Prevalence of Abdominal Obesity and Metabolic Syndrome in Children and Adolescents: A Community Based Cross-Sectional Study

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Abstract

Background: Although the prevalence of abdominal obesity and metabolic syndrome has been widely studied in the adult population, little is known about it in children and adolescents especially in developing countries. This study aimed to determine the prevalence of abdominal obesity and metabolic syndrome among children and adolescents in Yazd Greater Area, Iran; over the period of 2016-2017.

Methods: This study was part of a larger national study with a cross-sectional design. Using multistage cluster random sampling method, 1035 children, and adolescents of both sexes aged 6-18 yr were randomly selected from rural and urban districts in Yazd Greater Area, Iran. Components of metabolic syndrome, and anthropometry measured in the standard situation.

Results: The prevalence of abdominal obesity in children 6-10 yr old was 13.2% in boys versus 24.7% in girls. The overall prevalence of metabolic syndrome according to International Diabetes Federation (IDF) criteria in adolescents aged 10-18 yr old was 7.6% (9.4% in boys). The most prevalent metabolic syndrome components were low HDL-cholesterol (56.2%) and abdominal obesity (27.8%).

Conclusion: Comparatively, the prevalence of metabolic syndrome in Yazd is high. Low HDL-cholesterol levels and abdominal obesity were the most common component, and family history of heart disease, BMI, and male gender were the main determinants of metabolic syndrome in adolescents.

Keywords: Abdominal obesity; Children and adolescents; Metabolic syndrome; Prevalence

Introduction

The metabolic syndrome in children and adolescents is challenging for families, investigators, and health policy makers. At the same time, doing screen and diagnosis of this syndrome in children and adolescents are potentially more important to control chronic diseases including
T2DM and cardiovascular disorders in later life (1). The diabetic and cardiovascular risk factors can be tracked from childhood to adulthood. Furthermore, metabolic syndrome brings more burden of disease in children and adolescents due to chronic characteristics of the disease (2). Hence, metabolic syndrome raises much more concerns in children and adolescents. Diagnosis of the metabolic syndrome and estimating its prevalence in children and adolescents is controversial due to different diagnostic criteria and different ethnic, age and sex specified cut-off points (3). Abdominal obesity and low HDL-cholesterol are the most prevalent risk factors observed in most studies (4). Furthermore, abdominal obesity is a key risk factor in the diagnosis of metabolic syndrome. According to IDF criteria diagnosis of the metabolic syndrome cannot be made in children under 10 yr old, instead abdominal obesity should be reported (3). Investigators from all around the world have reported different prevalence rates of the metabolic syndrome in adolescents among different populations and in various time frames. For instance, MacPherson, and colleagues have reported the prevalence of 2.1% among Canadian adolescents aged 10 to 18 yr (4). This rate in the United States was reported to be 4.2% to 9.2% using the Third National Health and Nutritional Survey 1988 to 1994 (5). According to IDF criteria, the prevalence of metabolic syndrome was variable from 4.1% to 6.7% in Iranian adolescents from 1990 to 2015 (6). On the other hand, when the National Cholesterol Education Program-Adult Treatment Panel III (ATP III) criteria have been applied and also among the adult population, the prevalence of metabolic syndrome is much more (7).

The metabolic syndrome components are strongly related to lifestyle; hence its prevalence is increasing in the societies with the nutritional transition and may be varied in different populations and may change during time. Although, the prevalence of metabolic syndrome has been widely studied in the adult population, still little is known about its prevalence in children and adolescents especially in developing countries. Therefore, this study aimed to determine the prevalence of abdominal obesity and metabolic syndrome among children and adolescents in Yazd Greater Area, in Iran.

**Materials and Methods**

**Study Design**

This was an analytical cross-sectional study which was a part of the Iranian Children and Adolescents’ Psychiatric Disorders Study (IRCAP), a national project implemented in all provinces of Iran (8).

**Sampling**

One thousand and thirty-five children and adolescents aged 6-18 yr were selected by multistage cluster random sampling method from Yazd greater area according to postal code during 2016-2017. The sampling method and process are fully described in the IRCAP study (9).

**Inclusion and Exclusion Criteria**

Inclusion criteria were as follow: Being an Iranian citizen (residents at least for one year in Yazd district), and age range of 6 to 18 yr. Children and adolescents with severe physical illnesses were excluded.

