Official Journal of the European Paediatric Neurology Society

Original article

Cerebral palsy: Phenotypes and risk factors in term singletons born small for gestational age

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ARTICLE INFO

Article history:
Received 18 June 2014
Received in revised form
3 December 2014
Accepted 9 December 2014

Keywords:
Cerebral palsy
Intra-uterine growth restriction

ABSTRACT

Background and objectives: Children born small for gestational age (SGA) are at increased risk of developing cerebral palsy (CP). The pathophysiology behind this association remains unclear. We compare the clinical profile of children with CP born SGA to other children with CP. We hypothesize that differences noted will support antenatal causes of CP in children born SGA.

Methods: We conducted a retrospective cohort study of term singletons with CP, extracting data from the Canadian Cerebral Palsy Registry. SGA was determined as birth weight for gestational age and sex below the tenth percentile.

Results: Mothers of children with CP born SGA were more likely to be of African-American ethnicity (RR 2.54, 95% CI 1.20–5.39), have intrauterine infections (RR 2.22, 95% CI 1.09–4.50) and have gestational hypertension (RR 1.78, 95% CI 1.06–3.00). Children with CP born SGA had smaller head circumferences at birth ($p < 0.001$) and higher frequencies of emergency cesarean-section (RR 1.53, 95% CI 1.22–1.92), birth asphyxia (RR 1.53, 95% CI 1.0–2.32), and placental abnormalities (RR 1.45, 95% CI 1.00–2.10). Children with CP born SGA had greater fine motor (RR 1.46, 95% CI 1.02–2.11), gross motor (RR 1.53, 95% CI 1.12–2.10) and communication impairment (RR 1.24, 95% CI 1.10–1.40), and a higher frequency of cognitive impairment (RR 1.33, 95% CI 1.06–1.69).

Conclusion: Children with CP born SGA have different clinical factors and phenotypic profiles than other children with CP. These differences support the hypothesis of antenatal and perinatal causes of CP in children born SGA. Future case control studies would be desired to further define this causal pathway.

Abbreviations: CP, cerebral palsy; GMFCS, gross motor function classification system; IQ, intellectual quotient; IUGR, intra-uterine growth restriction; MACS, manual ability classification system; NE, neonatal encephalopathy; PW/BW ratio, placental weight to birth weight ratio; SGA, small for gestational age.

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http://dx.doi.org/10.1016/j.ejpn.2014.12.005
1090-3798/

1. Introduction

Cerebral palsy (CP) is the most common cause of motor impairment in childhood affecting approximately 2 in 1000 live-born children.[1] CP is characterized by multiple co-morbidities which contribute to the overall high burden of disease.[2] Children born small for gestational age (SGA) are recognized to be at increased risk for both neonatal encephalopathy (NE) and CP,[3–9] with multiple theories proposed on the possible causal pathways. Although an antenatal insult affecting both brain and intrauterine development is possible,[9] children born SGA are also at increased risk of adverse perinatal events which can also contribute to the development of CP. In a cohort of term singleton children with CP, we set out to investigate differences in clinical profiles between children born SGA and other children with CP. We hypothesize that children born SGA will have greater prenatal risk factors with a similar phenotypic severity than other children with CP.

2. Methods

We conducted a retrospective cohort study of term singleton children with a diagnosis of CP. Cases were extracted from the Canadian Cerebral Palsy Registry, which includes participating centers from the following provinces: British Columbia, Alberta, Ontario, Quebec, Nova Scotia, and Newfoundland. The diagnosis of CP was established at 2 years of age based on a consensus definition,[10] and was confirmed when possible at a follow-up appointment at 5 years of age along with updates on co-morbidities and standardized motor function classifications. Information regarding the pregnancy and delivery was obtained by interview with the mothers and review of the maternal chart. Information was also gathered about perinatal history, CP profile and co-morbidities through review of the children's charts.[2,11] Consent was obtained from the parents at the interview before inclusion in the registry and ethics approval was obtained from all sites prior to registry enrollment.

