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Identifying Insulin Resistance and Metabolic Syndrome According to Homeostasis Model Assessment of Insulin Resistance (HOMA IR) Indexes Amoung 6-14 Age of Children Who are Obese and Non-Obese

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ABSTRACT :

***Object**: As a result of unbalanced nutrition and lack of physical activity, the prevalence of obesity is increasing in all countries. In the future, it is expected to be greater public health problem. The purpose of these studies is to demonstrate the insulin resistance in earlier period of life to avoid possible complications of obesity.*

***Material and method**: We selected randomly children who admitted to Haydarpaşa Numune Training and Research Hospital Department of Pediatrics between March 2011 and October 2011. The anthropometrical measures were assessed and classified as obese and non-obese children. Fasting blood sample was obtained to measure insulin, HDL, LDL, triglyceride and cholesterol serum level. HOMA-IR indexes was calculated and HOMA –IR value above 2,5 was accepted as insulin resistance.*

***Results**: In the study population, we examined 107 children and 47% of the children were male and 53% female. 61, 7% of children were obese and 38, 3% were non-obese. Hypertension were detected in 19,6 % (n=21) of children. There was a positive correlation between HOMA – IR level and total cholesterol and triglycerides levels (r=0.1). According to WHO criteria, we detected metabolic syndrome in 24 of 107 subjects When we looked at the relation between insulin resistance and metabolic syndrome, 70,8% of children with metabolic syndrome had Homa –ır value above 2,5.*

***Conclusion**: Obesity is a significant public health problem in worldwide. As in adulthood, childhood onset obesity contributes to an increased prevalence of cardiovascular risk factors. Therefore obesity is an alarming problem of public health even for developing countries. The prevention of the obesity is the most important solution so particular strategies should be developed by the states to prevent obesity.*

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***Key words**: Childhood Obesity, Metabolic Syndrome, Insulin Resistance*

ÖZET :

***Giriş ve Amaç**: Dengesiz beslenme ve azalmış fiziksel aktivite bütün ülkelerde obezite sıklığını arttırmaktadır. Obezitenin ileride daha büyük bir halk sağlığı problem olacağı tahmin edilmektedir. Bu çalışmanın amacı, yaşamın erken döneminde insulin direncini tespit edip, obezitenin muhtemel komplikasyonlarını önlemektir.*

***Materyal ve Metod:** Mart 2011 – Ekim 2011 tarihleri arasında Haydarpaşa Numune Eğitim Araştırma Hastanesi Çocuk Polikliniğine başvuran çocuklar randomize olarak seçilmiş ve antropometrik ölçümleri yapılarak, obez ve obez olmayanlar olarak sınıflandırılmıştır. Çocuklardan insulin, HDL, LDL, trigliserid ve kolesterol değerleri ölçülmesi için açlık kan örneği alınmıştır. Hesaplanan HOMA – IR değerinin 2,5 ve üzeri değerler insulin direnci olarak kabul edilmiştir.*

***Bulgular**: Çalışmaya katılan 107 çocuğun %47'si erkek, %53'ü kız idi. %61,7'si obez, %38,3'ü obez değildi. Hipertansiyon sıklığının %19,1 (n=21) olarak tespit ettik. Bununla birlikte, özellikle kolesterol ve trigliserid değerleri ile HOMA – IR yüksekliği arasında pozitif korelasyon tespit edilmiştir. WHO kriterlerine göre 107 katılımcının 24 tanesinde metabolik sendrom tespit edildi. Homa – Ir yüksekliği ile metabolic sendrom arasındaki ilişki değerlendirildiğinde, metabolic sendrom tanısı alan çocukların %70,8'inde Homa –ır değeri 2,5 üzeri tespit edilmiştir.*

***Sonuç**: Dünya genelinde obezite önemli bir halk sağlığı sorunudur. Erişkinlerde olduğu gibi, çocukluk çağında görülen obezite, hipertansiyon, trigliserid yüksekliği, HDL düşüklüğü ve bozulmuş glukoz toleransı gibi kardiyovasküler risk faktörlerinin sıklığını arttırmaktadır. Bu nedenden dolayı, gelişmekte olan ülkelerde dahi önemli bir halk sağlığı problemidir. Bu problemlemin en önemli çözümü obezitenin önlenmesi olup buna yönelik önemli stratejiler geliştirilmelidir.*

***Anahtar kelimeler**: Çocukluk Çağında Obezite, Insulin Direnci, Metabolik Sendrom*

INTRODUCTION

As a result of unbalanced nutrition and lack of physical activity, the prevalence of obesity is increasing in all countries. Obesity related disorders are second degree prevalent after tobacco related causes of death in United States (1,2). Nowadays, obesity is a major problem and in the future, it is expected to be greater public health problem.

