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Impact of selected risk factors on motor performance in the 3rd month of life and further motor

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Abstract

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29 Background. Proper motor development can be influenced by a range of risk factors. The resulting motor performance can be assessed through quantitative and qualitative analysis of 30 31 posture and movement patterns.

Methods. This study was designed as the cohort follow-up of the motor assessment and aimed to demonstrate, in a mathematical way, the impact of particular risk factors on elements of motor performance in the 3rd month and the final motor performance in the 9th month of life. Four hundred nineteen children were assessed (236 male and 183 female), including 129 born preterm. In all children, a physiotherapeutic assessment of the quantitative and qualitative development at the age of 3 months was performed in the prone and supine positions. The neurological examination at the age of 9 months was based on the Denver Development Screening Test II and the evaluation of reflexes, muscle tone (hypotonia and hypertonia), and symmetry. The following risk factors were analyzed after the neurological consultation: condition at birth (5-minute Apgar score), week of gestation at birth, intraventricular hemorrhage, respiratory distress syndrome, and the incidence of intrauterine hypotrophy and hyperbilirubinemia determined based on medical records.

Results. A combination of several risk factors affected motor development stronger than any 44 45 one of them solely, with Apgar score, hyperbilirubinemia, and intraventricular hemorrhage 46 exhibiting the most significant impact.

47 Conclusions. Premature birth on its own did not cause a substantial delay in motor 48 development. Nonetheless, its co-occurrence with other risk factors, namely intraventricular 49 hemorrhage, respiratory distress syndrome and hyperbilirubinemia, notably worsened motor 50 development prognosis. Moreover, improper position of the vertebral column, scapulae, 51 shoulders, and pelvis in the third month of life may predict disturbances in further motor 52 development.

Keywords: Infant; Motor development; Risk factors; Qualitative analysis; Cerebral palsy

Introduction

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Certain conditions must be met for the motor development to proceed correctly, such as correct genetic imprint and properly functioning central nervous system, comprising normal mental development, fully-working senses, and proper motor outcome (Vojta V, Peters A, 2007; Illingworth R, 2012; Hadders-Algra, 2004). Adequate cognitive development plays an essential part in allowing the child to perform a given task or function due to motivation: the natural desire to explore the world (Adolph & Hoch, 2019).

Proper motor development is influenced by various risk factors, previously discussed by several authors. The most important biological risk factors include the type of delivery (Lee, Han & Lee, 2012), low 5-minute Appar scores (Bulbul et al., 2020), respiratory distress syndrome (RDS) (Janssen et al., 2008), intrauterine hypotrophy, hyperbilirubinemia (Wusthoff & Loe, 2015), and intraventricular hemorrhage (IVH) (Bulbul et al., 2020; Tatishvili et al., 2010; Wildin et al., 1995).

Motor development follows a specific pattern, conserved across the human population, permitting the development of homogeneous assessment methods. Such evaluation should be based on quantitative and qualitative components appropriate for a given developmental stage (Gajewska et al., 2013; Gajewska, Sobieska & Moczko, 2014). Furthermore, it should allow detecting delays or abnormalities in motor skills to provide a basis for therapy plan development and make it possible to prognose further motor development.

There is no consensus on a "gold standard" uniform functional assessment in pediatric physiotherapy in Poland. Similarly, there is currently no unified methodology for neurological evaluation.

Available in Poland and worldwide, general movements assessment (GMs) offers a notable degree of cerebral palsy predictability. Regrettably, defining therapeutic goals based on this method is often challenging. The Alberta Infant Motor Scale (AIMS) is an excellent assessment tool but has not yet been validated in Poland. However, in our opinion, it does not sufficiently capture the qualitative issues, which often tend to be crucial during the therapy. Furthermore, the Test of Infant Motor Performance (TIMP) was designed to detect developmental delays in children younger than fourth months. It is reported in the literature that a treatment plan can be prepared based on this scale, but it does not allow to predict which child will develop cerebral palsy accurately. However, after a thorough analysis of the test and an attempt to use it, based on the experience of many physiotherapists, we believe that it does not

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meet the standard requirements, as it is challenging to identify the main problem and assign an appropriate therapy on its basis.

Previous publications have shown that the most appropriate moment for the assessment to predict further motor development is the third month of life (Vojta V, Peters A, 2007; Hadders-Algra, 2004; Gajewska et al., 2013; Gajewska et al., 2014). In line with this idea, a quantitative and qualitative evaluation scale for motor development in the third month of life was presented and validated through inter and intraobserver reliability analysis. Furthermore, it was compared with a neurological evaluation method based on the Denver Developmental Screening Test II, commonly used in Poland, supplemented with reflexes, muscle tone, and symmetry/asymmetry testing. The results regarding its usefulness were published in several scientific publications (Gajewska et al., 2013; Gajewska, Sobieska & Moczko, 2014; Gajewska et al., 2015).

