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ORIGINAL PAPER

Smoking and smoking cessation during early pregnancy and its effect on adverse pregnancy outcomes and fetal growth

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Abstract Maternal smoking during pregnancy is a significant threat to the fetus. We examined the association between active maternal smoking and smoking cessation during early pregnancy with newborn somatometrics and adverse pregnancy outcomes including preterm delivery, low birth weight, and fetal growth restriction. One thousand four hundred mother–child pairs with extensive questionnaire data were followed up until delivery, within the context of a population-based mother–child cohort study (Rhea study), in Crete, Greece, 2007–2008. Comparing smokers to nonsmokers, the adjusted odds ratio (OR) was 2.8 [95% confidence interval (CI), 1.7, 4.6] for low birth weight and 2.6 (95%CI: 1.6, 4.2) for fetal growth restriction. This corresponded to a 119-g reduction in birth weight, a 0.53-cm reduction in length, and a 0.35-cm reduction in head circumference. Smoking cessation early during pregnancy modified significantly these pregnancy outcomes indicating the necessity for primary smoking prevention.

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Introduction

The impact of maternal smoking during pregnancy and its relative consequences on fetal and infant development is well-acknowledged [23, 26, 33]. Smoking during pregnancy, among other effects, impairs placental development directly or indirectly by reducing blood flow, which can create a hypoxic environment and lead to reduced provision of oxygen and micronutrients [33]. The existing scientific literature clearly underlines the existence of an association between smoking and adverse pregnancy outcomes, including miscarriage, ectopic pregnancy, stillbirth, and neonatal death [1, 5, 7]. Furthermore, the possible effect of smoking on reproductive outcomes, including low birth weight (LBW), small for gestational age (SGA), fetal growth restriction (FGR), and preterm delivery (PD) is also of significant interest. Several studies have found an association between smoking and LBW, SGA, and FGR [6, 8, 9, 13, 18, 29, 32]. On the other hand, for many women, pregnancy is perceived as a time of change through which expecting mothers may modify their health practices, one of the most significant of which would be to stop smoking [15, 28]. However, regardless of the existence or the extent of any formal intervention, smoking cessation during pregnancy has been shown to reduce LBW and PD [17].

Despite the existing literature, it is of significant interest to study the effect of maternal smoking during pregnancy on infant somatometrics having taken into account other possible confounding factors that could have an effect on fetal growth potential [such as

maternal height, pre-pregnancy body mass index (BMI), parity, ethnicity, and fetal sex], which could allow to better differentiate between infants who are small because their in utero growth has been restricted and infants who are small, but have reached their individual growth potential [10, 16]. Within the context of a population-based prospective cohort study of pregnant women and their children in Crete, Greece (Rhea study), we examined the association between active maternal smoking and smoking cessation early during pregnancy, and newborn somatometrics (infant weight, length, and head circumference), LBW, and PD in the offspring.

Methods

Study design and population

The "Rhea" mother–child cohort is a study of pregnant women (Greek and immigrants) who are residents of the prefecture of Heraklion in Crete, Greece. All women who became pregnant for 1 year from February 2007 until February 2008 were contacted and asked to participate in the study. The first contact was performed around the third month of pregnancy where the first major interview took place, while exposures were also assessed through additional questionnaires that were performed during the second and third trimester of pregnancy, respectively, in which extensive information on smoking habits was noted. A final interview was performed after birth, which provided us with all the necessary information in regards to birth outcomes together with data abstracted from hospital records. In all cases, trained interviewers administered the comprehensive computer-assisted, face-to-face interviews. The study was approved by the ethical committee, and all participants provided written informed consent. After excluding multiple births, stillbirths, miscarriages, and women who participated in the study but provided us with uncompleted questionnaire data, a total population of 1,400 pregnant women remained for the current analysis.

Sociodemographic and lifestyle determinants

Information on both maternal and paternal sociodemographical characteristics was collected as also extensive questionnaire information on both their self-reported smoking habits. Smoking status was classified into three categories. Nonsmokers were classified as the women who did not report smoking at any time for at least 3 months prior to pregnancy, ex-smokers were classified as those who reported smoking sometime within the 3 months prior to pregnancy and/or some time during the first 12 weeks but who had quit since, while active smokers were classified as those who self-reported to smoke 3 months prior to pregnancy, during early pregnancy, and during the time of interview, approximately at week 12 of gestation.

