Original Article

Study of Neuro-developmental Outcome of Preterm Babies Using Risk Stratification Score at a Tertiary Care Hospital

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Introduction : Recent advances and improvements in technology in Neonatal Intensive Care Unit (NICU) over the past few decades have increased the survival of preterm infants. India ranks first amongst the number of preterm birth. Though the survival of preterm babies have increased Neuro-developmental morbidity amongst such babies still persist. Through this study we aim to establish a risk stratification tool and predict neurodevelopmental delay at 1 year of age.

Materials and Methods : A total number of 77 babies were enrolled in the study after fulfilment of inclusion and exclusion criteria. Follow up till 1 year of age of corrected gestational age was done. Development assessment was done through Child Development Centre (CDC) grading, Amile-Tison Angle, Developmental Observation Card, Trivandrum Developmental Screening Chart and development quotient. Vision and Hearing Assessment was also done.

Conclusion : Neuro-developmental outcome prediction at 1 year of age is inadequate and proper long term follow up is needed. Overall preterm babies needing extensive resuscitation and 5 minute APGAR <6 had much poor neurological outcome.

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Key words **: Neuro-development outcome, Neurodevelopment delay, Preterm, Amiel-tison angle, CDC grading, Trivandrum Developmental Screening Chart (TDSC).**

Every year, an estimated 15 million babies are born preterm and this number is rising[1]. India ranks first amongst the number of preterm births with 3.5 million premature birth annually and incidence of 7-9% and constantly rising. Low birth weight is an important cause of morbidity & mortality in the developing countries like India[2].

Understanding the causative etiology of preterm birth is the most integral part for evaluating risks and formulating preventive protocols. WHO has developed new guidelines for reducing preterm births and improving outcomes of premature babies[1]. Out of 10 elements recommended by WHO antenatal corticosteroids, tocolytics, magnesium sulfate and Kangaroo Mother Care are currently included in India's Clinical Standards of Preterm Care at hospital level.

The survival of preterm babies has increased due to improvement in the quality of Perinatal Care Implementation of WHO recommended guidelines and advances made in Obstetric and Neonatal Intensive Care.

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Editor's Comment :

- Every neonate if screened timely can have improved quality of life.
- Simple assessment tool for evaluating risks and establishment of preventive protocols is essential at present to reduce preterm morbidity and mortality.
- Antenatal care is essential for good outcome of the neonate.
- Follow-up of high risk neonates should be done timely to evaluate and intervene in case of developing Neuro-development disability.

Every attempt is made for survival without disability but such babies are at substantial risk for future neurodevelopmental delay. The major adverse Neuro-developmental outcomes which can be associated with preterm birth include Cerebral Palsy, impairment in Motor and Cognitive Function, visual and auditory deficits and behavioral problems. Early prediction of such morbidities and timely appropriate intervention can prevent or modify many of these disabilities. And for this a well-structured follow up program for high risk neonates with good compliance is the need of the hour.

Materials and Methods

The present study is an prospective-observational study which was carried out in Department of Paediatrics at Tertiary Care Hospital. Over a period of 6 months from preterm infants were enrolled and then followed up till 1 year of age. A total 64 preterm

participated in the study in accordance to the inclusion and exclusion criteria. All preterm babies >34 weeks discharged from NICU and both inborn and out born babies referred in first 48 hours were included in the study. Preterm infants with Congenital Malformations, Congenital Heart Disorder, Intrauterine Infections, referred from outside after 48 hours and those transferred to another hospital before completion of care were excluded from the study. A questionnaire was formed to obtain information regarding participants. Demographical data, birth details and risk factors were obtained from case report file. Accordingly the babies were categorised into mild, moderate and severe risk based on the risk score obtained. Monthly follow up was taken of the enrolled preterm infants upto 1 year of age. Amiel-Tison Angle and Scarf sign was assessed every 3 months. Developmental Observational Card was used to check for achievement of major milestone and CDC grading of milestone was done at completion of 2, 4, 8 and 12 months. Trivandrum Developmental Screening Chart was used to screen children for developmental delay up to 1 year of corrected Gestational Age. Visual assessment was done to check for retina of prematurity and hearing assessment was done to check for deafness. Apart from this preterm babies head circumference was monitored and persistence of neonatal reflexes and presence of red flag signs for Cerebral Palsy was checked. Development quotient of each infant was assessed at 1 year of age. At the completion of 1 year outcome was predicted. Outcome was categorised into primary and secondary. Primary outcome was defined as death before 12 months of age post discharge or major Neuro-development delay in form of cerebral palsy, Mental impairment, Blindness and Profound Hearing loss. Secondary outcome was defined as normal baby or minor Neuro-development disability in form of refractive error/squint, impaired hearing not requiring assisted devices, growth delay and delay in achieving milestone in two or less than two domain.

