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EFFECTIVENESS OF THE LACEY ASSESSMENT OF PRETERM INFANTS TO PREDICT NEUROMOTOR OUTCOMES FOR PREMATURE BABIES AT TWELVE MONTHS CORRECTED AGE

¹Thanooja Naushad²N. Meena³Tushar Vasant Kulkarni

ABSTRACT

Background: The Lacey Assessment of Preterm Infants (LAPI) is used in clinical practice to identify premature babies at risk of neuromotor impairments, especially cerebral palsy. There is a shortage of studies on the Lacey assessment despite its wide clinical use. This study attempted to find the diagnostic accuracy of the Lacey assessment of preterm infants to predict neuromotor outcomes of premature babies at 12 months corrected age and to compare their predictive ability with brain ultrasound.

Methods: This prospective cohort study included 89 preterm infants (45 females & 44 males) born below 35 weeks gestation. An initial assessment was done using the Lacey Assessment of Preterm Infants (LAPI) after babies reached 33 weeks postmenstrual age. Follow up assessment on neuromotor outcomes was done at 12 months (± 1 week) corrected age using two standardized outcome measures, i.e., Infant Neurological International Battery and Alberta Infant Motor Scale. Brain ultrasound data were collected retrospectively. Data were statistically analyzed, the diagnostic accuracy of the Lacey Assessment of Preterm Infants (LAPI) alone and in combination with brain ultrasound was calculated.

Results: Fisher's exact test showed $p < .01$, indicating that there is an association between the Lacey Assessment of Preterm Infants (LAPI) and the neuromotor outcomes at one year corrected age. A combination of Lacey Assessment (LAPI) and brain ultrasound results showed higher sensitivity in predicting abnormal neuromotor outcomes than Lacey Assessment alone (80% vs. 66.7%, respectively). Lacey Assessment also showed high specificity (96.3%) and negative predictive value (97.5%).

Conclusion: Results of this study suggest that the Lacey Assessment of Preterm Infants (LAPI) can be used as a supplementary assessment tool for premature babies to identify those at risk of abnormal neuromotor outcomes. These findings have applications to identify premature babies eligible for early intervention services.

Keywords: Preterm, Lacey assessment of Preterm Infants, Neuromotor outcome.

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CORRESPONDING AUTHOR

¹Thanooja Naushad

Senior Physiotherapist
Latifa Women and Children Hospital, Dubai,
UAE. P O Box 9115.
Email: thanuphysio@gmail.com

²Lecturer, Physical Medicine and Rehabilitation
Annamalai University, Chidambaram, Tamil Nadu,
India. Email: roshmena@gmail.com

³Senior Specialist Registrar, Neonatology
Latifa Women and Children Hospital, Dubai, UAE.
P O Box 9115. Email: tushardips@yahoo.com



INTRODUCTION

Recent studies have shown that though there has been a significant increase in the proportion of premature infants who survive without major morbidities, they are still at high risk of developmental delay and neuromotor dysfunction (Moore et al., 2012; Pierrat et al., 2017) [1,2]. Hence regular follow up of babies born preterm is important to identify those with neurodevelopmental disabilities. Cost-effectiveness and lack of resources may hamper the follow up of all preterm babies born before 35 weeks of gestation (Leroux et al., 2013) [3]. The use of a neurological assessment tool specific to premature babies in the neonatal intensive care unit will, therefore, be effective in identifying those babies at particularly high risk for future neuromotor impairment.

The Lacey assessment of preterm infants (LAPI) was developed specifically for clinical use in the NICU as a longitudinal assessment tool to monitor the infant's development over time and to identify features indicating the risk of abnormal neurodevelopmental outcome (Lacey et al., 2004) [4]. When administered above 33 weeks postmenstrual age, Lacey assessment (LAPI) is reported to have 86% sensitivity and 83% specificity for subsequent Cerebral palsy (Lacey et al., 2004) [4]. Some studies have also shown superior sensitivity of the Lacey assessment when compared to brain ultrasound to predict cerebral palsy (Lacey et al., 2004; Marcroft et al., 2014) [4,5]. Though the Lacey assessment (LAPI) is widely used in clinical practice, it still has a limited evidence base (Marcroft et al., 2014) [5]. The only data that have been published investigating the diagnostic accuracy of the Lacey assessment - apart from the original study by Lacey et al., 2004 are that in a small retrospective review (James et al. 2017) [6]. These studies included babies born below 31 weeks gestation and were not representative of preterm babies born at later gestational ages.

