Mal J Nutr 16(2) : 207 - 217, 2010

Metabolic Syndrome Based on IDF Criteria in a Sample of Normal Weight and Obese School Children

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ABSTRACT

Metabolic syndrome was once reported only in adults but is now occurring more frequently in children. This study compared the incidence of metabolic syndrome and its components among normal and obese children using the 2007 International Diabetes Federation (IDF) pediatric definition for metabolic syndrome. Subjects comprised 78 school children aged 8-10 years, with 34 obese and 44 normal weight children. Body weight, height, and waist circumference (WC) were measured and body mass index was calculated. Clinical profiles measured included fasting blood glucose, triglyceride, HDL cholesterol, LDL cholesterol, total cholesterol, and blood pressure. Metabolic syndrome (MS) was defined using the 2007 IDF pediatric criteria. Obese subjects had a significantly ($p<0.001$) higher mean BMI (26.0 ± 3.6 kg/m^2) compared to normal weight subjects (15.1 ± 0.8 kg/m^2). Only one obese subject (1.3% of subjects) had metabolic syndrome based on the IDF definition, but all obese subjects had at least one component of metabolic syndrome. In comparison, no normal weight subjects had metabolic syndrome and only 9.1% of normal weight subjects had at least one component of metabolic syndrome. The most common component was central obesity, observed in 43.6% of subjects having WC equal to or greater than the 90th percentile. In concurrence with central obesity as the core feature of the IDF criteria, WC showed the strongest correlation with indicators of obesity such as BMI ($r=0.938$, $p<0.001$), fat mass ($r=0.912$, $p<0.001$) and fat-free mass ($r=0.863$, $p<0.001$). We conclude that the problem of metabolic syndrome is more prominent among obese children, although the incidence of MS as defined by the 2007 pediatric IDF criteria, is low in this population (1.3%).

Keywords: IDF Criteria, metabolic syndrome, normal weight children, obese children

INTRODUCTION

Metabolic syndrome (MS) is defined as a cluster of metabolic abnormalities including insulin resistance, hyperinsulinemia, glucose intolerance, dyslipidemia and hypertension that are associated with increased cardiovascular morbidity and mortality and risk for Type 2 diabetes (Reaven, 1988). Beyond these conditions, individuals with MS are also susceptible to polycystic ovary syndrome, fatty liver, cholesterol gallstones, asthma, sleep apnea, and some forms of cancer (Grundy *et al.*, 2004).

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The prevalence of MS had been reported more frequently among overweight children (Cook *et al*., 2003; Yoshinaga *et al*., 2005; Lee, Bacha & Arslanian, 2006). With increasing rates of childhood obesity, researchers have a growing interest in MS among children and adolescents. Of particular interest to Malaysia, a recent report from a nation-wide survey revealed a rise in the prevalence of overweight and obesity among children aged 6-12 years old; from 20.7% in 2001/2002 to 26.5% in 2008/2009 (Ismail *et al*., 2009).

However, studies among paediatric populations have used inconsistent and arbitrary definitions of MS. The prevalence of MS in children strongly depends on the chosen definition. For example, a large difference in prevalence is observed when child specific cut-offs were chosen (39-59% pre-valence) versus adult MS definitions (0-4% prevalence) (Golley *et al*., 2006).

The International Diabetes Federation (IDF) recently proposed a definition of MS for use in children and adolescents (Alberti, Zimmet & Shaw, 2007). Similar to the adult MS definition developed by IDF in 2005, the main focus of this new definition is central obesity characterised by waist circumference and two or more of the following four factors: elevated triglycerides, reduced HDL cholesterol, dysglycemia and high blood pressure (Alberti *et al*., 2007). The IDF definition was proposed for use in children aged 10-16 years. The IDF did not recommend the diagnosis of MS among pre-pubertal children unless the child has a family history of MS, type 2 diabetes mellitus, dyslipidaemia, cardiovascular disease, hypertension or obesity. However, parents themselves may be unaware of their risk, and with increasing global prevalence of childhood obesity, it is valuable to screen for MS risk factors at an earlier age.

Furthermore, prevention of metabolic syndrome should begin at an early age as children have higher motivation and are strongly influenced by family regarding behaviour change (AAP, 2006). Thus, the aim of this study was to compare the incidence of MS between obese and normal weight school children aged 8-10 years old using the IDF paediatric definition of MS.