The assessment of spontaneous motor activity involves a thorough analysis of posture and movement patterns. The quantitative evaluation determines the global pattern: the most advanced function (a milestone) exhibited by a child. While the movement does not need to be performed flawlessly, it is sufficient that the child manifests it in any way or at least strives to achieve it (Vojta V, Peters A, 2007). The qualitative assessment focuses on the individual elements that make up one global movement pattern, serving as an accurate analysis of its kinesiological content (Vojta V, Peters A, 2007). This assessment method allows to plan a therapy aimed at individual deficits and makes it possible to predict further motor development (Gajewska, Sobieska & Moczko, 2014; Gajewska et al., 2015).

Earlier publications mainly intended to demonstrate a proper analysis of the qualitative assessment of motor development and determine predictors of further motor development. However, we are aware that many risk factors can affect motor development and decided to evaluate them using a qualitative assessment-based scale. We decided to limit our analysis to the known biological risk factors which are supposed to have the strongest impact on motor development. We are aware that many other factors may influence motor performance and it should be studied further.

Hence, this study aims to mathematically determine the impact of particular risk factors on elements of motor performance in the 3rd month-old infants, as well as final motor performance in the 9th month of life.

Material and methods

Participants

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The study group consisted of children with no symptoms of impaired motor development, born at term or preterm (between weeks 28 and 37 of gestation), and children referred to the Clinic of Neurology for a periodic development assessment by a general practitioner, a pediatrician, or due to parents' concerns (weak head control during traction response or suspicion of delayed development).

The entire study population included 419 children: 236 boys and 183 girls, with 290 of them born at term and 129 preterms. The average birth week of the included infants was 38±3 (born at term 40±1 weeks; preterm 34±3 weeks), the mean body weight was 3100±814 g (born at term 3462±505 g; preterm 2282±788 g). Preterm children were assessed at the corrected age (Pin et al., 2009).

Exclusion criteria comprised genetic or metabolic disorders, severe congenital disabilities, or extreme preterm birth (below the 28th week of gestation). Moreover, no children with microcephaly or macrocephaly were included in the study.

Procedure

The study was designed as the cohort follow-up of the motor assessment. The examination was performed at the clinic of the Greater Poland Center for Child and Adolescent Neurology and the child clinic in the years 2018–2021. Calculation of the sample size, regarding the number of newborns per year in area, showed the required sample size of 383. We decided to gather even more population.

In all children, a physiotherapeutic qualitative assessment of motor performance at three months (completed three months but before completing four months) was performed in the prone and supine positions, as presented in previous publications (Gajewska et al., 2013; Gajewska, Sobieska & Moczko, 2014). During the assessment, a child was placed on the rehabilitation table, without clothes (so that the qualitative features could be accurately assessed), in a warm room, full-fed and well-rested. The examination lasted 10 to 15 minutes (Gajewska et al., 2013; Gajewska, Sobieska & Moczko, 2014).

The qualitative assessment included 15 elements in prone and supine positions (Tables 2 and 3, respectively).

In the prone position, the assessment involved: isolated head rotation; arm in front; forearm in an intermediate position; elbow outside of the line of the shoulder; palm loosely open; thumb outside, spine in segmental extension; scapula situated in medial position; pelvis in an intermediate position; lower limbs situated loosely on the rehabilitation table; foot in an

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intermediate position. In the supine position, the assessment involved: head symmetry; spine in extension; shoulder in a balance between external and internal rotation; wrist in an intermediate position; thumb outside; palm in an intermediate position; pelvis extended; lower limb situated in moderate external rotation and lower limb bent at the right angle at hip and knee joints; foot in an intermediate position – lifted above the rehabilitation table. Both sides were assessed for symmetrical parts of the body to exclude asymmetry. Each element was evaluated as 0 - performed only partially or entirely incorrectly, 1 - performed correctly. Each assessed element had to be observed at least three to four times during the test. The result was expressed as a sum of points (0-15 for prone and 0-15 for the supine position).

A neurologist examined the infants at nine months of age. The evaluation was based on the Denver Development Screening Test II (DDST II), the assessment of reflexes, muscle tone (hypotonia or hypertonia), and symmetry (Touwen BCL, 1976; Ślenzak J & Michałowicz R, 1973). The proper performance allowed to qualify a child as adequately developed for the 9th month of life. In case of irregularities, the neurologist indicated the maximum level of motor development achieved by a child. In the case of children in which cerebral palsy (CP) was suspected, the final diagnosis could be confirmed at 18 months of age (Figure 1).

Figure 1 near here

Previously, this type of examination was used in the assessment of children aged three months and the comparison between physiotherapeutic and neurological assessment showed high agreement, with high conformity coefficients (z = -5.72483, p < 0.001) (Gajewska et al., 2014).

