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Metabolic Syndrome and Risk Factors for Cardiovascular Diseases in Obese Children

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Abstract: To identify the prevalence of metabolic syndrome (MS) and risk factors for the development of cardiovascular diseases among Saudi children. Total of 510 Saudi child aged 9-12 years representing different socio-economic districts who were attending the outpatient clinics *at hospital of pediatric, King Saud Medical City,* Riyadh City, Kingdom of Saudi Arabia. They were randomly selected. Data were collected from the pediatric nutrition clinic (PNC) of the outpatient department (OPD); these children were referred to the nutrition clinic by the pediatricians for nutritional assessment and to be follow-up by dieticians for further nutritional treatment. A questionnaire was administered to the parents of all children. The questionnaire included socio-demographic data, the medical history comprised of medical illnesses such as hypertension in the subject or his or her parents. Also question related to the life style such as eating habits and exercise. Anthropometric and blood pressure were measured for all children. Body mass index (BMI) was calculated for all children. According to BMI the studied group divided into two subgroups; Overweight/obese = 180 and normal weight =300. Diagnostic criteria of MS was made based on the International Diabetes Federation's pediatric definition (IDF), namely waist circumference (WC) ≥ 90th percentile plus two or more of the following indices for all boys and girls: Triglycerides (TAG) ≥150 mg/dL (1.7 mmol/L), Blood pressure(BP) (Systolic ≥130 mmHg or Diastolic ≥ = 85 mmHg), fasting blood glucose (FB) ≥ 100 mg/dL (5.6 mmol/L) and high-density lipoprotein cholesterol (HDL-C) ≤ 40mg/dL (1.03 mmol/L). There was statistically significant difference between the two groups regarding to the family history of MS and diseases that were related to the MS $p<0.05$. Overweight/obese children had significantly worse clinical profiles and higher anthropometric parameters. The frequency of MS was 18% in overweight/obese children and the obese girls had significantly higher frequency of MS (10%) than obese boys (8%). MS was not observed in normal weight children. The overweight/obese poses a higher risk for developing the MS with high odds ratio ($p<0.05$) as compared to normal-weight individuals. It was observed from the present study that most predisposing factor for MS was obesity (O.R 6.31) followed by abdominal obesity (O.R 4.18), BP (O.R 3.62)and low (HDL-C) (O.R 2.93).

Key words: Metabolic syndrome · Anthropometric parameters · Obesity · Blood pressure and High-density lipoprotein cholesterol

INTRODUCTION

The rising rates of obesity in children and adults have been accompanied by an increase in the co occurrence of obesity-associated metabolic abnormalities known as the MS [1]. The underlying cause of the MS continues to challenge the experts but both insulin resistance and central obesity are considered significant factors [2]. Genetics, physical inactivity, ageing, pre inflammatory state and hormonal changes may have a causal effects but the role of theses may vary depending on ethnic group [3]. MS is recognized as the clustering of risk factors of obesity, insulin resistance, dyslipidemia and hypertension associated with the subsequent development of cardiovascular disease (CVD) and diabetes mellitus type 2 (DMT2) [4]. With the increasing prevalence of overweight and obesity worldwide, especially in children and youth, the "pediatrics metabolic syndrome" has received increasing attention from a public health perspective [5].

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Obesity is now considered as one of the important predisposing factors for many chronic diseases. Excessive weight has been a problem in developed countries and recently it started spreading in developing world [6]. Half of the obese children at age 6 were also obese at age 12 and the degree of obesity is predictive for adult obesity [7]. Reaven *et al.* [8] described the MS, explaining the link between insulin resistance and arterial hypertension, dyslipidemia, (DMT2) and other metabolic anomalies associated with CVD in adults. However, nowadays this problem is observed with ever greater frequency among children, particularly those with excess body mass. In addition to identifying obesity as an independent risk factor for CVD in pediatric populations, several studies have demonstrated strong links between MS and many co- morbidities and pathologies, such as insulin resistance, hyperinsulinemia, arterial hypertension, dyslipidemia and DMT2. Epidemiological studies have demonstrated an association between the growing incidence of chronic diseases, such as DMT2 and coronary disease, with reduced length of disease-free life, in line with increases in BMI and concomitant with population hyperinsulinemia [9].

