Congenital anomalies as risk factors for cerebral palsy and for severity of impairments

KJERSTI POSTMYR JYSTAD[1]*
KRISTIN MELHEIM STRAND[1]*
SOLVEIG BJELLMO[2]
STIAN LYDERSEN[3]
KARI KLUNGSØYR[4,5]
MAGNE STOKNES[1]
JON SKRANES[1,6]
GURO L ANDERSEN[1,7]
TORSTEIN VIK[1]

1 Department of Laboratory Medicine, Children's and Women's Health, Norwegian University of Science and Technology (NTNU), Trondheim; **2** Department of Obstetrics and Gynecology, Møre and Romsdal Hospital Trust, Ålesund; **3** The Regional Centre for Child and Adolescent Mental Health, NTNU, Trondheim; **4** Department of Global Public Health and Primary Care, University of Bergen, Bergen; **5** Domain for Health Data and Digitalisation, Norwegian Institute of Public Health, Bergen; **6** Department of Paediatrics, Sørlandet Hospital, Arendal; **7** The Cerebral Palsy Register of Norway, Vestfold Hospital Trust, Tønsberg, Norway.

Correspondence to Kjersti Postmyr Jystad, Njords veg 26c, 7035 Trondheim, Norway.
E-mail: kjersti.jystad@gmail.com

*Shared first authorship

ABBREVIATIONS

CPRN	Cerebral Palsy Register of Norway
MBRN	Medical Birth Registry of Norway

ABSTRACT

AIM To study the prevalence of congenital anomalies among children with cerebral palsy (CP) born at term or late preterm, and if CP subtypes and clinical manifestations differ between children with and without congenital anomalies.

METHOD This was a cross-sectional study using data from the Cerebral Palsy Register of Norway and the Medical Birth Registry of Norway. All children with congenital CP born at and later than 34 weeks' gestation in Norway from 1999 to 2009 were included. Anomalies were classified according to the European Surveillance of Congenital Anomalies classification guidelines. Groups were compared using Fisher's exact test, Kruskal–Wallis test, and the Mann–Whitney *U* test.

RESULTS Among 685 children with CP, 169 (25%) had a congenital anomaly; 125 within the central nervous system. Spastic bilateral CP was more prevalent in children with anomalies (42%) than in children without (34%; p=0.011). Children with anomalies less frequently had low Apgar scores (p<0.001), but more often had severe limitations in gross- and fine-motor function, speech impairments, epilepsy, severe vision, and hearing impairments than children without anomalies (p<0.03).

INTERPRETATION Although children with CP and anomalies had low Apgar scores less frequently, they had more severe limitations in motor function and more associated problems than children with CP without anomalies.

What this paper adds

- One in four children with cerebral palsy born at term or late preterm has a congenital anomaly.
- The added value of neuroimaging to detect central nervous system anomalies in children with cerebral palsy.
- Children with anomalies have more severe motor impairments.
- More severe clinical manifestations are not explained by perinatal complications as indicated by low Apgar scores.

Cerebral palsy (CP) is an umbrella term for a number of disorders of movement and posture, caused by a permanent, non-progressive injury to the immature brain.[1] The motor disorders are often accompanied by epilepsy, impairments of cognition, hearing, and vision. The causes of CP are considered to differ between children born very prematurely (i.e. before week 32) and in those born at term or late preterm (34+0 to 36+6 weeks). Interestingly, as opposed to the general population, congenital anomalies are more frequent in children with CP born at term than in preterm children.[2,3] A recent systematic review concluded that the most important risk factors for congenital CP in children born at term include low birth weight, congenital anomalies, and birth asphyxia.[4]

Previous studies have reported a prevalence of congenital anomalies ranging from 12% to 30% in children with CP,[2,3,5,6] probably reflecting differences in reporting, as well as definitions of congenital anomalies. Moreover, many congenital brain anomalies are not identified in the neonatal period, and documentation of such anomalies is likely to increase with the use of magnetic resonance imaging (MRI). Previous studies have found that children with cerebral anomalies have more severe CP than children without congenital anomalies.[5,6] Whether children with non-cerebral anomalies have more severe CP than children without anomalies remains unclear.[6,7]

Using data from the Cerebral Palsy Register of Norway (CPRN) and from the Medical Birth Registry of Norway, we aimed to (1) assess the risk of CP in children with anomalies recognized at birth or in the neonatal period among children born at term or late preterm; (2) describe the prevalence of congenital anomalies among children with congenital CP in Norway; and (3) identify differences in CP subtypes, motor function, and associated impairments in children with and without congenital anomalies.