Birth outcomes information—definition

Women were approached 1 or 2 days after birth during their stay at the maternity ward, and extensive information was collected regarding the gestational age (GA) at birth and the main newborn's somatometrics (weight, length/height, head circumference). GA was based on the interval between the last menstrual period and the date of delivery of the infant. When the menstrual estimate of GA was inconsistent by seven or more days in comparison to the first ultrasound measurement taken in the first trimester of pregnancy, a quadratic regression formula describing the relationship between crown-rump length and GA was used instead [31]. Hard copies of the three main ultrasound scans (nuchal translucency, second trimester, and Doppler) were hand collected by the interviewers, as no complete ultrasound base existed, with only the first untrasound used in the current analysis. PD is defined as gestation length <37 gestational weeks and LBW as a birth weight below 2,500 g. SGA based on weight (SwGA) is defined as a live-born infant below the tenth percentile of birth weight for GA in a referent population [11]. Accordingly, we defined SGA based on length (SlGA) and head circumference (SGA_hc). During the current analysis, Spanish growth curves were used to calculate SwGA, SlGA, and SGA_hc, as Greek ones do not exist [4].

We also developed a customized definition of impaired growth for the newborns of our study acknowledging their constitutional characteristics [3, 4]. We identified an infant as SGA if he/she does not achieve a standard weight for his/her GA and as FGR, an infant failing to achieve its genetic growth potential based on the calculated predicted weight. Maternal and newborn characteristics considered a priori were GA in weeks, maternal and paternal height (centimeters) and age (years), maternal pre-pregnancy weight (kilograms), primiparous mother, and infant sex. Sex and GA were considered as possible modifiers. A multivariable fractional polynomial linear regression model was used to predict birth weight, allowing polynomial terms for all continuous variables; considering up to degree 2 polynomials with powers {−2, −1, −1/2, 0, 1/2, 1, 2, 3}, we retained the model which best fitted regarding deviance [24]. The final model was obtained from a backward strategy retaining the variables with a p value lower than 0.05 and interactions terms with a p value lower than 0.1.

Table 1 Descriptive data and infant somatometrics for the study population of Rhea birth cohort study conducted in Greece, 2007– 2008

	Total n[a] (%)	Birth weight Mean in gr(SD)	Birth length Mean in cm (SD)	Head circumference Mean in cm (SD)
Singleton live births	1,400 (100)	3,153 (483)	50.3 (2.5)	34.1 (1.7)
Maternal age				
<30	695 (49.9)	3,155 (488)	50.3 (2.7)	34.1 (1.7)
≥30	699 (50.1)	3,162 (478)	50.4 (2.4)	34.2 (1.7)
Paternal age				
<30	312 (25.5)	3,128 (473)	50.3 (2.5)	34.1 (2.1)
≥30	910 (74.5)	3,165 (484)	50.0 (2.4)	34.1 (1.6)
Maternal BMI				
Underweight	28 (2.2)	2,977 (534)*	49.9 (3.2)	33.6 (2.2)*
Normal	717 (55.8)	3,143 (461)*	50.4 (2.4)	34.0 (1.6)*
Overweight	538 (41.9)	3,186 (492)*	50.4 (2.5)	34.3 (1.8)*
Maternal Education				
Low	272 (21.0)	3,149 (489)	50.3 (2.7)	34.2 (2.1)*
Medium	652 (50.5)	3,165 (483)	50.4 (2.4)	34.1 (1.6)*
High	368 (28.5)	3,149 (461)	50.4 (2.3)	34.1 (1.5)*
Paternal education				
Low	474 (37.1)	3,154 (501)	50.3 (2.5)	34.1 (1.9)
Medium	540 (42.2)	3,167 (455)	50.3 (2.4)	34.1 (1.6)
High	265 (20.7)	3,140 (489)	50.4 (2.4)	34.1 (1.6)
Marital status				
Married	1,292 (98.3)	3,158 (482)	50.3 (2.5)	34.1 (1.7)*
Single	22 (1.7)	3,083 (328)	50.3 (2.0)	33.4 (0.9)*
Parity				
Primipara	507 (38.4)	3,163 (496)	50.3 (2.6)	34.1 (1.7)
Multipara	814 (61.6)	3,156 (473)	50.3 (2.4)	34.2 (1.8)
Maternal origin				
Greek	1,264 (90.3)	3,143 (484)	50.3 (2.5)	34.1 (1.7)
Non-Greek	136 (9.7)	3,244 (460)	50.8 (2.3)	34.4 (1.8)
Smoking				
Nonsmoker	843 (64.1)	3,171 (473)*	50.4 (2.4)*	34.2 (1.7)
Ex-smoker	216 (16.4)	3,207 (465)*	50.6 (2.4)*	34.1 (1.6)
Smoker	256 (19.5)	3,059 (498)*	49.8 (2.6)*	33.9 (2.0)

