

Turkish Validity and Reliability of the Hammersmith Infant Neurological Examination (HINE) with High-Risk Infant Group: A Preliminary Study

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What is already known on this topic?

- The Hammersmith Infant Neurological Examination (HINE) is important for following up on high-risk infants with neurodevelopmental problems.

What this study adds on this topic?

- The Turkish translation of The HINE was found to be readily understandable and easy to use.
- The HINE scores were consistent with 3 different methods (magnetic resonance imaging, general movements, and Bayley Scales-III) of predicting neurodevelopmental outcomes in the first year to identify infants at risk for delayed motor and cognitive performance.

ABSTRACT

Objective: The purpose of this study was to establish the reliability of the Turkish translation of the Hammersmith Infant Neurological Examination in infants at 8-12 months corrected age and compare Hammersmith Infant Neurological Examination scores to other predictive assessments.

Materials and Methods: Perinatal risk factors, term-age magnetic resonance imaging, general movements at 3-month corrected age, and 12-month corrected age The Bayley Scales of Infant and Toddler Development, Third Edition (BSID-III) scores were obtained in 35 high-risk infants. The Hammersmith Infant Neurological Examination was evaluated using intra-rater and inter-rater reliability. Hammersmith Infant Neurological Examination scores were compared to the findings from the three other assessments.

Results: Intra-rater and inter-rater reliability was high (intraclass correlation coefficient = 1.00; intraclass correlation coefficient = 0.969, $P < .001$, 95% CI = 0.939-0.984, respectively). Global Hammersmith Infant Neurological Examination scores were significantly lower in infants with magnetic resonance imaging evidence of brain injury than without ($P < .05$) and in infants without general movements Fidgety movements ($P < .05$), than with. There was a significant positive correlation between global Hammersmith Infant Neurological Examination scores and Bayley Scales-III cognitive ($P < .001$), language ($P < .001$), and motor composite scores ($P < .001$).

Conclusion: This study strongly supports the use of the Turkish translation of the Hammersmith Infant Neurological Examination. Users found it readily understandable and easy to use, and the scores were consistent with 3 different methods of predicting neurodevelopmental outcomes. These findings will aid the early diagnosis, management, and support for children with neurodevelopmental problems.

Keywords: HINE, infant, reliability, validity

INTRODUCTION

High-risk infants may have long-term neurodevelopmental problems.^{1,2} particularly after hypoxic-ischemic encephalopathy (HIE), cystic periventricular leukomalacia (cPVL), and intraventricular hemorrhage (IVH).³

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The follow-up procedure of high-risk infants requires a broad-based approach in order to detect neurodevelopmental problems early.¹ One problem that requires early detection is cerebral palsy (CP), which is associated with neurodevelopmental difficulties.⁴ A combination of methods has shown high rates of predictive validity for the early diagnosis of CP,^{5,6} such as term-age magnetic resonance imaging (MRI), Prechtl's Qualitative General Movement Assessment (GMA) of Fidgety Movements (FMs), and the Hammersmith Infant Neurological Examination (HINE).^{5,6} The HINE, whose reliability and validity have been well established,⁷ has not been translated into Turkish.

Establishing the reliability of the Turkish translation of the HINE is needed. High-risk infant follow-up programs provide guidance for referral of infants for early interventions.⁸ In such programs, the HINE has been proven successful in predicting locomotor/gross motor functions in preterms with a probable diagnosis of CP, or in 3- to 14-month-old infants diagnosed with HIE.⁹ The interrater reliability and correlation coefficients for the HINE were found to be good in typically developing infants.⁷ Currently, there exist no studies examining intra-rater reliability, researcher reliability, and concurrent validity of the Turkish HINE in high-risk infants. The aims of our study were to develop a Turkish translation of the HINE and to determine its reliability and validity in a cohort of infants at high risk of CP.

MATERIALS AND METHODS

The study was developed in 3 stages:

Stage 1: Translation and Pilot Testing

For translation, the principles of Beaton et al were followed.¹⁰ The HINE was translated from English to Turkish by 2 native Turkish-speaking physiotherapists fluent in English. It was then back-translated into English by two English-speaking physiotherapists, also fluent in Turkish. All 4 physiotherapists agreed on a Turkish version. The pilot study involved 15 pediatric physiotherapists, experienced with applying the HINE, who each assessed one of 15 infants. They were asked how they understood and applied each item of the HINE and to express any difficulties they experienced. Through this process, a final version of the Turkish translation of the HINE was created considering the points raised during the pilot testing.

Stage 2: Reliability

This was undertaken by 2 physiotherapists, R1 and R2, one of whom had been involved in the translation. They had similar experience with handling high-risk infants and the use of the HINE. The first section of the finalized Turkish translation of the HINE was administered in 35 infants (not including those from the pilot study) and scored by R1 at baseline (R1-T1). Evaluations were video-recorded in HD for detailed observation. The same physiotherapist made a second assessment (R1-T2) from the original video recording for intra-rater reliability at a 2-week interval. The other physiotherapist (R2) scored the HINE examination from the video recordings separately (R2) and was blinded to the scoring of R1 for the inter-rater reliability. The evaluations by R1 and R2 were used for inter-rater reliability, while the evaluations made by R1 were used for intra-rater reliability. The total score and 5 sub-section scores from the same infants were compared between raters. Reliability for sections 2 and 3 was not assessed. Neither of these 2 physiotherapists

(R1-R2) administering HINE in this study was aware of the infant's medical history or the results of the neonatal neurologic examination.

