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Perinatal and family factors associated with preadolescence overweight/obesity in Greece: The GRECO study

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KEYWORDS Obesity; Adolescence; Pre- and post-natal factors

Abstract *Objective*: To explore associations of perinatal and family factors with preadolescence overweight and obesity in a sample of Greek schoolchildren.

Methods: A nationwide cross-sectional study among 2093 students $(10.9 \pm 0.72 \text{ years}, 44.9\% \text{ boys})$ and their parents were conducted. Anthropometric (e.g., height, weight, mother's body mass index (BMI) at the time of the study and at conception), socio-demographic (e.g., age, education, socio-economic status), diet and other major lifestyle characteristics (e.g., smoking, alcohol intake, physical activity and inactivity) and perinatal factors (e.g., breast- and formula-feeding) were collected with validated questionnaires. Height and weight of students were measured. Overweight/obesity was classified using IOTF cut-offs. Multivariable logistic and linear regression analyses were used to identify major independent factors of overweight/obesity among preadolescents and factors related with the percentage change of mother's BMI, respectively.

Results: Increased age at pregnancy [odds ratios (OR) = 0.95, 95% Confidence Interval (CI): 0.93–0.97], higher BMI at conception (OR = 1.17, 95% CI: 1.12–1.22) and heavy smoking (OR = 2.02, 95% CI: 1.23–3.33) were positively associated with child's overweight/obesity status. Moreover, mother's age and TV viewing, indicating inactivity, were the strongest factors of the percentage increase in mother's BMI ($b \pm se = 0.23 \pm 0.07$, p = 0.002; $b \pm se = 0.32 \pm 0.10$, p = 0.002, respectively).

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Conclusions: Preadolescent obesity is associated with mother's pre-pregnancy weight, age and heavy smoking at conception and mother's BMI change after gestation.

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1. Introduction

Childhood and adolescent obesity is now an epidemic, as an alarming increase has been noted in the prevalence of overweight and obesity throughout Europe and especially in the Mediterranean countries [1]. This is also depicted in several Greek studies [2,3] as adulthood obesity can be tracked back to early life [4]. Therefore, it is important to study the main causes of obesity in youth. Fetus growth in the uterus and the first years of life have been proposed to affect an offspring's later development, body composition and health status [5-6], although there have been some confounders to this hypothesis. In the uterus, the fetus experiences a period of rapid growth, multiplication of the cells and differentiation of the organs, while during infancy the function and development of the brain, metabolism and other physiological mechanisms are regulated. Thus it is important to investigate perinatal factors and their predictive role in obesity progression. Pre-pregnancy weight [7,8], weight increase during gestation [7,9], gestational age [10,11], smoking habits before and during pregnancy [12-17], alcohol [10,11] and coffee [18] consumption during the same period, birth weight [9,19,20] and breastfeeding duration and lifestyle of the mother during lactation [21,22] have been found to be strongly related to an elevated risk of overweight and obesity, either directly or through mediating factors, such as fetal growth restriction [18] and rapid weight gain [22]. In addition, the Fleurbaix-Laventie Ville Santé Study in France [23] showed that mother's body mass index (BMI) is a significant factor of her children's BMI after puberty, giving more ground for research in the field of prospective effect of mother's weight on the likelihood of having an overweight/obese offspring.

Relative studies in Greece have evaluated the link between factors associated with overweight or obesity in childhood [24] and adolescence [25]. However, information regarding the association of perinatal and family environment on the prevalence of overweight/obesity is limited. Thus, this work, as a part of the GRECO (Greek childhood obesity) study, aimed to investigate the perinatal and family factors that are related to the prevalence of children's overweight/obesity and the factors associated with mother's weight gain. As a benefit, the results of this work may assist the development of health promotion programs focused on preventing obesity.

2. Methods

In order to provide national estimates of overweight and obesity among Greek schoolchildren, as well as to evaluate possible risk factors, a nationally representative survey, the GRECO study, was performed among fifth and sixth grade students of primary schools aged 10–12 years old.

2.1. Study's sampling procedure

The study was carried out from October 2008 to 2009. total of 4786 children May А (10.9 ± 0.75 years, 49.3% boys) were voluntarily enrolled in the study (participation rate 95%). The number of schools that agreed to participate in the study was 117 from 10 regions all over the country. All participating children were informed about the aims and the procedures of the study, and their parents signed parental consent forms. A more detailed description of the sampling procedure has been reported elsewhere [3].

