Prepregnant reproductive risk and subsequent birth outcome among Scandinavian parous women

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SUMMARY

This study examined the impact of maternal prepregnant stature, smoking, and past reproductive characteristics on gestational length, birthweight, weight-for-gestation, and crown heel length. Analyses were based on 5722 para one and two Caucasian women in Trondheim and Bergen (Norway) and Uppsala (Sweden) who had a singleton pregnancy and who were interviewed before 20 completed weeks of gestation. Data included information about previous induced and spontaneous abortions, prepregnant weight and height, smoking, course and outcome of previous pregnancies with special reference to preterm and low birthweight (LBW) births, and perinatal deaths. Number of adverse outcome predictors was counted for each woman and birth outcomes were analysed by that number. Separate univariate and multivariate analyses examined the impact of the individual risk characteristics. Mean birthweight, crown heel length, and gestational length were significantly related to number of prepregnant risk characteristics with a dose response decrease from 3750 g, 51.2 cm, and 39.6 weeks to 2955 g, 47.7 cm, and 37.7 weeks for women with zero and six risk factors, respectively. Both univariate and multivariate analyses showed that prepregnant weight, a previous LBW birth, and cigarette smoking around conception were the strongest birthweight predictors with a mean BW reduction of 424 g (95% CI 373, 475 g) and 130 g (95% CI 112, 157 g) for a previous LBW birth and 10 cigarettes per day, respectively. As 88% of birthweight variation was left unexplained by these prepregnancy characteristics, it may be concluded that the major risk factors are either unknown or that main predictors of birthweight, such as life style factors, exert their effect *during* gestation, or both.

Key words: Pregnancy, risk factor, parous women, birth outcome

INTRODUCTION

With decreases in mortality and morbidity from other perinatal problems, adverse pregnancy outcome related to low birthweight has become relatively more important. Low birthweight is either due to preterm delivery, intrauterine growth retardation, or a combination of the two. The public health importance of these conditions has been emphasized repeatedly and their prevention is an important challenge in perinatal care (1-4).

A detailed medical, social, and reproductive history taken early in pregnancy is regarded as a cornerstone in every antenatal care programme (5). Whereas the purpose of the medical and social history is to unveil every circumstance, including life style habits, that might have a negative impact on the course and/or outcome of pregnancy, the reproductive history of parous women will include the outcome of previous births, i.e. complications during pregnancy, gestational length, mode of delivery and obsterical events, as well as status and anthropometry of the newborn. The underlying idea is that the available information enables the clinician to make a better risk assessment of the present pregnancy that includes the prediction of a newborn whose weight is lighter than expected.

There is considerable evidence that shows the association between smoking in pregnancy and low birthweight (6-8). Also, it has been shown that mothers have a tendency to repeat the outcome of pregnancy, e.g., a small-for-gestational age (SGA) newborn, in successive births (9). Still, it is unclear whether the latter tendency is the result of a genetic, exogenous, or combined influence. A cross-generational effect has been shown where a mother who was herself SGA had a higher risk of having an SGA child compared to a mother who was not SGA (10). The predictive properties of maternal stature, recurrent abortions, or a previous perinatal death on the outcome of subsequent births have been less well documented (11-13). The aim of the present paper was to study the association between a set of prepregnant maternal characteristics and subsequent birth outcome in a population of parous women.

MATERIAL AND METHOD

Data stem from the Scandinavian part of the National Institute of Child Health and Human Development (NICHD) Successive Small-for-Gestational Age Births Study. This is a multicenter study that was organized at the Universities of Trondheim and Bergen in Norway, and Uppsala in Sweden. A detailed background and description of the study has been published (14).

Recruitment of pregnant women in Norway was based on referrals from general practitioners and obstetricians in Trondheim and Bergen who had agreed to refer their eligible patients to the antenatal clinic at the University hospital for a series of special antenatal visits. In Sweden, women were recruited from all antenatal care centers in Uppsala county, which were under the direct supervision of the Uppsala obstetrical department. Study recruitment took place from January 1, 1986 through March 1988.

