Original Article (Research paper)

Evaluation of Extended Sick Neonate Score (ESNS) to predict neurodevelopmental outcome at one year of age

Dr. Aanchal Sachdeva[1], Dr. J Shrivastava[2], Dr. N Shrivastava[3], Dr. A Agrawal[4]

[1]Postgraduate resident, Department of Pediatrics, GMC, Bhopal
[2]Professor and Head, Department of Pediatrics, GMC, Bhopal
[3]Assistant Professor, Department of Pediatrics, GMC, Bhopal
[4]Associate Professor, Department of Pediatrics, GMC, Bhopal

Corresponding Author: Dr. J Shrivastava

ABSTRACT

Background: Various scoring systems are extensively applied in neonatal intensive care unit(NICU) to predict the immediate outcome of neonates and ESNS is one of those. None of the study in literature has used ESNS as long term predictor of morbidity in terms of neuro developmental outcome who survived in neonatal period.

Aims and Objectives:

Primary Objective:-. To determine immediate outcome of sick newborn using ESNS.

Secondary Objective:- To assess applicability of ESNS for predicting neuro developmental outcome at one year of age.

Methods: It was a hospital based prospective cohort study conducted over eighteen months in which 220 term neonates admitted were enrolled and the required parameters for ESNS were assessed. Immediate outcome was documented in terms of death, discharge and duration of stay. Neuro-developmental outcome between 12±3 months of age was assessed by The Bayley scales of infant and toddler development (Bayley – 4).

Results: Mortality rate was 48.2% in neonates with ESNS score <13 while only 1.5% in neonates with ESNS score of ≥13. The sensitivity for predicting immediate outcome was 75.8% and specificity of 95.2%. While to predict long term neuro-developmental impairment, 85% cases were developmentally delayed in ≥1 domain in ESNS <13 group while only 6.5% in ESNS ≥13 group. Cut off score of 13 had sensitivity of 95% and specificity of 88%(p <0.001).

Conclusion: ESNS can predict immediate outcome as well as long term neuro-developmental outcome with satisfactory sensitivity and specificity.

Keywords: Extended sick neonate score (ESNS), neuro-developmental impairment, neonatal mortality and morbidity, Bayley 4 scale

1. INTRODUCTION

Neonatal period – is the most vulnerable time for a child's survival. Neonatal interventions are mainly focused on reducing mortality and progressing towards Millennium Development Goal 4 (child survival). Among the survivors of NICU graduates, long term neuro-developmental morbidity has been found to be 37%.[1]Many neonates may survive major insults without any evidence of impairment because of the plasticity of the developing brain,

however in some newborns it is seen that the insults can cause varying degrees of long-term neuro-developmental morbidity[2].

For predicting the severity of illness and immediate outcome of newborns many scoring systems have been in use for many years like[3]: CRIB (Clinical Risk Index For Babies), CRIB-II , SNAP (Score For Neonatal Acute Physiology), SNAP II, SNAPPE(Score for Neonatal Acute Physiology Perinatal Extension), NTISS (National Therapeutic Intervention Scoring System). These are empirically validated illness severity and mortality risk scores for newborn intensive care.[4,5] . SNS (Sick Neonate Score) is also a useful to predict outcome of sick neonates in resource restricted settings[6]. ESNS was devised by Ray S et al[7] ,which is compilation of 9 clinical parameters which include respiratory efforts, heart rate, oxygen saturation(Spo2), blood sugar, blood pressure, axillary temperature, capillary refill time, moro reflex and Downes score.

All these scores can predict the outcome during hospital admission and in terms of mortality. Few studies are done previously using these mortality scores for predicting developmental outcome and one of those was using CRIB therefore present study was conducted to know the applicability of ESNS for predicting immediate as well as neuro-developmental outcome at one year of age by using Bayley 4.

Aims and Objectives

Primary Objective: to determine immediate outcome of sick newborn using ESNS.

Secondary Objective: to assess applicability of ESNS for predicting neuro-developmental outcome at one year of age.

2. MATERIALS AND METHODS

Study design-It was a hospital based prospective cohort study conducted over a period of eighteen months from March 2020 to August 2021 in paediatrics department of tertiary care hospital in Central India and the study was approved by Institutional Ethical Committee.

Participants-All NICU admitted term babies (≥37 weeks) irrespective of their indication of admission constituted the study population. Newborns with fatal congenital anomalies and requiring urgent surgical intervention were excluded from the study. Also neonate who are admitted after 7 days of life are not included as correct assessment of gestational age couldn't be done. Neonates who developed neurological illness or injury after the neonatal period during phase of follow up were also excluded.

