Anthropological Review • Vol. 84(1), 37–49 (2021)

ANTHROPOLOGICAL REVIEW
Available online at: https://doi.org/10.2478/anre-2021-0007

The influence of neonatal infections on the development of cerebral palsy

Marta Sternal, Barbara Kwiatkowska, Krzysztof Borysławski, Agnieszka Tomaszewska

Department of Anthropology, Wroclaw University of Environmental and Life Sciences, Wroclaw, Poland

ABSTRACT: One of the most significant biological factors predisposing to cerebral palsy (CP) are infections. The paper aims to analyze neonatal infections' influence in the risk of CP development with consideration of all significant risk factors including single, twin, full-term and pre-term pregnancies.
278 children with CP attending the chosen school-educational centers in Poland were included in the questionnaire. The control group included data obtained from the medical documentation of 435 children born in Limanowa County Hospital, Poland. Socio-economic factors, factors connected with pregnancy, and the coexisting disorders and diseases in children were taken into consideration. Constructed models of logistic regression were applied in the statistical analysis.
Neonatal infections increase the risk of CP development in all children (odds ratio (OR) 5.1, 95% confidence interval (CI) 2.6–9.8), children from single pregnancies (OR 5.8, 95% CI: 3.0–11.29), full-term (OR 6.2, 95% CI: 3.2–12.3), and single full-term pregnancies (OR 6.0, 95% CI: 3.0–12.0). The influence of neonatal infections in the risk of CP development in children from pre-term and single premature pregnancies was not indicated.
Neonatal infections are an independent risk factor for CP development in newborns from full-term pregnancy (>37 weeks of pregnancy). The patho-mechanism of CP is different in children from full-term and premature pregnancy and results from interrelating factors are discussed in this paper.

KEY WORDS: palsy, twin birth, pre-term birth, term birth

Introduction

Cerebral palsy (CP) encompasses various movement and posture disorders, coexisting with other adverse symptoms due to permanent damage of the encephalon in the early stages of its development. These disorders may change with age. Cerebral palsy does not constitute a determined morbid entity but an etiologi-

Original Research Article Received: October 24, 2020; Revised: February 11, 2021; Accepted: February 14, 2021
DOI: 10.2478/anre-2021-0007

cally and clinically diverse syndrome. Epidemiological assessments of occurrence frequency of CP vary according to the maximum and minimum age limit for the diagnosis (Martin 1960; Jarvis et al. 1985; Pharoah et al. 1987; Jaskulski and Zgorzalewicz 1993; Grether et al. 1996; Spinillo et al. 1997; O'Shea et al. 1998; Robertson et al. 1998; Liu et al. 1999; Zgorzalewicz et al. 2001; Winter et al. 2002; Wu and Colford 2002; Grether et al. 2003; Jacobsson et al. 2002; Jacobsson and Hagberg 2004; Koman et al. 2004; Tran et al. 2005; Ancel et al. 2006; Korzeniewski 2006; Costantine et al. 2007; Öztürk et al. 2007; Platt et al. 2007; Robertson et al. 2007; Hjern and Thorngren-Jerneck 2008; Himmelmann et. al. 2010;Brooka et al. 2014; Chang et al. 2015; Froslev-Friis 2015). In Poland, CP frequency is estimated to be ~2.0–2.5 in every 1000 live births (Jaskulski and Zgorzalewicz 1993; Michałowicz 2001; Zgorzalewicz et al. 2001; Milewska et al. 2011).

The second important risk factor (after prematurity) for CP are infections. Many etiological studies (Grether et al. 2003; Lang et al. 2012; Murphy et al. 1995; Grether and Nelson 1997; Yoon et al. 1997; Kornacka et al. 2009; Girard et al. 2009; Pappas et al. 2014; Strunk et al. 2014) reveal a strong correlation between perinatal infections and damage to the encephalon. Brain autopsies of fetuses and ultrasonic examinations show a significant increase in the occurrence of periventricular leukomalacia (PVL) in newborns whose mothers have had a medical history of infections, as well as in newborns with systemic inflammatory response syndrome (SIRS). Increasing evidence based research supports the hypothesis that infections are a major risk factor for encephalic abnormalities, as characterized by alterations in white matter and pathogenesis of CP (Grether et al. 2003; Lang et al. 2012; Murphy et al. 1995; Grether and Nelson 1997; Yoon et al. 1997; Kornacka et al. 2009; Girard et al. 2009; Pappas et al. 2014; Strunk et al. 2014).

Innate and perinatal infections, which most often are the result of toxoplasmosis, listeriosis, flu and rubeola viruses, rubella, as well as herpes viruses, may impair neurological development.

