Original Article

Developing a Cerebral Palsy Risk Score for Newborns

Chuenchom Chueluecha MD[1], Warangkana Deeprasertdamrong MD[1], Paskorn Sritipsukho MD[2,3]

[1] Department of Rehabilitation Medicine, Faculty of Medicine, Thammasat University, Pathum Thani, Thailand

[2] Department of Pediatric, Faculty of Medicine, Thammasat University, Pathum Thani, Thailand

[3] Center of Excellence in Applied Epidemiology, Thammasat University, Pathum Thani, Thailand

Background: Cerebral palsy (CP) causes developmental delays, affecting quality of life. Many risk factors are theorized however, no total risks summary exists, nor a CP prediction score for newborns. The result is under surveillance, treatment delays, and non-rectifiable complications.

Objective: To establish total risk factors and create a prediction score for assessing CP neonatal risk before discharge. A prediction score has great utility for medical professionals and parents in screening high-risk patients and developing adequate monitoring systems.

Materials and Methods: Using a case-controlled retrospect of children aged 0 to 2 years, born at Thammasat University Hospital, Thailand between 2005 and 2014, prenatal, perinatal, and postnatal risks were compared between children without CP as control, and those diagnosed with CP as case, by multivariable logistic regression. Predictors were assessed with area under the receiver operating characteristic (AuROC), odds ratio (OR), 95% confidence interval (CI), p-value, and clinical predisposition. Logistic regression was applied, including calibration, validation, and categorization of risk.

Results: Cerebral and non-cerebral malformations, multi-fetal gestation, low birthweight, and neonatal sepsis were found as potential predictors, scoring 3, 1.5, 1, 2, 2.5, respectively, AuROC being 0.86 (95% CI 0.79 to 0.92). Low, moderate, and high-risk groups were set with scores of less than 1, 1.5 to 3, and more than 3.5, respectively.

Conclusion: The present predictive CP risks and scoring system shows excellent discrimination power. If newborns were categorized in the high-risk group, close monitoring and surveillance are needed.

Keywords: Cerebral palsy, Risk score, Prenatal, Perinatal, Postnatal

Received 16 June 2020 | Revised 14 October 2020 | Accepted 15 October 2020

J Med Assoc Thai 2021;104(2):240-6

Website: http://www.jmatonline.com

Cerebral palsy (CP) is a predominant source of childhood disability[1] and a movement disorder affecting muscle tone or posture. Its root cause is damage to the immature, developing brain[2], which impedes development, contracts muscles, and impairs muscle control. Various complications occur such as joint contracture, pressure ulcers, and pneumonia[3], affecting self-help, patient socialization, and familial relationships. Those may increase patient care costs. CP is believed to have multiple risk factors[4,5], and there has been no total CP risk summary for neonates, nor criteria for risk assessment prior to discharge. It is highly probable that under surveillance occurs, along with subsequent treatment delays, and possibly irreversible complications.

The authors attempted to establish the risk factors and create a prediction score for assessing CP neonatal risk before discharge. A prediction score has great utility for medical professionals and parents, especially in smaller hospitals lacking specialists. The present CP risk prediction score may aid general practitioners or nurses in screening high-risk patients and developing adequate monitoring systems.

Correspondence to:

Chueluecha C.

Department of Rehabilitation Medicine, Faculty of Medicine, Thammasat University, Pathum Thani, 12120, Thailand.

Phone: +66-2-9269834, +66-89-4584620, **Fax**: +66-2-9269793

Email: puaichuenchom@hotmail.com

ORCID: 0000-0002-9242-4702

How to cite this article:

Chueluecha C, Deeprasertdamrong W, Sritipsukho P. Developing a Cerebral Palsy Risk Score for Newborns. J Med Assoc Thai 2021;104:240-6.