In this study, we included singleton children born at term, as defined by a gestational age of 37 weeks or more at delivery, with a birth weight and gestational age recorded. Growth for gestational age was determined for these patients using data from the Canadian Reference for birth weight for gestational age.[12] SGA was defined as a birth weight for gestational age falling below the 10th percentile by gestational age and sex for singletons, including both symmetric and asymmetric growth restriction (Fig. 1).

Variables were extracted from the registry regarding antenatal and perinatal factors, CP profiles and co-morbidities. Intrapartum asphyxia was defined as the presence of moderate or severe neonatal encephalopathy accompanied by at least 3 of the following: an apgar score below 6 at 5 min, a cord pH below 7.0, a base excess above 12, an abnormal fetal heart rate on antenatal cardiac monitor (tachycardia > 160 beats/minute or bradycardia < 120 beats/minute), presence of meconium, need for intubation, delay in spontaneous respiration, need for resuscitation, multisystemic involvement, or abnormal imaging results suggestive of acute hypoxic ischemic changes. Placental weight was also noted, and a placental to birth weight ratio (PW/BW ratio) was calculated. These ratios were then classified into percentiles, according to the latest Canadian reference standards.[13]

Children were assessed at 2 years of age or older, and re-assessed by 5 years of age to update their motor ability profile (GMFCS and MACS) as well as presence of comorbidities. Cognitive assessment is usually done after 4 years of age. The method of assessment is entered in the registry, however various scales were used across centers. When available, the severity of the cognitive impairment was also captured, as determined by the available psychology evaluation in the child's chart. Difficulties in communication were captured in the registry based on evaluations in speech pathology available in the child's chart. The registry captured whether or not communication difficulties are present, and further specify if

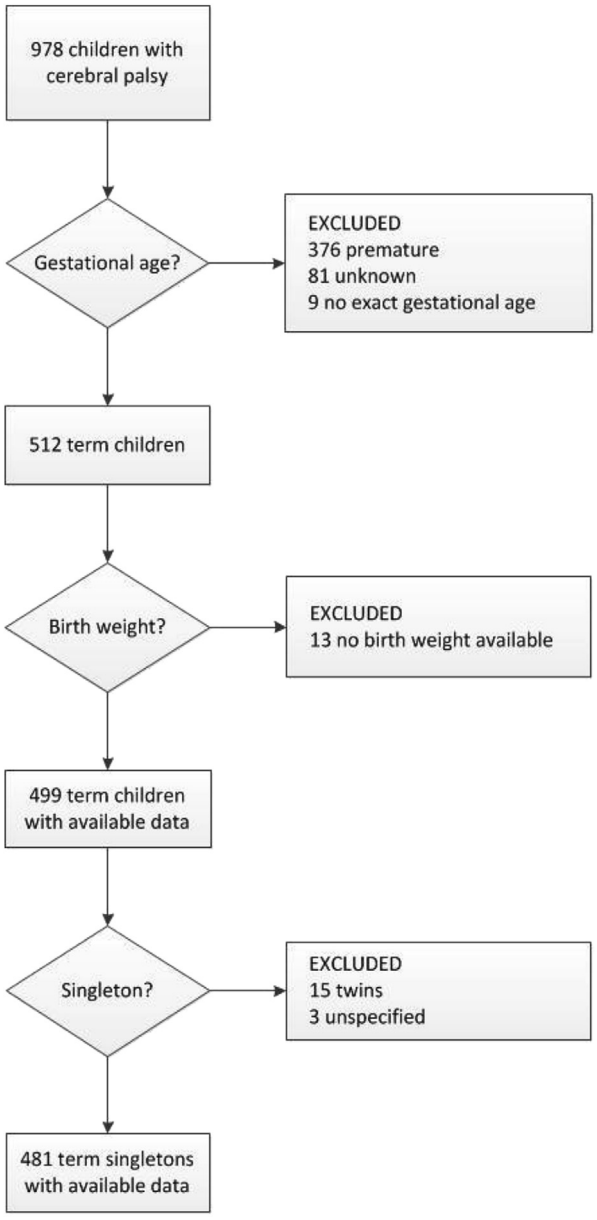

Fig. 1 – Selection process.