

# СРПСКИ АРХИВ

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## Cranial ultrasound as a complementary method to the general movements assessment in preterm infants for predicting the neurological outcome – a single center experience

Кранијални ултразвук као комплементарна метода процени општих покрета код превремено рођене деце за предвиђање коначног неуролошког исхода – искуство једног центра

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### Кранијални ултразвук као комплементарна метода процени општих покрета код превремено рођене деце за предвиђање коначног неуролошког исхода – искуство једног центра

#### SUMMARY

#### Сажетак

**Introduction/Objective** Implementing cranial ultrasound (CUS) into daily clinical practice represented a major advance in the diagnosis and treatment of newborns. Preterm birth is considered a risk factor for abnormal neurological development. The study aimed to evaluate the significance of CUS in preterms as a complementary method to the general movements assessment, for predicting neurological outcomes. Study was focused on a cohort of infants without significant neonatal morbidity.

**Methods** The study included 160 preterms, and was designed as a prospective clinical study. Statistical analysis included cranial ultrasound findings and the assessment of spontaneous motor activity in the first 5 days after birth ("Writhing" period), perinatal data, and pregnancy data.

**Results** The statistically significant association was between the group of infants in whom cerebral palsy was recorded in the final neurological outcome and abnormal CUS findings (p < 0.001). A statistically significantly more frequent pathological CUS finding was found in preterms born before 30 weeks of gestation (p < 0.001), newborns born by cesarean section (p < 0.001), and those who had an Apgar score of less than 8 in the first and fifth minutes after birth (p < 0.001). The specificity of the normal CUS is 86% but increases to 100% when combined with the normal finding of general motor activity in preterms.

**Conclusions** This research confirms that CUS can be a significant method for predicting neurological outcomes. It can provide data for the critical use of different methods of monitoring premature children, and can rationalize their examinations.

**Keywords:** preterm infants; cranial ultrasound; general movements; Prehtl's method; neurodevelopmental outcome

Увод/Циљ Примена ендокранијалног ултразвука (ЕУЗ) у свакодневној клиничкој пракси представља велики напредак у дијагнози и лечењу новорођенчади. Превремени порођај сматра се фактором ризика за поремећај неуролошког развоја. Циљ студије био је да се процени значај ЕУЗ код превремено рођене деце као комплементарне методе процени општих покрета, за предвиђање коначног неуролошког исхода. Студија је била фокусирана на кохорту новорођенчади без значајног неонаталног морбидитета.

Методе Студија је обухватила 160 превремено рођене деце и осмишљена је као проспективна клиничка студија. Статистичка анализа је обухватила налазе ЕУЗ и процену спонтане моторичке активности у првих 5 дана након рођења (Writhing период), перинаталне податке и податке о трудноћи. Резултати Статистички значајна повезаност постојала је између групе деце код које је церебрална парализа забележена у коначном неуролошком исходу и абнормалних налаза ЕУЗ (р < 0,001). Статистички значајно чешћи патолошки ЕУЗ налаз пронађен је код превремено рођене деце пре 30. недеље гестације (р < 0,001), новорођенчади рођене царским резом (р < 0,001) и оних који су имали Апгар скор мањи од 8 у првом и петом минуту након рођења (p < 0.001). Специфичност нормалног ЕУЗ је 86%, али се повећава на 100% када се комбинује са нормалним налазом опште моторичке активности код превремено рођене деце.

Закључак Ово истраживање потврђује да ЕУЗ може бити значајна метода за предвиђање неуролошких исхода, може пружити податке за критичку употребу различитих метода праћења превремено рођене деце и може рационализовати њихове прегледе.

Кључне речи: превремено рођена деца; ендокранијални ултразвук; општи покрети; Прехтлова метода; неуроразвојни исход

#### INTRODUCTION

Motor development in newborns, infants, and young children relies on the health of the central nervous system (CNS), influenced by genetic patterns and external stimuli. Mental and motor development are closely connected, with significant neurological changes occurring within the

first days and months of life. To assess these changes accurately, repeated evaluations, or developmental monitoring, are essential, as a single assessment may not detect certain neurological issues due to the immature CNS's variable responses [1, 2, 3].