**Procedure**

Trained researchers visited the participants’ home, introduced the study and described the protocol and invited the parents to participate in their children in the study after obtaining informed consent.

The interviewers collected the demographic data, as well as family history of heart disease. The criterion for family history of heart disease was having at least one first-degree relative with a diagnosis of any heart disease. Then the participants were referred to the Afshar Hospital for performing specialized tests, anthropometrics and other measurements.

In the beginning, an experienced nurse took their systolic and diastolic blood pressure three times, 15-20 min after the arrival. Blood pressure every
Time was taken from the right hand of the participants, in a sitting position and by using an automatic digital blood pressure device (Automatic Blood Pressure Monitor, Model M3 Comfort, Omron Co. Osaka, Japan). We used the mean of three measurements as the participant's blood pressure. All measurements were performed in standard positions and with calibrated tools.

The nurse took venous blood from participants after 8 to 12 h of fasting for measuring fasting blood sugar and dyslipidemia including the measure of triglycerides, total cholesterol, LDL, and HDL. Then blood samples were centrifuged for serum separation. To assess fasting blood glucose and triglyceride a biochemical auto-analyzer, model BT 3000 (Italy) and PARS Azmoon Kits (Pars Azmoon Kit, Pars Azmoon Inc., Tehran, Iran) were used. Bionic kits also were used to assess high-density lipoprotein cholesterol and low-density lipoprotein cholesterol. Overall, 216 participants refused to give blood samples and at this point attrition rate was about 21%.

In addition, the nurse measured anthropometric indices including weight, height, body mass index, and waist circumference. Weight was measured using calibrated digital scale while patients were in minimal clothing and height was measured by a standard wall-height-gauge while subjects were standing without shoes and in standard position. Waist circumference was measured using a non-stretchable tape measure at the middle space between the lowest rib and the iliac crest over minimal clothing at the end of exhalation. They also recorded clinical symptoms relating to heart disease including heart palpitations, shortness of breath and chest pain in children and adolescents.

**Definition of the metabolic syndrome components**

In this study we used the most consensus diagnostic criteria for the metabolic syndrome in children and adolescents from the International Diabetes Federation (IDF) (3) as follows: For children 6 to <10 yr old, the metabolic syndrome cannot be diagnosed, only ≥90th percentile of waist circumference (WC) was considered for abdominal (central) obesity. We used the national age and gender specified cut-offs according to CASPIAN study (10). For children 10 to <16 yr old, the metabolic syndrome diagnosed with abdominal obesity (national cut-offs for≥90th percentile of waist circumference (10)) and the presence of two or more of other criteria for metabolic syndrome i.e. hypertriglyceridemia (≥150mg/dl), low HDL-chol. (<40mg/dl), high blood pressure (systolic BP≥130 or diastolic BP≥85 mm Hg), increased plasma glucose (FPG≥100mg). For children older than 16, the diagnosis of metabolic syndrome included abdominal obesity (defined as waist circumference ≥ 90th percentile with ethnicity age and gender specified cut-offs for Iranians (10)) and the presence of two or more metabolic syndrome criteria’s i.e. hypertriglyceridemia (≥150mg/dl), low HDL-chol. (<40mg/dl in males and <50mg/dl in females), high blood pressure (systolic BP≥130 or diastolic BP≥85 mm Hg), increased plasma glucose FPG≥100mg) or previously diagnosed T2DM.

We defined overweight as ≥95th percentile of national age and sex specified cut-offs for BMI(11), at risk for overweight as ≥85th to <95th percentile of national age and sex specified cut-offs for BMI, and normal weight was defined as <85th percentile of national age and sex specified cut-offs for BMI(12). For feasibility of comparisons between studies, we also used specified cut-off points of BMI for age and gender-based on Centers for Disease Control and Prevention 2000 (13).

