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Lifecourse relationship between maternal smoking during pregnancy, birth weight, contemporaneous anthropometric measurements and bone mass at 18 years old. The 1993 Pelotas Birth Cohort

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ABSTRACT

Background: Maternal smoking during pregnancy is associated with short-term and also long-term harmful effects on offspring.
Objective: The aim of this study is to evaluate the associations of maternal smoking during pregnancy with offspring bone health at 18 years old, and the role of birth weight and contemporaneous height, weight and body mass index (BMI) in this association.
Data from the 1993 Pelotas Birth Cohort were analyzed using path analysis stratified by sex.
Adolescents at 18 years old ($N = 1512$ males, 1563 females).
DXA-determined total body bone mineral density (BMD) and bone mineral content (BMC) were assessed at 18 years old.
Results: Each additional cigarette smoked during pregnancy was associated with a lower BMC by −4.20 g in males (95% CI −8.37; −0.05), but not in females [−2.22 g (95% CI −5.49; 1.04)]; weaker inverse associations were observed for BMD. This inverse association was explained by the influence of maternal smoking on birth weight and contemporaneous anthropometry, particularly height. A 1 kg higher birth weight was associated with a higher BMC by around 144 g in males and by around 186 g in females, and also with a higher BMD by around 0.019 g/cm^2 in males and by around 0.018 g/cm^2 in females, respectively.
Conclusions: Lifecourse analysis using path models has enabled to evaluate the role of mediators in the associations of maternal smoking during pregnancy and birth weight with bone mass in the offspring, thus generating improved understanding of the etiology of bone health and the importance of early life experiences.

1. Introduction

Evidence has shown that smoking during pregnancy is harmful to the newborn (1–4), especially affecting birth weight (2,3,5). In recent years there has been growing interest in the impact of early life events including smoking during pregnancy (6), and birth weight (7,8) on height during childhood and adolescence (9) and on bone health as an attempt at better understanding how these exposures contribute to the pathophysiology of osteoporosis (10,11).

Maternal smoking, diet and physical activities levels are thought to contribute to the in-utero modulation of bone mineral acquisition (11). Osteoporosis is a medical condition of global public health concern because of the consequences of low-energy fractures in individuals with this disease (12). Those who have low accumulation of calcium in the bones have a high risk of osteoporotic fractures during their adult life (12) because of high rates of bone loss in adulthood (10,13). It is thus important to understand the potentially-modifiable factors which promote or inhibit the gain of bone mass during childhood and adolescence.

Few studies have examined the association between maternal smoking during pregnancy and bone mass in offspring. Jones et al. described an inverse association with spine and femur BMD at 8 years old (14); however this effect was not seen in a second follow-up visit

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when the offspring were 16 years old (15). Macdonald-Wallis et al. reported that maternal smoking during pregnancy was associated with higher BMC in girls aged 10 (6), but given the similar associations of maternal and paternal smoking in pregnancy, the authors concluded that the association was not likely to be causal.

In light of the scant existing evidence on this topic, especially among adolescents, the aim of this study was to evaluate the association of maternal smoking during pregnancy with BMD and BMC in participants from the 1993 Pelotas Birth Cohort at age 18, as well as to assess the potential role of birth weight, and height, weight and body mass index (BMI) at 18 years old as mediators in this association.

2. Methods

All live born infants born in 1993 to mothers who were residents of the urban area of Pelotas, a city located at southern Brazil, were eligible to participate in the birth cohort study. A total of 5249 newborns were included in the study (16 refusals). More detailed information about methodology and follow-up of the cohort study have been published previously (16). The analyses shown here are based on the perinatal study and on the follow-up at age 18 years.

At the perinatal survey the mothers or caretakers answered a questionnaire on health, smoking during pregnancy and socioeconomic conditions. Mothers reported the number of cigarettes smoked per day during the pregnancy in a questionnaire and it was analyzed as a continuous variable in order to allow for a potential dose–response; coefficients can thus be interpreted as the change in outcome/mediator for each additional cigarette smoked during pregnancy. Birth weight was measured by hospital staff with 10-g precision pediatric scales calibrated regularly by the research team. In the current analysis birth weight was evaluated in kilograms and analyzed as a continuous variable.

At the follow-up when participants were 18 years old, a total of 4106 adolescents were assessed (follow-up rate of 81.4%). At this time, tests were performed to assess body composition including bone densitometry by dual-ray absorptiometry (DXA) using a Lunar Prodigy Advance Bone Densitometer (GE, Germany) by two trained technicians. A total of 3855 participants (94% of those attending the follow-up) had their entire body scanned. DXA is currently the gold standard for estimating bone mass (17).