Special clinical attention is drawn to newborns who have some risk of developing disorders of CNS. The most common perinatal factors are prematurity, low birth weight of the newborn, low Apgar score, multiple pregnancies, birth trauma, inadequate presentation of the fetus, and termination of delivery by cesarean section (C-section) [3–6]. Premature newborns (born before the age of 37 weeks) have a higher risk of sudden death syndrome and complications in general, compared to full-term infants [7, 8, 9].

Apart from the neurological and neurokinesiological examination of newborns and infants, additional diagnostic methods used in clinical practice to detect neurological abnormalities are cranial ultrasound (CUS) examination and magnetic resonance imaging. Implementing CUS into daily clinical practice represented a major advance in the diagnosis and treatment of newborns [10–13].

The general motor assessment (GMA) in premature infants is defined as a high-certainty method for predicting neurological outcomes. Still, this type of examination should only be performed by a trained and certified physician, which is not available in every hospital [14, 15, 16]. For that reason, this study aimed to evaluate the significance of the initial CUS in preterms as a widely available, complementary method of examination to GMA for predicting neurological outcomes.

### **METHODS**

This study was designed as a prospective clinical study and included preterm infants (gestational age  $\leq$ 37 weeks), born in the Gynecology and Obstetrics Clinic of the University Clinical Center Niš between 2012 and 2014. It was performed in line with the principles of the Declaration of Helsinki and approved by the Ethics Board of the University Clinical Center Niš (No. 5718/1).

During this study period, 7142 children were born at the University Clinical Center Niš. Among them, 629 (8.8%) were born prematurely. All children who had any serious perinatal complications such as sepsis, necrotizing enterocolitis and lung disease were excluded from the study. Besides, some of the preterm infants were excluded from the study due to: the presence of deformities or congenital anomalies, as well as genetic syndromes of a newborn, invalid

video of the newborn motions, parents' refusal to participate in the study, or non-attendance in the follow-up in our institution. A two-year follow-up was completed for 160 preterm infants and they were analyzed in this study.

For each infant included in the research, detailed perinatal data were taken: gender, gestational age/gestational weeks (GW) (< 30 weeks; 30–37 weeks), body weight at birth, body length at birth, head circumference, Apgar score value at the 1st and 5th minute, data on method of delivery (C-section or not), data on multiple (twin) pregnancy and CUS findings.

GMA was carried out according to the basic principles of the Prechtl method within 5 days after the birth ("Writhing" period) and was based on video analysis and performed by a licensed person for GMA expertise [14, 15, 16]. To get good video recordings (lasting up to 25 minutes), the baby needed to be awake, calm, not crying, with open eyes, without irregular breathing, and in moving ("State 4"). For premature babies younger than 36 GW, recordings were made when they started moving, even if they were asleep.

General movements (GMs) were classified into four types [14, 15, 16]:

1. Normal Writhing Movements (N): smooth, twisting movements with low to moderate strength and slow to moderate speed, oval or twisting in shape.

2. Poor Repertoire (PR): limited variety and less complex than normal (baby starts a movement but doesn't finish it, making the sequence look incomplete or broken).

3. Cramped Synchronized Movements (CS): abnormal movements where the muscles of the body and limbs tighten and relax at the same time; movements are stiff and lack the smooth flow of normal writhing movements.

4. Chaotic Movements (CH): sudden, jerky movements with very large and random motions of the arms and legs, uncoordinated with a lack of smoothness or pattern.

Definitive neurological outcome was assessed based on a detailed neurological examination at the age of 24 months (corrected calendar age). The examination was performed by a certified neurologist specializing in pediatric neurology. Neurological outcome was classified as normal findings (completely normal neurological findings); minimal neurological dysfunction (MND), according to TINE criteria (Touwen Infant Neurological Examination) or non-specific signs without clear and definitive signs of cerebral palsy [17, 18]; cerebral palsy (CP) according to Surveillance of Cerebral Palsy in Europe (SCPE) criteria [19].

