

Neuro-Developmental follow up of high-risk newborns using hammersmith-dubowitz method

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Abstract

Background and Objectives: High risk infants are prone to delay in neurological development due to perinatal damage sustained by the brain and nervous tissue. Despite being on regular follow-up, delayed neurological development is often missed even by experienced examiners as most of the examination and history are subjective. We aim to validate an objective scoring system- the Hammersmith-Dubowitz neurological exam which was extensively researched and developed taking into consideration normal responses from a normal cohort. **Materials and Methods:** Over a period of two years, 112 infants were categorized as high-risk newborns and were followed up for a period of one year of age. The children underwent detailed milestone assessment, physical and neurological examination by two independent examiners along with objective scoring with Hammersmith infant neurological exam. Any abnormality in these tests was considered delayed development. **Results:** Of the 112 infants, 102 came for at least one follow up and 81 completed one year follow up with a mean follow up duration of 9.42 months. On the combined assessment scale of developmental, physical and complete neurological examination 7.84% infants were found to be abnormal. However, on objective assessment with Hammersmith neurological examination 16.67 % of the infants were found to have abnormal neurological development. **Conclusion:** Hammersmith neurological examination is a useful objective scoring tool to identify delayed neurological development early.

Key words: Hammersmith neurological exam, High risk infant, Objective neurological assessment

Introduction

The two important aspects of neonatal care are the fragility of a neonate and the consequences which can result from management of such a patient which greatly impacts his/her future. A second's delay might lead to years of morbidity and dependence especially when the damage is Neurological. High-risk newborns (HRNB) are especially vulnerable to neurological damage and its complications [1,2]. Early identification of these children can help in better management of their disability [3,4].

The neurological assessment of newborns has evolved through several stages to reach a modern era. The current standard of examination is using one of the many scoring scales to objectively assess the neurological status and express it in numbers or other

forms so that a uniform scale exists for their measurement and comparison irrespective of the examining person. The prominent of these scales include Infant Motor Profile (IMP), Harrison Infant Neuromotor Test (HINT), Alberta Infant Motor Scale (AIMS), Hammersmith Infant Neurological Examination (HINE), Bayley Scales of Infant Development II (BSID), Amiel-Tison neurological assessment, Peabody Developmental Motor Scales (PDMS).

The neonatal behavioral assessment scale (NBAS); Neurobehavioral assessment of the preterm infants (NAPI); the Assessment of preterm infant's behaviour (APIB); the Neonatal intensive care unit network neurobehavioral scale (NNS); and Dubowitz scale. Of these HINE is proved in multiple studies to be more comprehensive and superior in identifying delayed neurological development and milestone progress [5,6].

Manuscript received: 6th June 2019

Reviewed: 16th June 2019

Author Corrected: 20th June 2019

Accepted for Publication: 24th June 2019

The use of scales like HINE has enabled early identification of infants with delayed neurological development and early behavioral changes. These scales are specifically designed as screening tests to identify children at risk for these conditions. These include various components like motor, sensory, behavioral and milestones.

Most of these scales requires prior training and experience whether by formal or informal means for their use. The main criticism against these scales are the fact that administration of such an objective examination is time-consuming, requires expertise and children may not be available for follow-up.

Moreover, these scales are effective only when done serially and well documented. The clinical effectiveness of these scales considering the above said factors in a clinical environment that exists in India is not proven to date. Thus the questions arise - Are these scales effective in our clinical setting? Will the follow-up compliance be good in our country, where there is high prevalence of poverty and illiteracy? Will these scales reduce the need for unnecessary investigations in the infant population at risk?

Since the purpose of infant follow-up in first year of age is to identify impairments as early and broadly as possible and to provide guidance for families. Their choice of standardized assessment is heavily influenced by feasibility and prognostic considerations. In particular, examinations need to balance the demands of clinical imperatives and time constraints.

We selected the HINE for implementation in this study because it is a well-studied neurological examination in healthy or high-risk infants and is an objective scale and results are expressed in numbers easily understandable and without controversy.

