ISCHEMIA-MODIFIED ALBUMIN AS AN OXIDATIVE STRESS BIOMARKER IN OBESE CHILDREN

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ABSTRACT

Objective: *Ischemia modified albumin (IMA) is a marker that is considered as an oxidative stress biomarker. In this study we investigated the IMA levels, an oxidative stress marker, in obesity that leads to free radical formation, in children.*

Material and Method: *Fifty obese and fifty normal weighted children as a control were included in the study. Blood samples were collected for biochemical parameters and serum IMA values.*

Results: *Serum IMA levels were significantly higher in obese group than non-obese group (p<0.001). Median and minimum-maximum IMA values of obese and control groups were 930 (min: 673-max 1332) and 864 (min:496-max:1068) respectively.*

Conclusion: *IMA may be used as an important marker to show oxidative stress in childhood obesity.*

Keywords: *Ischemia modified albumin, obesity, child, insulin resistance, body mass index* ***Nobel Med 2015; 11(2): 80-84***

OBEZ ÇOCUKLARDA OKSİDATİF STRES BELİRTECİ OLARAK İSKEMİ-MODİFİYE ALBUMİN

ÖZET

Amaç: İMA (iskemi modifiye albumin) oksidatif stres biyomarkırı olarak kabul edilen bir belirteçtir. Bu çalışmada çocuklarda serbest radikal oluşumuna yol açan obezitede oksidatif stres belirteci olan İMA seviyelerini araştırdık.

Materyal ve Metot: Elli obez ve kontrol grubu olarak da elli normal ağırlıklı çocuk çalışmaya alındı. Biyokimyasal parametreler ve serum İMA değerleri için kan örnekleri toplandı.

Bulgular: Serum İMA değerleri obez grupta obez olmayan gruba göre anlamlı yüksekti (p<0,001). Medyan ve minimum-maksimum İMA değerleri sırası ile 930 (min: 673-max 1332) ve 864 (min:496-max:1068) idi.

Sonuç: Çocukluk çağı obezitesinde İMA oksidatif stresi göstermede önemli bir belirteç olarak kullanılabilir.

Anahtar kelimeler: İskemi modifiye albümin, obezite, çocuk, insulin direnci, vücut kitle indeksi **Nobel Med 2015; 11(2): 80-84**

INTRODUCTION

Obesity is an energy metabolism disorder due to excess fat deposition in the body. Apart from a being disorder, it is a potential hazard for both physical and psychological diseases.[1] Obesity in childhood is important not only for children but also for every period of life because many of adulthood obesity starts at early periods of life.[2] Childhood obesity is found to be associated with a lot of chronic condition as cardiac diseases, hyperlipidemia, hyperinsulinemia, hypertension and early atherosclerotic changes.[3-6]

As well as most common diagnostic parameter of obesity, body mass index (BMI) is an indirect indicator of body fat. In children using an age- and sex-specific percentile for BMI rather than the BMI categories used for adults is more convenient because children's body composition varies as they age and varies between boys and girls. Overweight is defined as a BMI at or above the 85th percentile and lower than the 95th percentile for children of the same age and sex and obesity is defined as a BMI at or above the 95th percentile for children of the same age and sex.[7]

Obesity is a chronic and inflammatory condition that triggers free oxygen radicals. It causes hyperglycemia, decreased antioxidant defense with decreased muscle activity, impaired lipid profile and increased blood pressures. It is known that as a result of excess fat tissue, non-esterified fatty acids and cytokine levels increase and also levels of adiponectin and plasminogen activator inhibitor I increase. As a result risks of insulin resistance, endothelial dysfunction and cardiovascular disease increase. These show that there is an oxidative stress in obesity.[8,9]

Reactive oxygen species and free hydroxyl radicals occur during tissue hypoxia. These free radicals modify the albumin at the amino or N-terminal side and as a result albumin's binding capacity of transition elements, and the end product is known as ischemia-modified albumin (IMA).[10-13] In recent studies, it is shown that free oxygen radicals formed as a result of ischemia, acidosis or oxidative stress increase IMA levels.[10,13,14] Recently, IMA is being considered as an oxidative stress marker. It is shown that IMA levels were increased in diseases causing non-cardiac hypoxia and oxidative stress such as chronic kidney disease, hypercholesterolemia, systemic sclerosis and type 2 diabetes mellitus. The most common utilization is in early myocardial injury.[14-20] Currently there have been studies ongoing about the IMA levels and the oxidative stress in adult and childhood obesity. Piva et al. found that IMA levels increased in overweight and obese subjects.[21]

In this prospective study, we aimed to study IMA levels in childhood obesity as an oxidative stress marker.

