Diabetologia (2006) 49:2614–2617
DOI 10.1007/s00125-006-0408-z

SHORT COMMUNICATION

The associations of birthweight, gestational age and childhood BMI with type 2 diabetes: findings from the Aberdeen Children of the 1950s cohort

D. A. Lawlor · G. Davey Smith · H. Clark · D. A. Leon

Received: 22 January 2006 / Accepted: 25 July 2006 / Published online: 21 September 2006

Abstract
Aims/hypothesis The aim of this study was to examine the associations of birthweight, gestational age and childhood BMI (assessed at a mean age of 5 years) with a self-report of a doctor diagnosis of diabetes in middle age.
Methods We studied a birth cohort of 5,793 individuals who were born between 1950 and 1956 in Aberdeen, Scotland, and who responded to a questionnaire administered in 2000.
Results Birthweight and gestational age were inversely associated with diabetes. These associations remained with additional adjustment for indicators of childhood and adult socioeconomic position, maternal complications of pregnancy, adult smoking, adult BMI and simultaneous adjustment for each other: the adjusted odds ratio per unit increase in birthweight z score was 0.73 (95% CI 0.60–0.88), the odds ratio per week increase in gestational age was 0.91 (95% CI 0.82–1.00) and odds ratio for preterm birth was 2.04 (94% CI 1.18–3.53). The positive association of childhood BMI with diabetes was attenuated on adjustment for adult BMI.
Conclusions/interpretation In this population, who were born in the 1950s, poor intrauterine growth and preterm birth are associated with an increased risk of diabetes.

Keywords Birthweight · BMI · Body Mass Index · Childhood · Diabetes · Epidemiology · Preterm

D. A. Lawlor (✉) · G. Davey Smith
Department of Social Medicine, University of Bristol,
Canynge Hall, Whiteladies Road,
Bristol BS8 2PR, UK
e-mail: d.a.lawlor@bristol.ac.uk

H. Clark
The Dugald Baird Centre for Research on Women's Health,
University of Aberdeen,
Aberdeen, UK

D. A. Leon
Department of Epidemiology and Population Health,
London School of Hygiene and Tropical Medicine,
London, UK

Introduction

Risk of diabetes may be determined by exposure to risk factors that exert their effects in the perinatal, infancy and childhood periods. Lower birthweight is associated with an increased risk of type 2 diabetes in studies conducted in populations born in the early part of the 20th century [1]. More recently, a study found that extreme preterm birth (≤32 weeks) was associated with insulin resistance in childhood (age 4–10 years) [2], but to our knowledge, no previous study has examined the association of gestational age with adult diabetes. Childhood BMI has been found to be positively associated with glucose intolerance in childhood [3, 4], but few studies have examined its association with later diabetes in adulthood.

The aim of this study was to examine the associations of birthweight, gestational age and childhood BMI (measured at a mean age of 5 years) with diabetes in a cohort of individuals from Aberdeen, Scotland, who were born between 1950 and 1956.

Subjects and methods

Data from the Aberdeen Children of the 1950s cohort study were used. Described in detail elsewhere [5, 6], the cohort consists of 12,150 individuals who were born in Aberdeen between 1950 and 1956. We excluded all multiple births (n=316). In 2000, a questionnaire was sent to all surviving participants who were still living anywhere in the UK. Responders were asked whether they had ever been diagnosed with diabetes and, if so, their age at diagnosis and current treatment. In the main analyses we only included individuals born as singletons and who responded to this questionnaire (n=5,803). Diabetes was defined on the basis of self-report in this questionnaire. Ten participants were excluded because they indicated that they had been diagnosed with diabetes prior to age 20 years; all of these participants were currently using insulin. Thus, we present analyses on 5,793 participants, amongst whom there were 113 (2%) with a self-report of a doctor diagnosis of diabetes occurring after age 20 years. In sensitivity analyses using the whole cohort and basing the outcome on hospital admissions data the results were essentially the same.

Data on birthweight, gestational age, father's occupational social class, gravidity, pregnancy-induced hypertension, antepartum haemorrhage, maternal age at birth and maternal height were abstracted from the Aberdeen Maternal and Neonatal Database, which collects these data prospectively using research standard protocols [5]. Height and weight at school entry were measured during routine school entry medical exams. The mean (SD) age of the children at the time of their school medical exam (when their height and weight were assessed) was 4.9 (0.7) years. In the follow-up questionnaire, participants were asked to record their weight and height. Adult occupational social class, educational attainment and smoking history were also obtained from the questionnaire [7].

Multivariable logistic regression was used to assess associations. There was no evidence that any associations differed between female and male subjects (all p values for interactions with sex were >0.6), and therefore all results are presented for both sexes combined.