The HINE is an easily performed and relatively brief standardized and scorable clinical neurological examination for infants aged between 2 and 24 months, accessible to all clinicians, with good inter-observer reliability even in less experienced staff. It has no associated costs such as lengthy certifications or proprietary forms. The use of the HINE optimality score and cutoff scores provides prognostic information on the severity of motor outcome.

The HINE can further help to identify those infants needing specific rehabilitation programs. It includes 26 items assessing cranial nerve function, posture, quality, and quantity of movements, muscle tone, and reflexes

and reactions. Each item is scored individually (0, 1, 2, or 3), with a sum score of all individual items (range 0 to 78). A questionnaire with instructions and diagrams is included on the scoring sheet, similar to the Dubowitz neonatal neurological examination. Optimality scores for infants three to 18 months are based on the frequency distribution of neurological findings in a typical infant population: when an item is found in at least 90% of infants, it is considered optimal [7].

Sequential use of the HINE allows the identification of early signs of cerebral palsy and other neuromotor disorders, whereas individual items are predictive of motor outcomes. For example, in preterm infants assessed between six- and 15-months corrected age, scores greater than 64 predict independent walking with a sensitivity of 98% and specificity of 85% [8]. Conversely, scores less than 52 were highly predictive of cerebral palsy and severe motor impairments [9].

Materials and Methods

Place of Study: NRI medical college and hospital, Chinakakani.

Study Design: Prospective observational study.

Period of Study: October 2016 to September 2018.

Study Population: The present study was a single-centre, prospective observational study. It studies the ability of Hammersmith infant neurological examination (HINE) scoring system in identifying infants with developmental delay among the high-risk TERM newborns delivered at NRI Medical College and Hospital from October 2016 to September 2018.

As a part of the study, all the TERM infants delivered at our hospital were considered for eligibility. As all the infants were delivered at the same institute and all were term only those satisfying criteria for high-risk newborns were included. Infants born out of both normal vaginal delivery and caesarean section were included in the study. The inclusion criteria were as follows:

Selection Criteria, Inclusion Criteria: All high-risk term newborns were included in the study with the criteria for high risk being- 1. Major morbidities such as chronic lung disease, intraventricular haemorrhage, and periventricular leucomalacia 2. Perinatal asphyxia - Apgar score 3 or less at 5 min and/or hypoxic-ischemic encephalopathy 3. Surgical conditions like Diaphragmatic hernia, Tracheo-oesophageal fistula 4. Small for date (97th centile) 5. Mechanical ventilation

for more than 24 hours 6. Persistent prolonged hypoglycemia and hypocalcemia 7. Seizures 8. Meningitis.9. Shock requiring inotropic/vasopressor support 10. Infants born to HIV-positive mothers 11. Twin to twin transfusion 12. Neonatal bilirubin encephalopathy 13. Major malformations 14. Inborn errors of metabolism / other genetic disorders 15. Abnormal neurological examination at discharge

Exclusion Criteria: Those who refused consent or refused to come for follow-up due to geographical or personal reasons. 2. Mortality during the period of study 3. Patients who withdrew treatment and were discharged against medical advice were excluded.

Procedures and Methods of Data Collection: After the newborn is delivered, he/ she are assessed for eligibility to be recruited. If the infant falls under the high-risk category the infant is assessed with HINE neonatal assessment at discharge. Any neurological damage identified is immediately referred to the specialist clinic.

Once the child is recruited, basic data and maternal data were noted including all possible risk factors. After discharge, the children were followed up over the phone and were called for repeat follow up examinations at 3, 6, 9 and 12 months [10], coinciding with their vaccination schedule.

The children were administered the HINE infant scoring system and the scores were documented. Any infants with low scores were referred to a specialist clinic and these children were in close follow up along with regular examinations.

Those children identified with the low score were followed up to note any improvement in the score with intervention. A score of < 60 as a sign of retardation and referred for further management and investigations.

Results

Number of Subjects: 112 A total of 2173 potential newborns were screened for recruitment. Of which 112 were high-risk term newborns. All the infants were admitted to NICU with different diagnoses and were treated appropriately.