doi.org/10.35755/jmedassocthai.2021.02.11570

Materials and Methods

The present paper was an exclusive retrospective case control study of neonatal CP risk factors in children aged 0 to 2 years, born at Thammasat University Hospital, Thailand between 2005 and 2014. The study population was those children diagnosed with CP with no neurological disorders from neonatal stroke, intracerebral hemorrhage, subgaleal hematoma, thrombotic disease, or other disorders of the nervous system that may later prove to be progressive conditions. Patients who suffered an accident or infection fatal to the nervous system after

discharge from the hospital, or patients appearing to have nervous system disorders noted upon physical examination prior to discharge, were excluded. Cases with CP were selected using standard criteria as a permanent disorder of movement, muscle tone, or posture caused by non-progressive damage to the immature, developing brain[2]. Babies, without CP, who were born in the same day or near the target population formed the control, with a target: normal population of 1:10. The present study sample size was calculated using the odds ratio (OR) and probability of exposure among non-case patients in accordance with various risk factor data[6,7]. The sample size was determined to be at least 40 cases with 400 controls. Statistical analysis was done using Stata, version 14 (StataCorp LP, College Station, TX, USA).

The authors analyzed and compared various risk factors in children with CP, as case, and children without CP, as control, by exploring all potential predictors included intrapartum maternal characteristics, neonatal characteristics, and perinatal events before discharge. Exact McNemar's probability test was used and defined what was statistically significant at p-value less than 0.05. Area under the receiver operating characteristic (AuROC) classified each risk factor's power. The determination of best risk factors for the present study predictive model was done by selecting variables from adjusted OR, p-value, AuROC, and clinical correlations using binary logistic regression. A stepwise approach created the predictive variable set, and the model's discrimination power was tested with AuROC.

Next, an individual risk rating and total risk score was designed by logistic regression. A score for the selected CP predictor variables was assigned to each of the two populations, with "yes" (means having risk factors) and "no" (no risk factors), then the total score for each was calculated. The model performance by discrimination measurement was distributionally plotted in bar graphs, with AuROC values of non-parametric ROC. Calibration was measured by comparing observed and predicted risk plots. The model was tested using the Hosmer-Lemeshow goodness-of-fit-test. Prediction was then done by separating the CP predictive variables into different levels. Levels were specified by predictive scores according to the increased risk curve and positive likelihood ratio (LHR+). Internal validity was tested by the bootstrap method.

The present research was approved by the Research Ethics Subcommittee on Human Research, Faculty of Medicine, Thammasat University on November 24, 2016 (Research Project Code MTU-EC-RM-1-181/59). Informed consent for participation and publication has been obtained.

Operational definitions

Fetal growth restriction (FGR): birthweight of newborn under the tenth percentile for weight as compared to the same population at the time of gestation[8]

Term: babies born at or after 37 weeks of pregnancy[9]

Preterm: born before 37 weeks of pregnancy[9]

Low birthweight: birthweight less than 2,500 g, regardless of gestational age[10]

Fetal distress: fetus does not receive oxygen adequately during labor, signs or symptoms are characterized using abnormal electronic fetal heart rate (FHR) monitoring or meconium-stained amniotic fluid[11]

Chorioamnionitis: pregnancy with "inflammatory or an infectious" disorder of the chorion, amnion, or both, diagnosis based on fever presenting with one or more of the following:

1. Fetal tachycardia (greater than 160 bpm for 10 minutes or longer)
2. Maternal white blood cell (WBC) count greater than 15,000 per microliter in absence of corticosteroids
3. Purulent fluid from the cervical os (cloudy or yellowish thick discharge confirmed visually on speculum exam coming from the cervical canal)
4. Biochemical or microbiologic amniotic fluid results consistent with microbial invasion of the amniotic cavity[12]

Premature rupture of membranes or prelabor rupture of membranes (PROM): the rupture of the chorio-amnionic membrane before the onset of labor[13], both in term and preterm labor

Maternal sepsis: two or more Systemic Inflammatory Response Syndrome (SIRS) criteria associated with proven or clinically suspected infection in pregnancy during labor:

1. Temperature higher than 38°C or lower than 36°C
2. Heart rate greater than 90 per minute
3. Respiratory rate greater than 20 per minute or $PaCO_2$ smaller than 32 mmHg (4.3 kPa)
4. WBC count greater than 12,000 per mm^3 or less than 4,000 per mm^3 or more than 10% immature bands[14]