Data Analysis : Data were entered in Microsoft excel 2016 and analysis was carried out using SPSS version 21 (Figs 1 & 2).

Statistical Test : Chi-square test with level of significance <0.05 and Odds ratio was used for as statistical test to test various associations.

Age (months)	Adductor angle	Popliteal angle	Dorsiflexion angle	Scarf sign
0-3	40°-80°	80°-100°	60°-70°	Elbow does not cross midline
4-6	70°-110°	90°-120°	60°-70°	Elbow crosses midline
7-9	110°-140°	110°-160°	60°-70°	Elbow goes beyond axillary line
10-12	140°-160°	150°-170°	60°-70°	

Fig 1 — Amiel – Tison Angle and scarf sign

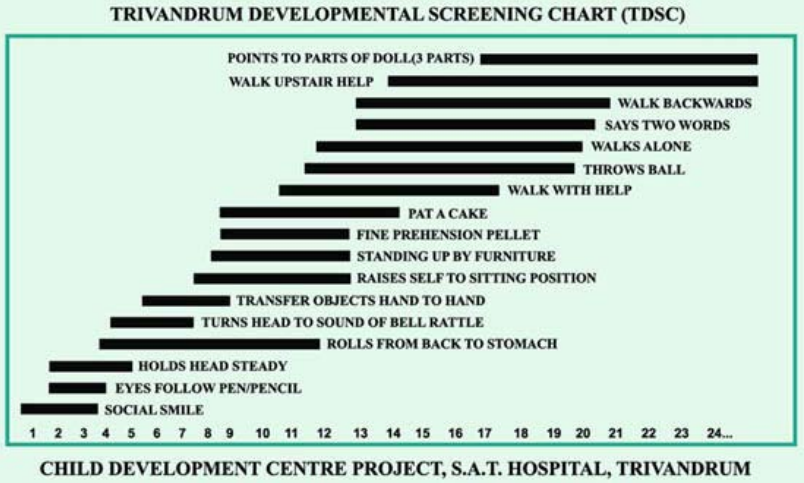

Fig 2 — Trivandrum Developmental Screening Chart

Observation

Odds ratio >1 indicates a significant association with a poor outcome and <1 indicates a significant association towards better or normal outcome. In univariate model, the risk factors associated with poor primary outcome are 5 minutes APGAR < 6, birth weight <1200 g, extensive resuscitation at birth, ventilation for >7 days, maternal hemoglobin <8g/dl, Gestational age <30 week, Sepsis, Encephalopathy, Abnormal Neurological examination at discharge and incomplete or no antenatal steroids received, in order of strength and were found to be statistically significant (Table 1).

Shock, Hypoglycemia, Abnormal Neuro-sonogram and history of previous preterm delivery or primi mother are also inclined towards poor primary outcome but they are statistically insignificant (Table 2).

Babies with low risk had better outcome than those with high risk score. The Chi-square statistic is 6.96 and p-value is <0.008 (<0.05) which is statistically significant (Tables 3 & 4).

Death or major Neuro-developmental Disability (NDD) was seen in 28 (36.3%) babies and minor NDD or normal outcome was seen in 39 (50.6%) babies (Table 5).