Eight of the infant's parents were not willing to come for further follow-up or be a part of the study. 22 infants were discharged against medical advice and 19 infants died during treatment due to various causes. Of the 112 infants discharged from the NICU, all were assessed and were called for a repeat assessment at 3, 6, 9, and 12 months coinciding with their vaccination schedule. Of the 112 infants, only 102 presented for one follow up at least.

The infants were stratified based on normal and abnormal HINE. Under both the groups, some infants lost to follow-up.

And the infants with abnormal HINE scores underwent necessary interventions after which some of them showed improved HINE scores on further follow-ups.

The infants with normal scores were followed up to one year or further for any neurological deficits or significant delay in milestones.

All these infants were followed up for a period of one year with interval assessments at 3, 6, 9 and 12 months of age coinciding with their vaccination schedule. The children underwent detailed milestone assessment, physical and neurological examination by two independent examiners with a minimum two years of experience in newborn assessment along with objective scoring with Hammersmith infant neurological exam.

Any abnormality in these tests was considered delayed development. The follow-up ended after one year from birth. All the data was compiled and statistically analysed.

Statistical Methods: Descriptive and inferential statistical analysis has been carried out in the present study. Significance is assessed at 5% level of significance.

The following assumptions on data are made. Assumptions: 1. Dependent variables should be normally distributed, 2. Samples drawn from the population should be random, Cases of the samples should be independent. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

Ethical Considerations: 1. Approval to carry out the study was sought from the Department of Pediatrics, NRI Medical College and Ethics Committee, NRI Medical College, Chinnakakani. 2. The nature and benefits of the study were explained to the parents of the infants in a language they understood. 3. Consent was obtained by signature or thumbprint on the consent form

Table-1: Normal and abnormal HINE groups follow-up.

Normal group on follow up	3months	6months	9months	12months
Normal group lost to follow up	85	79	74	68
Abnormal group lost to follow up		6	5	6
Abnormal group lost to follow up	17	14	10	7
Abnormal group improved to normal		1	1	2
		2	3	1

A total of 112 newborns were selected as high-risk term newborns fulfilling the inclusion criteria who were assessed at the time of discharge and advised to come for follow up. At 3 months of age, 102 infants came for follow-up of which 85 had normal HINE scores and 17 had abnormal HINE scores whereas 10 infants lost to follow up. At 6 months of age, 95 infants came for follow-up of which 79 had normal HINE scores, 14 had abnormal HINE scores, 2 infants from the abnormal group improved to normal HINE scores making a total of 81 infants with normal scores whereas 7 infants lost to follow-up. At 9 months of age, 89 infants came for follow-up of which 74 had normal HINE scores, 10 had abnormal HINE scores, 3 infants from abnormal group improved to normal HINE scores making a total of 79 infants with normal scores whereas 6 infants lost to follow-up. At 12 months of age, 81 infants came for follow-up of which 68 had normal HINE scores, 7 had abnormal HINE scores, 1 infant from abnormal group improved to normal HINE score making a total of 74 infants with normal scores whereas 8 lost to follow-up.

Out of the 112 high-risk term newborns included in the study, 50.9% (57 out of 112) were female babies and 49.1% (55 out of 112) were male. 51 of infants completed 38 weeks of gestation, 16 completed 39 weeks and 8 completed 40 weeks of gestation. 55 infants were born through lower segment caesarian section and 57 infants through normal vaginal delivery. 21 of the infants weighed less than 2.5kg and 91 of them weighed equal to or greater than 2.5kg.

Of the 112 high risk term newborns, 96(85.7%) were not ventilated whereas 16 (14.3%) of them were ventilated using a mechanical ventilator.

Out of the 112 high-risk term newborns include in the study , at 3 months follow up - a total of 91.1% (102 out of 112) babies came for follow-up of which 75.9% (85 out of 102) had normal HINE scores and 15.2% (17 out of 102) had abnormal HINE scores and 8.9% (10 out of 112) lost to follow-up.

