ORIGINAL ARTICLE

Does intrauterine growth restriction affect quality of life in adulthood?

Dale Spence, Fiona A Alderdice, Moira C Stewart, Henry L Halliday, Angela H Bell

Arch Dis Child 2007;**92**:700–703. doi: 10.1136/adc.2006.102947

See end of article for authors' affiliations

Correspondence to: Dr Dale Spence, Nursing and Midwifery Research Unit, Queen's University Belfast, 10 Malone Road, Belfast BT9 5BN, UK; d.spence@qub.ac.uk

Accepted 19 March 2007
Published Online First 5 April 2007

Objective: To compare health-related quality of life in 50-year-old adults who were born at term (⩾37 to 42 weeks' gestation) with intrauterine growth restriction (IUGR; birth weight <10th centile) and a group born at term without IUGR (⩾10th centile).
Design: Case control study.
Setting: A large regional maternity hospital in Northern Ireland.
Subjects: 235 adults who were born between 1954 and 1956 in the Royal Maternity Hospital, Belfast. 111 subjects born with IUGR and 124 controls with normal birth weight for gestation were compared.
Main outcome measure: Health-related quality of life in adulthood was assessed using the Short Form-36 Health Survey (SF-36).
Results: The two groups reported similar health-related quality of life on each of the eight dimensions of the SF-36 and there were no significant differences between them. Adjusting for potential confounding variables did not alter this conclusion.
Conclusions: The similarity of SF-36 scores indicated that those born with IUGR did not perceive this to adversely influence health-related quality of life at 50 years of age compared with those with normal birth weight.

Intrauterine growth restriction (IUGR) has been defined as a "concept signifying a fetus has not achieved its optimal growth".[1] Previous research has concentrated on groups defined by weight at birth with generally short- or medium-term outcomes. Our study took account of weight for gestational age and considered very long-term outcomes for term infants with IUGR. For the purpose of this study, babies with IUGR are defined as those born at term with birth weight <10th centile.[2]

It is widely accepted that risks of various chronic diseases in adulthood may have their origins before birth.[3] The Barker hypothesis links size at birth with risk of disease in adulthood. However, it was the effect of low birth weight rather than IUGR that formed the basis of Barker's original studies[4] as the gestational ages of babies in his early cohorts were unknown. Further studies have subsequently confirmed that birth weight is inversely correlated with blood pressure in later life,[5] coronary heart disease,[6 7] non-insulin dependent diabetes[8 9] and stroke.[6 10] Psychological and social effects of low birth weight have been shown in studies from the National Birth Cohorts, raising the likelihood of a complex interplay of biological and social processes across the life course. Recent research into early life risk factors for obesity in childhood found a significant association with catch-up growth between birth and 2 years.[11] Slower postnatal weight gain may actually have a long-term beneficial effect and reduce the risk of obesity and cardiovascular disease in adulthood.[12]

Health-related quality of life is now considered an important outcome measure for healthcare interventions in adults.[13] There is increasing focus in health services research on the effect of health state changes on quality of life for the individual. Quality of life in early adulthood (19–22 years) has not been found to be affected by being born preterm or with very low birth weight.[14] Many of the follow-up studies to date have focussed on low birth weight, preterm rather than term, growth-restricted infants, as information on gestational age is not always available or reliable.

There are major gaps in the knowledge of long-term effects of IUGR. In this study, our aim was to determine whether health problems reported in adult life, in particular health-related quality of life at age 50 years, are associated with IUGR at birth.

METHODS

Identifying babies weighing <10th centile

The UK 1990 Growth Reference Charts were used to establish birth centile.[15]

Study population

The cohort consisted of babies who were born in the Royal Maternity Hospital, Belfast between 1954 and 1956 and who were traced and assessed in adulthood at the age of about 50 years. Information on each birth between 1954 and 1956 (n = 6366) was manually abstracted and entered on a database. Gestational age was calculated based on the first day of the last menstrual period (LMP)[16–18] and birth weight recorded in pounds and ounces was converted to grams.