To identify the prevalence of MS and risk factors for the development of cardiovascular diseases among Saudi children.

MATERIALS AND METHODS

The subject studied constituted 510 Saudi child representing different socio-economic districts who were attending the outpatient clinics *at hospital of pediatric, King Saud Medical City,* Riyadh City, Kingdom of Saudi Arabia. They were randomly selected. Their ages ranged between 9 and 12 year. This study was carried out in studying year 2012-2013. Data were collected from the pediatric nutrition clinic (PNC) of the outpatient department (OPD), these children were referred to the nutrition clinic by the pediatricians for nutritional assessment and to be follow-up by dieticians for further nutritional treatment. Their main problems were obesity, diabetes, anemia and others. Exclusion criteria include subjects with any congenital abnormalities or cancer diseases.

Tools of the Study: A questionnaire was administered to the parents of all children and was considered consent for their children's participation in the study. The interview was carried out by the researcher for approximately 20 minutes for each subject, at the outpatient diet clinic. At the beginning of the interview, the purpose was explained to the mother and assurance was given that all information will be treated with strict confidentiality and will be used for research purpose only. The patients/subjects medical record number was used to complete the medical history. The questionnaire included socio-demographic data, age, sex, parent's educational levels, occupation of the parents, medical history which was comprised of medical illnesses such as hypertension in the subject or his or her parents. Also question related to the life style such as eating habits and exercise.

Anthropometric Measurements: Anthropometric measures comprised height, weight, midarm circumference, subscapular, triceps and skin fold thickness, WC, Hip circumference and Waist to hip ratio (WHR). Height was measured to the nearest cm by stadiometer, obtained without shoes, back straight with buttocks and shoulders touching a wall and head forward. Weight was measured, to the nearest 0.5 Kg, by a spring balance. Calibration of the scale was made on a daily basis using two different standard weights. The child was weighed in light clothes (no shoes or heavy outer garments). BMI used as an indicator for obesity and was defined as weight over height squared: [wt in kg/ (ht in m) ^{2}], Obesity was defined as $\geq 95^{th}$ percentile [10], under weight $<5^{th}$. Percentile and over weight: BMI>85 percentiles. The midarm circumference was measured after measuring the left upper arm length was measured from the acromion to the olecranon with the metal tape. The child's forearm was raised to make 90° angle during the measurement. The midpoint between the acromion and olecranon determined and marked on the dorsal surface of the arm. The triceps skinfold was measured between the acromion and olecranon and the subscapular skinfold was measured below the tip of inferior angle of scapula. The measurement was performed three times during the examination. Percentiles for the anthropometric measures as weight and height [10], midarm circumference [11]. Triceps and skinfold thickness [10] were obtained. The measurements of the present study were related to age and sex and plotted on the percentile curves. WC was measured to the nearest cm at the level of umbilicus with the subject standing and breathing normally. Hip circumference was measured on the under wear at the most protruding part of the buttocks to the nearest cm. WHR was defined as the ratio of waist circumference to the hip circumference in centimeters [12].

Blood Pressure Examination: Blood pressure was measured for all children using random zero sphygmomanometer [13]. The child was seated at rest

for at least 5 minutes before measurement. Two successive readings were taken approximately one minute apart [14]. The children were considered hypertensive if they were on ≥ 95th percentile for both systolic and diastolic blood pressures.

Diagnostic Criteria: MS was diagnosed based on the IDF pediatric definition [15], namely waist circumference ≥ 90th percentile plus two or more of the following indices for all boys and girls:

- TAG ≥150 mg/dL (1.7 mmol/L).
- Bp (Systolic ≥130 mmHg or Diastolic ≥ 85 mmHg).
- FBG ≥100 mg/dL (5.6 mmol/L) (more than
- HDL-C ≥ 40 mg/dL (1.03 mmol/L).

