

# Risk Factors Associated with Cerebral Palsy in Newborns

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## ABSTRACT

*The aim of this study was to investigate the risk factors associated with cerebral palsy (CP). For this purpose, a total of 55 newborns were investigated in the case control design study, with a total of 55 additional newborns that were matched to the cases. All patients were recruited in University Clinical Hospital Mostar and other institutions in the region between 1997–2005. The comparison of the Apgar score did not seem to show significant differences between cases and controls (odds ratio [OR]=1.15, 95% confidence intervals [CI] 0.36–3.69). Hypoxia was more common in the CP group (36.3% vs. 5.4% in the control group;  $p<0.001$ ). Additionally, cases were more frequently exposed to the infections ( $p<0.001$ ), intracranial hemorrhage ( $p=0.002$ ), premature delivery, before the 28th gestation week ( $p=0.027$ ), as well as the premature delivery during the 28–34 gestation week ( $p=0.001$ ), and 34–38 gestation week ( $p=0.018$ ). Accordingly, small birth weight was associated with cases more often than controls ( $p=0.003$ ). Bleeding during pregnancy was also more common in cases than controls ( $p=0.032$ ), while the breech presentation, emergency cesarean section, hydrocephalus, placenta disorders and pre-eclampsia were not associated with CP. The results suggest that CP cases were more commonly exposed to numerous risks, which all seem to contribute to the increased chances of CP. Traditional indicator, poor Apgar score was not found to be significantly associated with the CP.*

**Key words:** cerebral palsy, dyslalia, risk factors, apgar, Bosnia and Herzegovina

## Introduction

Cerebral palsy is a serious complication recorded in some newborns, which affects their development and causes a substantial problem for the family and the overall society. Therefore, it is of high interest to understand why some newborns acquire this disease, in order for the physician to be able to reduce the risks. Numerous studies have so far been able to identify some risk factors, broadly described as the factors that contribute to the pregnancy being termed pregnancy under risk. These include e.g. early gestation, various complications in mother, placenta or fetus.

## Materials and Methods

This study was based on the children with cerebral palsy, recruited from the University Clinical Hospital Mostar and two private institutions, the holy family Mostar and Široki Brijeg. The recruitment period included all recorded cases from 1997 and 2005 (N=55). In

addition, a control was assigned to each case, recruited amongst the children with dyslalia. The controls were matched according to the gender and age ( $\pm 2$  years). A number of parameters were recorded, including pregnancy records, birth procedures, maternal status and some newborn characteristics. Statistical analysis was performed in the SPSS v 13 (SPSS Inc, Chicago, IL).

$\chi^2$ -test was used in the analysis, with odds ratios calculated between cases and controls.

## Results

Among the total of 55 cases, 28 (50.9%) were males and 27 (49.1%) were females ( $\chi^2=0.02$ ,  $p=0.893$ ). Apgar scores between the first and fifth minute were not different between the cases and controls (Table 1). The type of delivery also did not show any significant differences between cases and controls (Table 2). Hypoxia was signifi-

**TABLE 1**  
APGAR SCORES IN 1<sup>ST</sup> AND 5<sup>TH</sup> MINUTE IN CASES AND CONTROLS

Apgar score	Median (interquartile range)		OR	95% CI
	Cases	Controls		
1 <sup>st</sup> min	7.0 (4)	9.0 (1)	1.15	0.36–3.69
5 <sup>th</sup> min	9.0 (3)	10.0 (0)	0.13	0.01–1.88