Childhood onset obesity has an impact on insulin resistance, type 2 diabetes, hypertension, hyperlipidemia, liver and kidney disease. At the same time, it increases the risk of adulthood obesity and cardiovascular disease (CVD) (3). For these reasons, childhood onset obesity has been considered as a major public health problem and particular strategies have been developed by the states in order to prevent it.

The metabolic syndrome also called as insulin resistance syndrome or X syndrome is a common disorder that causes many chronic diseases. Childhood onset obesity precedes the hyperinsulinemic state. The metabolic syndrome was firstly defined at 1988 by Reaven but nowadays, metabolic syndrome has been defined by diverse criteria like National Cholesterol Education Programme (NCEP), World Health Organization(WHO) or International Diabetes Federation (IDF)(4).

A parallel relationship is present between development of obesity and type 2 diabetes, at here the key mechanism is insulin resistance. The Insulin resistance is main mechanism in many complications caused by obesity therefore various new tests have been developed in order to determine the resistance. Some of them, homeostasis model assessment for insulin resistance (HOMA-IR), quantitative sensitivity check index (QUICKI), oral glucose tolerance test have been used (5,6).

In this study our aim is to evaluate HOMA-IR indexes in childhood onset obesity to determine insulin resistance related with metabolic syndrome, hypertension, hyperlipidemia, type 2 diabetes, liver and kidney disease.

RESEARCH DESIGN AND METHOD

Study Population

In this study, we selected randomly obese and non obese children who admitted to Haydarpaşa Numune Training and Research Hospital Department of Pediatrics between March 2011 and October 2011. Samples included in this study that have systemic disease, endocrine, neurologic disease and a history of chronic drug use were excluded from this study. The anthropometrical measurements were assessed by trained observers. Weight and height were measured with the subjects wearing light clothes and without shoes on. The body mass indexes (BMI) was calculated (weight in kilograms divided by the square the height in meters) and classified as obese and non-obese children by World Health Organization (WHO) recommendation.

Biochemical Analysis and Definition of Metabolic Syndrome

Blood samples were obtained for biochemical analysis after a 12-hour over night fast. Plasma glucose level was measured with the enzymatic calorimetric method and insulin level was calculated and measured by radioimmunoanalysis method. HOMA-IR indexes was calculated by the formula: HOMA-IR = fasting plasma insulin (μU/ml) x fasting plasma glucose (mmol/L)/22,5 . HOMA –IR value above 2,5 was accepted as insulin resistance.

Cholesterol, low density lipoprotein (LDL), high density lipoprotein and triglycerides were also calculated in all patients. Abnormalities in the fasting levels of triglycerides, total cholesterol, LDL and HDL were adjusted for age and sex (7). Blood pressure measurement was taken from all subjects while they are in sitting position and at rest for ten minutes. If the blood pressures were higher than 95 percent according to age and sex we defined them as having high blood pressure level. Metabolic syndrome was consider according to WHO's criteria if three or more of the following criteria were present: BMI >95th percentile, abnormal glucose intolerance, hypertension >95th systolic level, dyslipidemia (triglyceride >105 mg/dl for be-

low 10 age and >136 mg/dl for above 10 age or HDL<35mg/dl or total cholesterol below 5th percentile).

Statistical analysis

The findings of this study was analyzed using the program SPSS (Statistical Package for Social Science) for Windows (version 16.0). The data was reported as mean ± standard deviation (SD) or median / interquartile range, according with the normal distribution status. Student t test and Oneway Anova test were used in comparison within normal distribution status. We used Kruskal Wallis is test for comparison of abnormal distrubition status. Qualitative data was compared with Ki – square and the results were evaluated within 95% standart deviation and p value <0.05 statistically significant.