Stage 3: Validity

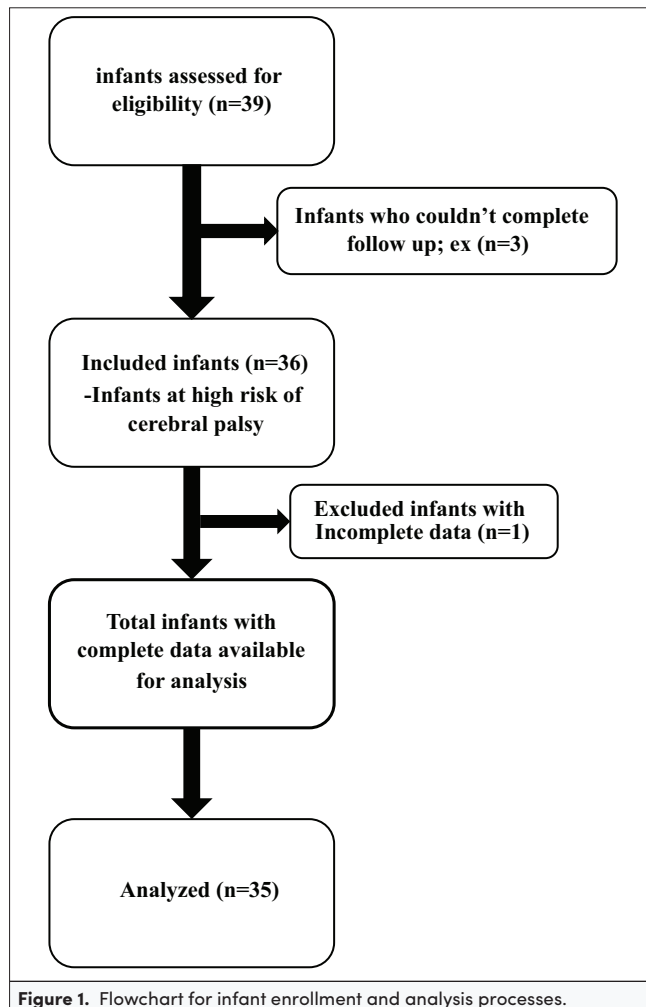
Validity was determined by comparing the HINE results with those of GMA and brain MRI. Additionally, the HINE global scores were correlated with developmental quotients from the Bayley Scales of Infant and Toddler Development (BSID-III) at 12 months. GMA was performed in all infants on 2 occasions from video recordings during the 4-week period at the corrected age (CA) of 12-16 weeks. MRI was undertaken at term-equivalent age (TEA, 38-41 weeks post-menstrual age) as recommended by the neonatologist. BSID-III was administered in all infants at 8-12 months CA by the first rater (R1).

Participants and Measurements

This preliminary study was conducted with 35 high-risk infants, but the study is continuing to evaluate high-risk infants and healthy peer aged between 3 and 12 months. The present study included 35 high-risk infants referred to physiotherapy by a neonatologist. According to the post hoc power analysis using the correlation coefficients between BSID-III and HINE, the power ranges between 94% and 99% for 35 sample sizes. Informed written consents were obtained from families. Age correction was used for all evaluation and outcome data. All examinations were carried out at the Department of Paediatrics. The infants included in the study are shown in Figure 1. Any infant admitted to the Neonatal Intensive Care Unit (NICU) at term with neurological problems and any preterm infant with an abnormal MRI or a complicated neonatal course was eligible (Table 1). Infants were excluded if they had disorders affecting peripheral movements, metabolic/genetic disorders, or infants still dependent on mechanical ventilation at 3 months post-term age. To use the HINE, permission was obtained from the webmaster of the Hammersmith Neurological Examination website.¹¹ The study was conducted in accordance with the Declaration of Helsinki. Ethical committee approval was received from the SANKO University Non-invasive Clinical Research Ethics Committee (Approval No: 16/6). Clinical Trial study registry identifier is NCT04259177.

