Prevalence of metabolic syndrome in obese prepubertal and pubertal children

Obez prepubesçel ve pubesçel çocuklarda metabolik sendrom prevalansı

Ayça TÖREL ERGÜR

ABSTRACT

Aim: Obesity associated with metabolic syndrome is characterized by glucose intolerance, insulin resistance, type 2 diabetes mellitus, dyslipidemia and other hormonal disorders in childhood. Unfortunately, if the preventive measures are not taken in time they become obese in the adult age. The prevalence of metabolic syndrome in the pediatric age group is still not well known in our country. The purpose of our study is to evaluate the prevalence of metabolic syndrome and other metabolic characteristics in the obese prepubertal and pubertal children.

Material and methods: We studied 70 obese children and adolescents. Each child was subjected to detailed examination including anthropometric measures, blood testing (biochemistry, blood fasting glucose, renal and hepatic function tests, lipids, electrolytes, hormonal testing including free T3, free T4, TSH, thyroid autoantibodies, fasting insulin levels and oral glucose tolerance test). The criteria of metabolic syndrome were defined according to modified WHO criteria. Homeostasis model assessment of insulin resistance (HOMA-IR) parameters were used as index of insulin resistance.

Results: Metabolic syndrome was found in 18.8% of cases. Metabolic syndrome was found in a significantly higher rate in the pubertal prepubertal group (P > 0.05). The data related with glucose homeostasis; fasting hyperinsulinemia, impaired glucose tolerance were 33.3% and 5.5% in the prepubertal group, where it was 64.7% and 23.5% in the pubertal group, respectively. Hypertension was observed in four pubertal cases (11.7%). Dyslipidemia were identified in 41.6% and 41.1% in prepubertal and pubertal groups, respectively, with no significant differences (P < 0.05).

Conclusion: Metabolic syndrome prevalence especially abnormal glucose homeoostasis among the obese pediatric age group was quite high. We suggested that, early diagnosis, regularly follow-up and if needed, treatment will prevent beta-cell destruction and development of type 2 diabetes mellitus in these cases.

Key words: Childhood obesity, obesity prevalence, metabolic syndrome, diabetes mellitus
ÖZET

Amaç: Çocukluk çağında Metabolik Sendrom (MS), ilişkili obezite glukoz intoleransı, insülin direnci, tip 2 diabet, dislipidemi ve diğer hormonal bozukluklarla karakterizedir. Ne yazık ki Maalesef bu olgular koruyucu önlemler alınmadığı taktirde erişkin yaşamda obez hale gelecektir. Pediatrik yaşta MS prevelansı ülkemizde halen iyi bilinmemektedir. Bu amaçla çalışmamızda prepubertal ve pubertal çocuklarda MS ve diğer metabolik özelliklere ait prevelansın değerlendirilmesi amaçlandı.

Gereç ve Yöntemler: 70 obez çocuk çalışmaya alındı. Antropometrik ölçümleri içeren detaylı muayenesi yapılan herbir çocuğa, kan biyokimyası; kan şekeri, renal ve hepatik fonksiyon testleri, lipidler, elektrolitler, hormonal değerlendirme için fT3, fT4, TSH tiroid otoantikorları, açlık insülin seviyeleri ve OGTT uygulandı. Metabolik sendrom kriterleri modifiye WHO kriterlerine göre tanımlandı. “Homeostasis model assessment of insulin resistance” (HOMA-IR) parametresi insülin rezistans indeksi olarak kullanıldı.

Bulgular: Tüm olgularda MS prevalansı %18,8 olarak saptandı. MS prepubertal gruba göre pubertal grupta anlamlı derecede yüksekti (P > 0,05). Glukoz homeostazına ilişkin bulgular, prepubertal grupta açlık hiperinsülinemisi, bozulmuş glukoz toleransi olup sırasıyla %33,3 ve %5,5 idi. Aynı bulgular pubertal grupta sırasıyla %64,7 ve %23,5 idi. Hipertansiyon 4 (%11,7) pubertal vakada gözlendi. Prepubertal ve pubertal grupta dislipidemi sırasıyla %41,6 ve %41,1 olarak saptandı. Bu yönü ile anlamlı farkılık yoktu (P < 0,05).