The following risk factors were analyzed after the neurological consultation: condition at birth (5-minute Apgar score), week of gestation at birth, intraventricular hemorrhage (IVH) (in some children, brain sonography was performed after birth, while all infants were subjected to this examination at the second month of corrected age; intraventricular hemorrhages (IVH) were classified into four grades of severity, as indicated by Papile), respiratory distress syndrome (RDS), and the incidence of intrauterine hypotrophy and hyperbilirubinemia determined based on medical records.

The study was approved by the Research Ethics Committee of Poznan University of Medical Sciences and registered under no. 22/10 (07-01-2010). Children recruited for the study were patients/clients of the Child Neurology Center. All parents/caregivers written agreed to participate in the study, as apart from routine assessment and therapy, no extra visit was necessary.

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Due to the nature of the variables, the results were presented as medians with quartiles (Me, Q25-Q75) and analyzed using non-parametric tests (the Mann-Whitney U test, Kruskal-Wallis ANOVA, Dunn's post hoc test). The assumed statistical significance level was p<0.05.

The association between pairs of nominal categorical variables was tested using the following tests:

- 1) To measure the magnitude of the association between two nominal variables without regard to the dimensions of the r x c contingency table Cramer's V coefficient was used in place of Pearson's chi-square statistics; the higher the coefficient, the stronger the association;
- 198 2) To measure the proportion of variation between interrelated nominal variables the
 199 Goodman-Kruskal's Tau test was used; the higher the result the more substantial the influence
 200 of one variable on another;
- 3) To estimate the best predictors of the impact of particular risk factors on the final assessment in the 9th month of life, the ordered logit analysis was performed. The dependent variable was measured on the ordinal scale, while all other predictors were expressed on the binary scale. For the significant models (p<0.005), P>[z] was given, along with the pseudo R² value.

In both cases, exact probability values (instead of asymptotic p-values) were calculated using StatXact-11 Cytel Studio v.11.1.0.

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Results

As no sex-related differences were found in previous studies, this parameter was not investigated (Gajewska et al., 2013; Gajewska, Sobieska & Moczko, 2014)

Qualitative assessment at the age of 3 months

The assessment at the age of 3_months is expressed as the sum of elements, in the proneand supine positions (enumerated in the tables 2 and 3, respectively), with a_max=imum value
of 15 points.

The neurological assessment is expressed as the month of maximal development reached by each child at the age of 9 months (presented in table 1).

Impact of particular risk factors on motor performance at the age of 9 months

First, the impact of individual risk factors or their combination on the qualitative assessment of motor skills in the 3rd month of life and the maximum skill level achieved at nine months were investigated. The details of this analysis are presented in Table 1. Prematurity

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itself was not a factor affecting motor development in the 3rd month of life. However, it should be noted that there were no children with three or four risk factors that were not born prematurely.

A low (4-7 points) 5-minute Apgar score resulted in a statistically significant difference in the prone position (z = 2.88, p = 0.012) compared to children born in good condition. In contrast, the difference in the supine position was not significant. However, it must be pointed out that there was a substantial difference in the number of subjects in these subgroups. Furthermore, there were not enough children with a poor score (0-3) to perform statistical analysis (see Table...).

Hyperbilirubinemia substantially impacted motor performance in the 3rd month of life and caused a delay in 7 out of 14 children (when analyzed as a single factor) (see Table...).

All children with a suspicion of CP in the 9th month of life did not perform correctly in the 3rd month. This diagnosis was confirmed at 18 months (nine participants were diagnosed with tetraplegia and one with diplegia). Children with tetraplegia failed to perform any of the evaluated elements in the prone and supine positions (scored 0 points), and only one child finally diagnosed with diplegia (weight 3210 g; born on the 40th week of gestation) scored 6/15 points in the supine position (hands, thumbs, external rotation of the lower limbs). Out of 10 children with suspicion of CP, four were affected by grade I IVH, one with grade II IVH, five with RDS, one with hyperbilirubinemia, and one with hypotrophy. When the total number of risk factors was taken into account, four children finally diagnosed with CP were not affected by any risk factor, one suffered from hypotrophy, four were affected by two risk factors (IVH + RDS), and one was affected by three (IVH + RDS + hyperbilirubinemia) (see Table ...).

The type of delivery (vaginally, n = 224; Caesarean section, n = 158; forceps delivery, n = 23; vacuum, n = 14) did not entail significant differences in the 3^{rd} month of life or the maximum development at nine months of age.

Children born prematurely and at term, without risk factors, achieved a similar maximum development level. Almost half of the children born prematurely and with additional risk factors showed delayed motor development and CP in extreme cases. In contrast, most children born at term but affected by risk factors still achieved the proper level of motor development (see Table ...).

It seems that prematurity does not cause a significant delay in motor development. Still, in combination with risk factors, IVH, RDS, and hyperbilirubinemia, it results in a notably worse motor development prognosis (see Tables...).

