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Smoking overrules many other risk factors for small for gestational age birth in less educated mothers

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ABSTRACT

Background

Although there is convincing evidence for the association between small for gestational age (SGA) and socioeconomic status (SES), it is not known to what extent explanatory factors contribute to this association. The objective was to examine to what extent risk factors could explain educational inequalities in SGA

Study design

In this study fully completed data were available for 3793 pregnant women of Dutch origin from a population-based cohort (ABCD study). Path-analysis was conducted to examine the role of explanatory factors in the relation of maternal education to SGA.

Results

Low-educated pregnant women had a higher risk of SGA offspring compared to the high-educated women (OR 1.98; 95% CI 1.35 – 2.89). In path-analysis, maternal cigarette smoking and maternal height explained this association. Maternal age, hypertension, chronic disease, late entry into antenatal care, neighbourhood income, underweight, environmental cigarette smoking, drug abuse, alcohol use, caffeine intake, fish intake, folic acid intake, anxiety, and depressive symptoms did not play a role in the association between maternal education and SGA birth.

Conclusion

Among a large array of potential factors, the elevated risk of SGA birth among low-educated women appeared largely attributable to maternal smoking and to a lesser extent to maternal height. To reduce educational inequalities more effort is required to include low-educated women especially in prenatal intervention programs such as smoking cessation programs instead of effort into reducing other SGA-risk factors, though these factors might still be relevant at the individual level.

INTRODUCTION

Small for gestational age birth (SGA) is strongly related to perinatal mortality and morbidity.[49,50] SGA infants, usually defined as birth weight below the 10th population centile on the basis of gestational age, are for instance more likely to have necrotizing enterocolitis, respiratory distress syndrome,[51] hypoglycaemia,[52] and adverse neurologic outcome.[53] Moreover, SGA born adults may have an increased risk of type 2 diabetes mellitus and ischemic heart disease.[54] Therefore, reducing the incidence of SGA is of paramount importance.

SGA results from complex interactions between factors of the mother, fetus, and environment.[32] Many risk factors, including cigarette smoking,[28] short stature,[55] caffeine intake,[56] and maternal psychosocial stress,[29] have been identified. Furthermore, SGA has been associated with socioeconomic status (SES).[57,58] Some researchers reported that social deprivation was independently associated with SGA,[59] but the majority of researchers suggested that after adjustment for known mediating factors, socioeconomic status may not be a relevant independent contributor to birthsize.[30] Although much research has focussed on socioeconomic differences in SGA, little research has evaluated the underlying pathways. Some studies highlighted a single factor, such as maternal smoking, and late entry into antenatal care[32] as explanatory factors in the relation between SES and SGA. From a public health point of view it is of interest to assess and compare the effects of different explanatory factors on the relation of SES to SGA. Furthermore, it is not known whether any residual socioeconomic disparities remain after adjustment for strongly suspected mediators.[30] In the present study we applied maternal education as an indicator of SES, as it was described as the best predictor of socioeconomic differences in birth outcomes.[58]

The aim of the present paper is therefore (i) to assess the association between SGA and maternal education and (ii) to examine to what extent risk factors could explain educational inequalities in SGA. This study was conducted in a large population based cohort and involved ethnic Dutch participants only to avoid bias by ethnic background.[30]

METHODS

The present study is part of the ABCD study, a population-based birth cohort study. Details of this study were described previously.[43] In brief, between January 2003 and March 2004 all pregnant women in Amsterdam, the Netherlands, were invited to participate during their first antenatal visit with their obstetric caregiver. In total 12 373 women were informed about the study and 8266 women returned the pregnancy questionnaire (median gestational age 12.95; IQR 2.43 weeks; response rate 67%) and were enrolled in the study. For the present study, twin pregnancies (n=135) were excluded, because birth weight differs between singleton and multiple births. In addition, participants with missing data on education (n=69) were

excluded. Those with a Dutch ethnicity, defined if both mother and grandmother were born in the Netherlands, were selected for the present study, leaving 3919 participants in our study population. Furthermore, still births (n=31), births below 24 weeks of gestation (n=2), and termination of pregnancy (n=9) were excluded, as well as participants with missing data on birth weight (n=44) and gestational age (n=6). Moreover, 44 cases were excluded because of at least one missing covariable. Finally, there were 3783 participants with fully completed data. The Institutional review boards of the participating hospitals approved the study. All mothers gave written informed consent. The ABCD study complies with the principles laid down in the Declaration of Helsinki.

