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Original Article

Risk Factors Associated with General Movement Quality in Infants

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Abstract

Background: The quality of general movements assessment, used to assess individual infant from birth to 20 weeks of age, has emerged as one of the most reliable and valid predictors of severe neurological impairments. Aim: To investigate the risk factors for the quality of general movements, which is a predictive value for brain dysfunction in infants. **Method:** 618 cases at the stage of writhing movements and 539 cases at the stage of fidgety movements were selected for assessment of the quality of general movements. The risk factors for the quality of general movements in infants were analysed by ANOVA, chi-square test, and multivariate logistic regression. **Results:** Multivariate logistic regression analysis showed that the factors that were significantly correlated with the quality of general movements at the stage of writhing movements included delivery gestational age (OR=0.762, *P*<0.001), birth weight (OR=0.264, *P*<0.001), severe asphyxia (OR=2.445, *P*=0.012), and intrauterine distress (OR=4.865, *P*<0.001). The factors that were significantly correlated with the quality of general movements at the stage of fidgety movements were delivery gestational age (OR=0.786, *P*=0.003), birth weight (OR=0.217, *P*<0.001), severe asphyxia (OR=3.765, *P*=0.001), and hyperbilirubinaemia (OR=2.640, *P*=0.028). **Conclusions:** Low delivery gestational age, low birth weight, severe asphyxia, hyperbilirubinaemia and intrauterine distress are risk factors and predictors for abnormal general movements in infants.

Key words Fidgety movements; General movements; Infant; Risk factor; Writhing movements

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Introduction

Prechtl's general movements (GMs) assessment, the best functional method to predict cerebral palsy (CP) in high-risk infants, can most reliably predict CP in high-risk infants with a reported sensitivity of 98% (95% confidence interval, CI 74-100%) and specificity of 91% (95% CI 83-93%).[1] The presence of poor repertoire (PR) at 1 month post-term seemed to predict lower neurodevelopmental scores at two years, especially in the domain of eye and hand coordination.[2] Abnormal fidgety (AF) movement is an early marker for complex minor neurological dysfunction at puberty.[3] The presence of cramped synchronised (CS) general movements during[4] preterm and term age and the absence of fidgety (F^-) movements are strong predictors for later CP diagnosis.[5-7] A 2004 report concluded that 70 to 80% of CP cases are due to prenatal factors and that birth asphyxia plays a relatively minor role (<10%).[8] The major risk factors for CP during pregnancy include advanced maternal age (≥35 years), multiple pregnancy, medicine use in early pregnancy, harmful environment, recurrent vaginal bleeding during pregnancy, pregnancy-induced hypertension, and intrauterine growth retardation.[9] Kaandorp and Kieviet also found that premature delivery, low birth weight, and asphyxia of newborn[10,11] are independent risk factors of CP. The risks correlated with preterm birth increase as delivery gestational age decreases, and vulnerability remains in preterm infants.[12] The prevalence of developmental delay for preterm infants is two-fold compared with full term infants,[13] the cognitive outcomes are slightly lower in intelligence quotient (IQ) and poorer in neurodevelopmental, as well as psychomotor outcomes.[14,15] Several studies[16] have reported the effects of asphyxia on the quality of GMs. The infants with abnormal GMs can receive scientific, reasonable treatment at an early stage, which may promote healthy development of the children.[17]

Methods

This was a prospective study, conducted at Qilu Hospital of Shandong University, the Affiliated Hospital of Qingdao University and Union Hospital of Fujian Medical University in China, aimed to investigate the risk factors that affect the quality of general movements.

The inclusion criteria were as follows: all infants born in participating obstetrics clinics, ranging from 3 days after birth to 15 weeks of corrected age.

The exclusion criteria were as follows: infants died from a disease during the study, had central nervous system infection, genetic and metabolic disease, chromosomal disease, congenital abnormality, brain malformation, tumours of the central nervous system, and whose mother could not recall when the last period took place.