METHOD

Study design

This study, linking data from the CPRN with the Medical Birth Registry of Norway (MBRN), consists of two parts. Part one, which assessed the risk of CP in children with congenital anomalies, was a prospective population-based study including all

singleton babies with a gestational age from 34 to 43 weeks born in Norway between 1 January 1999 and 31 December 2009. Part two was a cross-sectional study of children with congenital CP from the same cohort, and assessed clinical characteristics in children with CP and congenital anomalies.

In part one of the study, we used data on congenital anomalies collected only through the MBRN. This register was established in 1967 and one of its aims is to monitor congenital anomalies and other adverse pregnancy outcomes. The register is based on compulsory notification of all births in Norway, and data are prospectively recorded.[8] Information on congenital anomalies is based on the newborn examination by a physician, usually a paediatrician, during the first days after birth. Since 1999, the MBRN also receives information from the neonatal intensive care units of all neonatal diagnoses, including congenital anomalies for infants transferred to such a unit after birth.

In part two of the study, we included data on congenital anomalies from the CPRN. In the CPRN, data on congenital anomalies are collected by clinicians working in the 21 child habilitation centres in Norway. Registration in the CPRN is consent based, and children are recorded in the register at the time when the diagnosis is suspected and after the diagnosis has been confirmed, detailed information is recorded when the children are 5 years old[9]. Linkage of the registers was done using the unique national identification number assigned to every child at birth.

Study participants

A flowchart of the study population is shown in Figure S1 (online supporting information). A total of 609 527 singleton babies with a gestational age between 34 and 43 weeks were born in Norway during the study period; 790 of these were registered with CP in the CPRN. Exclusion of children with postneonatal CP and children whose diagnoses were only suspected but had not yet been confirmed at 5 years of age (*n*=117), left 609 410 children for analysis, including 685 (1.1 per 1000) children with CP.

Study variables

Exposure variables

We defined and categorized congenital anomalies (hereafter referred to as 'anomalies') according to the European Surveillance of Congenital Anomalies classification guidelines[10] (accordance with these guidelines, only major anomalies were included. For example, patent ductus arteriosus and pulmonary artery stenosis are included as anomalies only in term infants (>37 weeks). Anomalies were divided into anomalies of the central nervous system (CNS) ('CNS anomalies') and anomalies outside the CNS ('non-CNS anomalies'). Children with both CNS and non-CNS anomalies were assigned to the group with CNS anomalies. In line with the European Surveillance of Congenital Anomalies guidelines, we calculated gestational age and sex-specific standard deviation (SD) scores for head circumference, and defined microcephaly as a head circumference greater than 3 SD below the mean.

Outcome variables

CP was classified according to the criteria proposed by the Surveillance of Cerebral Palsy in Europe into spastic unilateral, spastic bilateral, dyskinetic, ataxic, and non-classifiable CP.[11] Severity of CP was evaluated based on CP subtype and gross- and fine-motor function, as well as by presence of the associated impairments feeding difficulties, impairments of speech, severe hearing and visual impairments, and epilepsy.

Gross-motor function was classified according to the Gross Motor Function Classification System,[12] and fine motor function according to the Bimanual Fine Motor Function system.[13] Speech function was classified using a scale developed by the CPRN into normal, slightly indistinct, indistinct, very indistinct, and no speech.[14] Although this scale has not been validated, it has provided the basis for the development of the Viking speech scale.[15] Severe vision impairment was defined as being blind, that is having a best-corrected visual acuity of less than 6/60 (<0.1) on the best eye.[14] Severe hearing impairment was defined as a loss of hearing of greater than 70 dB before correction on the best ear.[14]

Information on the use of antiepileptic drugs (yes or no) was used to identify children with active epilepsy, and the presence of gastrostomy (yes or no) was used as a proxy for severe feeding difficulties.