Main variables

The years of education after primary school were obtained by questionnaire. Maternal education was categorized[58] as low (less than 6 years), mid (6 to 10 years), and high (more than 10 years). Newborns were categorized as SGA if their birth weight was below the 10th percentile for gestational age on the basis of gender and parity specific standards from the Perinatal Registration of the Netherlands (PRN).[60]

Covariables

Possible covariables that might explain the association between maternal education and SGA were selected according to the literature[27,30] and were obtained from the pregnancy questionnaire. Covariables were: maternal height (cm; continuous), neighbourhood income (continuous), chronic health problem (no/yes), pregnancy-induced hypertension (yes/no), pre-existing hypertension (yes/no), maternal age (continuous), maternal cigarette smoking (no/yes: yes when at least one cigarette per day), environmental smoking (no/yes: yes when at least one cigarette per day), anxiety (State-Trait Anxiety Inventory [STAI]), non-medical drug abuse (no/yes), underweight (body mass index kg/m^2 < 18.5: yes/no), depressive symptoms (Center for Epidemiologic Studies Depression scale [CES-D]), late entry into antenatal care (<18 weeks, ≥ 18 weeks), alcohol consumption (no/yes), folic acid supplementation (yes/no), fatty fish intake (< 10 grams, 10-20 grams, > 20 grams), caffeine intake (< 100 grams, 100-200 grams, 200-300 grams, > 300 grams). A chronic health problem was categorized as yes if the mother reported a chronic disease that is associated with SGA, like asthma (n=57), thyroid disease or thyroid medicine use (n=24), and leiomyoma (n=2). Chronic health problems like renal disease and severe maternal heart condition were not reported. Neighbourhood income data (not based on the questionnaire) were registered by Statistics Netherlands, based on mean income per individual in a neighbourhood (sum of income divided by the number of residents in a neighbourhood) in euro's divided by 1000. The CES-D is designed to determine depressive symptoms in the week previous to the acquisition of the questionnaire. The CES-D is a 20-item scale (each item is scored on a four-point scale), which was found to have good validity and reliability.[61] Depressive symptoms were categorized as low (reference: 20-29),

mid (30-41) or high (42-80). Anxiety was assessed using the Dutch version of the STAI,[62] which is a 20 items with each 4-points scale. Anxiety was categorized as low (reference: 20-34), mid (35-48), or high (49-80). Pre-existing hypertension and pregnancy-induced hypertension were defined combining self-reported data from the questionnaire and data from the PRN, as described previously.[63]

Statistical analysis

Differences in general characteristics among educational levels were tested with ANOVA analysis for continuous normally distributed variables and a Chi-square test for categorical variables. To explore the associations of covariates with SGA, logistic regression analyses were performed. Path-analysis mediation models were used to identify potential determinants of SGA that may explain the relation of SGA to SES. Each path model consists of the following regression equations: A regression equation that describes the relationship between SGA and SES (adjusted for all the mediators), and the regression equations describing the relationship between each mediator and SES. Using path-analysis, the regression equations were estimated simultaneously accounting for the correlation between explanatory factors.[64] Only factors that were associated with both maternal education and SGA ($p < 0.1$) were considered as possible explanatory factors in the relation of maternal education to SGA and were included in further analyses. The objective of the analyses was to evaluate the extent to which determinants of SGA mediated the former association. Associations between maternal education and the mediating risk factors were modelled with the maximum likelihood algorithm implemented in M-PLUS using weighted least squared parameter estimates and a probit link.[65] Categorical variables were treated as continuous latent response variables. The indirect effects of the mediating risk factors were determined by calculating the product of the coefficients along a path. For the binary outcome (SGA birth), we used the standardized coefficients.[64] The proportion of the relationship between SGA and SES mediated by each of the mediators was determined by dividing each of the corresponding indirect effects by the absolute total effect.[66] The assumptions required to test mediation hypotheses were met, although we cannot assert that associations were not confounded.[67] Maternal education was included as categorical variable with high-education as reference group. SPSS 15.0, SPSS Inc., Chicago, USA was used for the univariate analyses and M-PLUS (Muthen and Muthen) was used for the path-analysis mediation models. A p-value < 0.05 was considered as significant.

RESULTS

General characteristics of the study population are described in Table 2.1. Low-educated women more often were multiparous, were younger, had a shorter height, lived in a lower-income neighbourhood area, and were more likely to have a late entry into antenatal care. They generally scored poorer on lifestyle and lifestyle-related characteristics (e.g. more smoking and more anxiety), except for alcohol consumption (less in low-educated women).