**Statistical analysis**

All data were analyzed using SPSS (IBM Corp. Released 2010. IBM SPSS Statistics for Windows, Ver. 19.0. Armonk, NY: IBM Corp) and STATA version 11 (StataCorp. 2009. Stata Statistical Software: Release 11. College Station, TX: StataCorp LP.). The prevalence of metabolic syndrome in children above 10 yr was measured in subgroups of gender, and BMI categories including normal weight (<85th percentile), at risk for overweight (85th to <95th percentile), and overweight (95th ≤ percentile). We used the Chi-square test to compare the prevalence of meta-
bolic syndrome between subgroups. We also performed the logistic regression analysis to define potential predictors of the metabolic syndrome in children and adolescents above 10 yr old. In children younger than 10 yr old, the only prevalence of abdominal obesity was reported instead of the metabolic syndrome. The $P$-values below the 0.05 were considered as statistical significance.

**Ethics Statement**

This study was approved by the ethics committee of National Institute for Medical Research Development (ethical code: IR.NIMAD.REC.1395.001) and Shahid Sadoughi University of Medical Sciences in Yazd, Iran (IR.SSU.Rec.1396.49). The consent was taken from children and adolescents to participate in this study. The consent completed for participants younger than 15 yr of age by their parent and for participants aged 15 to 18 yr by parents or by the adolescents. Independent of age, all children and adolescents were assented to participate. All information about children and adolescents and their families remained confidential.

**Results**

The participants of this study included 456 male (44.1%) and 579 female (55.9%). Of them, 402 (38.8%) were 6 to 9 yr and 633 (61.2%) were 10 to 18 yr old. The mean age of participants was 11.3 yr ±3.8, the mean BMI 19.5 kg/m$^2$ ± 5.0 (Table 1).

| Variable                  | Boys (mean±SD) | Girls (mean±SD) | Total (mean±SD) |
|---------------------------|----------------|-----------------|-----------------|
| Age (yr)                  | 11.6 ± 3.7     | 11.0 ± 3.9      | 11.32±3.8       |
| Height (cm)               | 147.7±22.3     | 144.4±18.1      | 145.8±20.1      |
| Weight (kg)               | 46.3±23.5      | 42.0±17.4       | 43.9±20.4       |
| BMI (kg/m$^2$)            | 19.8±5.5       | 19.2±4.6        | 19.5±5.0        |
| Waist circumference (cm)  | 71.4±16.3      | 68.7±12.3       | 69.9±14.3       |
| Systolic blood pressure (mmHg) | 102.1±14.4 | 98.8±11.3       | 100.3±12.9      |
| Diastolic blood pressure (mmHg) | 68.5±10.0 | 69.3±10.0       | 69.0±10.0       |
| TG (mg/dl)                | 87.9±46.2      | 88.6±37.2       | 88.3±41.6       |
| HDL (mg/dl)               | 40.6±13.8      | 42.5±13.4       | 41.6±13.6       |
| FBS (mg/dl)               | 89.5±10.0      | 87.4±8.4        | 88.4±9.2        |

The most prevalent component of the metabolic syndrome in our study was low HDL-cholesterol (56.2%) followed by abdominal obesity (27.8%). All of the metabolic syndrome components were highly associated with body mass index (BMI) (Table 2). According to IDF definition for metabolic syndrome, the diagnosis is valid in adolescents of 10 yr or older. In adolescents of our study with 10 to 18 yr old, the prevalence of the metabolic syndrome was 7.6% (9.4% in boys and 6.0% in girls). Alternatively, the prevalence of abdominal obesity has been reported in children younger than 10 yr; (13.2% abdominal obesity in boys vs. 24.7% in girls). Then, we have performed subgroup analysis according to BMI categories (both national and CDC cut-offs) of normal weight, at risk for overweight and overweight and we found that prevalence of the metabolic syndrome rises with BMI (Table 3). Afterwards, we entered the variables into the logistic regression model. The chance of having metabolic syndrome in male adolescents older than 10 yr was 1.6 times more compared to females (95% CI: 0.8 to 2.9). Moreover, ORs of the metabolic syndrome in adolescents older than 10 yr, respectively, were 1.7 and 5.9 for subjects at risk for overweight and overweight. The OR for the metabolic syndrome in those with a family history of heart disease was 1.58 (95% CI: 0.80 to 3.07) compared to those without the family history of heart disease.
Increased plasma glucose, high blood pressure (systolic BP≥130 or diastolic BP≥85 mm Hg), triglycerideemia (≥150mg/dl), low HDL-chol. (<40mg/dl in males and <50mg/dl in females), increased plasma glucose FPG≥100mg/dl, hyper-triglyceridemia (≥150mg/dl), low HDL-chol. (<40mg/dl in males and <50mg/dl in females), high blood pressure (systolic BP≥130 or diastolic BP≥85 mm Hg), increased plasma glucose FPG≥100mg/dl or previously diagnosed T2DM.