Covariates

From the birth registry, we obtained data on the mothers (age and parity), pregnancies (gestational age, mode of delivery, and multiple pregnancies), and neonates (sex, birth weight, birth length, head circumference at birth, and Apgar scores). Small for gestational age was defined as a birth weight greater than 2 SD below the mean, calculated according to Norwegian sex and gestational age-specific values for singletons.[16]

Statistical analysis

SPSS Statistics version 21 (IBM, Armonk, NY, USA) was used to analyse the data. $p<0.05$ were considered statistically significant. We used logistic regression to estimate odds ratios with 95% confidence intervals (CIs) for CP in children with congenital anomalies vs children without anomalies. In these analyses, odds ratios were close approximations to relative risks. Fisher's exact test was used to analyse differences in proportions between three groups, and if the result was statistically significant we proceeded with Fisher's exact test to decide which groups differed. Similarly, we used the Kruskall–Wallis test and the Mann–Whitney *U* test for ordinal variables. This procedure preserves the family-wise error rate when comparing three groups.[17] CIs for a proportion were calculated using the Wilson Score method, as recommended by Newcombe and Altman.[18]

Ethics

The study was approved by the Regional Committee for Medical and Health Research Ethics in mid-Norway (reference number 046-02). Parents provided written informed consent allowing their children to be registered in the CPRN and to link data to the MBRN.

RESULTS

The risk of CP in children with congenital anomalies

Among 609 410 children born in Norway between 1999 and 2009, 15 714 (2.6%) had a major congenital anomaly recorded in the MBRN. Table SI (online supporting information) shows maternal and infant characteristics of children with and without a congenital anomaly. A higher proportion of children with anomalies was born in breech position (7% vs 3%), twice as many were born small for gestational age (3.7% vs 1.5 %), and children with anomalies had lower Apgar scores at 5 minutes vs children without anomalies.

Of 15 714 children with anomalies registered in the MBRN, 76 were diagnosed with CP (4.8 per 1000) resulting in a nearly fivefold increased risk of CP compared with children without anomalies (Table I). The risk of CP associated with anomalies in specific organ systems is shown in Table I. Anomalies of the CNS were associated with a 90-fold increased risk of CP. In particular, among 111 children with congenital hydrocephalus, 25 had CP. Cardiac anomalies and anomalies of the digestive tract were also associated with increased risk of CP (Table I).

Clinical characteristics in children with CP and congenital anomalies

At 5 years of age, a further 93 children with CP had been diagnosed with a congenital anomaly, in addition to the 76 diagnosed at birth. Thus, among 685 children with CP, 169 (24.7%; 95% CI 21.6%–28.0%) had a congenital anomaly. Anomalies of the CNS were present in 125 (18.2%; CI 15.5%–21.3%) children, and 22 of these also had a non-CNS anomaly (Table II). The most common CNS anomalies were hydrocephalus, congenital cerebral cysts, and anomalies of the corpus callosum.

Maternal age, small for gestational age status, and sex did not differ between children with or without anomalies (Table SII, online supporting information). Children with anomalies had slightly lower mean gestational age and birth weight than children without anomalies (Table SII), whereas birth length and head circumference at birth did not differ between the groups (data not shown). Rates of caesarean section were 30% in children both with and without anomalies, but children with anomalies

were less often delivered by emergency caesarean section, and 88% of them had Apgar scores at 5 minutes between 7 and 10 vs 72% among children without anomalies ($p<0.001$, Mann–Whitney *U* test) (Table SII).

The spastic unilateral CP subtype was less prevalent, whereas the spastic bilateral CP subtype was more prevalent in children with anomalies than in children without (Table III). A similar difference was found between children with CP and CNS anomalies vs children with CP without anomalies, but the difference in the distribution of CP subtypes between these two groups did not reach statistical significance (Table IV). In contrast, the distribution of CP subtypes differed significantly between children with non-CNS anomalies and children without ($p=0.001$; Table IV). Interestingly, 18% of the children with non-CNS anomalies had dyskinetic CP vs 9% of children without anomalies. The proportion of children with Apgar scores between 7 and 10 was lower in children with non-CNS anomalies (75.0%) and in children without anomalies (71.2%) vs children with CNS anomalies (92.7%) ($p<0.001$, Kruskall–Wallis test).