Maternal urinary tract infection (UTI): pregnancy-related UTI includes all clinical types:

1. Asymptomatic bacteriuria (ASB)

Table 1. Univariate and multivariable analysis of cerebral palsy risk factors

Risk factor	CP (n=49); n (%)	No CP (n=561); n (%)	Univariate analysis		Multivariable analysis	
			OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Neonatal characteristics						
Cerebral malformation	7 (14.29)	1 (0.18)	93.83 (11.28 to 780.66)	<0.001	250.43 (26.29 to 2,385.48)	<0.001
Non-cerebral malformation	14 (28.57)	5 (0.89)	44.71 (15.24 to 131.25)	<0.001	16.04 (2.83 to 90.86)	0.002
Prenatal events						
Fetal growth restriction	11 (22.45)	42 (7.68)	3.48 (1.66 to 7.30)	0.001		
Multi-fetal gestation	10 (20.00)	6 (1.06)	23.29 (8.06 to 67.35)	<0.001	5.42 (0.55 to 52.88)	0.146
Perinatal events						
Preterm	24 (48.98)	13 (2.30)	40.69 (18.56 to 89.21)	<0.001	4.00 (0.66 to 24.34)	0.132
Low birthweight	26 (52.00)	3 (0.53)	172.91 (52.82 to 565.99)	<0.001	32.60 (5.31 to 199.96)	<0.001
Apgar score 5-minute, score <7	6 (12.24)	0 (0.00)	167.21 (9.27 to 3,017.42)*	<0.001		
Fetal distress	5 (10.00)	15 (2.65)	4.07 (1.42 to 11.72)	0.009	5.19 (0.88 to 30.66)	0.069
Uterine and cord abnormalities	3 (6.00)	0 (0.00)	83.36 (4.24 to 1,637.36)*	0.004		
Maternal infection	9 (18.00)	2 (0.35)	61.79 (12.92 to 295.43)	<0.001		
Postnatal events						
Neonatal jaundice	12 (24.00)	4 (0.71)	44.29 (13.63 to 143.89)	<0.001	4.56 (0.26 to 80.01)	0.299
Neonatal seizure	3 (6.00)	0 (0.00)	83.34 (4.24 to 1,637.36)*	0.004		
Neonatal encephalopathy	3 (6.00)	0 (0.00)	83.34 (4.24 to 1,637.36)*	0.004		
Congenital infection	3 (6.38)	0 (0.00)	88.96 (4.52 to 1,749.34)*	0.003		
Neonatal sepsis	17 (34.00)	1 (0.18)	290.55 (37.51 to 2,250.41)	<0.001	63.15 (5.03 to 793.09)	0.001
Use of mechanical ventilator	14 (29.70)	0 (0.00)	475.35 (27.77 to 8,136.42)*	<0.001		

CP=cerebral palsy; OR=odds ratio; CI=confidence interval

* Penalized maximum likelihood estimation

2. Acute cystitis
3. Acute pyelonephritis[15]

Neonatal sepsis: a clinical infection or sepsis that diagnosed and treated by a physician with or without positive hemoculture:

1. Difficulty feeding
2. Convulsions
3. Movement only when stimulated
4. Respiratory rate greater than 60 per minute
5. Severe drawing in of breath (chest) and axillary temperature higher than 37.5°C or lower than 35.5°C
6. Cyanosis and grunting[16]

Results

The present study included 49 patients diagnosed with CP and 561 children without. Neonatal and maternal characteristics, prenatal, perinatal, and postnatal risks, evidence of differences were measured as p-value. The univariate (OR) and multivariable (adjusted OR) analysis of CP risk are shown in Table 1. Cerebral and non-cerebral malformations, multi-fetal gestation, preterm, low birthweight, fetal distress, neonatal jaundice, and neonatal sepsis were risks adjusted OR 250.43, 16.04, 5.42, 4.00, 32.60, 5.19, 4.56, and 63.15, respectively. Cerebral and non-cerebral malformations, multi-fetal gestation, low birthweight, and neonatal sepsis were deemed predictors, with risk ratings of 3, 1.5, 1, 2, 2.5, respectively, adding up to 10 points (Table 2).