2.2. Measurements: Anthropometry, obesity and underweight definition

All measurements were conducted by trained personnel (i.e., nutritionists and dietitians) of the Unit of Human Nutrition of the Agricultural University of Athens. All measurements were performed during morning hours. Body weight was recorded to the nearest 10 g with the use of a digital scale (Tanita TBF 300) and with subjects standing without shoes in light clothing. Standing height was measured using a portable stadiometer (Leicester height measure) to the nearest 0.1 cm without shoes, with the head positioned according to the Frankfort plane. BMI was calculated by dividing weight (kg) by standing height squared (m²). Obesity and overweight measures among children were calculated using the IOTF (International Obesity Task Force) age- and gender-specific BMI cut-off criteria [26].

2.3. Dietary and physical activity assessment

Dietary assessment was based on a validated, selfreported, semi-quantitative food frequency questionnaire (FFQ), including 48 food items commonly used in the local Greek cuisine [3,27]. The KIDMED index (Mediterranean Diet Quality Index for children and adolescents) was used to evaluate the degree of children's adherence to the Mediterranean diet [28]. Physical activity status was measured using the Physical Activity Questionnaire for Older Children (PAQ-C) [3,29].

2.4. Information obtained by parents/ guardians

Information on parents' demographic characteristics, such as parents' age, years of education, annual household income, employment status (i.e., non-working vs. private sector, public sector, freelance), profession, type of occupation (i.e., manual, mixed, non-manual), and ownership of the residence, were collected via a questionnaire that was given to the children's parents/guardians.

Of the 4786 guestionnaires obtained by the children, 2138 were also answered by their parents (45% participation rate). Parents' body height (m) and weight (kg) were self-reported and used to calculate parents' BMI (kg/m^2) and to define parents' overweight (BMI 25–29.9 kg/m²) and obesity (BMI \geq 30 kg/m²), according to the World Health Organization classification for adults. Parents' lifestyle characteristics, such as physical inactivity (measured by hours of TV viewing/week), physical activity status (yes vs. no) and quality of diet, according to MedDietScore were also collected. MedDiet-Score (range 0-55) is used to evaluate parents' adherence to the Mediterranean Diet, with high values indicating high adherence to this particular regime [30].

Participants' mothers were additionally asked to complete a questionnaire regarding their demographic and lifestyle characteristics during pregnancy. Specifically, they were asked about their age (years) at pregnancy, body weight (kg) at conception, weight gain during pregnancy (kg), total period of gestation (weeks), smoking habits at conception, gestation and lactation (none, 1-9cigarettes/day, 10–20 cigarettes/day, \geq 20 cigarettes/day, in all cases), coffee intake at gestation (none, 1 cup/day, \geq 2 cups/day), alcohol intake at gestation and lactation (none, 1 drink/day, ≥ 2 drinks/day) and for the number of exclusive and total (i.e., along with formula milk intake) months of breast feeding. The percentage (%) change of mother's BMI was also calculated as the difference between the current BMI (at the time of the study) and the BMI at conception according to the following formula: $(BMI_{(current)} - BMI_{(conception)}) \times 100/BMI_{(current)}$.

2.5. Working sample

In this paper, data from 2093 children $(10.9 \pm 0.72 \text{ years}, 44.9\% \text{ boys})$ were used, in which information about weight and height was available, as well as a completed parents' questionnaire. The studied sample could be considered as representative of the overall study population (i.e., the 4786 children included for analysis in the GRECO study) as regards children's age and BMI distributions (both *p*'s > 0.05), but not gender (*p* < 0.05), and region (*p* < 0.01).