[a] Note that the differences in the numbers are due to missing values

*$p<0.05$

The final model included the following as covariates: GA, infant sex (male), maternal (MH), and paternal height (PH), pre-pregnancy weight (MW), as well as the interaction of GA with maternal weight (MW×GA). The expected birth weight (BW) was predicted from a regression model from the equation: $\mathrm{BW} = 96.48(\mathrm{GA} - 38.44) + 150\,\mathit{Male} - 32.94(\mathrm{MW} - 64.59) + 3083.8(\sqrt{(\mathrm{MW} \times \mathrm{GA}}/\mathrm{GA1000}.1000) - 1.58) + 7.92(\mathrm{MH} - 163.5) + 4.2(\mathrm{PH} - 177.08) + 3136.0$. The model explained 32% of the total variance in birth weight. We classified a neonate as fetal weight growth restricted (FwGR) if his/her actual birth weight fell below the tenth percentile of the predicted birth weight distribution according to the above model.

Statistical analyses

Bivariate associations between dependent and the independent variables were studied using Pearson's chi-square test for categorical variables or Student's t test for continuous ones. We used unconditional logistic and linear regression to estimate crude and adjusted odds

ratios (ORs) or β coefficients and 95% confidence intervals (95% CIs) for the association of exposure and birth outcomes. ORs were adjusted for maternal age at delivery (continuous variable), maternal education (“”low and medium level, ≤12 years of school/high level: university or technical college degree), ethnicity (Greek/non-Greek), parity (nulliparous/multiparous), and infant sex (boy/girl). We also adjusted for GA when using infant weight, length, and head circumference as a continuous variable in linear regression models. All statistical tests were two-sided, and values of $p<0.05$ were considered statistically significant. The statistical package Stata 10.0 was used to perform the analysis.

Results

In this prospective cohort study, 1,400 pregnant women with complete data on smoking habits during pregnancy and infant data were recruited. The majority of the mothers were nonsmokers (64.1% $n=843$), while 35.9% ($n=472$) reported any smoking during pregnancy, of which half quit during the first 12 weeks of gestation leaving thus 19.5% ($n=256$) of the women active smokers after week12. Among the newborns, 182 (13%) were classified as preterm, 96 (7%) as LBW, 79 (6%) as SwGA, 38 (3%) as SlGA, 137 (11%) as SGA_hc, 102 (9%) as FwGR, 81 (7%) as FlGR, and 92 (8%) as FGR_hc. Mean infant birth weight

Table 2 Birth outcomes for the study population of Rhea birth cohort study conducted in Greece, 2007–2008

	Total n[a] (%)	Preterm n (%)[a]	Low birth weight, n (%)[a]	Fetal weight growth restricted, n (%)[a]	Fetal length growth restricted, n (%)[a]	Fetal growth restricted by head circumference, n (%)[a]
Singleton live births	1,400 (100)	182 (13)	96 (7)	102 (9)	81 (7)	92 (8)
Maternal age						
<30	695 (49.9)	88 (51)	48 (53)	54 (54)	41 (51)	42 (46)
≥30	699 (50.1)	84 (49)	42 (47)	46 (46)	39 (49)	49 (54)
Paternal age						
<30	312 (25.5)	36 (23)	23 (27)	34 (35)*	20 (27)	27 (31)
≥30	910 (74.5)	120 (77)	61 (73)	64 (65)*	55 (73)	61 (69)
Maternal BMI						
Underweight	28 (2.2)	4 (3)	5 (6)*	3 (3)	4 (5.0)	4 (4)
Normal	717 (55.8)	84 (52)	48 (56)*	55 (54)	40 (50.0)	55 (60)
Overweight	538 (41.9)	73 (45)	32 (38)*	44 (43)	36 (45.0)	33 (36)
Maternal education						
Low	272 (21.0)	42 (26)	20 (23)	25 (25)	16 (20)	17 (19)
Medium	652 (50.5)	82 (50)	47 (55)	50 (49)	43 (53)	47 (51)
High	368 (28.5)	40 (24)	19 (22)	27 (27)	22 (27)	28 (30)
Paternal education						
Low	474 (37.1)	64 (39)	34 (40)	39 (39)	23 (29)	31 (34)
Medium	540 (42.2)	65 (40)	36 (42)	41 (4)	41 (51)	44 (48)
High	265 (20.7)	34 (21)	16 (19)	20 (20)	16 (20)	17 (18)
Marital status						
Married	1,292 (98.3)	168 (99)	87 (99)	100 (99)	79 (99)	88 (98)
Single	22 (1.7)	1 (1)	1 (1)	1 (1)	1 (1)	2 (2)
Parity						
Primipara	507 (38.4)	60 (36)	40 (45)	44 (43)	30 (37)	34 (37)
Multipara	814 (61.6)	108 (64)	48 (55)	58 (57)	51 (63)	57 (63)
Maternal origin						
Greek	1,264 (90.3)	172 (9)*	92 (96)	94 (92)	74 (91)	86 (94)
Non-Greek	136 (9.7)	10 (56)*	4 (4)	8 (8)	7 (9)	6 (6)

