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Effect of maternal smoking on birth weight of twins: a study from the Dutch Twin Register

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Abstract

Since twins weigh about 20% less than singletons at birth, maternal smoking may be a more severe risk for them than for singletons. Therefore, the effect of maternal smoking during pregnancy on birth weight was investigated in a group of 5376 twins. All necessary information was collected by a questionnaire filled out by the mother of the twins. Gestational age explains more than 75% of the variance in birth weight. Other effects were tested with gestational age as a covariate. Apart from zygosity (DZ twins weigh more than MZ twins), birth order (first born twins weigh more than second born twins) and sex (boys weigh more than girls), there was a very significant birth weight reducing effect (more than 8%) maternal smoking as well as a significant influence of maternal age (young mothers give birth to smaller children). There were no interactions with maternal smoking.

Keywords: Birth weight; Maternal age; Maternal smoking; Sex; Twins

1. Introduction

Low birth weight is a risk condition for the health and development of children. This has been documented convincingly [e.g. 8,10,11,25]. These investigations show that of the very low birth weight (VLBW) children — children with a birth weight

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below 1500 g — about one in three children has either behavioral or learning problems or both, whereas this is about one in seven among children with a low or normal birth weight. Hack et al. [7] confirmed these results and found in addition, a subnormal headsize ($\leq$ mean for that particular age – 2 S.D.) in 13% of the children at 8 months. That category of VLBW infants, i.e. those with perinatal growth failure, particularly underscored on tests of cognitive abilities at 8 years of age. A recent study among more than 20 000 Israeli boys showed a very significant lowering of IQ (measured during a medical examination for military service at the age of about 18 years) when birth weight was below the average the total group. This effect (tested after elimination of several confounding factors) appeared to be proportional to the birth weight shortage, even within the normal birth weight range (2500–3500 g) [20]. Lower birth weight has been found to be associated with higher death rates from ischemic heart disease in adulthood [1] as well as a poorer adult lung function [2].

Twins, weighing at birth on average 1000 g less than singletons may be considered a special risk group.

One condition that has a known depressing influence on fetal growth and birth weight is cigarette smoking by the mother during pregnancy. This effect has been demonstrated by several investigators [5,21,22,24] and was also found in the offspring of smoking-discordant female monozygotic twins: children of the smoking twin weighed about 127 g less than those of their birth order matched non-smoking co-twin [9].

Nicotine may decrease the utero-placental blood flow and thus reduce birth weight [19,23]. Recent animal research [12,13,18] has furnished evidence that prenatal exposure to nicotine may lead to long lasting impairment of β-adrenergic and α_1-adrenergic function, which could explain (in part) the type of effects of VLBW as reported by investigators like McCormick et al. [11] and Veen et al. [25]. Of course, smoking is not the only reason for low birth weight, i.e. there can be more than one causal path with low birth weight as an intervening condition, that lead to later developmental disturbances. It appears that, on average, the birth weight of children from mothers who smoke during pregnancy is about 200–250 g lower compared with children from non-smoking mothers [24]. The risk of low birth weight will therefore be higher among children whose mothers smoked during pregnancy.

Another condition that has a known negative effect on birth weight is 'being a twin'. On average, twins weigh about 700–800 g less than singletons [3,16]. This is more than 20% of the average birth weight of singletons and considerably more than the effect of maternal smoking. Thus, in twins the low birth weight risk is affected additively by their twin status and (eventually) by the smoking behavior of their mother. In the above mentioned study of McCormick et al. [11], about 0.65% of the children had a birth weight less than 1500 g (VLBW). In the twin sample used in the present study, 4–5% belong to the VLBW category, which is about seven times more than in singletons!

The purpose of the present study is therefore to estimate the effect of maternal smoking on the birth weight of twins. Since zygosity, sex and birth order have separate contributions to birth weight [3,16], these factors will be taken into consider-

ation as well, especially because of possible interactions with maternal smoking habits. In addition, the influence of maternal age will be considered, since in a Swedish study [6] it was found that maternal age potentiates the effect of smoking on birth weight: greater in older women than in younger ones. Because gestational age is known to be the most important — but at the same time most obvious — factor affecting birth weight, all the above mentioned specific potential factors that may influence birth weight are tested after correction for the effect of gestational age, by handling gestational age as a covariate in the ANCOVA's (analysis of covariance).

2. Method

2.1. Subjects

About 40% of all twins born in the Netherlands since the end of 1986 are registered in the Dutch Twin Register. Parents have given their written permission to list their family in the Register and their willingness to cooperate in future research. Once a year, a questionnaire is mailed to them, the first shortly after the birth of the twins, asking about several health and behavioral characteristics, zygosity, birth weight, etc. The total sample comprises 3275 twin pairs (6550 individuals). Information about at least one of the relevant variables was lacking for some twins, but data were complete for 5376 subjects.

