MATERNAL OBESITY - A RISK FACTOR FOR METABOLIC SYNDROME IN CHILDREN

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Abstract

Objective. *To determine the association between the metabolic syndrome in children (MS) and the pre-pregnancy nutritional status of the mother.*

Design and methods. *A total number of 180 children aged between 6-19 years were examined. Self reported data about parents and their children were collected. The children underwent physical examination; weight, height, waist circumference, blood pressure (BP) were measured. The nutritional status of the children was assessed by body mass index (BMI) and laboratory tests needed to diagnose MS were performed. IDF criteria for MS were used in children 10 years and older, and age and gender specific cut-off points in children younger than 10 years. The mothers were classified in the normal weight, overweight and obese categories according to the pre-pregnancy BMI. The statistical analysis of the data was descriptive and inferential analysis. In the bivariate analysis of the association between qualitative variables, we used the Chi-Square test and the exact Fisher test. The statistical analysis was performed with SPSS v 13.0.*

Results. *73 (40.55%) children were normal weight, 54 (30%) were overweight and 53 (29.44%) were obese. None of the normal weight children, 16 (29.60%) of the overweight and 23 (43.40%) of the obese ones had MS; 125 (69.44%) of the mothers were normal weight, 44 (24.44%) were overweight and 11 (6.11%) were obese.*

Pre-pregnancy maternal BMI was significantly associated with offspring MS in both genders, obese children and in the 10-16 age group.

Conclusions. *Pre-pregnancy maternal overweight/obesity represents a risk factor for offspring MS. The results are very difficult to compare between studies because of different cut-off values and definition of MS in children. If prevention is the goal rather than treatment, the perinatal period may be an important focus for future research.*

Keywords: obesity, overweight, metabolic X syndrome, child, fetal programming, risk factors.

Introduction

Obesity and its related diseases represent a threat for the population health and lifestyle, considering the increased prevalence of the disease in the last decades.

The prevalence of obesity among women of child-bearing age is increasing, in the USA 34% are obese and 59.5% overweight. In Europe the prevalence ranges between 6.2% - 36.5% with geographical variations, higher in Central, Eastern and Southern Europe than in Western and Northern Europe [1,2].

This increase is the result of several factors, lifestyle playing an important role. Emerging and increasing evidence suggest the role of factors acting early in the life of the individual and their long term influence on the metabolism, therefore pregnancy represents a critical period. One of these factors is the maternal overweight/obesity.

Recent studies on animals suggest the alteration of the oocytes quality, the influence of maternal obesity on the conception product being previous to fertilization. The

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obesity risk in offsprings of females with weight excess at the time of conception is maintained even if the diet is normal during pregnancy. Several modifications of the body composition occur, such as the increase in intramuscular fat content and altered expression of genes important in muscle growth and metabolism, leading to insulin-resistance. The maternal obesity influences the appetite, the physical activity, the structure and the function of the muscular tissue, as well as the alteration of adipocytes biology on a long-term basis [3].

An association between the obesity of the child and the BMI of the mother before and during pregnancy may be observed in humans, too. Alterations were observed in the newborn body composition if the mother had weight excess, such as an increase of the quantity and percentage of fat tissue. It seems that these associations are maintained into adulthood [3].

The increase of fatty tissue and the weight of the newborns from obese mothers are the result of metabolic changes during pregnancy (decrease of insulin sensitivity, increase of insulin resistance), as opposed to normal weight women, thus affecting the foetus-placenta development and growth [4].

Boney and co., studying a group of children of mothers with gestational diabetes and a group of children of mothers without gestational diabetes, found the same association between the maternal obesity and MS in children, the odds of MS being twice greater in children with obese mothers [5]. This would suggest that the foetal hyperinsulinemia in foetuses of overweight/obese mothers without gestational diabetes, is due to maternal hyperglycaemia, but with values below the threshold for the diagnosis of gestational diabetes. There is a relation between high BMI of the mother and hyperinsulinemia of the developing child (showed via determination of the C peptide from the umbilical cord) [6]. The high insulin secretion in offsprings of overweight/obese women is maintained during the entire life of the child [5].