METHODOLOGY

A total of 932 school children were screened from three primary schools at Keramat Zone, Kuala Lumpur. The three schools were selected from a pool of eight national primary schools with more than 1000 students in Keramat Zone. Screening indicated that 17.9 % were obese, 13.5% were overweight and 61.1 % were normal weight using the WHO (2007) BMI-for-age growth reference. Of these children, 89 were enrolled after obtaining written, informed consent from their parents. The inclusion criteria for participation were children aged 8 to 10 years, healthy at the time of study, and free from medication, diseases or conditions that may affect growth or body composition. Forty subjects with BMI-for-age at +2SD or more were categorised as obese whereas 49 subjects with BMI-for-age between -1SD and median were categorised as normal weight. The study protocol was approved by the Medical Research and Ethics Committee of Universiti Kebangsaan Malaysia. Data were collected from July to November 2008. Each participant was required to complete physical and biochemical measurements at their respective schools, and a socio-demographic information questionnaire was completed by their parents.

With regard to physical characteristics, height was measured using a SECA Bodymeter 208 (SECA, Germany) to the nearest 0.1 cm, and weight was measured to the nearest 0.1 kg using a Tanita digital scale Model TBF-300 (Tanita Corporation, Japan). Body mass index (BMI) was calculated and subjects were categorised into obese and normal weight categories based on reference to the WHO (2007) growth reference for children 5-19 years of age. Fat percentage, lean body mass and total body water were

measured using a bioelectrical impedance device Impedimed model IMP DF50 (Impedimed Limited, Australia). Waist circumference was measured midway between the lateral border of the ribs and the uppermost lateral iliac crest using a tape measure to the nearest 0.1 cm. Blood pressure (BP) was measured in a sitting position with a standard manual sphygmomanometer and size-appropriate cuff. Systolic BP was determined by the onset of the 'tapping' korotkoff sound while diastolic BP was defined as the 5th phase of the korotkoff sound.

All children and their parents received specific written instructions on preparations for clinical measurements. Children were asked to fast overnight, and blood sampling was conducted on the following morning. Venous blood was drawn for analysis of plasma lipid and glucose concentrations. Fasting plasma glucose, serum total cholesterol and triglycerides were determined using enzymatic colorimetric methods, HDL cholesterol was determined with enzymatic elimination method and LDL cholesterol was calculated using the Friedewald formula. All parameters were measured by an Advia 2400 Clinical Chemistry Auto Analyser (Siemens Medical Solution, USA).

Participants were defined as having MS based on the paediatric definition of the International Diabetes Federation (Alberti *et al*., 2007). According to these definitions, an individual has MS if he/she has increased central adiposity and at least two of the following criteria: (1) triglyceride ≥1.7 mmol/L (≥150 mg/dL), (2) HDL cholesterol <1.03 mmol/L (<40 mg/dL), (3) systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg, (4) fasting plasma glucose ≥5.6 mmol/L (≥100 mg/dL) or previous diagnosis of Type 2 diabetes mellitus. For all participants, central obesity was defined as equal to or above 90th percentile of WC based on Hong Kong WC percentile charts for children (Sung *et al*., 2008).

Statistical analysis was performed using Statistical Package for the Social Sciences version 11.0 (SPSS, Inc., Chicago, IL, USA). Means and standard deviation were used to summarise variables. Between the two groups, differences in metabolic profiles, physical characteristics, socio-demographic characteristics and risk of MS were tested using parametric (independent *t*-tests, chi square test) and nonparametric tests (Mann-Whitney U test). Bivariate correlation analysis was performed using the Spearman correlation. The level of significance was set at $p<0.05$.

RESULTS

Of the 89 enrolled subjects, only 78 subjects had complete data and were included in data analysis. The remaining 11 subjects were either absent during the measurement day or blood samples were not obtained for various reasons.

Table 1 shows the socio-demographic and physical characteristics of the participants from both groups. The obese group (9.2 ± 0.9 years) was not significantly older than the normal weight group (9.2 ± 0.8 years). Although the obese group was more financially affluent than the normal weight group, the difference was not statistically significant ($p>0.05$). Similarly, no significant difference was observed for other socio-demographic variables. However, the obese group had significantly higher values for all physical characteristic variables compared to the normal weight group ($p<0.001$).