2.2. Data

All information in the present report was acquired from questionnaires filled out by the mother. Data were collected on zygosity, birth order (age, i.e. first or second born), sex of the twins and age of the mother. Zygosity was assessed (with a questionnaire) shortly after birth and once again when the twins were about 2 years of age. For 1540 pairs, the zygosity determination was based on the first questionnaire (including also the opinion of the obstetrician, obtained via the mother) and for the remaining pairs on combined information from both the first and the second questionnaire. The use of a questionnaire for zygosity determination leads to an estimated proportion of misclassifications (among same sex twin pairs) of about 4–5% [4,14,15].

Maternal smoking during pregnancy was assessed in three categories: 'not at all' (not), 'sometimes' or 'regular'. This method of assessment of maternal smoking habits does not reflect the real number of cigarettes smoked but allows grouping of mothers on an ordinal scale and produces a low probability of 'denying' with regard to the highest answer category.

Sex, birth order, gestational age and maternal age could be reliably reported by the mother.

3. Results

Gestational age did not covary with smoking habits of the mother. Because gestational age is the most important factor influencing interindividual variability in birth weight, all reported analyses have been carried out with gestational age as a

covariate. The effects of sex and birth order were tested on the individual birth weights in one ANCOVA (analysis of covariance), carried out with the statistical package 'Systat 5.0' The effects of zygosity, maternal smoking and maternal age were tested on the sum weights of the twin pairs in one ANCOVA. For that analysis, the continuous variable 'maternal age' was categorized in three groups: 'young' (below 26 years of age); 'average' (between 26 and 33 years of age); and 'old' (33 and over).

All the main effects were significant (Table 1). None of the interactions reached significance. When the ANCOVA's are carried out on either the older or the younger twin, results remain the same, apart from small irrelevant shifts in *F*-values and the necessary omission of 'birth order' as an independent factor.

4. Discussion

The present study confirms several effects on birth weight: boys weigh more than girls, MZ twins are heavier than DZ twins, and first born twins weigh more than second born. In addition, it appears that young mothers give birth to twin babies of lower birth weight compared with older mothers. It is possible that maternal pregravid weight and/or maternal weight gain during pregnancy have confounded this effect, since these values are in general positively associated with both birthweight of the resulting child and age of the mother. However, we could not allow for this possible confounding effect because we did not have the information on pregravid weight and on weight gain.

Table 1
Significant main effects on birth weight of sex, zygosity, birth order, maternal smoking and maternal age

Factor	Average birth weight (S.D.)			*F*-value (df)[a]	*P*-value
Sex	Boys:	Girls:		96.1	<0.0001
	2566	2462		(1,5657)	
	(536)	(537)			
Zygosity	MZ:	DZss:[b]	DZos:[b]	8.8	<0.0002
	4828	4976	4986	(2,2673)	
	(973)	(969)	(999)		
Birth order	First:	Last:		34.9	<0.0001
	2545	2482		(1,5657)	
	(534)	(542)			
Smoking	Not:	Sometimes:	Regular:	83.7	<0.0001
	5140	4920	4730	(2,2673)	
	(994)	(1015)	(895)		
Maternal age	Young:	Average:	Old:	12.1	<0.0001
	4936	5007	5098	(2,2673)	
	(1009)	(972)	(965)		

[a]Where possible corrected for potential confounding with gestational age; sex and birth order are analyzed on individual birth weights; zygosity, maternal smoking and maternal age on sum weights.
[b]DZss, dizygotic twin pair, members having the same sex; DZos, twin pair of which one member is male and the other female.

The potentiating influence of maternal age on the weight reducing effect of maternal smoking — as found by Cnattingius [6] for singletons — could not be confirmed in the present study.

The effect of maternal smoking (i.e. the difference between not smoking and regular smoking) is about 200 g, which is about the same as has been repeatedly found in singletons, but also the same as in triplets as we recently found [17], i.e. the effect is the same per individual child in absolute terms, irrespective whether the child is part of a multiple or not. This is an indication that the condition that is responsible for the birth weight reduction of the fetuses is completely localized in the mother (most likely as suboptimal placental function) and can not be ascribed to some form of distribution of tobacco smoke constituents over the individual members of the multiple. Thus, proportionally, the effect in twins is more severe, and this holds even stronger for the younger of a pair, because that one already has a lower birth weight. One may say that maternal smoking increases the probability of a twin being 'low birth weight' or LBW (<2500 g) by about 16%, whereas the probability of a twin being 'very low birth weight' (VLBW, ≤ 1500 g) increases by about 4%, i.e. among twins from non-smoking mothers, 4.7% have a birth weight <1500 g; maternal smoking increases this to 8.5%.

In the near future these twins will be surveyed and one of the questions that will be addressed is whether, within the known relationship between birth weight and quality of behavioral development, a specific mediating contribution of maternal smoking can be distinguished from other factors affecting birth weight.

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