**TABLE 2**  
TYPES OF DELIVERY IN CASES AND CONTROLS INCLUDED IN THE STUDY

Type of delivery	Number (%)				p	OR	95% CI
	Unexposed		Exposed				
	Cases	Controls	Cases	Controls			
Cesarean section	49 (47.6)	54 (52.4)	6 (85.7)	1 (14.3)	0.113	6.61	0.77–56.88
Emergency cesarean section	52 (49.5)	53 (50.5)	3 (60.0)	2 (40.0)	1.000	1.53	0.25–9.53
Breech	53 (49.1)	55 (50.9)	2 (100.0)	0 (0.0)	0.495	n/a	n/a
Hipoxya	35 (40.2)	52 (59.8)	20 (87.0)	3 (13.0)	<0.001	9.91	2.74–35.87
Infection	39 (41.5)	55 (58.5)	16 (100)	0 (0)	<0.001	n/a	n/a
Intracranial hemorrhage	43 (44.3)	54 (55.7)	12 (92.3)	1 (7.7)	0.002	15.07	1.89–120.50
Premature water burst	49 (50.0)	49 (50.0)	6 (50)	6 (50)	0.999	1.00	0.30–3.32
Hydrocephalus	50 (47.6)	55 (52.4)	5 (100)	0 (0)	0.057	n/a	n/a
Premature birth (less than 28 gestational weeks)	49 (47.1)	55 (52.9)	6 (100)	0 (0)	0.027	n/a	n/a
Premature birth (28–34 gestational weeks)	43 (43.9)	55 (56.1)	12 (100)	0 (0)	0.001	n/a	n/a
Premature birth (34–38 gestational weeks)	42 (45.2)	51 (54.8)	13 (76.5)	4 (23.5)	0.018	3.95	1.20–13.01
Birthweight less than 1500g	46 (45.5)	55 (54.5)	9 (100)	0 (0)	0.003	n/a	n/a
Pregnancy bleeding	47 (46.5)	54 (53.5)	8 (88.9)	1 (11.1)	0.032	9.19	1.11–76.22
Placenta disorders	50 (47.6)	55 (52.4)	5 (100)	0 (0)	0.057	n/a	n/a
Preeclampsia	52 (49.5)	53 (50.5)	3 (60)	2 (40)	0.999	1.53	0.25–9.53

Fisher's exact test was used; n/a not available

cantly more frequently present in the cases than controls ( $\chi^2=15.89$ ,  $p<0.001$ ), with odds ratio (OR) of 9.91 (95%CI 2.74–35.87). Additionally, infections were more commonly reported in cases than controls ( $\chi^2=18.72$ ,  $p<0.001$ ; Table 2). Furthermore, intracranial hemorrhage was more common in cases, with OR of 15.07 (Table 2).

Premature births (less than 28 gestational weeks) were more common in cases, as were premature births between 28<sup>th</sup> and 34<sup>th</sup> gestation weeks (Table 2). Even in the latest premature birth group, cases were significantly more frequent than controls, suggesting that premature birth was strongly associated with CP (Table 2). Finally, low birth weight (less than 1500 g) was also more common in cases, but without sufficient number of cases for odds ratios to be calculated (Table 2).

Finally, the analysis of the risk factors from prenatal period suggested only that bleeding in pregnancy was significant risk factors, while the remaining characteristics did not exhibit significant association with CP (Table 2).

## Discussion

Recognizing possible neurological risk in newborns is of great importance for their further development, especially in the early stages when the repair opportunities are still large<sup>1</sup>. As the main result, this study suggested that the Apgar score is not as good predictor as it was traditionally considered to be<sup>2,3</sup>. It was the lack of oxygen that was the most commonly associated with the adverse outcomes, a finding that was reported in a number of studies<sup>4–6</sup>. Furthermore, a number of potential events, related to both birth and the pregnancy can affect the perinatal outcome<sup>6</sup>. Local lack of oxygen leads to the loss of energy needed to maintain homeostasis and consequently leads to the neuronal necrosis<sup>7</sup>. These necroses can then lead to various clinical manifestations of in the underdeveloped brain, contributing to fetal encephalopathy. The results of this study support the role of hypoxia in the CP development. Yet, it should be noted that only a third of all CP cases were exposed to hypoxia, while the remaining number was not exposed<sup>6</sup>. This lead

to an interesting suggestion, that fetal brain of the healthy fetus during the childbirth shows amazing resistance to the lack of oxygen, if the fetus has entered the delivery process unharmed<sup>4-6</sup>. The true question is why then such resistance is lost? So far, co-natal infections were attributed with the increased risks of hypoxic damage. The amount of evidence for this is rather small, proven in either histological results of clinical studies<sup>3,8</sup>. Some other disorders were also implied, such as the maternal hyperpyrexia<sup>3,8</sup>. The results of this study confirm such statements, suggesting that cases were more often exposed to infections.

Furthermore, CP and neural damage seemed to have been associated with shorter gestation and lower birth weight, which usually account 1.5% of the population and has a survival rate of 50%<sup>9</sup>. Due to these facts, this group of newborns is usually characterized with a total prevalence of CP of 10% and other mild neurological deficits of up to 50%<sup>9,10</sup>.

