Associations between antenatal and perinatal risk factors and cerebral palsy: a Swedish cohort study

Anna Jöud,1 Andréa Sehlstedt,1 Karin Källén,2 Lena Westbom,3 Lars Rylander1

ABSTRACT

Objectives To investigate known and suggested risk factors associated with cerebral palsy in a Swedish birth cohort, stratified by gestational age.

Setting Information on all births between 1995 and 2014 in Skåne, the southernmost region in Sweden, was extracted from the national birth register.

Participants The cohort comprised a total of 215 217 children. Information on confirmed cerebral palsy and subtype was collected from the national quality register for cerebral palsy (Cerebral Palsy Follow-up Surveillance Programme).

Primary and secondary outcome measures We calculated the prevalence of risk factors suggested to be associated with cerebral palsy and used logistic regression models to investigate the associations between potential risk factors and cerebral palsy. All analyses were stratified by gestational age; term (≥37 weeks), moderately or late preterm (32–36 weeks) and very preterm (<32 weeks).

Results In all, 381 (0.2 %) children were assigned a cerebral palsy diagnosis. Among term children, maternal preobesity/obesity, small for gestational age, malformations, induction, elective and emergency caesarian section, Apgar <7 at 5 min and admission to neonatal care were significantly associated with cerebral palsy (all p values<0.05). Among children born moderately or late preterm, small for gestational age, malformations, elective and emergency caesarian section and admission to neonatal care were all associated with cerebral palsy (all p values <0.05), whereas among children born very preterm no factors were significantly associated with the outcome (all p values>0.05).

Conclusion Our results support and strengthen previous findings on factors associated with cerebral palsy. The complete lack of significant associations among children born very preterm probably depends on the small number of children with cerebral palsy in this group.

INTRODUCTION

Cerebral palsy (CP) is one of the most common physical disabilities in children, with a prevalence of 2–2.5 per 1000 live births. There is usually a large gap in time from the occurrence of the brain damage until a CP diagnosis can be verified, which complicates the study of possible aetiologies.

The total prevalence of CP in the developed world has been relatively stable since the 1950s, although the distribution of different CP subtypes and severity levels have changed during the decades. Increased survival of newborns in successively earlier gestational age, with initially high incidences of cerebral insults, contributed to an increasing CP prevalence during a period. Lately, a decreased CP prevalence has been seen in several gestational age groups. A better understanding of the aetiology and risk factors for CP would hopefully result in more preventive measures. A decrease in the number of cases would be of immense benefit on the individual as well as on the socioeconomic level.

Birth asphyxia was long thought to be the main cause of CP. Although the definition of birth asphyxia has varied, it has often been based on different non-specific clinical signs, not taking into account that a newborn infant has a very limited range of responses. A study investigating 23 papers on intrapartum risks of CP found that the definitions of birth asphyxia as well as CP were heterogeneous and concluded that confusion of proximal effects with causes have overestimated the association between birth asphyxia and CP.

Many other risk factors have been identified...
and it is now widely agreed on that the aetiology of CP is multifactorial and that birth asphyxia is one of many associated factors, including not only perinatal, but also antenatal and postnatal factors. Some of these factors may be causal, while some may be a part of a series of events that together may be causal. Some factors may not be causal but predictive, or simply signs that the well-being of the fetus or neonate is somehow compromised.

Many antenatal and perinatal factors associated with CP are modified by gestational age. Therefore, stratifying analyses on gestational age can help to clarify the importance of different risk factors within different gestational ages.

The aim of the present study was to, within one birth cohort, investigate multiple known and suggested factors associated with CP stratified by gestational age.

METHOD

Data sources

Information about all children born in Skåne (the southernmost county in Sweden with a population of 1 286 584 in December 2014) in 1995–2014 was identified from the regional medical birth register Perinatal Revision South (PRS). In Sweden, maternal healthcare and delivery service is free of charge and almost all women attend antenatal care. PRS contains obstetric and neonatal data on all children born in the Southern Healthcare Region of Sweden, since 1995. Information about CP diagnoses was retrieved from the Cerebral Palsy Follow-up Surveillance Programme (CPUP) in December 2016. CPUP was created in 1994 and Skåne was part of the register from the start. It was approved as a national healthcare quality register by the Swedish National Board of Health and Welfare in 2005. CPUP uses the definition of CP recommended by Surveillance of Cerebral Palsy Europe (SCPE). Validation of the CP diagnosis and subtype classification for children born in 1994–2012 has been performed by one paediatric neurologist, LW, in cooperation with the patients’ doctor. Information about congenital malformations and syndromes were extracted from both PRS and CPUP. Certain minor abnormalities were excluded (preauricular appendices, single umbilical artery, minor skin malformations and undescended testicles).