Biochemical Profile: Blood analysis for: 1. Triglycerides TAG and High HDL-C and low density lipoprotein cholesterol LDL-C [16], FBG fasting blood sugar and Oral glucose Tolerance Test. Fasting plasma venous glucose =7.0 mmol/l (126 mg/dl) OR 2. Hour oral glucose tolerance test (OGTT) (with 75g with glucose) plasma venous glucose =11.1 mmol/l (200mg/dl) [17].

Statistical Analysis: Data were expressed as mean ± S.E. and were analyzed statistically using SPSS version 12.0 software (SPSS, Chicago, III), the variables were compared using T-test and Chi- square test. Differences were considered statistically significant at P ≥ 0.05. Pearson correlation and stepwise regression analysis were used to investigate the relationships between MS and anthropometric measurements [18].

RESULTS

Table 1 describes the socio-demographic characteristic of the studied group. BMI was calculated for all children. According to BMI the studied group divided into two subgroups (Over weight/obese=180) and normal weight =300. The mean age of the sample was

Table 1: Socio-demographic characteristics of the studied groups

	Over weight Obese No (180)		Normal -weight No (300)		
Description	No	%	No	%	P
Mean age (years)	10±2.81	10±1.12			
Range	9-12	9-12			
Gender					
Boys	86	48	141	47	>0.05
Girls	94	52	159	53	
Father's education					
Read & write	61	34	99	33	>0.05
Preparatory, Secondary	68	38	108	36	
University	51	28	93	31	
Mother's education					
Read & write	97	54	36	12	<0.05
Preparatory, Secondary	61	34	198	66	
University	22	12	66	22	
Father's occupation					
Professional	79	44	117	39	>0.05
Employee	88	49	162	54	
Manual	13	7	21	7	
Mother's occupation					
Working	40	22	231	77	<0.05
House wife	140	78	69	23	
Family income					
Sufficient and saving	92	51	180	60	>0.05
Sufficient	79	44	102	34	
Insufficient	9	5	18	6	
Family history of M.S	52	29	3	1	<0.05
Family history of diseases that were related to M.S:					
Hypertension	56	31	15	5	<0.05
Heart disease	36	20	12	4	
Diabetes	23	13	9	3	
Hypercholesterolemia	18	10	6	2	
The combination of them	13	7	3	1	
Negative history	34	19	255	85	

Table 2: The prevalence of obesity among studied children according to percentile

	Studied group (No 510)	
BMI and growth charts	No	%
Normal weight BMI range between 5-85th percentile.	300	58
Under weight >5th percentile	30	6
Over weight: BMI >85 percentiles	100	20
Obese: BMI > 95 percentiles	80	16

Table 3: Comparison of anthropometric measurements, blood pressure, biochemical characteristics of the studied groups

Parameters	Over weight /obese (180) (mean ±S.D)	Normal weight (300) (mean ±S.D)
Anthropometric measurements		
Mid arm	20.7±6*	15.1±2
Triceps	13.2±5.1*	10±1.1
Sub scapular	11.7±21.4*	8.1±0.1
Waist circumference (cm)	76.3±7.8**	53±4.7
Hip circumference (cm)	91.9±7.8**	70.8±2
Waist height ratio	0.5±1.1**	0.4±0.1
Waist hip ratio	0.8±0.1**	0.7±2.1
Height (cm)	132.1±21.19**	126.2±6.2
Weight (kg)	46.9±21.3*	26.7±5.6
BMI (kg/m^2)	26.9±6.6**	16.6±2.5
Blood pressure		
Systolic blood pressures	121.4±4.3 **	99.6±2.3
Diastolic blood pressures	79.5±2.2**	62.9±11.4
Biochemical characteristics		
Fasting blood pressure (mmol/L)	4.0±1.1	4.1±0.1
Triglycerides (mmol/L)	1.9±0.1**	0.7±0.2
HDL-cholesterol (mmol/L)	0.8±0.1**	1.6±0.4
LDL-cholesterol (mmol/L)	4.2±2.4*	3.0±0.1
Total cholesterol (mmol/L)	5.7±0.3	5.1±2.7

**Significance at p<0.001, * significance at p<0.05

Tablet 4: The metabolic risk factors in overweight/obese and normal-weight children