A total of 618 infants born in obstetrics clinics between October 2011 and December 2014 and had follow-up visits in the clinic were studied. All 618 cases were evaluated at the stage of writhing movements among them, 539 out of 618 cases were evaluated at the stage of fidgety movements, and the rest of 79 cases lost contact at the fidgety movement stage. The minimum delivery gestational age was 28 weeks and 6 days, whereas the maximum was 41 weeks and 4 days. The lowest and highest birth weights were 970 g and 4110 g, respectively. Three hundred twenty-nine out of 618 cases at the writhing movement stage were boys and the rest of 289 were girls. The mean delivery gestational age was 34.23± 2.7 weeks and the mean birth weight was 2.92± 0.54 kg. At the fidgety movement stage, 281 boys and 258 girls were included. The mean delivery gestational age was 34.15±2.43 weeks and the mean birth weight was 2.90± 0.57 kg. Based on the results of GMs, 618 cases were divided into normal writhing movement group (n=408), poor repertoire group (n=167), and cramped-synchronised group (n=43) at the writhing age. At the fidgety age, 539 cases were divided into the normal fidgety movement group (n=501), abnormal fidgety movements group (n=16), and absence of fidgety movement group (n=22).

The risk factors were investigated and registered. The database was established. Values were assigned to the variables, and the data were analysed using statistical software. Twenty perinatal factors that could be correlated with GMs were collected.

Asphyxia, which refers to no spontaneous breathing or respiratory depression after birth, leading to hypoxaemia, hypercapnia and metabolic acidosis, is an important cause of neonatal death and disability in children.[18,19] Severe asphyxia meets the diagnostic criteria: (1) Profound metabolic or mixed academia (PH<7.00) on an umbilical cord arterial blood sample, if obtained; (2) An Apgar score of 0 to 3 for longer than 5 minutes; (3) Neonatal neurologic manifestations, such as, seizures, coma, or hypotonia; (4) Multisystem organ dysfunctions, for example, cardiovascular, gastrointestinal, haematologic, pulmonary, or renal system.[19]

Fetal distress, life-threatening health syndrome due to hypoxia and acidosis of the fetus in utero, is an important cause of neonatal asphyxia and even death. The fetal distress can be displayed with two or more of the following

symptoms: (1) abnormal fetal movement, for example first increased fetal movement, and then decreased movement; (2) fetal heart rate monitoring: no stress test (NST) is non-reactive type, frequently late decelerations or decreased variability in the fetal heart rate; (3) the fetal heart rate ≥160 bpm or ≤120 bpm; (4) too little amniotic fluid, with amniotic fluid index (AFI) ≤50 mm.[20]

Birth weight of less than 2500 g was considered as low birth weight.[21] Low gestational age was defined as less than 37 weeks.[22] Hyperbilirubinaemia was defined as a total serum bilirubin level of >220.6 μmol/L in mature birth, TSB>256.5 μmol/L in premature delivery.[22]

Assessment of GMs[23]

GMs can be observed in fetuses as young as 9 weeks of postmenstrual age. In infants without neurological dysfunction, GMs continue in a similar pattern until about the end of the second month postterm, which is then followed by a gradually emerging new GMs pattern.

Normal GMs are gross movements, involving the whole body. They may last from a few seconds to several minutes or longer. What is particular about them is the variable sequence of arm, leg, neck and trunk movements. Their intensity, force and speed increase and decrease, and they have a gradual beginning and end. The majority of sequences of extension and flexion movements of arms and legs is complex, with superimposed rotations and often slight changes in direction of the movement. These added components make the movements fluent and elegant and create the impression of complexity and variability.[24]

During term age and during the first postterm months, GMs are commonly referred to as writhing movements. The best observing time for writhing movements was from the 3rd day after birth to corrected age of 4 weeks (according to the expected date of delivery). GMs of a writhing pattern are characterised by small to moderate amplitude and by slow to moderate speed. Fast and large extensor movements may occasionally break through, particularly in the arms. Typically, such movements are elliptical in form; this component creates the impression of a writhing character of movement.[24]

Types of abnormal GMs during preterm, term and early postterm ages are:[24]

Poor repertoire of GMs (PR): A sequence of the successive movement components is monotonous and movements of the different body parts do not occur in the complex way as seen in normal GMs.

Cramped-synchronised GMs (CS): CS are atypical and lack fluency, variation, and complexity. CS are also stereotyped in nature (limb and trunk muscles contract and relax nearly simultaneously).