Discrimination measures and clinical prediction score calibration were given as distribution percentages within the CP risk score. Results for the present study controls were 97.15% at 0, 1.07% at 1 point, 0.89% at 1.5 points, 0.53% at 2, 0.18% at 2.5, and 0.18% at 3. The cases were 26.53% at 0, 2.04% at 1.5, 4.08% at 2, 8.16% at 2.5, 16.33% at 3, 10.20% at 3.5, 16.33% at 4.5, 2.04% at 5.5, 6.12% at 6, 4.08% at 7, 2.04% at 7.5, and 2.04% at 8.5. AuROC of the total risk score using non-parametric ROC was 0.86 (95% CI 0.80 to 0.93). Plotting consistency could be seen between observed and predicted risk, as shown in Figure 1; Hosmer-Lemeshow goodness-of-fit was p=0.32.

The authors divided CP prediction risk into three groups. Low risk had a score of 1.0 or less, having 13 cases (26.53%) in the group with CP, and 551 cases (98.22%) in the group without CP: LHR+ 0.27 and

Table 2. Best multivariable clinical predictors, odds ratio, 95% CI, logistic regression beta coefficient (β) and assigned item scores

Predictors	OR	95% CI	p-value	Beta	Score
Cerebral malformation					
No	1.00	Reference	-	-	0
Yes	227.79	24.75 to 2,096.18	<0.001	5.43	3
Non-cerebral malformation					
No	1.00	Reference	-	-	0
Yes	16.34	3.22 to 83.02	0.001	2.79	1.5
Multi-fetal gestation					
No	1.00	Reference	-	-	0
Yes	6.079	0.91 to 40.74	0.063	1.81	1
Low birthweight					
No	1.00	Reference	-	-	0
Yes	52.65	11.22 to 246.99	<0.001	3.96	2
Neonatal sepsis					
No	1.00	Reference	-	-	0
Yes	143.89	14.41 to 1,437.01	<0.001	4.97	2.5

OR=odds ratio; CI=confidence interval

95% CI 0.00 to 0.02. Moderate risk was a score 1.5 to 3.0; there were 15 cases (30.61%) in the group with CP and 10 cases (1.78%) in those without: LHR+ 17.17 and 95% CI 9.30 to 64.57. High risks were those with a score of 3.5 or higher. There were 21 cases (42.86%) in the group with CP, but none found in the children without (0.00%): LHR+ ∞ as shown in Table 3. Internal validation using the bootstrap method had AuROC value 0.73 (95% CI 0.61 to 0.86).

Discussion

Theoretically, there are multiple variables surrounding neonatal CP risk. The present study aim was to increase awareness, especially in general practitioners, by exploring, outlining, and comparing all possible causes. This included both neonatal and maternal characteristics, as well as prenatal, perinatal, and postnatal risk factors. Cerebral and non-cerebral malformations, multi-fetal gestation, low birthweight, and neonatal sepsis are CP predictors easily observed in clinical practice. Furthermore, these five factors can be readily diagnosed without specialized tools as they are not complicated and have clear diagnostic criteria.

In view of each CP predictors, cerebral and non-cerebral malformations present as the risk for CP in accordance with other studies[17,18]. Multi-fetal gestation, twin pregnancy[19,20] has a strong relationship with CP, but triplets have an even stronger connection[19]. Low birthweight was documented