2.6. Statistical analysis

Results are presented as mean (SD) for the normally distributed variables, as median (25th percentile, 75th percentile) for the skewed ones and as frequencies for the categorical. The normality of the distributions regarding continuous variables was tested using graphical methods (i.e., p-p plots and histograms). Differences in the distribution of various characteristics between normal weight and overweight/obese participants were assessed using the *t*-test (for the normally distributed variables, i.e., weight of neonates at birth, mother's age at pregnancy, mother's BMI at conception, mother's current BMI, % increase in mother's body mass index) and the Mann-Whitney test (for the skewed, i.e., mother's weight gain during pregnancy, total weeks of gestation, months of exclubreastfeeding, and months of total sive breastfeeding). Associations between categorical variables were tested using Pearson's chi-square test (i.e., smoking habits at conception, gestation and lactation; coffee intake at gestation; alcohol intake at gestation and lactation). Unadjusted logistic regression analyses were used to evaluate the association of pre- and post-natal factors on the likelihood of overweight/obesity in preadolescents. To account for residual confounding, multivariable logistic regression models for each one pre- and post-natal factor were also estimated after adjustment for children's age, sex, physical activity level (according to the IPAQ score) and quality of diet (according to the KIDMED index) (Multivariable 1). Moreover, all factors that were found to be significantly associated with overweight/obesity among preadolescents in previous analyses were included in multivariable logistic regression analysis, after checking for co-linearity

(children's age, gender, physical activity and quality of diet adjusted) (Multivariable 2). The Wald test was used to hierarchy the factors that contribute the most to the model. Hosmer-Lemeshow statistic was used to test models' goodness-of-fit. Results are presented as odds ratios (OR) with their corresponding 95% Confidence Intervals (95% CI). Furthermore, a multivariable linear regression model was also performed to evaluate the factors that may be associated with the % change of mothers' BMI. Results are presented as $b \pm se$ along with their corresponding 95% CI. Weighting factors, according to children's age (i.e., 10-14) and gender distribution (i.e., boys/girls) by prefecture (i.e., Attica region, Central Greece, Peloponnese, Ionian islands, Epirus, Thessaly, Macedonia, Thrace, Aegean island, Crete) were applied to all analyses performed. All tested hypotheses were two-sided; p-value < 0.05 was considered statistically significant. SPSS version 18.0 software was used for all calculations (SPSS, Inc., Chicago, IL, USA).

3. Results

The prevalence of overweight/obesity among preadolescents according to IOTF cut-offs for the working sample (n = 2093) was 42% and did not differ from the prevalence reported for the total sample (i.e., 41%, n = 4786, p = 0.44) [3]. The distribution of pre- and post-natal anthropometric and lifestyle characteristics between normal weight and overweight/obese participants is presented in Table 1.

In order to accurately evaluate the association of pre- and post-natal factors with the likelihood of being an overweight/obese preadolescent, further analysis was applied and results are presented in. Unadjusted logistic regression analysis for the assessment of pre- and post-natal factors was performed, according to the observed differences in the distribution of the tested characteristics in both children's BMI groups. Results based on the unadjusted logistic models suggest that mother's age before pregnancy was inversely associated with the likelihood of being an overweight/ obese preadolescent (OR = 0.96, 95% CI: 0.94-0.98). On the contrary, mother's BMI at conception, and thus % change of mother's BMI, and heavy smoking at conception and gestation were positively associated with the likelihood of being an overweight/obese preadolescent. Specifically, 1 kg/m² increase of mother's BMI at conception was associated with 13% increase in the likelihood being an overweight/obese child of during preadolescence (95% CI: 1.08-1.18), while smoking >20 cigarettes/day before pregnancy and >10 cigarettes/day at gestation was associated with 2.45 and 2.84 higher odds of being an overweight/obese preadolescent, respectively (95% CI: 1.68–3.58 and 1.47–5.48, respectively). Results do not seem to alter when models were adjusted for children's age, gender, physical activity status (as measured by the IPAQ score) and quality of diet (as measured by the KIDMED index). Furthermore, children's age, gender, physical activity status (as measured by the IPAQ score), quality of diet (as measured by the KIDMED index), mother's age and BMI at conception, % change of mother's BMI and smoking habits at conception and at gestation were included in a multivariable logistic model. Results confirmed the previous findings. Moreover, 1% increase in mothers' BMI was associated with 2% increase in the likelihood of being an overweight/obese child during preadolescence (95% CI: 1.01-1.03) (Table 2).