Source population

The source population consists of all children born in Skåne between the years 1995 and 2014. There were 250,629 registered births during this 21 years study period. Multiple births, those with unknown gestational age or gestational age registered as <20 or ≥43 weeks, children with unknown birth weight or birth weight more than 5 SD from the mean, stillbirth/perinatal death as well as children who were born after 2012 (since their CP diagnosis had not yet been validated in accordance with the follow-up programme and did not have a determined subtype), were excluded from the study. This left a cohort of 215,217 children of whom 381 had CP that was not due to postnatally acquired brain injury (figure 1).

Statistical analyses

The children were grouped into three categories based on gestational age: term (week ≥37 + 0), moderately or late preterm (week 32–36 +6) and very preterm (week <32) births. Descriptive analyses were carried out to investigate the proportion of each of the suggested CP-associated factors. To examine the strength of the association between the factors and CP, we used univariate logistic regression generating ORs and 95% CIs. If there were less than 10 individuals in the CP or no CP group, univariate logistic regression analysis was not performed. The variables that were statistically significantly (p<0.05) associated with CP in the respective gestational age group, were included in the multivariable models. The first model investigated the association between the antenatal factors and CP. In the second model, perinatal factors were added, to elucidate to what extent the antenatal risk scores were mediated by those factors.

All statistical analyses were performed in Stata Statistical Software: release V.14.

PATIENT AND PUBLIC INVOLVEMENT

In this study, no patient or public involvement took place.

RESULTS

Out of the 215,217 children included in the study (figure 1), 206,618 (96 %) were born at term, 7,355 (3.4 %) where born moderately or late preterm and 1244 (0.6 %) were born very preterm (table 1). There were 381 children with CP in total, 268 (70.3 %) were born at term, 56 (14.7 %) were born moderately or late preterm and 57 (15.0 %) were born very preterm. Unilateral spastic CP was the most common type in the children born term and moderately or late preterm, while bilateral spastic CP was most common among those born very preterm (table 2). In the descriptive table 1, it is evident that for some variables there were none or very few (n<10) affected in one or more of the gestational age groups (table 3).

Children born term

The risk factors significantly associated with CP in the univariate analyses were: maternal overweight/obesity, small for gestational age, malformation, induction, delivery by elective or emergency caesarian section, Apgar at 5 min below 7 and admission to neonatal care unit (table 3). In the multivariable model including only the antenatal factors, the estimates remained similar to the univariate estimates (table 4). In the multivariable model including also perinatal factors, the effect estimates of malformation decreased but remained significant. Small for gestational age was no longer significantly associated with CP while emergency caesarian, Apgar at
5 min <7 and admission to neonatal care were, however, with lower effect estimates than in the univariate analyses.

**Children born moderately or late preterm**

The variables significantly associated with CP in the univariate analyses were: small for gestational age, malformation, delivery by elective or emergency caesarian section and admission to neonatal care (table 3). In the multivariable model, that only include antenatal factors, small for gestational age and malformation remain significantly associated with CP. Finally, in the multivariable model, that also include perinatal variables, the effect estimates, for being small for gestational age is decreased and no longer significant (table 4). Malformation indicates a significantly increased risk of CP in the second model as well as admission to neonatal care, while the effect estimates for emergency or elective caesarian section are lowered and no longer statistically significant.

**Children born very preterm**

No variables were significantly associated with CP in the logistic regression analyses.

**DISCUSSION**

In this population-based study among children from the Southern part of Sweden where we had the possibility to include a number of factors simultaneously, both antenatal and perinatal factors are associated with CP. The most pronounced associations observed among term as well as moderately or late preterm born children were for malformation and admission to neonatal care unit. Our results, given the relatively large sample and reliable data from the pregnancy period until delivery and the neonatal period, give weight to factors that have been shown to be associated with CP in prior studies.