Chaotic general movements (Ch): Movements of all limbs are of large amplitude and occur in a chaotic order without any fluency nor smoothness. They consistently appear to be abrupt.

Between 2 and 5 months of age, fidgety movements (FMs) become apparent: these show smaller amplitudes of circular shape, lower speed, and a higher variability in acceleration.[24]

FMs were judged as abnormal if they were:

(a) Absent (F^-): FMs are never observed from corrected age of 9 to 15 weeks. Other movements can, however, be commonly observed.
(b) Abnormal (AF): they look like normal FMs but their amplitude, speed, and jerkiness are moderately or greatly exaggerated.

Video-based Assessment[25]

All infants were video recorded while partially dressed in active wakefulness. Each recording lasted for 30 minutes excluding periods of crying. Two digital video recordings were made of each infant: For term infants, the assessment of writhing movements was at 1 month, the assessment of fidgety movements was at 3 months. For preterm infants, the assessment of writhing movements was at 1 month corrected age, and the second at 3 months corrected age, the age at which fidgety movements should be present. If the result was abnormal (PR, CS, F^-, or AF), the infant should be recorded again after three days, until the results reach two consistent conclusions. If the infant had a fever, he or she should be recorded again after the temperature returns to normal. If the infant was hypoglycaemic, a rerecording was performed after blood sugar became stable. The latest recording time could not be more than 1 week after the prescribed time. The quality of GMs was assessed independently by two observers who were blinded to the group assignments of the participants. In cases of disagreement, the video recordings were reassessed and an agreement was reached after a discussion. All observers had successfully completed a 7-day basic course of Prechtl's assessment of general movements.

Statistical Analysis

All statistical analyses were conducted using IBM SPSS statistical software Ver.21 (IBM Corp.). Multivariate logistic regression analysis was conducted to obtain the odds ratios (OR) for the result of GMs after adjusting the variables showed significant correlation in one-factor analysis of variance (ANOVA) or chi-square test. ANOVA was used in measurement data (the data is normally distributed). Chi-square test was used in enumeration data. Wilcoxon rank sum test was used for ranked data. *P* values <0.05 were considered statistically significant.

Results

Possible Perinatal Factors Correlated with GMs

The twenty perinatal factors (Table 1) that might be correlated with GMs included delivery gestational age, birth weight, fetal distress, prolonged labour, threatened abortion, cord entanglement, multiple birth or single birth, meconium-stained amniotic fluid, diabetic mother, placenta previa, cesarean section, early pregnancy (3 months) infection, intracranial haemorrhage, Apgar score (1 minute), severe asphyxia, pregnancy induced hypertension, Hypoglycaemia, hyperbilirubinaemia, convulsion of newborn and gender as the object of investigation that come from prenatal, natal, and postnatal.

Risk Factors of GMs at the Writhing Movements Stage

The twenty perinatal factors that might be correlated with GMs were collected and analysed using one-factor ANOVA and chi-square test. Among these factors, five factors that showed significant correlation in both tests, including delivery gestational age, birth weight, severe asphyxia, fetal distress, and Apgar score (1 minute) (Tables 1 & 2), were analysed using logistic regression. The differences among the three groups in delivery gestational age, birth weight, severe asphyxia, and fetal distress were statistically significant (Table 3).

Risk Factors of GMs at the Fidgety Movements Stage

The twenty perinatal factors that might be correlated with GMs were collected and analysed using one-factor ANOVA or chi-square test. Among these factors, five factors which showed significant correlation in both tests, including delivery gestational age, birth weight, severe asphyxia, hyperbilirubinaemia and fetal distress (Table 4) were analysed using logistic regression. The differences among the three groups in delivery gestational age, birth weight, severe asphyxia, and hyperbilirubinaemia were statistically significant (Table 5).

Correlations of Writhing Movements with Birth Weight and Delivery Gestational Age

Delivery gestational age (r=-0.374) and birth weight (r=-0.281) were negatively correlated (*P*=0.01) with the GMs. The lower the birth weight or the younger the delivery gestational age, the more severe the degree of abnormal GMs at the writhing movement stage.