According to the previous model, the % increase in mother's BMI was one of the most important factors associated with preadolescence overweight/ obesity (Wald test = 1641, p < 0.0001), followed by mother's BMI at conception and mother's age at pregnancy. Therefore, characteristics that may be associated with this change (i.e., mother's age, educational status, type of occupation, employment status, physical inactivity and activity and dietary habits) have been considered as factors associated with mother's % increase in BMI. Results revealed that one year increase in mother's age was associated with 0.23 kg/m² change in mother's BMI (se = 0.07, 95% CI: 0.08, 0.37), adjusted for all previously mentioned factors. In addition, sedentary lifestyle (as measured in hours of TV viewing per week) was associated with a % increase in mother's BMI ($b \pm se = 0.32 \pm 0.10$, 95% CI: 0.12-0.51) (Table 3).

4. Discussion

This study examined pre- and post-natal factors that influence the prevalence of overweight and obesity in preadolescents in Greece. The perinatal factors which were found to have a strong association with overweight/obesity were high maternal weight at conception and maternal heavy smoking (>20 cigarettes per day) at conception, even after adjustment for confounding factors. High maternal age at gestation was inversely associated with overweight and obesity. Moreover, as far as mother's weight change from conception to the time of the study is concerned, results revealed

	n	Normal-weighted (n = 1216)	Overweight/obese (n = 877)	p [‡]
Weight of neonates at birth (g)	1412	3261 (541)	3328 (519)	0.01
Mother's age at pregnancy (years)	1726	28.5 (4.9)	27.6 (4.6)	<0.001
Mother's body mass index at conception (kg/m^2)	1927	21.4 (2.8)	22.5 (3.2)	<0.0001
Mother's current body mass index (kg/m ²)	2074	23.6 (3.6)	25.0 (4.3)	<0.0001
% Increase in mother's body mass index*	1870	8.4 (9.7)	9.1 (10)	<0.0001
Mother's weight gain during pregnancy (kg)	1768	13.0 (10.0, 18.0)	14.0 (10.0, 19.0)	<0.0001
Smoking habits at conception (%)				<0.0001
No	1205	63	56	
1–9 cigarettes/day	321	15	17	
10–20 cigarettes/day	361	18	18	
>20 cigarettes/day	129	4.2	9.1	
Smoking habits at gestation (%)				<0.0001
No	1791	90	85	
1–9 cigarettes/day	210	9.3	12	
≥10 cigarettes/day	40	1.1	3.1	
Smoking habits at lactation (%)				<0.0001
No	1795	92	90	
1–9 cigarettes/day	159	7.4	9.0	
≥10 cigarettes/day	10	0.5	0.8	
Coffee intake at gestation (%)				<0.0001
No	831	42	39	
1 cup/day	1027	51	51	
≥2 cups/day	158	7.2	10	
Alcohol intake at gestation (%)				<0.0001
No	1986	96	97	
≥1 drink/day	86	4.4	3.3	
Alcohol intake at lactation (%)				0.004
No	1870	96	96	
≥1 drink/day	82	4.3	4.1	
Total weeks of gestation	1365	38.0 (36.0, 40.0)	38.0 (36.0, 40.0)	0.58
Months of exclusive breastfeeding	1514	2.0 (0.5, 4.0)	2.0 (1.0, 5.0)	0.10
Months of total breastfeeding	1815	3.0 (1.0, 6.0)	3.0 (1.0, 6.0)	0.93

Table 1 Differences between pre- and post-natal factors distribution (i.e., anthropometric and lifestyle characteristics) regarding to children's obesity status.[†]

* % Increase in mother's body mass index has been calculated as the difference between mother's current body mass index (at the time of the study) and body mass index at conception.

[†] Normally distributed continuous variables are presented as mean (standard deviation), while skewed as median (25th percentile, 75th percentile) and categorical as frequencies.

[†] *p*-Values were derived through comparisons between normal-weighted and overweight/obese children using *t*-test for normally distributed variables, Mann–Whitney test for skewed and Pearson's chi-square for categorical.

that an increase in mother's body weight may result in a considerable increase in the odds of having an overweight/obese offspring. Despite the limitations derived from the cross-sectional design, the results presented here have a considerable public health impact since they send out a clear message to the mothers that their lifestyle is associated with their offspring's health.

The weight of the mother at conception affects fetal growth and is an indicator for later obesity.

High pre-pregnancy weight may even double the odds for the 2-year-old offspring to be obese, as observed in the past [7]. Markedly, the odds ratio for the pre-pregnancy weight revealed a stronger association with preschoolers' obesity than with newborns and this effect seems to be strong in adolescence, too. More specifically, Kuhle *et al.* showed that for maternal pre-pregnancy weight over 80 kg, compared with a body weight less than 60 kg, the OR was 4.42 [8].