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Proper development manifests in achieving all the postural and Motor motor characteristics listed in the scale, i.e., the maximum sum of points (see Table...). Its reduction indicates deficits/abnormalities and may herald/predict developmental delay. Therefore we have evaluated whether risk factors in infants could coincide with reduced assessment scores. The effect of risk factors on the total qualitative assessment in the prone and supine positions was analyzed.

The result of the detailed qualitative assessment of motor performance was first presented in the form of a sum of points obtained to demonstrate to what extent individual risk factors or their combination reduces the level of functioning. The results of this analysis are presented in Table 1. The final development level of children with a given risk factor or their combinations in the 9th month of life was also indicated. Then, we investigated which risk factors influenced specific motor components assessed in pronation and supination. The results of this analysis are presented in Tables 2 and 3, respectively. Only the statistically significant values were given.

The last column of these tables indicates which motor element assessed in the 3rd month of life was critical (had a significant effect) to the child's achievement of the maximum level of motor development assessed at nine months of age. The tables only include the values for those elements of motor evaluation for which statistical significance was obtained. Statistical significance suggests that given risk factors disturbed the correct position or function in the examined children at the third month of life.

The differences of the "sum in the prone position" (H = 49.08, p = 0.000) and "sum in supine position" (H = 47.69, p = 0.000) variables depending on the number of risk factors were statistically significant, while the difference investigated using the post hoc test was as followed: without risk factors / two risk factors p = 0.002; without risk factors / three risk factors p = 0.003. Depending on the type of risk factors in the studied children, it was also possible to demonstrate the differences in the "sum in the prone position" (H = 52.81, P = 0.004) and "sum in supine position" (H = 13.21, P = 0.022) variables were significant, but detailed comparisons failed to achieve significance.

Table 1 near here

Next, the influence of particular risk factors on motor elementsperformance, investigated in the prone and supine positions, was studied. Six risk factors were included in the analysis: prematurity, 5-minute-Apgar score lower than 8, the presence of IVH, RDS, hyperbilirubinemia, and hypotrophy. Only reduced 5-minute Apgar score, IVH and hyperbilirubinemia were repeatedly significant and were presented in Tables 2 and 3.

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Subsequently, we analyzed which elements of motor skills, assessed qualitatively in the prone and supine positions in the 3rd month of life, had the most significant impact on the maximal level of motor performance, evaluated by the neurologist at the age of nine months. The axial features, namely the spine, scapulae, and pelvis, showed the highest impact. The results of this analysis are listed in detail in Tables 2 and 3.

Table 2, Table 3 near here

The elements in the prone position which best determined the proper prognosis of motor development included: correct curvatures of the vertebral column, scapula situated in the medial position, pelvis in the intermediate position, lower limbs situated loosely on the rehabilitation table, while in the supine position these comprised: proper curvatures of the vertebral column, shoulder in a balance between external and internal rotation, pelvis extended, lower limbs bent at a right angle at hip and knee joints, foot in the intermediate position, lifted above the rehabilitation table.

Discussion

Some authors point out that the early detection of motor abnormalities is relatively difficult (Crnković et al., 2011). Thus, it seems advisable to examine diagnostic methods that would make it possible to detect children at risk of abnormal development at the earliest possible time, irrespectively of the risk factors involved.

The primary finding is that none of the singular risk factors universally recognized as the most dangerous (prematurity, IVH, RDS, hyperbilirubinemia) is responsible for severe motor development impairment. However, the higher the number of coinciding risk factors, the worse the prognosis for motor development.

The percentage of premature births is 7.1% in Europe (Caring for tomorrow—EFCNI) and approximately 6.5% in Poland (GUS Roczniki Demograficzne -Statistics Poland, 2011). It was shown that RDS, IVH and sepsis, hypoglycemia, hypernatremia, and hypothermia are the factors causing developmental delay and potentially leading to unfavorable long-term neurodevelopmental consequences (Khan et al., 2012; Stephens & Vohr, 2009).

Our studies demonstrated that it was not prematurity itself but in combination with other risk factors that worsened the prognosis of proper motor development. However, it should be noted that there were no children with an extremely low gestational age in the investigated group who could exhibit a delay despite being examined at the corrected age.

Many authors report that the CP diagnosis is often made too late, and rehabilitation, which could help improve the affected children's condition, is implemented with a significant

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delay (Morgan et al., 2015). Novak et al. (2017) identified two diagnostic pathways for infants at risk of developing CP (Novak et al., 2017). About 50% are infants from the risk group with certain factors, such as prematurity, fetal growth disorders, encephalopathy, genetic defects, convulsions, are diagnosed under five months of age (corrected age). Infants with no such medical/–clinical history are diagnosed later in life, based on the second pathway. The first disturbing symptoms in such infants include a delay in motor development (e.g., lack of sitting ability at nine months of age, or a clear one-sided preference, visible only when performing more complex actions (e.g., griping) (Novak et al., 2017).

