

## Familial aggregation of the components of metabolic syndrome

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### ABSTRACT

**Objective:** To investigate cardiometabolic factors in children of parents with metabolic syndrome (MetS), and to determine the association of these factors among children and their parents.

**Methodology:** This cross-sectional study was conducted as part of the baseline survey of a longitudinal study. According to inclusion/exclusion criteria, 800 children of parents with diagnosed MetS were selected by convenience sampling. Cardiometabolic data including fasting blood glucose (FBG), serum triglyceride (TG), total cholesterol (TC), body mass index (BMI), waist circumference (WC), and fat mass percentage (FMP) were collected and analyzed. Data regarding children's diet and their psychological state were also recorded by validated questionnaires. Mean of continuous variables were compared by one-way ANOVA and correlations between continuous variables were determined by the Pearson correlation test.

**Results:** After excluding cases with missing data, information for 746 children (58% boys) and their parents was analyzed. Among children, TG was significantly correlated with BMI, WC, and FMP ( $p=0.001$ ,  $r=0.24$ ;  $p<0.0001$ ,  $r=0.25$ ; and  $p=0.01$ ,  $r=0.19$ , respectively). Additionally, TC was significantly correlated with WC ( $p=0.02$ ). There were significant correlations between mother's FBG with children's BMI and WC ( $p=0.01$ ,  $r=0.27$ ; and  $p=0.00$ ,  $r=0.29$ , respectively). Children of fathers and mothers with high BMI had significantly increased TC ( $p=0.04$ , and  $p=0.02$ , respectively). There was an inverse significant correlation between mood score and systolic blood pressure ( $p=0.03$ ). There were also correlations between carbohydrates in children's diets and WC ( $p=0.02$ ,  $r=0.34$ ), and a near significant inverse correlation between nut consumption in diet and TC ( $p=0.05$ ,  $r=-0.22$ ).

**Conclusions:** The current study showed the association of various factors on cardiometabolic risk factors in children and the relationship between these factors in children and in their parents. In addition to genetic predisposition, the familial aggregation of anthropometric measures underscores the role of obesogenic families in the development of cardiometabolic risk factors.

**KEY WORDS:** Cardiometabolic syndrome, Children, Familial pattern.

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### INTRODUCTION

Metabolic syndrome (MetS) refers to a group of risk factors that collectively increase the risk for cardiovascular disease and diabetes. The syndrome may be physiologically characterized by insulin resistance, glucose intolerance, dyslipidemia, hypertension, and obesity.<sup>1,2</sup> Recent studies have shown changes in the epidemiological aspects of MetS in terms of its escalating prevalence and decrease in its average age of onset. These trends suggest that MetS will continue to be a significant health issue in children and adolescents in the future.<sup>3,4</sup>

There is a growing body of evidence that suggests obesity in children and adolescents is associated with short- and long term risks, notably of cardiometabolic disorders and related morbidity and mortality.<sup>5</sup> Childhood obesity and MetS are becoming an increasing global public health burden. Identifying the determinants of MetS is an important step in prevention and early treatment. Obesity, lifestyle habits, family history, and genetic factors are known contributing factors for the development of MetS.<sup>6</sup> Although the heritability of MetS has not been reported directly, significant genetic components have been reported for all of its major features including insulin resistance, obesity, hypertension, and dyslipidemia.<sup>7-12</sup> Several studies have investigated the familial aggregation of the MetS and its components; positive family history of diabetes and/or hypertension are shown to significantly increase risks.<sup>13,14</sup>

Many studies have investigated the relationship between metabolic states in young and old age. Some have compared the metabolic state of children with their parents in order to evaluate the role of familial factors, while others have conducted longitudinal studies from childhood to adulthood. According to these studies, offspring birth weight could be used as a useful surrogate for maternal metabolism during pregnancy<sup>15</sup>, and there is an association between size at birth and the risk of diabetes and cardiovascular disease (CVD) in later life.<sup>16</sup> A study on the familial aspects of the MetS and CVD risk factors reported that parents of obese children are at six times higher risk of being obese than parents of non-obese children. The corresponding figures for hypertension and hypertriglyceridemia are 15 and 5 times, respectively. These findings indicated that detection of several clinically apparent and silent CVD risk factors in children may predict increased CVD risk in their parents.<sup>17</sup>

Similar to many other developing countries, Iran is facing a rapid epidemiologic transition and lifestyle change. In turn, a considerably high prevalence of obesity and MetS in adults<sup>18</sup> and children<sup>19</sup> has been reported. In the present study, we aimed to investigate various cardiometabolic factors in children of parents with MetS and to determine the inter-relationships of these factors between children and their parents.