The antenatal factor most strongly associated to CP among term children was malformations, suggested as a potential risk factor from earlier studies. Those delivered by caesarian section were also more likely to later receive a CP diagnosis. This result is in line with earlier studies and is most likely due to underlying causes leading to surgery. There has been a big increase in caesarian sections the last decades but the CP rates have remained relatively stable. Admission to neonatal care was strongly associated with CP, which can both be because of detrimental factors not recognised in this material such as perinatal infections and because of early signs of CP.

Stillborn or neonatal deaths were not included in this study. It is likely that the same factors that could give rise to symptoms, which would later in life qualify for a CP-diagnosis would also increase the risk of dying before birth.

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**Figure 1** Children included and excluded in the study. Several exclusion criteria may be present in one child. CP, cerebral palsy.
Table 1 Prevalence of characteristics among term (≥37 weeks), moderately or late preterm (32–36 weeks) and very preterm (<32 weeks) children, respectively, with and without cerebral palsy (CP)

| Characteristic                          | Term (≥37 weeks) | Moderately or late preterm (32–36 weeks) | Very preterm (<32 weeks) |
|-----------------------------------------|------------------|------------------------------------------|--------------------------|
|                                         | n=20618          | n=7355                                   | n=1244                   |
|                                         | CP=268           | CP=56                                    | CP=57                    |
|                                         | No CP=206–350    | No CP=7299                                | No CP=1187               |
| Antenatal                               |                  |                                          |                          |
| Pregnancy length (days mean ±SD)        | 277.9 (±10.0)    | 279.2 (±9.0)                             | 241.4 (±10.6)            |
| Maternal age (years mean ±SD)           | 29.9 (±5.6)      | 29.8 (±5.1)                              | 30.2 (±5.9)              |
| Maternal weight (kg mean ±SD)           | 69.3 (±14.6)     | 68.0 (±13.1)                             | 72.1 (±15.0)             |
| Maternal BMI, kg/m²                      |                  |                                          |                          |
| <18.5                                   | 6 (2.2)          | 4852 (2.4)                               | 1 (1.8)                  |
| 18.5–24.9                               | 134 (50.0)       | 117291 (56.8)                            | 26 (46.4)                |
| 25.0–29.9                               | 72 (26.9)        | 47576 (23.1)                             | 15 (26.8)                |
| ≥30.0                                   | 30 (11.2)        | 21160 (10.3)                             | 6 (10.7)                 |
| Missing                                 | 26 (9.7)         | 15471 (7.5)                              | 8 (14.3)                 |
| Smoking in early pregnancy              |                  |                                          |                          |
| No                                      | 232 (86.6)       | 179770 (87.1)                            | 44 (78.6)                |
| 1–9 cigarettes/day                      | 21 (7.8)         | 15748 (7.6)                              | 7 (12.5)                 |
| ≥10 cigarettes/day                      | 11 (4.1)         | 6953 (3.4)                               | 2 (3.6)                  |
| Missing                                 | 4 (1.5)          | 3879 (1.9)                               | 3 (5.4)                  |
| Country of origin                       |                  |                                          |                          |
| Nordic                                  | 226 (84.3)       | 177608 (86.1)                            | 51 (91.1)                |
| Europe, North America, Australia        | 12 (4.5)         | 7648 (3.7)                               | 3 (5.4)                  |
| Other                                   | 30 (11.2)        | 20989 (10.2)                             | 2 (3.6)                  |
| Missing                                 | 0                | 105 (0.1)                                | 0                        |
| Parity                                  |                  |                                          |                          |
| Primipara                               | 121 (45.2)       | 92408 (44.8)                             | 26 (46.4)                |
| Not primipara                           | 142 (53.0)       | 112242 (54.4)                            | 30 (53.6)                |
| Missing                                 | 5 (1.9)          | 1710 (0.8)                               | 0                        |
| Infant sex                              |                  |                                          |                          |
| Male                                     | 147 (54.9)       | 105744 (51.2)                            | 34 (60.7)                |
| Female                                   | 121 (45.2)       | 100606 (48.8)                            | 22 (39.3)                |
| Thyroid dysregulation                   | 2 (0.8)          | 3951 (1.9)                               | 13 (23.2)                |
| Chorioamnionitis                        | 0                | 167 (0.1)                                | 1 (1.8)                  |
| Diabetes mellitus type 1                | 2 (0.8)          | 1314 (0.6)                               | 0                        |
| Gestational diabetes                    | 6 (2.2)          | 3995 (1.9)                               | 2 (3.6)                  |
| Severe preeclampsia                     | 2 (0.8)          | 735 (0.4)                                | 1 (1.8)                  |
| Weight deviation                        |                  |                                          |                          |
| SGA                                      | 18 (6.7)         | 5252 (2.6)                               | 14 (25.0)                |
| AGA                                      | 230 (85.8)       | 190469 (92.3)                            | 38 (67.9)                |
| LGA                                      | 20 (7.5)         | 10629 (5.2)                              | 4 (7.1)                  |
| Any kind of malformation                | 21 (7.8)         | 5375 (2.6)                               | 11 (19.6)                |
| Chromosomal abnormalities               | 1 (0.4)          | 132 (0.1)                                | 0                        |
| Bleeding in second or third trimester   | 3 (1.1)          | 1561 (0.8)                               | 5 (8.9)                  |
| Epilepsy                                | 1 (0.4)          | 1091 (0.5)                               | 0                        |