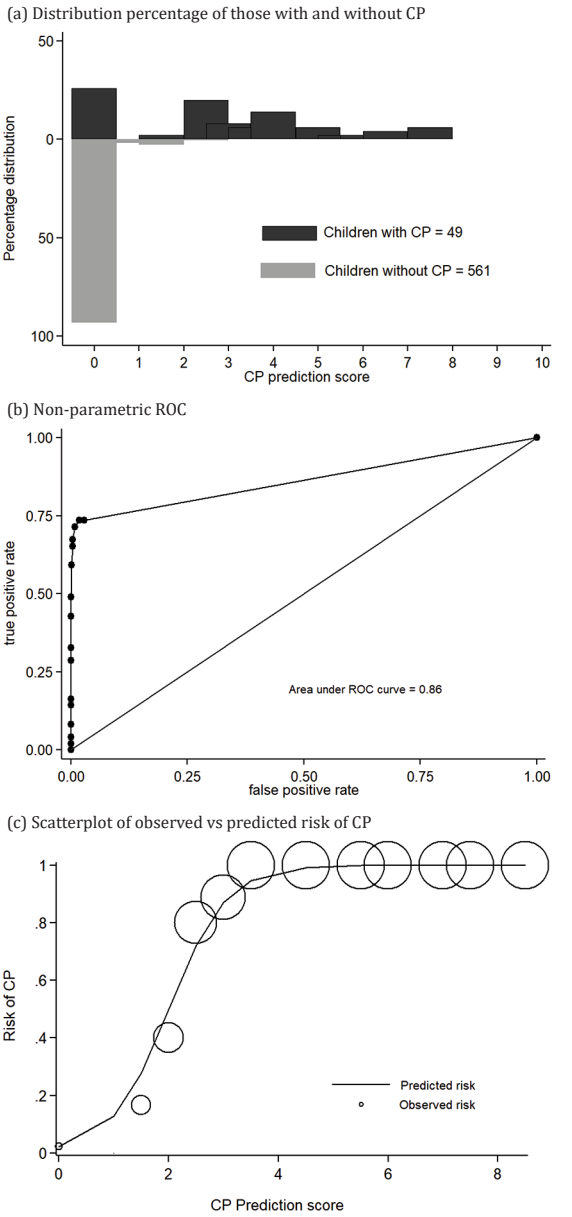

Figure 1. Discrimination measures and clinical prediction score calibration: (a) Distribution percentage of those with and without CP, (b) Non-parametric ROC, (c) Scatterplot of observed vs. predicted risk of CP.

as a notable risk and found in conjunction with an increased CP prevalence, especially for children weighing 1,000 to 1,499 g to 59.18 per 1,000 live births[21]. Neonatal sepsis, the typical sequela after neonatal sepsis was neurodevelopmental impairment (14%), 8% had CP and growth retardation[22], this is reported as a strong risk for CP in all gestational age groups[23].

As mentioned, the adjusted OR was determined

Table 3. Distribution of cases vs controls into low, moderate and high probability categories, LHR+ and 95% CI

Probability categories	Score	Cases (n=49); n (%)	Controls (n=561); n (%)	LHR+	95% CI	p-value
Low	≤1.0	13 (26.53)	551 (98.22)	0.27	0.00 to 0.02	<0.001
Moderate	1.5-3.0	15 (30.61)	10 (1.78)	17.17	9.30 to 64.57	<0.001
High	≥3.5	21 (42.86)	0 (0.00)	∞	-	<0.001
Mean±SD	-	2.99±2.32	0.04±0.28			<0.001

LHR+=likelihood ratio of positive; CI=confidence interval; SD=standard deviation

by logistic regression when there were significant differences ($p<0.05$) between the two groups. An Apgar score at 5 minutes of less than 7, uterine and cord abnormalities, neonatal seizure, neonatal encephalopathy, congenital infection, and ventilator use, only appeared in the case group. Therefore, the authors used the penalized maximum likelihood estimation for these variables and the risk difference model. However, when comparing these results with the prediction model obtained by the multivariable logistic regression, the AuROC performance and log likelihood did not differ significantly. In addition, AuROC of the model was 0.86, thus, the predictive set's ability to identify CP was considered excellent[24]. Score accuracy was consistent in comparing observed to predicted risk plots, fitting the present model ($p=0.32$).