## METHODOLOGY

The study was approved by the Research Committee of Isfahan University of Medical Sciences. All parents gave written informed consent

after receiving information about the study, and oral consent was obtained from children. This study was conducted among children aged 8 to 10 years living in Isfahan, Iran. According to the inclusion criteria, children were eligible for the study if they were of Iranian origin, 8–10 years of age, lived with biological parents, and had at least one biological parent with a diagnosis of the MetS. Children with chronic medical problems, chronic medication use, craniofacial abnormalities or other signs associated with genetic syndromes, and those on special diets were not included in the study.

Participants were visited by a trained physician and data obtained from interview and physical examination were recorded using questionnaires validated in a pilot study. Measurements of anthropometric parameters (weight, height, and waist circumference) and blood pressure were conducted using standard protocols. For parents, MetS and its components were defined according to the Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III or ATP III).<sup>20</sup>

Using BMI and WC percentile ranks, children were classified to normal or high BMI<sup>21</sup> and normal or high WC.<sup>22</sup> Similarly, parents were also categorized to normal or high BMI.<sup>23</sup> Body fat mass percent (FMP) was determined via dual energy absorptiometry using an Omron body fat monitor (Omron, Kyoto, Japan) that was validated in our previous studies.<sup>24</sup> For laboratory examinations, blood samples of participants were obtained by trained nurses from the left antecubital vein following 12 hours of fasting. Serum total cholesterol (TC), low-density lipoprotein cholesterol (LDL), triglycerides (TG), and fasting blood glucose (FBG) were measured enzymatically. Serum high-density lipoprotein cholesterol (HDL) was determined after precipitation of low-density and very low-density lipoproteins with dextran sulfate-magnesium. Children's psychological states were assessed by a validated short mood and feelings questionnaire (Child Version, SMFQ). In this questionnaire, higher mood scores were correlated to more depressed mood.<sup>25</sup> Children's diet was studied by a validated food frequency questionnaire (FFQ). Daily diet was recorded in detail and categorized into groups of carbohydrates, proteins, and fats with related sub categories.

**Statistical analysis:** Statistical analyses were performed using the SPSS statistical package. We used one-way analysis of variance (ANOVA) to compare mean of continuous variables between two groups and *post hoc* analysis for more than two

groups. Correlations between continuous variables were determined by the Pearson correlation test. P-values less than 0.05 were considered statistically significant.

## RESULTS

This study comprised 800 participants. After excluding cases with missing data, information for 746 children (58% boys) and their parents was analyzed. The mean age of children was  $8.87 \pm 0.15$  years (range: 8-10). Specific characteristics and cardiometabolic factors of boys and girls are presented in Table-I.

Comparison of cardiometabolic factors between sexes showed significantly higher FMP and FBG in boys ( $p=0.02$ , and  $p=0.04$ , respectively). Correlations between metabolic factors and anthropometric indices among children and among children and their parents were also analyzed showing that among children, TG was significantly correlated with BMI, WC and FMP ( $p=0.001$ ,  $r=0.27$ ;  $p<0.0001$ ,  $r=0.31$ ; and  $p=0.01$ ,  $r=0.19$ , respectively) as well as TC with WC ( $p=0.02$ ).

Metabolic factors were compared between children with normal and high BMI and normal and high WC. There was a significant difference in FMP, systolic blood pressure (SBP), diastolic blood pressure (DBP), and TG between children with normal and high BMI. Among the normal and high WC groups, FMP, SBP, TG, TC and LDL were significantly different (Table-II).