CUS examination was performed with LOGIQTM (GE Healthcare) machine with a highfrequency linear probe (7–11 MHz) within five days after the birth. Repeat CUS examination was performed two weeks after the birth, but statistical analysis included only the findings of the first examination. All CUS examinations were performed by the same person and categorized into five groups of interest (according to the guidelines from the ELGAN study [13] and Prechtl's recommendations [14, 15, 16]):

- CUS 1 normal finding;
- CUS 2 hyperechogenicity of the brain parenchyma lasting up to 14 days;
- CUS 3 hyperechogenicity of the brain parenchyma that lasts longer than 14 days;
- CUS 4 intraventricular hemorrhage;
- CUS 5 periventricular leukomalacia.

The medical doctor who analyzed spontaneous motor activity in newborns and the medical doctor who analyzed CUS findings did not have access to any results or data on the newborns. Statistical analysis was conducted using SPSS ver. 20.0 (IBM, Chicago, USA). The normality of continuous variables in defined groups was determined. Anthropometric mode values were presented as percentiles based on child growth standards. Continuous variable comparisons between groups utilized the Mann-Whitney test, while qualitative variables were analyzed with Pearson's  $\chi^2$  test. For category variables with samples less than 5, Pearson  $\chi^2$  or Fisher's exact tests were used. To evaluate the CUS method, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic odds ratio (DOR) were calculated based on normal CUS findings and final neurological outcomes. A two-tailed p-value of < 0.05 was considered statistically significant.

#### RESULTS

A statistically significant difference in neurological outcome after 24 months existed between infants born before and after 30 weeks (p < 0.001). Lower body weight of newborns (p < 0.001), body length (p < 0.05), and Apgar score at the 1st and 5th minute (p < 0.001) were statistically significantly associated with a worse neurological outcome. The prevalence of different types of GMs in the observation period of up to 5 days differed statistically significantly between the different outcomes (p < 0.001). The outcome after a follow-up of 24 months was normal in 124, qualified as MND in 22, and diagnosed as CP in 14 preterm infants (Table 1).

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Pathological CUS findings were statistically significantly more common in preterms born before 30 GW (p < 0.001), delivered via C-section (p < 0.001), and those with an Apgar score < 8 at both the 1st and 5th minutes after birth (p < 0.001) (Table 2).

Among six preterm infants with an Apgar score of 1 in the 1st minute, four scored 2 and two scored 5 in the 5th minute. Four developed CP, with two having scores of 1 and 2, and two with scores of 1 and 5. All CP cases showed hyperechogenicity of brain parenchyma detectable for up to 14 days. Additionally, two preterms diagnosed with MND had scores of 1 in the 1st minute and 2 in the 5th minute, with hyperechogenicity lasting longer than 14 days. Due to the small sample size, more research is necessary to draw definitive conclusions about this subgroup.

Previously determined statistically significant clinical characteristics of preterm infants for the final outcome also showed a statistically significant relation with CUS findings (Table 3).

Table 4 indicates that deviations from normal CUS findings are smallest in subjects with a normal final neurological outcome. A significant association was observed between CP in the final outcome and abnormal CUS findings (p < 0.001). Pathological CUS findings varied significantly among the groups based on final neurological outcomes (normal, MND, CP) (p < 0.05). Altered findings were most prevalent in subjects with CP and least frequent in those with a normal outcome.

Table 5 indicates that a normal CUS finding has a high specificity of 72.2% for a normal final neurologic outcome, though its sensitivity is lower at 67.8%. The specificity of normal CUS finding improves when assessing outcomes without CP or with CP. Combining CUS and GMA achieved 100% specificity and PPV in ruling out deviations from normal neurologic outcomes.

### DISCUSSION

Periventricular subependymal hemorrhage and intraventricular hemorrhage are complications that usually occur in the first days after birth and are characteristics of premature babies. Frequency of these hemorrhages in newborns who weigh < 1500 g and are < 32 GW of age, is up to 25%. In newborns who weigh < 1000 g, this frequency is up to 40%. Extremely low birth weight and extremely low gestational age, represent a good predisposition for long-term complications, including CP/MND [9, 20].