Among Major NDD Cerebral Palsy (66.6%) was the most common NDD seen followed by hearing impairment (25%) and in Minor NDD majority of the

Table 1 — *Odds ratio for risk factors associated with poor primary outcome*

Risk Factors	Signifi-cance	Odds ratio	95% CI	
Gestational age ≤30 week	0.0001	9.65	3.088	30.15
Primi/Previous Preterm	0.690	1.26	0.39	4.00
Maternal anemia- Hb <8g%	0.0356	10.36	1.17	91.7
Birth weight <1200g	0.0002	58.7	7.01	491.98
Male	0.659	0.8	0.30	2.13
IUGR	0.605	0.75	0.25	2.2
Multiple gestation	0.054	0.12	0.01	1.03
Resuscitation	0.0001	20.40	5.72	72.64
5 min APGAR <6	0.002	90.7	5.07	1621.00
Ventilation >7 days	0.004	7.76	1.91	31.51
Sepsis	0.039	9.31	1.11	77.67
Hypoglycemia	0.951	1.05	0.21	5.11
Shock	0.059	5.04	0.93	27.20
Incomplete/ No antenatal steroids	0.002	7.00	2.04	23.98
Abnormal Doppler	0.444	0.68	0.25	1.8
Abnormal neuro-sonogram	0.152	2.06	0.76	5.54
Encephalopathy	0.002	9	2.22	36.33
Hyperbilirubinemia	0.659	0.80	0.30	2.13
NEC	0.629	0.45	0.01	11.46
PDA	0.394	0.26	0.01	5.69
Abnormalneurological examination on discharge	0.009	8.76	1.71	44.68

Table 2 — *Risk score of outcome obtained*

Risk Score	Present study		KIMS study	
	Normal Outcome	Abnormal Outcome	Normal Outcome	Abnormal Outcome
Low (1,2)	11 (55%)	9 (45%)	188 (95.5%)	9 (4.5%)
High (3,4,5)	1 (8.3%)	11 (91.6%)	23 (82.2%)	5 (17.8%)
Total	12	20	197	28

Table 3 — *Comparison of different outcome with KIMS study*

Outcome	Present study(n=64)	KIMS study(n=225)
Incidence of Major NDD	17.9%	6.2%
Mean birth weight	1455.9g ± 345.71 gram	1425 ± 376 gram
Mean gestational age	31.7 ± 2.19 week	30.6 ± 2 week
ROP requiring laser	1.5 % δ 30 week	37% - <28 week 9.5% - 29-30 week 5.7% - 31-33 week
Refractive error requiring spectacles	2.9%	3.5%
Squint	7.46%	1.3%

preterm had vision impairment in form of refractive error or squint (41.1%) followed by delayed development (35.29%) (Table 6).

Out of 12 babies having abnormal ATA 8(66.6%) had Major NDD and 4 (33.3%) had Minor NDD. Trivandrum Developmental Screening Chart (TDSC) was delayed in 28 (41.7%) babies of the study population from which 12 (42.8%) had developed Major NDD and 16 (55.1%) had Minor NDD (Table 7).

Table 4 — *Distribution of outcome*

Primary outcome(n = 28) (36.3%)	Major NDD Death	12 (15.5%) 16 (20.7%)
Secondary outcome(n = 39) (50.6%)	Minor NDD Normal	17 (22%) 22 (28.5%)
Lost to follow-up		10 (12.9%)
Total		77

Majority of the babies with abnormal neurological examination had major NDD (81.8%) and none had normal outcome at the end of 1 year follow up.

Discussion

Total 77 babies enrolled in our study over period of 6 months. Out of 77 babies, 13 babies died before discharge (16.8%) and remaining 64 (83.1%) were followed up. Out of 64, 10 babies were lost to follow up. During follow up, 3 babies died out of which 2 died within 3 months because of severe Septicemia which was due to mismanaged feeding. And one baby expired by 8 months of age due to respiratory illness. The remaining 51 were followed up till 1 year of corrected age. In a study by Astbury *et al*[3], it was found that the Neuro-developmental delay also may be under-estimated at 1 year of age. Voss *et al* have concluded that atleast 6 year outcome may be necessary to derive meaningful conclusions[4].