	Unadjusted		Multivariable 1 †		Multivariable 2 [‡]	
	OR	95% CI	OR	95% CI	OR	95% CI
Weight of neonates at birth (kg)	1.00	1.00-1.00	1.00	1.00-1.00	_	_
Mother's age at pregnancy (years)	0.96	0.94–0.98	0.96	0.94-0.98	0.94	0.92-0.97
Mother's body mass index at conception (kg/m ²)	1.13	1.08-1.18	1.13	1.09-1.18	1.17	1.12-1.22
Mother's % increase of body mass index* (kg/m ²)	1.01	1.00-1.02	1.01	1.00-1.02	1.02	1.01-1.03
Smoking habits at conception [§]						
0 cigarettes/day	1.00	_	1.00	_	1.00	_
1–9 cigarettes/day	1.28	0.99-1.65	1.26	0.98-1.63	1.32	0.99-1.77
10–20 cigarettes/day	1.10	0.86-1.41	1.09	0.85-1.40	0.97	0.70-1.36
>20 cigarettes/day	2.45	1.68-3.58	2.43	1.66-3.56	2.02	1.23-3.33
Smoking habits at gestation [§]						
0 cigarettes/day	1.00	_	1.00	_	1.00	_
1–9 cigarettes/day	1.34	1.00-1.80	1.32	0.99-1.78	1.31	0.87-1.97
≥10 cigarettes/day	2.84	1.47-5.48	2.84	1.46-5.54	2.24	0.88-5.67

Table 2Results from logistic regression analysis for the assessment of the main effect of pre- and post-natal factors onthe likelihood of being an overweight/obese pre-adolescent.

* % Increase in mother's body mass index has been calculated as the difference between mother's current body mass index (at the time of the study) and body mass index at conception.

[†] *Multivariable 1* regression models adjusted for children's age, gender, physical activity status (according to IPAQ score) and quality of diet (according to KIDMED score).

* *Multivariable* 2 regression model adjusted for children's age, gender, physical activity status (according to IPAQ score), quality of diet (according to KIDMED score) and all other factors (i.e., mother's age at pregnancy, mother's body mass index before conception, mother's % body mass index change, smoking habits at conception and gestation).

^s *p*-Trend = 0.001 for the univariate adjusted models in both cases.

Table 3Results from linear regression analysis to evaluate the association of mother's socio-demographic and lifestylecharacteristics on the % increase of mother's body mass index* (kg/m²).

	b ± se	(95% CI)
Mother's age (years)	0.23 ± 0.07	(0.08, 0.37)
Mother's educational status (years)	-0.13 ± 0.11	(-0.34, 0.07)
Mother's type of occupation		
Manual	Reference	
Mixed	-1.49 ± 1.02	(-3.48, 0.51)
Non-manual	-2.48 ± 1.16	(-4.75, -0.20)
Mother's job status		
Non-working [†]	Reference	
Free lancer	-0.84 ± 1.03	(-2.86, 1.17)
Private sector	-0.82 ± 0.97	(-2.73, 1.09)
Public sector	1.35 ± 1.02	(-0.66, 3.35)
TV viewing (hours/week)	0.32 ± 0.10	(0.12, 0.51)
Intense physical activity (yes vs. no)	-1.05 ± 0.57	(-2.16, 0.06)
MedDietScore (0–55)	0.06 ± 0.03	(-0.01, 0.13)

 * % Increase in mother's body mass index has been calculated as the difference between mother's current body mass index (at the time of the study) and body mass index at conception.

[†] Category includes unemployed, housekeeping and retired.

In addition, previous research in the field of parents' weight change throughout their offspring's life is scarce. In only one French study, maternal adiposity and its effect on the adiposity of the child was assessed [23]. Several phenomena could account for this pattern of correlations. First, a cumulative effect of a shared familial environment could strengthen the parent—child correlation over time. Secondly, with puberty, additional genetic factors may be involved in hormone secretions

related to subcutaneous adiposity development and then participate in these stronger parent—child correlations in post- rather than the pre-pubertal period. Obviously, this merits more research in order to confirm or refute this hypothesis.