It is worth noting that Novak et al. (2017) suggest diagnostics only after the age of 5 months, while in our studies (repeatedly), children who were diagnosed with CP at the age of 18 months showed large motor deficits at three 3 months of age (; they did not perform any, or only performed 2-3 activities of the assessed 15 in pronation and supination) (Gajewska et al., 2013; Gajewska, Sobieska & Moczko, 2014; Gajewska et al., 2015).

However, early detection of motor deficits may support therapy for children at risk of CP and those who will eventually only develop a developmental delay. Moreover, in the third month of life, it could be noticed that they did not perform all of the observed functions correctly, or at least did not achieve the maximum score.

The most crucial aim of the study was to demonstrate whether it is possible to associate specific risk factors with a motor delay up to the occurrence of CP. It has been shown that intraventricular bleeding, respiratory disorders, and hyperbilirubinemia had the most significant impact on motor development. It is also worth emphasizing that these factors, acting not individually but in combination, had the most significant effect on motor development delay.

Apart from the statement that children with particular risk factors developed more slowly, it was shown that their performance in the 3rd month was worse. Only a detailed qualitative assessment can detect these minor deviations from normal development that affect motor progress.

At the same time, detection of disorders in the 3rd month of life allows for the implementation of early physiotherapy, following commonly accepted canons. The pronation score seems to reflect better the discrete deficits seen in children born with a poorer 5-minute Apgar score. The ability to overcome the forces of gravity is probably a good indicator of both the proper development of muscle strength and the maturity of the nervous system.

Hence, we suggest that diagnostics should be performed very early, already at three-3 months. Even if the diagnosis of CP may be delayed until 18 months, rehabilitation should be implemented as early as any worrying symptoms are noticed.

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The qualitative assessment conducted at the age of 3 months is a reliable prognosis of motor development at 9-months of age, with a crucial role played by proximal characteristics related to the axial skeleton (spine-scapulae-shoulders-pelvis). The precise determination of which motor development elements are impaired also allows for the implementation of appropriate therapy.

The predictive value of the commonly used Bayley scale is being undermined (highly unstable delay classifications, low sensitivities, and poor positive predictive values), and the need for a new, more effective tool used to predict motor development and allow early therapeutic intervention is emphasized (Lobo et al., 2014).

Since there is no globally recognized "gold standard" method of functional assessment, it was impossible to compare the results of this study with such a standard or to calculate the confidence intervals or odds ratio. The only point of reference was the neurological examination, and more specifically – the level of motor development assessed at the age of 9 months. This age was chosen as this is the usual time for assuming the standing position (Vojta V, Peters A, 2007; Gajewska, Sobieska & Moczko, 2014). Achieving this milestone (with the support of furniture or an adult) reflects the achievement of complete motor control and guarantees further proper motor development (including walking).

We demonstrated that even as an isolated risk factor, hyperbilirubinemia had a substantial negative impact on motor development. In combination with prematurity, this impact was even more prominent.

Another important risk factor for developmental disorders and CP is the increasing severity of IVH (Fily et al., 2006; Spittle et al., 2009). Measures of brain structure and function are by far the most predictive of neurodevelopmental outcomes. Preterm infants with ventricular dilatation and IVH showed worse motor test results than those without IVH (Vollmer et al., 2006). IVH in children born prematurely leads to worse psycho-motor assessment outcomes and more frequent CP occurrence (Klebermass-Schrehof et al., 2012). In our study, in the group of children who obtained bad scores, IVH was much more frequent. In the studies by Sherlock et al., (2005), patients with IVH grade IV showed up to four times higher percentages of abnormal results than grade I patients (Sherlock et al., 2005). However, we could not confirm this finding due to the small number of children with IVH included in our study.

The risk of the RDS occurrence is inversely proportional to the newborn's gestational age—: Hit occurs in 1% of all newborns and in nearly 70% of infants born before the 28th week of gestation (Shonkoff JP & Meisels SJ, 2000). In our study, RDS occurred mainly in children whose motor development was assessed as inferior in our study. However, it should be stressed

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that these children were not born extremely prematurely.

The analysis of risk factors and their impact on motor development in the investigated group was similar to that of other authors. It is believed that there is a critical need for collaboration among experts to determine early predictive factors and neuroprotective therapies (Khan et al., 2012). Furthermore, while hyperbilirubinemia proved to be a highly burdening factor, even children who suffered from many complications of similar severity occasionally showed proper development and reached maximal performance at nine months.

Four children whose diagnosis of tetraplegia was ultimately confirmed at the age of 18 months were not affected by any risk factors but scored zero 0 during the quantitative assessment in the 3rd month, both in prone and supine positions. Qualitative and quantitative evaluation makes it possible to focus on motor delays or disorders as early as in the 3rd month of life. According to McIntyre et al. (2011), 50% of CP cases are diagnosed in infants born at term in whom no risk factor has been identified (McIntyre et al., 2011).