Caucasian women with a singleton pregnancy and one or two previous births (defined as a delivery after 20 completed weeks) were eligible for enrollment. A total of 6354 parous women were recruited and referred to one of the respective centers prior to 20 completed weeks of gestation. However, 6.8% (432) of the referred women were excluded because they did not fulfil study criteria. E.g., several women had aborted (229), some (34) had a twin pregnancy, while the remainder (169) had either gone beyond 20 weeks or were excluded due to ethnic or language incompatibilities. For various reasons, mostly social constraints, another 3.1% (200) of the referred women failed to come to the first study visit despite the fact that they had agreed to participate. Those women were also excluded.

The present analyses regard the remaining 5722 eligible women who entered the study and were interviewed and examined by a study midwife at one of the three University obstetrical departments. The antenatal risk characteristics that were used in the analyses were recorded at the first visit and were defined as follows:

Low body mass (Ponderal) index: (Prepregnant weight/Height^2) * 1000. A value below 2.00 kg/m^2 corresponded to the lower quartile.
Previous abortion: One spontaneous second trimester or two induced abortion(s).
Previous preterm birth: A previous delivery before 37 completed weeks gestation.
Previous low birthweight (LBW) birth: A previous first birth below 2700 grams (female) or 2800 grams (male), or a second birth below 2800 grams (female) or 2900 grams (male).
Previous perinatal death: A previous stillbirth (after 28 weeks gestation) or death of a newborn within the first week of life.
Smoking: Women who reported that they were daily smokers around the time of conception.

Other definitions:

Expected date of delivery: Expected date of confinement (EDC) was based on the last menstrual period (LMP) if it was regarded as certain to within ± 3 days by the woman, if she had not used oral contraception within the last six months, and if the EDC based on the LMP did not differ by more than ± 14 days compared to the EDC based on ultrasonography. If the opposite were the case, the latter EDC was used.
Small-for-gestational age (SGA): Birthweight below 15th percentile-for-gestation according to Norwegian population based percentile charts (15).

Data were analyzed with the SAS PC version (SAS Institute Inc. 1987). Different analytical techniques (Student's t-test, chi-square statistics, Pearson's r, analysis of variance (ANOVA), and stepwise linear regression modeling) were employed and observed differences with $p< 0.05$ were considered statistically significant.

RESULTS

Maternal characteristics

As shown in table 1, para one and two mothers differed significantly in several respects. While there were no differences in terms of prepregnancy weight and smoking habits, para one mothers were significantly younger, had lower body mass index, fewer abortions, premature and low birthweight births, as well as fewer perinatal deaths.

Table 1. Maternal characteristics of para 1 and para 2 women in the Scandinavian part of The NICHD Successive Small-for-Gestational Age Births Study (N=5722).

Maternal characteristic*	Para I (N=4090)	Para II (N=1632)	p value
Age (SD)	29.1 (4.2)	31.6 (4.2)	<.001
Prepregnancy weight (SD)	61.0 (9.5)	61.5 (9.8)	n.s.
Body Mass Index (SD)	2.19 (0.31)	2.22 (0.32)	<.001
Previous late or ≥ 2 induced abortion(s)	4.3%	5.5%	<.05
Previous premature birth(s)	6.8%	11.0%	<.001
Previous perinatal death(s)	0.9%	3.6%	<.001
Proportion of smokers	33.7%	34.2%	n.s.
Mean daily number of cigarettes (SD)	3.9 (6.3)	4.0 (6.6)	n.s.
Previous LBW birth	7.5%	13.5%	<.001

* For description of characteristics; see text

Analysis of risk characteristics

The prevalence of the defined risk characteristics, regardless of parity, is shown in figure 1 and varied from 33.4% (smoking) to 1.6% (perinatal death). Except for low body mass, which was 25% by definition, the prevalence of the other prepregnant risk characteristics ranged between 4.6% (abortion) and 9.2% (previous LBW birth). There was a highly significant correlation between the latter characteristic and a previous preterm birth (Pearson's r=0.6; p<0.001) which was considered in the multivariate analyses. Also, a test for collinearity showed that prepregnancy weight and body mass index could not be used simultaneously in the multivariate analysis.

