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## General movements as a predictive tool of the neurological outcome in term born infants with hypoxic ischemic encephalopathy



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#### ABSTRACT

*Background:* At a time of increasing high risk neonates, an assessment method is needed that can reliably predict neurological deficits at an early age.

*Aims:* The objective of this study was to determine whether the assessment of fidgety movements (FMs) will predict the neurological outcome of infants with hypoxic ischemic encephalopathy (HIE).

Study design: This study employed a prospective and descriptive plan.

*Subjects:* The study sample consisted of 15 infants (8 male and 7 female) born at term. Video recording of FMs were analyzed at 3 to 5 months' infants, who identified with perinatal asphyxia and neonatal HIE. FMs were classified as present or absent.

*Outcome measures*: At 12–18 months age, the infants' developmental outcome was classified as normal or abnormal according to the Infant Neurological International Battery test. "Abnormal outcome" was denoted as poor motor or neurological outcome such as cerebral palsy, whereas "Normal outcome" denotes normal motor and neurological outcomes.

*Results*: The predictive values of FMs were: a sensitivity 0.80 (95% CI: 0.44–0.96), a specificity 1.00 (95% CI: 0.47–1.00), and the accuracy 0.87 (0.57 to 1.00).

*Conclusions:* FMs assessment improves our ability to predict later neurodevelopmental outcomes in term born children with neonatal HIE.

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#### 1. Introduction

Cerebral palsy (CP) is a neurodevelopmental condition which manifests early in childhood, usually before 18 months of age [1].The predictors of CP are; perinatal asphyxia, preterm birth, low birth weight, white matter disease, severe intraventricular hemorrhage, cerebral infarction and deep grey matter lesions [2–4].

Hypoxic–ischemic encephalopathy (HIE) is characterized by clinical and laboratory evidence of acute or sub-acute brain injury due to asphyxia leading to hypoxia and acidosis [5]. Often, the underlying cause and the exact timing of brain injury remain uncertain. HIE is an important cause of permanent damage to CNS tissues that may result in neonatal death or manifest later as CP or developmental delay. Frequency of HIE is reported to be high in developing countries although exact figures are not available. About 20–30% of infants with HIE die in the neonatal period, and 33–50% of survivors are left with permanent neurodevelopmental abnormalities such as CP, and cognitive impairment [5,6].

There is a strong interest in the early detection of predictive signs of developmental disorders in at risk infants, as this offers the opportunity for intervention at young age, when the central nervous system is most plastic [7]. Animal studies emphasize that the environment can enhance or alter brain development [8,9]. General movements (GMs) are part of an infant's spontaneous movement repertoire [10]. Observation of movement patterns in preterm and term infants from birth up to 20 weeks' post term age predicts later CP [11–14], and minor neurologic dysfunction [15].

GM-assessment is based on visual Gestalt perception. Normally, GMs comprise the entire body and manifest themselves in variable sequences of arm, leg, neck and trunk movements. They appear and disappear gradually, varying in intensity and speed. Rotations and frequent slight variations of the direction of motion make them look complex, though smooth [12,13].

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GMs occurs in age-specific patterns. During the post-term age of 3 to 5 months, they are described as 'fidgety movements (FMs)', i.e. small movements of the neck, trunk and limbs in all directions and of variable acceleration [12,13].

The assessment of the FMs has been shown to be a highly valid predictor of neurodevelopmental impairments, specifically in the case of the identification of CP [10,16]. A recent review of 15 studies on the predictive value of FMs reported a sensitivity > 91% and a specificity > 81% [16]. The most comprehensive study, in which more than 900 children participated, revealed a sensitivity of 98% and a specificity of 94% [17].

Previous studies demonstrated that GM and white matter abnormality on MRI are predictive of motor development at 12 months age in at risk children [18]. Although MRIs may require transportation of infants to a specialist facility, GM assessment is more feasible because it is done at the bedside [19]. In our country in which brain imaging techniques such as diffusion weighted MRI and magnetic resonance spectroscopy for clinical routines are rare, GM-assessment is a valuable tool for the assessment of the integrity of the nervous system.

The aim of this study was to determine the predictive value of FMs in infants with HIE, in setting with limited access to brain imaging techniques.

#### 2. Participants and methods

This study employed a prospective and descriptive plan. During the years 2012–2013, neonates with HIE, that were admitted to the Neonatal Intensive Care Unit (NICU) at Mosavi University Hospital, Zanjan, Iran, enrolled in the study. This NICU is an III level (subspecialty) neonatal intensive care center admitting high-risk patients, and the only referral hospital in this area.

The study group consisted of term and near-term neonates (gestational age  $\geq$  35 weeks') presenting with asphyxia. Asphyxia was diagnosed if an infant had one of these symptoms: need for neonatal resuscitation, Apgar score < 5 on 5 min, or symptoms of fetal distress (such as; amniotic fluid meconium stain, or FHR disturbance), arterial blood gas (ABG) with PH < 7 or BE = -16[5,6]. Children were assigned into the study group, if they have signs of neonatal encephalopathy as indicated by a Sarnat score  $\geq 2$  [20], by a neonatologist with experience in the field.

