Case-control study of intrapartum care, cerebral palsy, and perinatal death

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Abstract

Objective—To investigate the relation between suboptimal intrapartum obstetric care and cerebral palsy or death.

Design—Case-control study.

Setting—Oxford Regional Health Authority.

Subjects—141 babies who subsequently developed cerebral palsy and 62 who died intrapartum or neonatally, 1984-7. All subjects were born at term of singleton pregnancies and had no congenital anomaly. Two controls, matched for place and time of birth, were selected for each index case.

Main outcome measures—Adverse antenatal factors and suboptimal intrapartum care (by using predefined criteria).

Results—Failure to respond to signs of severe fetal distress was more common in cases of cerebral palsy (odds ratio 4.5; 95% confidence interval 2.4 to 8.4) and in cases of death (26.1; 6.2 to 109.7) than among controls. This association persisted even after adjustment for increased incidence of a complicated obstetric history in cases of cerebral palsy. Neonatal encephalopathy is regarded as the best clinical indicator of birth asphyxia; only two thirds (23/33) of the children with cerebral palsy in whom there had been a suboptimal response to fetal distress, however, had evidence of neonatal encephalopathy; these 23 formed 6.8% of all children with cerebral palsy born to residents of the region in the four years studied.

Conclusion—There is an association between quality of intrapartum care and death. The findings also suggest an association between suboptimal care and cerebral palsy, but this seems to have a role in only a small proportion of all cases of cerebral palsy. The contribution of adverse antenatal factors in the origin of cerebral palsy needs further study.

Introduction

The relation between the quality of care which is given to a mother during labour and delivery and the death of her baby or cerebral palsy in her surviving child is a continuing source of debate involving obstetricians, paediatricians, parents, and lawyers.

Evidence from epidemiological studies has suggested that only a small proportion (3-13%) of all children with cerebral palsy have had signs of intrapartum stress.^{1,2} It is unclear what proportion of these could have been prevented by a different management.

In 1984 Niswander *et al* published a case-control study in which they were unable to show an association between intrapartum care that was predefined as suboptimal and cerebral palsy.⁴ Only 34 children with cerebral palsy were included in this study, however, some of whom were born preterm and who probably had cerebral palsy because of cerebral haemorrhage and ischaemia occurring postnatally. If, as suggested,

less than 13% of all children with cerebral palsy have signs of intrapartum stress,³ and only some of these are avoidable by different care, this study probably lacked the precision to detect this small group of children.

We have replicated the case-control study, excluding from our cases of cerebral palsy children who were born preterm or of a multiple pregnancy and those with a known congenital anomaly. In this way we anticipated that the cases of cerebral palsy remaining would include those most likely to be associated with suboptimal intrapartum care—that is, obstetrically preventable.

By using this case series we tested the null hypothesis that compared with controls, cases of cerebral palsy among singleton babies born at term without congenital anomaly are not more likely to have been preceded by intrapartum care defined by preset criteria and considered by clinical consensus to be suboptimal.

Deaths occurring during labour or after birth among singleton babies who are born after 37 weeks of gestation and who have no major congenital anomaly or evidence of severe infection are widely considered to be those which are most likely to be obstetrically preventable. In the study of Niswander *et al* there was indeed an association between fetal death and suboptimal care.⁴ By using the same case-control design we planned to test a second hypothesis that compared with controls, intrapartum or neonatal deaths among singleton babies born at term without congenital anomaly are more likely to have been preceded by intrapartum care defined by preset criteria and considered by clinical consensus to be suboptimal.

It is now widely accepted that many cases of cerebral palsy are likely to have an antenatal origin. This is supported by the observation that antenatal risk factors such as poor fetal growth and pre-eclampsia occur more commonly among mothers of babies with cerebral palsy than in a control population.^{3,6} Further, it is possible that signs of fetal distress in babies who later manifest cerebral palsy may reflect previous antenatal factors rather than an acute intrapartum hypoxic event.⁷ Antenatal risk factors and evidence of intrapartum distress are therefore important potential confounding variables—that is, they can be associated both with the risk of suboptimal care (more complex clinical decisions would be needed in the cases than in the controls) and with the outcome of cerebral palsy or death (the antenatal factors themselves have a causal role in cerebral palsy or death). Hence, any observed association of suboptimal care and death or cerebral palsy would need to take antenatal risk factors into account.

Subjects and methods

CASE SELECTION

Cerebral palsy—Children with cerebral palsy born in 1984-7 who were singleton deliveries, born at 37

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weeks' gestation or more, and who had no congenital anomaly or postnatal cause were identified from the Oxford region register of early childhood impairments.⁸ The definition of cerebral palsy used by the register is that of a permanent impairment of voluntary movement or posture presumed to be due to permanent damage to the immature brain.

Gestational age for all groups was estimated by using a combination of accurate menstrual dates and an ultrasound scan performed before 20 weeks' gestation. If the menstrual date was inaccurate or there was a discrepancy of more than 14 days between menstrual date and the scan estimate of gestation, the date from the scan was used. The register includes children of mothers who were resident within the Oxford health region at the time of delivery. Multiple sources of ascertainment are used to compile the register, and the condition of the children is determined at the age of 3 and 5 years.

Deaths—Intrapartum stillbirths and deaths occurring after birth among babies born at 37 weeks' gestation and with no major congenital anomaly and with no evidence of severe infection were identified from copies of death certificates (previously obtained by the Oxford region register of early childhood impairment) and from the records of each maternity unit.

SELECTION OF CONTROLS

Two controls for each case were selected by identifying in each hospital delivery book the two babies born immediately before the index case. Only singleton babies born at 37 weeks' gestation or after and with no major congenital anomaly were included. Controls were drawn from all 10 of the hospitals in the region that provide obstetric care.

