) kontrol alındı. Antropometrik ölçümler, serum trigliserid,total kollesterol, yüksek dansiteli lipoprotein kollesterol (HDL), düşük dansiteli lipoprotein kolesterol (LDL), Alanin aminotransferaz(ALT) Asparta aminotransferaz (AST), ürik asit, hemogloulin, , trombosit sayısı, MPV, PDW tüm hastalarda bakıldı. İnsulin direnci homostatik model assesmant (HOMA-IR) kullanarak ve oral glikoz yükleme testi (OGTT) yapılarak belirlendi.

Bulgular: Ürik asit değerleri obez grupta anlamlı yüksek saptandı. Ancak trombosit indeksleri arasında istatistiksel anlamlı fark bulunamadı. Trombosit sayısı, MPV,PDW değerleri insulin direnci olan, olmayan ve control grubunda istatistiksel olarak anlamlı farklı saptanmadı. Buna ragmen MPV HOMA-IR değeri, trombosit sayısı ,ALT ve LDL arasında arasında negatif yönde korelasyon varken MPV ile PDW arasında pozitif korelasyon saptandı.

Sonuç: Obezite ile trombosit sayısı, PDW ve MPV arasındaki ilişki daha önce gösterilmiştir. Biz düşündüğümüz gibi trombosit indeksleri ile obezite derecesi arasında bir ilişki saptayamadık. Ancak insulin direncini belirlemede seçilmiş hastalarda ürik asit düzey ölçümü daha yararlı olabilir.

Anahtar kelimeler: Çocukluk çağı, trombosit, ortalama trombosit volümü, trombosit dağılım genişliği

INTRODUCTION

Childhood obesity continues to represent a major public health problem, and it is reported to have increased by three fold in the last four decades in the USA (1). Obesity in the childhood period can potentially have its long term metabolic effects in adulthood, even after the resumption of normal weight. Obesity-related complications such as hepatic steatosis or Type 2 diabetes can now be

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monitored from early childhood [1-3].

Obesity accounts for a low-graded inflammatory process with an increase in platelet numbers and the incidence of thrombosis. This is a serious predisposing factor particularly in cardiovascular (CVS) disease. The underlying mechanism is due to the increase in the circulating interleukin-6 (IL-6) secreted from adipose tissue [2]. IL-6 is an important indicator of proliferation of megakaryocytes and megakaryopoiesis. MPV is a parameter that is used to determine platelet activation. High MPV indicates increased platelet size, implying, more active platelets in terms of both metabolic and enzymatic processes. Increased MPW (mean platelet width) is also considered an independent risk factor in cardiovascular disease[3]. One of the most important complications of obesity-related is cardiovascular diseases due to underlying atherosclerosis which is a likely result of platelet activation [4].

Studies have shown higher platelet numbers and MPV parameters in obese adults than normal population[5]. MPV has been used as a parameter in monitoring early atherosclerosis, metabolic syndrome and nonalcoholic steatohepatitis [5]. Our study aims to predict the obesity related complications in children by using a simple hematological test and to examine the relationship between MPV and PDW values, and the insulin resistance.

MATERIALS AND METHODS

Children attending the paediatric obesity clinic at from October 2013 to March 2014 were included in the study. Children with a body mass index above 95 % were enrolled in the study. Anthropometric measurements such as body weight, height, body mass index and waist circumference were performed in all subjects. Patients with Type 2 diabetes, Cushing's disease, and those on corticosteroids and medications affecting both the numbers and function of platelets were excluded. Routine complete blood counts (platelets, MPW and PDW), uric acid, lipid levels, AST, ALT, fasting blood glucose, insulin levels and HOMA-IR values were obtained. Complete blood counts were measured using Beckman Coulter automatic counter. Insulin resistance was calculated based on the HOMA-IR model (fasting insulin x blood sugar/22.5). Oral glucose tolerance test (1,75g/kg of glucose) was performed on subjects with HOMA-IR values higher than 4 and/or subjects with physical examination findings of insulin resistance including acanthosis nigricans, skin tags and hyperkeratosis pilaris. Subjects with fasting plasma glucose level >100 mg/dL on the oral glucose tolerance test were classified as subjects with impaired fasting glucose, those having plasma glucose level 140 mg/dl at 120 minutes were classified as impaired glucose tolerance, those with insulin level >70 IU/ml at a20 minutes and/or peak insulin >150 mIU/ml and the total insulin levels>300mIU/ml were regarded as metabolically affected obese subjects with hyperinsulinism. Patients were divided into three groups: obese, obese with insulin resistance and control.