Body mass status	Overweight/obese (N0: 180)				Normal weight (No: 300)			
Gender	Boys		Girls		Boys		Girls	
Risk factor	No	%	No	%	No	%	No	%
o/risk factor	11	6	11	6	138	46	150	50
+1/risk factor	36	20	37	21	3	1	9	3
+2/risk factor	25	14	27	15	0	0	0	0
+3/risk factor	11	6	13	7	0	0	0	0
+4/risk factor	4	2	5	3	0	0	0	0
Total	87	48	93	52	141	47	159	53

Table 5: Comparison between overweight/obese and normal-weight children in regard to MS

	Overweight/obese (No: 180)		Normal weight (No: 300)		
MS	No	%	No	%	Odd's Ratio P value
Yes	32	18	0	0	p<0.05
No	148	82	300	100	

10±2.8.1 years that ranges from 9 to12. Most of the children's fathers received below essential education (38%) in group 1 (over weight /obesity) compared to (36%) group 2(normal weight) and 28% were university graduates in group 1 compared to (31%) group 2, 49% of fathers were employees in group 1 compared to(54%) group 2, most of the mothers received below essential education read and write (54%) in group 1 compared to (12%) in group 2 and 22% of both group were university graduates. There was no statistically significant difference

between the two groups regarding to the education and occupation of father as well as the family income p>0.5, however there was statistically significant difference between the two groups regarding to the education and occupation of the mother p<0.5. The majority of mothers were house wives. On describing the family income; most of the families of the studied group were sufficient and saving. As regards family history of MS 29% in group 1 compared to only 1% in group 2. There was statistically significant difference between the two groups regarding to family history of MS and diseases that were related to the MS p<0.5. As regards family history of diseases that were related to the MS, 31 % of group1 have hypertension, compared to (5%) in group 2, 20% of group1 have heart diseases compared to (4%) in group 2, 13% of group1 have diabetes compared to (3%) in group 2 and 10% of group1 have hypercholesterolemia compared to (2%) in group 2.

Modified BMI for age was used to define obesity in children, 58 % of children with normal weight range was between 5 - 85th percentile while 20 % of children with BMI >85 percentiles (more than) (overweight), 6 % (30) under weight<5th. Percentile and 16% of children with BMI>95 percentiles (obese) (Table 2). Anthropometric and biochemical characteristics of the children are shown in Table 3 Overweight/obese children had significantly worse clinical profiles and higher anthropometric parameters [height, weight, BMI, hip circumference (HC), (WHR), waist-to-height ratio (WHtR), TG, HDL-C, SBP and DBP, $p < 0.001$; LDL-C $p < 0.05$ compared to normal-weight children except for TAG and FBG. Clustering of cardiovascular risk factors was abundantly present in overweight/obese children as compared to normal weight children; 6% among overweight/obese children had no risk factor; however, 20%, 14%, 6 % and 2% in overweight/obese boys children had 1, 2, 3 and 4 risk factors respectively compared to 21%, 15%, 7% and 3% in overweight/obese girls for CDV. The frequency of CVD risk factors in normal weight children was 46 % in boys and 50% in girls had none but the frequency of 1 risk factors was 1% and 3%, respectively (Table 4). The frequency of MS was 18% in overweight/obese children. It is important to note that obese girls had significantly higher frequency of MS (10%) than obese boys (8%). MS was not observed in normal weight children. The overweight/obese poses a higher risk of developing the MS with high odds ratio (p<0.05) as compared to normal-weight individuals (Table 5). Regarding the association between MS and different predisposing factor, it was observed from the present study that the most predisposing factor for MS was obesity BMI (O.R 6.31) followed by abdominal obesity (O.R 4.18), BP (O.R 3.62), Low (HDL-C) (O.R 2.93), family history of MS (O.R 2.34), life style (O.R 1.97), genetic liability (O.R 1.89) and lastly the gender (O.R 1.80) (Table 6).