Children with CP and anomalies had more severe gross- and fine-motor impairments ($p=0.004$ and $p=0.013$, respectively), poorer speech function ($p=0.001$), and a higher proportion had epilepsy ($p<0.001$) and severe vision and hearing impairments ($p=0.001$ and $p=0.017$, respectively) than children without anomalies (Table V). The same differences were found when we compared children with CNS anomalies with children without anomalies (Table V). In addition, the prevalence of gastrostomy was higher in children with CNS anomalies than in children without anomalies (Table V). Children with non-CNS anomalies displayed a similar distribution of gross- and fine-motor function, as well as speech function and severe hearing impairment, as children with CNS anomalies, but compared to children without anomalies, the difference in distribution reached statistical significance only for severe hearing impairment (Table V). In contrast to children with CNS anomalies, children with non-CNS anomalies had a similar prevalence of epilepsy and severe vision impairment as children without anomalies (Table V).

DISCUSSION

We found that term or late preterm born babies with congenital anomalies recognized at birth or in the neonatal period had a fivefold increased risk of CP. While approximately every tenth child with CP was diagnosed with a congenital anomaly in the neonatal period, this was the case for every fourth child with CP at the age of 5 years. The subtype spastic unilateral CP was less prevalent, while spastic bilateral CP was more prevalent in children with anomalies than in children without. It is, however, noteworthy that a relatively high proportion of children with non-CNS anomalies had dyskinetic CP. Furthermore, children with CP and anomalies had more severe motor impairments and were more likely to have associated impairments than children with CP without anomalies. It may also be noteworthy that children with CP and anomalies had higher Apgar scores than children with CP without anomalies.

Strengths and limitations

A strength of this study is the prospective recording of data in the MBRN and that the diagnosis of CP was confirmed when the children were at least 5 years old. Further, the study was restricted to term or late preterm born singletons to exclude confounding by multiple birth and by very or moderately preterm birth. Low *p*-values were obtained for most of the results. However, caution is needed when interpreting results with *p*-values between $p<0.05$ and $p<0.01$ owing to multiple comparisons. Nonetheless, most of the findings were highly statistically significant; moreover, the results were all in the same direction. We therefore consider it unlikely that chance findings explain the main results. Although children with non-CNS anomalies had more severe motor- and associated impairments than children without anomalies, most of these results did not reach statistical significance. The latter is probably owing to the low number of children with non-CNS anomalies, and these results should be interpreted with caution.

The CPRN registers children with CP from all over Norway, and the national material is a strength of our study. During the observation period, approximately 81% of children with CP in Norway were included in the CPRN, and a validation study has indicated that the distribution of CP subtypes in the CPRN is unbiased.[19] Similarly, the MBRN covers the entire population of newborn infants. A weakness of the study

is that the MRI images of the children were interpreted by different radiologists working at different hospitals. It makes some variation in how the images were interpreted possible, and could thus theoretically influence how malformations of the CNS were reported.

Information on anomalies was collected both from the CPRN and the MBRN. Out of the total of 169 children registered with a congenital anomaly, 24 were identified exclusively through the MBRN (mainly non-CNS anomalies), whereas 93 were identified exclusively through the CPRN. Thus, the use of information from both registers increased case ascertainment and is a strength of the study.

Comparison with other studies

Using data on anomalies only from the MBRN, we found a fivefold increased risk of CP in children with anomalies recognized at birth or in the neonatal period.