PREDEFINED CRITERIA FOR CARE

Before the study the criteria for care based on those used in the study done by Niswander *et al*⁴ were reviewed by every obstetrician in the region. Agreement could not be reached on which items should be included in the assessment of antenatal care, but after a lot of discussion a consensus was reached on the criteria for suboptimal intrapartum care (appendix 1). The criteria for suboptimal resuscitation after delivery were based on the recommendations of the Royal College of Obstetricians and Gynaecologists.⁹ At the request of some of the obstetricians a further category was added to which a mother could be assigned if the researchers considered that care was suboptimal in aspects not covered by the five predefined groups.

MONITORING OF FETAL HEART RATE

At the time of the study continuous electronic fetal monitoring was widely used in all 10 obstetric units in the region. Some of the mothers in the study who did not have continuous electronic fetal monitoring had cardiotocography performed on admission and again intermittently during labour; the remainder had intermittent auscultation. It was accepted practice that if there were signs of abnormalities in the fetal heart rate on intermittent auscultation, continuous electronic fetal monitoring was started.

The terms used to describe and classify the cardiotocogram were those used in the Dublin trial of continuous monitoring of fetal heart rate.¹⁰ A decision was made that there had been a suboptimal response to signs of intrapartum fetal distress when the criteria in appendix 1 were met. This was almost always based on evidence from continuous cardiotocography. If the observations recorded in the notes of mothers who had not been continuously monitored (or who had been monitored but the cardiotocogram was missing) clearly showed that the specified time limits for responding to

fetal distress had been exceeded, these mothers were also considered to have had suboptimal care.

ASSESSMENT OF HOSPITAL NOTES

The obstetric notes of mothers included in the study were obtained. All information about the outcome of the baby was masked by a researcher who did not participate in the review of the notes; and the notes were reviewed by a researcher blind to the neonatal condition and the child's outcome.

The following antenatal characteristics, considered to be possible confounding factors, were abstracted from the notes by a researcher with experience in obstetrics: previous poor obstetric outcome, existing maternal disease such as diabetes, renal disease, induced conception, raised maternal serum concentration of α fetoprotein, intrauterine growth retardation, pre-eclampsia, bleeding after 20 weeks' gestation, oligohydramnios, polyhydramnios, prolonged rupture of the membranes, and postmaturity (appendix 2). The obstetric history was considered to be complicated if one or more of these factors was present.

A systematic review of the events during labour and delivery including the original cardiotocographic recordings and the events immediately after birth was carried out. At the end of the review of each set of notes the researcher made an assessment of intrapartum care within the five predefined categories, designating care as optimal or suboptimal. Finally, aspects of care considered suboptimal that were not included in the five predefined categories were recorded.

A second observer (a consultant obstetrician), also blind to the outcome of the baby and using the same criteria, then made an independent assessment of the quality of intrapartum care. When there was disagreement between the two observers a third person was asked to act as arbiter. This was rarely necessary as the criteria were so precise.

Finally, information from the paediatric notes was abstracted, including the condition at delivery and evidence of neonatal encephalopathy.¹¹ We defined neonatal encephalopathy as depression at birth, based on an Apgar score at 1 minute of ≤ 6 , followed by evidence of neonatal neurological abnormality such as lethargy, coma, impaired respiration, and seizures or changes in tone, or both. Babies with transient jitteriness were excluded. Babies who seemed neurologically normal after birth and developed seizures after the first three days of life were not considered to have neonatal encephalopathy.

ETHICS APPROVAL

The approval of all eight district ethics committees in the Oxford health region was obtained before the start of the study.

STATISTICAL METHODS

Based on the study of Niswander *et al*,⁴ we assumed that suboptimal care would be present in between 3% and 13% of controls. One hundred and fifty cases of cerebral palsy and 80 cases of death with the selected characteristics were available for study. We predicted that the study would be large enough to detect a relative risk associated with suboptimal care of 2.3 for cases of cerebral palsy and an increased risk of 3.5 for cases of death with 80% power and at a significance of 5%.

Analysis entailed the comparison of the two case series, cerebral palsy and death, with their controls matched for hospital and time of birth. The relative odds for particular antenatal and intrapartum characteristics and the likelihood of the presence of these characteristics was estimated by using only matched sets, usually triads (a set of a case and two matched

controls). When one of the two intended controls was unavailable, either because the case notes were missing or when information regarding that particular characteristic was missing, a combination of matched pairs (a set of one case and one matched control) and matched triads was used. The relative odds were based only on discordant sets—that is, sets in which the presence or absence of the characteristics differed between cases and controls.^{12,13} The results of all comparisons are given as odds ratios (95% confidence intervals) estimated by matched analysis with maximum likelihood techniques implemented by conditional logistic regression. This was carried out by using the computer program EGRET.¹⁴

The odds ratio is an estimate of the odds of suboptimal care among cases relative to the odds of suboptimal care among controls; if the odds ratio is above one it implies that the cases had a higher chance of suboptimal care than the controls. The 95% confidence intervals give the range of values on each side of the odds ratio within which we can assume with 95% certainty that the true value lies.

Further analysis was performed to examine the confounding effect of having had a complicated antenatal history on the association of cerebral palsy and quality of care. Adjusted odds ratios for these were estimated by using conditional logistic regression.

Results

CASES OF CEREBRAL PALSY

There were 339 children with cerebral palsy on the regional register who were born in 1984-7 to mothers resident in the region. Of these, 123 (36%) were born before 37 weeks of gestation and 216 babies were born at term. Among these term infants 27 (8%) had cerebral palsy of postnatal origin, 40 (12%) had evidence of a congenital anomaly or of a prenatal origin, and two (0.6%) were multiple births, all of whom were excluded from the study. The 147 (43%)

remaining children were the cases of cerebral palsy for study.