There is an interesting finding, showing that the shortest gestation group had lesser odds of having CP. This finding might be associated with the occurrence of leukomalacia, with 7–17% in premature births and 26% in fetuses with less than 34 weeks of gestation, based on the optimal technology and best possible approach<sup>9,11</sup>. This could be associated with developmental phases of the brain growth and the dynamics of the changes that occur during the fetal life, associated with the subplate zone development<sup>9,12,13</sup>. This zone is the most developed during the 22<sup>nd</sup>–32<sup>nd</sup> weeks of gestation, the period after which it disappears<sup>9</sup>. This is why some newborns with very short gestation may have more favorable outcomes than those born closer to the term<sup>9</sup>.

Overall, the results of this study contribute to the knowledge of the fetal neuronal risks, suggesting that a number of factors need to be taken into account when dealing with high risk pregnancies and newborns.

## REFERENCES

1. BOŠNJAK-NAD K, *Gynaecol Perinatol*, 13 Suppl 2 (2004) 56. — 2. GAFFNEY G, SELLERS S, FLAVELL V, *BMJ*, 308 (1994) 743. — 3. NELSON KB, GREYER JK, *Am J Obstet Gynecol*, 179 (1998) 507. — 4. BADAVIDI N, KURINCZUK JJ, KEOGH JM, *BMJ*, 317 (1998) 1549. — 5. BADAVIDI N, KURINCZUK JJ, KEOGH JM, *BMJ*, 317 (1998) 1554. — 6. ŠKRABLIN S, *Gynaecol Perinatol*, 13 (2004) 31. — 7. AZZOPARDI D, WAYAT JS, CADT EB, *Pediatr Res*, 25 (1989) 445. — 8. WU YW, COLFORD Jr JM, *JAMA*, 284 (2000) 2996. — 9. MEJAŠKI-BOŠNJAK V, GOJ-
- MERAC T, ĐURANOVIĆ V, KRAKAR G, *Gynaecol Perinatol*, 13 (2004) 41. — 10. PAPILE LA, BURSTEIN J, BURSTEIN R, KOFFER H, *Pediatrics*, 92 (1978) 529. — 11. De VRIES L, EKEN P, GROENENDAL F, HAASSTERT IC, MEINERS LC, *Neuropediatr*, 24 (1993) 263. — 12. KOSTOVIĆ I, JUDAŠ M, *Croat Med J*, 39 (1998) 107. — 13. KOSTOVIĆ J, LUKINOVIĆ N, JUDAŠ M, BOGDANOVIĆ N, MRZLJAK L, ZEČEVIĆ N, *Metab Brain Dis*, 4 (1989) 17.

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## ČIMBENICI RIZIKA POVEZANI SA CEREBRALNOM PARALIZOM

### SAŽETAK

Cilj ovog istraživanja bio je istražiti rizične čimbenike povezane s pojavom cerebralne paralize (CP). U tu svrhu analizirani su podaci 55 djece sa jednako toliko kontrola koje su imale glosolaliju. Djeca su u istraživanje uključena na temelju dolaska u Kliničku bolnicu Mostar i dvije druge ustanove tijekom 1999–2005. godine. Usporedba Apgar rezultata nije ukazala na značajnu razliku između slučajeva i kontrola (omjer šansi [OR]=1,15, 95% interval pouzdanosti [CI] 0,36–3,69). Hipoksija je bila češća kod slučajeva (36,3% vs. 5,4%;  $p < 0,001$ ). Slučajevi su češće bili izloženi infekcijama ( $p < 0,001$ ), intrakranijalnom krvarenju ( $p = 0,002$ ), preranom porodu, prije 28. tjedna gestacije ( $p = 0,027$ ), kao i porod tijekom 28–34. tjedna gestacije ( $p = 0,001$ ), pa i 34–38. tjedna gestacije ( $p = 0,018$ ). Također, i manja porodna težina bila je povezana s CP ( $p = 0,003$ ). Krvarenje tijekom trudnoće je isto tako bilo češće zabilježeno među slučajevima nego kontrolama ( $p = 0,032$ ), dok stav zatkom, hitan carski rez, hidrocefalus, poremećaji funkcije placente i preeklampsija nisu bili povezani s povećanim rizikom CP. Rezultati ovog istraživanja ukazuju na mnogostruke rizične čimbenike koji mogu doprinijeti pojavi CP. Tradicionalni čimbenici poput Apgar rezultata nisu bili povezani sa pojavom CP.