Strengths and limitations

The presented paper is based on a large and homogenous study group, and the implemented statistical analysis, not commonly used in similar research, is accordingly adjusted to the hypothesis. Qualitative analysis was performed in the third month of life, regarded as a crucial time point to predict further development, allowing to plan therapy or social support in cases of expected disability.

A relatively short follow-up (up to nine months) is the only limitation of the study.

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Conclusions

It was not prematurity itself but its combination with risk factors (IVH, RDS, hyperbilirubinemia) that made the prognosis of proper motor development worse. Children with a motor delay at nine months of age demonstrated a lower quality of movement as early as in the 3rd month of life. Furthermore, qualitative assessment allowed to identify high-risk children and predict the degree of delay.

Axial skeleton characteristics (vertebral column, scapulae, shoulders, pelvis) and prone responses were the best determinants of the proper prognosis of motor development.

Ethics approval and consent to participate

The study was approved by the Research Ethics Committee of Poznan University of Medical Sciences and registered under no. 22/10 (07-01-2010). The study was conducted at the Center for Child and Adolescent Neurology Clinic between 2018 and 2021, following the ethical guidelines of the 1964 Helsinki declaration and its later amendments.

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Table 1. Risk factors, motor performance at 3rd month and final motor performance at 9th

Comentado [R43]: Identify abbreviations, e.g., CP: cerebral

Qualitative assessment was expressed as the sum of particular elements in the prone and supine positions (Median and Quartiles (Q) 25 and 75, for a maximum of 15 points). The final assessment was performed by the neurologist at the age of 9 months and is expressed as a number of children who reached the given level of motor performance (number and percentage).

Comentado [R44]: Because we are talking about different groups, with different dimensions, percentage gives a more understandable and comparable proportional occurrence aths...)

			Final	assessmer	nt (motor p	erformar	ice (r	naths)	
Number of risk factors, group (full term or preterm), and gestation weeks (mean±standard deviation) Quality in the prone position Median (Q25-Q75)	Quality in	Quality in	<u>level in months)</u>						
	the supine position Median (Q25-Q75)	Suspected CP	6th month	7th month	8th month	9th month	-		
no risk factors, n=254 gestation age 39.5 ± 1.1	<u>15 (10-15)</u>	<u>15 (13-15)</u>	1 (%)	<u>9</u>	<u>24</u>	<u>8</u>	212	_	
$\frac{1 \text{ risk factor, n=}112}{\text{gestation age}}$ $\frac{36.7 \pm 2.6}{\text{gestation age}}$	<u>15 (9-15)</u>	<u>15 (11-15)</u>	<u>3</u>	<u>2</u>	<u>8</u>	<u>6</u>	<u>93</u>	_	
1 risk factor, n=80 preterm only gestation age 35.4 ± 1.8	<u>15 (10-15)</u>	<u>15 (11-15)</u>	<u>3</u>	<u>1</u>	<u>5</u>	<u>3</u>		omentado [R45]: Keep same identification format along ble	
2 risk factors, n=28 gestation age 34.1 ± 3.0	<u>8 (2-12)</u>	10 (6-15)	<u>2</u>	<u>4</u>	<u>3</u>	<u>3</u>	<u>16</u>	_	
$\frac{\text{preterm+1 risk factor, n=25}}{\text{gestation age}}$ $\frac{33.5 \pm 2.4}{\text{preserved}}$	8 (2-15)	<u>11 (6-15)</u>	1	<u>4</u>	<u>3</u>	<u>3</u>	<u>14</u>		
$\frac{\text{preterm+2 risk factors.}}{\text{n=18}}$ $\frac{\text{gestation age}}{31.7 \pm 3.1}$	<u>5 (0-12)</u>	<u>6 (0-15)</u>	<u>3</u>	<u>2</u>	<u>6</u>	1	<u>6</u>	_	
preterm+3 risk factors, n=6 gestation age 31.7 ± 3.1	0 (0-5)	0 (0-4)	1	1	<u>2</u>	Ξ	<u>2</u>	_	