The paper aims to analyze neonatal infections' in influencing CP development with consideration of all significant risk factors including single, twin, full-term and pre-term pregnancies.

Material and methods

Participants

A group of 278 children with diagnosed CP, born in the years 1976–2010 who attended educational-therapeutic centers in Poland, were included in the study. The tool used in the research was a questionnaire filled in by the mothers of children with CP or by the closest caregiver. Data were collected in 40 Polish centers involved in the care and rehabilitation of children with CP.

The control group included data from medical documentation of 435 neonates born without congenital abnormalities, genetic syndromes, metabolic disorders, or other hereditary diseases in the years 1990–2010 in Limanowa County Hospital in the Name of God's Mercy, Poland (Polish: Szpital Powiatowy Imienia Miłosierdzia Bożego w Limanowej). Data on mothers and neonates were collected based on available medical documentation (hospitalization information card, nursing information, midwife information, and newborn information cards

– information concerning parents and the state of the neonate). The following parameters were evaluated during this study: systemic inflammatory response syndrome (SIRS), elevated CRP level, diagnosed fungal, bacterial, or viral infection or antibiotic therapy.

Data collection

This paper constitutes a part of more substantial research aimed at selecting independent risk factors for the development of CP from demographic, antenatal, perinatal, and neonatal factors. The questionnaire was divided into three parts in order to determine risk factors for CP. Factors impacting pregnancy and parturition are significant for the etiology of CP. Therefore, the first part of the questionnaire was devoted to the mother's pathological, familial, and obstetric history. It included questions concerning the parturition, pregnancy, gynecological disorders, as well as information about the child's father. The second part of the questionnaire included questions concerning medical and anthropological information, as well as information relating to the occurrence of the coexisting disorders and diseases of the child. The last part of the questionnaire was devoted to environmental diagnosis concerning family structure, residence, education, the parents' profession, and the mother's material situation during pregnancy.

Cases of acquired CP, cases with innate hydrocephalus in the course of genetic syndromes (Arnold-Chiari malformation, Dandy-Walker syndrome), as well as cases with innate microcephalus, were excluded from the study.

Study design

According to epidemiological research, the etiology of CP is different in premature newborns and the full-term ones, as well as newborns from single and twin pregnancy. Hence, a division of material into groups regarding single and twin full-term pregnancies (≥37 weeks of pregnancy) and premature pregnancies (<37 weeks of pregnancy) was carried out in order to obtain a reliable assessment of CP risk level (Table 1).

It was assumed in previous studies that the primary predictors of CP are the age of a pregnancy (week of the end of pregnancy) and multiple pregnancies(single/twin pregnancy). Accordingly, the research procedure strove to show that depending on various pregnancy stages, CP risk factors may be different. There-

Table 1. Quantity of children with CP and control group included in the analyses

Name of the group	N	%
All children	713	100.0
Children from single pregnancies	669	93.8
Children from twin pregnancies	44	6.2
Children from full-term pregnancies	548	76.9
Children from premature pregnancies	165	23.1
Children from full-term, single pregnancies	527	96.2
Children from full-term, twin pregnancies	21	3.8
Children from premature, single pregnancies	142	86.1
Children from premature, twin pregnancies	23	13.9

fore, the models estimating the risk should be different as well. Groups isolated in the material in view of single, twin, full-term, and premature pregnancy were significantly different regarding CP's etiopathogenesis. Therefore, it was initially assumed that there were variables differentiating the above-mentioned groups. The planned one-dimensional analyses with variables such as birth weight, birth length, age of the pregnancy, birth order, and sex were aimed at comparative characteristics of children with CP and the control group. It was also aimed to determine of variables which after the introduction of logistic regression models would serve as covariates controlling the appropriate statistical conclusion.

Statistical analyses

To evaluate the probability of the occurrence of CP several logistic regression models were planned in connection to the affiliation with the appointed group and the existence of covariates:

- simple model determining strict quotient of chance (OR) of the occurrence of CP in view of the researched factors in each group,
- adjusted model which considers the influence of the covariates designates in the one-dimensional analyses,
- full model which considers, apart from covariates and significant risk factors, also the influence of father's and mother's age (so that it is possible to assess the independent influence of mother's and father's age in connection to the analyzed factors and group affiliation).

In order to lower the risk of the occurrence of a diluted matrix of answers, the production of logistic regression with aggregation and without the aggregation of data was considered in the planned research. Additionally, considering the possibility of covariants' obliquity, the regression models with transformed variables were planned.

To ultimately assess the independent risk factors of CP, a logistic regression model considers all factors significant in multidimensional analyses such as demographic factors, antenatal, perinatal and neonatal factors, and significant covariates.