Table 2 shows the univariate analysis of birthweight for births of women with and without each risk characteristic. The mean birthweights were significantly lower for women *with* the characteristics and the differences ranged between 137 g (previous abortion) and 444 g (previous LBW birth). One exception was a history of previous perinatal death which showed borderline significance. Still, that risk factor was included in the multivariate analysis.

The number and proportion of women by number of risk factors are shown in table 3. Overall, almost 80% of the women had no (43.4%) or only one (34.6%) recorded risk characteristic. Table 3 also shows the outcome of pregnancy in terms of mean birthweight in grams, birthlength (crown heel) in cm, and gestational length in completed weeks by number of risk factors. There was a decrease in mean birth outcomes from 3750 g, 51.2 cm, and 39.6 weeks to 2955 g, 47.7 cm, and 37.3 weeks for women with zero and six risk factors, respectively. Analyses of variance showed that all these differences were highly significant (p <0.001). The dose response relationship between number of risk characteristics and birthweight is also shown in figure 2. Separate analyses of variance showed the same significant decrease in mean birthweight, birthlength, and gestational length by number of risk factors for para one and two women, and for male and female newborns (p<0.001; data not shown).

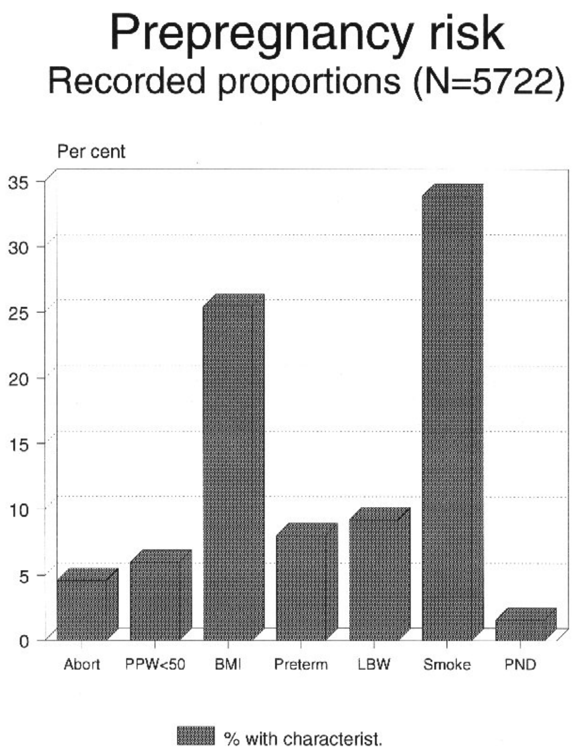

Figure 1. Proportion of prepregnant risk characteristics among parous Scandinavian women (N=5722). **Legends**: Abort=Previous abortion; PPW<50=Prepregnancy weight below 50 kg; BMI=Body Mass Index; Preterm=Previous preterm birth; LBW=Previous low birthweight birth; Smoke=Smoking around time of conception; PND=Previous perinatal death.

Table 2. Univariate analysis of mean birthweight for women with and without seven selected prepregnant risk characteristics (N=5722).

Risk characteristic	Women with risk characteristic; Mean birthweight (SD)	Women without risk characteristic; Mean birthweight (SD)
Previous late or ≥ 2 induced abortion(s)	3473 (732)	3610** (575)
Prepregnancy weight < 50 kg	3302 (557)	3623*** (580)
Body mass (Ponderal) index < 25th percentile (= 2.00 kg/m^2)	3469 (565)	3650*** (583)
Previous preterm birth(s)	3319 (634)	3629*** (572)
Previous low birth weight newborn	3201 (605)	3645*** (565)
Smoking around time of conception (= yes)	3470 (605)	3673*** (582)
Previous perinatal death(s)	3463 (739)	3606* (580)