The prevalence of SGA was 12.3% in the low-educated group whereas the prevalence was 6.6% in the high-educated group. Compared to the women with high education, the women with low education had an increased risk of delivering an SGA infant (OR 1.98; 95% CI 1.35 – 2.89, Table 2.2). Covariables that were indicated as possible explanatory factors were: maternal age, height, underweight, cigarette smoking, and caffeine intake. All other covariables were neither associated with maternal education nor were associated with SGA (Table 2.2).

The path-analysis model was used to explain the associations of maternal education with SGA (Figure 2.1). The left part of Figure shows that low-education was associated with younger maternal age, shorter maternal height, less caffeine intake, and higher odds of being exposed to tobacco during pregnancy. The right part of Figure shows that the odds of being SGA increased with increasing maternal age, decreasing maternal height, and in particular with cigarette smoking.

Table 2.3 illustrates the indirect effects of low-education on SGA through mediating risk factors involved maternal age, maternal height, and maternal cigarette smoking. There was no indirect effect of caffeine intake and underweight. The indirect effect of maternal smoking on the association between low maternal education and SGA was 0.45 (95% CI 0.28; 0.63), which is the product of the regression equations along that path reported in Figure (1.57*0.29). The total effect was 0.68, which was the sum of the absolute value of the direct effect plus the sum of the absolute values of the indirect effects. Maternal cigarette smoking explained about 66% of the association between maternal education and SGA (0.45/0.68*100) In addition, maternal height explained about 9% of this association. As maternal age was positively associated with SGA, but negatively associated with low maternal education, maternal age had a negative indirect effect and therefore masks rather than explains the association between maternal education and SGA (-13%). After adjustment for mediators, the association of maternal education with SGA was no longer statistically significant.

Table 2.1. General characteristics by maternal educational level

		Educational level			
	Total	High	Mid	Low	p-value*
	(n = 3783)	(n = 2134)	(n = 1339)	(n = 310)	
Pregnancy characteristics					
Infant gender (% boys)	50.2	50.8	48.3	53.9	.14
Maternal age, yr (SD)	32.1 (4.2)	32.8 (3.3)	31.7 (4.5)	29.5 (6.2)	<.001
Parity (% primipara)	60.2	60.5	61.3	53.5	.04
Maternal height, cm (SD)	171.5 (6.2)	171.9 (5.9)	171.2 (6.5)	169.8 (6.4)	<.001
Pregnancy-induced hypertension (%)	9.4	8.7	10.4	10.0	.13
Pre-existing hypertension (%)	3.3	2.8	4.0	3.5	.14
Chronic disease (%)	2.2	2.3	2.3	1.3	.49
Late entry into antenatal care (%)	4.5	3.8	4.9	7.4	.01
Neighbourhood					
Neighbourhood income (SD)	12.7 (2.5)	13.1 (2.5)	12.4 (2.4)	11.6 (2.4)	<.001
Lifestyle habits					
Underweight (%)	4.1	4.0	3.7	6.8	.047
Maternal cigarette smoking (%)	7.3	2.2	9.3	33.2	<.001
Environmental cig. smoking (%)	19.5	11.9	24.6	49.7	<.001
Non medical drug abuse (%)	2.4	1.5	2.8	6.8	<.001
Alcohol use (%)	29.3	35.5	23.4	12.6	<.001
Caffeine intake (%)					.001
< 100 grams	25.5	23.3	27.0	33.9	
100 – 200 grams	32.2	32.1	32.6	31.6	
200 – 300 grams	22.0	23.3	21.1	16.5	
> 300 grams	20.3	21.2	19.3	18.1	
Fatty fish intake (%)					<.001
< 10 gram	29.6	22.9	35.8	48.7	
10-20 gram	41.7	44.0	40.6	30.3	
> 20 gram	28.7	33.0	23.6	21.0	
Folic acid intake (%)	90.4	93.1	89.3	76.5	<.001
Psychological					
Anxiety (%)					<.001
Low	50.3	55.0	47.4	30.6	
Mid	39.4	36.5	41.5	50.3	
High	10.3	8.5	11.1	19.0	
Depressive symptoms (%)					<.001
Low	52.3	57.1	49.4	31.6	
Mid	38.2	34.6	40.3	53.5	
High	9.6	8.6	10.4	14.8	
Outcome					
SGA (%)	7.2	6.6	6.9	12.3	.001

*Significance levels for continuous normally distributed variables were based on one-way ANOVA and for categorical variables on Chi-square test.