Prechtl found that increased brain tissue echodensity is temporary and has limited prognostic value when lasting less than two weeks [12]. Other studies recommend the first CUS on the third day after birth and a follow-up before the end of two weeks [21]. In our study, 96 subjects

(60%) had normal CUS findings at the first examination. Among them, 10 had MND, and 2 were diagnosed with CP. Both infants were born before 30 GW, suggesting that their early preterm birth affected the maturation of their CNS.

Our study on CUS findings shows differences compared to existing literature, likely due to the smaller sample sizes often used in those studies [21]. For instance, a large study of premature infants born after 33 weeks of gestation noted pathological CUS findings in 13%. The authors highlighted that even slight differences in gestational age can affect CUS specificity, complication rates, and neurological outcomes [22]. While some studies report that C-section is not significantly linked to poor neurological outcomes, factors like Apgar scores and head circumference are associated with these outcomes [22, 23]. In contrast, our study found a significant association between C-section delivery and unfavorable neurological outcomes, likely influenced by the overlap of low Apgar scores and head circumferences in C-section cases.

The availability of CUS as a diagnostic method and its application in daily clinical practice represented a major diagnostic advance. In recent study, normal CUS finding has a PPV for the final normal neurological outcome of 89.4% and PPV increases to 97.9% for a final neurologic outcome that excludes CP. These results indicate that the subjects with a normal finding on the CUS may have a pathological neurological outcome and it correlates with the already described studies. Recent research supports the fact that the pathological CUS finding has a predictive value for later neurological deviations. The sensitivity of these findings was not high, which indicates the need to follow up on the development of children who, in the first 5 days after birth, had abnormal findings, either during the examination by CUS or during the GMA. Pathological CUS findings are statistically significantly more frequent in subjects who had CP in the final outcome (p < 0.05).

The diagnostic odds ratio of CUS finding without pathology in all examined combinations is >1, which implies the ability of the single method to determine the final outcome. DOR doubles in the case of determination of non-CP/CP in the final outcome (DOR = 10.26) compared to normal/abnormal determination (DOR = 5.42). A DOR value >10 indicates excellent diagnostic value. Results combining CUS and GMA are impressive. In the case of determining DOR about non-CP/CP in the final outcome as well as normal/abnormal final outcome, DOR tends to infinity because in no one case of both normal CUS findings and normal GMA findings did MND or CP develop.

In this study, 100% of preterm infants with periventricular leukomalacia developed CP, which is in agreement with the research of other authors who indicate the high predictive value of this finding for the later development of CP [24]. All subjects with a finding of intraventricular hemorrhage had one of the pathological outcomes (MND/CP), in the final outcome. Periventricular echodensity in the frontal white matter, which disappeared for up to 14 days, did not affect spontaneous motor activity, but periventricular echodensity in the same zone lasting longer than 14 days was associated with abnormal development of spontaneous motor activity.

A recent study included a limited number of preterm infants due to various exclusion criteria, primarily focusing on those born at or above 30 GW, which comprised 90% of participants. Most infants were not delivered via C-section or from twin pregnancies. After a 24-month follow-up, most subjects showed normal neurological findings; however, the majority of those who developed CP were born before 30 GW (14 out of 16). This suggests that insufficient maturity of CNS may be a contributing factor. Given that preterm infants with serious complications were excluded from this study, it should be emphasized that results show the prognostic values of CUS and GMA for relatively "low-risk" preterm infants. This fact represents a limiting factor for the generalizability of our results.

Future research should involve more infants (both "low-risk" and "high-risk"), especially those under 30 GW, and a more detailed categorization of CUS and neurological outcomes could enhance the findings' applicability.

Studies indicate that preterm infants can show abnormal GM in the first week after birth, often due to factors like electrolyte imbalances or changes in cerebral blood flow, despite later having normal neurological outcomes. To prevent misleading results, it's recommended that the first GM evaluation be conducted after the first week [25]. In our study, we performed the first GMA earlier due to some newborns leaving the maternity ward before this period, following Prechtl's recommendations [14, 15] while excluding those with significant complications. All newborns with normal GM findings at the initial evaluation had a normal neurological outcome at 24 months.