Sample size-Sample size was calculated based on sensitivity and specificity of ESNS which was found in previous study–

Sensitivity $N_{se} = \frac{(Z_{1-a/2})^2 \times se \times (1-se)}{(d)^2}$ Specificity $N_{sp} = \frac{(Z_{1-a/2})^2 \times sp \times (1-sp)}{(d)^2}$

Taking value of sensitivity 92.6% and specificity 93.2% at a cut off of 11 in previous study by Ray et al for term cohort by ESNS, sample of 27 subjects with the outcome (died) and 27 without the outcome (survived) will be at least required to detect above sensitivity and specificity with 10 % precision and 95% confidence interval. We enrolled 220 neonates so as to have enough number of subjects remaining for follow up considering attrition.

After taking informed consent eligible neonates were enrolled. Antenatal history including the risk factors was recorded. The details of indication for admission, anthropometry, vital parameters were recorded for all registered neonates. Gestational age was assessed using New Ballard score. On arrival ESNS of all neonates was documented.

Ethical clearance: The approval was obtained from the Institutional Ethical Committee of the Gandhi Medical College, Bhopal (Letter No. 523/MC/IEC/2020; dated 04/01/2020)

Table 1– The Extended Sick Newborn Score System(ESNS)

Parameter	Score 0	Score 1	Score 2
Respiratory effort	Apnea	rate >60 ±retractions	Rate 40-60/min
Heart rate(bpm)	Bradycardia/asystole	>160	100-160
Mean blood pressure	$<5^{th}$ percentile	$5\text{-}50^{th}$	$>50^{th}$
Axillary temperature (degree Celsius)	<36	36.0-36.5	36.5-37.5
Capillary filling time (s)	>5	3-5	<3
Random blood sugar (mg/dl)	<45	45-60	>60
Spo2 (%in room air)	<85	85-92	>92
Moro reflex	Absent	Depressed/exaggerate	Corresponding to gestational age
Modified Downes' score*	>6	2-6	0-2

*modified Downes' score represent a composite score including five parameters (each carrying 0,1,2 points, with minimum score 0 to maximum score 10) i.e. respiratory rate, retraction, grunt, cyanosis, air entry.

Immediate outcome was documented in terms of death, discharge and duration of stay. Treatment given during hospitalization and course of stay was recorded. Long term outcome in terms of neurodevelopment was assessed by the Bayley 4 scale between 12±3 months of age.

The Bayley-4 Scale was used to assess the child's neuro development on follow up. Bayley was applied by certified Bayley person. ESNS was not disclosed/provided at the time of Bayley application. Developmental delay was classified "at risk" if a Bayley-4 score was below 85 (lying less than -2SD) on any of the domain like language, cognitive, or motor scales and as a "delayed" if score was below 70 (lying more than -2SD). Development was assessed in all the five domains that is cognitive, language, motor, socio-emotional, adaptive behavioural. The scores derived from all 5 domains in terms of raw score were converted to scaled/standard scores by the age specific score conversion tables. Summing up of scaled scores was done and recorded in percentile rank table. Using these scores developmental growth was plotted individually for each domain and sub-domain in the graphs provided with Bayley 4 scale. The confidence interval was derived using the plot and interpretation of the growth was done in terms of standard deviation.

Analysis-Data were analyzed and statistically evaluated using SPSS software, version 25 (Chicago II, USA). Quantitative data was expressed in mean, standard deviation while qualitative data were expressed in percentage. ROC (Receiver Operating Characteristic) curve was prepared using ESNS score to predict neuro-developmental outcome and based on Youden index cutoff value was calculated and sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of ESNS score was calculated. p' value less than 0.05 was considered statistically significant. Reporting has been done as per STARD checklist.