The outcomes were whole body BMD (grams per square centimeter, g/cm^2) and BMC (grams, g). Both measures were analyzed as continuous variables. Contemporaneous anthropometric measures collected at 18 years included body weight (kilograms), height (centimeters) and BMI (kg/m^2).

The correlations between our exposures and outcomes were assessed using Pearson correlation test. To understand the relationships between maternal smoking during pregnancy, offspring birth weight, offspring concurrent anthropometric condition at age 18 and offspring bone mass, a path analysis using the structural equation modeling command in Stata (sem) was performed, with Fig. 1 depicting our hypothesized relationships between the variables. In this model one can notice that we wished to test whether maternal smoking during pregnancy had a direct effect (i.e. not mediated by any other variable in our analysis model) on BMD/BMC (dotted line) in addition to the indirect effects (i.e. the association mediated through birth weight and contemporaneous anthropometric measures) (solid line). Mediation by height, weight and BMI were each considered separately. Also, the total effect (entire association, comprising both the 'direct' and 'indirect' effects) of maternal smoking and the total effect of birth weight were calculated (total effect = indirect + direct).

We made the a priori decision to stratify all analyses by gender based on the evidence from literature about sexual differences in bone acquisition (10,18). Variables from the perinatal survey used as confounders (group 1) in the adjusted analysis were: partner smoking during pregnancy as a dichotomous variable (smoker/non-smoker); family income (wages); maternal education (years of schooling); maternal skin color (white/non-white); maternal age (years); maternal height (cm); and gestational age (weeks) estimated from the last menstrual period or using the Dubowitz score (19) when information on the last menstrual period was not available. Variables from the 18 year old follow-up (group 2) included in the model as confounders were: smoking (no/yes if the adolescent use to smoke at least one time per week), alcohol consumption (frequency of alcohol consumption per month), physical activity (score of minutes per day during leisure time measured by the International Physical Activity Questionarie short version), and calcium intake (adjusted by total calories consumption) (see Fig. 1). Confounders from group 1 remained in all the models. Confounders from group 2 were added to the model when contemporaneous mediators were evaluated.

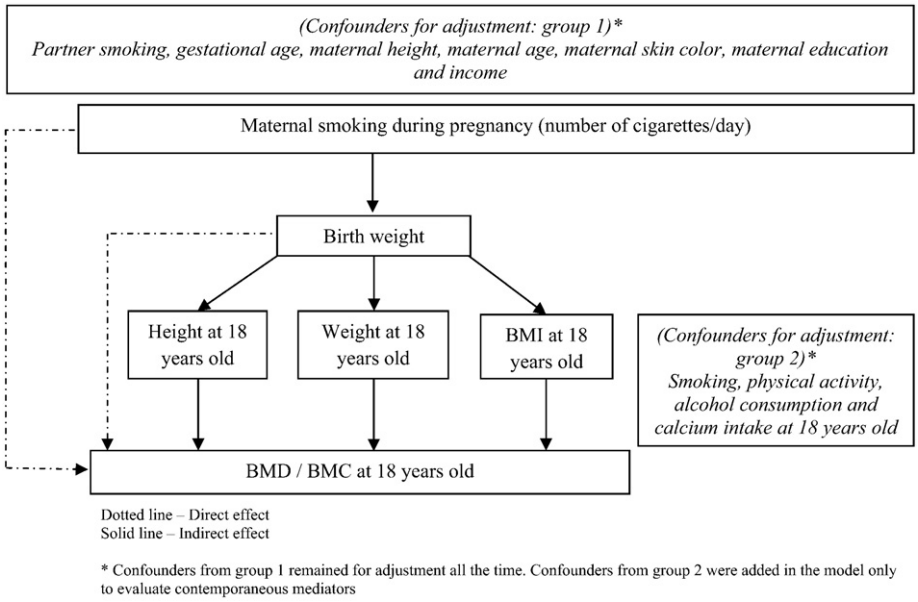

Fig. 1. Analytical model to evaluate the association between number of cigarettes/day smoked by the mother during pregnancy and total body bone mass density (BMD) and bone mineral content (BMC) at 18 years old, and assessing how much of this relationship is mediated by birth weight and current height, weight and body mass index (BMI) at 18 years.