Correlations of Fidgety Movements with Birth Weight and Delivery Gestational Age

Delivery gestational age (r=-0.305) and birth weight (r=-0.180) were also negatively correlated (*P*=0.01) with the GMs. The lower the birth weight or the younger the delivery gestational age, the more severe the degree of abnormal GMs at the fidgety movement stage.

Table 1 Valuation of the influential factor associated with the quality of GMs

Variables	Risk factor	Valuation and description
X1	Delivery gestational age	Numerical variables
X2	Birth weight	Numerical variables
X3	Fetal distress	No=0, Yes=1
X4	Hyperbilirubinaemia	No=0, Yes=1
X5	Severe asphyxia	No=0, Yes=1
X6	Cord entanglement	No=0, Yes=1
X7	Whether the newborns are twins	No=0, Yes=1
X8	Meconium-stained amniotic fluid	No=0, I grade =1, II grade =2, III grade =3
X9	Whether the mother is diabetic	No=0, Yes=1
X10	Placenta previa	No=0, Yes=1
X11	Cesarean section	No=0, Yes=1
X12	Early pregnancy (3 months) infection	No=0, Yes=1
X13	Intracranial haemorrhage	No=0, Yes=1
X14	Apgar score (1 minute)	Numerical variables
X15	Threatened abortion	No=0, Yes=1
X16	Pregnancy induced hypertension	No=0, Yes=1
X17	Hypoglycaemia	No=0, Yes=1
X18	Prolonged labour	No=0, Yes=1
X19	Convulsion of newborn	No=0, Yes=1
X20	Gender	Female=0, Male=1

Table 2 One factor ANOVA and chi-square test for GMs result at the writhing movement stage

Variables	Group			F(χ^2)	P value
	N	PR	CS		
Delivery gestational age, weeks, mean (SD)	34.73 (2.80)	33.50 (2.10)	32.27 (2.17)	26.415	<0.001
Birth weight, mean (SD)	3.05 (0.46)	2.73 (0.54)	2.39 (0.63)	49.932	<0.001
Severe asphyxia, number (Yes/No)	38/370	77/90	22/21	(115.495)	<0.001
Fetal distress, number (Yes/No)	47/361	85/82	30/13	(140.326)	<0.001
Apgar score (1 minute) mean (SD)	9.14 (1.42)	8.73 (1.55)	7.70 (2.40)	19.051	<0.001

Table 3 Odds ratio for GMs result at the writhing movement stage

Variables	Regression coefficient	Standard error	Wald	df	P	OR	95% Confidence intervals
Delivery gestational age	-0.272	0.048	32.657	1	0.000	0.762	0.694-0.836
Birth weight	-1.332	0.210	40.027	1	0.000	0.264	0.175-0.399
Severe asphyxia	0.894	0.354	6.378	1	0.012	2.445	1.222-4.895
Fetal distress	1.532	0.333	22.608	1	0.000	4.865	2.535-9.344

Table 4 One factor ANOVA and chi-square test for GMs result at the fidgety movement stage

Variables	Group			F(χ^2)	P value
	F	AF	F⁻		
Delivery gestational age, weeks, mean (SD)	34.46 (2.78)	34.43 (1.86)	31.73 (2.43)	10.626	<0.001
Birth weight, mean (SD)	2.99 (0.50)	2.79 (0.37)	2.15 (0.81)	28.950	<0.001
Severe asphyxia, number (Yes/No)	97/404	12/4	9/13	(32.920)	<0.001
Hyperbilirubinaemia, number (Yes/No)	261/240	12/4	18/4	(10.425)	0.005
Fetal distress, number (Yes/No)	177/324	11/5	8/14	(7.484b)	0.024

Table 5 Odds ratio for GMs result at the fidgety movement stage

Variables	Regression coefficient	Standard error	Wald	df	P	OR	95% Confidence intervals
Delivery gestational age	-0.241	0.077	9.680	1	0.003	0.786	0.675-0.915
Birth weight	-1.527	0.309	24.344	1	0.000	0.217	0.118-0.398
Severe asphyxia	1.326	0.383	12.008	1	0.001	3.765	1.799-7.969
Hyperbilirubinaemia	0.971	0.441	4.843	1	0.028	2.640	1.112-6.266

Discussion

GMs at writhing age mainly correlated with asphyxia related illness.[16] While perinatal asphyxia is an obstetric complication that strongly affects the central nervous system.[26] In our study, a total of 618 cases at the writhing movement stage and 539 cases at the fidgety movement stage were selected for assessment of GMs. We found that low delivery gestational age, low birth weight, severe asphyxia, and intrauterine distress are high-risk factors and predictors of abnormal general movements at the stage of writhing movements. Low delivery gestational age, low birth weight, severe asphyxia, and hyperbilirubinaemia are high-risk factors and predictors of abnormal general movements at the stage of fidgety movements.