Exclusion criteria were as follows: birth before 35 weeks' gestation, chromosomal defects or a known syndrome, birth malformations of the central nervous system or neuromuscular disease and heterogeneous series of clinical conditions such as: moderate to severe intra ventricular hemorrhage (IVH), small for gestational age (SGA), and infants with diabetic mother, that affects the quality of GMs [12].

Gestational age was calculated from antenatal ultrasound scans. Brain imaging of infants was not accessible and none of HIE children had been treated with hypothermia.

Data had been collected at birth and the infants' spontaneous movements were recorded at fidgety movements' period (aged 3 to 5 months), and the neurological outcomes were assessed at 12–18 months' of age.

Seven to ten minute video recordings were made of the spontaneous motility of each infant at a mean age of 14 weeks' (range = 12 to 20 weeks). The recordings were made during periods of active wakefulness between feedings, with the infant partly dressed and lying in supine position [21]. The room temperature was maintained between 22 °C and 24 °C, in order not to affect the infants' behavior and quality of movements. The blinds were closed, the lights were kept dimmed, and the noise level was at minimum, in order to prevent any possible distraction around the infant during the recording.

The video recordings were evaluated by two pediatricians, who had successfully completed the basic GM Trust training courses, according to Prechtl's method of GM assessment [12]. Pediatricians were not familiar with the participants' clinical histories, and the neurological examination. Each infant's video recording was analyzed (on the day of

the recording, and not separately), to determine whether normal, abnormal or absent fidgety movements were displayed, according to the following descriptions [12]:

- Normal fidgety: small movements of moderate speed and variable acceleration of neck, trunk and limbs in all directions that is continual in the awake infant except during fussing and crying.
- Abnormal fidgety: larger amplitude movements than normal fidgety movements, with moderately exaggerated speed and jerkiness.
- Absent fidgety: fidgety movements are not observed.

At age 12–18 months, a pediatric neurologist with experience at outpatient clinic performed a complete neurological examination, according to the Infant Neurological International Battery (Infanib) recommended by Ellison [22,23]. He was blinded to the infants' fidgety movement results, as well as to the infants' perinatal history and previous assessment results.

The Infanib has 20 items which assess the infant condition in supine, prone, sitting, standing and suspended position for body tone and posture, primitive reflexes and French angles from 4 to 18 months [22].

The Infanib assisted in describing specific upper motor neuron abnormalities, such as muscle tone and reflexes. Both the psychometric properties, and the reliability and validity of the Infanib, have been well established and reported in the literature [24] and in Iran [25].

The Persian Infanib cut-off points were used for assessing motor performance at 12–18 months' age [26]. According to the Infanib, the assessed infants were classified in three categories: normal (scored >1 SD below the mean), mild to moderate abnormal (scored between 1 to 2 SD below the mean) and moderate to severe abnormal (scored more than 2 SD below the mean) [22,26]. Infants were defined and ranked as: 1) "normal clinical outcome" if they had normal scores on the Infanib, 2) "abnormal clinical outcome" if they had "mild to moderate" or "moderate to severe" abnormal scores on the Infanib, and/or an abnormal neurological outcome such as CP, at 12–18 months of age.Data was analyzed with SPSS software, version 19.0 (IBM SPSS Statistics, Chicago, IL, USA). Sensitivity, specificity, as well as accuracy and 95% confidence intervals, and Cramer's V (to illustrate the association between fidgety movements and outcome), were calculated.

The study was approved by Zanjan University Ethics Committee. Written informed consent was also obtained from the parents of the infants who participated in the study and for publication of the results.

#### 3. Results

Totally 40 infants were found to be eligible for the study. Ten infants were excluded due to having SGA (N = 1), severe IVH (N = 2), diabetic mother (N = 1), and birth before 35 weeks' gestation (N = 6). Twelve infants died before they could undergo the video recording. At 3 months' corrected age, 18 children had GM assessment. At 12–18 months 15 (83%) of surviving children were assessed with the Infanib test. Therefore, 15 infants were assigned in the study group, with birth weight (gr), gestational age (week) and admission's age (month) [mean  $\pm$  SD; (2800  $\pm$  234), (37.3  $\pm$  1.1), (15.8  $\pm$  1.9)]. Two infants had meconium staining and 6 of 15 had FHR abnormalities. Arterial blood gas values and Apgar score after 5 min [median; range] were 6 (4–7), and 4 (2–7). Clinical characteristics of the study group are listed in Table 1.

At fidgety movements' period, 7 infants (47%) displayed normal and 8 infants (53%) did not display FMs and their movements were classified as absent.

At 12–18 months of age, 5 infants had normal and 10 had abnormal clinical outcome. Of the 8 infants who were noted as displaying absent FMs, all of them develop abnormal outcome. In 2 of 7 children with the presence of FMs, abnormal outcome was identified (Table 1).

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