Based on clinical profiles, the obese group had higher diastolic blood pressure (DBP), systolic blood pressure (SBP), LDL cholesterol, triglycerides (TG) and total cholesterol compared to the normal weight group, but significant differences ($p<0.05$) between the two study groups were only

Table 1. Characteristics of the subjects according to weight category (mean ± SD)

Variables	*Obese(N=34)*	*Normal(N=44)*
Sociodemography		
Age (years)	9.2 ± 0.9	9.2 ± 0.8
Family income (RM)	3594 ± 3398	2765 ± 2232
Number of siblings	3.5 ± 1.4	4.1 ± 1.3
Number of family members	5.6 ± 1.4	6.0 ± 1.2
Birth weight (kg)	3.3 ± 0.5	3.2 ± 0.4
Physical characteristics		
Height (cm)	137.6 ± 6.1***	131.0 ± 7.2
Weight (kg)	49.4 ± 9.6***	25.9 ± 3.5
BMI (kg/m^2) †	26.0 ± 3.6***	15.1 ± 0.8
Fat mass (kg)	20.0 ± 5.7***	4.6 ± 2.0
Fat-free mass (kg)	29.4 ± 4.5	21.3 ± 2.5***
Waist circumference (cm) †	79.9 ± 8.8***	53.7 ± 3.4
Hip circumference (cm) †	87.5 ± 7.4***	66.1 ± 3.6
Biochemical characteristics		
Diastolic blood pressure (mmHg) †	65.0 ± 8.5***	57.4 ± 4.9
Systolic blood pressure (mmHg)	108.6 ± 10.4***	93.3 ± 6.0
HDL cholesterol (mmol/L) †	1.2 ± 0.2***	1.4 ± 0.2
LDL cholesterol (mmol/L)	3.2 ± 0.7	3.0 ± 0.6
Fasting blood glucose (mmol/L)	4.9 ± 0.3	5.0 ± 0.3
Triglycerides (mmol/L) †	1.1 ± 0.5*	0.9 ± 0.4
Total cholesterol (mmol/L) †	5.0 ± 0.8	4.9 ± 0.8

*p<0.05, *** p<0.001 significant difference between groups; independent *t*-test.
† Mann-Whitney U test.

observed for DBP, SBP, and triglycerides. Additionally, HDL cholesterol was significantly lower in the obese group than in the normal weight group (p<0.05). Surprisingly, the normal weight group had a slightly higher mean fasting blood glucose (5.0 ± 0.3 mmol/L) compared to the obese group (4.9 ± 0.3 mmol/L, p>0.05) (Table 1). Further analysis based on gender found that only fasting blood glucose was significantly different between normal weight boys and girls (Table 2).

Among the individual components of MS, a large waist circumference was the most common. All obese subjects had central obesity, whereas none of the normal weight subjects were centrally obese. This was followed by high triglycerides (11.1%), low HDL cholesterol (6.7%) and high fasting blood glucose (6.7%). As with absolute fasting blood glucose values, the frequency of high fasting blood glucose was also higher in normal weight group (4.5%). Only one subject from the obese group had MS based upon the IDF pediatric definition. However, 82.4% of obese subjects had at least one component of MS. In contrast, only 9.1% of normal weight subjects had at least one component (Table 3).

Several components of MS showed a significant positive relationship with obesity indicators (fat mass and BMI), except HDL cholesterol, LDL cholesterol and fasting blood glucose (p<0.001) (Table 4). Similar correlations were also observed between fat free mass and the various components of MS.

Table 2. Comparison of metabolic components between groups (mean ± SD)

Variables	*Obese*			*Normal*		
	Boy (n=20)	*Girl (n=14)*	*p*	*Boy (n=22)*	*Girl (n=22)*	*p*
Diastolic BP (mmHg)	64.3 ± 8.0	66.0 ± 9.4	0.551	64.3 ± 8.0	66.0 ± 9.4	0.715†
Systolic BP (mmHg)	108.7 ±10.6	108.6 ±10.6	0.972	93.3 ± 6.6	93.2 ± 5.4	0.941
HDL cholesterol (mmol/L)	1.2 ± 0.3	1.3 ± 0.7	0.495	1.5 ± 0.3	1.4 ± 0.2	0.414†
LDL cholesterol (mmol/L)	3.2 ± 0.6	3.2 ± 0.8	0.992	3.1 ± 0.7	3.0 ± 0.6	0.923
Fasting blood glucose (mmol/L)	5.0 ± 0.3	4.9 ± 0.3	0.350	5.1 ± 0.3	4.8 ± 0.3	0.019†
Triglycerides (mmol/L)	0.9 ± 0.4	1.3 ± 0.7	0.103	0.8 ± 0.3	1.0 ± 0.6	0.206†
Total cholesterol (mmol/L)	4.9 ± 0.8	5.1 ± 0.9	0.429	4.9 ± 0.9	4.9 ± 0.6	0.844†

p = significant difference between gender, independent *t*-test.
† Mann-Whitney U test.