Study ethics

The Scottish Multicentre Research Ethics Committee and local research ethics committees plus the Scottish Privacy Advisory Committee approved the revitalisation of the Children of the 1950s cohort. All record linkage was undertaken by the Information and Statistics Division (ISD) of the Scottish Office, who provided us with an anonymised dataset for analysis.

Results

Birthweight showed a small positive correlation with BMI in childhood (Pearson's correlation coefficient [r]=0.14, p<0.001), but was not correlated with adult BMI (r=0.02, p=0.11). There was a positive correlation between childhood and adult BMI (r=0.21, p<0.001). Adult BMI was associated with diabetes, with an odds ratio per 5 kg/m^2

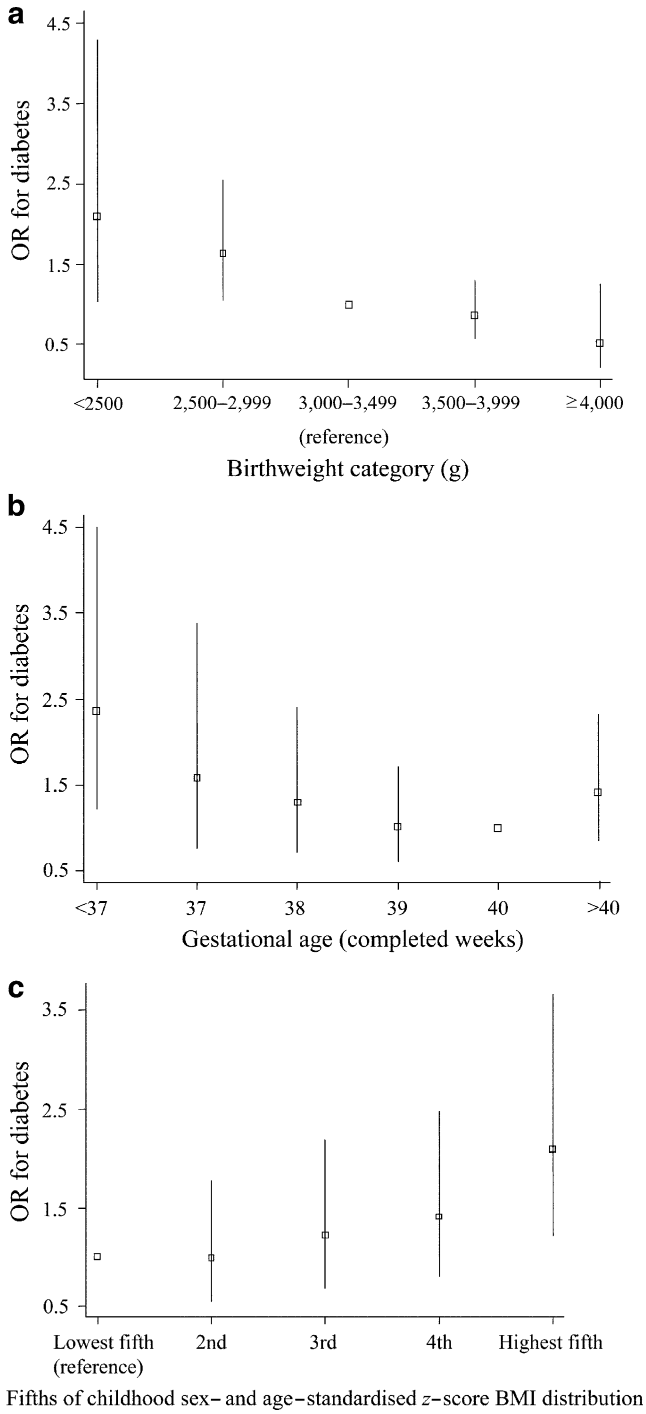

Fig. 1 Sex-adjusted and year of birth-adjusted associations (OR with 95% CIs) of birthweight (**a**), gestational age (**b**) and childhood BMI z score (**c**) with adult type 2 diabetes risk among a cohort of 5,793 subjects (113 diabetes cases). **a** p value for linear trend <0.001; **b** p value for linear trend=0.04, p quadratic=0.3; **c** p value for linear trend=0.002

adjusted for sex, year of birth and use of weight scales of 1.65 (95% CI 1.43–1.90). This association was unaltered by adjustment for indicators of early life socioeconomic position, birthweight, gestational age, childhood BMI, adult social class and adult smoking.

Birthweight and childhood BMI were linearly associated with diabetes, and there was weak evidence of a linear association between gestational age and diabetes (Fig. 1). The associations of lower birthweight, earlier gestational age and being born preterm with diabetes remained with adjustment for any covariates (Table 1). The association between childhood BMI and diabetes was attenuated towards the null with adjustment for adult BMI. When all three of birthweight, being born preterm and childhood BMI were included simultaneously in a model, the inverse association between birthweight and positive association of preterm birth with diabetes remained.