Sonuçlar: Obez pediatrik yaş grubunda özellikle anormal glukoz homeostazını içeren MS prevelansı belirgin yüksek saptandı. Sonuç olarak bu olgularda erken tanı, düzenli izlem ve gerekirse tedaviyle, beta hücre yıkımının ve tip 2 diabet gelişiminin önlenileceği düşünebilir.

Anahtar kelimeler: Çocukluk çağı obezitesi, obezite prevelansı, metabolik sendrom, diabetes mellitus

Introduction

Obesity in early childhood increases the risk of premature illnesses and early death, raising public health concerns. Recent studies showed that prevalence of nutritional deficiencies and infectious diseases decreased while morbidity due to other causes such as diabetes and cardiac diseases in the pediatric age-group increased [1]. The prevalence of the diseases associated with obesity may be affected by environmental factors, lifestyle changes and economical status. Although the prevalence of childhood obesity was previously reported to be between 9.1-12.8% in Turkey [2], it seems that its prevalence still steadily increasing.

Since there is insufficient data for the prevalence of metabolic syndrome in obese prepubertal and pubertal children in our country, in this study we aimed to search the clinical, metabolic and biochemical characteristics and prevalence of metabolic syndrome of 70 obese children and adolescents.

Material and Methods

The study group consisted of 70 children and adolescents (the mean age 10.7±2.9 years old) with obesity. All the cases were admitted to Kırıkkale University, Department of Pediatric Endocrinology and Diabetes. All the cases underwent a detailed physical examination, pubertal staging and anthropometric evaluation such as chronological age, height, weight, standing height. Height was expressed as SD score, body mass index as BMI: weight (kg)/ height (meters) [2]. Children with BMI exceeding 95th percentile for age and sex is termed as obese [3]. The pubertal development stage was assessed by the same pediatric endocrinologist using the criteria of Tanner Stages [4]. In the physical examination, acanthosis nigricans reflexing insulin resistance was evaluated in each case (Figure 1).

![Figure 1. Appearance of axillary acanthosis nigricans](image-url)
Written informed consent was obtained from the parents. The inclusion and exclusion criteria of the study are shown in Table 1.

**Table 1.** The inclusion and exclusion criteria

| The inclusion criteria                                                                 | The exclusion criteria                                                                 |
|--------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|
| 1. Cases between 4-17 years of age without any chronic disease and infection of any kind such as cardiac, renal, hepatic, diabetes, cancer, psychiatric diseases. | 1. Cases with a prior major illness; cardiac, renal, hepatic, cancer, psychiatric diseases and, type 1 or 2 diabetes. |
| 2. BMI > 95th percentile for age and gender based on the standards of the Centers for Disease Control and Prevention (CDC) | 2. Cases taking medications such as glucocorticoids. |

Blood fasting glucose, renal and hepatic function tests, lipids (total cholesterol, triglycerides, low-density lipoprotein-cholesterol (LDL), triglycerides, high-density lipoprotein-cholesterol (HDL), electrolytes, hormonal testing such as fT3, fT4, TSH, thyroid autoantibodies, fasting insulin levels. and an oral glucose tolerance test were performed in all cases. An oral glucose tolerance test (OGTT) was performed using a dose of 1.75g glucose/kg body weight (maximum of 75 g). Venous blood samples were obtained at 0, 30, 60, 120, 180 minutes to measure plasma glucose and plasma insulin levels in the morning by venipuncture after a night fasting [5]. Plasma glucose level was determined by the glucose oxidase method, plasma insulin was measured by using IMMULITE immunoassay. The criteria for obesity and metabolic syndrome, defined by WHO was shown in Table 2 [3].

**Table 2.** Criteria of metabolic syndrome which was defined as having ≥ 3 of the following components

| 1. Obesity                                                                     | BMI > 95th percentile for age and sex |
|--------------------------------------------------------------------------------|-------------------------------------|
| 2. Abnormal glucose homeostasis                                               | ≥ 100 mg/dl |
| Impaired fasting glucose                                                      | prepubertal > 15 mU/L; pubertal > 30 mU/L |
| Fasting hyperinsulinemia                                                      | OGTT 120 min; 200 mg/dl > plasma glucose level ≥ 140 mg/dl |
| Impaired glucose tolerance                                                    |                                      |
| 3. Hypertension                                                              | systolic blood pressure > 95th percentile for age and sex |
| 4. Dyslipidemia                                                              |                                      |
| Triglycerides                                                               | < 10 years; > 102 mg/dl and > 10 years; > 136 mg/dl |
| Low LDL-c                                                                  | < 35 mg/dl |
| High Total-c                                                                | > 95th percentile |

Homeostasis model assessment of insulin resistance (HOMA-IR) parameter (fasting insulin × fasting glucose / 18 / 22.5) was used as index of insulin resistance [6]. A cut-off HOMA-IR level of > 2.5 in children and; >4 in adolescents was used to identify an insulin-resistance status [6].