Hammersmith Infant Neurological Examination

The HINE is a simple, standardized, and scorable test for the clinical neurological evaluation of 2- to 24-month-old infants. It has 3 sections: (1) neurological examination (26 items, scored) evaluating cranial nerve function, posture, movements, tone, reflexes, and reactions, (2) motor milestones (8 items, unscored), and (3) behavior (3 items, unscored). Each of the 26 items is scored first separately (as 0, 1, 2, or 3, half scores), and then, the total score is calculated with a maximum score of 78. The total score can be classified as optimal or suboptimal. Optimal scores are based on the frequency distribution of neurological findings in the population observed in at least 90% of infants in the age range under examination.⁹ The optimal scores for term-born infants between 9 and 12 months are ≥ 73 . Scores found in 9- to 18-month-old preterm infants with normal neonatal brain imaging and the ability to walk independently at 2-year all had scores > 64 .¹² The HINE optimal scores and cut-off scores for predicting the ability to walk or sit or the likelihood of developing CP can provide vital prognostic information regarding future motor



development⁹ and help to determine whether infants might benefit from a specific and early rehabilitation programs. Detailed instructions of the HINES are available freely on the web.¹¹

Novak identified a HINE score of <73 at 6, 9, and 12 months as a risk for developing CP.⁶ Most children in our study had a HINE score <73. We then compared our data to those of Frisone et al.¹² who found that HINE scores <64 at 9- to 18-month-old in infants born preterm were predictive of independent walking, and scores < 52 were predictive of independent sitting but not walking by year 2.¹² We therefore used 64 as cut-off to identify children at high risk of not walking and developing CP. Frisone et al.¹² reported that the optimality scores were not affected by the gestational age of the child or the age at which they were examined between 9 and 18 months uncorrected age. In a later study by Romeo et al.¹³ showed that HINE scores at 9 and 12 months fell sharply with the increasing severity of CP, and all children with CP levels II-V on the Gross Motor Function Classification Scale (GMFCS) had a HINE score <64.¹³ Therefore, in the present study, we compared MRI and FMs findings with suboptimal and optimal HINE scores according to Frisone et al.¹²

Prechtl's General Movements Assessment

General movements (GMs) are the spontaneous movement repertoire present from early foetal life until 20 weeks post-term. From birth to 8 post-term weeks, they have a "writhing"

character and then till about 20 weeks a "fidgety" character. Two specific abnormal movement patterns reliably predict CP: (1) a persistent pattern of cramped-synchronized GMs up to 8 post-term weeks and (2) the absence of the fidgety character from 8-20 post-term weeks. FMs are classified as (a) normal (F+), (b) absent (AF), when normal FMs are never observed, and (c) abnormal (F-). All infants were examined for FMs at least twice using 5-minute video recordings from 9- to -20-week-post-term via video recordings. Recordings were made by physiotherapist R1 when infants were in a supine position in a quiet and well-lit room and outside feeding times. FMs were then assessed from the video by a different pediatric physiotherapist.

Brain MRI

Some of the infants who had cranial ultrasonography damage underwent MRI (n = 19) at term equivalent age (TEA, 38-41 weeks CA) due to abnormal cranial ultrasound (cUS) findings. The neuroimaging reports were assessed by 2 independent radiologists blinded to all clinical information except gestational and postnatal age. In this study, comparing the HINE to MRI findings at term age, we decided to use a robust marker of the integrity of the cortical-spinal tracts at term age, that is, the state of myelination of the posterior limb of the internal capsule (PLIC) as an imaging predictor of CP.¹⁴⁻¹⁶ The radiologists grouped the infants as 1. *Extremely unlikely to develop CP.* Normal imaging or minor anomalies such as IVH grade 1-2. PLIC was of normal.

2. *Unclear, CP is possible, but unlikely,* scans showed some evidence of damage but symmetrical myelin was present in the PLICs. Examples were IVH grade 3, HIE damage not involving the basal ganglia or thalami (BGT), PLIC, the pyramids, or periorlandic area.

3. *Very likely to develop CP.* Evidence of brain damage or malformation involving the motor structures with abnormal/absent myelination in the PLICs. Examples were IVH grade IV, cystic PVL, HIE with BGT involvement, or brain malformation with involvement of the motor cortex and any abnormal PLICs.

The Bayley Scales of Infant and Toddler Development, Third Edition (BSID-III)

The BSID-III is a neurocognitive assessment used to evaluate infants from 0 to 42 months and to monitor their development with 5 domains: cognitive, language (receptive and expressive communication), motor (fine and gross motor), social-emotional, and adaptive functions.¹⁷ The first 3 domains were assessed. To allow comparison of results from the 5 domains, a composite score is calculated for each domain (mean, 100 ± 15). A composite score below -2 standard deviation (SD) (<70) is considered a severe delay for all domains. At 12 months CA, all infants were assessed with the BSID-III by physiotherapist (R1) in a quiet and bright room with their parents.

Statistical Analysis

The number of examinations needed for the reliability study was calculated at 5% significance level, with an effect size of 0.61, $\alpha = 0.05$, 80% power based on adaptation study conducted in an Indian population, and determined to be 25.¹⁸ However, considering the possibility of 10% loss, the sample size was set at 30.