The analysis was carried out in the STATISTICA 12.5 software. A comparative characteristic of children with CP and control group children were analyzed using Mann-Whitney U tests, Student's t-tests for independent samples (in regard to groups), and for non-parametric data the Chi-square test. Variables that differentiated the groups of children with CP and from control group and rendered statistically significant were included in the analyses' main component. This allowed the separation of non-correlated covariates, which were included in further multidimensional analyses. The OR chance quotient was calculated to establish the relation between the researched variables and CP. The OR value was given together with the estimation measurement in the form of a 95% range of confidence, giving the significance level p for the Wald's Chi-square test. The data adjustment was checked by means of Pearson's Chi-square statistics, deviation statistics, calibrated Pearson's Chi-square statistics and calibrated deviation statistics. Adjustment measurement of the model was expressed through Cox-Snell and Nagelkerke's coefficient and Hosmer-Lemeshow's test.

Results

One-dimensional analyses showed that in the group of all children and the group of children from single pregnancies, birth weight and length, birth order, as well as the age of the pregnancy, significantly differentiated children with CP and children from the control group. However, in children from twin pregnancies, sex, birth order, and pregnancy age, were significant factors in differentiating children with CP from children in the control group (Table 2).

Table 2. Comparative characteristics of all children from the studied and control groups and separately for single and twin pregnancies

All children			
Variables	CP children group N=278	Control group N=435	*p* level
Sex m/f	152/126	219/216	NS
Birth weight (g)	440.0–5600.0 2554.9±997.2	1290.0–5170.0 3367.1±552.0	<0.001
Birth length (cm)	20–65 50.0±7.2	41–63 54.8±3.1	<0.001
Birth order	1–9 2.0±1.3	1–15 2.6±1.8	<0.001
Age of pregnancy (week of pregnancy) <37 Age of pregnancy (week of pregnancy) ≥37	126 151	39 396	<0.001
Children from single pregnancies			
Variables	CP children group N=250	Control group N=419	*p* level
Sex m/f	136/114	217/202	NS
Birth weight (g)	440.0–5600.0 2615.2±1005.6	1430.0–5170.0 3403.87±514.07	<0.001
Birth length (cm)	20–65 50.3±7.12	45–63 54.9±2.9	<0.001
Birth order	1–9 2.0±1.3	1–15 2.6±1.8	<0.001
Age of pregnancy (week of pregnancy) <37 Age of pregnancy (week of pregnancy) ≥37	106 141	35 381	<0.001
Children from twin pregnancies			
Variables	CP children group N=28	Control group N=16	*p* level
Sex m/f	16/12	2/14	<0.01
Birth weight (g)	830.0–3750.0 2025.7±745.4	1290.0–3230.0 2403.1±650.4	NS
Birth length (cm)	33–63 47.4±7.0	41–56 49.9±4.4	NS
Birth order	1–4 1.8±1.0	1–5 2.6±1.5	<0.05
Age of pregnancy (week of pregnancy) <37 Age of pregnancy (week of pregnancy) ≥37	20 8	4 12	<0.01

Data expressed as the group's quantity, the range of changeability or mean and standard deviation, *p* level from the *t*-Student test, Mann-Whitney U test, or Chi-square test, not significant NS.

Children from full-term pregnancies and full-term single pregnancies, birth eight and length, as well as birth order, were statistically significant different in between children with CP and the control group. However, in children from full-term twin pregnancies, the differentiating variables were sex and birth order (Table 3).

Variables in children such as those born to premature pregnancies, both twin and single pregnancies, birth weight, and length were statistically significant between children with CP and the control group. However, in children from premature twin pregnancies, none of the variables were statistically significant (Table 4).

After analyzing the main components, birth weight and birth order were included in the logistic regression models as covariants (controlling the appropriate statistical deduction) in the group of all children, and children from full-term single pregnancies on the basis of absolute values of the load. However, in the group

Table 3. Comparative characteristics of children from full-term pregnancies, full-term single pregnancies, and full-term twin pregnancies from the studied and control group