Statistical analysis: For the statistical analysis SPSS (Inc Version 11.0 software) statistical programs was used. The results are expressed as mean and median values in qualitative variables and as a percentage. Abnormal glucose homeostasis (insulin resistance) parameters and metabolic syndrome prevalence’s in the prepubertal and pubertal groups were estimated by chi-square test. The differences were tested by Student’s test. Statistical significance was taken as P < 0.05.

**Results**

The study group consisted of 70 cases (ages between 4.6 to 16.3 years) with obesity. The general characteristics, anthropometric values, glucose and lipid metabolism features of all the cases are shown in Table 3.

**Table 3.** Clinical characteristics of the cases

| Case (n) | 70 |
|---------|----|
| Female  | 36 |
| Male    | 34 |
| Age (year) | 10.7 ± 2.9 |
| BMI (w/h2 ;kg/ m2) | 26.7 ± 4.5 |
| Systolic BP (mmHg) | 109.8 ± 14.1 |
| Diastolic BP (mmHg) | 69.9 ± 9.9 |
| Fasting glucose (mg/dl) | 88.3 ± 9.2 |
| Fasting insulin (IU/L) | 20.7 ± 15.4 |
| Glucose / insulin | 9.07 ± 6.3 |
| IRHOMA | 3.48 ± 3 |
| OGTT 120'glucose (mg/dl) | 114 ±25.8 |
| OGTT 120'insulin (mg/dl) | 88.9 ± 17.4 |
| Total-cholesterol (mg/dl) | 179.9 ± 32.4 |
| Triglycerides (mg/dl) | 126.7 ± 76.1 |
| HDL-cholesterol (mg/dl) | 48.4 ± 8.8 |
| LDL-cholesterol (mg/dl) | 106.9 ± 29.9 |
Of the 70 obese children, 56 (80%) had a positive family history for obesity. Achantosis nigricans was determined in 20% of the cases. Achantosis nigricans and hypertension were significantly more common in pubertal cases ($P < 0.05$). OGGT performed in 70 cases and the total abnormal glucose homeostasis was identified in 67.1%, hyperinsulinemia in 48.5%, impaired glucose tolerance in 14.3% and none of the cases were determined as having impaired fasting glucose. Hyperinsulinemia, impaired glucose tolerance, high triglycerides were also more frequent in pubertal than prepubertal children. There was no significant differences in the prevalence of metabolic syndrome by gender. Table 4 shows the prevalence of metabolic syndrome of prepubertal and pubertal cases. In this according with metabolic syndrome was found in 20 (58.8%) cases in pubertal cases, 12 (33.3%) cases in prepubertal cases. Metabolic syndrome was significantly more frequent among pubertal cases than prepubertal cases.

Ten cases were diagnosed as subclinical hypothyroidism. The mean serum TSH level was 6.1 ± 1.24 IU/L. Thyroid autoantibody positivity was not observed in any of the cases.

**Discussion**

Recent studies have shown an increase in the prevalence of metabolic syndrome in obese children and adolescents [1]. The metabolic syndrome is defined by a combination of obesity, hypertension, dyslipidemia, abnormal glucose metabolism such as hyperinsulinism, insulin resistance, impaired fasting glucose tolerance, impaired glucose tolerance and/or type 2 diabetes mellitus [1]. Besides obesity, low birth weight, increased gain in body mass in early childhood, decreased pubertal insulin sensitivity and clinical markers of insulin resistance (acanthosis nigricans, polycystic ovarian syndrome, premature adrenarche) increased risk of metabolic syndrome [7]. The prevalence of obesity and associated metabolic syndrome in children and adolescents still seems to steadily increasing in Turkey. So obesity in children and adolescents has become a major public health issue in our country. Obese children have a high risk to become obese adults with a high risk for the occurrence of type 2 diabetes, cardiovascular, orthopaedic, bone and other diseases. The most effective tool for prevention of metabolic syndrome is to avoid the development of childhood obesity. Unfortunately, besides several studies, there is not enough knowledge about the prevalence of glucose and/or lipid abnormalities and metabolic syndrome in obese children in Turkey.