Table-2: Determinants of HINE at 3 months follow up.

variable	Category	HINE at 3 months				P value
		Abnormal (<60)		Normal(GE 60)		
		count	%	count	%	
Sex	Female	8	16	42	84	1
	Male	9	17.3	43	82.7	
GA	37	9	20.5	35	79.5	0.12
	38	3	8.6	32	91.4	
	39	2	12.5	14	87.5	
	40	3	42.9	4	57.1	
Mode of delivery	LSCS	7	14	43	86	0.6
	NVD	10	19	42	80.8	
Birth weight	<2.5	3	15	17	85	1
	GE 2.5	14	17.1	68	82.9	
ventilation	No	13	14.8	75	85.2	0.24
	Yes	4	28.6	10	71.4	

Out of the 112 high-risk term newborns include in the study , at 6 months follow up - a total of 84.8% (95 out of 112) babies came for follow-up of which 72.3% (81 out of 95) had normal HINE scores and 12.5% (14 out of 95) had abnormal HINE scores and 15.1% (17 out of 112) lost to follow-up.

Table-3: Determinants of HINE at 6 months follow up:

variable	category	HINE at 6 months				P value
		Abnormal		Normal		
		count	%	count	%	
Sex	Female	6	13.3	39	86.7	0.78
	Male	8	16	42	84	
GA	37	8	20.5	31	79.5	0.28
	38	3	9.1	30	90.9	
	39	1	6.3	15	93.8	
	40	2	28.6	5	71.4	
Mode of delivery	LSCS	5	10.9	41	89.1	0.39
	NVD	9	18.4	40	81.6	
Birth weight	<2.5	2	11.1	16	88.9	1
	GE2.5	12	15.6	65	84.4	
ventilation	NO	11	13.4	71	86.6	0.4
	YES	3	23.1	10	76.9	

Out of the 112 high-risk term newborns include in the study, at 6 months follow up - a total of 84.8% (95 out of 112) babies came for follow up of which 72.3% (81 out of 95) had normal HINE scores and 12.5% (14 out of 95) had abnormal HINE scores and 15.1% (17 out of 112) lost to followup.

Table-4: Determinants of HINE at 9months.

Variable	Category	HINE at 9 months				P value
		Abnormal		Normal		
		count	%	Count	%	
Sex	Female	5	11.9	37	88.1	1
	Male	5	10.6	42	89.4	
GA	37	6	16.2	31	83.8	0.35
	38	3	9.4	29	90.6	
	39	0	0	15	100	
	40	1	20.0	4	80	
Mode of delivery	LSCS	3	7	40	93	0.32
	NVD	7	15.2	39	84.8	
Birth weight	<2.5Kg	1	6.3	15	93.8	0.68
	2.5	9	12.3	64	87.7	
ventilation	No	7	9.2	69	90.8	0.16
	Yes	3	23.1	10	76.9	

At 9 months followup, a total of 79.46% (89 of 112) babies came for follow up, of which 11.23% (10 of 89) babies had abnormal HINE scores and 88.76%(79 of 89) babies had normal HINE scores and 20.53% (23 of 89) babies were lost to follow up.

Table-5: Showing HINE at 12 months follow up.

Variables	Category	HINE at 12 months				P value
		Abnormal		Normal		
		Count	%	count	%	
Sex	Female	4	10.3	35	89.7	0.71
	Male	3	7.1	39	92.9	
GA	37	5	13.9	31	86.1	0.24
	38	1	4.0	24	96	
	39	0		15	100	
	40	1	20.0	4	80	
Mode of delivery	LSCS	3	7.5	37	92.5	1
	NVD	4	9.8	37	90.2	
Birth weight	<2.5	1	6.7	14	93.3	1
	2.5	6	9.1	60	90.9	
Ventilation	Yes	6	8.6	64	91.4	1
	No	1	9.1	10	90.9	

Out of the 112 high-risk term newborns include in the study, at 12 months follow up - a total of 72.3% (81 out of 112) babies came for followup of which 66.1% (74 out of 81) had normal HINE scores and 6.3% (7 out of 81) had abnormal HINE scores and 27.7% (31 out of 112) lost to followup.