The proportion of children with CP and anomalies in this study (24.7%; 95% CI 21.6%–28.0%) is higher than has been found in previous studies by Rankin et al. (15%),[5] Pharoah (11%),[20] Garne et al. (12%),[3] and Croen et al. (19%),[2] but lower than reported by Blair et al. (32%).[6] Variations in ascertainment and inclusion criteria between studies can most likely explain much of the discrepancy. In contrast to our study, Blair et al. also included minor anomalies.[6] Pharoah[20] and Garne et al.[3] relied on data only from CP registers. Rankin et al. used data both from anomaly registers and CP registers;[5] however, in their study only 20% of the children with CP had been examined with cerebral MRI.[21] In our study, 87% of children with CP and anomalies and 82% of children with CP without anomalies underwent cerebral MRI, probably partly explaining the high prevalence of anomalies in our study. Moreover, previous studies including very preterm born children found a higher proportion of anomalies in those born at or near term vs more preterm born children.[3,5] Thus, as we only included children born at 34 weeks and later, this could, to some extent, explain the higher prevalence of anomalies found in our study compared with most previous studies.

Approximately three out of four children (75%) with CP with anomalies had an anomaly of the CNS, and this is similar to what has been observed in the studies by

Rankin et al. (80%)[5] and Garne et al. (72%).[3] In these and other studies, microcephaly and hydrocephalus were the most common cerebral malformations. However, in our study the most common CNS anomalies were hydrocephalus, cystic anomalies of the brain, and anomalies of the corpus callosum. Diagnosing and interpreting hydrocephalus may be difficult, as hydrocephalus does not have to be present before birth as a congenital anomaly but can result from brain injuries during or after birth. This is mostly a problem in very preterm born children, owing to posthaemorrhagic hydrocephalus. In our study 25 of the 34 children with hydrocephalus were diagnosed at birth, and as we only included children born at 34 weeks and later we consider misclassification of postneonatal-acquired hydrocephalus as congenital hydrocephalus unlikely to be a significant problem in our study. In accordance with previous studies, the most common non-CNS anomaly in our study was cardiac anomaly.[5,6]

Garne et al.[3] and Rankin et al.[5] have previously found increased risks for ataxic CP in children with cerebral anomalies compared with children without anomalies. In our study, however, spastic bilateral CP was more prevalent in children with CNS anomalies than in children without (44% vs 34%), and dyskinetic CP was twice as prevalent in children with non-CNS anomalies than in children without anomalies (18% vs 9%). In contrast to Garne et al.[3] and Rankin et al.,[5] we included only term and near-term children, and a different distribution of cerebral anomalies could explain the difference. Although our study is the smallest of these three, the study by Rankin et al. included only 24 children with ataxic CP.[5] Garne et al. relied on CP registries to collect data on malformations,[3] whereas we used data from both the CPRN and the MBRN, which may have increased ascertainment. Our results are likely in line with those of Blair et al. reporting that the association between cerebral anomalies and CP was strongest for the CP subtypes with the most extensive involvement, including spastic quadriplegia.[6]

In accordance with our findings, Rankin et al.[5] and Blair et al.[6] found that children with CNS malformations had more severe CP than children without malformations. Towsley et al. also found cerebral malformations to be significantly associated with the presence of comorbidities.[22] Some studies have suggested that children with cerebral malformations may tolerate birth less well than children without malformations, leading to an increased risk of further brain damage resulting in a more severe CP.[3,23] However, in our study children with anomalies, in particular those with

CNS anomalies, had higher Apgar scores at 5 minutes than children without anomalies. This could be in line with McIntyre et al.,[24] who reported that congenital anomalies were present in over half of children with CP who did not have hypoxic-ischaemic encephalopathy. Thus, our results suggest that congenital brain anomalies per se have more serious consequences for later function than other aetiologies of CP, unrelated to perinatal events.

Among children with non-CNS anomalies, the dyskinetic CP subtype was more prevalent, and the proportion of children with low Apgar scores was similar to children with CP without anomalies. This finding suggests that in this group perinatal events may play a larger role in the causal chain leading to CP, than for children with CNS anomalies. The distribution of gross- and fine-motor function, as well as speech function and severe hearing impairment, was similar to children with CNS anomalies, but only hearing impairment differed significantly from children without anomalies. We believe this is owing to low statistical power and consider our findings in line with those of Blair et al.,[6] reporting an increased risk for severe CP and associated impairments also in children with non-CNS anomalies. In contrast to Blair et al.,[6] we found no increase in epilepsy or severe vision impairment in children with non-CNS anomalies.