Changes of the fat and protein metabolism may be noticed along the glucose metabolism changes, especially in the case of excessive alimentary intake of the mother. Increased serum glucose levels of the mother, free fatty acids and amino acids produce permanent alterations in the regulation of the appetite, the neuronal and endocrine systems and the energetic metabolism of the foetus, thus determining obesity and a high risk of metabolic syndrome in the subsequent life of the individual [7].

Studies have evidenced metabolism disturbances in obese women during pregnancy and support Baker and Gluckman's hypothesis arguing the "foetal origins" of the diseases, subsequently named the "Developmental Origins of Adult Health and Disease" (DOHaD). Therefore one may assume that the influence the maternal obesity on the child starts during intrauterine life and continues throughout the life of the individual [4,8,9].

Objective of the Study

To determine the association between metabolic syndrome in children and the pre-pregnancy nutritional status of the mother.

Design and methods

We performed a cross sectional retrospective study in a group of 180 subjects, children aged between 6-19 years old, referred to the Paediatric Clinic 2 of Cluj-Napoca, and children from 2 schools in the same city. The study was performed during the period 2005-2010. The parents of the children gave their informed consent to use the data in this study. We obtained the approval of the medical ethics committee of the Pediatric Emergency County Hospital.

Data on the parents and maternal anthropometric data at the time of conception (pre-pregnancy nutritional status) were obtained by anamnesis. The children were measured: weight, height, waist circumference (WC) and blood pressure (BP). We calculated the body mass index (BMI) for the children and the mothers

The laboratory tests performed were: fasting glucose level, oral glucose tolerance test, fasting insulin level, total

Table I. Metabolic syndrome in children-definition criteria.

Age	WC	TG	HDL	BP	Glucose
<10 years	>p90	>p90 and/or ≥150 mg/dl	<p10 and/or <40 mg/dl	>p90	gl ≥100 mg/dl and/or OGTT ≥200 mg/dl and/or HOMA-IR >2.5
10-16 years	>p90	≥150 mg/dl	<40 mg/dl	BPs ≥130 mmHg BPd ≥85 mmHg	gl ≥100 mg/dl and/or OGTT ≥200 mg/dl and/or HOMA-IR >2.5
>16 years	Girls ≥80 cm Boys ≥94 cm	≥150 mg/dl	Girls <50 mg/dl Boys <40 mg/dl	BPs ≥130 mmHg BPd ≥85 mmHg	gl ≥100 mg/dl

WC: waist circumference; HDL: high-density lipoprotein cholesterol; BP: blood pressure BPs systolic BPd diastolic; gl: fasting glucose; OGTT: oral glucose tolerance test.

cholesterol, HDL cholesterol, triglycerides.

We defined the metabolic syndrome according to IDF criteria for children and adolescents [10]. Considering there is no clear definition of this syndrome in children younger than 10 years old, we used age and gender specific cut-off points, as mentioned in the table, according to each variable [11-15]. The definition used in this study is presented in the table I. We considered a MS diagnosis if at least 3 of 5 criteria were present, based on the latest IDF recommendations in adults [16].

Subjects were distributed into 3 age groups (younger than 10 years, between 10-16 years old and older than 16 years) according to the MS definition in children, into two groups by gender and into 3 groups according to the nutritional status. The nutritional status of the children was assessed based on the BMI and the groups of normal weight, overweight and obese children according to the IOTF references were established [17]. The children were also grouped depending on the pre-pregnancy nutritional status of the mother, BMI: <25 kg/m^2 normal weight, between 25-29.99 kg/m^2 overweight, ≥30 kg/m^2 obese. Only those with idiopathic obesity were included in this study, we excluded the mothers and children with obesity due to other causes and children with diseases which might influence the laboratory tests.

Statistical method

The statistical analysis of the data was descriptive and inferential analysis. In the bivariate analysis of the association between qualitative variables, we used the Chi-Square test and the exact Fisher test. The quantification of the association was estimated by the odds ratio (OR) and the 95% confidence interval. The significance level for all tests was α=0.05. Thus, the type 1 error rate we are willing to assume is 5%. Test significance is given by the bilaterally observed significance level, p<0.05. The exact Fisher test was used if at least 20% of the theoretical frequencies were less than 5. The statistical analysis was performed with SPSS v 13.0.