Continued
or during the neonatal period. If so, the estimates in this study would be affected towards the null.

The link between low parental socioeconomic status (SES) and the risk of having a child with CP have been suggested\(^2\) and since low SES are linked to the overall risk of preterm birth this could be the pathway.\(^2\) Several studies have also found that the effect of SES on the prevalence of CP remains after adjusting for possible mediators such as gestational age and birth weight.\(^2\) We do not have a specific marker of SES in this study, but smoking is inversely related with SES in Sweden.\(^2\) In this study, smoking in early pregnancy is not significantly associated with CP, and thus does not support an association between low SES and increased risk of CP. In relation to low birth weight, especially SGA has been identified as a risk factor for CP in term babies,\(^2\) however, we did not find that in ours study.

Genetic involvement has been identified in CP, but we do not have any genetic information in this study, except about occasional genetic syndrome. Depending on genetic susceptibility, environmental factors might be more or less detrimental and understanding such relations better might open up for directed preventive measures.\(^2\) In combination with this registry study, maternal early pregnancy biobank blood samples from most of the participants are available, and will be analysed regarding toxicological risk factors. Another way to further understand the complexity between different risk factors and CP would be to combine registry data with a biobank that include important biomarkers including genetic markers from the participants themselves.

An important strength of the study lies in our population-based study design. Many prior studies have studied one or a few suggested risk factors at a time whereas our design allowed us to investigate several previous suggested factors associated with CP simultaneously. Moreover, the data were routinely and prospectively collected, which is an important strength since it eliminates the risk for recall bias.

Another strength of our study is the large sample size that enabled us to stratify all analyses on gestational age. Still, it is important to bear in mind that preterm birth itself is an abnormal event, why a control group matched on prematurity contains, per definition, neonates born preterm due to some kind of pathological process,\(^2\) which affects the risk estimates. This must be taken into account

### Table 1

| (n(%)) Unless otherwise stated | Term n=206618 | Moderately or late preterm n=7355 | Very preterm n=1244 |
|-------------------------------|--------------|----------------------------------|---------------------|
| CP n=268 | No CP n=206–350 | CP n=56 | No CP n=7299 | CP n=57 | No CP n=1187 |
| PROM | 6 (2.2) 9304 (4.5) 11 (19.6) 2165 (29.7) 15 (26.3) 301 (25.4) | | | | |
| Mode of delivery | | | | | |
| Vaginal | 177 (66.0) 168106 (81.5) 22 (39.3) 4630 (64.3) 21 (36.8) 391 (32.9) | | | | |
| Vaginal Instrumental | 13 (4.9) 9700 (4.7) 1 (1.8) 181 (2.5) 0 4 (0.3) | | | | |
| Sectio, elective | 23 (8.9) 11066 (5.4) 6 (10.7) 382 (5.2) 1 (1.8) 33 (2.8) | | | | |
| Sectio, emergency | 51 (19.0) 14146 (6.9) 26 (46.4) 2027 (27.8) 34 (59.7) 756 (63.7) | | | | |
| Breech vaginal delivery | 1 (0.4) 1088 (0.5) 1 (1.8) 114 (1.6) 1 (1.8) 19 (1.6) | | | | |
| Placental abruption | 6 (2.2) 280 (0.1) 6 (10.7) 192 (2.6) 4 (7.0) 115 (9.7) | | | | |
| Placenta praevia | 2 (0.8) 609 (0.3) 1 (1.8) 203 (2.8) 2 (3.5) 60 (5.1) | | | | |
| Maternal fever in labour | 1 (0.4) 1427 (0.7) 2 (3.6) 75 (1.0) 0 35 (3.0) | | | | |
| Induction | 37 (13.8) 18676 (9.1) 3 (5.4) 705 (9.7) 1 (1.8) 7 (0.6) | | | | |
| Agp at 5 min below 7 | 40 (14.9) 1750 (0.1) 9 (16.1) 296 (4.1) 14 (24.6) 311 (26.2) | | | | |
| Admission to neonatal care | 112 (41.8) 11820 (5.7) 51 (91.1) 4266 (58.5) 57 (100) 1133 (95.5) | | | | |