Clinical implications

Our results suggest that a high proportion of children with CP born at term or late preterm have congenital anomalies (25%), and that three of four such anomalies are within the CNS. Thus, our findings support that cerebral MRI should be included as a diagnostic tool in all children with CP. Furthermore, it suggests that particular caution is required when interpreting causes of CP in the absence of cerebral imaging. Moreover, our study highlights the importance of gathering information on congenital anomalies on CP children from multiple sources in prevalence studies.

In light of the more severe motor and associated impairments found in children with CNS anomalies, we would encourage future studies of early-intervention programs in children with CP to include a description of the proportion of children

with anomalies. This would enable assessment of whether the effectiveness of intervention may be influenced by the presence of anomalies.

Conclusion

Congenital anomalies are recognized as a major contributor to CP in children born at term or late preterm. Children with CP and cerebral anomalies have more impaired gross-motor function and more often associated problems than children with CP without anomalies. Our results suggest that this may be true also for children with CP and non-cerebral anomalies. Our results did not support the notion that the more severe clinical manifestations of CP among those with CNS anomalies were caused by perinatal events.

Supporting information

The following additional material may be found online:

Table SI: Maternal and infant characteristics where the child was diagnosed with or without a congenital anomaly in the Medical Birth Registry of Norway.

Table SII: Maternal and infant characteristics in children with cerebral palsy with and without congenital abnormalities.

Figure S1: Study population.

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Table I: Odds ratios (OR) with 95% confidence intervals (CI)[a] for cerebral palsy (CP) in children with congenital anomalies recorded in the Medical Birth Registry of Norway (MBRN)

	CP		
	Yes (*n*=685)	No (*n*=608 725)	
	n (%)	*n* (%)	OR (95% CI)
Congenital anomaly recorded in the MBRN			
Yes	76 (11)	15638 (3)	4.7 (3.7–6.0)
No	609 (89)	593 087 (97)	
CNS anomaly			
Yes	36 (5)	375 (0.1)	90 (63.4–128)
No	649 (95)	608 350 (99.9)	
Hydrocephalus			
Yes	25 (4)	86 (0.01)	268 (171–421)
No	660 (96)	608 639 (99.99)	
Cardiac anomaly			
Yes	25 (4)	5361 (1)	4.3 (2.9–6.4)
No	660 (96)	603 364 (99)	
Chromosome anomaly			
Yes	4 (1)	966 (0.2)	3.6 (1.3–9.9)
No	681 (99)	607 759 (99.8)	
Abdominal wall anomaly			
Yes	0 (0)	199 (0.03)	NA

No	685 (100)	608 526 (99.97)	
Digestive anomaly			
Yes	7 (1)	707 (0.1)	8.9 (4.2–18.8)
No	678 (99)	608 018 (99.9)	

[a]Logistic regression analyses. CNS, central nervous system; NA, not applicable.

Table II: Congenital anomalies among 169 Norwegian children with cerebral palsy born in the period 1999–2009

CNS anomalies[a]	*n* (%)	Non-CNS anomalies	*n* (%)
Hydrocephalus	34 (27)	Heart anomalies	18 (41)
Anomalies of the corpus callosum	15 (12)	Syndromes[b]	9 (20)
Congenital cerebral cysts	15 (12)	Muscle-skeleton anomalies	6 (14)
Microcephaly	11 (9)	Urogenital anomalies	4 (9)
Holoprosencephaly	3 (2)	Gastrointestinal anomalies	2 (5)
CNS anomalies outside the brain[c]	2 (2)	Eye anomalies	2 (5)
Other[d]	39 (31)	Airway anomalies	1 (2)
Unspecified	6 (5)	Other[e]	2 (5)
Total	125 (100)	Total	44 (100)

[a]Twenty-two of the 125 children (17.6%) with central nervous system (CNS) anomalies also had non-CNS anomalies. These included five children with heart anomalies, four with gastrointestinal anomalies, three with eye anomalies, three with urogenital anomalies, one with musculoskeletal anomalies, four with syndromes, one with cleft hard platelet, and one with anomalies in the liver. [b]Down syndrome, other specified chromosome abnormalities, Potter syndrome, Aicardi syndrome, deletion of short arm of chromosome 5 and ring chromosome 13. [c]Spina bifida and syringomyelia. [d]Other specific anomalies of the brain, other unspecified anomalies of the brain, other reduction deformities of the brain, septo-optic dysplasia, microgyria, macrocephaly, Arnold Chiari syndrome and brain tumour, unspecified. [e]Incontinetia pigmenti, renal agenesis.