Table 6: Association between metabolic syndrome and different risk factors

	MS	
Items	O.R (95%CI)	P value
Obesity (BMI ≥ 95 percentile)	6.31	<0.01
Abdominal obesity (WC)	4.18	<0.01
BP	3.62	<0.01
Low HDL-C	2.93	<0.01
Family history	2.34	<0.01
Life style	1.97	<0.05
Genetic	1.89	<0.05
Gender	1.80	<0.05

DISCUSSION

Nowadays the problem of MS is observed with ever greater frequency among children, particularly those with excess body mass. The prevalence of overweight and obese children in our study was 36%; higher than in an earlier study by Wee *et al.* [19] who reported that the prevalence of overweight and obese children in metropolitan Kuala Lumpur was 34.2% and by Ismail *et al.* [20] who reported an increase from 20.7% in 2002 to 26.5% in 2008 using the WHO growth reference in 6-12 year-old children in Peninsular Malaysia. The present study revealed that the prevalence of obesity was 20% (who have BMI ≥ 95th percentile), the prevalence of overweight and obesity in our study was 20% and 16% respectively which was higher than that reported from Abha City, where over weight and obesity for age group 6-18 years were 11.0 % and 15.9%, respectively [21].

In the present study, the prevalence of overweight and obese girl's children was increased compared to overweight and obese boy's children. This is consistent with Figueroa *et al.* [22] in Alabma, USA, who concluded that the prevalence of childhood obesity and associated complication was significantly greater in girls at age 5 years (23% in blacks and 10% in whites) than boys (13% in blacks and 6% in whites). The prevalence of obesity in our study was more than in neighborhood countries like Qatar, they reported that, 3.2% and 8.8% were overweight and 1.6% and 5.4% of both boys and girls were obese, respectively [23]. The data in our study showed that girls children were more obese than boy's children. This could be explained by reduced activities

levels of the girls in the school or out the school. Farghaly *et al.* [21] evaluated the life style and dietary habits of school students, reported that, overweight and obesity were significantly more prevailing among girls of primary schools. It was observed that low level of mother's education have been associated with obesity in children (Table 1).This may be due to that mothers has no nutritional education. This is in agreement with those reported by Kromeyer *et al.* [24] who observed that there was an association between overweight and lower mother's education in both sexes, which implies that the environmental factors as low level of education plays a major role in obesity development. With the increasing trend of childhood obesity worldwide, it is not surprising that there is an increase the prevalence of MS [1]. The prevalence of children suffering from MS in our study was18%, broken down as 10% of the girls and 8% of the boys, this agreement with study of Ferreira *et al.* [25] who reported that the prevalence of the studied children in Brazil in 2007 suffering from MS was 17.3%, broken down as 10.7% of the boys and 25% of the girls. These figures are comparable with the results of another study that analyzed schoolchildren from a rural community in the USA and found figures of 10% for boys and18%for girls aged 7 to 18 years [26]. Also in agreement with our study are the results of the Bogalusa Heart Study which found that 17.2% of children aged 5 to 10 years exhibited three or more risk factors for CVD [27].

It was observed from the present study that overweight/obese children pose a higher risk for developing the MS with high significant ($p<0.05$) as compared to normal-weight individuals. This result is in agreement with those obtained by Wee *et al.* [19] who reported that 5.3% of overweight/obese children in metropolitan Kuala Lumpur had the MS with only 12% of the overweight/obese group being free from the MS risk factors. This is in sharp contrast to 83.9% of the normal-weight children who were free from all risk factors. The overweight/obese children pose a higher risk for developing the MS with O.R of 16.3 as compared to normal-weight individuals. A hospital-based study by Taha *et al.* [28] reported that obese Saudi children and adolescents have multiple risk factors associated with MS. In Kuala Lumpur, another study reported that Ms was found in 1.3% of children aged 7 to 9 years [29]. Our results revealed that overweight/obese children had significantly higher anthropometric and biochemical indices compared to normal-weight counterparts except for TAG and FBG, this is supported by Wee *et al.* [19] and Misra and Vikram [30] suggested that high FBG will only be visible when other metabolic components start appearing. Regarding association between MS and different predisposing factor, it was observed from Table 6 that the most predisposing factor for MS was obesity (O.R 6.3). This is in accordance with Reaven [8]. The second most predisposing factor for MS was abdominal obesity (O.R 4.18) WC is typically used as a surrogate measure of abdominal obesity. With the present health risks of central fat distribution it is of little surprise that WC is the first criteria in determining the risk of the MS [31].