GMA has better predictive value in later periods of development, with the best predictive value in "fidgety" period (50–54 GW) [14, 15, 16]. Recognizing the importance of initial examinations and effectively incorporating them into practice is crucial for timely therapy application. This study suggests that developing a prognostic model for predicting neurological outcomes in a larger, multicentric study could be beneficial. This model should integrate GMA and CUS findings along with statistically significant perinatal clinical characteristics and pregnancy data from preterm cases.

#### CONCLUSION

This study highlights the strong link between clinical characteristics, CUS findings, and neurological outcomes in preterm infants. Pathological CUS findings were more prevalent in those born before 30 weeks of gestation, delivered by C-section, and with lower Apgar scores. Normal CUS results were highly specific for normal neurological outcomes, especially when combined with GMA. Prolonged hyperechogenicity and conditions like periventricular leukomalacia were significant predictors of CP. These findings underscore the importance of early multimodal diagnostics, particularly CUS and GMA, in predicting long-term neurological outcomes and guiding interventions.

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Conflicts of interest: None declared.

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		Out	come after 24 mo	Summarized			
<b>Clinical characte</b>	eristics	Normal	MND CP		(n - 160)	р	
		(n = 124)	(n = 22)	(n = 14)	(11 – 100)		
<sup>a,b</sup> Gestational age		25 (20, 26) GW	25 (22, 25) GW	20 (27, 20) GW	35 (27-36) GW	0.014	
mode (min-max)		55 (29-50) CW	33 (33–33) G W	29 (27–29) U W	33 (27–30) G W	0.014	
$\geq 30$ week	KS .	122 (98.39%)	22 (100%)	0 (0%)	144 (90%)	< 0.001	
< 30 wee	ks	2 (1.61%)	0 (0%)	14 (100%)	16 (10%)	< 0.001	
<sup>a</sup> S or	Female	60 (48.39%)	10 (45.45%)	8 (57.14%)	78 (48.75%)	0.78	
Sex	Male	64 (51.61%)	12 (54.55%)	6 (42.86%)	82 (51.25%)	0.78	
aTruina	No	92 (74.19%)	18 (81.82%)	14 (100%)	124 (77.5%)	0.070	
1 WIIIS	Yes	32 (25.81%)	4 (18.18%)	0 (0%)	36 (22.5%)	0.079	
<sup>a</sup> Caesarean	No	80 (64.52%)	12 (54.55%)	6 (42.86%)	98 (61.25%)	0.227	
section	Yes	44 (35.48%)	10 (45.45%)	8 (57.14%)	62 (38.75%)	0.227	
<sup>b</sup> Birth weight (g)		2150 (2000-	1750 (1350-	1320 (1250–	2125 (1250-		
mode (min-max)		2350)	2400)	1350)	2400)	< 0.001	
mode in percentiles		18.9%	3.4%	57.1%	18.9%		
<sup>b</sup> Birth body length (cm)		45(42-47)	11 (13-15)	30 (35, 10)	14 (42 47)		
mode (min-max)		43 (42-47) 24 5%	1/ 0%	55 2%	1/ 0%	0.021	
mode in percentil	es	24.370	14.970	55.270	14.970		
<sup>b</sup> Head circumfere	nce (cm)	30 (29_32)	30 (28-32)	28 (26-29)	30 (26-32)		
mode (min-max)		7 5%	7.5%	75.2%	7 5%	0.114	
mode in percentil	es	7.570	1.570	15.270	7.570		
<sup>b</sup> Apgar score							
(1– minute)		8 (8–9)	8 (8-8)	6 (1–7)	8 (1–9)	< 0.001	
mode (min-max)							
<sup>b</sup> Apgar score							
(5– minute)		9 (8–9)	8 (8-8)	7 (5–8)	9 (5–9)	< 0.001	
mode (min–max)							
<sup>a</sup> GMs within 5 days							
N		94 (75.81%)	0 (0%)	0 (0%)	94 (58.75%)		
PR		30 (24.19%)	22 (100%)	2 (14.29%)	54 (33.75%)	< 0.001	
CS		0 (0%)	0 (0%)	12 (85.71%)	12 (7.5%)	0.001	
СМ		0 (0%)	0 (0%)	0 (0%)	0 (0%)		