In this study, our primary objective was to investigate the diagnostic accuracy of the Lacey Assessment of preterm infants (LAPI) to predict neuromotor outcomes of premature babies born below 35 weeks gestation at 12 months corrected age using standardized outcome measures. Our secondary objective was to compare Lacey assessment (LAPI) with brain ultrasound for predicting neuromotor outcomes at 12 months of corrected age.

MATERIALS AND METHODS

The subjects in this study were 89 preterm infants (45 females and 44 males) who were admitted in the neonatal intensive care unit of Latifa Women and Children Hospital, Dubai, during the year 2018. Participants were selected as a sample of convenience. The study was approved by the Dubai Scientific Research and Ethics committee (DSREC-SR-08/2017_04) of the Dubai Health Authority. Preterm babies born less than 35 weeks gestation and with birth weight, less than 2.5kg were included in the study. Infants diagnosed with genetic/ chromosomal abnormalities, metabolic disease, musculoskeletal or neuromuscular

conditions, or other congenital anomalies were excluded.

Signed informed consent was obtained from parents of babies who met the inclusion criteria. The babies were examined using the Lacey assessment (LAPI) after they reached 33 weeks postmenstrual age. At least two assessments were completed prior to discharge from the neonatal unit. The assessment was done following all the guidelines in the Lacey assessment manual (Lacey et al., 2015) [7]. Developmental scores were calculated, and babies were classified into one of the two groups - usual or monitor based on LAPI findings. After discharge from the NICU, all babies were reassessed at 12 months (± 1 week) corrected age using the Infant Neurological International Battery and the Alberta Infant Motor Scale. Based on the INFANIB scores, babies were classified as Normal, Transiently abnormal, or Abnormal. In this study, the compromised neuromotor outcome was defined as INFANIB categories of transiently abnormal or abnormal together with AIMS score < 5 th centile. Babies who were in the transient group in INFANIB had some neurological signs without a diagnosis of cerebral palsy, and those in the abnormal category had cerebral palsy. Diagnosis of cerebral palsy was further verified from neurologists' notes in the infant's case file. Cut off score to identify motor developmental delay in AIMS was fixed at 5th centile based on earlier studies on preterm babies (Darrah et al., 1998; Song et al., 2018) [8,9].

Data were analyzed using SPSS version 21. Statistical significance of the Lacey Assessment (LAPI) to predict neuromotor outcomes at 12 months corrected age was calculated using Fisher's exact test. Brain Ultrasound data were analyzed retrospectively and were compared with the Lacey assessment (LAPI) to predict final neuromotor outcomes at one year. Sensitivity, specificity, positive and negative predictive value, and likelihood ratio were calculated for Lacey assessment and for a combination of Lacey assessment with brain ultrasound.

RESULTS

Eighty-nine babies were recruited for the initial Lacey assessment (LAPI). Their demographic and clinical characteristics are given in Table 1.

Table 1: Characteristics of babies who underwent LAPI assessment

Category	Type	Number	Percentage
Sex	Female	45	50.6
	Male	44	49.4
GA	<28	17	19.1
	28-32	50	56.2
	≥ 32	22	24.7
Type of Birth	Multiple Birth	40	44.9
	Single birth	49	55.1
Type Of Delivery	C section	69	77.5
	Normal Delivery	20	22.5