Children from full-term pregnancies			
Variable	CP children group N=152	Control group N=396	*p* level
Sex m/f	86/66	203/193	NS
Birth weight (g)	2180.0–5600.0 3307.4 ±540.3	1480.0–5170.0 3453.3±472.5	<0.01
Birth length (cm)	35–63 54.3±3.9	46–63 55.2±2.7	<0.05
Birth order	1–9 1.9±1.2	1–5 2.6±1.5	<0.001
Children from full-term, single pregnancies			
Variable	CP children group N=143	Control group N=384	*p* level
Sex m/f	80/63	201/183	NS
Birth weight (g)	2225.0–5600.0 3339.7±529.7	2050.0–5170.0 3479.3±446.3	<0.01
Birth length (cm)	35–63 54.4±3.9	46–63 55.3±2.6	<0.05
Birth order	1–9 1.9±1.2	1–15 2.6±1.8	<0.001
Children from full-term, twin pregnancies			
Variable	CP children group N=9	Control group N=12	*p* level
Sex m/f	6/3	2/10	<0.05
Birth weight (g)	2180.0–3750.0 2801.1±470.9	1480.0–3230.0 2620.8±548.9	NS
Birth length (cm)	49–63 52.9±4.9	47–56 51.8±2.8	NS
Birth order	1–4 1.8±0.9	1–5 3.2±1.4	<0.05

Data expressed as the group's quantity, the range of changeability or mean and standard deviation, *p* level from the *t*-Student test, Mann-Whitney U test or Chi-square test, not significant NS.

of children from premature pregnancies and from premature, single pregnancies, only the birth weight was included in the model. In children from full-term twin pregnancies and premature twin pregnancies, no covariants were designated. These groups were too small to estimate the maximum likelihood method in the logistic regression models.

Among all logistic regression models estimating the risk of CP for neonatal factors, the adjusted model for covariants with data aggravation was selected to interpret data. This model was characterized by the higher ratio of correctly classified cases quotient to incorrectly classified cases quotient. Additionally, due to the insignificant y-intercept, the correctness of the estimated simple model (insignificant y-intercept in the estimation of parameters in the group of children from premature and premature, single pregnancies) and transformed model was lower than in the adjusted model.

Table 4. Comparative characteristics of children from premature pregnancies, premature, single pregnancies, and premature twin pregnancies from the studied and control group

Children from premature pregnancies			
Variable	CP children group N=126	Control group N= 39	*p* level
Sex m/f	66/60	16/23	NS
Birth weight (g)	440.0–4600.0 1644.9±572.8	1290.0–3580.0 2491.3±499.4	<0.001
Birth length (cm)	20–65 44.5±6.6	41–57 50.2±3.6	<0.001
Birth order	1–9 2.1±1.4	1–7 2.2±1.3	NS
Children from premature, single pregnancies			
Variable	CP children group N=107	Control group N=35	*p* level
Sex m/f	56/51	16/19	NS
Birth weight (g)	440.0–4600.0 1642.4±581.0	1430.0–3580.0 2576.0±485.7	<0.001
Birth length (cm)	20–65 44.5±6.7	45–57 50.8±3.1	<0.001
Birth order	1–9 2.2±1.5	1–7 2.3±1.3	NS
Children from premature, twin pregnancies			
Variable	CP children group N=19	Control group N= 4	*p* level
Sex m/f	10/9	0/4	NS
Birth weight (g)	830.0–2360.0 1658.4±540.2	1290.0–2300.0 1750.0±502.1	NS
Birth length (cm)	33–55 44.6±6.4	41–48 44.8±3.8	NS
Birth order	1–4 1.9±1.1	1 1 ± 0	NS

Data expressed as the group's quantity, the range of changeability or mean and standard deviation, *p* level from the *t*-Student test, Mann-Whitney *U* test, or Chi^2 test, not significance NS.

Considering the influence of neonatal infections, it was noticed that neonatal infections had a higher risk for CP in the group of all children, children from single, full-term pregnancies and full-term, and single pregnancies. It was estimated that in the group of all children and children from single pregnancies, neonatal infections increased the risk of CP four times (respectively OR 4.0, 95% CI: 2.3–7.0 and OR 4.2, 95% CI: 2.3–7.5). However, in the group of children from full-term pregnancies, the risk was increased by 4.4 (OR 4.4, 95 % CI: 2.4–8.2), children from full-term, and single pregnancies (OR 4.6, 95% CI: 2.4–8.6) (Table 5).

Applying the constructed logit models, a selection of potential independent variables significantly influencing CP occurrence was performed. Based on the collection of the obtained significant variables (among demographic factors, antenatal, perinatal, and neonatal factors), an estimation employing the full model (all significant factors adjusted to covariates) was performed to obtain a model projecting the influence of neonatal infections as an independent risk factor of the development of CP in individual groups.

Having included neonatal infections into the final model, it was confirmed that neonatal infections increased the risk of development of CP in the group of all children (OR 5.1, 95% CI: 2.6–9.8), children from single pregnancies (OR 5.8, 95% CI: 3.0–11.3), full-term (OR 6.2, 95% CI: 3.2–12.3), and single full-term pregnancies (OR 6.0, 95% CI: 3.0–12.0) (Table 6). The influence of neonatal infections on the risk of CP development in children from premature and single premature pregnancies was not indicated.