CASES OF DEATHS

There were 1129 babies who were registered as stillbirths or who died in the first week of life among babies born in 1984-7 to mothers resident in the region.¹⁵ Of these, 63 (6%) were singleton babies delivered at or after 37 weeks of gestation who did not have a major congenital anomaly or evidence of severe infection and who died either during labour or delivery (17 (27%)) or after birth (46 (73%)).

CONTROLS

The total number of babies who we planned to include as controls was 420; 294 as matched controls for the cases of cerebral palsy and 126 as the matched controls for those who died.

CASES AND CONTROLS AVAILABLE FOR STUDY

One hundred and forty seven cases of cerebral palsy were thought to be suitable for inclusion in the study. Permission to include babies born within the eight district health authorities of the region had been obtained from the local ethics committees but not for babies born outside the region. We decided, therefore, that controls for the nine children with cerebral palsy born outside the region could not be selected. Thirty one records either could not be found or contained insufficient information to apply the criteria for care. We then excluded data on two children with cerebral palsy as we discovered that they had evidence of major congenital anomaly. The numbers remaining who were then available for study were 141 with cerebral palsy (257 controls) and 62 perinatal deaths (119 controls), a total of 573 participants (table I).

From these, 125 matched triads and an additional three matched pairs (a set of a case and one matched control) were available for the matched cerebral palsy analysis ($n=128$). Fifty nine matched triads and one additional matched pair were available for the matched analysis of deaths and controls ($n=60$). Hence, 381/441 (86%) of the intended cases of cerebral palsy and controls were used and 179/189 (95%) of deaths and controls were available for study.

ANTENATAL RISK FACTORS

All antenatal risk factors, except breech presentation, were more common in cases of cerebral palsy than controls. The increased incidence was significant at the 5% level, however, only for existing maternal illness (odds ratio 2.3; 95% confidence interval 1.1 to 5.0) and pre-eclampsia (2.0; 1.2 to 3.4; table II).

The incidence of antenatal complications was also higher among the cases of death, particularly severe pre-eclampsia (12.0; 1.5 to 99.7) and intrauterine growth retardation (3.3; 0.8 to 13.9), although the latter was not significant at the 5% level.

TABLE I—Numbers of participants in study of cerebral palsy and intrapartum/neonatal death and intrapartum care

No of subjects	Cerebral palsy		Deaths	
	Cases	Controls	Cases	Controls
Intended for study:	147	294	63	126
Not available:				
Out of region	0	18	0	0
Hospital records missing	4	19	1	7
Late exclusion (congenital anomaly)	2	0	0	0
Available for study (matched triads and pairs):	141	257	62	119
Case plus two controls	125		5	
Case plus one control	3		1	
Case plus no control	13		2	
No case plus two controls	2		0	
Triads and pairs for matched analysis	128		60	

TABLE II—Antenatal variables among cases of cerebral palsy and death and controls expressed as numbers (percentages) and odds ratios (95% confidence intervals)

Variable	Cerebral palsy			Deaths		
	Cases (n=128)	Controls (n=253)	Odds ratio* (95% confidence interval)	Cases (n=60)	Controls (n=119)	Odds ratio* (95% confidence interval)
Previous poor obstetric outcome	6 (4.7)	9 (3.6)	1.8 (0.7 to 4.8)	4 (6.7)	7 (5.9)	0.9 (0.3 to 3.1)
Existing maternal disease	18 (14.1)	14 (5.5)	2.3 (1.1 to 5.0)	7 (11.7)	8 (6.7)	2.3 (0.7 to 7.5)
Induced conception	6 (4.7)	7 (2.8)	1.7 (0.6 to 5.1)	1 (1.7)	1 (0.8)	2.0 (0.4 to 20.0)
Raised α fetoprotein	2 (1.6)	3 (1.2)	1.4 (0.2 to 10.3)	3 (5.0)	0	
Intrauterine growth retardation	14 (10.9)	15 (5.9)	2.1 (0.9 to 4.3)	5 (8.3)	3 (2.5)	3.3 (0.8 to 13.9)
Severe pre-eclampsia	11 (8.6)	6 (2.4)	3.7 (1.4 to 9.9)	6 (10.0)	1 (0.8)	12.0 (1.5 to 99.7)
All pre-eclampsia	41 (32.0)	49 (19.4)	2.0 (1.2 to 3.4)	12 (20.0)	17 (14.3)	1.6 (0.7 to 3.7)
Bleeding after 20 weeks	4 (3.1)	5 (2.0)	1.3 (0.7 to 2.4)	2 (3.3)	4 (3.4)	1.0 (0.4 to 2.3)
Oligohydramnios	4 (3.1)	6 (2.4)	1.4 (0.4 to 5.3)	1 (1.6)	1 (0.8)	2.0 (0.1 to 32.0)
Polyhydramnios	3 (2.3)	4 (1.6)	1.6 (0.3 to 8.4)	1 (1.6)	0	
Prolonged rupture of membranes	3 (2.3)	4 (1.6)	2.4 (0.4 to 15.0)	1 (1.6)	0	
Postmaturity	1 (0.8)	0		1 (1.6)	0	
Breech presentation	4 (3.1)	13 (5.1)	0.7 (0.2 to 2.1)	5 (8.3)	4 (3.4)	3.3 (0.8 to 14.0)

*Odds ratios estimated by matched analysis.

Overall, 62/128 (48.4%) children with cerebral palsy and 28/60 (46.7%) babies who died were considered to have had a complicated antenatal history (having one or more of the antenatal characteristics in appendix 2). Of the controls for cerebral palsy, 90/253 (35.6%) had one or more antenatal risk factors present and 31/119 (26.1%) of the controls for death. A complicated antenatal history was more likely among cases of cerebral palsy than controls (1.8; 1.2 to 2.8) and among cases of death than controls (2.8; 1.3 to 5.8).