Table 2.2. Logistic regression for SGA with determinants adjusted for maternal education

		OR (95% CI)
Maternal education (reference: high)		
Mid		1.06 (0.80 – 1.38)
Low		1.98 (1.35 – 2.89)
Pregnancy characteristics		
Maternal age		1.04 (1.01 – 1.08)
Maternal height		0.94 (0.92 – 0.96)
Pregnancy-induced hypertension (reference: no)		1.30 (0.89 – 1.92)
Pre-existing hypertension (reference: no)		1.65 (0.93 – 2.93)
Chronic disease (reference: no)		0.83 (0.33 – 2.06)
Late entry into antenatal care (reference:<18 weeks)		1.21 (0.70 – 2.10)
Neighbourhood		
Neighbourhood income		0.97 (0.92 – 1.02)
Lifestyle habits		
Underweight (reference: no)		1.90 (1.16 – 3.09)
Maternal cigarette smoking (reference: no)		3.06 (2.11 – 4.43)
Environmental cigarette smoking (reference: no)		1.24 (0.91 – 1.67)
Non medical drug abuse (reference: no)		1.59 (0.83 – 3.05)
Alcohol use (reference: no)		1.09 (0.83 – 1.44)
Caffeine intake (reference: < 100 grams)	100 – 200 grams	0.95 (0.67 – 1.35)
	200 – 300 grams	1.34 (0.93 – 1.91)
	> 300 grams	1.42 (0.99 – 2.03)
Fatty fish intake (reference > 20 grams)	10-20 grams	0.97 (0.72 – 1.31)
	< 10 grams	0.83 (0.60 – 1.16)
Folic acid intake (reference: no)		0.80 (0.52 – 1.25)
Psychological		
Anxiety (reference: low)	Mid	0.98 (0.75 – 1.28)
	High	1.10 (0.73 – 1.65)
Depressive symptoms (reference: low)	Mid	0.94 (0.72 – 1.22)
	High	0.97 (0.63 – 1.50)

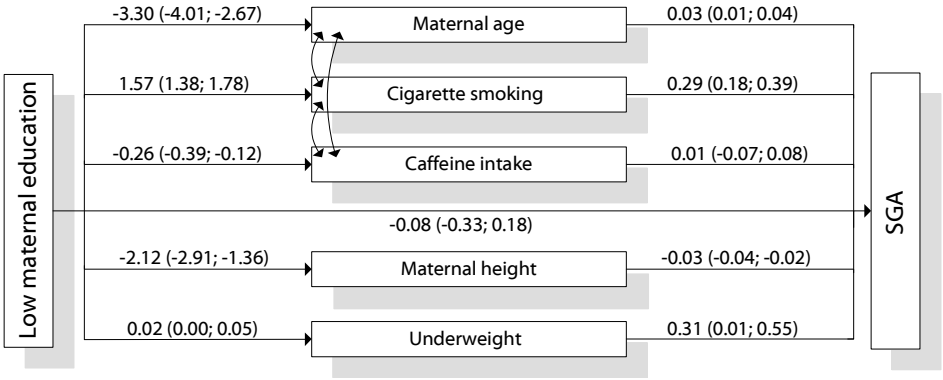

Figure 2.1. The 5 regression equations, with SGA and each of the potential mediators as the outcomes, are represented by single-headed arrows. Double-headed arrows refer to the correlation between potential mediators. The product of the coefficients reflects the weight of the path with the 95% confidence intervals in parentheses.

Table 2.3. Indirect effects of mediators on the association between low maternal education and SGA (95% CI) and proportion mediated.

	Indirect effects	Proportion mediated (%)
Maternal age	-0.09 (-0.14 – -0.03)	-13
Maternal cigarette smoking	0.45 (0.28 – 0.63)	66
Maternal height	0.06 (0.03 – 0.09)	9
Total effect*	0.68 (0.30 – 1.06)	
Total indirect effect**	0.60 (0.42 – 0.79)	

*Total effect=Total indirect effect+abs(-0.08).
**Total indirect effect=abs(-0.09)+abs(0.45)+abs(0.06).