Table 3. Incidence and clustering of metabolic syndrome components according to the IDF paediatric definition (expressed as number (%))

Components	*Obese (N=34)*	*Normal (N=44)*	*Overall*
Individual components of metabolic syndrome			
Low HDL cholesterol	2 (5.9)	1 (2.3)	3 (6.7)
High triglycerides	4 (11.8)	1 (2.3)	5 (11.1)
High waist circumference	34 (100.0)	0	34 (75.6)
High blood pressure	0	0	0
High fasting blood glucose	1 (2.9)	2 (4.5)	3 (6.7)
Metabolic syndrome	1 (2.9)	0	1 (1.3)
Number of components			
0	0	40 (90.9)	40 (51.3)
1	28 (82.4)	4 (9.1)	32 (41.0)
2	5 (14.7)	0	5 (6.4)
3	1 (2.9)	0	1 (1.3)
4	0	0	0
5	0	0	0

The metabolic syndrome is defined as having central obesity (waist circumference ≥ 90th percentile) plus at least two of the following criteria: (1) triglyceride ≥ 1.7 mmol/L (≥150 mg/dL); (2) HDL cholesterol <1.03 mmol/L (<40 mg/dL); (3) systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 85 mmHg; and (4) fasting plasma glucose ≥ 5.6 mmol/L (≥ 100 mg/dL).

Participants with a self-reported family history of diabetes, cardiovascular disease, hypertension or hypercholesterolemia were at 2.4 times (95% CI: 0.93-6.341) higher risk of developing MS (Figure 1). Those with a family history of these diseases had a significantly higher mean diastolic blood pressure (p<0.05) (Table 5). Of the subjects who reported a family history of these diseases (34.6% of subjects), the majority had a family history of high blood pressure (28.2%) and diabetes (23%), and 5.1% reported a family history of all the mentioned diseases. The only subject that had MS in

Table 4. Relationship between metabolic components and obesity indicators

Variables	*Correlation Coefficients (r)*		
	Fat mass (kg)	*BMI*	*Fat-free mass (kg)*
Diastolic blood pressure (mmHg)	0.521 ***	0.505 ***	0.462 ***
Systolic blood pressure (mmHg)	0.687 ***	0.682 ***	0.732 ***
HDL cholesterol (mmol/L)	-0.514 ***	-0.430 ***	-0.371 **
Fasting blood glucose (mmol/L)	-0.035	0.081	0.159
Triglycerides (mmol/L)	0.234 *	0.166	0.247 *
Waist circumference	0.912 ***	0.938 ***	0.863 ***
LDL cholesterol (mmol/L)	-0.007	-0.024	0.016

* $p<0.05$, ** $p<0.01$, *** $p<0.001$, Spearman correlation.