Statistical analysis

All data were analyzed using SPSS 18 software. Student's t test was used to compare mean and differences between the three groups, and $p<0.05$ was considered statistically significant. Pearson's correlation analysis was used to identify any correlation between variables.

RESULTS

267 obese subjects (160 F) were enrolled in the study. The mean age was 11.6±3.5 years. There was no differences in the platelet counts, MPV and PDW value between males and the females in the obese group (Table 1). Differences between patients with obesity, control group and obesity with IR were evaluated depending on whether the Homa-IR value exceed 4. Although MPV values in patients with insulin resistance were higher compared to the non-obese group and the control group, the differences were not statistically significant.

In addition, no difference determined in platelet count and hemoglobin levels between all three groups. As expected, ALT and uric acid values significantly differed among in these three groups (Table 2). At assessment using OGTT, when compared the groups with and without hyperinsulinism, whereas no difference was determined in terms of MPV and PDW, and platelet numbers (Table 3). MPV was negatively correlated with ALT and PLT, whereas HOMA-IR, BMI and PDW exhibited a positive correlation (Table 4).

Table 1. Demographic and clinical characteristics of study population according to gender

	Obesity Girls n 160	Obesity Boys n 107	P	IR Girls n 27	IR Boys n 40	P
Age (Years)	11.6± 3.2	11.1± 3.2	0.311	12.4± 2.8	12.9 ±2.29	0.380
BMI (kg/m2)	28± 5	28 ±4.6	0.351	30± 5	31± 4	0.468
BMI SDS	2.7 ±1.1	2.3± 0.55	0.01	2.8 ±0.88	2.4± 0.44	0.008
Hbg(gr/dl)	12.8± 0.91	13.2 ±1.1	0.00	12.8± 0.98	13.6 ±1.1	0.00
PLT	318573± 74911	347631 ±231440	0.426	301181± 54498	313285± 85947	0.421
PDW(fl)	11.6 ±1.8	11.4± 2.3	0.906	11.8± 1.6	11.6± 1.8	0.638
MPV(fl)	9.9± 0.89	9.6± 1.3	0.158	10 ±0.79	9.9 ±0.88	0.376
LDL(mg/dl)	96± 27	100± 25	0.315	97 ±29	101± 29	0.534
TG(mg/dl)	105 ±50	101± 47	0.478	115 ±52	107 ±44	0.444
Uric acid(mg/dl)	4.7± .95	5.1± 1.2	0.016	4.9 ±0.98	5.8 ±1	0.00
Plasma glucose	88± 7.7	90± 9	0.106	91± 7.9	93 ±10	0.220
Insulin	17± 10	15 ±8.6	0.122	24 ±6.7	24 ±6.8	0.880
Homa IR	3.9 ±2.5	3.4± 2	0.185	6± 2.3	5.6± 1.5	0.377
ALT(u/l)	20± 16	26 ±16	0.016	23± 23	37± 22	0.010

BMI: Body mass Index, Plt: platelet, PDW: Platelet distribution width, MPV: Mean platelet volume, LDL: lowdensitylipoprotein, TG:Trigliserid, HOMA-IR: using homeostasis model of assessment of insulin resistance, ALT: Alanine aminotransferase

Table 2. Comparison of clinical and laboratory parameters between patients with Obesity with IR (group 1), without IR (group 2), and healthy controls (group 3).