Discussion

We have shown that lower birthweight and being born preterm are associated with an increased risk of diabetes in a cohort born in the 1950s. The positive association of childhood BMI with diabetes appears to be mediated via the positive association of childhood BMI with adult BMI in this cohort.

The main limitation of this study is the use of self-report of a clinical diagnosis of diabetes rather than an assessment based on fasting blood measurements. Since type 2 diabetes is asymptomatic and obesity is a major risk factor, it is possible that the strong association between adult BMI and diabetes is exaggerated as a result of the tendency for a doctor to preferentially screen for diabetes in adults who are overweight. If this is the case, the association of childhood BMI with diabetes may have been underestimated when adjusted for adult BMI. The age at ascertainment of diabetes in this study was 46–50 years, and several individuals who will go on to develop diabetes will be too young for this to have occurred yet. Thus, our results refer to individuals with diabetes diagnosed in early middle-age. The agreement between self-report and medical record diagnoses of diabetes is good [8], and our analyses using inpatient hospital discharge records were very similar to those for the main analyses using self-report. Self-report of adult weight and height may be biased, but the association between adult BMI and diabetes in this study, consistent with other studies using measured BMI, suggests that there is no major bias. Loss to follow-up, though consistent with other birth cohorts (63% response to the questionnaire in adulthood), may have resulted in selection bias [9]. However, there was no difference in hospital admission rates for diabetes between questionnaire responders and

Table 1 Multivariable associations of birthweight, preterm birth and childhood BMI with adult diabetes in 5,793 participants (113 cases of diabetes)

	Adjusted odds ratio (95% CI)					
	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
Birthweight (per kg)	0.50 (0.36–0.71)	0.51 (0.36–0.72)	0.50 (0.35–0.72)	0.53 (0.37–0.75)	0.49 (0.34–0.71)	–
Birthweight (per gestational age and sex-standardised *z* score)	0.74 (0.61–0.89)	0.74 (0.61–0.90)	0.74 (0.61–0.90)	0.76 (0.63–0.93)	0.74 (0.61–0.90)	0.73 (0.60–0.88)
Gestational age (per week of completed gestation)	0.90 (0.82–0.99)	0.90 (0.82–0.99)	0.90 (0.82–0.99)	0.90 (0.82–0.99)	0.91 (0.82–1.00)	0.91 (0.82–1.00)
Born preterm vs not	2.14 (1.25–3.67)	2.10 (1.23–3.61)	2.10 (1.23–3.61)	2.11 (1.23–3.62)	2.02 (1.17–3.50)	2.04 (1.18–3.53)
BMI at primary school entry (per age- and sex-standardised *z* score)	1.22 (1.10–1.36)	1.22 (1.10–1.36)	1.22 (1.10–1.36)	1.23 (1.10–1.37)	1.07 (0.96–1.19)	1.07 (0.95–1.19)

Model 1: Adjusted for sex and year of birth
Model 2: As model 1 plus indicators of childhood socioeconomic position that might confound the associations: father's occupational social class at birth, mother's gravidity, mother's height and mother's age at birth
Model 3: As model 2 plus complications of pregnancy that might confound the associations: gestational hypertension and antepartum haemorrhage
Model 4: As model 3 plus adult indicators of socioeconomic position and smoking that might confound the associations by reflecting parental socioeconomic position: adult occupational social class, educational attainment and adult smoking
Model 5: As model 4 plus adult BMI, which might mediate the associations
Model 6: As model 5 but with simultaneous adjustment for birthweight *z* score, gestational age/preterm birth and childhood BMI, to assess their independent associations

non-responders, and associations were essentially the same when based on Scottish hospital admissions data. We had no information on maternal gestational diabetes or family history of diabetes and were therefore unable to assess the effect of these on any associations that we observed. Gestational diabetes results in greater birthweight, and would therefore not explain the association of lower birthweight with future diabetes. Adjustment for other complications of pregnancy did not result in attenuation.

The magnitude of the association that we have found between birthweight and diabetes is similar to that found in earlier studies of individuals born in the earlier decades of the 20th century [1]. The stability of the association in cohorts born across the first half of the 20th century suggests that the underlying mechanism is not strongly influenced by the profound improvements in infant and maternal health that have occurred over this period. For example, between 1901 and 1905, infant mortality was 130 per 1,000 in Scotland, whereas between 1941 and 1945 it had decreased to 80 per 1,000, and a marked decline over the subsequent decade led to a rate of 37 per 1,000 between 1951 and 1955 [10], the period during which participants in the current study were born.

