Effects of birth weight, gestational age, and maternal obstetric history on birth prevalence of cerebral palsy

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SUMMARY A register of children with cerebral palsy born to mothers resident in the Mersey region from 1966 to 1977 was compiled from health service records. Frequency distributions and prevalences of birth weight and gestational age differed for those with hemiplegia, diplegia, and quadriplegia. In particular, the children with diplegia showed a bimodal frequency distribution. Children of normal birth weight with diplegia had a higher prevalence of severe mental retardation than those of low birth weight. These differences may be due to survival bias and may not be of aetiological importance. Furthermore, the mothers of diplegic infants had a significantly higher proportion of spontaneous abortions, stillbirths, and low birthweight infants in their obstetric history. This suggests that prenatal factors predominate in the aetiology of diplegia.

The association between cerebral palsy and prematurity was first recognised in 1826, when Joerg noted that 'too early and unripe born fetuses may present a state of weakness and stiffness in the muscles persisting until puberty or later'.¹ Subsequently Little in 1834 observed that contracture of the arms and legs occurred in premature infants² and later gave his classic description of cerebral palsy, in which the association with prematurity was again noted.³

More recently the association of cerebral palsy with retardation of intrauterine growth has been highlighted. Alberman showed in a case control study that birth weight was unduly low for gestational age in infants with spastic diplegia and quadriplegia and concluded that some prenatal factor was responsible.⁴ McDonald, in a follow up of low birthweight infants, also found that birth weight and gestational age were independent risk factors for cerebral palsy,⁵ an observation that was subsequently confirmed by both case control and longitudinal cohort studies.⁶

The bimodal frequency distribution of birth weight of infants with spastic diplegia was first recognised by Childs and Evans⁷ and has been confirmed by others.^{8–10} On the basis of this bimodality and the clinical differences between the two subgroups it was proposed that the aetiological factors leading to paraplegia and diplegia of low birthweight infants differed from those operating among infants of normal birth weight.

The relevance of birth weight and gestational age

as risk factors for cerebral palsy is assuming increasing importance with current trends in obstetric and neonatal management. These include the early recognition of growth retardation followed by induction of labour, and the technological developments in neonatal intensive care with the ability to keep progressively smaller infants alive. In the light of these developments we report the association between birth weight and gestational age in a geographically delineated cohort of patients with spastic cerebral palsy born from 1966 to 1977 and relate it to the observed prevalence of the syndrome.

Methods

A register was compiled of all patients with cerebral palsy born in the years 1966–77 whose mothers' area of residence at the time of birth was within the boundary of the Mersey Regional Health Authority. As the mother's area of residence was the criterion for inclusion infants born within the region but whose mothers' area of residence was outside were excluded, but those born outside whose mothers' area of residence was within the region were included. These inclusion and exclusion criteria were applied because denominator data for live births obtained from birth registration documents are published according to the mothers' area of residence at the time of birth.

The register was compiled from several sources, including the handicap registers of all health districts

in the region, the national register of families claiming family disability allowance maintained by the Rowntree Trust in York, records of children attending schools for the educationally subnormal and the physically handicapped, and a search by the Office of Population Censuses and Surveys (OPCS) of all death certificates in which cerebral palsy featured as the underlying cause of death.

The type of cerebral palsy was categorised from information in the clinical records of each child. The notes of all doubtful cases were reviewed by one of us (LR). The spastic and mixed spastic syndromes provided the material on which this report is based. Patients with symmetrical or nearly symmetrical spasticity of the legs with lesser or no involvement of the arms were designated as having spastic diplegia. Patients with unilateral spasticity of one arm or one leg, or both, were designated as having hemiplegia, and those whose arms and legs were equally affected, were designated as having spastic quadriplegia.