In our study the prevalence of abnormal glucose metabolism in obese cases was found as 67.1%. None of the cases had impaired fasting glucose or type 2 diabetes, while 10 obese
cases had impaired glucose tolerance. In a study from Southern Italy, the prevalence of insulin resistance was found as 40.8% in obese children and as 41.2% in obese adolescents. None of the subjects had impaired fasting glucose or diabetes as in our study, while 4 obese patients had impaired glucose tolerance (4%). According to this study; impaired glucose tolerance is still rare whereas insulin-resistance is already detectable in more than 40% of obese children and adolescents in Southern Italy [8]. Their observations confirm that metabolic risk factors can be found at a very early age and strengthen the case for implementing programs for prevention and treatment of childhood obesity. In a study from Spain, the prevalence of insulin resistance in obese children was found 35.8%, impaired glucose tolerance was found in 7.4%, but there was no case with type 2 diabetes mellitus [8]. Our findings as high prevalence of insulin resistance in obese children, were in conformity with both studies.

In another study; Wiegand et al reported that the prevalence of abnormal glucose tolerance and type 2 diabetes were 7.5% and 1.2%, respectively in 491 obese European children and adolescents [9]. Accordingly, the incidence of childhood obesity and type 2 diabetes is an increasing problem in Europe. Impaired glucose tolerance and type 2 diabetes are far more common in obese European children of Caucasian origin than previously thought. Therefore, using fasting glucose levels as the main screening tool appears to be insufficient in detecting these children. Wiegand et al reported that the percentage of type 2 diabetes in the obese pediatric cases was very high [9]. In our study we did not determine type 2 diabetes in the obese cases. An increased prevalence of type 2 diabetes mellitus in obese children and adolescents, especially in specific ethnic subgroups was observed. The prevalence of type 2 diabetes mellitus in a large group of 520 Caucasian children and adolescents with obesity living in Germany was assessed. They reported that 1.5% (n=8) of the obese cases were type 2 diabetes while impaired fasting glucose was detected in 3.7% (n=19) and impaired glucose tolerance in 2.1% (n=11) of the patients [9]. Screening for diabetes in severely obese children and adolescents (BMI-SDS > 2.5) was therefore recommended [9].

In an extensive work, “Bogalusa Study” made by Chen et al on children at pediatric age group the metabolic syndrome was found to be 4% in white and 3% in black children [10]. In another extensive research made on Finnish children and adolescents investigating cardiovascular risk factors, the incidence of metabolic syndrome was determined as 4% [11]. In USA, in the third National Health and Nutrition Research during 1988-1994 the metabolic syndrome frequency was found to be 4.2% (6.1% in males and 2.1% in females) [12].

In the same investigation in obese adolescents (BMI > 95 percentiles) the frequency of metabolic syndrome was found to be 28.7% and in overweight cases (between BMI 85-95 percentiles) 6.8%. In a study made recently on obese adolescents of metabolic syndrome was found to be 30% and it was noted that with the decrease of insulin sensitivity, the metabolic syndrome components increased [13]. Babaoğlu et al. determined impaired fasting and glucose metabolism in 14.2% of 105 children aged 10-18 years in a multicentre study [14]. Atabek et al. found metabolic syndrome to be 27.2% in 169 obese children and adolescents [2].

In this study we determined MS in prepubertal cases considerably frequent. Some studies showed that, exposure to environmental factors in utero (maternal diabetes or obesity) increases the risk of developing childhood MS and also the risk of early stages of cardiovascular disease [15]. Longitudinal studies of Pima Indian children demonstrated that birth weight, i.e., either small for gestational age (SGA) or large for gestational age (LGA), exposure to diabetes in utero, and obesity are the major factors in the development of childhood MS [16].

As a conclusion, we think that Turkish clinicians should screen obese children and adolescents from the point of view of metabolic syndrome. Multicentre, population based diabetes screening programs in accordance with the model protocol suggested by WHO are essential for the estimation and determination of metabolic syndrome prevalence in Turkey.

Declaration of conflicting interests

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