Inclusion/exclusion criteria

Inclusion criteria were live, term (⩾37 to 42 weeks' gestation), singleton births. The study group consisted of growth-restricted babies (birth weight <10th centile) born at term. The control group was term, normal birth weight babies (⩾10th centile). Exclusion criteria were multiple pregnancies, babies born with major congenital abnormalities and surviving adults deemed inappropriate for the study by their general practitioner (GP).

Sample size calculation

The pre-study sample size calculation estimated that a minimum of 172 participants per arm (total 344) needed to be recruited to ensure that a true mean difference of 7% in any

Abbreviations: GP, general practitioner; IUGR, intrauterine growth restriction; LMP, last menstrual period; SDS, standard deviation score; SF-36, Short Form-36 Health Survey

dimension of the Short Form-36 Health Survey (SF-36) would be detected with 90% power. We assumed an overall drop-out rate of 40%, indicating that 280 participants per arm (total 560) needed to be approached.

Sample selection

The study and control groups were selected from 4667 births that met the inclusion criteria. Software from the Child Growth Foundation was used to adjust birth weight for gestation and gender and to convert these measures to standard deviation scores (SDS). SPSS (version 11) was used to identify the study group (n = 491). A random selection of the non-study group based on a one-to-one ratio formed the control group. Losses to follow-up, dropouts and non-participation were recorded at the various stages to enable the researcher (DS) to examine potential sample bias (table 1).

Tracing the sample selected

Maternal and birth details were forwarded to the Central Services Agency in Northern Ireland for tracing and matching with GPs if possible (n = 591). GPs made the initial contact with patients, after which a pack was posted to potential participants (n = 515), inviting them to take part in the study. If willing to participate, a consent form was returned to the researcher (n = 246) with a contact telephone number to arrange for a gender-specific questionnaire to be posted to the participant's home.

Measures

The primary outcome health-related quality of life was measured using the SF-36. This measures eight multi-item dimensions, including physical functioning, role limitation due to physical problems, role limitation due to emotional problems, social functioning, mental health, energy/vitality, pain and general health perception. In addition, the questionnaire was designed to obtain data related to family background, general health, use of health services, lifestyle and socio-economic factors, including social class[19] and Townsend deprivation index.[20]

Table 1 Recruitment to study

	Total	Cases	Controls
Central Services Agency (n = 982)			
Sample selected	982	491	491
Resident outside Northern Ireland	16	9	7
Deceased	14	7	7
Not traced	361	193	168
GP details	591	297	294
General practitioners (n = 591)			
Telephone reminders	145	82	63
Patient deceased	4	3	1
No record of patient	59	28	31
Inappropriate to contact patient	5	2	3
GP unhappy to assist	8	5	3
Patient address	515	249	266
Potential participants (n = 515)			
Reminders	260	121	139
Wrong trace	12	7	5
Wrong address	9	2	7
Resident outside Northern Ireland	4	3	1
Learning difficulties	3	3	0
Refusals	58	36	22
No response	183	88	95
Consent	246	117	129
Participants with consent (n = 246)			
Consent returned after study completed	3	2	1
Did not take part in study	8	6	2
Questionnaire and examination	232	108	124
Questionnaire only	3	3	0
Total study participants	235	111	124

Analysis

For each dimension item scores were coded, summed and transformed onto a scale from 0 (worst possible health state) to 100 (best possible health state). Mean scores between groups were initially compared using *t* tests. Multiple linear regression analysis was then undertaken to adjust for potential confounding variables.

RESULTS

Recruitment and response

Table 1 provides an overview of the recruitment and response of study participants. The overall groups (each n = 491) were similar in terms of available birth characteristics, including gender, gestational age, mode of delivery, maternal age and parity. Mean birth weight reflected the desired <10th or ⩾10th centile difference between groups. Actual study participants were also similar in terms of birth characteristics and, in addition, social class at time of study. The only significant difference was that the study group were more likely to have been born following a normal delivery than the comparison group ($\chi^2 = 10.24$, df = 3, p = 0.02) (table 2). At the time of the study, sociodemographic and lifestyle characteristics, such as education, employment, social class, marital status, and dietary, smoking and alcohol intake, did not differ significantly between groups.

