SHORT REPORT

Length of gestation is associated with mortality from cerebrovascular disease

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Recent studies reported on increased levels of adult cardiovascular risk factors in subjects born prematurely,[1] and on interactions between length of gestation and size at birth in their effect on cortisol metabolism,[2] and blood pressure.[3] The effect of fetal growth rate and the length of gestation on circulatory disease are explored in this study.

PARTICIPANTS, METHODS, AND RESULTS

In a cohort of 14 193 men and women born in Uppsala in 1915–1929, we studied the associations of fetal growth rate and length of gestation with the risk of death from ischaemic heart disease (ICD 7: 420–422; 8 and 9: 410–414; 10: I20–25) and cerebrovascular disease (ICD 7: 330–334; 8 and 9: 430–438, 10: I60–69). Occlusive strokes include ICD7: 332–334, ICD8: 432–436, ICD9: 433–436 and ICD10: I63–66. Data on deaths and emigrations were obtained by linkage to the population and death registers.

Socioeconomic circumstances at birth and neonatal characteristics, including gestational age (based on last menstrual period), were available for 96% of the subjects from hospital records. Data on social circumstances in adulthood included subjects' own social group, education, marital status, and household car ownership from 1960 census and were available for 96% of the 12 346 men and women who lived in Sweden in 1960.

Sex specific z scores of birth weight for each week of gestation were calculated using the cohort as a reference. The hypothesised independent effects of fetal growth rate and length of gestation were studied by combining the z scores for birth weight for gestational age with the length of gestation in the same model.

Analyses were restricted to singletons born at 30 or more completed weeks of gestation and 11 474 men and women were included in the multivariate analyses. Each participant

Table 1 Hazard ratios for death from ischaemic heart disease, cerebrovascular disease, and occlusive stroke (95% CI) in 11474 men and women born 1915–1929. Adjusted for age, period of birth, sex, and social characteristics (mother's civil status and social group when the study subject was born, and subject's own social group, education, marital status, and household car ownership from 1960 census)

	Ischaemic heart disease			Cerebrovascular disease			Cerebrovascular disease: occlusive stroke		
	Number of events	HR (95% CI) age, period, and sex adjusted	HR (95% CI) fully adjusted	Number of events	HR (95% CI) age, period, and sex adjusted	HR (95% CI) fully adjusted	Number of events	HR (95% CI) age, period, and sex adjusted	HR (95% CI) fully adjusted
Total number of events 1960–2001	1211			355			127		
Weight for gestational age (quintiles)									
Lowest	259	1.0	1.0	68	1.0	1.0	22	1.0	1.0
2nd	242	0.83 (0.70,0.99)	0.84 (0.71,1.00)	84	1.06 (0.77,1.45)	1.08 (0.78,1.49)	29	1.09 (0.63,1.90)	1.12 (0.64,1.96)
3rd	260	0.87 (0.73,1.03)	0.92 (0.77,1.09)	75	0.91 (0.66,1.27)	0.95 (0.68,1.32)	30	1.09 (0.63,1.90)	1.16 (0.66,2.01)
4th	218	0.74 (0.62,0.89)	0.77 (0.65,0.93)	69	0.83 (0.60,1.17)	0.87 (0.62,1.21)	22	0.80 (0.44,1.45)	0.86 (0.47,1.55)
Highest	232	0.76 (0.63,0.90)	0.80 (0.67,0.96)	59	0.70 (0.50,1.00)	0.74 (0.52,1.05)	24	0.82 (0.46,1.48)	0.89 (0.50,1.61)
p value heterog 4 df		0.007	0.035		0.136	0.225		0.673	0.764
p value linear trend		0.001	0.010		0.015	0.035		0.266	0.421
Gestational age (weeks)									
30–35	52	1.0	1.0	23	1.0	1.0	15	1.0	1.0
36–37	108	0.92 (0.66,1.28)	0.95 (0.68,1.32)	39	0.72 (0.43,1.20)	0.74 (0.44,1.25)	13	0.37 (0.18,0.78)	0.39 (0.18,0.82)
38–39	395	0.94 (0.70,1.26)	1.01 (0.75,1.35)	122	0.62 (0.40,0.97)	0.66 (0.42,1.03)	37	0.29 (0.16,0.53)	0.32 (0.17,0.58)
40–41	509	1.01 (0.76,1.35)	1.08 (0.81,1.44)	133	0.56 (0.36,0.88)	0.60 (0.38,0.94)	50	0.32 (0.18,0.58)	0.36 (0.20,0.65)
42+	147	1.06 (0.77,1.45)	1.09 (0.80,1.50)	38	0.57 (0.34,0.96)	0.60 (0.35,0.99)	12	0.28 (0.13,0.59)	0.29 (0.14,0.63)
p value heterog 4 df		0.663	0.775		0.148	0.234		0.007	0.015
p value linear trend		0.227	0.160		0.021	0.031		0.009	0.016

What is already known

- Higher rate of fetal growth is associated with a lower risk of circulatory disease.
- Recent studies reported on increased levels of adult cardiovascular risk factors in subjects born prematurely, and on interactions between length of gestation and size at birth in their effect on cortisol metabolism and blood pressure.

was considered at risk from the time of the 1960 census to date of emigration, death, or end of follow up (31 December 2001). The data were analysed by Cox regression in Stata. Results are adjusted for age, sex, and period of birth, with additional adjustments for social characteristics at birth and in adult life.

While higher rate of growth at any length of gestation was associated with a decreased risk of ischaemic heart disease, both higher rate of fetal growth and longer gestation were associated with a decreased risk of death from cerebrovascular disease (table 1). The risk of death from occlusive stroke in particular was decreased in subjects born after 36 or more weeks of gestation (table 1).

The effect of social characteristics at birth was particularly strong on mortality from cerebrovascular diseases, subjects born to families with lower social class being at a higher risk. The social characteristics in adulthood were more strongly associated with the risk of death from ischaemic heart disease. Adjustments for either did not appreciably affect the association of fetal growth rate or length of gestation with mortality from circulatory disease. There were no appreciable sex differences in the effect of weight for gestational age or length of gestation on risk of death from cerebrovascular disease.

What this study adds

- Shorter length of gestation is associated with higher mortality from cerebrovascular disease but not with ischaemic heart disease.
- The risk of death from occlusive stroke in particular is decreased in subjects born after 36 or more weeks of gestation.

Our results show that length of gestation is associated with mortality from cerebrovascular disease but not with ischaemic heart disease. The independent effect of length of gestation on risk of stroke seems plausible given the recent evidence on raised blood pressure,[3] and long term structural brain abnormalities in subjects born before term.[4]

Failure of earlier studies to show the adverse effect of prematurity on risk of stroke may be attributable to the lack of data on gestational age, restrictions to term births, or insufficient statistical power. The fact that parameters of fetal growth may be particularly linked to a certain type of stroke—rate of fetal growth being more strongly related to haemorrhagic strokes[5] and length of gestation to occlusive strokes—together with the difference in the composition of fatal and non-fatal cerebrovascular disease categories might have added to the difficulty of addressing this question. Given the potential implications for prevention of cerebrovascular disease, our results should be tested for consistency in other settings and the specific underlying mechanisms further elucidated.

Policy implications

Given the potential implications for prevention of cerebrovascular disease, our results should be tested for consistency in other settings and the specific underlying mechanisms further elucidated.

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Conflicts of interest: none declared.

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