EVENTS DURING LABOUR AND DELIVERY

There was no evidence of a significant difference at the 5% level between cases of cerebral palsy and controls in the incidence of induction of labour (1.2; 0.8 to 2.0), prolonged first or second stage of labour (1.0; 0.5 to 2.0 and 1.5; 0.7 to 3.3, respectively) or intrapartum haemorrhage (2.4; 0.4 to 15.0). Amniotic fluid stained with meconium, however, was more often present among cases of cerebral palsy than controls (3.0; 1.7 to 5.4).

Among perinatal deaths there were more cases than controls with intrapartum haemorrhage (5.3; 1.4 to 20.1) and evidence of amniotic fluid stained with meconium (12.3; 3.6 to 41.4).

About two thirds of cases of cerebral palsy and controls had continuous electronic fetal monitoring; there was no significant difference at the 5% level in the rate of continuous monitoring between cases and controls (table III). More cases of death than controls, however, were continuously monitored (3.3; 1.5 to 7.7).

Cardiotocograms (during the first stage) were missing in 14.6% (12/82) of cases of cerebral palsy in which continuous electronic fetal monitoring occurred and in a third (15/45) of cases of death. First stage cardiotocograms were missing in 12.4% (19/153) controls for cerebral palsy and 9.7% (6/62) controls for deaths. There was an increased likelihood of a missing cardiotocogram in the first stage in cases of death compared with controls (5.9; 2.1 to 20.9).

An ominous cardiotocogram[†] in both the first and second stage of labour was more common in cases of cerebral palsy than controls. This did not reach

significance for the first stage (1.9; 0.7 to 5.3), although it did for the second stage (5.6; 1.9 to 16.7). More cases of death than controls had an ominous cardiotocogram during the first stage of labour (22.4; 3.0 to 170.3); the difference in incidence of an ominous cardiotocogram in the second stage was not significant at the 5% level (7.7; 0.9 to 63.8).

CONDITION OF BABY

Babies with cerebral palsy and those who died were more depressed than their controls at the age of 5 minutes (table IV). Although all babies in this study were born after 37 weeks of gestation, 13 (10.2%) of those with cerebral palsy weighed less than 2500 g compared with four (1.6%) controls. This reflects an increased likelihood of retardation of fetal growth among children with cerebral palsy (8.2; 2.3 to 28.9); this was also more prevalent in cases of death than in controls (6.0; 1.2 to 29.7). Thirty seven (28.9%) of the cases of cerebral palsy and 31 (68.9%) of the 45 neonatal deaths had signs of neonatal encephalopathy; none of the controls had neonatal encephalopathy.

SUBOPTIMAL CARE

Table V shows the numbers and proportions of cases and controls in which there was a failure to provide optimal care in each of the five predefined categories.

Although one or more of the prespecified indications were present, continuous electronic monitoring was not used in 17 (13.3%) cases of cerebral palsy, 46 (18.2%) controls for cerebral palsy, 13 (21.7%) perinatal deaths, and 17 (14.3%) controls for death. There was no significant difference at the 5% level in the likelihood of failing to use continuous electronic fetal monitoring between cases of cerebral palsy and controls (0.7; 0.4 to 1.3) or between perinatal deaths and controls (1.8; 0.8 to 4.3).

Suboptimal instrumental delivery, as predefined, rarely occurred (two among cases of cerebral palsy and one perinatal death). The numbers were too small for a matched analysis.

Miscellaneous abnormalities in labour such as maternal pyrexia, severe bleeding requiring blood replacement, or a second stage lasting longer than

TABLE III—Intrapartum variables among cases of cerebral palsy and death and controls expressed as numbers (percentages) affected and odds ratios (95% confidence intervals)

Variable	Cerebral palsy			Deaths		
	Cases (n=128)	Controls (n=253)	Odds ratio* (95% confidence interval)	Cases (n=60)	Controls (n=119)	Odds ratio* (95% confidence interval)
Induction of labour	37 (28.9)	65 (25.7)	1.2 (0.8 to 2.0)	17 (28.3)	22 (18.5)	1.6 (0.8 to 3.2)
Duration of labour:						
First stage > 12 hours	15 (11.7)	31 (12.3)	1.0 (0.5 to 2.0)	9 (15.0)	13 (10.9)	1.6 (0.6 to 4.0)
Second stage > 2 hours	10 (7.8)	20 (7.9)	1.5 (0.7 to 3.3)	3 (5.0)	5 (4.2)	1.6 (0.3 to 8.1)
Epidural anaesthesia	34 (26.6)	50 (19.8)	1.3 (0.8 to 2.2)	12 (20.0)	20 (16.8)	1.3 (0.6 to 2.9)
Meconium stained liquor	31 (24.2)	25 (9.9)	3.0 (1.7 to 5.4)	20 (33.3)	6 (5.0)	12.3 (3.6 to 41.4)
Continuous electronic fetal monitoring done:						
First stage	82 (64.1)	153 (60.5)	1.2 (0.8 to 2.0)	45 (75.0)	62 (52.1)	3.3 (1.5 to 7.7)
Second stage	79 (61.7)	140 (55.3)	1.4 (0.9 to 2.3)	28 (46.7)	55 (46.2)	1.1 (0.6 to 2.1)
Missing cardiotocogram:						
First stage	12 (14.6)	19 (12.4)	1.4 (0.6 to 3.2)	15 (33.0)	6 (9.7)	5.9 (2.1 to 20.9)
Second stage	14 (17.7)	24 (17.1)	1.3 (0.6 to 2.8)	9 (32.1)	6 (10.9)	3.3 (1.0 to 12.8)
Ominous cardiotocogram†:						
First stage	16 (22.9)	14 (10.4)	1.9 (0.7 to 5.3)	20 (66.7)	4 (7.1)	22.4 (3.0 to 170.3)
Second stage	37 (56.9)	37 (31.9)	5.6 (1.9 to 16.7)	16 (84.2)	17 (34.7)	7.7 (0.9 to 63.8)
Intrapartum haemorrhage	3 (2.3)	3 (1.2)	2.4 (0.4 to 15.0)	8 (13.3)	3 (2.5)	5.3 (1.4 to 20.1)

*Odds ratios estimated by matched analysis.