### Table 2: Prevalence of the individual components of metabolic syndrome among children and adolescents of Yazd district, Iran, 2016-17

| Variable                        | Abdominal obesity N(%) | High blood pressure N(%) | High blood glucose N(%) | Low HDL-c N(%) | High TG N(%) |
|---------------------------------|-------------------------|--------------------------|-------------------------|----------------|--------------|
| **Sex**                         |                         |                          |                          |                |              |
| Total                           | 257(27.8)               | 76 (8)                   | 71 (9.1)                 | 438(56.2)      | 58 (7.4)     |
| Male                            | 121(27.4)               | 37 (8.9)                 | 41 (11.2)                | 209(57.3)      | 29 (7)       |
| Female                          | 136(28.1)               | 39 (7.3)                 | 30 (7.2)                 | 229(55.2)      | 29 (7)       |
| **BMI percentile**              |                         |                          |                          |                |              |
| (Iranian cut-off points)        |                         |                          |                          |                |              |
| Normal (<85th)                  | 21(3.5)                 | 35(7.6)                  | 25(4.5)                  | 236(51.5)      | 23(5)        |
| At risk (85th to <95th)         | 72(40.7)                | 9 (6.8)                  | 14(8.6)                  | 73(55.3)       | 12(9.1)      |
| Overweight (95th ≤)             | 148(83.3)**             | 26(14.9)*                | 31(14.7)**               | 120(69)**      | 22(12.6)*    |

**Significant at P≤0.0001 level; using Pearson Chi-Square test (Compared with normal weight and at-risk for overweight subjects)/** * Significant at P≤0.05 level; using Pearson Chi-Square test (Compared with normal weight and at-risk for overweight subjects)

### Table 3: Prevalence of the metabolic syndrome or abdominal obesity among children and adolescents in Yazd district, Iran, 2016-17

| Variable                        | N of valid cases (excluding missing) | N (%) of subjects with MetS* | P (Chi-Square test) | N of valid cases (excluding missing) | N (%) of subjects with abdominal obesity* | P (Chi-Square test) |
|---------------------------------|--------------------------------------|-----------------------------|---------------------|--------------------------------------|------------------------------------------|---------------------|
| < 10 years sex                  |                                      |                             |                     |                                      |                                          |                     |
| Male                            | 153                                  | -                           |                     | 152                                  | 20 (13.2)                                 | 0.006               |
| Female                          | 231                                  | -                           |                     | 231                                  | 57(24.7)                                  |                     |
| Total                           | 386                                  | -                           |                     | 383                                  | 77(20.1)                                  |                     |
| 10 years ≤ sex                  |                                      |                             |                     |                                      |                                          |                     |
| Male                            | 278                                  | 26(9.4)                     | 0.1                 | 290                                  | 101(34.8)                                 | 0.2                 |
| Female                          | 317                                  | 19(6.0)                     |                     | 325                                  | 99(30.5)                                  |                     |
| Total                           | 595                                  | 45(7.6)                     |                     | 615                                  | 200(32.5)                                 |                     |
| < 10 years BMI percentile*      |                                      |                             |                     |                                      |                                          |                     |
| Normal (<85th)                  | 238                                  | -                           |                     | 238                                  | 3(1.5)                                    | ≤0.001              |
| At risk (85th to <95th)         | 65                                   | -                           |                     | 66                                   | 12(18.2)                                  |                     |
| Overweight (95th ≤)             | 77                                   | -                           |                     | 79                                   | 62(78.5)                                  |                     |
| Total                           | 380                                  | -                           |                     | 383                                  | 77(20.1)                                  |                     |
| 10 years ≤ BMI percentile*      |                                      |                             |                     |                                      |                                          |                     |
| Normal (<85th)                  | 357                                  | 0(0.0)                      | ≤0.001              | 362                                  | 18(5)                                    |                     |
| At risk (85th to <95th)         | 100                                  | 10(10)                      |                     | 111                                  | 60(54.1)                                  | ≤0.001              |
| Overweight (95th ≤)             | 139                                  | 35(26.9)                    |                     | 142                                  | 122(85.5)                                 |                     |
| Total                           | 587                                  | 45(7.7)                     |                     | 615                                  | 200(32.5)                                 |                     |
| < 10 years BMI percentile†      |                                      |                             |                     |                                      |                                          |                     |
| Normal (<85th)                  | 277                                  | -                           |                     | 278                                  | 6(2.2)                                    | ≤0.001              |
| At risk (85th to <95th)         | 48                                   | -                           |                     | 48                                   | 21(43.8)                                  |                     |
| Overweight (95th ≤)             | 55                                   | -                           |                     | 57                                   | 50(87.7)                                  |                     |
| Total                           | 380                                  | -                           |                     | 383                                  | 77(20.1)                                  |                     |
| 10 years ≤ BMI percentile†      |                                      |                             |                     |                                      |                                          |                     |
| Normal (<85th)                  | 402                                  | 1(0.2)                      | ≤0.001              | 412                                  | 33(8)                                     | ≤0.001              |
| At risk (85th to <95th)         | 120                                  | 19(15.8)                    |                     | 131                                  | 99(75)                                     |                     |
| Overweight (95th ≤)             | 65                                   | 25(38.5)                    |                     | 72                                   | 68(94.4)                                   |                     |
| Total                           | 587                                  | 45(7.7)                     |                     | 615                                  | 200(32.5)                                 |                     |