APGAR	<7 at 1 minute	31	36.9
	<7 at 5minute	4	4.8
Birth Weight	<1kg	21	23.6
	<1.5kg	37	41.6
	<2kg	22	24.7
	<2.5kg	9	10.1
Medical Conditions	Chronic Lung Disease	16	18
	Respiratory Distress Syndrome	80	89.9
	Patent Foramen Ovale	28	31.5
	Neonatal Hyperbilirubinemia	79	88.8
	Anemia of prematurity	30	33.7
	Neonatal Sepsis	20	22.5
	Retinopathy of Prematurity	17	19.1
	Metabolic Bone Disease	14	15.9
	Small for Gestational Age	17	19.1
	Infant of Diabetic Mother	11	12.6
Brain Ultra Sound	IVH Grade I, II	15	17.9
	IVH Grade III, IV	3	3.6
	PVL	2	2.4
	Ventriculomegaly	3	3.6

After the initial Lacey assessment, Eighty-one babies (91%) were placed in the Usual group in LAPI, and eight babies (9%) were placed in the Monitor group. The distribution of these categories based on gestational age is shown in Table 2.

Table 2: LAPI categories based on gestational ages

Gestational Age	Usual	Monitor	Total
<28 weeks	12	5	17
28-32 weeks	48	2	50
≥32 weeks	21	1	22

From the table, it can be observed that babies born at lower gestational ages, especially those below 28 weeks, were more likely to be placed in the Monitor category in LAPI, implying compromised neuromotor function.

Outcome assessment: Babies were reassessed at 12 months corrected age (± 1 week) using INFANIB and the AIMS. One baby was lost to follow up for the final assessment. 6 babies had compromised neuromotor function at one year follow up. Three of these were diagnosed as cerebral palsy, of which two had spastic quadriplegic cerebral palsy, and one had spastic diplegia. The remaining three babies had a severe gross motor developmental delay with some neurological signs but were not diagnosed as Cerebral palsy. Five of the six babies with compromised neuromotor outcome were born at below 30 weeks gestation. Sixteen babies had gross motor developmental delay (<5th centile in AIMS), 10 of them had normal scores in INFANIB and hence was not included in the final list of babies with neuromotor compromise. All babies with transiently

abnormal or abnormal findings in INFANIB had AIMS score below 5th centile.

Table 3: Outcome assessment results based on gestational ages

Gestational Age	INFANIB				AIMS centile			
	Normal	%	Transient or Ab-normal	%	>5 th centile	%	≤5 th centile	%
<28 weeks	12	75	4	25	7	43.7	9	56.3
28-32 weeks	49	98	1	2	44	88	6	12
≥32 weeks	21	95.5	1	4.5	21	95.5	1	4.5

Table 3 shows that babies who were extremely preterm were more likely to develop abnormal neuromotor function at one-year corrected age

Lacey Assessment and final neuromotor outcomes at 12 months

Of the 81 babies classified by the Lacey assessment (LAPI) as usual, 79 babies had a normal neuromotor function in the final follow up. Of the seven babies classified as monitor, four had compromised neuromotor outcomes at one year. Probability testing using Fisher's exact test showed P-value <.01, indicating that there is an association between the Lacey assessment and the neuromotor outcomes at 12 months corrected age. The predictive ability of Lacey assessment was calculated and is shown in Table 4.

Table 4: The predictive ability of LAPI at one-year corrected age

Statistic	Value	95% CI
Sensitivity	66.67%	22.28% to 95.67%
Specificity	96.34%	89.68% to 99.24%
Positive Likelihood Ratio	18.22	5.24 to 63.38
Negative likelihood ratio	.35	0.11 to 1.07
Positive Predictive value	57.14%	27.71% to 82.26%
Negative predictive value	97.53%	92.72% to 99.19%
Accuracy	94.32%	87.24% to 98.13%