Correlations between children's and parent's cardiometabolic factors were also studied (Table-III). There was significant correlations between chil-

dren's TC and father's BMI, TC and LDL ( $p=0.004$ ,  $r=0.28$ ;  $p<0.0001$ ,  $r=0.62$ ; and  $p<0.0001$ ,  $r=0.65$ , respectively). Children's serum LDL was significantly correlated to father's TC and LDL ( $p=0.02$ ,  $r=0.39$ ; and  $p=0.005$ ,  $r=0.41$ , respectively). Mother's BMI was significantly correlated to children's BMI, WC and TG ( $p=0.006$ ,  $r=0.28$ ;  $p=0.01$ ,  $r=0.4$ ; and  $p=0.02$ ,  $r=0.28$ , respectively). Additionally, there were significant correlations between mother's FBG with children's BMI and WC ( $p=0.04$ ,  $r=0.32$ ; and  $p=0.002$ ,  $r=0.27$ , respectively).

Parents were also classified into two groups according to BMI (normal or high), and children's cardiometabolic factors were compared based on their parent's BMI state. Children of parents from the different BMI groups had significantly different TC values (father's BMI  $p=0.04$  and mother's BMI  $p=0.02$ ).

Evaluation of the effects of psychological factors on cardiometabolic parameters showed an inverse significant correlation between mood score and SBP ( $p=0.04$ ,  $r=-0.27$ ). Analysis of the different components of diet showed a significant correlation between carbohydrate consumption and WC ( $p=0.04$ ,  $r=0.42$ ) and near significant inverse correlation between nut consumption and TC ( $p=0.04$ ,  $r=-0.32$ ). There was no significant correlation between other diet components and cardiometabolic factors.

After excluding children being taken care of by only a father or mother (because they were only 7 cases), we compared two other groups. Serum TG was significantly higher in children being cared for by persons other than parents ( $132.3 \pm 46.98$  vs.  $102.8 \pm 37.17$  mg/dL, respectively,  $p=0.01$ ). There was no

Table-I: Children's characteristics.

	Boy (58.7%)	Girl (41.3%)	Total N=746 (100%)	P-value
Age(years)	8.57±0.14	8.71±0.35	8.87±0.15	0.28
Weight(kg)	32.28±8.95	33.64±9.88	32.28±9.32	0.32
Height(cm)	135.49±7.84	135.20±7.46	135.38±7.68	0.80
BMI (kg/m <sup>2</sup> )	17.37±3.57	18.23±4.29	17.70±3.88	0.13
WC(cm)	65.38±9.84	67.36±9.83	66.14±9.86	0.17
DBP(mmHg)	48.10±8.71	47.79±8.65	47.98±8.67	0.81
SBP(mmHg)	89.37±8.83	89.73±9.82	89.51±9.20	0.80
FBG(mg/dL)	86.53±8.87	83.96±8.06	85.55±8.64	0.04
TC(mg/dL)	169.55±30.47	170.01±31.18	169.72±30.65	0.92
LDL(mg/dL)	94.27±25.50	94.55±26.38	94.37±25.77	0.94
TG(mg/dL)	91.33±42.27	96.23±45.44	93.19±43.45	0.45
HDL(mg/dL)	53.84±11.43	54.34±15.06	54.03±12.89	0.80
FMP(%)	23.06±8.17	19.98±9.54	21.81±8.85	0.02

Values are presented as mean  $\pm$  SD BMI: Body mass index; WC: Waist circumference; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; FBG: Fasting blood glucose; TC: Total cholesterol; TG: triglycerides; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; FMP: Fat mass percent.

Table-II: Comparison of children's cardio-metabolic factors based on their anthropometric measures.