* 0.05<p<0.10 ** p<0.01 *** p<0.001

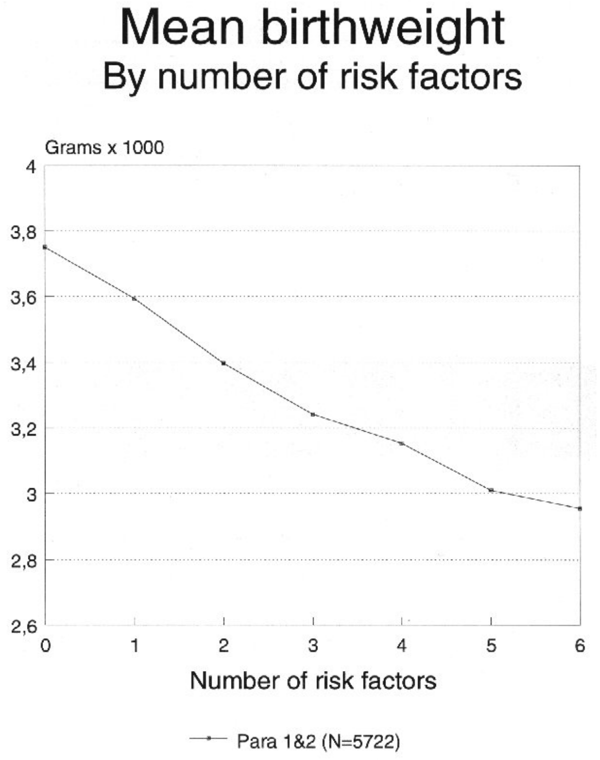

Figure 2. Mean birthweight (in 1000 grams) of the newborn by number of prepregnant risk characteristics among parous Scandinavian women (N=5722).

Table 4 shows the birth outcomes by various combinations of maternal risk, i.e. smoking, low body mass index, and a previous LBW birth. Whereas women with no risk characteristics constituted almost half of all the women (43.4%), women with only one made up another 21.1% (smoking), 14.1% (low body mass index), and 3.9% (previous LBW birth), respectively. Still, there was a gradual and significant decrease in the birth outcomes (3750 g, 51.2 cm, and 39.6 weeks vs. 2964 g, 47.8 cm, and 38.3 weeks) for women with no to women with all three risk characteristics ($p<0.001$). There was also an increase in the proportion of women with a birth below the 15th percentile among women who had one or more risk characteristics. While there was an overall proportion of 10.3%, it varied from 5.9% among women with none to 37.0% among women with all three risk characteristics and with crude odds that ranged from 0.55 to 5.39. However, the 95% confidence limits included the null value for women with only one risk factor.

Birthweight was modeled stepwise with the prepregnant risk characteristics. Due to the collinearity between maternal prepregnant weight and body mass index and the high correlation between previous preterm and low birthweight birth, body mass index and previous preterm birth were not entered into the model which examined the main effects as well as two- and three-way interaction terms. The final model, however, included only the main effects since none of the interaction terms met the appropriate significance level ($p<0.15$) to enter the model. The results of the stepwise procedure in terms of variable coefficients, partial prediction coefficient (R^2) and standard error are shown in table 5. For instance, a previous LBW birth was associated with an adjusted mean birthweight reduction of 424 g (95% CI 373, 475 g), whereas women who smoked 10 cigarettes per day around conception delivered newborns who on average weighed 131 g (95% CI 112, 157 g) less than non-smokers. Even if the multivariate model was highly significant ($p<0.001$), the explained birthweight variance for births in the present pregnancy was no better than 12% ($R^2 = 0.1196$).

DISCUSSION

These analyses examined the relative impact of selected prepregnant maternal risk characteristics on subsequent birth outcome among parous women. Based on a first interview with the 5722 study women around week 17 of gestation, seven risk characteristics were identified with reference to maternal stature, smoking, and previous reproductive history and birth outcomes.

Table 3. Number and proportion of women and birth outcomes by number of antenatal risk factors* in the Scandinavian part of The NICHD Study of Successive Small-for-Gestational Age Births Study (N=5722).