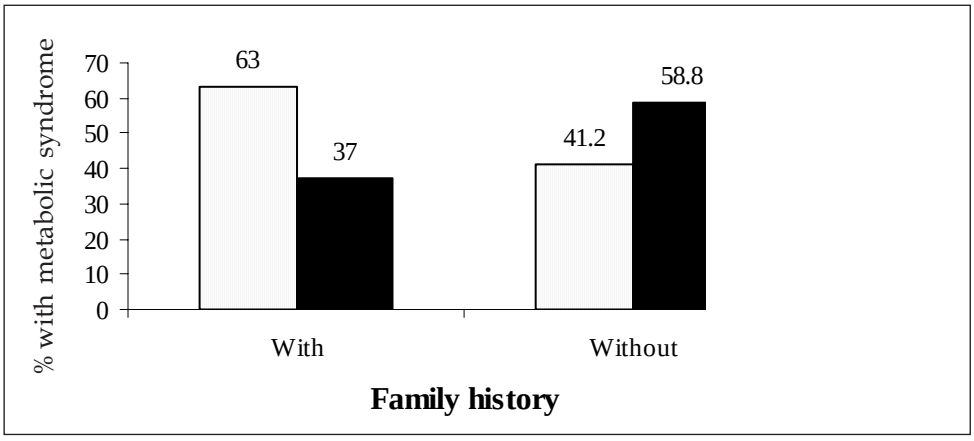

Figure 1. Risk of metabolic syndrome between groups with and without family history of diabetes mellitus, cardiovascular disease, high blood pressure and/or hypercholesterolemia. Subjects were categorised as at-risk of metabolic syndrome if they had at least one component of metabolic syndrome. Family history was based on self-report. Subjects who were unaware of family history for the above-mentioned diseases were categorised as 'without' family history.

this study (1.3% of subjects) reported having a family history of both diabetes and hypertension.

DISCUSSION

The incidence of MS among the participants was very low. Only one participant had MS as defined by central obesity, high triglycerides and low HDL cholesterol. Only the obese group had subjects with two or more MS components, with no significant gender-related difference ($p>0.05$; Pearson chi square). However, the prevalence of MS varies depending on the definition used. Among a similar age group of African American pre-adolescent females, prevalence of MS was reported to range from 0.4% to 23.0%, as defined by the National Cholesterol Education Program (NCEP)

Table 5. Comparison of metabolic profiles between groups with and without family history of diabetes mellitus, cardiovascular disease, high blood pressure and/or hypercholesterolemia

Variables	*With family history (n=27)*		*Without family history (n=51)*	
	Mean	*(SD)*	*Mean*	*(SD)*
Diastolic blood pressure (mmHg)	63.1	(8.5)	59.4 *	(6.9)
Systolic blood pressure (mmHg)	102.5	(10.1)	98.6	(11.6)
HDL cholesterol (mmol/L)	1.3	(0.2)	1.4	(0.3)
Fasting blood glucose (mmol/L)	5.0	(0.4)	4.9	(0.3)
Triglycerides (mmol/L)	1.1	(0.7)	0.9	(0.3)
Waist circumference	63.1	(14.4)	68.9 *	(14.2)

*$p<0.05$ significant difference between groups with and without family history; Mann-Whitney U test.

Adult Treatment Panel III, and from 0% to 15.3%, as defined by the World Health Organization criteria (Chi *et al*., 2006).

Various studies used criteria adapted from the NCEP but differ in the individual MS constituents measured and threshold levels (Cook *et al*., 2003; Yoshinaga *et al*., 2005). The most frequently applied definition of MS among children and adolescents was the definition by Cook *et al*. (2003) which was adapted from the NCEP (Ford & Li, 2008). Hence, the lack of a universally acceptable and applicable definition of MS makes it difficult to compare prevalence of MS across studies and diverse populations.

The first attempt to create a standardised paediatric definition of MS was presented by IDF in 2007 (Alberti *et al*., 2007). Ford *et al*. (2008) appeared to be the first to use this IDF paediatric definition. Based on the data from the National Health and Nutrition Examination Survey, the prevalence of MS was reported as the lowest at 4.5% compared with the other paediatric studies conducted in U.S.

The IDF paediatric definition of MS emphasises the key role of central obesity. Central obesity is an essential and not an optional component of MS (Alberti & Zimmet, 1998). In view of this, the IDF definition may under-estimate the number of normal weight individuals who are at higher risk for developing MS. Even though none of our normal weight subjects had central obesity, almost one in ten subjects exceeded the criterion for having one component of MS even at this young age.

Secondly, IDF suggested single cut-off values for all the components, except waist circumference. This contradicts with the multiple cut-off values dependent on gender, age, and ethnicity adopted in most MS studies involving children and adolescents (Cook *et al*., 2003; Cruz & Goran, 2004; Weiss *et al*., 2004).

Among all the components, one of the most prominent features of the IDF paediatric definition is the cut-off value for blood pressure at 130 mmHg systolic and 85 mmHg diastolic. Other studies with children or adolescents used a percentile chart adjusted for gender and height as recommended by National High Blood Pressure Education Program (NHBPEP) (Cook *et al*., 2003; Cruz & Goran, 2004; Weiss *et al*., 2004). Based on the cut-off value proposed by IDF (2007), none of the participants in this study had high blood pressure. In contrast, 15.4% had systolic blood pressure and 9.0% had diastolic blood pressure above the 90th percentile based on the US blood pressure percentiles adjusted

for age, gender and height (NHBPEWG, 1996).