Results

Of the 180 subjects, 98 (54.44%) were girls, 82 (45.55%) were boys. There were 78 (43.33%) under 10 years old, 90 (50%) between 10-16 years old, and 12 (6.66%) older than 16 years. According to the nutritional status of the children, we had 73 (40.55%) normal weight, 54 (30%) overweight and 53 (29.44%) obese (table II).

By analyzing the association between the pre-pregnancy nutritional status of the mother and the presence of the metabolic syndrome in children we noticed an increasing percentage of children with MS with increasing pre-pregnancy maternal BMI. A percentage of 12.8% of children with normal weight mothers (BMI <25 kg/m^2) had MS, the percentage increased to 38.6% in children with overweight mothers (BMI 25-29.99kg/m^2) and reached 54.4% in children whose mothers were obese (BMI ≥30 kg/m^2) at the time of conception. We found a statistically significant association between the pre-pregnancy nutritional status of the mother and the presence of MS in children (Chi-Square test, p<0.001) (table III).

Table II. Gender, age and nutritional status of the children.

Gender		Age		Nutritional status	
Girls	98 (54.44%)	< 10 years	78 (43.33%)	Normal weight	73 (40.55%)
Boys	82 (45.55%)	10-16 years	90 (50%)	Overweight	54 (30%)
		>16 years	12 (6.66%)	Obese	53 (29.44%)

Table III. Metabolic syndrome in children with overweight, obese and normal weight mothers.

pre-pregnancy BMI of the mother		MS present	MS absent	Total	Pearson Chi-Square
≥30	number of subjects	6	5	11	χ2=20.262
	%	54.5%	45.5%	100.0%	df=2
25 <30	Number of subjects	17	27	44	**p<0.001**
	%	38.6%	61.4%	100.0%	
<25	Number of subjects	16	109	125	
	%	12.8%	87.2%	100.0%	
Total	Number of subjects	39	141	180	
1 cells (16.7%) have expected count less than 5. The minimum expected count is 2.38.					

Table IV. Metabolic syndrome in children with overweight/obese and normal weight mothers.

pre-pregnancy BMI of the mother		MS present	MS absent	Total	Pearson Chi-Square
≥25	Number of subjects	23	32	55	χ2=18.950
	%	41.8%	58.2%	100.0%	df=1
<25	Number of subjects	16	109	125	**p<0.001**
	%	12.8%	87.2%	100.0%	**OR=4.89**
Total	Number of subjects	39	141	180	95%CI=2.313-10.365

A percentage of 41.8% of children with overweight or obese mothers at the time of conception had MS as opposed to 12.8% of children whose mothers were of normal weight at the time of conception. The relation was statistically significant p<0.001. The odds of having MS was 4.89 times higher in children whose mothers were overweight or obese at the time of conception (table IV).

The association between the pre-pregnancy nutritional status of the mother remained statistically significant analyzed by gender: 42.3% of the girls from overweight or obese mothers had MS versus 11.1% of the girls with normal weight mothers at the time of conception. For boys, the percentages were similar: 41.4% and 15.1% respectively.

The study on the association between pre-pregnancy nutritional status of the mother and MS in children was performed in the sub-groups of overweight and obese children; in the sub-group of normal weight children we had no subjects with MS (table V).

Among the overweight children having MS, 33.3% had overweight or obese mothers and 28.6% had mothers with normal weight. For the obese children we found a statistically significant association between the BMI of the mother at the time of conception and MS presence in children (p<0.05). A percentage of 55.9% of the obese children with overweight or obese mothers at the time of conception had MS versus only 21.1% of those with normal weight mothers. The odds of having MS in obese children with overweight/obese mothers with at the time of conception is of 4.75 (95%CI=1.302-17.327) (table VI).

In the analysis of the relation between the nutritional status of the mother at the time of conception and the presence of MS in children, in the 3 age groups, we observed increased percentages of MS in children from overweight or obese mothers versus those from normal weight mothers for all 3 age groups. The relation was statistically significant only for the 10-16 years age group. For this age group, a percentage of 48.0% of those with overweight or obese mothers presented MS versus 10.8% of those with normal weight mother at the time of conception (table VII).