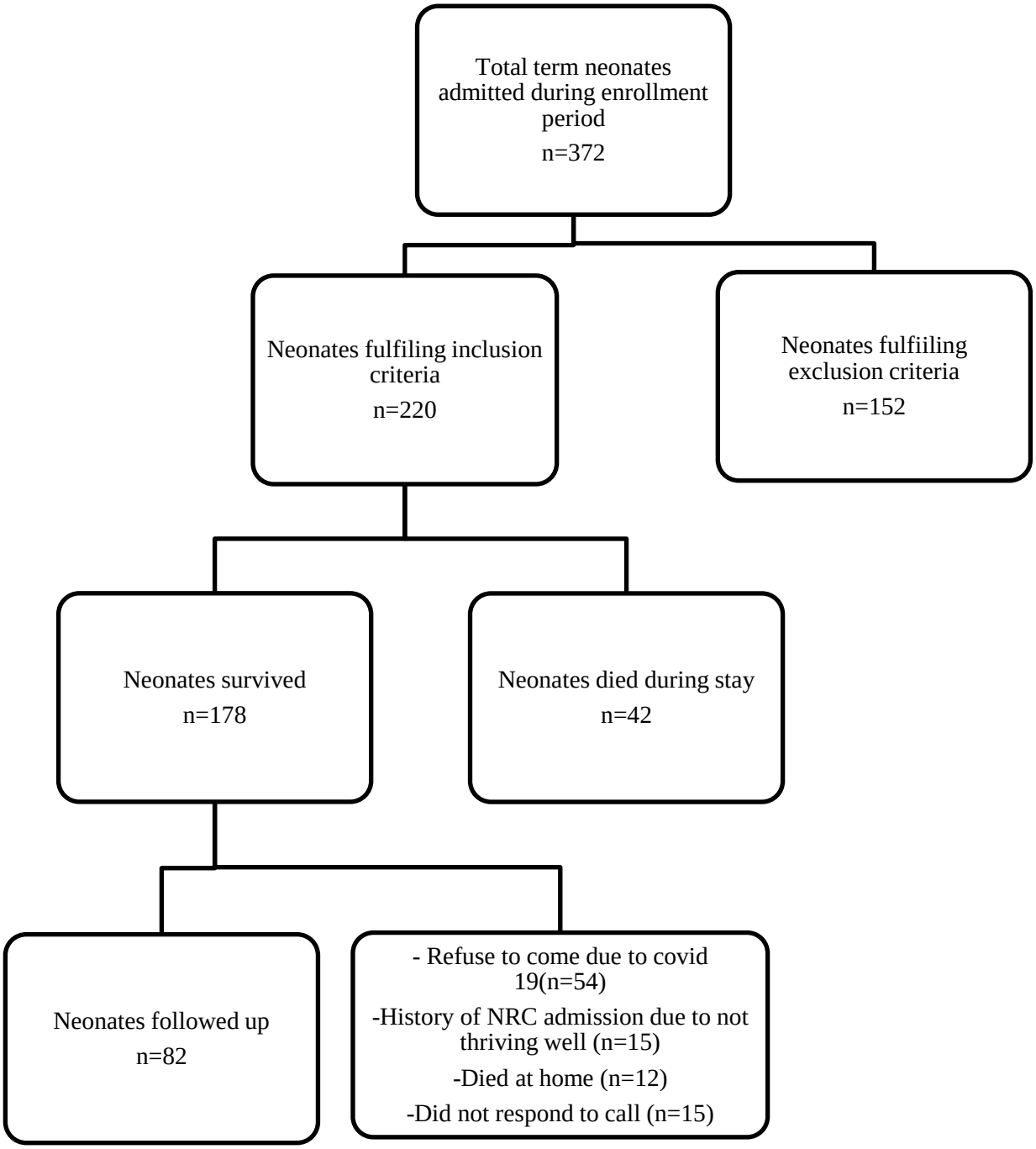

Figure 1- study flow chart

3. OBSERVATION & RESULTS

During the enrolment period of study i.e. from March 2020 to August 2020, among 372 admitted term newborns 220 fulfilled the inclusion criteria and 152 were excluded. Among 220 term newborns enrolled in study most of the newborns belong to age group of <24 hours [n=132 (60%)] followed by 4-7 days [n=45 (20.5%)]. There were 155 male (70.5%) and 65 female (29.5%) newborns in the study. 72 (32.7%) newborn had history of risk factors in pregnancy. Most common maternal risk factor was preeclampsia [n=21 (29.1%)] followed by premature rupture of membrane (>24hours) [n=16 (22.2%)] and others [n=16(22.2%)] which included thyroid disorder and Rh-negative pregnancy. Main indication of admission in NICU was birth asphyxia [92(41.8%)] followed by sepsis [n=44(20%)], respiratory distress [n=43(19.5%)], neonatal hyperbilirubinemia [n=34(15.5%)], shock [n=6(2.7%)] and haemorrhagic disease of newborn [n=1(0.5%)]. Mean ESNS score was found to be 13.16±3.06. There were 137(62.3%) neonates who scored ESNS ≥13 and 83(37.7%) neonates who scored <13.