Table III: Comparison of the distribution of cerebral palsy (CP) subtypes in children with or without congenital anomalies born at ≥34 weeks' gestation in Norway, 1999–2009

	Congenital anomaly		
	Present (*n*=169)	Absent (*n*= 516)	*p*[a]
CP subtype[a]			
Spastic unilateral	65 (38)	264 (51)	
Spastic bilateral	71 (42)	176 (34)	
Dyskinetic	16 (9)	47 (9)	0.011
Ataxic	12 (7)	27 (5)	
Unclassified	4 (2)	2 (0)	

Data are *n* (%). [a]Fisher's exact test for difference in proportions between the groups. [b]One missing in the congenital anomaly present group.

Table IV: The distribution of cerebral palsy (CP) subtypes among children born at ≥34 weeks' gestation, 1999–2009, with central nervous system (CNS) anomalies, with non-CNS anomalies, and without anomalies

	Congenital anomaly					
	CNS-anom-aly (*n*=125)	Non-CNS anom-aly (*n*=44)	No anom-aly (*n*=516)	*p*[a]	*p*[b]	*p*[c]
CP sub-types[d]						
Spastic unil	51 (41)	14 (32)	264 (51)			

ater al						
Spa stic bi- lat- eral	55 (44)	16 (36)	176 (34)			
Dy ski- neti c	8 (7)	8 (18)	47 (9)	0.0 02	0.102	0.001
Ata xic	9 (7)	3 (7)	27 (5)			
Un- clas si- fied	1 (1)	3 (7)	2 (0)			

Data are *n* (%). [a]Fisher's exact test for difference in proportion between the groups. [b]Fisher's exact test between the CNS-anomaly and no-anomaly group. [c]Fisher's exact test between the Non-CNS anomaly and no-anomaly group. [d]One missing in the CNS anomaly group.

Table V: Gross- and fine-motor function and associated impairments among children with cerebral palsy (CP) born at ≥34 weeks' gestational age, 1999–2009, with central nervous system (CNS) anomalies, with non-CNS anomalies, and without anomalies

	Co nge nita l ano mal y					

	CNS anomaly (*n*=125)	Non-CNS anomaly (*n*=44)	No anomaly (*n*=516	p^a	p^b	p^c
GMFCS[d]						
Level I–II	75 (62)	25 (61)	375 (75)			
Level III	8 (6)	3 (7)	19 (4)	0.006	0.004	0.067
Level IV–V	39 (32)	13 (32)	108 (21)			
MACS[e]						
Level I–II	66 (60)	24 (65)	337 (73)			
Level III	17 (15)	4 (11)	35 (7)	0.036	0.013	0.334
Level IV–V	28 (25)	9 (24)	91 (20)			
Speech function[f]						

Normal/slightly indistinct	63 (52)	22 (54)	339 (69)			
Indistinct	15 (12)	7 (17)	37 (8)	0.001	0.001	0.072
Very indistinct/no speech	43 (36)	12 (29)	114 (23)			
Epilepsy[g]						
No	70 (57)	33 (81)	380 (77)	<0.001	<0.001	0.702
Yes	52 (43)	8 (19)	113 (23)			
Severe visual impairment[h]						
No	100 (90)	35 (97)	453 (98)	0.003	0.001	1.0
Yes	11 (10)	1 (3)	11 (2)			
Severe hearing impairment[i]						
No	108 (95)	35 (92)	458 (99)	0.013	0.017	0.024
Yes	6 (5)	3 (8)	6 (1)			

Gastrostomy[j]						
No	95 (80)	40 (95)	442 (88)	0.025	0.018	0.209
Yes	24 (20)	2 (5)	59 (12)			