Table-6: Improvement in abnormal HINE scores.

Improved	frequency	Percentage
No	11	65
Yes	6	35
Total	17	100

Initially at the beginning of the study, it took around 15 to 20 minutes for the assessment of HINE score each time in a well cooperative infant. Gradually with repetitive assessments and experience, the time taken to examine decreased to a maximum of 5 minutes in a well cooperative infant. Just like Ballards scoring which initially took time for assessment but eventually with practice, it is routinely done easily, similarly HINE can also be performed easily over time. This makes it easier for use in regular clinical practice.

Discussion

Delayed neurological development is the leading cause of permanent disability in a newborn infant. Not only does it affect the infant alone, but also causes a major social and economic burden on the family who will have to manage a morbidly disabled child. In a developing country like India, the social effects of such a disabled child are multiplied manifold due to the scarce resources available for treatment and the poor financial means available with the family.

Ultimately these children due to lack of adequate care have high mortality rates within five years of life [10] Thus, identifying these children early is of prime importance. On looking up the various means for the assessment of these high-risk infants, we found the

Hammersmith Infant Neurological Examination (HINE). Though the HINE score has previously been evaluated in various settings, a complete prospective trail using it has never been done on the Indian population. Moreover, we used the scale exclusively in high-risk term infants as a screening tool in a specified population set to identify early developmental delay which is unique to our study. We have compared our study with various other studies and compared the results.

Demography and maternal factors: The gender distribution among the infants in our study is 49.1% male and 50.9% females which were not on expected lines with respect to the Indian population. However,

this can be explained by the lack of prenatal sex determination of these babies. The findings correlated with those of Zafar et al. performed in Indian population though in a different region. However, among the 31 infants lost to follow up 24(77.4%) were female infants which reflects the lack of importance given to the health of the female child among the low socioeconomic and low-income groups in Indian population. These findings are unique to our study.

Multiple maternal factors have been implicated in the neurological growth retardation in various studies in the west [1,5]. However when the factor of prematurity has been eliminated and the results analyzed no prenatal or maternal factors including mode of delivery affected the normal development of the nervous system of a newborn. The commonest gestational age was 37 and 38 weeks as seen in many Indian studies [10,11].

The mode of delivery is almost equal with 49.1% of children born out of LSCS and the rest were by NVD. Though these rates are significantly higher than the rest of the Indian population which is 17.2% [12,13], this can be explained by the fact that the study population consists of high-risk infants who in turn would have been high-risk deliveries or had fetal distress in the prenatal period.

The birth weight in our study was on lines with the rest of the Indian population. 16% of these high-risk newborns were ventilated. Considering the fact that those infants who expired during the course of the study were excluded this number might have been higher.

Fetal Outcomes: Perinatal asphyxia, neonatal seizures, RDS and Neonatal jaundice are the most common condition among infants classified as high-risk newborns. This correlates well with the data published by Simeonsson et al [14]. Overall in the study population with the use of the HINE score we were able to detect 15.1% of the infants had a significant delay in neurological development.

Though the number varies significantly in various studies ranging from 6.3% to 33%, [15,16] the relatively lower number in our 89 study though the study population is of high-risk infants can be explained by the following factors: a. This is not a population based study, it is among the infants treated at a tertiary care centre with a good NICU setup and availability of neonatologist throughout. b. The high rate of LSCS (49.1%) reflects the standard of care received by these infants and their mothers in the perinatal period. c. The careful follow-up and detection of these conditions. d.

The follow-up period is only upto one year which is a limitation as conditions like autism are not usually evident by one year of age. However since the main aim of the study was not to calculate the prevalence of the condition these findings need not be attributed major significance. 27.7% of the infants were lost to follow-up at the end of one year with most of them being female infants; The follow-up rate was good compared to other studies in this arena [5,6].