MATERIAL AND METHOD

Ethics approval was obtained through the Çanakkale Onsekiz Mart University Clinical Research's Ethics Committee. Fifty obese children with the BMI percentile above 95th percentile according to reference values of Turkish children of the same age and sex and fifty healthy children with normal weight (BMI percentile between 50 and 75) as a control group admitted to general policlinics between May 2012 and December 2012 were enrolled in the study.[22] In routine well child visits of control group, while taking blood samples for complete blood count screening, blood samples for IMA was collected.

From obese children blood samples were collected to analyze biochemical parameters and IMA. Samples for IMA were separated immediately by centrifugation at 4 °C and stored at -20 °C for further analysis. Liver steatosis was determined with ultrasonography for each subject.

Biochemical assay for IMA

The albumin cobalt binding test was analyzed according to the method defined by Bar-Or et al. In this method 200 µL serum was added to 25 µL of 0.1% (w/v) cobalt chloridine water solution. It was mixed gently and waited for 10 minutes for sufficient cobalt-albumin binding. Then 50 µL dithiothreitol (DTT) (1.5 mg/mL H_2O) was added as a colorizing agent. After waiting for two minutes 1.0 mL 0.9% NaCl was added to stop the cobalt binding process of albumin. Afterwards, the absorbance was measured in a spectrophotometer at 470 nm. A sample without DTT was used as a blank. The results were reported as absorbance units (ABSU).[11]

Biochemical assay for insulin and glucose

Plasma glucose was analyzed by glucose oxidase method and measured with Roche Cobas Integra 6000 modular autoanalyzer. Plasma insulin was measured by enzyme immunoassay method.

Statistical analysis

Data were analyzed using SPSS version 15.0 software (SPSS Inc.). Descriptive statistics were performed to summarize sample characteristics. The adjustment to normality for laboratory results was verified with the Kolmogorov-Smirnov test. There was more than one

Table 1. Sex, weight, height, BMI and BMI percentiles of children			
	Obese (n=50)	**Control (n=50)**	**p**
Sex			
Girl n (%)	27 (54)	25 (50)	
Boy n (%)	23 (46)	25 (50)	0.69**
Weight (kg)			
Girls (mean±SD)	46.2±18.4	27.3±10.9	<0.001*
Boys (mean±SD)	54.4±21.7	29.8±11.9	<0.001*
Height (cm)			
Girls (mean±SD)	135.5±17.4	133.2±16.9	0.21*
Boys (mean±SD)	140.7±20.6	139.7±20.1	0.24*
BMI (kg/m²)	25.2±4.3	16.1±3.8	<0.001*
Mean BMI percentile	>97	50-75	<0.001*

*: Mann-Whitney U test, **: chi-square test, **n:** number, **BMI:** body mass index

Table 2. Laboratory and radiological results of obese children	
Variables	**Median (Min-Max)**
Glucose (mg/dl)	89.00 (74.00-140.00)
Insulin (mIU/ml)	19.07 (4.00-52.00)
LDL (mg/dl)	102.50 (65.00-156.00)
HDL (mg/dl)	48.00 (29.00-86.00)
Triglyserid (mg/dl)	113.00 (40.00-346.00)
T. cholosterol (mg/dl)	178.50 (140.00-244.00)
IMA	930.00 (673.00-1332.00)
Cortisol (mg/dl)	13.02 (4.99-26.11)
CRP (mg/L)	0.36 (0.10-2.22)
Glucose/insulin ratio	5.21 (1.81-21.89)

parameter that is different in distribution so median and minimum-maximum values were used. The Chi-squared test was used to compare obesity and sex. To compare numerical parameters Mann-Whitney U test was used. A p value <0.05 was considered statistically significant.

RESULTS

A total of 100 cases were included in the study. Fifty were obese and fifty were normal weight children. Mean age of cases was 9.59±3.89. In obese group the mean BMI percentile was >97th percentile while in control group it was 50-75th percentile (Table 1).

Laboratory results obese children were summarized in Table 2. Median and minimum-maximum IMA values of obese and control groups were 930 (min:673-max:1332) and 864 (min:496-max:1068) respectively (Figure 1). In obese group IMA values were significantly higher (p<0.001).