Table 1. Clinical characteristics of subjects according to outcome after 24 months

MND - minimal neurological dysfunction; CP - cerebral palsy; GW - gestational weeks; min

- minimum; max - maximum; GM - general movements; N - normal writhing movements; PR

- poor repertoire; CS - cramped synchronized movements; CM - chaotic movements;

<sup>a</sup>Pearson's χ2 test;

<sup>b</sup> Mann–Whitney test

### Table 2. Distribution of normal and abnormal cranial ultrasound findings in relation to clinical

#### characteristics of preterms

		Cranial ultra	sound finding	
Clinical chara	cteristics	Normal (n = 96)	Abnormal (n = 64)	р
Sov	Female $(n = 78)$	52 (66.7%)	26 (33.3%)	0.108
Sex	Male $(n = 82)$	44 (53.7%)	38 (46.3%)	0.108
Castational and	$\geq$ 30 weeks (n = 144)	94 (65.3%)	50 (34.7%)	< 0.001
Gestational age	< 30 weeks (n = 16)	2 (12.5%)	14 (87.5%)	< 0.001
Truing	No (n = 124)	76 (61.3%)	48 (38.7%)	0.566
I wins	Yes $(n = 36)$	20 (55.6%)	16 (44.4%)	0.300
Cocorroop coation	No (n = 98)	70 (71.4%)	28 (28.6%)	< 0.001
Cesarean section	Yes $(n = 62)$	26 (41.9%)	36 (58.1%)	< 0.001
	9 $(n = 52)$	38 (73.1%)	14 (29.6%)	
Apgar score (1-minute)		52 (63.4%)	30 (36.6%)	< 0.001
	< 8 (n = 26)	6 (23.1%)	20 (76.9%)	
	9 (n = 90)	64 (71.7%)	26 (28.9%)	
Apgar score (5-minute)	8 (n = 52)	30 (57.7%)	22 (42.3%)	< 0.001
	< 8 (n = 18)	2 (11.1%)	16 (88.9%)	

Pearson's  $\chi^2$  test

M

C		1					
Clinical chara	cteristics	CUS 1	CUS 1 CUS 2		CUS 4	CUS 5	р
		(n = 96)	(n = 36)	(n = 20)	(n = 6)	(n = 2)	
	$\geq$ 30 weeks (n = 144)	94 (65.3%)	30 (20.8%)	18 (12.5%)	2 (1.4%)	0 (0%)	< 0.001
Gestational age	< 30 weeks (n = 16)	2 (12.5%)	6 (37.5%)	2 (12.5%)	4 (25%)	2 (12.5%)	< 0.001
	No $(n = 98)$	70 (71.4%)	16 (16.3%)	8 (8.2%)	2 (2%)	2 (2%)	0.002
Cesarean section	Sarean section $\frac{\text{Yes}}{(n=62)}$ 26 (41.9%) 20	20 (32.3%)	12 (19.4%)	4 (6.5%)	0 (0%)	0.002	
	9 (n = 52)	38 (73.1%)	12 (23.1%)	2 (3.8%)	0 (0%)	0 (0%)	
Apgar score (1-minute)	8   (n = 82)	52 (63.4%)	16 (19.5%)	12 (14.6%)	2 (2.4%)	0 (0%)	< 0.001
	< 8 (n = 26)	6 (23.1%)	8 (30.8%)	6 (23.1%)	4 (15.4%)	2 (7.7%)	
Apgar score (5-minute)	9 (n = 90)	64 (71.1%)	18 (20%)	8 (8.9%)	0 (0%)	0 (0%)	
	8   (n = 52)	30 (57.7%)	10 (19.2%)	8 (15.4%)	8 (8.9%)	2 (3.8%)	< 0.001
	< 8 (n = 18)	2 (11.4%)	8 (44.4%)	4 (22.2%)	4 (22.2%)	0 (0%)	