Health-related quality of life

Both groups reported similar health-related quality of life on each dimension of the SF-36 and there were no significant differences between them. Adjusting for potential confounding variables did not alter this conclusion (table 3).

DISCUSSION

Most follow-up studies of those born preterm or with very low birth weight examine quality of life in childhood or adolescence, with only a few extending to early adulthood. Less is

Table 2 Birth characteristics of study participants

	IUGR group (n = 111)	Control group (n = 124)
Gender		
Male	46 (41)	52 (42)
Female	65 (59)	72 (58)
Mean gestational age in weeks (SD)	40.0 (1.4)	40.0 (1.5)
Mean birth weight in grams (SD)	2613 (347)	3460 (491)
Maternal parity		
0	78 (70)	77 (62)
1	13 (12)	25 (20)
2	11 (10)	7 (6)
⩾3	9 (8)	15 (12)
Mode of delivery*		
Normal	83 (75)	86 (69)
Forceps	22 (20)	18 (15)
Breech	0 (0)	9 (7)
Caesarean	6 (5)	11 (9)
Mean maternal age in years (SD)	27.7 (5.4)	27.7 (5.1)
Social class group		
1	0 (0)	3 (2)
2	14 (13)	21 (17)
3	19 (17)	18 (15)
3M	48 (43)	50 (40)
4	16 (14)	14 (11)
5	11 (10)	15 (12)
Missing	3 (3)	3 (2)

Values are number with percentage in parenthesis unless stated otherwise.
*$\chi^2 = 10.2$, df = 3, p = 0.02.

Table 3 Short Form 36 Health Survey (SF-36) sub-dimensions before and after adjustment for confounding variables

SF-36	IUGR group, n = 111, mean (SD)	Control group, n = 124, mean (SD)	Mean difference, unadjusted (95% CI)	p Value	Mean difference, adjusted* (95% CI)	p Value
Physical function	86.3 (21.5)	82.9 (23.7)	3.4 (−2.5 to 9.2)	0.26	4.4 (−1.3 to 10.1)	0.13
Role limitation due to physical problems	83.3 (32.7)	80.6 (35.9)	2.7 (−6.2 to 11.6)	0.55	4.8 (−3.8 to 13.3)	0.27
Role limitation due to emotional problems	79.9 (34.9)	81.7 (35.1)	−1.8 (−10.9 to 7.2)	0.69	0.2 (−8.3 to 8.7)	0.96
Social functioning	85.8 (22.9)	86.0 (23.8)	−0.2 (−6.3 to 5.8)	0.94	1.1 (−4.7 to 6.8)	0.71
Mental health	72.3 (19.3)	73.4 (19.7)	−1.1 (−6.1 to 3.9)	0.67	0.4 (−4.4 to 5.1)	0.88
Energy/vitality	61.1 (21.7)	61.0 (21.1)	0.1 (−5.4 to 5.6)	0.98	1.5 (−3.8 to 6.8)	0.58
Pain	76.9 (25.6)	76.8 (24.1)	0.1 (−6.3 to 6.5)	0.98	1.3 (−4.9 to 7.6)	0.68
General health perception	70.1 (21.6)	71.0 (20.1)	−0.9 (−6.3 to 4.4)	0.74	0.3 (−5.0 to 5.6)	0.90

*Adjusted for gender, social class at birth, marital status, education, Townsend deprivation index and age at time of study.

known about health-related quality of life in later adult life and there is little information on those born with IUGR. Health-related quality of life is regarded as an increasingly important outcome measure for healthcare interventions, and health status measures are significant determinants of health care utilisation.[13] The SF-36 is used worldwide to assess quality of life and general health, and covers a wide range of areas that may be adversely affected by illness. It has undergone validity testing in the UK, including assessment of its content, criterion and construct validity.[21] In our study, the scores on each domain of the SF-36 were similar to published UK age-related norms for males and females aged 45–54 years.[22] Comparable findings have been reported in a study using the SF-36 to assess quality of life in 19–22 year olds who had been born very preterm.[14]

Our study indicates that adults who were born with IUGR do not perceive themselves to have worse health-related quality of life than their normally grown peers. It could be argued that participants in this study have survived the short-term effects of IUGR and although they see themselves as being healthy, this needs to be assessed by formal physical examination. The impact of being born with IUGR should not be underestimated in terms of later health and wellbeing.