On determining immediate outcome in 220 newborns, 42(19.09%) newborns died while 178 (80.9%) survived and were discharged. On assessment of ESNS and immediate outcome it was found that 98.5% (n=135 out of 137) newborns who scored ≥13 got discharged and only 1.5% (n=2) died but among neonates who scored <13 only 51.8% (n=43 out of 83) got discharged and 48.2% (n=40) died. Thus mortality rate was 48.2% in neonates with ESNS score <13 as compared to mortality rate of only 1.5% in neonates with ESNS score ≥13. The sensitivity of ESNS for assessing immediate outcome came out to be 75.8% and specificity of 95.2%($p<0.001$).

On comparing duration of hospital stay with ESNS score, score <13 was associated with increased stay (15.61+/-6.77 days) as compared to ESNS score ≥13 (6.33+/- 2.99 days) which is statistically significant ($p<0.001$).

Among 178 survivors, 82 subjects completed the follow up till one year of age since the period of study was affected by peaks of COVID-19 pandemic. In newborns who underwent developmental assessment 74.3% (n=61) were found to be developmentally normal in all the 5 domains while 23.2% (n=19) were found to have developmental delay in one or more domains.

Figure 2 is showing ROC curve which was prepared using ESNS score to predict neuro developmental outcome and based on Youden index cutoff value was calculated and sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of ESNS score was calculated.

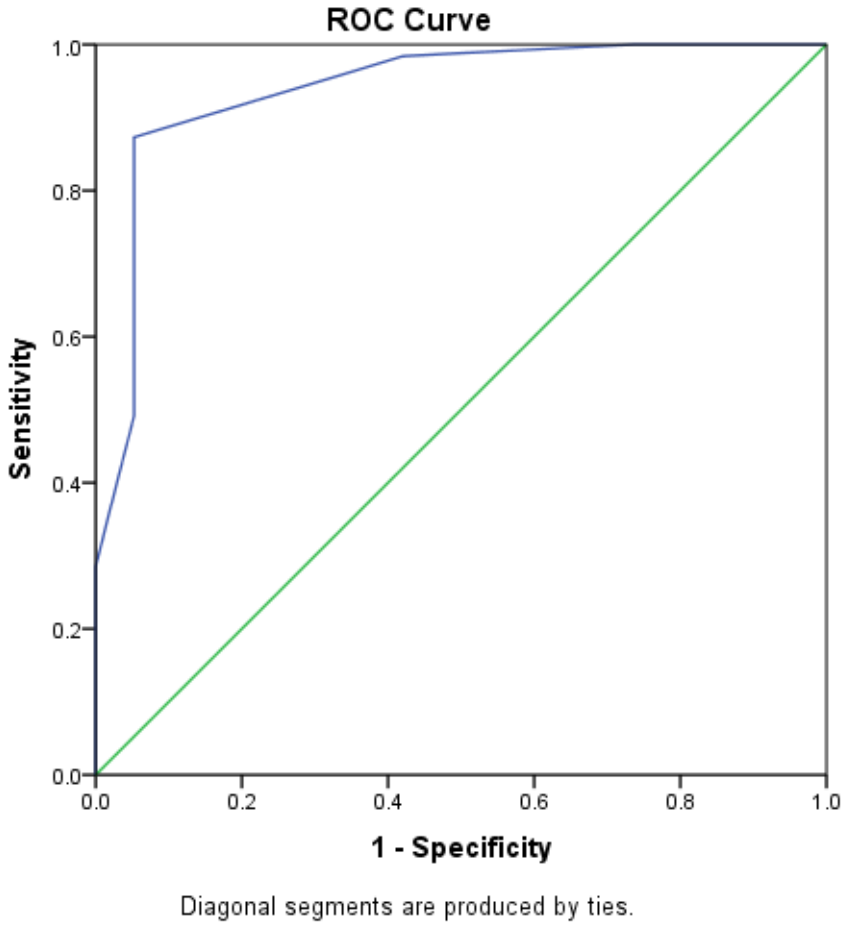

Figure 2: ROC Curve analysis using ESNS score to predict neuro-developmental impairment

Table 2 represent diagnostic performance of ESNS score to predict neuro developmental impairment in different domains. Using ROC curve the best cut off value was calculated to be score of 13 which gives 94.7% sensitivity, 87.3% specificity, 69.23% PPV and 98.21% NPV to predict cognitive, language and motor impairment. While in the domains of social emotional and adaptive behavior impairment with same cut off value of 13, sensitivity was 100% for both the domains, specificity was 91.8% & 88.89%, PPV was 80.77% & 73.08% respectively and NPV was 100% for both.