[a] Note that the differences in the numbers are due to missing values

*$p<0.05$

recorded was 3,153 g (±483), the mean length at birth was 50 cm (±3), and the mean head circumference was 34 cm (±2). A comparison between main sociodemographic characteristics of the study population and the main newborn somatometrics at birth was performed, and the results are included in Table 1 (in which the completeness of the data set for each variable is also presented). The mean birth weight and head circumference were found to differ significantly between underweight, normal, and overweight women (pre-pregnancy weight), with overweight women having newborns with the highest birth weight. Head circumference was higher among married women when compared to single and among low educated women when compared to medium and high educated women ($p<0.05$). Additionally, Table 2 provides information on the distribution of birth outcomes in relationship with maternal, paternal, and sociodemographic characteristics. Specifically, PD was found to be associated with maternal ethnicity, while LBW and FwGR were found to be related with maternal BMI and paternal age, respectively ($p<0.05$). No further differences were noted.

The percentage of preterm deliveries, LBW, and fetal growth restricted infants was higher among smokers in comparison to nonsmokers (Table 3), while no differences were observed between women who quit smoking in early pregnancy and nonsmokers. A logistic regression analysis was preformed to adjust for the effect of possible confounding factors (Table 4). The comparison between active vs. nonsmokers showed a greater than a twofold increase in risk regarding LBW, adjusted OR 2.78 (95%CI, 1.69, 4.59), SwGA OR 2.63 (95%CI, 1.55, 4.49), SGA_hc OR 2.38 (95%CI, 1.53, 3.69), FwGR OR 2.58 (95%CI, 1.60, 4.17), FGR_hc OR 2.31 (95%CI, 1.37, 3.88) after adjustment for origin, smoking during pregnancy, parity, maternal education, maternal age, and infant sex. Finally, children of women who quit early during pregnancy in comparison to never smokers had no different risk of giving birth of a LBW, SwGA, SGA_hc, FwGR, and FGR_hc infant. No statistically significant increased risk for PD was revealed when comparing smokers or ex-smokers with nonsmokers.

Table 5 shows the association of infant weight, length, and head circumference at birth examined as continuous variables, in regards to continued smoking or smoking cessation early during pregnancy. A statistically significant reduction for infant weight (β coefficient=−119 g; 95%CI, −177 to −62), infant length (β coefficient=−0.53 cm; 95% CI, −0.88 to −0.19), and head circumference at birth (β coefficient=−0.35 cm; 95%CI, −0.60 to −0.10, respectively) was revealed when comparing active smokers with nonsmokers. Smoking cessation early during pregnancy was found to eliminate the differences in birth weight, length, and head circumferences. Infant weight, length, and head circumference at delivery in ex-smokers were similar to those of nonsmokers.

Discussion

Our results indicated an almost threefold increase in risk in LBW and fetal growth restricted babies among smokers in regards to almost all of their somatometrics, while active smoking was associated with a 120–150 g reduction in birth weight. Quitting early during pregnancy (before week 12) was found to minimize differences in fetal growth in comparison to nonsmokers. These findings reinforce the current clinical guidelines that stress the importance of smoking cessation early during pregnancy.