| Subtypes | Term n=268 | Moderately or late preterm n=56 | Very preterm n=57 | Total n=381 |
|-----------|------------|-------------------------------|-------------------|-------------|
| Unilateral spastic | 95 (35.5) | 22 (39.3) | 11 (19.3) | 128 (33.6) |
| Bilateral spastic diplegia | 55 (20.5) | 20 (35.7) | 41 (71.9) | 116 (30.5) |
| Bilateral spastic tetraplegia | 10 (3.7) | 0 | 1 (1.8) | 11 (2.9) |
| Dyskinetic | 60 (22.4) | 6 (10.7) | 1 (1.8) | 67 (17.6) |
| Ataxic | 32 (11.9) | 5 (8.9) | 2 (3.5) | 39 (10.2) |
| Non-classifiable | 16 (5.9) | 3 (5.4) | 1 (1.8) | 20 (5.3) |

AGA, Appropriate for gestational age; BMI, body mass index; LGA, Large for gestational age; PROM, Prelabor rupture of membranes; SGA, Small for gestational age.
Table 3  Univariate estimates obtained from logistic regressions between antenatal and perinatal factors and cerebral palsy (CP) among term (≥37 weeks), moderately or late preterm (32–36 weeks) and very preterm (<32 weeks) children, respectively