	Body mass index (BMI)			Waist circumference (WC)			Total
	Normal BMI n=123	High BMI n=70	p-value	Normal W.C n=123	High W.C	p-value	n=193
FMP(%)	17.57±6.60	29.11±7.38	<0.0001	17.76±6.88	27.59±8.07	<0.0001	21.82±8.86
SBP(mmHg)	87.86±9.24	92.49±8.43	<0.0001	87.80±9.75	91.13±8.32	<0.0001	89.52±9.21
DBP(mmHg)	46.24±8.17	51.11±8.73	<0.0001	46.35±8.10	49.06±9.30	0.06	47.98±8.67
FBG(mg/dL)	85.79±9.20	85.15±7.69	0.63	85.24±8.88	86.63±7.29	0.30	85.56±8.67
TC(mg/dL)	168.27±33.45	172.09±25.21	0.42	164.77±29.78	176.52±26.83	0.01	169.65±30.72
LDL(mg/dL)	93.48±28.24	95.81±20.99	0.56	89.88±24.92	99.05±23.18	0.02	94.32±25.83
TG(mg/dL)	84.87±38.80	108.75±47.07	<0.0001	82.72±31.07	108.34±51.97	<0.0001	93.47±43.39
HDL(mg/dL)	54.18±11.39	53.76±15.38	0.83	54.69±11.30	54.60±15.58	0.96	54.03±12.93

Values are presented as mean ± SD BMI: Body mass index; WC: Waist circumference; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; FBG: Fasting blood glucose; TC: Total cholesterol; TG: triglycerides; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; FMP: Fat mass percent.

significant difference in other obesity indices and cardiometabolic factors.

Comparing metabolic factors of children according to the number of household members revealed no significant differences. There were also no significant differences in metabolic factors in relation to the children's order in the family, and there was no significant difference in metabolic factors of children according to parents' education level.

## DISCUSSION

In the current study, children of parents with MetS were more prone to develop cardiometabolic complications even in the early years of life. This is likely due to both familial and environmental factors. These findings underscore the importance of drawing additional attention to primary prevention for children of parents with MetS. This population would benefit from early screening as well as special lifestyle modifications to prevent long-term complications.

Although many researchers have studied the potential contribution of genetic and environmental influences on cardiometabolic syndrome components, most of these estimations are only available

for a subset of components and they vary widely.<sup>26,27</sup> In addition, very limited experience is available from developing countries. The present study assessed both familial and environmental factors on cardiometabolic risk factors in children of parents with MetS. Significant correlations between children's and parent's lipid profile can be interpreted in two ways. The first expresses the effects of genetic and familial relationships. Lipid metabolism is controlled by heritable factors, and due to this genetic similarity, lipid profile is significantly correlated between parents and children.

Therefore, this high correlation could be equivalent to the high heritability of plasma lipid and lipoprotein concentrations. This hypothesis is consistent with prior research findings that have identified genes which effect lipid and lipoprotein concentrations, or the lipid response to dietary change. For example, genetic polymorphisms for proteins involved in lipoprotein metabolism (ex. apolipoprotein E, cholesterylester transfer protein, and hepatic lipase) have been either identified as candidate genes for cardiovascular risk or found to modify the lipid response to dietary change.<sup>28,29</sup> The second interpretation revolves around the effect of

Table-III: Pearson Correlation coefficients (r) between children's and parents' cardio-metabolic factors.

Children	Fathers							Mothers						
	BMI	WC	FBG	TC	LDL	TG	HDL	BMI	WC	FBG	TC	LDL	TG	HDL
BMI	0.19	0.18	-0.04	0.17	0.19	0.14	-0.22	0.28*	0.41	0.32*	-0.11	-0.10	0.03	-0.04
WC	0.14	0.17	-0.01	0.20	0.17	0.16	-0.21	0.20*	0.30	0.27*	0.00	0.00	0.07	0.04
FBG	-0.05	0.23	0.26	-0.18	-0.13	0.12	-0.12	0.04	0.06	0.14	0.00	-0.02	0.07	0.10
TC	0.28**	0.21	-0.02	0.62**	0.64**	0.20	0.09	-0.11	0.02	-0.03	0.19	0.06	0.05	0.24*
LDL	0.19	0.20	-0.27	0.39*	0.41**	0.13	0.13	-0.12	-0.05	0.02	0.12	0.02	0.09	0.19
TG	-0.14	0.07	0.00	0.24	0.22	0.19	0.02	0.28*	0.05	0.06	-0.02	-0.03	0.13	0.05
HDL	0.21*	0.04	0.19	0.28	0.24	0.06	-0.11	-0.12	0.08	-0.16	0.06	-0.02	-0.12	0.24*

\*P-value<0.05; \*\*P-value<0.01

BMI: Body mass index; WC: Waist circumference; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; FBG: Fasting blood glucose; TC: Total cholesterol; TG: triglycerides; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; FMP: Fat mass percent.

common environmental factors such as dietary and physical activity habits. Because most of the children in this study were living with their parents, the diet is a common factor within the family and can affect both groups in similar ways. To eliminate biases due to common diet, we need another study on children with lifestyles independent of their parent's. However, this may not be easily performed for children within this age range.