Discussion

The weight gain and the metabolic changes during childhood are the result of the interaction of various factors, including the genetic predispositions and the lifestyle (alimentation, physical activity) that developing

Table V. Metabolic syndrome in girls and boys with overweight/obese and normal weight mothers.

Girls		MS		Total	Pearson Chi-Square
pre-pregnancy BMI of the mother		present	absent		
≥25	Number of subjects	11	15	26	$\chi2$=11.895
	%	42.3%	57.7%	100.0%	df=1
<25	Number of subjects	8	64	72	**p<0.001**
	%	11.1%	88.9%	100.0%	**OR=5.86**
Total	Number of subjects	19	79	98	95%CI=2.012-17.109
Boys		MS		Total	Pearson Chi-Square
pre-pregnancy BMI of the mother		present	absent		
≥25	Number of subjects	12	17	29	$\chi2$=7.022
	%	41.4%	58.6%	100.0%	df=1
<25	Number of subjects	8	45	53	**p=0.014**
	%	15.1%	84.9%	100.0%	**OR=3.97**
Total	Number of subjects	20	62	82	95%CI=1.383-11.396

Table VI. Metabolic syndrome in overweight and obese children with overweight/obese mothers.

Overweight		MS		Total	Fisher's Exact Test
pre-pregnancy BMI of the mother		present	absent		
≥25	Number of subjects	4	8	12	p=0.734
	%	33.3%	66.7%	100.0%	
<25	Number of subjects	12	30	42	
	%	28.6%	71.4%	100.0%	
Total	Number of subjects	16 29.60%	38	54	
Obese		MS		Total	Pearson Chi-Square
pre-pregnancy BMI of the mother		present	absent		
≥25	Number of subjects	19	15	34	$\chi2$=6.019
	%	55.9%	44.1%	100.0%	df=1
<25	Number of subjects	4	15	19	**p=0.021**
	%	21.1%	78.9%	100.0%	**OR=4.75**
Total Number of subjects		23 43.40%	30	53	95%CI=1.302-17.3027
Overweight and obese		39 36.45%	68	107	

2 cells (33.3%) have expected count less than 5. The minimum expected count is 3.04.

Table VII. Metabolic syndrome in three age group children with overweight/obese mothers.

<10 years prepregnancy BMI of the mother		MS present	MS absent	Total	Fisher's Exact Test
≥25	Number of subjects	7	17	24	p=0.211
	%	29.2%	70.8%	100.0%	
<25	Number of subjects	8	46	54	
	%	14.8%	85.2%	100.0%	
Total	Number of subjects	15	63	78	
1 cells (25.0%) have expected count less than 5. The minimum expected count is 4.62.					
10-16years prepregnancy BMI of the mother		MS present	MS absent	Total	Pearson Chi-Square
≥25	Number of subjects	12	13	25	$\chi 2$=15.028
	%	48.0%	52.0%	100.0%	df=1
<25	Number of subjects	7	58	65	**p<0.001**
	%	10.8%	89.2%	100.0%	**OR=7.64**
Total	Number of subjects	19	71	90	95%CI=2.522-23.192
> 16 years prepregnancy BMI of the mother		MS present	MS absent	Total	Fisher's Exact Test
≥25	Number of subjects	4	2	6	p=0.242
	%	66.7%	33.3%	100.0%	
<25	Number of subjects	1	5	6	
	%	16.7%	83.3%	100.0%	
Total	Number of subjects	5	7	12	

early during the childhood [18]. The family is one of the most important components influencing the metabolic risk factors in children. The studies of the genetic-lifestyle interaction demonstrated the capacity of the environment to influence the genetic predisposition [19].

The prevalence of the metabolic syndrome in our study was high, 43.3% in obese children and 36.45% in obese and overweight children, within the range of other studies using IDF definition (16.4%-44.2%); in Europe the median prevalence was 21% with range between 8.9%-50% [20]. Studies in our country using IDF definition revealed a prevalence of metabolic syndrome in obese children between 20% [21] and 58% [22]. The high prevalence and variations in the prevalence may be due to the small sample size.