Particular risk factors, as single or in combinations

	Г	T		1		1	
Apgar 5th minute	[7;4]	4;4	1	_	_	_	Comentado [R46]: Explain what is this
0-3, n=2 4-7, n=14	8 (0-11)	12 (0-15)	2	1	=	2	9
$\frac{4-7}{8-10}$, n=403	<u>15 (9-15)</u>	<u>15 (11-15)</u>	<u>7</u>	<u>17</u>	<u>43</u>	<u>16</u>	<u>320</u>
-	11 (0.15)	15 (5 15)					-
IVH, n=9 I° n=5	11 (9-15) 6;11;15;15;15	15 (5-15) 8;15;15;15;15	<u>-</u>	<u>1</u> 1	<u>1</u> 1	<u>-</u>	Comentado [R47]: Identify all abbreviations
II° n=1	7	8,13,13,13,13 15	=	=	=	=	Comentado [R48]: And classifications
<u>III° n=1</u>	<u>15</u>	15	=	=	=	=	Comentado [R49]: Explain what is this
Hiperbilirubinemia,							
$\frac{\text{riperofitationerita}}{n=14}$	<u>11 (6-15)</u>	9 (4-15)	Ξ	1	<u>3</u>	<u>3</u>	<u>7</u>
Hypotrophy,	15 (15-15)	15 (15-15)	Ξ	Ξ	1	<u>1</u>	<u>8</u>
<u>n=10</u>			_	_			
preterm+							
hyperbilirubinemia,	<u>10 (1-15)</u>	<u>10 (9-15)</u>	Ξ	<u>1</u>	<u>2</u>	<u>1</u>	<u>6</u>
<u>n=10</u>							
I I I I I I I I I I I I I I I I I I I							
preterm+IVH+RDS, n=10	<u>5 (0-15)</u>	<u>10 (0-15)</u>	<u>3</u>	1	<u>2</u>	=	<u>4</u>
<u>n-10</u>							
preterm+RDS,	400151515	4;12;12;15;15;1					
<u>n= 6</u>	4;8;8;15;15;15	<u>5</u>	Ξ	<u>1</u>	Ξ	<u>1</u>	<u>4</u>
mustamm + IV/II							
<u>preterm+IVH,</u> n= 6	6;7;9;11;15;15	6;6;9;11;15;15	Ξ	<u>1</u>	<u>1</u>	<u>1</u>	<u>3</u>
preterm+IVH+							
hyperbilirubinemia,	0;0;2;12;15	0;2;7;15;15	=	Ξ	<u>3</u>	=	<u>2</u>
<u>n=5</u>							
preterm+IVH+RDS+							
hyperbilirubinemia,	0;0;0;15	0;0;0;11	<u>1</u>	Ξ	<u>1</u>	Ξ	<u>2</u>
<u>n=4</u>							
preterm+hypotrophy,	200	0.6.6					
<u>n=3</u>	<u>2;0;0</u>	0;6;6	<u>1</u>	Ξ	Ξ	1	<u>1</u>
4 177711 4 1							
<u>preterm+IVH+hypotrophy</u> n= 2	<u>7;7</u>	<u>6;6</u>	Ξ	<u>1</u>	Ξ	<u>1</u>	Ξ.
<u> </u>							
RDS+hyperbilirubinemia,	7.15	4.15					2
<u>n=2</u>	<u>7;15</u>	<u>4;15</u>	=	=	=	Ξ	<u>2</u>
<u>IVH+RDS,</u>	<u>0</u>	<u>0</u>	=	=	=	=	<u>1</u>
<u>n=1</u>	_	_		_			
preterm+hypotrophy+							
hyperbilirubinemia,	<u>0</u>	<u>0</u>	Ξ	Ξ	<u>1</u>	Ξ	=
<u>n=1</u>							
preterm+IVH+hypotrophy+							
hyperbilirubinemia,	<u>5</u>	<u>4</u>	=	=	<u>1</u>	=	<u>=</u>
<u>n=1</u>							
preterm+RDS+hypotrophy							
+hyperbilirubinemia, n=1	<u>0</u>	<u>0</u>	Ξ	1	=	Ξ	=
peronnaomema, n_n		1		1	1		

<u>Table 2.</u> The impact of risk factors on individual elements of motor development, was studied in the 3rd month in the prone position.

Comentado [R50]: Missing data for body side parameters

For each pair of variables, the values of Cramer's V coefficient, confidence interval, and Goodman and Kruskal Tau coefficient are given, along with the exact p-value. The ordered log it analysis (ologit) was used to assess the particular elements' impact on reaching the standing posture in the 9th month. The dependent variable was measured in the ordinal scale, while all other predictors were expressed in the nominal (binary) scale. For the significant models (p<0.005), P>[z] was given, along with the pseudo R^2 value.

	Side of	Crai	mer's V, G-K-Tau,	p	ologit	
Qualitative characteristic s in the prone position	the body (right= R. left=L)	Apgar 5 th minute lower than 8	<u>IVH</u>	hyperbilir ubinemia	Crucial for final assessmen t at 9th month	
<u>Isolated head</u> <u>rotation</u>		0,1782 (0,0718- 0,2846); 0,0318; p=0,007	0,1984 (0,0917- 0,3952); 0,0394; p=0,0001	0,1676 (0,0610- 0,2742); 0,0281; p=0,0010	=	
Arm in front,	<u>R</u>					
forearm in an intermediate position, elbow outside of the line of the shoulder	<u>L</u>					
Palm loosely	<u>R</u>					
<u>open</u>	<u>L</u>					
	<u>R</u>					
Thumb outside	<u>L</u>					
Spine segmentally in extension		0,1244 (0,0222- 0,2267); 0,01550; p=0,0187	0,1972 (0,0965- 0,2979); 0,0389; p=0,0001	0,1992 (0,0982- 0,3001); 0,0397; p=0,0001	0.074; 0.3389 Con	nentado [R51]: Does not comply criteria
Scapula situated in the medial position	<u>R</u>	0,2114 (0,1232- 0,2997); 0,0447; p=0,0000	0,1992 (0,1013- 0,2971); 0,0379; p=0,0001	0,2168 (0,1194- 0,3142);	0.002; 0.3389	