The mother's hospital obstetric record was used to obtain the child's birth weight. Denominator numbers of live births in the Mersey region for determining the prevalence of infants with cerebral palsy at birth were obtained from the Registrar General's and OPCS tables of birth registration. Grouped birthweight specific data for infants weighing 2500 g or less were obtained from the LHS 27/1 returns compiled by the Department of Health and Social Security (DHSS) from birth notifications. Numbers of live born infants weighing over 2500 g were obtained by subtracting notifications of births of 2500 g or less from total birth registrations.

To subdivide the denominator data for infants weighing over 2500 g into 500 g categories national data from England and Wales were used to obtain the proportion of infants in each category and these were applied to the total population of live births in the Mersey region to estimate the number of births in each birthweight category.¹¹

Gestational age at birth was obtained from the hospital obstetric records for 540 cases in which the date of the last menstrual period was fairly certain. In an additional 51 cases an estimate of gestational age was found in the paediatric records. To obtain the denominator for the number of births in each gestational age group the proportions in each group in the 1970 British birth cohort were applied to all live births in the Mersey region.¹² Data from 1970 related to single births only. The 1970 cohort had to be used because there is no other routinely published source of data giving the frequency distribution for gestational age.

Appropriateness of birth weight for gestational age allowing for sex was determined by reference to

standard charts giving third, 10th, and 50th centiles.¹³ Data on the number of previous spontaneous abortions, stillbirths, live births, and infants weighing 2500 g or less were obtained from each mother's obstetric record.

Almost all the children were assessed by a clinical psychologist at least once, usually when school placement was being considered. Various assessment procedures were used. Where possible mental ability was classified according to intelligence quotient (IQ). Severe retardation was determined by an IQ of <50, moderate retardation by an IQ of 50–69, and normal or minimal retardation by an IQ of ≥70.

The significance of differences between proportions was calculated using χ^2 low column analysis.

Table 1 *Type of spastic cerebral palsy classified by sex*

	No (%) with hemiplegia	No (%) with diplegia	No (%) with quadriplegia
Male infants	114 (58)	81 (54)	149 (60)
Female infants	83 (42)	68 (46)	98 (40)
Total	197 (100)	149 (100)	247 (100)
Male:female ratio	1.4:1	1.2:1	1.5:1

Fig 1 *Birthweight frequency distribution of cerebral palsy.*

Results

The study population comprised 593 cases of spastic cerebral palsy. Table 1 shows the cases according to type of cerebral palsy and sex. There was a preponderance of male patients, and the three categories of syndrome showed similar male:female ratios.

BIRTH WEIGHT AND SPASTIC CEREBRAL PALSY

Fig 1 shows the frequency distributions of birth-weight for the three types of spastic cerebral palsy. Excluded from this analysis were five cases in whom there was no record of birth weight (two with diplegia and three with quadriplegia).

The hemiplegic and quadriplegic infants showed a unimodal distribution which was shifted to the left compared with the distribution of all live births in England and Wales. Those with diplegia showed a bimodal distribution with the major peak among the low birthweight infants. The differences in the frequency distribution of birth weight of the infants with spastic cerebral palsy were explained when the birthweight specific prevalences were examined (fig 2). (In this analysis the infants with cerebral palsy born in 1966 had to be excluded because denominator data on the numbers of live births in each birthweight category in the Mersey region were not available.) There was an exponential rise in the

prevalence with decreasing birth weight in all three subgroups of spastic cerebral palsy, but the rise was most pronounced for those with diplegia. Thus the bimodality of the frequency distribution of birth weight in those with diplegia derived from a combination of the high rates among those of lower birth weight, even though the denominators were small, and the large numbers of births at the higher end of the birthweight frequency distribution.

GESTATIONAL AGE AND SPASTIC CEREBRAL PALSY

In two cases (one of diplegia and one of quadriplegia) the gestational age was not recorded in either the maternal obstetric or the paediatric notes; the analysis was based on the remaining 591 cases.