Another important point is that correlations are not limited only to lipid profiles. Significant correlations between mothers FBG with children's WC, BMI and FMP imply that there are correlations among all components of MetS.

This study showed significantly higher TG levels in children cared for by people other than their biological parents. Because the population of our study was children of parents with MetS, they were genetically predisposed to this disorder. Keeping children with their biological parents may lead to a better caring situation that can prevent symptoms of MetS. Parents' insight in dealing with MetS and their knowledge of managing it can result in limiting environmental predisposing factors in their children.

It is important to note that the psychological state of children who are cared for by people other than their biological parents is different. In the most cases, non-biological parents who keep these children pay more attention to them and try to compensate their emotional problems by encouraging them to eat. They also assist them in daily activities more than biological parents. This could lead to more dietary intake and less activity. These conditions can lead to a disturbed lipid profile in these children. As previous studies have concluded, environmental factors such as diet and exercise are shared within families.<sup>30,31</sup> Therefore, parents suffering from MetS may provide better diets and encourage exercise for their children because of their higher awareness regarding MetS.

We also studied obesity anthropometric indices and its associated effects on children's health conditions. While many people believe that obesity and its related changes are problems of adulthood, studies support the theory of early onset of metabolic changes along with childhood obesity. Children with increased WC had significantly higher TG, TC, LDL, FMP, and SBP. These findings confirm the importance of central obesity in childhood. BMI is an indicator of general obesity, and studies have described relationships between higher BP and increasing BMI.<sup>32-34</sup> In our study, when chil-

dren were classified based on BMI percentiles TG, FMP, SBP, and DBP were significantly lower in the normal BMI group. Our results confirm previous studies in adults that report WC is most associated with cardiometabolic factors, followed by BMI and health risks.<sup>35</sup>

With regards to the effects of diet on cardiometabolic factors among children, we found significant correlations between WC and carbohydrate consumption. This implies the importance of addressing the problem of overconsumption of starchy foods, which is common among many Iranian families. Significant correlations between WC and carbohydrate consumption supports the important role of carbohydrates in childhood obesity. This is consistent with data reported in another study concerning the unfavorable nutritional status caused by high carbohydrate diets found among kindergarten children in Crete.<sup>36</sup> Analyzing children's daily diet also showed that nuts can improve lipid profile. This finding is consistent with previous reports on the association between nut consumption and improved lipid profiles, suppression of oxidative stresses, and increased support of antioxidant systems, leading to reduced risk of cardiovascular diseases.<sup>37</sup> Despite high fat content in many nuts, recent studies have shown that the unsaturated fatty acid content is responsible for their lipid-lowering effects.<sup>38-41</sup>

Cardiometabolic syndrome was also studied in relation with psychological factors. The hypothesis that psychological factors influence BP goes back to at least 100 years.<sup>42</sup> In the current study, children were assessed for psychological status, and we found that among all cardiometabolic components, only SBP was affected by psychological factors. Our results confirmed the old hypothesis: "the more depressed mood, the less systolic blood pressure". Previous publications have shown this result in adults during long-term investigations. For example, a study of adults in Norway reported that symptoms of anxiety and depression predicted lower blood pressure 11 years later.<sup>42</sup> Our results among children are in line with this study. In general, our findings are consistent with other familial studies on cardiometabolic risk factors.<sup>43,44</sup> and underscore the importance of family-centered interventions.

## CONCLUSION

This study showed the association of different factors on cardiometabolic risk factors in childhood and their relationship with their parents. Additional

research must be conducted to determine the exact influence of each of these factors. In particular, familial and environmental factors must be studied independently to account for limitations such as the "common diet" among family members. Long-term studies on both parents and their children are needed to better understand the effects of familial factors and genetic-environmental interactions.

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