*Using Iranian data set for BMI percentiles
† Using CDC2000 data set for BMI percentiles
¶ For children 6 to <10 yr old, which according to IDF the diagnosis of metabolic syndrome cannot be made, instead, only ≥90th percentile of waist circumference with national age and gender specified cut-offs

The metabolic syndrome diagnosed for children 10 to <16 yr old, with abdominal obesity (national cut-offs for≥90th percentile of waist circumference) and the presence of two or more of other criteria for metabolic syndrome i.e. hyper-triglyceridemia (≥150mg/dl), low HDL-chol. (<40mg/dl), high BP (systolic BP≥130 or diastolic BP≥85 mm Hg), increased plasma glucose FPG≥100mg/dl. For children older than 16, abdominal obesity (wc ≥ 90th percentile with ethnicity age & gender specified cut-offs for Iranians and the presence of two or more metabolic syndrome criteria’s i.e. Hyper-triglyceridemia (≥150mg/dl), low HDL-chol. (<40mg/dl in males and <50mg/dl in females), high blood pressure (systolic BP≥130 or diastolic BP≥85 mm Hg), increased plasma glucose FPG≥100mg/dl or previously diagnosed T2DM.

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Table 4: Variables associated with metabolic syndrome upon logistic regression analysis

| Variable                          | Univariate analysis | Multivariate analysis |
|-----------------------------------|---------------------|-----------------------|
|                                  | Crude OR (95% CI)   | P-value               |
| Gender                           | 1.6 (0.8 to 2.9)    | 0.12                  |
| Family history of heart disease  | 1.58 (0.80 to 3.07) | 0.18                  |
| Region of living                 | 1.20 (0.29 to 5.54) | 0.72                  |
| Subjects at risk for overweight  | 1.7 (0.41 to 6.7)   | 0.33                  |
| Overweight subjects              | 5.9 (1.3 to 8.1)    | <0.001                |
|                                  | 1.9 (0.21 to 5.1)   | 0.99                  |

CI: Confidence Interval
* adjusted by gender, Family history of heart disease, Region of living, and age

The OR for the metabolic syndrome in the urban regions was 1.20 (95% CI: 0.29 to 5.54) compared to the rural regions. In multivariate analysis after adjusting for gender, Family history of heart disease, Region of living, and age none of the variables remained in the model and the ORs of BMI categories were not significant (Table 4).

Discussion

In this study, based on IDF criteria, the prevalence of the metabolic syndrome in children and adolescents aged 10 to 18 yr was 7.6% (9.4% in boys and 6% in girls) which is relatively high. Moreover, in children below 10 yr prevalence of abdominal obesity was even higher (20.1%). This is the first study reporting the prevalence of metabolic syndrome and abdominal obesity in children and adolescents in Yazd Greater Area and one of the few province-wide studies in Iran. Worldwide, investigators have reported different prevalence rates using different diagnostic criteria. Using modified diagnosis criteria of ATP III, the prevalence of metabolic syndrome was reported in American adolescents to be 9.2% (5). The prevalence rate of 10.1% in 12 to 19 yr age group based on 2001–2010 National Health and Nutrition Examination Survey was reported in the USA (14). While usually much lower prevalence rates have been reported using IDF criteria. Different prevalence rates were reported for the metabolic syndrome in the same population (0.9% using IDF criteria versus 11.4% using de Ferranti-modified ATP III criteria) (15). While 2.1% of metabolic syndrome were reported among Canadian adolescents aged 10 to 18 yr using IDF criteria (4).