This can be attributed to clubbing the infant examination schedule with that of the vaccination schedule. Since the vaccination compliance in India is upto 85% in semi-urban and urban areas [12] we sought to replicate these numbers and partially succeeded. With combining of the vaccination schedule and infant examination at 3rd months, 6th month, 9th month and one year we were able to achieve high follow up rates and hence recommend the same to be replicated in future studies to maintain high follow up rates at least upto one year of age. Moreover prior education of the patients about the need for regular follow up, maintaining a database of contact details including the telephone numbers and months contact over telephone also resulted in better followup and sustenance rates.

Hammersmith Infant Neurological Examination: With the use of HINE score, we were able to identify 17(15.1%) infants with abnormal neurological development as early as at 3rd month of age. Of these infants, 6 of the 17(35.5%) improved back to normal HINE score by one year with appropriate referral and early initiation of treatment.

Thus HINE score helped identify these infants early and improved outcomes with early identification. The sensitivity of Hammersmith Score was 90.9% in our study with a specificity of Hammersmith Score nearly 100%. The positive predictive value was 100%. Mean duration of detection of developmental delay using the hammer smith score was 5.1 months. Only one patient was detected with delay in milestones with a normal neurological examination.

The objective scoring system of the HINE assessment gives a clear-cut picture of the neurological development status of the infant and is very useful to identify these children early. Similar findings were noted in two studies by Romeo et al. [17,18] using HINE assessment. Of the various assessments evaluated by multiple authors, [19,20,21,22] the HINE assessment is definitely better in many aspects as it is holistic, comprehensive, short, uncomplicated and requires minimum training.

Use of HINE score in routine OPD follow-up of high-risk newborns is rewarding and helps in early identification of infants requiring special treatment and other assistance. This has been proved in our study that by serial follow-up of these infants we can improve the overall outcomes with timely intervention and referral.

With regular use of HINE score in our daily clinical practice we were able to definitely state that though in the initial days of use it was time consuming and was not easy to master as time passed we were able to perform the follow up examination of each infant within 5 minutes duration thus obtaining vital information for the management of the infant. As the HINE score can be done serially, it can also be used to assess the response to intervention as it was successfully demonstrated by us with an improvement of 6 of 17 children with timely intervention. There are no extra costs involved as the HINE assessment is available free of cost, needs no extra training and is noninvasive. As children also do not experience any pain or discomfort the compliance by parents is also high.

Though the use of HINE is highly rewarding in the follow-up of a high-risk newborn, it is time-consuming and can become a hurdle to daily work if performed on every infant. Since the incidence of delayed neurological development in normal infants is quite less, its use as a screening tool in regular population is limited. It is best used as a screening tool in the high-risk population and as a follow-up tool to monitor progress of borderline cases and to assess improvement or deterioration in children with proven developmental delay. More studies need to be done with use of the HINE scale among high-risk infants to further gauge the efficiency of this scale at identifying and improving outcomes in infants with delayed neurological development. More widespread training should be available to all pediatricians to easily and quickly perform this examination without confusion, and hence be able to identify infants at risk of delayed development.

Conclusion

Hammersmith Infant Neurological examination (HINE) can be used to objectively assess and follow-up neuro-developmental outcomes in high-risk newborns • Hammersmith Infant Neurological examination can be used serially in infants upto one year of age. • Identification of infants with delayed development and correlate factors causing the same. • HINE can be used as a neurological screener tool in Clinical practice • HINE objective score can be done in a regular clinical

setting in OPD within 5 minutes with practice and has good inter-observer reliability • HINE offers early detection of neuro-developmental delay through follow-ups at regular intervals • HINE objective score with early interventions provides better outcomes

What this study adds

1. HINE can be used as a neurological screening tool in clinical practice in Indian setting.
2. HINE scores allows for quantitative evaluation of neurological findings and developmental trajectories
3. It increases the diagnostic precision but does not increase the overdiagnosis.

Funding: Nil, **Conflict of interest:** None initiated,

Permission from IRB: Yes

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How to cite this article?

Lakshmi Priya C, Sravanthi N. L, Vijayalakshmi B, Kantakumari P. Neuro-Developmental follow up of high-risk newborns using hammersmith-dubowitz method. *Int J Pediatr Res*. 2019; 6(06):277-285. doi:10.17511/ijpr.2019.i06.03

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