Table 3 Birth outcomes distribution among non- smokers, ex– and current smokers during pregnancy (Greece 2008)

	Non-smokers, n^a (%)	Ex-smokers, n^a (%)	Smokers, n^a (%)	p value
Preterm delivery	107 (12.9)	24 (11.3)	38 (15.3)	<0.001
Low birth weight	47 (5.8)	10 (4.7)	31 (12.5)	<0.001
Small for gestational age[b]				
Small for gestational age by weight	41 (5.1)	8 (3.8)	27 (11.2)	0.001
Small for gestational age by length	24 (3.1)	1 (0.5)	11 (5.0)	0.024
Small for gestational age by head circumference	72 (9.4)	19 (9.4)	42 (19.3)	<0.001
Fetal growth restricted[c]				
Fetal weight growth restricted	51 (6.9)	16 (8.0)	34 (15.5)	<0.001
Fetal length growth restricted	57 (8.0)	4 (2.0)	20 (10.0)	0.005
Fetal growth restricted by head circumference	45 (6.4)	19 (9.9)	27 (13.7)	0.003

[a] Note that the differences in the numbers are due to missing values

[b] *SwGA*, *SlGA*, and *SGA_hc* small for gestational age based on infant weight, length, and head circumference at birth, respectively

[c] *FwGR*, *FlGR*, and *FGR_hc* fetal growth restricted based on infant weight, length, and head circumference at birth, respectively

Table 4 Odds ratios and 95% confidence intervals for birth outcomes associated with smoking exposure from a birth cohort study conducted in Greece, 2007–2008

	Active vs. nonsmoking[c]		Ex- vs. nonsmoking[c]	
	Unadjusted OR 95% CI	Adjusted OR 95% CI	Unadjusted OR 95% CI	Adjusted OR 95% CI
Preterm delivery	1.22 (0.82, 1.83)	1.28 (0.84, 1.94)	0.86 (0.54, 1.38)	0.90 (0.56, 1.46)
Low birth weight	2.33 (1.45, 3.76)	2.78 (1.69, 4.59)	0.8 (0.39, 1.62)	0.82 (0.41, 1.67)
Small for gestational age[a]				
Small for gestational age by weight	2.36 (1.42, 3.93)	2.63 (1.55, 4.49)	0.73 (0.34, 1.59)	0.74 (0.34, 1.62)
Small for gestational age by length	1.64 (0.79, 3.39)	1.84 (0.88, 3.88)	0.15 (0.02, 1.13)	0.16 (0.02, 1.22)
Small for gestational age by head circumference	2.30 (1.52, 3.49)	2.38 (1.53, 3.69)	1.00 (0.59, 1.69)	1.10 (0.63, 1.88)
Fetal growth restricted[b]				
Fetal weight growth restricted	2.48 (1.56, 3.95)	2.58 (1.60, 4.17)	1.17 (0.65, 2.10)	1.16 (0.64, 2.11)
Fetal length growth restricted	1.27 (0.75, 2.18)	1.32 (0.77, 2.28)	0.24 (0.09, 0.67)	0.23 (0.08, 0.66)
Fetal growth restricted by head circumference	2.32 (1.40, 3.85)	2.31 (1.37, 3.88)	1.6 (0.92, 2.82)	1.55 (0.87, 2.77)

Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were obtained from logistic regression, adjusting for origin, parity, maternal education, maternal age, and infant sex

[a] *SwGA*, *SlGA*, and *SGA_hc* small for gestational age based on infant weight, length, and head circumference at birth, respectively

[b] *FwGR*, *FlGR*, and *FGR_hc* fetal growth restricted based on infant weight, length, and head circumference at birth, respectively

[c] Reference group

LBW is an important risk factor for perinatal morbidity and mortality and thus continues to be the leading preventable cause of pregnancy complications in otherwise low-risk women [2, 14, 19]. Cigarette smoking during pregnancy has been previously associated with LBW in a number of studies and has been causally indicated to cause a reduction of 100–300 g, while other research has indicated even an almost 500-g reduction among populations with certain metabolic gene polymorphisms [8, 13, 18, 22, 30, 32].