There are a few studies investigated the prevalence of metabolic syndrome in children and adolescents in Iran. The Age-modified standards of the National Cholesterol Education Program-Adult Treatment Panel III (ATP III) criteria were used in the context of Tehran Lipid and Glucose Study. They have reported 10% of metabolic syndrome in district 13 of Tehran (16). In the framework of the CASPIAN study (2003-2004) on children and adolescents based on ATP III criteria have reported 14% of metabolic syndrome (14% in boys and 13% in girls) (17). In Ahvaz, southwest of Iran, the prevalence of metabolic syndrome has reported to be 9% (11% in boys and 7% in girls) based on modified ATP III criteria (18).

In Isfahan, 4.8% of metabolic syndrome were reported in children and adolescents using the IDF criteria (19). In framework of the Isfahan Healthy Heart Program performed from 2000 to 2007, using IDF criteria in Arak and Isfahan provinces (center of Iran) have reported the prevalence of 2.8% among girls and 6.6% among boys, while metabolic syndrome prevalence rates according to de Ferranti criteria were 14.4% among boys and 10.9% among girls (20). It also reported 5.2% metabolic syndrome in urban areas and 3.3% in rural areas using IDF criteria. Alike us, almost all of the previous reports studied, have found that metabolic syndrome mostly occurs in boys, and in urban regions (6, 14, 16-18, 20). Furthermore, some revealed gender role in this regard (21). Our study is in accord with other studies reported the abdominal obesity and low HDL-cholesterol are among the most prevalent risk factors of metabolic syndrome in children and adolescents (16, 22, 23). Poor dietary...
habits, low physical activity or genetic characteristics of the study population may cause this. We have observed variations in the prevalence of metabolic syndrome in adolescents. Different definitions of the metabolic syndrome and different cut-off points explain for some of the diversity observed in the prevalence of this syndrome in different districts. Moreover, diversity in lifestyle, domestic dietary habits and different levels of physical activity can be the explanation of this diversity. Previous domestic studies reported higher metabolic syndrome have used ATP III criteria which are very similar to IDF criteria except for Rigorous cut-offs for hypertriglyceridemia (e.g. Triglyceride ≥ 110 mg/dl in ATP III vs. Triglyceride ≥ 150 mg/dl in IDF). i.e. the ATP III criteria are more inclusive.

In our study, chance of having metabolic syndrome is dramatically increased in overweight adolescents. Independent of kind of the diagnosis criteria, all previous studies have also reported such observation. Some pieces of evidence have noted that body weight disorders in childhood can be developed to eating disorders, adulthood obesity, adulthood metabolic syndrome and its related psychiatric and somatic disorders in later life (24-27). This emphasis on the priority of action against childhood obesity by family and community nutritional education and more physical activity in favor of weight management (28).

**Limitations**

Lack of consensus about national growth charts and cut-off points make it hard to pick-up the best study. Furthermore, due to cross-sectional nature of this study, we can’t infer the causal relationships.

**Conclusion**

The prevalence of metabolic syndrome among children and adolescents in Yazd province is high compared to other studies. Low HDL-cholesterol levels and abdominal obesity were the most common component of metabolic syndrome. The abdominal obesity was mostly observed in girls but clustering it with other components of metabolic syndrome especially lower HDL-c in males caused the overall prevalence rate of the metabolic syndrome to be higher in boys. Family history of heart disease, living in urban areas, having higher BMI and being the male gender were the main determinants of metabolic syndrome in adolescents. Hence, the researchers and health policy makers should focus to solve the puzzle of low HDL-cholesterol and high abdominal obesity in children and adolescents especially in high-risk subgroups of overweight, urban residents, and boys.

**Ethical considerations**

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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**Conflict of interests**

None

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