Our study revealed that the hypertension was the risk factor for MS with high O.R 3.62; this is in agreement with study of Ferreira *et al.* [25] who reported that arterial hypertension (systolic or diastolic) was present in 14.3% of the boys and 16.7% of the girls. Several investigators have reported the link between obesity and hypertension [32]. Longitudinal studies of Pima Indian children have demonstrated that obesity was the major factors in the development of childhood hypertension [33]. Prevalence of hypertension in urban Asian Indian children have been shown to be 4.5% in those with normal BMI, 15.3% in overweight children and 43% in obese children. Even in rural areas, a 6.8% prevalence of sustained hypertension was reported in overweight children compared with 61.7% in obese children [34]. Our study revealed that the low (HDL-C) was a risk factor for MS with high O.R 2.93, this is in agreement with study of Ramzan *et al.* [35] who reported that MS was associated with low HDL-C and it plays a major role in the contribution to the MS.

Also this is supported with study of Vikram *et al.* [36] who reported that the overweight and obesity in children and adolescent in Urban Asian Indian was significantly associated with dyslipidemia (hyper TAG and low levels of HDL-C). Our study revealed that the family history of MS was a risk factor for MS in children with O.R 2.34, this is in agreement with study of Vikram *et al.* [36] who reported recently that, in Asian Indian children, children had MS with O.R for development of DM T2 was 86.4 (95% confidence interval 17.0-438.5) who had a high WHRt and a family history of DM T2 in a first-degree relative [37] this is in contrast to a study conducted by Wee *et al.* [19] who reported that there was no significant association between family history of disease with the MS group. Our study revealed that the life style was a risk factor for MS with O.R 1.97. These results are consistent with those obtained by Fisberg *et al.* [38, 39] who reported that regular participation in physical activity with eating healthy diet strongly influences health status and reduce risk of obesity and overweight which related to

CVD. Also, Physical exercise was lowering factor that blood lipids are one of risk factor for hypertension. This could be explained by the fact that, exercise will increase energy requirement and decrease fat deposition. Gibson *et al.* [40] and Al-Rukban [41] found that family history and lack of physical activity were associated with adolescent obesity. This could explain the increased prevalence of obesity due to eating dense energy food with lack of exercise [42]. It is postulated that aggregation of adiposity within families is due to shared genes and environments. It was reported that genetic factors may play a role in obesity more than in over weight [43]. This could be explain by the fact that, obesity aggregates within families because of shared genes and environments, children may had the same parents dietary habits and life style such as eating high calorie foods and lack of exercise [44]. Similar findings were obtained by Eldamaty *et al.* [45] who stated that there was an association between overweight and obesity and food habits as well as activity level. This was in agreement with study of Misra *et al.* [46] who reported recently that therapeutic lifestyle changes, maintenance of high levels of physical activity and normal weight are most important strategies. Pharmacologic therapy for individual components of the MS is occasionally needed.

Our study revealed that the genetic was a risk factor for MS with O.R 1.89; this is in agreement with study of Butte [47] who reported that significant heritability and pleiotropy seen for the components of the MS indicate a strong genetic contribution.

Our study revealed that the age a risk factor for MS. These data is consistent with those of Ferreira *et al.* who used National Cholesterol Education Program NCEP ATP III diagnostic criteria and classified10.7% of boys and 25% of girls with the MS. Some have suggested that higher numbers of girls are reported to have the MS due to hormonal changes and subsequent central body fat accumulation, especially during puberty [48].

CONCLUSION

The MS in children is an important clinical marker of hypertension and coronary heart disease in adults. Obese children exhibited a high prevalence of MS with more risk factors. In the light of these findings intervention measures are necessary in order to prevent excessive weight gain during childhood. Our findings suggest that preventive interventions should focus not only on obesity, but also to related diseases. This requires strategies and coordinated efforts at all levels (family, schools, community and government) to reduce the tendency of overweight and obesity.

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