RESULTS

In the study population, we examined 107 children and 47% of the children were male and 53% female. The distribution of obesity, 61, 7% (n=66) of children were obese and 38, 3% (n=41) were non-obese and also all clinical and demographic characteristics are shown in the table 1. There were no statistical differences between in weight status by sex. However incidence of the obesity was increased with increasing age.

	Obese	non obese
Male	30 (45%)	20 (48%)
Female	36 (55%)	21 (52%)
Age	10,8±2,5	9,3±2,5
BMI	27,3±2,5	17,7±3,1
Systolic pressure (mmHg)	115±12,1	95,3±10,5
Insulin resistance	40 (60%)	4 (9%)
Metabolic syndrome	23 (34%)	1 (2%)

BMI (body mass index)

Tablo 1: Gender, age, systolic blood pressure and body mass index distribution on obese and non obese children

Hypertension were detected in 19,1 % (n=21) of children. When we looked at distribution of the obesity within hypertensive children, all hypertensive children were obese at the same time and any hypertensive children were detected within non obese. Especially total cholesterol and triglyceride level were higher in obese children than non obese. This data was a statistically significant (p<0.05). There were no statistical differences between obese and non obese children according to other parameters of the lipid profiles (Table 2).

	Obese	Non obese	P value
Hypertension	21 (19,1%)	0,0	<0,05
Total cholesterol	165,5±26,8	142,3±31,3	<0,05
Triglyceride	121,0±50,4	71,8±26,3	<0,05
LDL	94,1±24,9	82,9±28,2	>0,05
HDL	47,8±11,0	50,3±11,5	>0,05

LDL: low density lipoprotein, HDL: high density lipoprotein

Tablo 2: Blood pressure and lipid profile among obese and non obese children

In our study, insulin resistance was accepted if the HOMA-IR index is above 2,5. In this population mean HOMA-IR level was 2, 8 ± 2, 4. However, mean HOMA-IR index in the obese children was 3,6 ± 2,8 and in the non obese group was 1,7 ± 1,2. Insulin resistance was detected in 60% (n=40) of obese children and 9% (n=4) of non obese (p<0,05). There was no statistically difference in HOMA – IR index by gender. When we looked at the distribution of insulin resistance among total cholesterol, triglycerides and LDL level there was a positive correlation between HOMA – IR level and total cholesterol and triglycerides levels (r=0.1). However, no positive correlation was detected between HOMA-IR and LDL – HDL cholesterol level (Table 3).

	HOMA – IR≥2,5	HOMA-IR<2,5
Obese	40(60%)	26(40%)
Non obese	4(9%)	37(91%)
Total cholesterol	162,5±28,9	151,6±31,0
Triglyceride	119,1±51,9	83,2±37,7
LDL	91,4±25,1	89,1±28,2
HDL	48,5±11,7	49,3±10,8

Tablo 3: Obesity distribution and mean cholesterol, triglyceride and LDL level according to HOMA – IR (insulin resistance)

When insulin resistance was compared with body mass indexes (BMI) there was statistically significant relation within these groups so frequency of insulin resistance was increased with increasing BMI (Table 4).

According to WHO's metabolic syndrome criteria, we detected metabolic syn-

drome in 24 of 107 subjects (%22, 4). There were no statistically differences in frequency of metabolic syndrome by sex and age groups. Additionally, among the obese children, 34, 8% of obese children had three or more metabolic syndrome criteria. When we looked at the relation between insulin resistance and metabolic syndrome, 70, 8% of children with metabolic syndrome had insulin resistance (HOMA-IR level ≥ 2, 5). At the same time, only 29,2% of children without insulin resistance (HOMA-IR<2,5) had three or more metabolic syndrome criteria(P<0.05) (table 5).