In our study, the BMI of the mother was significantly associated with the MS of the child, with the percentage of those with MS proportional with overweight/obesity of the mother at the time of conception. The odds of MS in children increased almost fivefold for those with overweight or obese mothers. The significant association is consistent with the literature, but the percentage of those with MS in our study was up to four times higher (Hirschler 8.5% vs 41.8%), and the odds of developing MS double (OR: Boney 1.8 Ekelund 1.61 vs 4.89). This might be explained by the various definitions of MS used, the age of the subjects included in the study, the obesity type of the mother [5,23,24].

Hirschler, in his initial studies, found a significant correlation between maternal abdominal-type obesity (assessed by WC) and MS in children, even stronger than with the metabolic risk factors, including MS of the mother. The subsequent studies which included 5 anthropometrical indices of the mother do not show any significant differences between their capacity to identify children with MS or overweight risk, the best association being the relation with the waist circumference of the mother. Pre-pregnancy BMI cut-off value which predicts the metabolic syndrome in children, as result of this study, was suggested as 30 kg/m^2, within the range of 27-30 kg/m^2 for optimal specificity and sensibility [18,23].

The effect of intrauterine conditions on the foetus seems to extend throughout the entire life of the individual, by affecting the body composition, the insulin secretion, the insulin resistance, but also the appetite and the lifestyle via the central nervous system by several mechanisms demonstrated only in animal models [3,5]. In our study, we found a significant association between the overweight/obesity of the mother and the MS of the child only within the 10-16 years age group where we used the recommended non-modified IDF definition for this age group. Ekelund found an increase of the odds of developing MS at the age of 15 of 1.36 times higher than at the age of 10.

The association of the overweight/obesity of the mother with the MS of the child was significant in both genders, with close percentages of the girls and boys with MS and having overweight/obese mothers, similar with other results in literature [5]. However the odds of having MS in girls was higher than in boys (5.86 vs. 3.97) in our study, as opposed to the results obtained by Ekelund, where the boys odds was 2.63 times higher than girls (the study was performed in children with obese and normal weight mothers).

The significant association between the overweight/obesity of the mother and the presence of MS only in obese children, considering that we had no normal weight children with MS, raises questions regarding the existence of the relationship between the overweight of the mother and the

MS of the children, or whether there is just a link between MS and child's obesity. Considering the small percentage of normal weight children with MS, the relatively small number of the group can limit the results.

Significant differences between the BMI of children with MS and children without MS and the BMI of the mother were also highlighted by the European Youth Hearth Study. Although the maternal BMI was significantly and independently associated with the MS of the child and BMI, the same relationship was not found in respect to the metabolic components of the MS. Therefore it could be argued that the adiposity of the mother determines the MS of the child via his adiposity, considering the well known association between the obesity of the mother and the increased weight at birth and further obesity of the child. The difference as compared to our study is the MS definition used, the central-type obesity being a *sine qua non* condition for the MS definition.(24) The weight of the mother before the pregnancy was determined by anamnesis, which might have influenced the accuracy of the data, given the time lapsed since the childbirth. Therefore a prospective study could bring more data.

The conclusions of this study are limited by its cross sectional design. Due to the small sample size, the statistical significance of the prevalence of MS in our study was limited. It shows the association between the MS of the child and the risk factors, but it cannot directly predict subsequent complications.

Conclusions

The overweight/obesity of the mother represents a risk factor for the metabolic syndrome of the child, especially in obese children. Further studies are needed in order to clarify the way in which the weight excess of the mother influences the development of the metabolic syndrome in children, directly or via the obesity of the child. Both genders are similarly affected by the overweight/obesity of the mother.

Considering the studies design differences, the population differences, the lack of a unanimously accepted definition of the metabolic syndrome of the child, the studies using different definitions, the various cut-off values of metabolic syndrome elements, the results are difficult to compare.