	Group 1 (N=88)	Group 2 (N=179)	Group 3 (N=51)	P
Age (years)	12± 2.6	10.8± 3.4	11.3 ±4.2	0.01
BMI (kg/m2)	30 ±4.6	27 ±4.5	18.5± 3.4	0.00
BMI SDS	2.6± 0.73	2.5± 1	-0.26± 1	0.00
PLT	305720± 67788	342520± 185650	312734± 88118	0.125
MPV(fl)	10±0.8	9.7± 1.2	9.8± 0.77	0.248
PDW (fl)	11.7± 1.7	11.3± 2.3	11.6 ±1.9	0.394
Hbg(gr/dl)	13 ±1.1	12.9± 0.99	12.8± 1.2	0.277
AST (u/l)	24± 11	22± 6	24 ±5.4	0.139
ALT(u/l)	28 ±23	20 ±9	18 ±9.6	0.00
TG (mg/dl)	112 ±48	99 ±48	_	0.160
LDL(mg/dl)	99 ±29	97 ±25	_	0.980
Homa-IR	5.9 ±2.1	2.4± 1	_	0.00
Uric acid(mg/dl)	5.3±1.11	4.6± 1	4 ±0.99	0.00

BMI: Body mass Index, Plt: platelet, PDW:Platelet distribution width, MPV: Mean platelet volume, LDL: lowdensitylipoprotein, Hg: Hemogram, TG:Trigliserid, HOMA-IR: Homeostasis model of assessment of insulin resistance,AST: Aspartate amino trensferase ALT: Alanine aminotransferase

Table 3. Differences between OGTT-performed patients with and without hyperinsulinism

	Hyperinsulinism (+) (n=67)	Hyperinsulinism(-) (n=25)	P
Age(years)	12.9 ±2.4	13.7± 2.4	0.173
BMI(kg/m2)	31 4.8	30± 3.6	0.235
BMI SDS	2.9± 1.4	2.5± 0.6	0.237
MPV(fl)	10.0± 0.85	10.2± 1.07	0.585
PDW(%)	11.8± 1.7	11.7± 3.4	0.867
AST(u/l)	25 ±11	20.4 ±5.8	0.036
ALT(U/L)	31± 25	19 ±7.8	0.031
HBG(gr/dl)	13.2± 0.97	12± 1.3	0.369
Uric acide	5.4± 1	4.9± 1.04	0.022
TG(mg/dl)	125 ±55	122± 59	0.834
LDL(mg/dl)	100± 29	101± 24	0.876
PLT(/mm3)	306151 ± 65007	294440± 79885	0.474
Homa-IR	5.2± 2.5	3.6±1.4	0.003

Table 4. Correlation between laboratory parametres in patients

		MPV	HomaIR	BMI	plt	PDW	ALT
MPV	Pearson Correlation	1	.049	.182**	-.507**	.699**	-.037
	Sig. (2-tailed)		.453	.002	.000	.000	.566
	N	287	238	279	284	280	242
HomaIR	Pearson Correlation	.049	1	.416**	-.103	.003	.256**
	Sig. (2-tailed)	.453		.000	.104	.958	.000
	N	238	254	252	249	244	242
BMI	Pearson Correlation	.182**	.416**	1	-.078	.107	.205**
	Sig. (2-tailed)	.002	.000		.175	.066	.001
	N	279	252	310	300	295	263
Plt	Pearson Correlation	-.507**	-.103	-.078	1	-.442**	.003
	Sig. (2-tailed)	.000	.104	.175		.000	.961
	N	284	249	300	308	303	260
PDW	Pearson Correlation	.699**	.003	.107	-.442**	1	.047
	Sig. (2-tailed)	.000	.958	.066	.000		.454
	N	280	244	295	303	303	256
ALT	Pearson Correlation	-.037	.256**	.205**	.003	.047	1
	Sig. (2-tailed)	.566	.000	.001	.961	.454	