	HOMA-IR≥2,5	HOMA-IR <2,5
10-25p	1(9,1%)	10(90,9%)
25-50p	0	11(100%)
50-75p	0	9(100%)
75-95p	3(30%)	7(70%)
>95p	40(80,6%)	26(39,4%)

P<0,05 - p: percentile

Tablo 4: insulin resistance and body mass index relation

	HOMA – IR ≥2,5	HOMA – IR<2,5
Metabolic syndrome		
Yes	17(70,8%)	7(29,2%)
No	27(32,5%)	56(67,5%)

P<0,05

Tablo 5: Metabolic syndrome and HOMA – IR (insulin resistance)

DISCUSSION

Up to last decade, metabolic syndrome was known as an adulthood disease. Nowadays, childhood obesity is accepted a major risk factor for metabolic syndrome related to insulin resistance. Multiple definitions of the metabolic syndrome have been proposed for adults by WHO, the National Cholesterol Health Program's Adult Panel III, the European Group for the Study of Insulin Resistance and the International Diabetes Federation, which all agreed on the essential components (glucose intolerance, central obesity, hypertension and dyslipidaemia) but differed in detail (8). In our study, we used WHO's criteria for definition of metabolic syndrome in children .WHO has defined metabolic syndrome by three or more of the following criteria: BMİ is above 95 percentile, fasting glucose intolerance, arterial hypertension, dyslipidemia (high triglyceride and cholesterol level or low HDL level)(9).

Not only obesity is an independent risk factor for cardiovascular diseases but also main determinant for metabolic syndrome. Ferreira et al. reported mean HOMA –IR level was higher in female (3,8±2,2) than male (2,6±1,3) in 52 obese children. Additionally, majority of the obese children has at least one cardiovascular risk factor (10). In our study, metabolic syndrome was found 22, 4% of children and mean HOMA-IR level was higher in females (3,3±3,1) than males (2,3±1,2). According to this study, the obese children also had one or more additional cardiovascular risk factors especially hypertension, hyperlipidemia or insulin resistance.

Bao et al. searched insulin level in 5 – 9 ages of children and explained that children with high insulin level had abnormal lipid profile and high arterial blood pressure. Therefore, they emphasized that high insulin level triggers risk factors for CVD and metabolic syndrome (11). In current study, we also reported that hypertension, high cholesterol, and triglyceride and LDL level were more frequent in the insulin resistance group.

There is no certain cutoff level of HOMA-IR for definition of insulin resistance. Additionally, many determinations have been developed for this definition. We also used cutoff HOMA –IR level as ≥ 2,5 for insulin resistance. In South America, Caceres et al. studied 61 obese children between 5-18 years of ages and searched the relation between insulin resistance and the components of metabolic syndrome. They reported insulin resistance 39,4% of the obese, high triglyceride level 42,6% and high blood pressure 24,5% of these obese children(12). In our study overall prevalence of insulin resistance (36%) is similar to that found in the study of Caceres even if they accepted insulin resistance as HOMA – IR ≥ 3, 5. We also found positive correlation between hypertension and HOMA –IR level like Caceres' study. In current study, 70,8 % (n=17) of children with metabolic

syndrome had insulin resistance. We found insulin resistance more frequently in children who have components of metabolic syndrome. Insulin resistance was detected in 57, 1% of hypertensive children. Likewise there was insulin resistance in 64,5% of high triglyceride group and 63,6% of high cholesterol group.Varness et al. explained that insulin resistance onset in childhood is the triggering factor for occurrence of metabolic syndrome and cardiovascular disorders (13). Similarly, hypertension, dyslipidemia and obesity were found frequently in children with insulin resistance (HOMA-IR ≥2,5) in our study. These results show that risk factors for cardiovascular disease seen in adulthood already begin in childhood. Therefore childhood obesity and also insulin resistance are more serious problem associated with a wide range of illness and death in later life.

Finally, obesity is a significant public health problem in worldwide. As in adulthood, childhood onset obesity contributes to an increased prevalence of cardiovascular risk factors, such as hypertension, hypertriglyceridaemia, low-HDL and impaired glucose metabolism (14). The clustering of these factors, which is associated with insulin resistance and found in humans who are overweight more often than normal weight, is called metabolic syndrome , also known as syndrome X, insulin resistance syndrome and deadly quartet (15). Nowadays, lack of physical activity and unbalanced feeding behavior increase the prevalence of obesity and obesity related disorders. Therefore obesity is an alarming problem of public health even for developing countries. The prevention of the obesity is the most important solution of the alarming problem so particular strategies should be developed by the states to prevent obesity

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