References

1. Berghöfer A, Pischon T, Reinhold T, et al. Obesity prevalence from a European perspective:a systematic review. BMC Public Health, 2008; 8:200.
2. Flegal KM, Carroll MD, Ogden CL, Curtin LR. Prevalence and trends in obesity among US adutls. JAMA, 2010; 303:235-241.
3. Drake AJ, Reynolds RM. Impact of maternal obesity on offspring obesity and cardiometabolic disease risk. Reproduction, 2010; 140:387-398.
4. Catalano PM, Ehrenberg HM. The short- and long-term implications of maternal obesity on the mother and her offspring. BJOG, 2006; 113(10):1126-1133.
5. Boney CM, Verma A, Tucker R, Vohr BR. Metabolic syndrome in childhood:associationwith birth weight, maternal obesity and gestational diabetes mellitus. Pediatrics, 2005; 115:290-296.
6. McIntyre & HAPO Study Research Group. Hyperglycaemia and adverse pregnancy outcome (HAPO) study: associations with maternal body mass index. Br J Obstet Gynaecol, 2010; 117:575-584.
7. Armitage JA, Poston L, Taylor PD. Developmental origins of obesity and the metabolic syndrome: the role of maternal obesity. Hor, 2008.
8. Whitaker RC. Predicting preschooler obesity at birth: the role of maternal obesity in early pregnancy. Pediatrics, 2004; 114:29-36.
9. Gluckman PD, Hanson MA, Pina LC. The developmental origins of adult disease. Matern Child Nutr, 2005; 1:130-141.
10. Zimmet PZ, Alberti G, Kaufman F, Tajima N, et al. The metabolic syndrome in children and adolescents: the IDF consensus. Diabetes Voice, 2007; 52(4):29-32.
11. McCarthy HD, Jarrett KV, Crawley HF. The development of waist circumference percentiles in British children aged 5.0±16.9y. Eur J Clin Nutr, 2001; 55:902-907.
12. Daniels SR, Greer FR, Committee on Nutrition. Lipid screening and cardiovascular health in children. Pediatrics, 2008; 122:198-208.
13 National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Pediatrics, 2004; 114:555-576.
14. Madeira IR, Carvalho CN, Gazolla FM, de Matos HJ, Borges MA, Bordallo MA. Cut-off point for homeostatic model assessment for insulin resistance (HOMA-IR) index established for receiver operating characteristic (ROC) curve in the detection of metabolic syndrome in overweight pre-puberatal children. Arq Bras Endocrinol Metabol, 2008; 52(9):1466-1473.
15. Report of a WHO/IDF consultation. Definition and diagnosis of diabetes mellitus and intermediate hyperglicaemia, 2006.
16. Alberti KGMM, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome:a joint interim statement of the International Diabetes Federation Task Force on epidemiology and prevention; National Heart, Lung, and Blood Institute; American Heart Association; Word Heart Federation; International Atherosclerosis Society; and International Association for the study of Obesity. Circulation, 2009; (120):1640-1645.
17. Cole TJ, Bellizzi MC, Flegal KM, Dietz W. Establishing a standard definition for child overweight and obesity wordwide:international survey. BMJ, 2000; 320:1240-1243.
18. Hirschler V, Roque MI, Calcagno ML, Gonzales C, Aranda C. Maternal waist circumference and the prediction of children`s metabolic syndrome. Arch Pediatr Adolesc Med, 2007; 161(12):1205-1210.
19. Bouchard C. Childhood obesity: are genetic differences involved? Am J Clin Nutr, 2009; 89:1494S-1501S.
20. Fried A, Craig L, Turner S. The prevalence of metabolic syndrome in children: a systematic review of the literature. Metab Syndr Relat Disord, 2013; X(X):1-10.
21. Pop A. Riscul dezvoltării sindromului metabolic la copilul obez. Teză de doctorat, 2011, cap VI.
22. Puha Preda M, Matasaru S. Sindromul metabolic în obezitatea

copilului. Practica Medicală, 2011; VI(2):155-161.
23. Hirschler V, Molinari C, Beccaria M, Maccallini G, Aranda C. Comparation of various maternal anthropometric indices of obesity for identifying metabolic syndrome in offspring. Diabetes Technol Ther, 2010; 12(4):297-305.
24. Ekelund U, Anderssen S, Andersen LB, et al. Prevalence and correlates of the metabolic syndrome in a population-based sample of European youth. Am J Clin Nutr, 2009; 89:90-96.