Discussion

General and local infections (lung, skin, eyeball, umbilical cord, kidney, meningitis infections) often occur in the neonatal period. The occurrence of such infections are the result of newborns having undeveloped protective mechanisms against pathogens, viruses, and bacteria. Additionally, newborns have a deficient migration of phagocytic cells to infection sites, and an insufficient number of spare leukocytes in the bone marrow. Also, together with incomplete activation of

Table 5. The estimation of logit models for the occurrence of CP with consideration of the influence of neonatal infections in individual groups of children

Group	OR (95% CI)	Wald's test
All children	4.0 (2.3–7.0)	$p = 0.000001$
Children from single pregnancies	4.2 (2.3–7.5)	$p = 0.000002$
Children from full-term pregnancies	4.4 (2.4–8.2)	$p = 0.000003$
Children from full-term, single pregnancies	4.6 (2.4–8.6)	$p = 0.000004$

Table 6. The estimation of logit models for the occurrence of CP with consideration of the influence of neonatal infections in individual groups of children

Group	OR (95% CI)	Wald's test
All children	5.1 (2.6–9.8)	$p < 0.000001$
Children from single pregnancies	5.8 (3.0–11.3)	$p < 0.000001$
Children from full-term pregnancies	6.2 (3.2–12.3)	$p < 0.000001$
Children from full-term, single pregnancies	6.0 (3.0–12.0)	$p < 0.000001$

fixators, neonatal neutrophils destroy pathogens less effectively than in adults. Contrary to healthy newborns, neutrophils in sick newborns tend to have an increased deficiency in pathogen elimination function (Marcdante and Kliegman 2014).

All neonatal infections, especially SIRS, are dangerous as they may lead to neonatal deaths, damage to kidneys, lungs, hearing, cognitive function impairment, as well as CP. On the basis of available research, it can be argued that the risk of CP development increases with the occurrence of neonatal infections (Yoon et al. 1997; Reddihough and Collins 2003; Soleimani et al. 2003; Kułak and Sobaniec 2004; Steenwinckel et al. 2004; Stoll et al. 2004; Greenwood et al. 2005; Wilson-Costello et al. 2005; Costantine et al. 2007; Škrablin et al. 2008; Gilbert et al. 2010; Milewska et al. 2011; Decembrino et al. 2014; Strunk et al. 2014; Pilypiene et el. 2015).

The confirmation of this is the authors' research – in more than 42% newborns, disorders that may be causatively connected with the discussed disease's occurrence. In newborns from the group of children with CP, airway inflammation (53.8%), meningitis (12.8%), sepsis (7.7%), or innate infections (3.2%) were more often observed in comparison with newborns from the control group. Lung inflammation had the largest proportion among the above-mentioned diseases. The obtained results are compliant with earlier observations by (Michałowicz 2001).

The deficiency of antibacterial and antiviral defenses contributes to neonatal infections, especially in newborns' with low birth weight (Kornacka et al. 2009; Marcdante and Kliegman 2014). Systemic inflammatory reaction occurs in 1:1500 newborns from full-term pregnancies and 1:250 from premature pregnancies. Furthermore,, six fold higher occurrence of sepsis in preemie is connected with larger immaturity of the immune system (Marcdante and Kliegman 2014).

It was shown in the conducted research that neonatal infections are a strong predictor of CP in the group of all children, children from single, full-term pregnancies and full-term, single pregnancies. The influence of neonatal infections in CP development in children from premature and single premature pregnancies was not indicated. However, it was connected with the smaller quantitative representation of this group of newborns. Simultaneously, it should be underlined that the relevant research highlights the influence of different factors in the occurrence of CP in premature newborns (Murphy et al. 1995; Grether et al. 1996; Dammann and Leviton 1997; Spinillo et al. 1997; O'Shea et al. 1998; Jacobsson et al. 2002; Steenwinckel et al. 2004; Stoll et al. 2004; Wilson-Costello et al. 2005; Platt et al. 2007; Robertson et al. 2007; Škrablin et al. 2008; Sellier et al. 2010; Decembrino et al. 2014; Pappas et al. 2014; Stunk et al. 2014; Pilypiene et al. 2015).

The conducted statistical analyses showed that birth weight and order are significant covariates that change the estimated parameters' values. Therefore, they should be used as control variables to assess risk factors of CP. Additionally, the conducted multidimensional analyses showed that depending on the group (twin, single, full-term, premature pregnancies), the risk factors of CP were different, and models estimating the percentage of CP incidence should be developed. Further research regard-

ing consideration of twin, full-term twin, and premature twin pregnancies is indispensable in order to determine all independent risk factors of CP.