Table 1. Physical Characteristics of the Infants

| | Minimum | Maximum | Mean ± SD | |
|--|-----------|-----------|--------------|-------------|
| Birth weight (g) | 500 | 3500 | 1877 ± 885 | |
| Gestational age (w) | 25 | 40 | 32.97 ± 4.37 | |
| Age at HINE (m) | 8 | 12 | 10.25 ± 1.43 | |
| | n (%) | | sex n (%) | |
| | | Female | Male | |
| Preterm | 26 (74.3) | 10 (38.5) | 16 (61.5) | |
| Term | 9 (25.7) | 3 (33.3) | 6 (66.7) | |
| Total (n = 35) | 35 | 13 | 22 | |
| Infant diagnoses, GM fidgety movements, and MRI findings | | | | |
| | n = 35 | | % | |
| Prematurity+RDS+LBW | 5 | | 14.3 | |
| SGA+IUGR | 3 | | 8.6 | |
| Kernicterus | 1 | | 2.9 | |
| RDS | 9 | | 25.7 | |
| BPD | 3 | | 8.6 | |
| Asphyxia and encephalopathy | 9 | | 25.7 | |
| Sepsis with chorioamnionitis | 2 | | 5.7 | |
| ELBW+RDS+ PROM | 3 | | 8.6 | |
| GMs fidgety movement characteristics | | | | |
| | n = 35 | | % | |
| F+ | 29 | | 82.9 | |
| F- | 6 | | 17.1 | |
| AF | 0 | | 0 | |
| MRI findings at term equivalent age | | | | |
| | n = 19 | % | Term (n) | Preterm (n) |
| Normal (classification 1 – all normal PLIC) | 9 | 47.3 | 4 | 5 |
| IVH (grade 3) (classification 2) | 2 | 10.5 | 1 | 1 |
| IVH (grade 2)+ severe WM injury (classification 3) | 1 | 5.2 | 1 | 0 |
| IVH (grade 1)+ severe WM injury (classification 1) | 1 | 5.2 | 1 | 0 |
| PVL (classification 3) | 2 | 10.5 | 0 | 2 |
| Hypomyelination of PVA (classification 1) | 3 | 15.7 | 0 | 3 |
| Bilateral subcortical hyperintensity+ PVL (classification 3) | 1 | 5.2 | 0 | 1 |
| PLIC myelin not seen (classification 3) | 6 | 32 | 2 | 4 |

SD, standard deviation; RDS, respiratory distress syndrome; BPD, bronchopulmonary dysplasia; LBW, low birth weight; ELBW, extremely low birth weight; IUGR, intrauterine growth retardation; IVH, intraventricular hemorrhage, MRI, magnetic resonance imaging; n, number; PROM, preterm rupture of membranes; PVL, cystic periventricular leukomalacia; SGA, small for gestational age; PLIC, posterior limb of the internal capsule; PVA, periventricular area; F+, fidgety movements present; F-, fidgety movements absent; AF, abnormal fidgety; g, grams; w, weeks; m, months.

The data were analyzed using the Statistical Package for Social Sciences, version 25.0 software (SPSS Inc.; Chicago, IL, USA). Descriptive statistics are given as mean and SD for continuous variables and frequency and percentage values for qualitative variables. The reliability of the HINE was evaluated with test-retest/intra-rater and inter-rater reliability. The validity of the scale was evaluated with concurrent validity. Test-retest reliability was assessed by intra-class correlation coefficient and paired *t*-test by comparing HINE scores at different times obtained by the same rater (R1-T1 and R1-T2); inter-rater reliability (R1-T1 and R2) was assessed using intra-class correlation coefficient and paired *t*-test by comparing scale scores obtained by the 2 different raters. The validity of the HINE scale was evaluated with independent samples *t*-test, Cramer's V coefficient by comparing to the MRI findings and FMs, and Pearson's correlation coefficient between BSID-III composite scores at 12 months CA and the HINE total score.

RESULTS

In total, 35 high-risk infants were examined using the HINE between 8 and 12 months CA (mean, 10.25 months). The primary diagnosis, gestational age (GA), birth weight, prenatal risk factors, evidence of respiratory illness, sepsis, convulsions at discharge were recorded from the neonatal charts (Table 1).

Reliability

Inter-rater reliability of the HINE was high (n = 35, ICC = 0.96, P < .001, 95% CI = 0.93-0.98) for all the sub-score sections (Table 2). For the test-retest reliability, there was no significant difference between the mean of the global and sub-sections of the HINE scores obtained by the same rater (R1-T1 and R1-T2) (P = 1.00). ICC values for the cranial nerves, posture, movement, tone, reflexes & reactions, and global scores were also reliable (Table 2).