Strengths and weaknesses of the study

Our study used good quality historical records allowing us to assess the effect of low birth weight in relation to gestational age at term on outcomes in adulthood. This was the first study which examined health-related quality of life in adults aged 50 years who had been born with IUGR. We acknowledge that estimates of gestational age were inevitably made without the benefits of modern ultrasound as this cohort was born in the 1950s. On the other hand, the absence of such technological support places more reliance on clinical information such as accurate recording of LMP and estimated date of delivery.

As with any long-term retrospective study, problems were encountered in tracing the sample. Adults in our study had had no previous interim assessments in a research context and therefore the invitation to participate could not have been expected. The overall response rate is comparable to that in a study by Barker *et al*,[23] which also involved follow-up 50 years after birth and recorded similar measures.

The sample size calculation for our study was based on the primary outcome, quality of life. More subjects than anticipated were lost at the initial stage of tracing before identification of potential participants, and this should be considered when planning similar studies. This loss was higher than anticipated as there had been a 75% success rate when tracing was undertaken as part of preliminary work related to our study. Despite this, a total of 235 out of the required 344 participants (68% of the estimated sample size) were included in the study. In a post-study power assessment this was sufficient to give 85% power to detect a difference of 8% in any SF-36 dimension as statistically significant.

Mortality is an important aspect of ill health. We were unable to assess this formally as 361 of the 982 potential participants could not be traced by the Central Services Agency. However, of those traced, mortality rate was evenly distributed between the two groups studied, making an overall difference between all potential participants less likely.

The SF-36 is a generic measurement of health status and its use allowed wider comparison with other studies. Further research investigating a more holistic subjective view of patients' health-related quality of life would make an important contribution to this area of study.

What is already known on this topic

- There is an inverse relationship between birth weight and the prevalence of chronic diseases in adulthood as proposed in the Barker hypothesis.
- IUGR increases mortality and morbidity in the neonatal period, but there is limited information on its effect on health-related quality of life in adulthood.

What this study adds

- This study took account of gestational age and birth weight.
- There were no differences in health-related quality of life as assessed by SF-36 scores in 50-year-old adults who had been born at term with IUGR compared with normal birth weight controls.

ACKNOWLEDGEMENTS

We acknowledge the statistical support of Dr Christopher C Patterson, Queen's University Belfast and methodological advice from Professor George Davey Smith, University of Bristol. We especially thank all those who participated in the study.

Authors' affiliations

Dale Spence, Fiona A Alderdice, Nursing and Midwifery Research Unit, Queen's University Belfast, Belfast, Northern Ireland, UK
Moira C Stewart, Department of Child Health, Queen's University Belfast, Belfast, Northern Ireland, UK
Henry L Halliday, School of Medicine and Dentistry, Queen's University Belfast, Belfast, Northern Ireland, UK

Angela H Bell, Health Promotion Agency, CEMACH Office, Belfast, Northern Ireland, UK

Funding: The Research and Development Office for Health and Personal Social Services in Northern Ireland provided funding for this study.

Competing interests: None.

Ethical approval: Queen's University of Belfast Research Ethics Committee approved this study (reference number 56/00).