The authors are aware of the limitations of the retrospective method. Consequently, , further studies should be conducted by the prospective method as well. Additionally, the broad time range of this study may have influenced the obtained results. Changes of socioeconomic factors, elements of life quality and development of medicine might influence the mothers. Although, the authors were aware of this limitation, the data were collected in as many as 14 voivodships, in 40 medical centers and the size of the research group was a condition of its representativeness. Also, it should be emphasized that although people with CP consist of a large group, they live dispersed throughout the Poland. It is not possible to narrow down the group in terms of the time period, since the group would simply become unrepresentative. Moreover, The statistical analyses indicated that birth weight, length and birth order, as well as the age of the pregnancy were significant accompanying variables, which considerably changed the values of estimated parameters. Hence they should be used as controlling variables when attempting to assess risk factors of CP. Besides, the multivariate analyses showed that, depending on the category (twin, singleton, term, preterm births), risk factors of CP were different, and models estimating the probability ratio of CP should be taken into account. Further studies are necessary, considering twin pregnancies, twin term and twin preterm births, in order to identify all independent risk factors of CP.

Conclusion

The present study examined the influence of neonatal infections in the development of CP. Neonatal infections are an independent risk factor of CP development in newborns from full-term pregnancy (>37 weeks of pregnancy). The pathomechanism of CP is different in children from full-term and premature pregnancy and results from the overlapping of many factors discussed in this paper. Our study demonstrated the need to include basic clinical information, as well as also other factors(i.e. infections, diseases, studies). Future studies should consider different types of CP presentations. We also suggest that extending the studies to include a greater number of twin pregnancies and the health of the mothers and fathers (including obesity, drug and alcohol intake) would be beneficial. The need to focus on this aspect of research denotes that there are many pathogenic factors of CP that remain unexplained.

The Authors' contribution

MS conceived the paper, collected the data, performed statistical computations and drafted the manuscript; BK was project supervisor, co-edited the final version of the manuscript; KB performed statistical computations and co-edited the final version of the manuscript; AT performed statistical computations, drafted the manuscript, co-edited the final version of the manuscript.

Conflict of interest

The authors declare that there is no conflict of interest.

Corresponding author

Agnieszka Tomaszewska, Department of Anthropology, Institute of Biology, Wroclaw University of Environmental and Life Sciences, Poland, Kożuchowska 5, 51-631 Wroclaw, Poland
e-mail: agnieszka.tomaszewska@up.wroc.pl

References

Ancel P, Livinec F, Larroque B, Marret S, Arnaud C, Pierrat V, Dehan M, N'Guyen S, Escande B, Burguet A, Thiriez G, Picaud JCh, André M, Bréart G, Kaminski M. 2006. Cerebral Palsy Among Very Preterm Children in Relation to Gestational Age and Neonatal Ultrasound Abnormalities: The EPIPAGE Cohort Study. Pediatrics 117:828–35.

Brooks J, Strauss DJ, Shavelle RM, Tran LM, Rosenbloom L, Wu YW. 2014. Recent trends in cerebral palsy survival. Part I: period cohort effects. Dev Med Child Neurol 56:1059–64.

Chang M, Ma H, Lu T. 2015. Estimating the prevalence of cerebral palsy in Taiwan: A comparison of different case definitions. Res Dev Disabil 36:207–12.

Costantine MM, How HY, Coppage K, Maxwell RA, Sibai BM. 2007. Does peripartum infection increase the incidence of cerebral palsy in extremely low birth weight infants? Am J Obstet Gynecol 196(5):6–8.

Dammann O, Leviton A. 1997. Does prepregnancy bacterial vaginosis increase a mother's risk of having a preterm infant with cerebral palsy? Dev Med Child Neurol 39:836–40.

Decembrino L, Pozzi M, Falcone R, Stronati M. 2014. Chorioamnionitis and neonatal outcome: early vs late preterm infants. Ital J Peadiatr 40:1–2.

Froslev-Friis Ch, Dunkfase-Heinl U, Holmgren Andersen JD, Stausbol-Gron B, Hansen AV, Garne E. 2015. Epidemiology of cerebral palsy in Southern Denmark. Danish Medical J 62(1):1–5.

Gilbert WM, Jacoby BN, Xing G, Danielsen BD. Smith LH. 2010. Adverse Obstetrical Events are Associated with Significant Risk of Cerebral Palsy. Am J Obstet Gynecol 203(4):1–5.

Girard S, Kadhim H, Roy M, Lavoie K, Brochu ME, Larouche A, Sebire G. 2009. Role of perinatal inflammation in cerebral palsy. Pediatr Neurol 40(3):168–74.