**Table 3.** Distribution of different cranial ultrasound findings in relation to previously

 significant clinical characteristics of preterms

CUS 1 – normal finding; CUS 2 – hyperechogenicity of the brain parenchyma lasting up to 14 days; CUS 3 – hyperechogenicity of the brain parenchyma that lasts longer than 14 days; CUS 4 – intraventricular hemorrhage; CUS 5 – periventricular leukomalacia;

Pearson's  $\chi^2$  test

Neurologic outcome	Normal		р				
	(n = 96)						
Normal	84 (67 74%)	40 (32 26%)					
(n = 124)	01 (07.7170)						
MND	10 (45 45%)	12 (54 550/)					
(n = 22)	10 (45.4570)		< 0.001				
СР	2(14,20%)	12 (85 710/)					
(n = 14)	2 (14.2970)						
	CUS 1	CUS 2	CUS 3	CUS 4	CUS 5		
	(n = 96)	(n = 36)	(n = 20)	(n = 6)	(n = 2)		
Normal	QA (67 740/)	28 (22 580/)	12 (0 6 9 9 / )	0 (00/)	0 (09/)		
(n = 124)	84 (07.74%)	28 (22.38%)	12 (9.08%)	0 (0%)	0 (0%)		
MND	10 (45 45%)	1 (19 1994)	6 (27 2794)	2 (0.00%)	0 (0%)	0.002	
(n = 22)	10 (43.4376)	4 (10.1070)	0 (27.2770)	2 (9.0978)	0 (0%)	0.005	
СР	2(14,200/)	4 (28 570/)	2 (14 200/)	4 (28 570/)	2(14,200/)		
(n = 14)	2 (14.29%)	4 (28.37%)	2 (14.29%)	4 (28.37%)	2 (14.29%)		

Table	4.	Distribution	of	different	cranial	ultrasound	findings	in	relation	to	different
neurolo	ogic	al outcomes									

MND – minimal neurological dysfunction; CP – cerebral palsy; CUS 1 – normal finding; CUS 2 – hyperechogenicity of the brain parenchyma lasting up to 14 days; CUS 3 – hyperechogenicity of the brain parenchyma that lasts longer than 14 days; CUS 4 – intraventricular hemorrhage; CUS 5 – periventricular leukomalacia

Pearson's x2 test

### **Table 5.** Distribution of different cranial ultrasound findings in relation to final neurological

		CUS finding	finding Sensitivity = 67			
		Normal	Abnormal	Specificity = 72.2%		
Nourological outcome	Normal	84 (67.7%)	40 (32.3%)	PPV = 89.4%	p = 0.005	
Neurological outcome	Abnormal	10 (27.8%)	26 (72.2%)	NPV = 39.4%		
				DOR = 5.42		
		CUS finding	,	Sensitivity = 63%		
		Normal	Abnormal	Specificity = 85.7%		
Nounale gigal outcome	Non-CP	92 (63%)	54 (37%)	PPV = 97.9%	p = 0.018	
Neurological outcome	СР	2 (14.3%)	12 (85.7%)	NPV = 18.2%		
			DOR = 10.26			
		CUS and GMA finding		Sensitivity = 51.6%		
		Normal	Abnormal	Specificity = 100%		
Nourological outcome	Normal	64 (48.4%)	60 (51.6%)	PPV = 100%	p < 0.001	
Neurological outcome	Abnormal	0 (0%)	36 (100%)	NPV = 37.5%		
				DOR = infinity		
		CUS and GMA finding		Sensitivity = 43.9%		
		Normal	Abnormal	Specificity = 100%		
Neurological outcome	Non CP	64 (43.8%)	82 (56.2%)	PPV = 100%	p = 0.038	
	СР	0 (0%)	14 (100%)	NPV = 14.6%		
				DOR = infinity		

#### outcomes and evaluation of the method significance

CUS – cranial ultrasound; CP – cerebral palsy; GMA – general movements assessment; PPV – positive predictive value; NPV – negative predictive value; DOR – diagnostic odds ratio Pearson's  $\chi^2$  test and determination of the sensitivity, specificity, PPV, NPV, and DOR