BMI: Body mass Index, Plt: platelet, PDW:Platelet distribution width, MPV: Mean platelet volume, LDL: lowdensitylipoprotein, TG:Trigliserid, HOMA-IR: Homeostasis model of assessment of insulin resistance, ALT: Alanine aminotransferase

DISCUSSION

Various parameters have been developed for early detection of obesity related complications that may occur in childhood. The complete blood count was used as a very simple test for early detection of increased mortality due to cardiovascular diseases contributed by insulin resistance. Increased PLT numbers and MPV levels have been associated with complications[6]. Our result showed PLT and MPW in obese subjects were higher than those of the control group. The IR was also higher in obese subjects than the non-obese group although the differences were not statically significant. However, as predicted no significant relationship was determined. These parameters have been examined in adults and studies have suggested that increased levels of MPV and PLT indicated the presence of active platelets as well as increasing the likelihood of thrombosis, although only new studies have been performed in pediatric patients. Even Çoban et al reported MPV as a good parameter in assessing the atherosclerosis and decreased MPV and PLT in subjects with dyslipidemia, controlled by diet and medications[7].

Increase in the parameters cited above are known to affect the likelihood of obesity progressing to atherosclerosis since this an inflammatory process. First study involving pediatric patients was performed in 2005, and increased levels of MPV were detected in obese children with NAFLD[8]. As an easily measured hematological parameter, MPV is still used to identify at risk patients in clinical practice. In our study, MPV levels were determined in the IR group, although the differences were not statistically significant, this can be used as a parameter of detecting any metabolic syndrome. These findings can be potentially used to monitor the likeliness of developing cardiovascular disease in adulthood as a result of exposure to increased inflammation in the childhood period contributed by obesity. In the study of Aypak et. al. reported a marked increase in PLT numbers and decreased MPV levels in children with metabolic syndrome, and suggested a correlation between PLT numbers and metabolic syndrome (METS) as well as increased probability of thrombosis[9].

MPV is an incidence of PLT, being a parameter easy to assess. The association between increased MPV level and cardiovascular diseases has been shown in adults. Increased level of MPV have particularly been reported in obese patients with diabetes mellitus and subjects with hypertension[10]. Another study conducted in 2013 examined the relationship between carotid artery intima media thickness and MPV in subjects with obesity in childhood. A positive correlation was determined with BMI increasing together with these two parameters[11].

Aslan et al. compared the levels of MPV in groups with or without NAFLD in childhood and showed a

significantly higher MPW in the group with NAFLD[12]. However, another pediatric study, by Aypak reported, high MPV levels in prepubertal girls with metabolic syndrome, suggesting that MPV can be used as a marker of metabolic syndrome criteria regardless of the mechanism involved[13]. Another study involving 13,000 subjects assessed relationship between MPV and diabetes, metabolic syndrome and glycemic control significantly elevated MPV levels were determined in patients with diabetes mellitus, abdominal obesity, metabolic syndrome and low HDL. Significantly correlation was identified between the MPW and glucose regulation especially in poorly controlled diabetic patients, even with strict 3 months control, HbA1c and MPV levels still low. However, no relationship was determined in this study between the presence or absence of metabolic syndrome and MPV[14]. Recent studies have reported significant relationship between MPV and decreased HDL and abdominal obesity in particular. Decreased MPV values have been recorded in individuals who lose weight[15].

Serum uric acid level is a more significant marker than platalet in determining obesity related complications such as dyslipidemia, hypertension and hepatosteatosis. Positive correlation between uric acid and BMI has been reported in many previous studies[16]. Uric acid can be used to evaluate degree of disease in childhood obesity. Uric acid is a more valuable parameter than PLT, MPV and PDW and reveal the degree of inflamatory process. A cut off value can be determined for routine evaluation of obese patients and this can be used to for early detection of complications. Although, not statifically significant, our study showed that MPW increased with obesity and insulin resistance. MPW is a relatively simple test which in combination with the platelet count that can be potentially be used to identify the a.t-risk patients and monitored through adulthood[17].

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