Greenwood C, Yudkin P, Sellers S, Impey L, Doyle P. 2005. Why is there a modifying effect of gestational age on risk factors for cerebral palsy. Arch Dis Child Fetal Neonatal Ed 90:141–6.

Grether J, Nelson KB, Emery S, Cummins SK. 1996. Prenatal and perinatal factors and cerebral palsy in very low birth weight infants. J Pediatr 128(3):407–15.

Grether J, Nelson KB, Walsh E, Willoughby RE, Redline RW. 2003. Intrauterine Exposure to Infection and Risk of Cerebral Palsy in Very Preterm Infants. Arch Pediatr Adolesc Med 157:26–32.

Grether JK, Nelson KB. 1997. Maternal infection and cerebral palsy in infants of normal birth weight. JAMA 278(3):207–11.

Himmelmann K, Hagberg G, Uvebrant P. 2010. The changing panorama of cerebral palsy in Sweden. X. Prevalence and origin in the birth-year period 1999-2002. Acta Paediatr 99:1337–43.

Hjern A, Thorngren-Jerneck K. 2008. Perinatal complications and socio-economic differences in cerebral palsy in Sweden – a national cohort study. BMC Pediatrics 8(49):1–7.

Jacobsson B, Hagberg G, Hagberg B, Ladfors L, Niklasson A, Hagberg H. 2002. Cerebral palsy in preterm infants: a population-based case-control study of antenatal and intrapartal risk factors. Acta Paediatr 91:846–951.

Jacobsson B, Hagberg G. 2004. Antenatal risk factors for cerebral palsy. Best Pract Res Clin Obstet Gynaecol 18(3):425–36.

Jacobsson B, Ladfors L, Milson I. 2004. Advanced Maternal Age and Adverse Perinatal Outcome. Am J Obstet Gynecol 104(4):727–32.

Jarvis SN, Holloway JS, Hey EN. 1985. Increase in cerebral palsy in normal birthweight babies. Arch Dis Child 60:1113–21.

Jaskulski T, Zgorzalewicz B. 1993. Zastosowanie komputerowego rejestru do badań nad epidemiologią mózgowego porażenia dziecięcego. Neurologia Dziecięca 2(3):13–9.

Koman AL, Smith PB, Shilt JS. 2004. Cerebral palsy. The Lancet 363:1619–31.

Kornacka MK, Bokiniec R, Bargiel A. 2009. Risk factors for preterm encephalopathy. Ginekol Pol 80(8):620–3.

Korzeniewski S. 2006. The Descriptive Epidemiology of Cerebral Palsy. Clin Perinatol 33:251–67.

Kułak W, Sobaniec W. 2004. Cerebral palsy in children in north-eastern Poland. Journal of Pediatric Neurology 2(2):79–84.

Lang TC, Fuentes-Afflick E, Gilbert WM, Newman T, Xing G, Wu YW. 2012. Cerebral palsy among Asian ethnic subgroups. Pediatrics 129(4):992–8.

Liu J, Li S, Lin Q, Li Z. 1999. Prevalence of cerebral palsy in China. Int J Epidemiol 28:949–54.

Marcdante KJ, Kliegman RM. 2014. Nelson Essentials of Pediatrics. 7th edition. Section 11, Gowen CW. Elsevier Saunders.

Martin JK. 1960. Cerebral Palsy in Manitoba. Can. Med. Assoc. J 82:411–7.

Michałowicz R. 2001. Mózgowe porażenie dziecięce. Warszawa: Wydawnictwo Lekarskie PZWL.

Milewska A, Mileańczuk-Lubecka BA, Kochanowski J, Werner B. 2011. Analiza czynników ryzyka mózgowego porażenia dziecięcego. Nowa Pediatria 4:79–84.

Murphy DJ, Sellers S, MacKenzie IZ, Yudkin PL, Johnson AM. 1995. Case-control study of antenatal and intrapartum risk factors for cerebral palsy in very preterm singleton babies. Lancet 346(8988):1449–54.

O'Shea M, Klinepeter KL, Dillard R. 1998. Prenatal Events and the Risk of Cerebral Palsy in Very Low Birth Weight Infants. Am J Epidemiol 147(4):362–9.

Öztürk A, Demirici F, Yavuz T, Yildiz S, Degirmenci Y, Döşoglu M, Avşar Y. 2007. Antenatal and delivery risk factors and prevalence of cerebral palsy in Duzce (Turkey). Brain Dev 29:39–42.