Lacey assessment and Brain ultrasound

In this study, abnormal brain ultrasound included those babies with varying grades of intraventricular hemorrhage (IVH), periventricular leukomalacia (PVL), or ventriculomegaly. On comparison with brain ultrasound, the Lacey assessment(LAPI) showed lower sensitivity (66.7% vs. 83.3%), superior specificity (96.3% vs. 77.9%), higher positive predictive value (57.1% vs. 22.7%), similar negative predictive value (97.53vs 98.36%) and better positive likelihood ratio (18.5 vs. 3.8) to predict neuromotor outcomes at one year of age. It was observed that of the 60 babies who had a 'usual' categorization in Lacey assessment (LAPI) and normal brain ultrasound, only one baby showed abnormal neuromotor outcomes in the final outcome assessment. Similarly, of the six babies who were in the 'monitor' category of Lacey assessment and had an abnormality in brain ultrasound, four were identified as having abnormal neuromotor outcome at 12

months corrected age. Neuromotor outcomes at 12 months corrected age of Lacey assessment (LAPI) in comparison with brain ultrasound is shown in Table 5.

Table 5: Brain ultrasound scan and neuromotor outcomes at one year

BUSS	Abnormal Outcome	Normal Outcome	Total
Abnormal	5	17	22
Normal	1	60	61

Diagnostic accuracy of a combination of LAPI and brain ultrasound was calculated, and results are shown in Table 6.

Table 6: The predictive ability of combined Lacey assessment and brain ultrasound at 12 months corrected age

Statistic	Value	95% CI
Sensitivity	80%	28.36% to 99.49%
Specificity	96.72%	88.65% to 99.60%
Positive Likelihood Ratio	24.40	5.83 to 102.14
Negative likelihood ratio	0.21	0.04 to 1.19
Positive Predictive value	66.67%	32.33% to 89.33%
Negative predictive value	98.33%	91.08% to 99.71%
Accuracy	95.45%	87.29% to 99.05%

On comparing tables 4 and 6, it can be said that a combination of Lacey assessment (LAPI) and brain ultrasound scan shows more strength to predict abnormal neuromotor outcomes of premature babies at one year corrected age, than LAPI assessment alone.

DISCUSSION

The results of this study indicate that Lacey assessment of preterm infants (LAPI) can be used as an effective screening tool in the neonatal intensive care unit, especially to identify babies at low risk of abnormal neuromotor outcomes. This study shows almost similar positive and negative predictive values as in the original study by Lacey et al., 2004 (57.1 vs. 57% and 97.5 vs. 96% respectively) [4]. The high specificity value, as found in this study, points to the ability of LAPI to predict for normality, as has been documented in similar studies (Lacey et al., 2004; Marcroft et al., 2014) [4,5]. This has clinical significance since a 'usual' outcome in Lacey assessment can be used to reassure parents who are anxious about their baby's future development. The sensitivity value of the Lacey assessment found in this study was lower than that was previously reported by Lacey et al. A retrospective review by Marcroft et al., 2014 [5] had also shown lower sensitivity values (75%) as compared to the original validation study. The sample size of our study was much lower compared to the original validation study by Lacey et al., 2004 [4] (n=89 vs. n=192 respectively), and babies were born at higher gestational ages (GA<35weeks vs. GA<31 weeks). Studies have established the fact that lower the gestational age higher is the neuro disability rates (Marret et al., 2013; Spittle et al., 2018) [10,11]. These factors could have contributed to the lower sensitivity values in this study, and it reflects the diagnostic accuracy of Lacey

assessment on a broader population of preterm babies of older gestational ages and birth weights. Moreover, the infants who were in the Monitor group in Lacey assessment had undergone early intervention, including physiotherapy or occupational therapy sessions, as per our hospital policy during the course of their development. This also might have influenced sensitivity calculations based on neuromotor outcomes at one year corrected age.