Data are *n* (%). [a]Kruskal Wallis test for differences in proportions between the three group. [b]Mann–Whitney test between the CNS anomaly group and the no-anomaly group. [c]Mann–Whitney test between the non-CNS anomaly group and the no-anomaly group. [d]Three missing in the CNS anomaly group, three in the non-CNS anomaly group, and 14 in the no anomaly group. [e]Fourteen missing in the CNS anomaly group, seven in the non-CNS anomaly group, and 53 in the no anomaly group. [f]Four missing in the CNS anomaly group, three in the non-CNS anomaly group, and 26 in the no anomaly group. [g]Three missing in the CNS anomaly group, three in the non-CNS anomaly group, and 23 in the no anomaly group. [h]Fourteen missing in the CNS anomaly group, eight in the non-CNS anomaly group, and 52 in the no anomaly group. [i]Eleven missing in the CNS anomaly group, six in the non-CNS anomaly group, and 52 in the no anomaly group. [j]Six missing in the CNS anomaly group, two in the non-CNS anomaly group, and 15 in the no anomaly group.

Supporting information

The following additional material were in the original article found online:

Table S1: Maternal and infants' characteristics where the child was diagnosed with or without a congenital anomaly (CA) in the Medical Birth Registry of Norway (MBRN).

	Congenital anomaly				
	Present N=15 714	% (100)	***Absent N= 593 696***	% (100)	p-value
Maternal age[a]					
≤19 year	363	(2)	14 088	(2)	
20-34 year	12 306	(78)	481 153	(81)	
≥35 year	3045	(20)	98 422	(17)	<0.001
Parity					
Nullipara	6685	(43)	243 146	(41)	<0.001
Multipara	9029	(57)	350 550	(59)	
Caesarean delivery[b]					
Planned	1428	(42)	32 622	(40)	
Acute	1993	(58)	49 847	(60)	0.011
Position					
Cephalic	14 298	(91)	567 665	(96)	
Breech	1157	(7)	19 139	(3)	
Transverse lie/other	259	(2)	6892	(1)	<0.001
Small-for gestational age (SGA)[c]					
Yes	579	(3.7)	8895	(1.5)	<0.001
Sex[d]					
Male	8637	(55)	303 922	(51)	<0.001
Female	7076	(45)	285 770	(49)	
Apgar score at 5 min[e]					

0-3	198	(1)	2107	(0.4)	
4-6	792	(5)	10706	(1.8)	
7-10	14 679	(94)	579 442	(97.8)	<0.001

[a] 33 missing in the absent group.
[b] 12293 missing in the CA present group and 511 227 in the absent group.
[c] 56 missing in the CA present group and 440 in the absent group.
[d] 1 missing in the CA present group and 4 in the absent group.
[e] 45 missing in the CA present group and 1441 in the absent group.

Table SII: Maternal and infant characteristics in children with cerebral palsy with and without congenital abnormalities.

Table S2: Maternal and infants' characteristics in children with cerebral palsy with and without congenital anomalies.

	Congenital anomaly			
	Present n=169	% (100)	***Absent n= 516***	% (100)
Maternal age				
≤19 year	6	(4)	13	(3)
20-34 year	120	(71)	404	(78)
≥35 year	43	(25)	19	(19)
Parity				
Nullipara	65	(43)	254	(49)
Multipara	104	(62)	262	(51)
Caesarean delivery[a]				
Planned	18	(37)	17	(11)
Acute	31	(63)	141	(89)
Position				
Cephalic	154	(91)	490	(95)
Breech	15	(9)	16	(3)
Transverse lie/other	0	(0)	10	(2)

Small-for gestational age (SGA)[b]				
Yes	13	(7.7)	34	(6.7)
Birthweight, mean (SD)	3300	(645)	3438	(673)
Gestational age in weeks, mean (SD)	38.7	(2.2)	39.2	(2.0)
Sex				
Male	94	(56)	305	(59)
Female	75	(44)	211	(41)
Apgar score at 5 min[c]				
0-3	5	(3)	53	(10)
4-6	15	(9)	92	(18)
7-10	147	(88)	367	(72)

SD, standard deviation
[a] 120 missing in the CA present group and 358 in the absent group.
[b] 9 missing in the absent group.
[c] 2 missing in the CA present group and 4 in the absent group.

Figure S1: Study population.