Research on maternal smoking during pregnancy and subsequent growth appears to have consistent outcomes. According to CESAR, a study performed in Central and Eastern Europe, the mean OR for six countries in the region was 1.26 [12], while the pooled OR in a large literature review of 14 studies that took place in Europe, Australia and North America was 1.52 [13]. In Greece, Moschonis et al. [24] reported an OR of 1.72 for preschoolers developing obesity when the mother was both a passive and an active smoker during pregnancy. Intrauterine exposure to tobacco smoke is proposed to have adverse effects on birth weight. In other words, children of smokers tend to be lighter at birth, but at the same time have a greater chance for developing obesity, while the OR increases with age, suggesting strengthening of the relationship over time [14]. Other reported data are also consistent with the present findings, suggesting a dose-depended association between pre-natal smoking and obesity [8,15]. In contrast, a study performed by Gilman *et al.* [16] failed to demonstrate a strong association between these two characteristics. Using a siblings' model and after adjustment for confounders, it was shown that family level factors influence the studied relation. Those findings are opposite to those of von Kries et al. [15], who proposed a strong influence by the intrauterine environment and not by the lifestyle of the parents. When analyzing smoking during the different trimesters of pregnancy and its impact on the risk of overweight/obesity, the outcomes were inconsistent [17].

The strong relation between a newborn's weight at birth and later obesity may be a proof for the crucial role of intrauterine growth in the development of obesity. A recent study performed by Kuhle et al. [8] in schoolchildren aged 10 and 11 years old was in line with the findings reported herein. Previously reported data have also supported that heavy newborns tend to become heavy children, with odds ratios (OR) varying from 1.50 to 2.30 [19]. In a large study in 10,683 children who were followed up until the age of 33, Parsons et al. [20] indicated that in younger age groups the association between birth weight and BMI was linear; however, as age increased, the association became more J shaped. It is noticeable that when controlling parental BMI, the association became stronger.

The results of previous Greek studies are similar. Panagiotakos *et al.* [25] support that birth weight over 3500 g increased the odds for overweight and obesity in girls (OR = 1.85) and Moschonis *et al.* [24] presented a protective effect of low birth weight against overweight in preschoolers (OR = 0.56). The latter lower the likelihood for later obesity, or the absence of any influence concerning obesity as it was noticed in the results of this study which was also encountered elsewhere in the literature [8].

Previously, no other Greek study has examined the factor of mother's weight at conception, as researchers usually focus their attention on excessive weight gain during pregnancy, which was positively associated with an elevated risk for overweight/obesity [7,9]. Findings of this study do not support these results, probably owing to the small percentage of mothers who were overweight/obese, according to self-reported data. However, a 5% increase in the likelihood of being an overweight/obese offspring during preadolescence was noticed for every kg increase in maternal body weight at conception. This increase is mainly attributed to physical inactivity of the mother after the birth of her offspring.

As far as smoking habits are concerned, data showed a strong relation between heavy smoking at conception and overweight/obesity at preadolescence. This could probably be explained by the lifestyle patterns of the parents, which could lead to the increased BMI of an offspring. According to findings of this study, another strong factor of preadolescent overweight/obesity was mother's age at gestation. The likelihood of being an overweight/ obese offspring was higher for younger mothers, although previous studies did not support this [7,24], probably owing to the limited mother's age span of the sample and predominantly around 40 years of age.

5. Limitations

This study does not evaluate all the perinatal factors, like diabetes during pregnancy, mother's nutritional habits, parity, complications during pregnancy, post-natal hospitalization and socioeconomic status, while a number of perinatal data were self-reported 10–12 years later in time resulting in probable recall bias. In addition, collected data regarding smoking and alcohol intake during pregnancy were not checked regarding their validity and reliability. Finally, cross-sectional studies include a number of limitations, as their main purpose is to evaluate prevalence and not to prove causality between different factors. Thus, the results presented here are lacking a causal basis, but may be helpful for stating future research hypotheses.

6. Conclusion

Childhood and adolescent obesity is claimed to have its origins in intrauterine and early life. This study was an effort to present a strong association between preadolescents' overweight/obesity and mother's pre-pregnancy weight, mother's weight change from conception until the time of the study, mother's age and smoking habits at conception and birth weight. Monitoring the effect that pre- and post-natal factors have on the levels of overweight and obesity in Greece is a task of high priority in order to plan an effective prevention strategy.

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