REFERENCES

1 **Kingdom J**, Baker P. *Intrauterine growth restriction. Aetiology and management*. London: Springer, 2000.
2 **Bakketeig LS**. Current growth standards, definitions, diagnosis and classification of fetal growth retardation. *Eur J Clin Nutr* 1998;**52**(Suppl 1):P94.
3 **Harding JE**. The nutritional basis of the fetal origins of adult disease. *Int J Epidemiol* 2001;**30**:15–23.
4 **Whittle MJ**. The management of intrauterine growth restriction. In: Rodeck CH, Whittle MJ, eds. *Fetal medicine: basic science and clinical practice*. London: Churchill Livingstone, 1999:773–84.
5 **Huxley RR**, Shiell AW, Law CM. The role of size at birth and postnatal catch-up growth in determining systolic blood pressure: a systematic review of the literature. *J Hypertens* 2000;**18**:815–31.
6 **Rich-Edwards JW**, Stampfer MJ, Manson JE, *et al*. Birthweight and risk of cardiovascular disease in a cohort of women followed up since 1976. *BMJ* 1997;**315**:396–400.
7 **Leon DA**, Lithell HO, Vâgerö D, *et al*. Reduced fetal growth rate and increased risk of death from ischaemic heart disease: cohort study of 15000 Swedish men and women born 1915–1929. *BMJ* 1998;**317**:241–5.
8 **McKeigue PM**, Lithell HO, Leon DA. Glucose tolerance and resistance to insulin-stimulated glucose uptake in men aged 70 years in relation to size at birth. *Diabetologia* 1998;**41**:1133–8.
9 **Rich-Edwards JW**, Colditz GA, Stampfer MJ, *et al*. Birthweight and the risk for type 2 diabetes mellitus in adult women. *Ann Intern Med* 1999;**130**:278–84.
10 **Eriksson JG**, Forsén TJ, Toumilehto J, *et al*. Early growth, adult income and risk of stroke. *Stroke* 2000;**31**:869–70.
11 **Reilly JJ**, Armstrong J, Dorosty AR, *et al*. Early life risk factors for obesity in childhood: cohort study. *BMJ* 2005;**330**:1357–63.
12 **Singhal A**, Lucas A. Early origins of cardiovascular disease: is there a unifying hypothesis? *Lancet* 2004;**363**:1642–5.
13 **Hofman A**, Jaddoe VWV, MacKenbach JP, *et al*. Growth, development and health from early fetal life until young adulthood: the Generation R Study. *Paediatr Perinat Epidemiol* 2004;**18**:61–72.
14 **Cooke RWI**. Health lifestyle and quality of life for young adults born very preterm. *Arch Dis Child* 2004;**89**:201–6.
15 **Wright CM**, Booth IW, Buckler JMH, *et al*. Growth reference charts for use in the United Kingdom. *Arch Dis Child* 2002;**86**:11–14.
16 **Hyppönen E**, Power C, Davey Smith G. Prenatal growth, BMI, and risk of type 2 diabetes by early mid-life. *Diabetes Care* 2003;**26**:2515–17.
17 **Strauss RS**. Adult functional outcome of those born small for gestational age. Twenty-six year follow-up of the 1970 British birth cohort. *JAMA* 2000;**283**:625–32.
18 **Kiserud T**, Maršál K. Ultrasound assessment. In: Kingdom J, Baker P, eds. *Intrauterine growth restriction:a practical approach*. London: Year Book Medical Publishers, 2000:205–38.
19 **Danesh J**, Gault S, Appleby P, *et al*. Postcodes as useful markers of social class: population based study in 26,000 British households. *BMJ* 1999;**318**:843–5.
20 **Townsend P**, Phillimore P, Beattie A. *Health and deprivation: inequality in the North*. Beckenham: Croom Helm, 1988.
21 **Jenkinson C**, Coulter A, Wright L. Short form 36 (SF36) health survey questionnaire: normative date for adults of working age. *BMJ* 1993;**306**:1437–40.
22 **Ware JE**, Snow KK, Kosinski M, *et al*. *SF-36 Health Survey: manual and interpretation guide*. Boston, MA: The Health Institute, New England Medical Center, 1993.
23 **Barker DJP**, Bull AR, Osmond C, *et al*. Fetal and placental size and risk of hypertension in adult life. *BMJ* 1990;**301**:259–62.