Pappas A, Kendrick DE, Shankaran S, Stoll BJ, Bell EF, Laptook AR, Walsh MC, Das A, Hale EC, Newman NS, Higgins RD. 2014. Chorioamnionintis and Early Childhood Outcomes among Extremely Low-Gestational-Age Neonates. JAMA Pediatrics 168(2):137–47.

Pharoah POD, Cooke T, Rosenbloom I, Cooke RWJ. 1987. Trends in birth prevalence of cerebral palsy. Arch Dis Child 62:379–84.

Pilypiene I, Drazdiene N, Dumalakiene I, Vezbergiene N, Bartkevičiene D, Šilkünas M, Bumbuliene Ž. 2015. The significance of fetal inflammatory response syndrome in early and later adaptation of premature infants. Arch Gynecol Obstet 291(1):67–72.

Platt MJ, Cans Ch, Johanson A, Surman G, Topp M, Torrioli M, Krageloh-Mann I. 2007. Trends in cerebral palsy among infants of very low birthweight (<1500 g) or born prematurely (< 32 weeks) in 16 European centres: a database study. The Lancet 369:43–50.

Reddihough DS, Collins KJ. 2003. The epidemiology and causes of cerebral palsy. Aust J Physiother 49:7–12.

Robertson ChMT, Svenson LW, Joffres MR. 1998. Prevalence of cerebral palsy in Alberta. Can J Neurol Sci 25:117–22.

Robertson ChMT, Watt M, Yasui Y. 2007. Changes in the Prevalence of cerebral Palsy for Children Born Very Prematurely Within a Population-Based Program Over 30 Years. JAMA 297(24):2733–40.

Sellier E, Anderson G, Surman G, Cans Ch. 2010. Trends in prevalence of cerebral palsy in children born with a birthweight of 2500 g or over in Europe from 1980–1998. Eur J Epidemiol 25(9):635–42.

Škrablin S, Maurac I, Banovič V, Bošnjak-Nadj K. 2008. Perinatal factors associated with the neurologic impairment of children born preterm. Int J Gynaecol Obstet 102:12–8.

Soleimani F, Vameghi R, Biglarian A. 2003. Antenatal and Intrapartum Risk Factors of Cerebral Palsy in Term and Near-term Newborns. Arch Iran Med 16(4):213–6.

Spinillo A, Capuzzo E, Orcesi S, Stronati M, Mario M, Fazzi E. 1997. Antenatal and delivery risk factors simultaneously associated with neonatal death and cerebral palsy in preterm infants. Early Hum Dev 48:81–91.

Steenwinckel JV, Schang AL, Sigaut S, Chhor V, Degos V, Hagberg H, Baud O, Fleiss B, Gressens P. 2004. Brain damage of the preterm infant: new insights into the role inflammation. Biochem Soc Trans 42(2):557–63.

Stoll BJ, Hansen NI, Adams-Chapman I, Fanaroff AA, Hintz SR, Vohr B, Higgins RD. 2004. Neurodevelopmental and Growth Impairment Among Extremely Low-Birth-Weight Infants With Neonatal Infection. JAMA 292(19):2357–65.

Strunk T, Inder T, Wang X, Burgner D, Mallard C, Levy O. 2014. Infection-induced inflammation and cerebral injury in preterm infants. The Lancet Infectious Diseases 14(8):751–62.

Tran U, Gray PH, O'Callaghan MJ. 2005. Neonatal antecedents for cerebral palsy in extremely preterm babies and interaction with maternal factors. Early Hum Dev 81(6):555–61.

Wilson-Costello D, Friedman H, Minich N, Fanaroff AA, Hack M. 2005. Improved survival rates with increased neurodevelopmental disability for extremely low birth weight infants in the 1990s. Pediatrics 115(4):997–1003.

Winter S, Autry A, Boyle C, Yeargin-Allsopp M. 2002. Trends in the Prevalence of Cerebral Palsy in a population – Based Study. American Academy Of Pediatrics 110:1220–5.

Wu YW, Colford JM. 2002. Chorioamnionitis as a risk factor for cerebral palsy: a meta-analysis. JAMA 284(11):1417–24.

Yoon BH, Jong JK, Romero R, Park KH, Gomez R, Choi JH, Kim IO. 1997. Amniotic fluid inflammatory cytokines (interleukin-6, interleukin-1beta, and tumor necrosis factor-alpha), neonatal brain white matter lesions, and cerebral palsy. Am J Obstet Gynecol 177(1):19–26.

Zgorzalewicz B, Mieszczanek T, Zgorzalewicz M. 2001. Epidemiologia opisowa mózgowego porażenia dziecięcego. Ortopedia Traumatologia Rehabilitacja 3(4):467–71.