Within this prospective cohort study, active smoking was found to be related to a reduction of 120 g in body weight, a 0.53-cm reduction in length, and a 0.35-cm reduction in head circumference, results almost identical to those found by Pickett et al., in their cohort of pregnant women in Boston, USA among current smokers [22]. Similarly, our results indicated an excess risk of 2.8 for active smoking on LBW, almost identical to the results presented by Suzuki et al. (OR, 2.9 for active smoking) and Chiolero et al. (OR, 2.7) but higher than that presented by others [6, 14, 29]. Recognizing the fetus's growth potential, active smokers were approximately two and a half times more likely to give birth to a baby that was either FGR or SGA, in regards to either their child's weight or the child's head circumference. This risk is similar to that noted by other studies, with

Table 5 Odds ratios and 95% confidence intervals for newborn somatometrics associated with smoking exposure from a birth cohort study conducted in Greece, 2007–2008

	Weight		Length		Head circumference	
	Crude β coefficient 95% (CI)	Adjusted β coefficient 95% (CI)	Crude β coefficient 95% (CI)	Adjusted β coefficient 95% (CI)	Crude β coefficient 95% (CI)	Adjusted β coefficient 95% (CI)
Active vs. nonsmoking						
Non smoking	Reference	Reference	Reference	Reference	Reference	Reference
Active smoking	−111.56 (−179.67, −43.45)	−119.29 (−176.76, −61.82)	−0.59 (−0.95, −0.22)	−0.53 (−0.88, −0.19)	−0.30 (−0.56, −0.05)	−0.35 (−0.60, −0.10)
Ex- vs. nonsmoking						
Nonsmoking	Reference	Reference	Reference	Reference	Reference	Reference
Ex-smoking	36.13 (−34.96, 107.23)	38.81 (−18.14, 95.77)	0.14 (−0.23, 0.51)	0.15 (−0.19, 0.48)	−0.12 (−0.37, 0.13)	−0.11 (−0.35, 0.13)

Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were obtained from logistic regression, adjusting for gestational age, origin, parity, maternal education, maternal age, and infant sex

the slight differences noted likely to be attributed to both different cigarette consumption and the inclusion of other confounding factors within the model used to define SGA infants within each study [6, 9, 29]. Furthermore, scientific evidence has indicated that active smoking during pregnancy is related to PD [6, 13]. Although we found an increased risk PD among smokers, differences were small and were not statistically significant.

There is limited existing evidence in the scientific literature, whether smoking cessation early during pregnancy can have an impact on birth outcomes [20]. Our results indicated that smoking cessation early during pregnancy (i.e., before week 12) was found to eliminate differences with nonsmokers. The child's head circumference at birth was found to be slightly smaller among ex-smokers in comparison to never smokers, but differences were small and not statistically significantly. The child's brain weight is directly related to its head circumference, and it has been pointed out that the neurodevelopmental, (cognitive and behavioral) effects noted among children exposed to active smoking in utero could be partially attributed to this reduction in brain size as also to the other toxic and constituents of tobacco smoke, such as nicotine [21, 25, 27]. Although smoking cessation early in pregnancy was not shown to negatively affect birth weight or length, the noted reduction in head circumference was one third that of active smokers, a fact that could indicate a possible critical window of exposure during the first 12 weeks on fetal brain development.

Study limitations and strengths

A significant strength of our study is its cohort design with individual follow-up of pregnancies to determine reproductive outcomes, which may allow us to investigate into causality. While previous studies have relied on information provided through hospital records to estimate GA (which is prone to substantial error), in our case, self-reported last menstrual period was collected from participants during the first trimester of pregnancy (when recall is more accurate) and were corrected based on the first ultrasound scan [12]. Furthermore, this is one of the few studies that prospectively investigated into the relationship between active smoking with SGA based on length and head circumference at birth and the only study to our knowledge to investigate on the role of smoking cessation early during pregnancy on head circumference, SGA_hc and FGR_hc. Although there are methodological advantages in the present study compared with previous studies, a number of important limitations remain that could affect the study results. Moreover, the assumption that we made by considering Spanish and Greek population similar in order to use the Spanish national birth somatometrics curves for SGA calculations (Greek ones do not exist) might have introduced some measurement error. It is for this reason that we also used a customized measure of fetal growth retardation for the study population. Regarding exposure assessment, we must state that smoking status was based on self-report and thus subject to response bias, while exposure to secondhand smoke was not taken into account as only active smoking was assessed,

Conclusions

In conclusion, in this population in Crete, active maternal smoking was associated with lower birth weight, birth length, and head circumference in newborns compared to those of non-smoking mothers. Smoking cessation early during pregnancy modified significantly these pregnancy outcomes. These results indicate the necessity for the promotion of smoking cessation early during pregnancy and the imperative role of primary smoking prevention, especially among women of reproductive age.

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Conflict of Interest The authors declare that they have no conflict of interest.

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