No. of risk factors	No. of women	Birthweight (SD)	Birthlength (SD)	Gest. length (SD)
0	2482 (43.4%)	3750 (546)	51.2 (2.4)	39.6 (2.1)
1	1981 (34.6%)	3593 (556)	50.5 (2.6)	39.5 (2.1)
2	830 (14.5%)	3398 (603)	49.8 (2.8)	39.0 (2.7)
3	314 (5.5%)	3243 (528)	49.3 (2.4)	38.8 (2.4)
4	83 (1.5%)	3153 (550)	48.6 (2.7)	38.5 (2.2)
5	29 (0.5%)	3009 (907)	47.6 (5.3)	38.0 (3.3)
6	3 (0.1%)	2955 (572)	47.7 (1.5)	37.3 (1.2)

* For description of risk factors; see text

Table 4. Number of women and birth outcomes[1] by various combinations of maternal prepregnancy risk characteristics in Scandinavian NICHD Successive Small-for-gestational age study (N=5722).

Risk characteristics	Number[2]	BW (SD)	BL (SD)	GL (SD)	Prop. SGA	Crude OR (95% CI)
None	2482 (43.4%)	3750 (546)	51.2 (2.4)	39.6 (2.1)	5.9%	0.55 (0.49;0.62)
Smoking	1210 (21.1%)	3571 (564)	50.4 (2.6)	39.5 (2.1)	11.5%	1.18 (0.96;1.44)
Low body mass index (BMI)	804 (14.1%)	3591 (536)	50.6 (2.2)	39.4 (1.9)	10.3%	1.01 (0.79;1.29)
Previous LBW birth	222 (3.9%)	3331 (646)	49.5 (3.2)	38.4 (39.3)	11.8%	1.17 (0.77;1.79)
Smoking + Low BMI	490 (8.6%)	3406 (535)	49.9 (2.4)	39.3 (2.2)	16.1%	1.79 (1.38;2.31)
Smoking + Prev. LBW birth	146 (2.6%)	3173 (544)	49.0 (2.9)	38.8 (2.2)	33.6%	4.73 (3.42;6.55)
Previous LBW birth + Low BMI	69 (1.2%)	3160 (403)	49.2 (2.0)	38.6 (2.0)	25.0%	2.97 (1.75;5.05)
Smoking + Low BMI + Previous LBW birth	92 (1.6%)	2964 (644)	47.8 (3.4)	38.3 (2.4)	37.0%	5.39 (3.65;7.94)

1) Analysis of variance (ANOVA) showed a significant difference for all continous outcomes: Birthweight (BW), birthlength (BL), and gestational length (GL); $p<0.001$.
2) 207 women had one or more other risk factors than those presented in table 4.

Table 5. Stepwise multiple regression of birth weight on selected prepregnancy characteristics among parous Scandinavian women (N=5722; Model $R^2 = 0.1196$).

Variable	Coefficient	Partial R^2	Standard error
Prepregnancy weight (kg)	12.664	0.0499	0.768
Previous LBW (yes/no)	–421.494	0.0438	26.299
Number of cigarettes around conception	–13.429	0.0225	1.152
Previous abortion (y/n)	–119.946	0.0017	35.359
Parity (2 vs 1)	38.082	0.0010	16.424
Previous perinatal death (y/n)	125.504	0.0007	60.066

Small-for-gestational age was defined as a birthweight below the nominal 15th percentile according to the used population based reference data (15). Recent analyses have shown that this cut off probably identifies better the true proportion of the 10 per cent lightest-for-dates newborns (14). Also, the definition of a previous LBW birth took into account the different birthweight distributions among newborns of separate gender and birth order (16).

The study included only parous women who expected their second or third child which may be regarded as a limitation of the study. Thus, no potential predictive properties of the prepregnant risk among nulliparous women could be considered. This limitation was a direct consequence of the overall design of the NICHD Small-for-Gestational Age Births Study (14).

One of the main strengths of the study was its population based nature and prospective design and that the risk characteristics were identified before the outcome of pregnancy was known. As an indication of the general, low risk of the population under study, three of four women (78%) had no or only one of the defined risk factors. Nevertheless, there was a significant decrease in birthweight, birthlength, and gestational length by number of risk characteristics. In addition to the mean birthweight difference of almost 800 g between newborns of mothers with no and six recorded risk factors, a dose response relationship was demonstrated by number of risk factors, regardless of the nature of the characteristics for the individual woman.