Table 2. Inter-Rater Reliability of the HINE in 35 High-Risk Infants

| Components of HINE | | Mean ± SD | ICC | 95% CI | P |
|--|-------------------|------------------|-------|-------------|--------|
| Neurological examination (n = 35) | | | | | |
| Cranial nerves | R1-T1 | 14.14 ± 2.54 | 0.993 | 0.987-0.997 | <.001* |
| | R2 | 14.20 ± 2.52 | | | |
| | <i>t</i> = -0.81° | <i>P</i> = .422 | | | |
| Posture | R1-T1 | 15.85 ± 2.85 | 0.906 | 0.813-0.952 | <.001* |
| | R2 | 15.97 ± 3.30 | | | |
| | <i>t</i> = -0.37 | <i>P</i> = .711 | | | |
| Tone | R1-T1 | 5.42 ± 1.48 | 0.842 | 0.686-0.920 | <.001* |
| | R2 | 5.48 ± 1.33 | | | |
| | <i>t</i> = -0.62 | <i>P</i> = .535 | | | |
| Movements | R1-T1 | 20.71 ± 2.51 | 0.962 | 0.925-0.981 | <.001* |
| | R2 | 21.97 ± 2.26 | | | |
| | <i>t</i> = -4.19 | <i>P</i> < .001* | | | |
| Reflexes & Reactions | R1-T1 | 12 ± 2.40 | 0.946 | 0.894-0.973 | <.001* |
| | R2 | 12.14 ± 2.86 | | | |
| | <i>t</i> = -0.70 | <i>P</i> = .483 | | | |
| Global score | R1-T1 | 68.20 ± 9.80 | 0.969 | 0.939-0.984 | <.001* |
| | R2 | 69.74 ± 10.79 | | | |
| | <i>t</i> = -2.559 | <i>P</i> = .015* | | | |
| Intra-rater reliability of the HINE in 35 high-risk infants | | | | | |
| Components of HINE | | Mean ± SD | ICC | 95% CI | p |
| Neurological examination | | | | | |
| Cranial nerves | R1-T1 | 14.14 ± 2.54 | 0.999 | 0.998-0.999 | <.001* |
| | R1-T2 | 14.17 ± 2.53 | | | |
| | <i>t</i> = -1.000 | 0.324 | | | |
| Posture | R1-T1 | 15.85 ± 2.85 | 1.00 | - | - |
| | R2-T2 | 15.85 ± 2.85 | | | |
| | <i>t</i> = - | <i>P</i> = - | | | |
| Movements | R1-T1 | 5.42 ± 1.48 | 0.993 | 0.986-0.996 | <.001* |
| | R1-T2 | 5.48 ± 1.31 | | | |
| | <i>t</i> = -1.435 | 0.160 | | | |
| Tone | R1-T1 | 20.71 ± 2.51 | 0.995 | 0.989-0.997 | <.001* |
| | R1-T2 | 20.80 ± 2.55 | | | |
| | <i>t</i> = -1.358 | 0.183 | | | |
| Reflexes & Reactions | R1-T1 | 12 ± 2.40 | 0.990 | 0.980-0.995 | <.001* |
| | R1-T2 | 12 ± 2.40 | | | |
| | <i>t</i> = 0 | 1.000 | | | |
| Global score | R1-T1 | 68.20 ± 9.80 | 1.00 | - | - |
| | R1-T2 | 68.20 ± 9.80 | | | |
| | <i>t</i> = - | <i>P</i> = - | | | |

HINE, Hammersmith Infant Neurological Examination; n, number; SD, standard deviation; *P*, *P* value; ICC, intraclass correlation coefficient; R1-T1, first rater's direct scorings; R2, second rater scores; R1-T2, second scoring of the first rater over video recording. **P* value is significant between the groups; °Paired *t* test, *P* < .05, *t*, *t* value.

Validity

MRI and GMA Findings

Nineteen infants had an MRI. Ten (52.7%) had evidence of abnormal findings and 9 (47.3%) normal findings (Table 1). Of the 10 infants with abnormal findings, 6 with abnormal/absent PLIC myelin were considered high risk for developing CP (15, 16). Twenty-nine (82.9%) had FMs (F+) and 6 (17.1%) had no FMs (F-) (Table 1).

HINE Scores and Term-Age MRI Findings

Nine infants with normal/very minor MRI findings had a mean HINE score of 72.11 ± 3.37. All had a HINE score >64 and 5 had ≥73. In the 10 infants with abnormal MRI findings, the mean

HINE score was 60.00 ± 14.77 (Tables 3 and 4). When the infants with abnormal scans were divided into those with a visible PLIC (n = 4) and those without (n = 6), the mean HINE scores were 72.25 (70-74) and 51.83 (36-74). Only 1 infant with absence of PLIC myelin had a HINE score >64 (Tables 3 and 4).

There was a significant difference in global HINE scores (*P* = .030) between infants with and without abnormal MRI findings and between infants with and without PLIC myelinization (*P* = .010) (Table 3). Abnormal MRI findings were moderately compatible with low HINE scores (Cramer's *V* = 0.567). The *V* value was not significant (0.272) when HINE scores were compared between infants with normal or

Table 3. Comparison of HINE with MRI and GMs Fidgety Movements and BSID-III Cognitive, Language, and Motor Composite Scores