We also found that delivery gestational age and birth weight were negatively correlated with the GMs, indicating that, the lower the birth weight or the younger the delivery gestational age, the more severe the degree of abnormal GMs at the writhing movement stage. Delivery gestational age and birth weight were negatively correlated with the GMs, indicating that the lower birth weight or the younger delivery gestational age, the more severe the degree of abnormal GMs at the fidgety movement stage.

Based on the analysis above, low delivery gestational age, low birth weight, severe asphyxia, and fetal distress are related to PR and CS. Low delivery gestational age, low birth weight, severe asphyxia, hyperbilirubinaemia, and fetal distress are related to AF and F^{-}, which may lead to developmental disorders in children, such as dyskinesia or learning difficulties. The infants with risk factors of GMs should receive early intervention which may improve GMs quality.[17]

What is the possible mechanism? Preterm birth and low birth weight carry a higher vulnerability to suffering brain insults compared to term infants. These babies can develop any kind of known brain lesions including those affecting the most premature babies (i.e.an intraventricular haemorrhage) and lesions affecting more typically term babies like asphyxia and stroke.[27] They were at much higher risk for destructive brain lesions that resulted in cystic necrotic white matter injury and secondary cortical and subcortical gray matter degeneration. Essentially complete myelination failure occurs in relatively uncommon but clinically significant necrotic lesions as a consequence of the degeneration of all cellular elements.[28] Several studies have identified that preterm survivors display significant reductions in the growth of the cerebral cortex and subcortical gray matter structures that include the basal ganglia, thalamus, hippocampus, and cerebellum.[29-33]

Global Cerebral Ischemia occurs following neonatal asphyxia and leads to harmful neurological consequences. In most cases, patients develop severe cognitive and motor impairments. The study focused on learning and memory deficits that are correlated with brain neuroanatomical reorganisation that appears after Global Cerebral Ischemia.[34] Lipid peroxidation has been implicated as a major mechanism of cellular membrane damage involved in asphyxia in the newborn piglet.[35] Hyperbilirubinaemia often exposes the affected infants to an elevated risk of acute bilirubin encephalopathy or its chronic form, kernicterus.[36] Bilirubin, a powerful antioxidant, also can act as a powerful but silent neurotoxin at the most vulnerable stage of preterm life. The impact is long-lasting with both functional and structural neurologic injury that alters the processing of afferent input and leads to disordered efferent function. Moreover, these perturbations can potentially arrest or retard the natural neural maturation and/or lead to disordered clinical extrapyramidal function, sensory processing of hearing, visual responses, and learning.[37] Hyperbilirubinaemia is a risk factor for GMs at the fidgety movement stage, but not at the writhing movements stage. The possible reason is that the short duration of hyperbilirubinaemia at the writhing movement stage cannot cause severe brain damage.

GMs generated from central pattern generator located in the brainstem, which may be regulated by corticospinal tract or reticulospinal tract. The central pattern generator may be damaged in the process of brain injury above by these high risks. If the central pattern generator is damaged, the quality of GMs may be affected.[38]

In summary, low delivery gestational age, low birth weight, severe asphyxia, hyperbilirubinaemia, and fetal distress are risk factors and predictors of abnormal GMs. The prevention of risk factors can prevent the occurrence of abnormal GMs, which can effectively predict and prevent neurological impairments of the newborns, especially premature infants.

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Conflict of Interest

The authors declare no competing financial interests.

Ethical Consideration

This study was approved by the Ethics Committee of Qilu Hospital of Shandong University, the Affiliated Hospital of Qingdao University and Union Hospital of Fujian Medical University. The methods were carried out in accordance with the approved guidelines. Informed consent was obtained from the parents. Photographs were redacted to prevent human subjects from being identified.

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