Given our definition of a previous abortion (one late spontaneous or two induced abortions), it turned out to be a stronger birthweight predictor than expected (11, 12). The rather weak association between a previous perinatal death and birthweight was more expected since the evidence for such an association has not been fully established (13). Of the significant characteristics in table 4, smoking and a previous LBW birth have been overwhelmingly documented as predictors of an adverse birth outcome (1-4,6-8,13), whereas maternal stature in terms of her prepregnant weight or – even more so – maternal body mass index has come into focus as a separate predictor more recently. E.g., other analyses of the NICHD study data have shown that proportional maternal weight gain during pregnancy is a strong predictor of intrauterine growth (16). We defined a low body mass index as the lowest 25 per cent of mothers which corresponded to the nominal value of 2.00 kg/m^2. For comparison, the 50th and the 75th percentile was 2.14 kg/m^2 and 2.33 kg/m^2, respectively.

The relationship between the birthweight of the mother and her offspring was assessed in a subset of 2072 pregnancies. Overall, there was a significant correlation between mother and newborn birthweights ($r=0.20$; $p<0.001$). Moreover, when the gender of the newborn was considered, there was a stronger correlation between mother and daughter ($r=0.24$; $p<0.001$) than mother and son ($r=0.17$; $p<0.001$) birthweights. Since data did not include the birthweight of all mothers and the subset of 2072 women were not representative of the whole study population (14), we chose not to enter this information in the multivariate model. However, the shown correlations agree with the growing literature on intergenerational effects and the probably inherited metabolic tendencies which determine fetal growth rate (9,10,18).

While the SGA prevalence was significantly lower among women without any of the prepregnancy risk characteristics (5.9%), smoking, a previous LBW birth, or low body mass index as the only risk factor increased the SGA prevalence about twofold. But whereas smoking and low body mass reduced the average birthweight by 167 g and 147 g, respectively, the average reduction among women with a previous LBW birth was 407 g. However, that substantial difference must be viewed in light of the gestational length which was one week shorter for the latter group of women, a finding that supports the argument for not entering previous preterm and LBW birth into the same multivariate model.

Various combinations of the risk characteristics further increased the crude odds for an SGA birth with smoking around conception combined with a previous LBW birth as the strongest set of predictors. Still, the highest SGA prevalence (37%) was seen among women with a history that included all three risk factors. The much lower birthweight among the latter women (2955 g) is probably the combined result of the prepregnancy risk impact and a significantly shorter than average gestational length (38.3 weeks). The latter finding compares favourably with the reported tendency that women repeat both gestational length and birthweight in successive pregnancies (9). Based on our results one might also include crown heel length.

Even if several statistically significant predictors were established in the multivariate analysis, we must acknowledge that they explain only 12% of the birthweight variability. Hence, our results correspond with others in terms of predictive properties of maternal prepregnant weight, a previous LBW birth, and smoking (1-4,6-8,13). Yet, they imply that when these well documented prepregnant predictors are considered, 88% of the birthweight variance still remains unexplained. For the clinician it is important to ackowledge the presence of the prepregnant risk factors discussed here, yet they will never serve as more than a discrete background scenery for other factors that influence fetal growth.

Maternal weight gain is greatly influenced by nutritional intake during pregnancy, and other analyses of the NICHD study data have shown that there are qualitative differences in food consumption, including coffee drinking, between smoking and nonsmoking pregnant women (19). E.g., mothers who smoked had a more unhealthy diet which influenced fetal growth negatively over and above that of smoking. In the present study the proportion who reported that they smoked around time of conception was alarmingly high (33.4%). Analyses of a subset of 751 smokers showed that 18% quitted during pregnancy and that the majority did so in the first trimester (8).

In conclusion, past reproductive history and prepregnant maternal characteristics yield significant prediction about subsequent birth outcome. However, our findings imply that major potential prepregnancy risk factor are still unknown and/or that the major outcome predictors exert their effect during gestation itself. In the latter case, the effect is probably strongly influenced by the woman's life style during pregnancy.

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