†Proportions based on number of mothers with available cardiotocograms.

TABLE IV—Baby's condition at delivery expressed as numbers (percentages) affected; odds ratios based on matched analyses (95% confidence intervals)

At 5 minutes of age:	Cerebral palsy			Deaths		
	Cases (n=128)	Controls (n=253)	Odds ratio* (95% confidence interval)	Cases (n=60)	Controls (n=119)	Odds ratio* (95% confidence interval)
Heart rate less than 100 beats/min	15 (11.7)	2 (0.8)	15.0 (3.4 to 65.6)	40 (66.6)	1 (0.8)	
Respiratory effort absent	15 (11.7)	1 (0.4)	30.0 (4.0 to 227.1)	44 (73.3)	1 (0.8)	
Apgar score < 2 at five minutes	8 (6.3)	0		39 (65.0)	0	
Birth weight < 2500 g	13 (10.2)	4 (1.6)	8.2 (2.3 to 28.9)	6 (10.0)	2 (1.7)	6.0 (1.2 to 29.7)

*Odds ratios estimated by matched analysis.

TABLE V—Failure to provide optimal care in five predefined categories (appendix 1) in cases of cerebral palsy and death and controls expressed as numbers (percentages) and odds ratios (95% confidence intervals)

Detail	Cases	Controls	Odds ratio* (95% confidence interval)	Adjusted odds ratio†
<i>Cerebral palsy</i>				
No of subjects	128	253		
Failure to use continuous electronic fetal monitoring (indication present)	17 (13.3)	46 (18.2)	0.7 (0.4 to 1.3)	0.7 (0.4 to 1.3)
Suboptimal instrumental delivery	2 (1.6)	0		
Miscellaneous group	7 (5.5)	15 (5.9)	1.0 (0.4 to 2.5)	1.0 (0.4 to 2.5)
Failure to respond to signs of fetal distress	33 (25.8)	18 (7.1)	4.5 (2.4 to 8.4)	4.3 (2.3 to 8.1)
Failure to respond to baby's condition after delivery	10 (7.8)	5 (2.0)	4.7 (1.5 to 15.0)	4.9 (1.5 to 16.1)
<i>Deaths</i>				
No of subjects	60	119		
Failure to use continuous electronic fetal monitoring (indication present)	13 (21.7)	17 (14.3)	1.8 (0.8 to 4.3)	1.7 (0.7 to 4.0)
Suboptimal instrumental delivery	1 (1.7)	0		
Miscellaneous group	3 (5.0)	4 (3.4)	1.6 (0.3 to 8.4)	1.4 (0.3 to 7.9)
Failure to respond to signs of fetal distress	30 (50.0)	8 (6.7)	26.1 (6.2 to 109.7)	24.4 (5.8 to 102.7)
Failure to respond to baby's condition after delivery	12 (20.0)	0		

*Odds ratios estimated on matched analysis.

†Odds ratios adjusted for complicated antenatal history.

two hours occurred infrequently, and there was no significant difference at the 5% level in the failure to respond optimally to these complications between cases of cerebral palsy and controls (1.0; 0.4 to 2.5) or between perinatal deaths and controls (1.6; 0.3 to 8.4).

There was an increased incidence of failure to respond optimally to clinical signs of fetal distress (as defined in appendix 1) in cases compared with controls. Clinical signs of fetal distress were diagnosed on the basis of continuous cardiotocography except in 12 mothers (two cases of cerebral palsy, two controls for cerebral palsy, seven cases of deaths, and one control for death) who were not continuously monitored or for whom the cardiotocogram was missing. In these, the observations recorded in the notes clearly showed that the criteria for fetal distress had been met. Just over a quarter of cases of cerebral palsy (33/128) did not meet the criteria for an optimal response compared with 7.1% (18/253) of controls for cerebral palsy (4.5; 2.4 to 8.4). There was a failure to respond optimally to fetal distress in half of the cases of perinatal death (30/60) compared with 6.7% (8/119) of the controls for death (26.1; 6.2 to 109.7). Of the 33 cases of cerebral palsy in which there had been a suboptimal response to fetal distress, 23 had signs of neonatal encephalopathy, suggesting that an acute intrapartum hypoxic event had occurred.

Although many cases of cerebral palsy and death were managed optimally in the neonatal period, in more cases of cerebral palsy than controls there seemed to be a failure to resuscitate optimally after delivery (4.7; 1.5 to 15.0). Twelve cases of death did not meet the criteria for optimal management after birth; no controls for death had suboptimal management after birth. The association of failure to resuscitate optimally and cerebral palsy or death can probably be explained largely by the higher incidence of neonatal depression among cases of cerebral palsy and death than their controls. The study was not sufficiently large to test this further.

Finally, after reviewing all circumstances not included in the five predefined categories, we considered that care had not been entirely optimal in a further six cases of cerebral palsy and 23 controls for cerebral palsy and 10 perinatal deaths and 11 controls for death. The problems in this category were diverse and included a variety of events such as rupture of a caesarean scar, repeated attempts to achieve delivery by forceps, inappropriate use of prostaglandin in the induction of labour, poor management of shoulder dystocia, and misjudgment of the position of the fetal head when applying rotational forceps. Events in this category occurred rarely, and they were equally distributed among cases and controls. As this category had not been predefined no further analysis was performed on this group.