				0,0470; p=0,0000			
	<u>L</u>	0,2199 (0,1301- 0,3096); 0,0483; p=0,0000	0,1916 (0,0916- 0,2917); 0,0367; p=0,0001	0,1408 (0,0393- 0,2423); 0,0198; p=0,0047			
Pelvis in the intermediate position		0,1235 (0,0106- 0,2364); 0,0153; p=0,0163	0,1732 (0,0617- 0,2847); 0,0300; p=0,0008	0,2610 (01500- 0,3720); 0,0681; p=0,0000	0.000	; 0.3389 Con	nentado [R52]: idem
Lower limbs	<u>R</u>						-
situated loosely on the substrate	<u>L</u>						_
Foot in	<u>R</u>						
intermediate position	<u>L</u>						

Table 3. The impact of risk factors on individual elements of motor development, was studied in the 3rd month in the supine position.

For each pair of variables, the values of Cramer's V coefficient and confidence interval and

 Comentado [R53]: See table 2 comments

For each pair of variables, the values of Cramer's V coefficient and confidence interval and Goodman and Kruskal Tau coefficient are given, along with the exact p-value. The ordered log it analysis was used to assess the particular elements' impact on reaching the standing posture in the 9th month. The dependent variable was measured in the ordinal scale, while all other predictors were expressed in the nominal (binary) scale. For the significant models (p<0.005), P>[z] was given, along with the pseudo R² value

	100	<u>Cra</u>	<u>ologit</u>		
Qualitative characteristics in supine position:	Side of the body, right=R, left=L	Apgar 5th minute lower than 8	<u>IVH</u>	<u>hyperbilirubinemi</u> <u>a</u>	Crucial for final assessment at 9th month
Head symmetry		0,1380 (0,0274- 0,02486);	0,1958 (0,0865- 0,3051);	0,1473 (0,0392- 0,2554);	=

		0,0190; p=0,0077	0,0383; p=0,0002	0,0217; p=0,0039	
Spine in extension		0,1244 (0,0222- 0,2267); 0,0155; p=0,0187	0,1972 90,0965- 0,2979); 0,0389; p=0,0001	0,1992 (0,0982- 0,3001); 0,0397; p=0,0001	0.060; 0.3219
Shoulder in balance between external	<u>R</u>	0,2196 (0,1122- 0,3269); 0,0482; p=0,0000	0,1979 (0,0883- 0,3075); 0,0392; p=0,0001	0,2059 (0,0967- 0,3152); 0,0424; p=0,0001	0.038; 0.3219
and internal rotation	<u>L</u>	0,0214 (0,1081- 0,3205); 0,0459; p=0,0001	0,2111 (0,1026- 0,3196); 0,0446; p=0,0001	0,2364 (0,1286- 0,3443); 0,0559; p=0,0000	0.070; 0.3219
Wrist in	<u>R</u>	2			
intermediate position	<u>L</u>		<u>?</u>		
	<u>R</u>			<u>?</u>	
Thumb outside	<u>L</u>				?
Palm in	<u>R</u>	<u>?</u>			
intermediate position	L				?
Pelvis extended (no anteversion, no retroversion)		0,1542 (0,0396- 0,2686); 0,0237; p=0,0036	0,1777 (0,0654- 0,2899); 0,0316; p=0,0006	0,2856 (0,1745- 0,3968); 0,0816; p=0,0000	0.063; 0.3219
Lower limb situated in moderate external rotation	<u>R</u>	0,2233 (0,0901- 0,3546); 0,0499;	0,1980 (0,0728- 0,3231); 0,0392;	0,1959(0,0724- 0,3194); 0,0384; p=0,0003	0.037; 0.3219

	<u>L</u>	0,2181 (0,0864- 0,3497); 0,0475; p=0,0000	0,1919 (0,0681- 0,3158); 0,0368; p=0,0004	0,2118 (0,0883- 0,3354); 0,0449; p=0,0001	0.127; 0.3219
Lower limb bent at a right angle at hip and knee joints, foot in intermediate position – lifting above the substrate	<u>R</u>	0,2009 (0,0740- 0,3278); 0,0404; p=0,0004	0,2196 (0,0947- 0,3391); 0,0470; p=0,0001	0,3185 (0,1965- 0,4404); 0,1014; p=0,0000	?
	<u>L</u>	0,1966 (0,0709- 0,3222); 0,0386; p=0,0005	0,2114 (0,0903- 0,3326); 0,0447; p=0,0001	0,3118 (0,1908- 0,4327); 0,0972; p=0,0000	?

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