Using this IDF (2007) definition, the determination of central obesity is highly dependent on the ethnic-specific percentile chart, which is not available in Malaysia. A waist circumference percentile chart based on a database of children in Hong Kong (Sung *et al*., 2008) with a cut-off equal or above 90th percentile was used instead. It was interesting to observe that all obese subjects had high WC, whereas none of the normal weight subjects had high WC. On the other hand, if a percentile chart based on a population of British children (McCarthy, Jarrett & Crawley, 2001) was used, the number of subjects categorised with elevated waist circumference would certainly be higher. All of the above mentioned reasons may lead to a lower prevalence of MS as reported. Hence, a major limitation of our study is the lack of a waist circumference percentile chart that is sensitive to the diverse population of Malaysian children.

However, irrespective of the definition used, MS had been reported more frequently in obese or overweight children in various studies (Weiss *et al*., 2004, Agirbasli *et al*., 2006, Yoshinaga *et al*., 2005). Even though no significant difference in MS incidence was reported between the groups in our study, certain components of MS (DBP, SBP and WC) worsened with increasing obesity as evidenced by the significant relationship between BMI and DBP (r=0.505, p<0.001), SBP (r=0.682, p<0.001) and WC (r=0.938, p<0.001). In contrast, HDL cholesterol showed a significant negative relationship to BMI (r=-0.430, p<0.001). In addition, our findings contradict that of Weiss *et al.* (2004), which showed that impaired glucose tolerance worsens with increasing obesity, and the findings of Sinha *et al.* (2002) which detected impaired glucose intolerance in 25% of obese children. The present study only observed a weak relationship for this component and high fasting blood glucose was slightly more prevalent in normal weight subjects (4.5%) as compared to obese subjects (2.9%).

Besides the positive relationship between MS components with obesity (fat mass and BMI), family history of hypertension, diabetes mellitus and cardiovascular disease are associated with increased risk of MS (Sung *et al*., 2003; Castillo *et al*., 2007; Kelishadi *et al*., 2008). Based on our findings, the risk of MS was 2.4 times higher (95% CI:0.930-6.341, p>0.05) in subjects with a family history of diabetes, hypercholesterolemia, high blood pressure or cardiovascular disease. However, no significant association was observed between subjects with and without family history of these diseases and risk of MS (p>0.05, Pearson Chi square). Thus for children below ten years, attention should not be placed on family history as proposed by IDF (Alberti *et al*., 2007). MS risk may be present even if children do not have a family history of the previously mentioned diseases (Chi *et al*., 2006). Results presented here show that 41.2% subjects without a family history of the mentioned diseases were at risk for MS. MS is a clustering of various inter-related factors and subjects that exceed the cut-off value for any component will be categorised as at-risk for MS (Huang *et al*., 2008). In short, interventions should be targeted at an early stage before the other components have developed. This reasoning is the basis for our decision to target children aged 8-10 years for enrolment. Hence, the existing proposed MS definition should be extended to include children below ten years old.

Last but not least, unfavourable lifestyle behaviours such as physical inactivity can elicit clinical consequences of MS (Li *et al*., 2007). Thus, future studies should investigate the role of physical inactivity in MS among young children. The current study was not designed to determine the prevalence or causes of MS but to provide a general picture of MS incidence between obese and normal weight children aged 8-

10 years old. The narrow age range limited the effect of age-related difference.

CONCLUSIONS

The incidence of MS was very low in this study as determined by the IDF pediatric definition of MS. The low incidence of MS may be due to the cut-off value used for blood pressure and the core feature of waist circumference. No obese subjects were free from any components of MS versus 90.9% of the normal weight subjects. The IDF proposes the diagnosis of MS among children above age ten, or those below age ten but with family history of diabetes mellitus, cardiovascular disease, high blood pressure or hypercholesterolemia. However, in view of global increases in childhood obesity, a consensus definition for MS in children below age ten would be useful for documenting prevalence and trends of MS among children.

ACKNOWLEDGEMENT

This study was funded by a MOSTI research grant (ScienceFund 06-01-02 SF0314). We wish to thank all participants, their parents, and school administrators for granting permission and for their support throughout the study.

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