As the authors' recommendation, high risk is defined as having a score 3.5 or more, there was an absence of any controls at this level (LHR+ ∞). Therefore, newborns with this score should be closely monitored by doctors every one to three months for the assessment of development, muscular tightness, and spasticity, especially during the first year. It would be prudent to continue this until school age. For those newborns in the moderate risk group (score 1.5 to 3.0) (LHR+ 17.17), they should have regular follow-ups with their doctors every three to six months, especially at any of the major developmental milestones such as sitting, standing, and walking. Neonates within the low-risk group (score of 1.0 or lower) (LHR+ 0.27) can have follow-ups and screening with nurses at every regular vaccination appointment and checkup, usually every six months.

Nonetheless, parents of all risk groups need to receive knowledge regarding the developmental levels and expectations according to age and other underlying diseases, as well as CP signs and symptoms, so parents can aid in surveillance.

Limitation

To the best of the authors' knowledge, there are no criteria for assessing the CP risk in newborns at present. The present research is a first attempt to create prediction scores for newborn CP risk, after delivery but before discharge. The authors considered this to be a crucial time in the sense in that infants at risk for CP would receive better monitoring. This would lead to early diagnosis and, hopefully, reduce associated complications. The authors believe this prediction score, or a modified version of it, is useful for small community hospitals without specialized doctors or sufficient medical personnel or resources. The predictive criteria can help general practitioners, other doctors, or even pediatric nurses screen children and determine risk groups requiring close monitoring.

However, as the present study was a retrospective case control containing children without CP, there are very few or no events for some risk factors. Therefore, the authors were unable to find the OR value in these situations as aforementioned and instead used penalized maximum likelihood estimation and the risk difference model, as stated before, AuROC performance and log likelihood did not differ significantly between the prediction model for multivariable logistic regression and this.

Further study in the context of other hospitals or clinics could provide some external validation in areas such as detection rate, false positives, false negatives, and challenges or obstacles. It would be insightful to measure medical staff and parental acceptance or cooperation implementing these guidelines. Finally, it is useful to have long-term studies on patient outcomes and detection rates that included both newborns who were assessed with the criteria and those who were not. Most importantly, the authors would like to know if the present prediction factors could ameliorate the CP detection rate. The authors hope all these ideas can move everyone forward to create a set of variables relevant for a wide variety of hospitals and settings.

Conclusion

Cerebral and non-cerebral malformations, multi-

fetal gestation, low birthweight, and neonatal sepsis were found to be CP risks. Even though the risk may not be as high, all medical professionals should also be vigilant with infants having fetal distress, preterm, or having neonatal jaundice. Using children without CP as controls for the present retrospective research led to having very few or absent events or risk factors in that group. This should be taken into consideration when designing future studies. Further long-term multicenter research would increase events in both control and case groups and permit a deeper analysis of possible associations with CP. Nonetheless, having an easy to use and understand score, from 0 to 10, and categories, from high, moderate, and low, for CP risks, such as the present study, can help all practitioners and parents determine which infants need to be closely, moderately, or regularly monitored for CP.

What is already known on this topic?

Many risk factors for CP are theorized from neonatal to maternal characteristics. There has been no total CP risk summary for neonates nor criteria for risk assessment prior to discharge.

What this study adds?

There has been no prediction score for assessing CP neonatal risk before discharge. The present CP prediction score can categorize newborns into low, moderate, or high-risk scoring by cerebral or non-cerebral malformations, multi-fetal gestation, low birthweight, and neonatal sepsis as risk predictors.

Acknowledgement

The research was supported by the Faculty of Medicine, Thammasat University, Thailand.

Conflicts of interest

The authors declare no conflict of interest.