Previous studies had focused on the use of LAPI as a diagnostic tool for cerebral palsy (Lacey et al., 2004; Marcroft et al., 2014) [4,5]. Current evidence points to a high rate of motor impairment in very preterm children, both including and excluding cerebral palsy (Williams et al., 2010) [12]. Transient signs may either progress to cerebral palsy or get resolved as children become older. It is reported that extremely preterm children with a history of transient neurological signs are at higher risk for lower cognitive and academic skills than those with normal neurological findings (Harmon et al., 2015) [13]. Hence, in our study, transient neuromotor abnormalities without the diagnosis of cerebral palsy are also considered as compromised neuromotor function. Compared to earlier studies (Marcroft et al., 2014) [5] which had relied on data collected from clinical notes, or discharge letters of infants to reach a diagnosis of cerebral palsy, in this study we have used valid and reliable clinical outcome measures like the INFANIB and AIMS to identify the abnormal neuromotor function. INFANIB is a tool for the assessment of the neurological integrity of infants till 18 months corrected age (Ellison et al., 1985) [14] and has established reliability for clinical and research purposes (Soleimani et al., 2007; Sung & Kang, 1997) [15,16]. AIMS is a valid measure of motor development in preterm infants and is applicable in clinical settings as a routine screening test to detect preterm infants with motor delay (Albuquerque et al., 2018; Fuentefria et al., 2017) [17,18]. The use of standardized outcome measures has helped in the uniformity of outcome measurement and thus facilitates replication of this study in a larger population by other researchers. Comparison of Lacey assessment categories with the AIMS centiles showed that 15 babies who had 'usual' categorization in Lacey assessment had AIMS scores $\leq 5^{\text{th}}$ centile, and 93% of them were born ≤ 30 weeks gestation. This finding highlights the need for longitudinal follow up of babies born very premature, irrespective of their initial assessment results prior to discharge from NICU.

Similar to a study by Marcroft et al. 2014 [5], the results of this study also showed that a combination of Lacey assessment and brain ultrasound results provides better diagnostic accuracy than LAPI results alone. In another study (Spittle, 2011) [19] has aptly remarked that "given the multitude of influences on development it is unlikely that clinicians and researchers will ever be able to predict with absolute certainty whether a child will go on to have cerebral palsy or another developmental impairment from a single assessment." Hence it is prudent to use clinical assessment tools like the Lacey assessment in combination

with neuroimaging results while considering future developmental outcomes for premature babies. This, in turn, facilitates more accurate early identification of at-risk or low-risk infants much prior to term age. Identifying preterm infants who are at high risk of neuromotor impairments is important for enrolling children in early intervention programs and counseling families (Spittle et al., 2011) [20].

In this study, we had done at least two serial Lacey assessments for each baby prior to their discharge from the neonatal unit. Though parent satisfaction was not measured, we had noticed that Lacey assessment could be an effective tool to enhance positive experiences for parents of premature babies in the neonatal unit. Pointing out baby's ability to hold head upright in a supported sitting or protectively turn their head to sides from prone position fascinates parents and attunes them to their otherwise 'fragile' babies abilities and may enhance positive interactions between infants and parents. It might also help them to understand the patterns of motor development of their premature baby and the progress achieved by babies over a period of time. This, in turn, attunes parents to baby's development and facilitates conversation between neonatal physiotherapists and parents, which is a vital aspect of parent education in the neonatal unit.

Based on the findings, the authors of this study recommend that Lacey assessment of preterm infants (LAPI) can be used as a supplementary clinical assessment tool to identify babies likely to develop abnormal neuromotor outcomes rather than a diagnostic tool for cerebral palsy as was initially proposed by Lacey et al., 2004.

CONCLUSION

The results of this prospective cohort study shows that the Lacey assessment can be used to identify those premature babies at risk of abnormal neuromotor outcomes. The strength of LAPI is its superior specificity, which helps to correctly identify babies who are likely to have a normal course of development. Lacey assessment, in combination with brain ultrasound, shows better diagnostic accuracy for predicting neuromotor outcomes at one-year corrected age. Thus, Lacey assessment can be a valuable neuromotor assessment tool for neonatal physiotherapists working in intensive care units and special care nurseries.

Study Limitations and future research

The main limitations of this study were the relatively small population recruited and shorter duration of follow up. Earlier studies on Lacey assessment had outcome measurements at 2 or 3 years as compared to one year in this study. Investigator was not blinded to the Lacey assessment results or medical history at the final assessment, and this might have been a cause of bias. Future studies in this area require long term prospective studies with a larger population and outcome measures that assess multiple domains of development.

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