51 babies were followed up from which 12 had major NDD, 17 had minor NDD and 22 had normal outcome. Out of 12 major NDD, 3 babies (25%) had hearing impairment requiring assisted devices and 1 baby (8.3%) had vision impairment (blindness in one eye) and rest 8 babies (66.6%) had Cerebral palsy. 39 babies fell into secondary outcome with 17 of them having minor developmental delay in form of delay in achievement of milestone in 2 or less than 2 domain in development quotient, impairment of hearing not requiring assisted devices and impairment of vision in form of squint or refractory error. 2(11.7%) of the babies had refractory error. 4 babies (23.5%) had impaired hearing but did not require assisted devices and 5 (29.4%) babies had squint.Regular follow up was carried and babies were assessed during each follow

Table 5 — *Distribution of Neurodevelopment Disability*

NDD		Total	Percentage
Major	Cerebral Palsy	8	66.6%
	Hearing Impairment Requiring Assisted Devices	3	25%
	Vision Impairment (Blindness)	1	8.3%
Minor	Delayed Development (2 or<2 Domain Affected)	6	35.29%
	Refractiveerror/Squint	7	41.1%
	Hearing Impairment Not Requiring Assisted Device	4	23.5%

Table 6 — *Abnormal results on Neuro-development parameters*

Parameter	Total	Major NDD	Minor NDD
Abnormal Amiel-Tison Angle(ATA)	12	8 (66.6%)	4 (33.3%)
CDC grading	13	8 (61.5%)	5 (38.4%)
TDSC (delayed)	28	12 (41.3%)	16 (55.1%)
Any delay (vision/hearing)	14	4 (28.5%)	10 (71.4%)

Table 7 — *Neurological examination versus outcome*

Neurological examination at discharge	Survived			Death post discharge	Total
	Major NDD	Minor NDD	Normal		
Normal	3 (6.9%)	15 (34.8%)	22(51.1%)	3(6.9%)	43
Abnormal	9(81.8%)	2(18.1%)	0	0	11
Total	12	17	22	3	54

up for their neuro-development and at 1 year of corrected age on basis of all the parameters used and development quotient deduced the outcome of babies were determined.

5 minute APGAR score <6 has an odds ration 90.7 for predicting death or Major Neuro-developmental delay. In the VON network study[5], the adjusted odds ratio is 2.06 for severe delay.

Abnormal Neuro-sonogram odds ratio was 2.06 and is one of the most consistent poor prognostic indicator in previous similar studies.

In a study by Fazzi *et al*[6], it was found that the sonographic abnormalities correlated more closely with neuromotor delay rather than cognitive delay which was seen in our study also.

Most of the studies from Western World even some decades ago, had a very low incidence of poor neurologic outcome of <20%[7]. But the studies from the developing world are different. In a study from Bangladesh in 2006, the incidence is 68% in <33 weeks of preterm babies.[8]In our study 53.2% babies had some form Neuro-developmental Disability either Major or minor.

Children who present with symptoms of Cerebral Palsy, earliest manifestations is abnormality in muscle tone. The variation in tone can be picked up early by method of evaluation devised by Amiel-Tison and abnormality of tone was measured with Amiel-Tison Angles (ATA). In present study total 12 babies had abnormal ATA out of which 8 went out to develop major NDD in form of Cerebral Palsy.

Though the initial neuromotor status lays the foundation of future cognitive development according to Piagets theory, the correlation may not be accurate.

Infants with mild to moderate abnormalities may improve with time. This is known as transient Neuromotor Dysfunction and in growing brain with plasticity, many infants become normal. The infants with severe early neurologic dysfunction is unlikely to make complete recovery and likely to have worst neurodevelopmental outcome[9].

Conclusion

From this study we concluded that the strongest association with a poor neurological outcome is seen with 5 minute APGAR score <6, birth weight <1200 gram, extensive resuscitation required at birth and Maternal Haemoglobin < 8g/dl. Growth delay was present proving catch up growth is inadequate at 1 year of corrected Gestational age. Long term follow up is needed for much accurate outcome. Parameters like ATA , CDC grading and TDSC chart can help in early recognition of Neuro-developmental disability. Early stratification of neonates with possibility of abnormal outcome can help in early intervention and moving towards an intact survival of high risk neonates. Standardized follow up program should be an integral part of every neonatal unit to improve the outcome of high risk neonates.

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