ADJUSTED ANALYSIS

We then calculated the likelihood of suboptimal intrapartum care by adjusting for the presence or absence of a complicated antenatal history (appendix 2). As can be seen the odds ratios were altered little by this adjustment.

Discussion

Over the past 10 years there has been a considerable change in the views held by obstetricians, paediatricians, and lawyers about the origin of cerebral palsy. For many years it had been assumed that most cases of cerebral palsy resulted from injury to the fetal brain around the time of birth as a result of trauma or hypoxia. Further, it was widely agreed that such injury was preventable.¹⁶

Views have changed after the accumulation of epidemiological evidence which strongly suggested that most children with cerebral palsy do not have intrapartum clinical signs which are assumed to reflect hypoxic stress in the fetus.¹⁷ It was also increasingly appreciated that these clinical markers of stress in labour and delivery are poorly predictive of cerebral palsy and that most babies with these markers do not later have cerebral palsy. Indeed, in 1990, it was stated that "brain damage from asphyxia appears very rare."¹⁸

Two explanations have been offered for the reported low incidence of adverse birth events in cerebral palsy. Firstly, it is possible that a hypoxic insult to the fetus results either in death or complete recovery—an all or none effect.¹⁹ Although this effect may have been observed in the past, the currently more active approach to the resuscitation of babies with severe asphyxia could result in the survival of damaged babies.

Secondly, intrapartum hypoxia is only one of several aetiological factors in cerebral palsy. The term cerebral palsy describes a group of conditions with clinical similarities but different aetiological pathways. In the Oxford region we have a population register of children with cerebral palsy. During the four birth years (1984-7) of the study, of the 132 743 babies registered as live born in the region, 339 are included on the cerebral palsy register. This is a prevalence rate for the birth cohort of 2.6/1000 live births (2.4/1000 live births if postnatal cases are excluded), which is comparable with other reported rates for the same birth years.^{20 21} Of the 339 children with cerebral palsy, a third were born preterm and were thus particularly vulnerable to haemorrhage and ischaemia in the first few days of life: in 27 (8%) the cerebral palsy arose after the first four weeks; and one in five born at term had signs of a congenital anomaly. The 43% (147/339) remaining were non-malformed term babies whose cerebral palsy was most likely to have been associated with adverse

birth events, some of which might have been preventable with different care.

MATERNAL AND ANTENATAL RISK FACTORS

It was clear, however, that even among this group other possible aetiological factors were present. The mothers of the children with cerebral palsy and those who died were at higher risk antenatally than the controls—for example, placental dysfunction as manifest by pre-eclampsia and failure of fetal growth were more likely to occur in both groups. This observation has two implications when we consider the origin of cerebral palsy. Firstly, it suggests that prenatal factors perhaps associated with chronic hypoxia in the fetus may result in damage to the developing brain. Neuropathological observations of prenatal ischaemic lesions in brain white matter associated with antenatal maternal complications support this hypothesis.^{22,23} A second possibility is that the vulnerability of the fetus to the normal stress of labour may be altered by prenatal factors, leading to intrapartum hypoxic damage under conditions which a normal fetus could resist.

INTRAPARTUM FETAL DISTRESS

Not only did the mothers of children with cerebral palsy and babies who died have more adverse antenatal factors than controls but also fetal distress as measured by an ominous cardiotocogram during the first stage of labour (among those who had a continuous electronic fetal monitoring and with an available and interpretable cardiotocogram) was recognised almost twice as often in cases of cerebral palsy than among controls and almost 10 times more often in cases of death than in the controls.

There are problems in estimating the true incidence of fetal distress in this study. Only two thirds of the cases of cerebral palsy and their controls had continuous electronic fetal monitoring and 15% of cardiotocograms were missing. Reasons for mislaid cardiotocograms are many but possibly several of these were abnormal interesting cardiotocograms, resulting in an underestimate of the incidence of ominous cardiotocograms among those continuously monitored. On the other hand, if routine practice was to start continuous electronic fetal monitoring when fetal heart abnormalities were suspected on intermittent auscultation, the rate of fetal distress may be lower among those not continuously monitored. A further constraint on the interpretation of the relative likelihood of fetal distress in cases and controls is imposed by the matched analysis. As only those with an available cardiotocogram could be included in this matched analysis the numbers of participants are low and 95% confidence intervals are wide.

From the data available, however, ominous cardiotocograms seemed to be more common among cases of cerebral palsy and death than among controls as was meconium staining of the amniotic fluid. Richmond *et al* reported fetal distress in 24% of term babies who developed the signs of cerebral palsy as being almost three times more common than among controls.²⁴ These clinical signs of intrapartum stress may in part reflect the increased antenatal risk factors, suggesting that in some cases of cerebral palsy and death there is a cascade of adverse events starting in pregnancy and continuing through labour.

SUBOPTIMAL CARE

It did seem from this study, however, that a further factor which might contribute to this sequence of events was suboptimal care. The criteria for suboptimal care used in this study were agreed by obstetricians throughout the region. Many of these criteria have never been subjected to rigorous evaluation, but they

represent a consensus among obstetricians of the minimum expected response to clinical events. They cannot be regarded as standards for clinical practice but rather the threshold below which care is, by consensus, not at present acceptable to practising obstetricians.