|                          | Term gestational age ≥37 | Moderately or late preterm gestational age 32–36 | Very preterm gestational age <32 |
|--------------------------|--------------------------|---------------------------------------------------|----------------------------------|
| **Antenatal**            |                          |                                                   |                                  |
| Maternal age (years)     |                          |                                                   |                                  |
| <20                      | 1.18 (0.53, 2.66)        | 2.58 (0.80, 8.36)                                 | 0.55 (0.07, 4.08)                |
| 20–39                    | ref                      | ref                                               | ref                              |
| ≥40                      | 1.46 (0.80, 2.67)        | 1.59 (0.49, 5.12)                                 | 0.31 (0.04, 2.31)                |
| Maternal BMI (kg/m²)     |                          |                                                   |                                  |
| <18.5                    | 1.08 (0.48, 2.45)        | 0.62 (0.08, 4.61)                                 | 0.88 (0.11, 6.73)                |
| 18.5–24.9                | ref                      | ref                                               | ref                              |
| >25                      | **1.30 (1.00, 1.68)**    | 1.27 (0.71, 2.26)                                 | 1.58 (0.89, 2.82)                |
| Smoking in early pregnancy|                          |                                                   |                                  |
| No                       | ref                      | ref                                               | ref                              |
| Yes                      | 1.09 (0.75, 1.58)        | 1.25 (0.61, 2.57)                                 | 1.26 (0.64, 2.49)                |
| **Country of origin**    |                          |                                                   |                                  |
| Nordic                   | ref                      | ref                                               | ref                              |
| Europe, North America, Australia | 1.23 (0.69, 2.20) | 1.51 (0.47, 4.86)                                 | 1.04 (0.31, 3.45)                |
| Other                    | 1.12 (0.77, 1.64)        | 0.33 (0.08, 1.37)                                 | 1.01 (0.42, 2.41)                |
| **Parity**               |                          |                                                   |                                  |
| Previous child/children  | ref                      | ref                                               | ref                              |
| No previous child        | 1.04 (0.81, 1.32)        | 0.71 (0.42, 1.20)                                 | 0.82 (0.47, 1.41)                |
| **Infant sex**           |                          |                                                   |                                  |
| Male                     | 1.16 (0.91, 1.47)        | 1.31 (0.77, 2.25)                                 | 1.67 (0.95, 2.96)                |
| Female                   | ref                      | ref                                               | ref                              |
| **Thyroid dysregulation (yes vs no)** | †                    | 1.86 (1.00, 3.47)                                 | 1.40 (0.73, 2.69)                |
| Weight deviation         |                          |                                                   |                                  |
| SGA                      | 2.84 (1.76, 4.59)[¶]     | 3.39 (1.83, 6.28)[¶]                              | 0.66 (0.32, 1.37)                |
| AGA                      | ref                      | ref                                               | ref                              |
| LGA                      | 1.56 (0.98, 2.46)        | 1.37 (0.49, 3.86)                                 | 1.24 (0.37, 4.14)                |
| Malformation (yes vs no) | **3.18 (2.03, 4.97)[¶]** | **4.77 (2.44, 9.30)[¶]** | †                              |
| **Perinatal**            |                          |                                                   |                                  |
| PROM (yes vs no)         | 0.58 (0.30, 1.12)        | 1.05 (0.57, 1.92)                                 |                                  |
| **Mode of delivery**     |                          |                                                   |                                  |
| Vaginal                  | ref                      | ref                                               | ref                              |
| Vaginal instrumental     | 1.27 (0.72, 2.24)        | 1.16 (0.16, 8.67)                                 | §                                |
| Sectio, elective         | **1.97 (1.28, 3.05)[‡]** | **3.31 (1.33, 8.20)***                            | 0.56 (0.07, 4.33)                |
| Sectio, emergency        | **3.42 (2.51, 4.68)[¶]** | **2.70 (1.53, 4.77)[‡]**                            | 0.84 (0.48, 1.46)                |
| Induction (yes vs no)    | **1.61 (1.14, 2.28)[‡]** | †                                                  | †                                |
| Apgar at 5min (below vs above 7) | **20.6 (14.66, 28.91)[¶]** | †                                             | **0.93 (0.50, 1.73)**            |
| Admission to neonatal care (yes vs no) | **11.82 (9.26, 15.07)[¶]** | **7.25 (2.89, 18.19)[¶]** | §                                |

ORs with 95% CIs are given. Bold values indicate 95% significant estimates.
*sign.<0.05.
†OR not calculated because n<10 in either CP or no CP-group.
‡sign.<0.01
§OR not possible to calculate because 100% in CP or no CP group.
¶sign.<0.001.
AGA, Appropriate for gestational age; BMI, body mass index; LGA, Large for gestational age; SGA, Small for gestational age.
when interpreting results of analyses stratified by gestational age. However, in this study, the focus of our analysis was to analyse the importance of different suggested risk factors within each gestational age group, and doing so we get an estimate of the relative importance of this risk factor for children that for one reason or another were born term, moderately or late preterm or very preterm.

Finally, and importantly, the use of the quality register CPUP for case ascertainment is a major strength, since all the CP cases have been diagnosed independently of

### Table 4 Univariate and multivariable estimates obtained from logistic regressions between antenatal and perinatal factors and cerebral palsy among term (≥37 weeks) and moderately or late preterm (32–36 weeks) children, respectively