The correlation between IMA and glucose/insulin ratio was examined in obese group with Spearman test. There was no statistically significant difference between IMA and glucose/insulin ratio (Spearman's rho =-0.104; p=0.471).

DISCUSSION

In our study it is found that IMA levels are significantly higher in obese children than non-obese children. Therefore we can suggest that oxidative stress due to obesity affects children beginning from early ages.

Childhood obesity has become a significant problem especially in developed and developing societies, due to high-calorie food consumption and restricted physical activity. It is going to be almost the most common chronic disease of childhood.[24]

Obese children can be considered quite charming and healthier by the parents sometimes. However, this cute image can be a triggering or preparing factor for many important problems for future life of this child. According to the data from the Bogalusa Heart Study it is clearly shown that 20% of obese children have at least one cardiovascular risk factor (hypercholesterolemia, hyperinsulinemia, hypertriglyceridemia, or hypertension), and it is emphasized multiple risk factors are associated with early atherosclerosis.[25] In addition, it is considered that adiposity especially in abdominal region in obesity can trigger atherosclerotic process and oxidative stress so that can cause vascular dysfunctions.[26]

Overproduction of free radicals due to obesity may cause modification of human serum albumin, causing increased IMA that seems to play a role as an oxidative stress marker.[15] Baysal et al. studied serum IMA levels, epicardial fat tissue thickness and hepatic parenchyma evaluation in obese children and adolescents.[27] They showed that IMA values are prominently high in metabolic syndrome. As well epicardial fat tissue thickness showed significant positive correlation with IMA levels.

Mehmetoğlu et al. studied IMA, total antioxidant status (TAS), total oxidant status (TOS), high-sensitivity C-reactive protein (hsCRP), serum lipid and insulin levels in adult obese subjects.[28] IMA, TOS, hsCPR values were found to be higher in obese subjects compared to control and TAS values were found to be lower. Also they showed that BMI and insulin levels are independent determinatives of IMA values. In our study TOS and TAS were not evaluated. Similar to their study we also found that IMA values are significantly higher in obese group compared to control. However there was no significant association between IMA values and CRP values. This difference

can be explained by the longer period of ischemic and inflammatory exposure in adults with increasing age compared to children.

Piva et al. reported that IL-6, urinary albumin and IMA values are significantly higher in obese adults compared to normal-weight and overweight ones while nitrate/nitrite ratio is lower.[29] And they suggested oxidative stress, endothelial dysfunction and inflammation in obese subjects cause these results. Different from our study this study included diabetic patients also.

Çağlar et al. have founded that IMA values are higher in patients with insulin resistance compared to patients without insulin resistance in their study on young women with polycystic ovary syndrome.[30] In our study there was no significant correlation between IMA values and insulin resistance. It is also known that serum lipid values substantially affect IMA levels.[31] Therefore differences in serum lipid values can cause differences in our study.

There are some limitations to our study. First, the other oxidative stress markers such as TOS, myeloperoxidase, malondialdehyde and TAS could not be studied. And follow up values of IMA after weight loss are not studied that would increase the correlation between IMA and obesity.

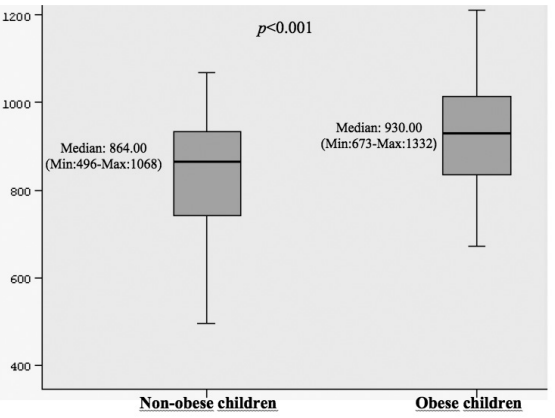

Figure 1. Comparison of IMA values of obese and non-obese groups. Median IMA value of obese children is significantly higher than IMA value of non-obese children (p<0.001)

CONCLUSION

In conclusion, IMA is a promising parameter of hypoxemia nowadays. It can show ischemia in obese children as it is an indicator of ischemia in many diseases. There are limited number of studies about childhood obesity and IMA. There were different results about different parameters. Therefore more comprehensive studies are needed to reveal importance of IMA on childhood obesity.

* The authors declare that there are no conflicts of interest.

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