By using these criteria, failure to respond either by taking a fetal blood sample or by delivery to signs considered by practising obstetricians to indicate distress in the fetus occurred almost four times more often among cases of cerebral palsy than in controls and 26 times more often in cases of death than in controls. Our findings need to be interpreted with great caution. Firstly, the presence of antenatal risk factors and intrapartum fetal distress may be important confounding variables. The likelihood of a suboptimal response to signs of fetal distress did not alter after adjustment for a complicated antenatal history, although it remains possible that some of the observed association may be accounted for by the higher incidence of fetal distress in cases of cerebral palsy than in controls. A larger study is needed to clarify this issue. Secondly, it is generally accepted that if a baby is not depressed at birth and is neurologically normal during the neonatal period, it is unlikely that there has been a preceding severe intrapartum hypoxic event.²⁵ A third (10/33) of the cases of cerebral palsy in which there was a suboptimal response to fetal distress did not have neonatal signs of encephalopathy. It is tempting to speculate therefore that among these children with no signs of encephalopathy intrapartum events or quality of intrapartum care had little to do with the evolution of cerebral palsy. In these children a preceding factor probably resulted in signs of fetal distress and later evidence of neurological deficit without an acute hypoxic episode. In the courts, however, as care did not meet standards which were agreed by clinicians, it would be difficult to mount a defence against the claim that negligence had a causal role in the child's cerebral palsy.

Thirdly, although our study was considerably larger than the two previously reported studies of the association of care and cerebral palsy,^{4,24} and our selection of cases of cerebral palsy increased the likelihood of showing an association between care and outcome, the numbers available for analysis were still small especially as we used a matched design. To explore further the association of antenatal and intrapartum factors and cerebral palsy combinations of large datasets of children with cerebral palsy will be needed. This would also allow an investigation of the possibility that some clinical subgroups of cerebral palsy, such as spastic quadriplegia, are more likely than others to be associated with intrapartum events—for example, spastic hemiplegia.

Finally, although our findings suggest an association between care and adverse outcome of pregnancy in some babies, it is clear that most cases of cerebral palsy and perinatal death are unrelated to suboptimal intrapartum care. Of the 339 children with cerebral palsy born to mothers resident in the region during the study period, only 6.8% (23/339) of cases occurred in non-malformed term singleton babies with signs of neonatal encephalopathy in whom there was evidence of failure to respond to signs of intrapartum fetal distress. Likewise, in only 30/1129 (2.7%) of all perinatal deaths during the study period was there failure to respond to intrapartum fetal distress in babies born at term.

In conclusion, we were unable to sustain our hypothesis that compared with controls cases of cerebral palsy among term singleton babies without a congenital anomaly are not more likely to have been preceded by suboptimal intrapartum care. Just as among term singleton non-malformed babies who die

Clinical implications

- Mothers of term, singleton, non-malformed babies who die or who later have cerebral palsy have an increased risk of a complicated antenatal course
- They also have an increased risk of having signs of intrapartum fetal distress and a sub-optimal response to this distress
- Only 7% of all children with cerebral palsy, however, have a history of suboptimal response to distress followed by signs of neonatal encephalopathy
- Most cerebral palsy in children born at term is likely to have an antenatal origin

intrapartum or soon after birth, there was an increased likelihood of a suboptimal response to clinical signs of fetal distress among this selected group of cases of cerebral palsy. We suggest that cerebral palsy (among singleton, term, non-malformed babies with neonatal encephalopathy) and death (during labour and delivery or soon after birth among singleton, term, non-malformed babies) form a continuum of adverse outcome related to care.

Our findings do support, however, the view that birth events, avoidable or unavoidable, are contributing factors in only a few cases of cerebral palsy. Even among this highly selected group of term, singleton, non-malformed cases of cerebral palsy over two thirds had no signs of intrapartum distress. The challenge for the clinician is the small group of children with cerebral palsy with apparently potentially avoidable intrapartum hypoxia; the challenge for researchers is to determine much more precisely the interrelations of chronic intrauterine hypoxia and other antenatal events, neonatal encephalopathy, and cerebral palsy.

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Appendix 1

Care was assessed under the following categories.

CONTINUOUS ELECTRONIC MONITORING OF FETAL HEART RATE

Care was considered suboptimal if there was a failure to use continuous electronic fetal monitoring in the presence of one or more of the following:

- Pre-eclampsia
- Diabetes
- Suspected retardation of intrauterine growth
- Pregnancy duration of greater than 42 weeks' completed gestation
- Suspected abruption
- Meconium
- Administration of prostaglandin or oxytocin to induce labour or oxytocin to accelerate labour
- Epidural
- Previous caesarean section
- Breech presentation
- Maternal fever

INSTRUMENTAL DELIVERY

Care was considered suboptimal if there was:

- Strong traction and more than three pulls used to achieve an instrumental delivery

Attempted forceps delivery when the head was not engaged
Breech extraction

MISCELLANEOUS ABNORMALITIES OF LABOUR

Care was considered suboptimal if there was:

- Inadequate blood replacement for severe bleeding
- Failure to investigate and treat maternal fever
- Failure to ensure delivery within two hours of commencing pushing in the second stage of labour

FAILURE TO RESPOND TO FETAL DISTRESS

Care was considered suboptimal if there was failure to respond within the specified time limit by taking a fetal blood sample or by delivery in the presence of:

- Prolonged bradycardia (< 100 beats/min) for 30 minutes
- Severe variable decelerations for 90 minutes
- Late decelerations for 90 minutes
- Severe tachycardia (> 180 beats/min) for 90 minutes
- (Response times were halved in the presence of meconium.)