| Comparison of HINE Scores According to MRI Findings | | | | | | | | |
|--|------------------|------|-----------------------|------|-------------------------------------|---------------------|----------|----------|
| MRI findings | | | Mean HINE scores ± SD | | PMA | <i>t</i> | <i>P</i> | |
| Normal scan | 9 | | 72.11 ± 3.37 | | 38.60 ± 1.05 | -2.522 ^a | .030* | |
| Any scan abnormality | 10 | | 60.00 ± 14.77 | | 38.90 ± 0.87 | | | |
| Infants not scanned | 16 | | 71.12 ± 4.20 | | 38.76 ± 1.05 | | | |
| PLIC findings in infants with abnormal scans | | | Mean HINE scores ± SD | | | | | |
| PLIC myelin seen | 4 | | 72.25 ± 2.75 | | | -2.822 ^a | .010* | |
| PLIC myelin not seen | 6 | | 51.83 ± 10.25 | | | | | |
| Agreement between MRI findings and HINE scores | | | | | | | | |
| | HINE < 64 | | HINE ≥ 64 | | Total (n = 19) | | | <i>P</i> |
| MRI findings | n | % | n | % | n | % | | |
| Normal | 0 | 0 | 9 | 100 | 9 | 100 | 0.567 | .013* |
| Abnormal | 5 | 50 | 5 | 50 | 10 | 100 | | |
| PLIC myelin seen | 4 | 100 | 0 | 0 | 4 | 100 | 0.272 | .389 |
| PLIC myelin not seen | 5 | 80 | 1 | 20 | 6 | 100 | | |
| Comparison between HINE scores and GMA | | | | | | | | |
| | n = 35 | | Mean ± SD | | <i>t</i> | <i>P</i> | | |
| F+ | 29 | | 71.58 ± 3.66 | | 6.948 ^a | .017* | | |
| F- | 6 | | 51.83 ± 13.77 | | | | | |
| Agreement between fidgety movements and HINE scores | | | | | | | | |
| | HINE < 64 | | HINE ≥ 64 | | Total (n = 35) | | <i>V</i> | <i>P</i> |
| | n | % | n | % | n | % | | |
| F+ | 1 | 3.4 | 28 | 96.6 | 29 | 100 | 0.799 | <.001** |
| F- | 5 | 83.3 | 1 | 16.7 | 6 | 100 | | |
| BSID-III cognitive, language, and motor composite scores in 35 infants at 12 months CA: correlation with the HINE global score | | | | | | | | |
| BSID-III in 35 infants at 12 months CA | Mean scores ± SD | | | | Correlation with global HINE scores | | | |
| Cognitive composite scores | 102.91 ± 25.73 | | | | <i>r</i> = 0.771; <i>P</i> < .001 | | | |
| Language composite scores | 109 ± 19.64 | | | | <i>r</i> = 0.553; <i>P</i> = .001 | | | |
| Motor composite scores | 89.83 ± 23.71 | | | | <i>r</i> = 0.715; <i>P</i> < .001 | | | |

^aIndependent sample *t* test; BSID-III, Bayley Scales of Infant and Toddler Development, Third Edition; CA, corrected age; GMA, general movements assessments; F+, fidgety movements present; F-, fidgety movements absent; HINE, Hammersmith Infant Neurological Examination; *V*, Cramer's *V* coefficient; MRI, magnetic resonance imaging; n, number; *P*, *P* value; PMA, postmenstrual age at scan; *r*, Pearson correlation coefficient; SD, standard deviation; **t*-test; *P* < .05%: percentage; *r*, Pearson correlation coefficient; PLIC, posterior limb of the internal capsule.

abnormal PLIC (within the group with some scan abnormality) (Table 3).

HINE Scores and GMA

Of the 29 infants with normal FMs (F+), the mean HINE score was 71.58 ± 3.66, and in the 6 infants with absent FMs, the mean HINE score was 51.83 ± 13.77. HINE scores were statistically different between infants with normal and abnormal FMs (*P* = .017). Five of 6 infants with F- had HINE scores <64, while only 1 infant with F+ movements had a HINE score <64. Thus, 83.3% of HINE scores <64 occurred in infants with F- and only 3.4% of HINE scores <64 occurred in infants with F+, a statistically significant finding (*V* = 0.799, *P* < .001) (Table 3).

HINE Scores and BSID-III Data

We compared the HINE scores and BSID-III scores. A significant positive correlation was found between the HINE global scores and BSID-III cognitive composite scores (*P* < .001, *r* = 0.771), language composite scores (*P* < .001, *r* = 0.553), and motor composite scores (*P* < .001, *r* = 0.715) (Table 3). Five of 10 infants with HINE scores <64 and with MRI damage had BSID-III motor scores <70 (Tables 4 and 5).

The prognostic value of the HINE in 8- to 12-month CA infants with a high risk of CP compared to their MRI findings, GMs, BSID-III, and HINE scores is shown in Tables 3-5.

DISCUSSION

In this study, the HINE scale was translated into Turkish. We found that the first, scorable part of the scale was reliable with high inter-rater ICC coefficient, consistent with previous studies.^{7,18} There was a strong correlation between the 2 scorings done by the first rater, at a 2-week interval, and the second scoring from a video, and the scoring made by the second rater confirming that the sub-scores of the scale can be scored objectively in 3 separate evaluations¹⁸ using video and by 2 different evaluators working in this specialty. When the same rater re-scored the examination from the video at an interval of 4-6 months, there was no significant difference from the original scoring. These data show that it is easy to apply one-to-one or via video. A clinically insignificant difference was found in the mean scores between raters in the tone assessment, which might have been caused by the second-rater scoring from the video recordings. This was in concurrence with the previous