The frequency distribution of gestational age was similar to that of birth weight for all three subgroups of spastic cerebral palsy, the diplegic infants again showing a bimodal distribution (fig 3). The gestational age specific prevalences increased with decreasing gestational age except among those whose gestational age was ≤ 28 weeks, where the prevalence was low (fig 4).

As with the frequency distribution of birth weight the bimodality of the gestational age curve for infants with diplegia was the consequence of the high prevalences among those infants whose gestational age was ≤ 36 weeks.

Fig 2 Birthweight specific prevalence rates of cerebral palsy.

Fig 3 Gestational age frequency distribution of cerebral palsy.

Fig 4 Gestational age specific prevalence rates of cerebral palsy.

Table 2 Appropriateness of associating birth weight and gestational age. Values are numbers (%) of infants

Centiles	Hemiplegia (n=197)	Diplegia (n=147)	Quadriplegia (n=244)
<3rd centile	22 (11.2)	25 (17.0)	39 (16.0)
<10th centile	48 (24.4)	50 (34.0)	87 (35.7)
<50th centile	130 (66.0)	114 (77.6)	157 (64.3)

APPROPRIATENESS OF ASSOCIATIVE BIRTH WEIGHT AND GESTATIONAL AGE

Table 2 shows the proportions of cases falling below the third, 10th, and 50th centiles on the charts of birth weight for gestational age. The analysis concerns 588 cases in which both birth weight and gestational age were recorded. In all three categories of cerebral palsy a disproportionate number were small for gestational age; 11.2%, 17.0%, and 16.0% of those with hemiplegia, diplegia, and quadriplegia, respectively, fell below the third centile. A higher proportion of infants with diplegia seemed to have retarded growth at birth, while those with hemiplegia showed the least growth retardation, but these differences were not significant.

MENTAL ABILITY AND BIRTH WEIGHT

There were 574 cases in which birth weight was known and a record of mental ability available. Table 3 shows mental ability in the three categories of cerebral palsy according to their birth weight groups. A greater proportion of those with quadriplegia showed severe mental retardation (64%, compared with only 24% and 13% among those with diplegia and hemiplegia, respectively).

In the very low birthweight group (≤ 1500 g), all three categories of cerebral palsy showed a greater proportion of infants with normal mental ability compared with the other birthweight groups (1501–2500 g and >2500 g).

MATERNAL OBSTETRIC HISTORY

All conceptions before the birth of each index case

Table 3 Mental ability by type of cerebral palsy and birth weight (Values are numbers (%) of infants)

Birth weight and diagnosis	Mental ability			All
	Normal	Moderately retarded	Severely retarded	
≤ 1500 g				
Hemiplegia	5 (83)	1 (17)	0 (0)	6
Diplegia	16 (76)	2 (10)	3 (14)	21
Quadriplegia	4 (40)	4 (40)	2 (20)	10
1501–2500 g				
Hemiplegia	27 (69)	6 (15)	6 (15)	39
Diplegia	39 (65)	10 (17)	11 (18)	60
Quadriplegia	10 (22)	8 (17)	28 (61)	46
>2500 g				
Hemiplegia	113 (74)	19 (13)	19 (13)	151
Diplegia	33 (50)	11 (17)	21 (32)	65
Quadriplegia	39 (22)	19 (11)	118 (67)	176
Total				
Hemiplegia	145 (74)	26 (13)	25 (13)	196
Diplegia	88 (60)	23 (16)	35 (24)	146
Quadriplegia	53 (23)	31 (13)	148 (64)	232

Table 4 Outcome of previous conceptions (Values are numbers (%) of infants)