One recent small study found that being born extremely preterm (≤32 weeks gestation) was associated with insulin resistance in childhood and that this association was independent of birthweight [2]. Our findings of an association between being born before 37 weeks and adult diabetes, to some extent, confirms this earlier finding. If the findings of this earlier study [2] and those of our study are replicated in other datasets, the increasing number of infants who are born preterm and survive into adulthood may represent an important population-attributable risk for diabetes. There was a tendency in our study for an increased risk of diabetes across the distribution of gestational age, which would suggest that interventions to increase gestational age towards term in all pregnancies might be important in the prevention of diabetes.

We found that childhood BMI, assessed, on average, at 5 years, was positively associated with diabetes, but this appeared to be largely mediated through the association of childhood BMI with adult BMI. The mean BMIs for both boys and girls in our cohort are similar to contemporary figures for European and US children, but only a small proportion were obese at age 5. Thus, it is possible that being obese in childhood may have an independent (of adult BMI) effect on future diabetes risk that we are unable to detect in this cohort. The emergence of type 2 diabetes in obese children [3, 4] is a clear indicator that one cannot be complacent about the risk associated with obesity in childhood.

In conclusion, we have found that lower birthweight and preterm birth are associated with an increased risk of diabetes in a cohort of individuals born in the 1950s. These findings highlight the importance of early life interventions to prevent diabetes.

Acknowledgements We are very grateful to R. Illsley for providing us with the data from the Aberdeen Child Development Survey and for his advice about the study. G. Ford played a crucial role in identifying individual cohort members and in helping us to initiate the process of revitalisation. S. Macintyre, D. Campbell, G. D. Smith, M. Hall, B. De Stavola, S. Morton, D. Batty, D. Godden, D. Kuh, G. Lewis and V. Östberg collaborated with the authors to revitalise the cohort. M. Beveridge assisted H. Clark in managing the revitalisation. We would also like to thank staff at the ISD (Edinburgh), GRO (Scotland) and NHSCR (Southport) for their substantial contributions, and J. Lemon, who undertook the linkage to the Aberdeen Maternity and Neonatal Databank. The Aberdeen Children of the 1950s Study was funded as a component project (G0828205) of a Medical Research Council Co-operative Group named 'Life-course and trans-generational influences on disease risk' (G9819083). A project on cognition and adult health in the cohort was funded by the Chief Scientist Office of the Scottish Executive Health Department. D. A. Lawlor is funded by a UK Department of Health Career Scientist Award. The views expressed in this paper are those of the authors and not necessarily of any funding body.

Duality of interest There is no duality of interest.

References

1. Forouhi N, Hall E, McKeigue P (2004) A life course approach to diabetes. In: Kuh D, Ben-Shlomo Y (eds) A life course approach to chronic disease epidemiology. Second edn. Oxford University Press, Oxford, pp 165–188
2. Hofman PL, Regan F, Jackson WE et al (2004) Premature birth and later insulin resistance. N Engl J Med 351:2179–2186
3. Fagot-Campagna A, Pettitt DJ, Engelgau MM et al (2000) Type 2 diabetes among North American children and adolescents: an epidemiologic review and a public health perspective. J Pediatr 136:664–672
4. Ehtisham S, Barrett TG, Shaw NJ (2000) Type 2 diabetes mellitus in UK children—an emerging problem. Diabet Med 17:867–871
5. Batty GD, Morton SMB, Campbell D et al (2004) The Aberdeen Children of the 1950s cohort study: background, methods, and follow-up information on a new resource for the study of life-course and intergenerational effects on health. Paediatr Perinat Epidemiol 18:221–239
6. Leon DA, Lawlor DA, Clark H, Macintyre S (2006) Cohort profile: the Aberdeen Children of the 1950s study. Int J Epidemiol 35:549–552
7. Lawlor DA, Batty GD, Morton SMB, Clark H, Macintyre S, Leon DA (2005) Childhood socioeconomic position, educational attainment and adult cardiovascular risk factors: findings from the Aberdeen children of the 1950s cohort study. Am J Public Health 95:1245–1251
8. Haapanen N, Miilunpalo S, Pasanen M, Oja P, Vuori I (1997) Agreement between questionnaire data and medical records of chronic diseases in middle-aged and elderly Finnish men and women. Am J Epidemiol 145:762–769
9. Nishiwaki Y, Clark H, Morton SM, Leon DA (2005) Early life factors, childhood cognition and postal questionnaire response rate in middle age: the Aberdeen Children of the 1950s study. BMC Med Res Methodol 5:16
10. Charlton J (1997) Trends in all cause mortality: 1841–1994. In: Charlton J, Murphy M (eds) The health of adult Britain: 1841–1994. The Stationery Office, London, pp 17–29