References

1. Kuban KC, Leviton A. Cerebral palsy. N Engl J Med 1994;330:188-95.
2. Bax M, Goldstein M, Rosenbaum P, Leviton A, Paneth N, Dan B, et al. Proposed definition and classification of cerebral palsy, April 2005. Dev Med Child Neurol 2005;47:571-6.
3. Weir KA, McMahon S, Taylor S, Chang AB. Oropharyngeal aspiration and silent aspiration in children. Chest 2011;140:589-97.
4. Himmelmann K, Ahlin K, Jacobsson B, Cans C, Thorsen P. Risk factors for cerebral palsy in children born at term. Acta Obstet Gynecol Scand 2011;90:1070-81.
5. Sukhov A, Wu Y, Xing G, Smith LH, Gilbert WM. Risk factors associated with cerebral palsy in preterm infants. J Matern Fetal Neonatal Med 2012;25:53-7.
6. Himpens E, Oostra A, Franki I, Vansteelandt S, Vanhaesebrouck P, den Broeck CV. Predictability of cerebral palsy in a high-risk NICU population. Early Hum Dev 2010;86:413-7.
7. Soleimani F, Vameghi R, Biglarian A. Antenatal and intrapartum risk factors for cerebral palsy in term and near-term newborns. Arch Iran Med 2013;16:213-6.
8. Blair EM, Nelson KB. Fetal growth restriction and risk of cerebral palsy in singletons born after at least 35 weeks' gestation. Am J Obstet Gynecol 2015;212:520.e1-7.
9. Palmer L, Blair E, Petterson B, Burton P. Antenatal antecedents of moderate and severe cerebral palsy. Paediatr Perinat Epidemiol 1995;9:171-84.
10. WHO: recommended definitions, terminology and format for statistical tables related to the perinatal period and use of a new certificate for cause of perinatal deaths. Modifications recommended by FIGO as amended October 14, 1976. Acta Obstet Gynecol Scand 1977;56:247-53.
11. American Pregnancy Association. Fetal distress: diagnosis, conditions & treatment [Internet]. 2015 [cited 2018 May 25]. Available from: https://americanpregnancy.org/healthy-pregnancy/labor-and-birth/fetal-distress-9221.
12. Higgins RD, Saade G, Polin RA, Grobman WA, Buhimschi IA, Watterberg K, et al. Evaluation and management of women and newborns with a maternal diagnosis of chorioamnionitis: summary of a workshop. Obstet Gynecol 2016;127:426-36.
13. Beckmann C. Premature rupture of membranes. In: Beckmann C, Ling FW, Barzansky BM, Herbert W, Laube DW, Smith RP, editors. Obstetrics and gynecology. 6th ed. Baltimore: Lippincott Williams & Wilkins; 2010. p. 213-6.
14. Morgan J, Roberts S. Maternal sepsis. Obstet Gynecol Clin North Am 2013;40:69-87.
15. Szweda H, Jóźwik M. Urinary tract infections during pregnancy - an updated overview. Dev Period Med 2016;20:263-72.
16. Opiyo N, English M. What clinical signs best identify severe illness in young infants aged 0-59 days in developing countries? A systematic review. Arch Dis Child 2011;96:1052-9.
17. Rankin J, Cans C, Garne E, Colver A, Dolk H, Uldall P, et al. Congenital anomalies in children with cerebral palsy: a population-based record linkage study. Dev Med Child Neurol 2010;52:345-51.
18. Nelson KB, Blair E. Prenatal factors in singletons with cerebral palsy born at or near term. N Engl J Med 2015;373:946-53.
19. Petterson B, Nelson KB, Watson L, Stanley F. Twins, triplets, and cerebral palsy in births in Western Australia in the 1980s. BMJ 1993;307:1239-43.
20. Grether JK, Nelson KB, Cummins SK. Twinning and

cerebral palsy: experience in four northern California counties, births 1983 through 1985. Pediatrics 1993;92:854-8.
21. Oskoui M, Coutinho F, Dykeman J, Jetté N, Pringsheim T. An update on the prevalence of cerebral palsy: a systematic review and meta-analysis. Dev Med Child Neurol 2013;55:509-19.
22. Haller S, Deindl P, Cassini A, Suetens C, Zingg W, Abu Sin M, et al. Neurological sequelae of healthcare-associated sepsis in very-low-birthweight infants: Umbrella review and evidence-based outcome tree. Euro Surveill 2016;21:30143.
23. Greenwood C, Yudkin P, Sellers S, Impey L, Doyle P. Why is there a modifying effect of gestational age on risk factors for cerebral palsy? Arch Dis Child Fetal Neonatal Ed 2005;90:F141-6.
24. Šimundić AM. Measures of diagnostic accuracy: basic definitions. EJIFCC 2009;19:203-11.