RESPONSE AFTER DELIVERY

Care was considered suboptimal if there was failure to apply intermittent positive pressure ventilation within two minutes of birth in the presence of:

- Persistent neonatal bradycardia (heart rate < 100 beats/min)
- Absent or minimal respiratory effort

Appendix 2

DEFINITIONS OF ANTENATAL CHARACTERISTICS CONTRIBUTING TO COMPLICATED OBSTETRIC CASES

Previous poor obstetric history—Previous intrauterine death, previous spontaneous abortion at ≥ 15 weeks' gestation, two or more spontaneous abortions at any gestation, previous neonatal death, previous live child with disability or handicap related to perinatal asphyxia, previous premature delivery

Existing maternal illness—Chronic hypertension, renal disease diagnosed by biochemical or radiological variables, or ongoing dialysis or the presence of renal transplantation, gestational or long standing diabetes, respiratory or cardiovascular disease, other chronic diseases

Pre-eclampsia—The presence of hypertension (diastolic blood pressure ≥ 90 mm Hg) and proteinuria (with or without accompanying biochemical and haematological changes). Pre-eclampsia was graded in four stages as used by the high risk pregnancy unit at the John Radcliffe Hospital (C W G Redman, personal communication). Non-proteinuric hypertension appearing for the first time in pregnancy was classified as grade 1

Severe pre-eclampsia—Significant proteinuria (≥ 0.3 mg/24 hours) or untreated diastolic blood pressure of ≥ 110 mm Hg or abnormal liver biochemistry or symptomatic pre-eclampsia. Pre-eclampsia leading to eclampsia was also included.

Antepartum haemorrhage—Vaginal bleeding after 20 weeks' gestation regardless of aetiology after exclusion of local haemorrhage of genital tract

Oligohydramnios—A clinical impression of reduced volume of amniotic fluid or preferably an ultrasound derived diagnosis of the largest vertical pool of ≤ 2 cm

Polyhydramnios—A clinical impression of increased volume of amniotic fluid or preferably an ultrasound derived diagnosis of a vertical pool of ≥ 8 cm

Suspected antenatal retardation of intrauterine growth—Usually an ultrasound derived diagnosis of a weight ≤ 10 th centile as estimated by serial measurement of the abdominal circumference, occasionally by clinical impression alone

Raised serum α fetoprotein—The finding of a raised maternal serum α fetoprotein of ≥ 2.5 multiples of the median with correct estimation of gestation and a singleton pregnancy in a normally formed fetus

Induced conception—Conception brought about by using stimulated cycles or by in vitro fertilisation, gamete intrafallopian transfer, or artificial insemination, usually for reasons of infertility

Prolonged rupture of membranes—Rupture of the membranes for > 24 hours' duration

Premature rupture of membranes—Rupture of the membranes before 37 completed weeks of gestation

Postmaturity—Pregnancy duration of greater than 42 completed weeks' gestation

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Relation between infection with *Helicobacter pylori* and living conditions in childhood: evidence for person to person transmission in early life

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Abstract

Objectives—To relate the prevalence of infection with *Helicobacter pylori* in adults to their living conditions in childhood to identify risk factors for infection.

Design—Prevalence study of IgG antibodies to *H pylori* (>10 µg IgG/ml, determined by enzyme linked immunosorbent assay (ELISA)) and reported living conditions and other socioeconomic factors in childhood.

Setting—Three factories in Stoke on Trent.

Subjects—471 male volunteers aged 18 to 65 years.

Main outcome measures—Seroprevalence and variables in childhood.

Results—Seroprevalence of *H pylori* increased with age (22/74 (29.7%) at <30 years v 29/46 (63%) at 55-65 years; $P < 0.001$ for trend) and was related to manual occupation (14/65 (21.5%) for non-manual v 162/406 (39.9%) for manual; $P = 0.003$). After data were adjusted for age and occupation subjects from large families, whose childhood homes were crowded or who regularly shared a bed in childhood, were significantly more likely to be seropositive (adjusted odds ratio (95% confidence interval) 2.15 (1.41 to 3.30) for crowding and 2.13 (1.38 to 3.30) for sharing a bed), but there was no relation with possession of a bathroom, inside toilet, refrigerator, or household pets in childhood.

Conclusions—Close person to person contact in childhood is an important determinant of seroprevalence of *H pylori* in adulthood, suggesting that the infection is transmitted directly from one person to another and may be commonly acquired in early life.

Introduction

Infection with *Helicobacter pylori* has been established as a major cause of chronic gastritis.¹ It also plays an important part in the development of peptic ulcer disease^{2,3} and has been implicated in the process of gastric carcinogenesis.⁴ Around half of adults may be

infected in developed countries, while this figure could be as high as 90% in developing countries,⁵ yet little is known about the way in which the infection is transmitted. No reservoir of organisms has been identified outside the human stomach, and, although reports have suggested that *H pylori* can be isolated from faecal material⁶ and dental plaque,⁷ these reports have yet to be confirmed.

Infection tends to cluster in families^{8,9} and in people living in crowded^{10,11} or closed environments,¹²⁻¹⁴ suggesting that person to person contact plays an important part in transmission. Infection has also been associated with poor hygiene,¹⁵ and it has been suggested that acquisition may commonly occur in childhood.¹¹

We aimed to relate infection with *H pylori* in adults to their living conditions in childhood by using the presence of circulating antibodies to *H pylori* as a marker of infection. Of particular interest was the effect of sharing a bed in childhood, previously reported by Galpin *et al*,¹⁰ and the possibility that this might explain some of the observed relations with overcrowding and lower socioeconomic status.

Data were collected as part of a larger study of gastritis in Stoke on Trent.

Subjects and methods

Male employees at two factories in Stoke on Trent and men attending a blood donation session at a third factory were invited to participate. Volunteers completed a questionnaire that included detailed questions about their living conditions during two periods of childhood (below 5 years and between 5 and 16 years) before attending an appointment when the information was checked for completeness and a blood sample (10 ml) was collected by venepuncture.

Serum samples were stored below 4°C until they could be transferred to a -40°C freezer at the end of each day. Samples were assayed for antibodies to *H pylori* by using an established enzyme linked immunosorbent assay (ELISA),¹⁶ with a cut off point

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