Table 4. Detailed Comparison of HINE Optimality Score at 8-12 Months CA with Term-Age MRI Findings, GMs Fidgety Movements, and 12-month BSID-III Scores

| MRI Findings (n = 19) | Optimal Score (73 or above) | Suboptimal Score (64-72.9) | Suboptimal Score (52-63.9) | Suboptimal Score (<52) |
|----------------------------|-----------------------------|----------------------------|----------------------------|------------------------|
| Normal (n = 9) | ***** | **** | | |
| Abnormal (n = 10) | | | | |
| PLIC myelin seen | ** | ** | | |
| PLIC myelin not seen | . | | ** | *** |
| Fidgety movements (n = 35) | | | | |
| F+ (n = 29) | ***** | ***** | . | |
| F- (n=6) | . | | ** | *** |
| BSID-III scores (n = 19) | | | | |
| Cognition | | | | |
| Score ≥ 70 | ***** | ***** | . | |
| Score < 70 | | | | **** |
| Language | | | | |
| Score ≥ 70 | ***** | ***** | . | *** |
| Score < 70 | | | | . |
| Motor | | | | |
| Score ≥ 70 | ***** | ***** | | |
| Score < 70 | | | ** | *** |

PLIC, posterior limb of the internal capsule; F+, fidgety movements present; F-, fidgety movements absent; BSID-III, Bayley Scales of Infant and Toddler Development, Third Edition; HINE, Hammersmith Infant Neurological Examination; MRI, Magnetic Resonance Imaging; CA, corrected age; GMs, general movements; n, number.

studies, where infants were evaluated for inter-observer agreement by 2 raters and they found that the interobserver correlation coefficient was close to 1.⁷⁻¹⁸

In terms of construct validity, the HINE cut-off value's predictive ability for CP compared to MRI and FMs agreed with the literature.^{6,9,19} GMA, HINE, and MRI assessments have been tested in high-risk infants demonstrating high sensitivity and specificity for detecting CP as early as 3 months CA for FMs, 5 months for the HINE, and term-age for the MRI. International Clinical Guidelines for the early identification of CP recommend the use of neuroimaging, Prechtl's GMA, and HINE.^{6,9,20} In our study, HINE scores were significantly lower in patients with MRI evidence of damage, compatible with the literature,²¹ and even more so, when the HINE scores were compared between infants with and without PLIC. It is well accepted that the absence of myelin in the PLIC at term age is a strong predictor of CP, better than an abnormal scan. As a result, the HINE was able to distinguish those with a higher risk of CP and vice versa compared to the MRI findings. Inevitably, not one test is perfect in predicting CP, and a combination of MRI findings, HINE score, and GMs are more accurate.^{21,22} Morgan et al²³ emphasized that 9-16% of infants with CP showed no detectable changes on MRI scanning. Those with hypotonic or ataxic forms are over-represented in this group. Therefore, a normal MRI cannot absolutely exclude the clinical diagnosis of CP.²³⁻²⁵ Our results were consistent with the good correlation between high-risk term age MRI findings and HINE results. Combination of neurological examination and brain imaging improved the prediction for abnormal outcome. The absence of FMs was associated with a high risk of CP as predicted from the HINE score in our study.^{6,25,26} Infants with F+ had significantly

higher HINE scores than those with F- (6, 21) but again the correlation was not perfect. But when comparing HINE scores (<64 or >64) between infants with normal or abnormal PLIC in this study, it was not predictive whether infants could walk independently between 9 and 18 months as Frisone et al's study.¹² This suggested that infants without PLIC should be followed up by increasing the sample size.

A standardized neurological examination combined with brain MRI/cUS was shown to improve the predictive value of brain MRI/cUS alone in terms of neurosensory outcomes in preterm infants.²⁷ Our predicted outcomes were not identical for MRI and FMs and we also detected developmental risk via HINE scores in infants with normal MRI findings/normal FMs, and vice versa.

Interestingly our results showed a strong linear relationship between the cognitive, language, and motor composite scores of the BSID-III and HINE, which supports recent data showing that early motor-cognitive assessments can be used for early prediction of CP.^{22,28} Similarly, it was reported that the HINE could provide prognostic information on neurodevelopmental outcome in a population of infants born preterm with/without CP.²⁹

One of the limitations of the study was that when documenting HINE scores during the examination, we observed that the time taken caused some distraction/irritation in infants. Next, the reliability and validity testing of the HINE was only performed in 8- to 12-month-old CA infants and we did not include a control group. These issues will be addressed in a subsequent study evaluating 3- to 12-month-old high-risk infants and healthy peer aged. This preliminary study was hampered by the small sample size. Also, the physiotherapist undertaking the BSID-III was not blind to findings from the other evaluations.