|                      | Term | Antenatal variables | Small or large for gestational age | Perinatal variables | Moderate or late preterm |
|----------------------|------|---------------------|-----------------------------------|---------------------|-------------------------|
|                      | n=206618 | n=187984 | n=187984 | n=7355 | n=7275 | n=7275 |
| **Univariate models** |      |           |                     |                     |                         |
|                      | Univariate models (same estimates as in table 3) | Multivariable models Including only antenatal variables | Multivariable models Including antenatal and perinatal variables |
| Maternal BMI (kg/m²) | <18.5 | 1.08 (0.48,2.45) | 1.07 (0.47,2.43) | 1.17 (0.52,2.67) |
|                      | 18.5–24.9 | ref | ref | ref |
|                      | >25 | 1.30 (1.00,1.68) * | 1.28 (0.98,1.66) | 1.10 (0.84,1.43) |
| Small or large for gestational age | SGA | 2.84 (1.76,4.59) ‡ | 2.24 (1.28,3.93) † | 1.07 (0.60,1.91) |
|                      | AGA | ref | ref | ref |
|                      | LGA | 1.56 (0.98,2.46) | 1.23 (0.73,2.09) | 0.88 (0.52,1.51) |
| Malformation (yes vs no) | 3.18 (2.03,4.97) † | 3.37 (2.13,5.33) ‡ | 2.07 (1.30,3.31) † |
| Induction (yes vs no) | 1.61 (1.14,2.28) † | 1.19 (0.82,1.75) |
| Delivery mode | Vaginal delivery | ref | ref | ref |
|                      | Vaginal instrumental delivery | 1.27 (0.72,2.24) | 0.71 (0.39,1.30) |
|                      | Elective cesarian section | 1.97 (1.28,3.05) † | 1.59 (1.00,2.53) |
|                      | Emergency cesarian section | 3.42 (2.51,4.68) † | 1.56 (1.08,2.24) * |
| Apgar at 5min (below vs above 7) | 20.6 (14.66,28.91) ‡ | 4.45 (2.88,6.83) † |
| Admission to neonatal care unit (yes vs no) | 11.82 (9.26,15.07) ‡ | 7.06 (5.19,9.62) ‡ |
| **Perinatal variables** |                      |                     |                     |                         |
|                      | Moderately or late preterm | n=7355 | n=7275 | n=7275 |
| Small or large for gestational age | SGA | 3.39 (1.83,6.28) ‡ | 2.93 (1.57,5.49) † | 1.72 (0.90,3.32) |
|                      | AGA | ref | ref | ref |
|                      | LGA | 1.37 (0.49,3.86) | 0.97 (0.30,3.16) | 0.91 (0.28,2.99) |
| Malformation (yes vs no) | 4.77 (2.44,9.30) † | 4.22 (2.14,8.32) ‡ | 3.35 (1.70,6.61) † |
| Delivery mode | Vaginal delivery | ref | ref | ref |
|                      | Vaginal instrumental delivery | 1.16 (0.16,8.67) | 0.95 (0.13,7.10) |
|                      | Elective cesarian section | 3.31 (1.33,8.20) * | 2.15 (0.85,5.44) |
|                      | Emergency cesarian section | 2.70 (1.53,4.77) | 1.61 (0.88,2.95) |
| Admission to neonatal care unit (yes vs no) | 7.25 (2.89,18.19) † | 5.05 (1.96,13.00) † |

One of the multivariable models includes only antenatal variables whereas the other model includes antenatal and perinatal variables. ORs with 95% CIs are shown.

Bold values indicate 95% significant estimates.

*sign.<0.05.
†sign.<0.01.
‡sign.<0.001.
BMI, body mass index.
this study. CPUP has very good coverage and includes in principle all children with CP in southern Sweden. The definition of CP used in the CPUP is the same as in earlier studies from Sweden and the SCPE. The ascertainment of CP in the region was solid; a senior neuropediatrician (LW) performed regular inventories to find all children with signs of CP in the area, and validated the CP diagnosis and subtype after the child’s fourth birthday. In conclusion, we investigated several of the previously suggested factors associated with CP in one population-based study. Many prior studies have been focused on studying one or a few factors at a time, whereas our design allowed us to investigate several factors simultaneously in one material. Our results support and strengthen previous findings.

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Patient consent for publication Not required.

Ethics approval The study was approved by the Regional Ethical Review Board, Lund, Sweden.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request. In the information given to the project participants, it was stated that the collected information would only be available to the researchers working on the project. This restriction on sharing data was a part of the documents reviewed and approved by the regional ethical review board, Regionala etikprövningsnämnden i Lund. A new application to the ethical review board is needed to let the board consider whether access to data about the participants could be given to external researchers. Applications can be sent via digital forms. Homepage: https://etikprövningsnaryl.se/. Phone: +46-10-475 08 00. The request for data can be sent to the guarantor of the project: Lars.rylander@med.lu.se.

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ORCID iD Anna Jöud http://orcid.org/0000-0001-7192-4911

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