Associations between ENPP1 rs1044498 gene polymorphism, anthropometric parameters and maternal obesity

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Introduction

Obesity is a major health problem in developed countries. The incidence of obesity is increasing in both children and adults, leading to major metabolic and cardiovascular complications. The ENPP1 (nucleotide pyrophosphatase /phosphodies-terase-gene) inhibits the sensitivity of insulin receptor, being considered a gene with a potential role in determining insulin-resistance and type 2 diabetes mellitus.

The aim of this study was to evaluate the impact of ENPP1 on maternal nutritional status, and its correlations with paraclinical and anthropometric parameters (mid-upper arm circumference - MUAC, and tricipital skinfold thickness - TST).

Material and method

We performed a cross-sectional study on 185 mothers admitted in a Tertiary Hospital from Romania. We divided the subjects into 2 groups: Group I - 52 mothers with high BMI (≥30) and Group II - 133 mothers with BMI<30 – control group. Both groups were assessed anthropometrically (MUAC, TST), clinically and genetically (the ENPP1 rs1044498 gene polymorphisms). The associations between genetic, anthropoetric, bioimpedance factors and maternal obesity were performed using Chi-square test, Student-t test and Mann-Whitney test. Data analysis was performed with R (v3.4.3).

The inclusions criteria were: maternal age above 18 years and single pregnancies.

The exclusion criteria were: intrauterine growth retardation as a result of congenital malformations, chronic disorders, intrauterine infections, the lack of complete clinical, paraclinical, anthropometric and genetic data, but also mothers who refused to sign the informed consent for themselves and for their newborns before the inclusion in the study.

Results:

The mean age of mothers included in the study was 28.10±5.80 years, over 50% of them having higher education, most of them being primiparas (56.2%), with a medium gestational weight gain of 17.1±6.2 kg. Of all 185 pregnant women, 11.4% were smokers, 5.90% presented preeclampsia and only 2.7% gestational diabetes.

We noticed that in obese mothers the wild genotype AA of ENPP1 rs1044498 gene polymorphism was more frequent than variant (AC+CC) genotype: 32 cases (61.5%) versus 20 (38.5%), while in control group 97 cases (72.9%) versus 36 (27.1%). We found no significant association between ENPP1 rs1044498 gene polymorphism and maternal obesity (p=0.129).

After adjusting for maternal covariates as maternal age, education level and parity, the presence of ENPP1 rs1044498 variant genotype (CT+CC) had an increased risk of pre-pregnancy overweight (adjusted OR=1.34; 95%CI:[0.65; 2.75]).

We did not find significant associations between the variant genotype of ENPP1 rs1044498 SNP and GWG status (Table 1). After controlling for maternal covariates such as maternal age, educational level, parity, smoking in pregnancy, the presence of ENPP1 rs1044498 SNP variant genotype (CT+CC) was not significantly associated with an increased risk of excessive GWG (adjusted OR=0.77; 95%CI:[0.34;1.71] and insufficient GWG: adjusted OR=0.89, 95%CI:[0.28;2.84]).

In obese group, the distribution values of the anthropometric parameters, such as MUAC (median [percentile 25%; percentile 75%]: 33.4[31.6; 35.6] vs. 28 [26.3; 29.2] mm), TST (25.7[21.9; 30.1] vs 14.8 [11.1; 19.7] mm) and the maternal weight after birth (86.65 [81.4; 95.3] vs. 67.5 [61.4; 72.1] kg) were significantly higher (p< 0.001).

Table 1. Associations between ENPP1 rs1044498 SNPs and GWG status

	Study sample n(%)	Underweigh t/normal n(%)	Overweight /obesity n(%)	p*	Insufficien t GWG n(%)	Normal GWG n(%)	Excessive GWG n(%)	p*
ENPP1 rs1044498 Maternal SNP								
AA	129 (69.7)	95 (70.9)	34 (66.7)	0.576	19 (70.4)	28 (66.7)	82 (70.7)	0.886
AC+CC	56 (30.3)	39 (29.1)	17 (33.3)		8 (29.6)	14 (33.3)	34 (29.3)	
A-allele	310 (83.8)	226 (84.3)	84 (82.4)	0.645	46(85.2)	68 (80.9)	196 (84.5)	0.166
C-allele	60 (16.2)	42 (15.7)	18 (17.6)		16 (29.6)	16 (19.1)	36 (15.5)	
p-value for HW	0.640	0.849	0.571		0.366	0.634	0.574	

Legend: GWG=Gestational weight gain; [®] Hardy-Weinberg equilibrium; * p-values obtained from Chi-square or Fisher's exact tests. ENPP1rs1044498 A>C: nucleotide pyrophosphatase/phosphodiesterase gene polymorphisms (AA=reference category); AA – homozygous for A allele; AC – heterozygous; CC - homozygous for C allele;

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In the studied sample, the mean BW was 3368 g±448, with 9.7% (18 cases) above 4000 grams. We did not find a significant difference between the mean in BW in the newborns whose mothers had an initial BMI ≥25 kg/m² in comparison to those from mothers with an initial BMI<25 kg/m². BW, MUAC and TST were significantly associated with maternal GWG status (p<0.001). In the post-test analysis, the mean BW was significantly different in newborns whose mothers had insufficient GWG in comparison to those from mothers with excessive GWG. Therefore, the mothers with excessive GWG had newborns with higher BW (Table 2).

Conclusions

In obese women, we identified significant higher values for anthropometric parameters as MUAC, TST and maternal weight after birth, but also a higher frequency of the wild genotype of ENPP1 rs1044498 gene polymorphism.

Disclosure of interest: “None Declared”.

Table 2. Relationship between studied gene polymorphisms and neonatal anthropometric bioimpedance characteristics

Factors	Birth weight (kg)		MUAC (cm)		TST (cm)	
	Mean±SD	p ⁺	Median[Q1;Q3]	p ⁺	Median[Q1;Q3]	p ⁺
BMI initial (kg/m ²)						
< 25	3.33±0.45	0.094	10.5[10.0;11.3]	0.075	2.8[2.3;3.4]	0.912
≥25	3.46±0.45		11.0[10.5;11.5]		2.9[2.4;3.2]	
GWG status						
Insufficient	3.11±0.49	<0.001	10.3[9.7;10.8]	0.005	2.3[2.0;2.8]	<0.001
Normal	3.28±0.43		10.5[10.2;11.4]		2.8[2.4;3.5]	
Excessive	3.46±0.42		11.0[10.5;11.5]		2.3[2.0;2.8]	
ENPPI rs1044498 Maternal SNP				0.149		
AA	3.35±0.43	0.333	10.5[10.0;11.3]	0.085	2.8[2.3;3.2]	0.208
AC+CC	3.42±0.49		11.0[10.3;11.5]		3.0 [2.4;3.4]	

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Legend: SD=standard deviation; Q1=first quartile; Q3=third quartile; * p-values obtained from Student-t test for independent samples, ANOVA test or nonparametric test (as Mann-Whitney or Kruskal-Wallis) BMI: Body mass index, BW: birth weight, MUAC: Middle upper arm circumference, SD: standard deviation, TST: Tricipital skinfold thickness. ENPP1 rs1044498 A>C: nucleotide pyrophosphatase/phosphodiesterase gene polymorphisms (AA=reference category); AA – homozygous for A allele; AC – heterozygous; CC - homozygous for C allele;

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