	Spontaneous abortions	Stillbirths	Low birthweight live births	Normal birthweight infants	Total conceptions
Hemiplegia	35 (14.0)	2 (0.8)	18 (7.2)	195 (78.0)	250 (100)
Diplegia	55 (24.6)	8 (3.6)	23 (10.3)	138 (61.6)	224 (100)
Quadriplegia	57 (12.6)	14 (3.1)	28 (6.2)	353 (78.1)	452 (100)

were classified according to whether the outcome had been a spontaneous abortion, a stillbirth, a live birth weighing ≤ 2500 g, or a live birth weighing >2500 g. A summary of the outcomes of all previous conceptions according to type of cerebral palsy is shown in table 4. The difference was highly significant; in particular, the mothers of diplegic infants had had a greater proportion of spontaneous abortions, stillbirths, and low birthweight infants than the mothers of hemiplegic or quadriplegic infants ($\chi^2=28.2$, df 6, $p=0.0001$).

Discussion

The bimodal frequency distribution of birth weight of the diplegic infants confirms previous observations.⁷⁻¹⁰ The interpretation that this bimodality is the result of different aetiological factors, however, requires reassessment. In support of this thesis Childs and Evans noted that the proportion of severely mentally retarded infants was greater among infants of normal birth weight than among those with birth weights of <2500 g.⁷ An alternative interpretation is that survival of infants in the two birthweight categories is biased according to the severity of brain damage, for which the marker is the degree of mental retardation. If this were so the low birthweight group would be less likely to show severe mental retardation because the most severely affected cases would have been aborted or died before the diplegia was recognised. In the normal birthweight group the severely mentally retarded have a better chance of survival because they do not have the additional hazard of prematurity. While the diplegic infants may not be a single entity, their aetiological subdivision cannot be justified on the basis of the bimodality of the birthweight distribution curve.

Another explanation of the higher proportion of severely mentally retarded among diplegic infants with normal birth weight could be that the longer the infant remains in a hostile intrauterine environment the greater the neurological deficit.

Drillien *et al* also noted differences between

premature and mature cases in the mothers' social class distribution, age at marriage, and fertility pattern and concluded that these were attributable to differences in aetiology.¹⁴ These results can, however, be explained by survival bias without invoking aetiological differences.

The survival bias is further evident on examination of the prevalences specific for gestational age. We have confirmed that infants with spastic cerebral palsy fail to grow normally in utero, with a disproportionate number, particularly of those with diplegia, being small for dates. Among infants with a very short gestational age (≤ 28 weeks) there is a sharp fall in the prevalence of cerebral palsy (fig 4). The sharp fall is likely to be an artefact of incomplete ascertainment because not only are the infants with cerebral palsy premature but their growth is retarded so that the chance of survival is severely compromised.

The bias introduced by differential survivals highlights the dangers inherent in advancing aetiological hypotheses on prevalence rather than incidence. In the current state of knowledge no study of cerebral palsy can provide data on incidence; at the very best only prevalence at birth can be determined because there is no method of ascertaining how many affected pregnancies are aborted or stillborn. Any factor that affects rates of abortion or stillbirth may also affect the prevalence of cerebral palsy at birth without being of aetiological importance. Even the ascertainment of prevalence at birth is incomplete because it is impossible to recognise all cases of cerebral palsy among those infants who die.

The higher proportions of spontaneous abortion, stillbirth, and low birthweight infants in the obstetric history of the mothers of diplegic infants lend support to the observation made by Dejerine that the aetiological factors leading to diplegia were prenatal in onset as opposed to those leading to hemiplegia, which were postnatal.¹⁵ Freud, who first used the term cerebral diplegia, noted the difference in symptoms between that syndrome and hemiplegia; the former showed a diffuse bilateral

symmetrical defect of the brain whereas the latter showed a gross lesion.¹⁶ In this context infants with quadriplegia should be subdivided into those with diffuse lesions, and who can be classified with diplegic infants, and those who have double hemiplegia. If such a distinction cannot always be made on clinical examination, technological advances such as ultrasound scanning, computed tomography or magnetic resonance imaging may help to delineate more precisely the epidemiology of the cerebral palsies and allow the formulation of specific aetiological hypotheses.

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