Table 5. Characteristics of 19 Infants with MRI at Term-Equivalent Age

| Characteristics of 9 Infants Without MRI Damage | | | | | | | | | | | |
|---|-------------------|--|----------------------|---|------------------|-----|--------------------|--------------------------|-------------------------|----------------------|--|
| GA/Sex | Birth Weight (kg) | Diagnosis, Prenatal Risk/Perinatal Risk | PMA at Scan in Weeks | MRI Abnormality | PLIC Myelin Seen | GMs | HINE Global Scores | BSID-III Cognitive Score | BSID-III Language Score | BSID-III Motor Score | |
| 40/F | 2.8 | Asphyxia | 41 | No | Yes | F+ | 75 | 130 | 106 | 97 | |
| 38/M | 3.3 | Asphyxia | 39 | No | Yes | F+ | 73 | 120 | 100 | 124 | |
| 39/M | 3.5 | Asphyxia | 40 | No | Yes | F+ | 75 | 140 | 135 | 103 | |
| 26/M | 1.0 | BPD | 38 | No | Yes | F+ | 67 | 95 | 97 | 85 | |
| 28/M | 1.09 | RDS+ PROM: +LBW | 38 | No | Yes | F+ | 74 | 120 | 124 | 112 | |
| 31/M | 1.6 | BPD | 37 | No | Yes | F+ | 71 | 135 | 112 | 118 | |
| 31/F | 1.43 | RDS | 37 | No | Yes | F+ | 71 | 120 | 138 | 94 | |
| 39/F | 3.48 | Asphyxia | 40 | No | Yes | F+ | 67 | 105 | 106 | 94 | |
| 28/F | 1.0 | RDS+ELBW+ PROM | 37 | No | Yes | F+ | 76 | 140 | 115 | 103 | |
| Characteristics of 10 infants with MRI damage | | | | | | | | | | | |
| GA/Sex | Birth Weight (kg) | Diagnosis, Prenatal Risk/Perinatal Risk | PMA at Scan in Weeks | MRI Damage | PLIC Myelin Seen | GMs | HINE Global Scores | BSID-III Cognitive Score | BSID-III Language Score | BSID-III Motor Score | |
| 28/F | 1.00 | PA, ELBW sepsis, convulsions, MV > 7d, BPD | 39 | Reduced myelin in PVA - bilateral | Yes | F+ | 74 | 110 | 118 | 85 | |
| 38/F | 2.60 | Chorioamnionitis sepsis, MV > 7d convulsions, | 39 | IVH-3 | No | F- | 61 | 55 | 77 | 46 | |
| 35/F | 2.30 | SGA, IUGR, multiple birth, MV > 7 d | 39 | IVH-3 | No | F- | 44 | 55 | 62 | 47 | |
| 35/F | 2.50 | SGA, IUDD, multiple birth, MV > 7d | 39 | Reduced myelin in PVA motor pathway | No | F- | 36 | 55 | 91 | 46 | |
| 34/M | 2.16 | Multiple birth, Asphyxia, MV > 7d | 39 | Bilateral subcortical hyperintensity+ PVL | No | F- | 74 | 90 | 79 | 79 | |
| 29/M | 1.25 | RDS, Multiple birth, PPROM, MV>7d | 37 | PVL | No | F- | 52 | 65 | 103 | 49 | |
| 25/F | 0.58 | Chorioamnionitis, ELBW, PROM multiple birth, MV > 7d | 38 | Reduced PVA myelin bilateral | Yes | F+ | 71 | 100 | 86 | 107 | |
| 36/F | 1.95 | SGA | 39 | Posterior PVL | Yes | F+ | 70 | 95 | 144 | 79 | |
| 38/M | 3.24 | Asphyxia high bilirubin, MV > 7d | 40 | Severe WM injury, IVH-2 | No | F- | 44 | 52 | 77 | 46 | |
| 38/M | 2.75 | Asphyxia low Apgar scores | 40 | Severe WM injury, IVH-1 | Yes | F+ | 74 | 70 | 103 | 61 | |

BPD, bronchopulmonary dysplasia; BSID-III, Bayley Scales of Infant and Toddler Development, third edition Composite scores; LBW, extremely low birth weight; F, female; F+, fidgety movements present; F-, fidgety movements absent; GA, gestational age; GMs, general movements; HINE, Hammersmith Infant Neurological Examination; IUGR, intrauterine growth retardation; IVH, intraventricular hemorrhage; M, male; MRI, magnetic resonance imaging; MV, mechanical ventilation; PA, placental abruption; PLIC, posterior limb of the internal capsule; PROM, premature rupture of membranes; PVA, periventricular area; PVL, cystic periventricular leukomalacia; RDS, respiratory distress syndrome; SGA, small for gestational age; WM, white matter; PMA, postmenstrual age; d, days; kg, kilograms.

CONCLUSION

It is concluded that the Turkish translation of the HINE has high inter-rater and intra-rater reliability. It is reliable and suitable for repeated measurements in clinical studies by the same/different raters. We found a high level of concordance and concurrent validity between the global HINE scores obtained by the physiotherapist assessment and MRI, GMA, and BSID-III assessments. This study provides strong evidence that the HINE is a reliable and valid measurement that can be used in the examination of infants at high-risk of neurodevelopmental problems. It supports the efficacy of the translation and confirms that the HINE works in the Turkish population. Our findings should encourage physicians and therapists to include the HINE in their follow-up practices in Turkey.

Ethical Committee Approval: This study was approved by Ethics committee of Gaziantep SANKO University, (Approval No: 16/6).

Informed Consent: Written informed consent was obtained from all infants' family who participated in this study.

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