DISCUSSION

The relation between maternal education and SGA birth is almost entirely explained by maternal cigarette smoking and for a small part by maternal height. Potential other explanatory factors such as hypertension, chronic disease, late entry into antenatal care, underweight, environmental cigarette smoking, alcohol use, drug abuse, folic acid intake, fish intake, caffeine intake, and psychological factors appear not to be responsible for educational inequalities in SGA offspring at the population level, though these factors could be meaningful in individuals.

Kramer et al.[30] described that it is not known whether any residual socioeconomic disparities remain after accounting for factors whose mediating roles are known or strongly suspected. Our results suggest that there is no independent association of maternal education with SGA. Furthermore, previous studies to socioeconomic disparities in SGA birth have primarily focussed on one or two factors at a time. As far as we know, this is the first study that simultaneously assessed an array of explanatory factors of educational inequalities in SGA birth in one study. Similar to others studies we found that maternal cigarette smoking largely contributes to socioeconomic inequalities in SGA.[31,32] In an extensive review, many other factors that may explain a small, additional portion of the disparity between socioeconomic groups were hypothesized as explanatory factors.[30] Explanatory factors were for example: psychosocial factors,[29] alcohol use,[68] and caffeine consumption.[69] However, there are no studies that have examined the contribution of these factors in the relation of SES to SGA offspring. Using path-analysis, which accounts for the correlation between explanatory variables, maternal cigarette smoking overrules other factors. To reduce educational inequalities in SGA offspring, we should therefore rather focus on cessation of maternal smoking instead of a reduction of other possible contributors.

Maternal cigarette smoking was the main factor in the relationship between maternal education and SGA offspring. In the literature, maternal education was not only associated with smoking, but also has been associated with the willpower to stop smoking in pregnancy. Women with a college degree were more often in the 'action stage', whereas women who attended only compulsory school were more often in a 'contemplative stage'.[70] In addition, maternal education was associated with successful cessation among the general population.[71] As continuing smoking during pregnancy was associated with psychosocial problems[72] and these problems were strongly related to maternal education, psychosocial problems might lie under the effect of smoking on the association between maternal education and SGA. An et al.[70] compared the reach, effectiveness, and costs of different modes of cessation assistance (treatment center, work-site, helpline, website) and concluded that the helpline was notable in comparison with other programs for serving those with less education. So least educated women should be approached proactively for smoking cessation.

Major strengths of the present study include the community-based sample, the prospective study design and the fact that many explanatory variables from multiple dimensions were available, enabling to assess their individual and independent contribution. However, it should be noted that in this large sample, explanatory variables were measured only in the first trimester. Whereas this might be a strength for some variables, e.g. folic acid use, it has been argued that other variables e.g. cigarette smoking, affect SGA birth especially in the last trimester. For example, in women who stopped smoking before 15 weeks' gestation, rates of SGA did not differ from those in non-smokers.[27] Explanatory variables were available from an extensive questionnaire, and we were able to 'explain' the educational inequalities. In a subgroup of 2875 women we tested the influence of maternal occupation in the association between maternal education and SGA, but adding maternal occupation did not influence the results. We used SGA as an outcome measure, which is a commonly used and clinically relevant composite measure from gestational age, parity, gender, and birth weight. However, this measure could not fully differentiate between physiological and pathological smallness as the growth curves for example do not reflect physiological variation because of maternal height or prematurity.[73] In our study, results did not change by excluding all preterm infants (n= 186). The moderate response rate and the fact that women with a non Dutch ethnicity were left out may affect generalizability, but educational inequalities were not confounded by ethnicity. Educational differences in SGA offspring among other ethnic backgrounds are an issue to be addressed in future studies. Finally, a statistical limitation have to be mentioned. It was argued that causal assumptions required for the validity of the decomposition method were not verifiable, so we have to point out that our results cannot be interpreted as causal effects.[67] On the other hand, many explanatory factors were based on well-known pathophysiologic mechanism, so causality is plausible.

CONCLUSION

Our results indicate that to a large extent, educational inequalities in SGA offspring are attributable to maternal cigarette smoking and to a small extent to maternal height, while many other pregnancy characteristics, lifestyle habits, and psychological factors appear not to play a role in the association between maternal education and SGA offspring. To reduce inequalities based on maternal education more effort is required to include least educated women especially in prenatal intervention programs such as smoking cessation programs. Reducing the prevalence of other risk factors of SGA offspring appears not to lead to a decrease of educational inequalities in SGA offspring, but might still relevant at the individual level for improving the offspring's health.