Table 2: Diagnostic performance of ESNS score to predict neuro-developmental impairment

	cognitive impairment	**language impairment**	**motor impairment**	**social emotional impairment**	**adaptive behavior impairment**
AUC	0.93	0.93	0.96	0.98	0.98
95% CI	0.87-1.0	0.87-1.00	0.92-0.99	0.96-1.0	0.96-1.0
p value	<0.001	<0.001	<0.001	<0.001	<0.001
Cut off value	13	13	13	13	13

Sensitivity	94.7%	94.7%	94.7%	100%	100%
Specificity	87.3%	87.3%	87.3%	91.8%	88.89%
Positive predictive value	69.23%	69.23%	69.23%	80.77%	73.08%
Negative predictive value	98.21%	98.21%	98.21%	100.0%	100.0%
Accuracy	89.02%	89.02%	89.02%	93.9%	91.46%

Among followed up neonates 75.6%(n=62) belonged to ≥13 ESNS group and 24.3% (n=20) belonged to ESNS <13.Among < 13 ESNS group, on assessment of cognitive,language and motor domain 75%(n=15) were found to have developmental delay & 25% (n=5) were developmentally normal while in socio-emotional and adaptive behavioural domain 85% (n=17)were found to have developmental delay & 15% (n=3) were developmentally normal . Newborns with ESNS ≥13 on follow up showed that 93.5 % (n=58) were neuro-developmentally normal in cognitive, motor, language and social-emotional domain while 6.5%(n=4) had developmental delay in one or more domain with p value of <0.001. When the same group of ≥13 ESNS score was assessed for adaptive behavioural domain, 96.8% (n=60) were found developmentally normal and 3.2% (n=2) were found delayed. This association was found statistically significant (p<0.001).

Table 3: Association of ESNS score with neuro-developmental outcome

	<13		**≥13**		**p value**
	No.	**%**	**No.**	**%**	
Cognitive delay					
Delay -nt (<-2SD)	5	25.0	58	93.5	<0.001
Delay +nt (>-2SD)	15	75.0	4	6.5	
Language delay					
Delay -nt (<-2SD)	5	25.0	58	93.5	<0.001
Delay +nt (>-2SD)	15	75.0	4	6.5	
Motor delay					
Delay -nt (<-2SD)	5	25.0	58	93.5	<0.001
Delay +nt (>-2SD)	15	75.0	4	6.5	
Social emotional impairment					
Delay -nt (<-2SD)	3	15.0	58	93.5	<0.001
Delay +nt (>-2SD)	17	85.0	4	6.5	

Adaptive behavior impairment					
Delay -nt (<-2SD)	3	15.0	60	96.8	<0.001
Delay +nt (>-2SD)	17	85.0	2	3.2	

4. DISCUSSION

In the present study ESNS is used to predict immediate outcome and long term morbidity of "term newborns" , where cut off was used as 13 which is found to have sensitivity of 95% and specificity of 88% while previous study done by Ray S et al on ESNS for Clinical Assessment and Mortality Prediction in Sick Newborns referred to Tertiary Care center showed ESNS of ≤11 had the best sensitivity of 85.9% and specificity of 89.8%. In their study ESNS was able to predict in- hospital mortality outcome for both the preterm and term infants(7).

In the present study ESNS was more in those who survived. It was evident that 98.5% (n=135) out of 137 of those who scored >13 got discharged and only 1.5% (n=2) died but in comparing with those who scored <13 only 51.8% (n=43) got discharged and 48.2%(n=40) died and p value was <0.001 for each observation. In comparing this with the study done by Sundaram et al., the median SNAP II was significantly higher in babies who died versus those who survived [median (IQR): 43 (36-53.5) vs 18 (16-37), p<0.001](8).

Similar study done by K. P. Mansoor et al, deduced MSNS(modified sick neonatal score) with cutoff score of ≤10 with 80% sensitivity and 88.8% specificity in predicting mortality. In their study expired newborns had statistically significant frequency of lower scores across each of the parameters (9). Their study was centered only for mortality prediction.

In present study ESNS <13 was associated with increased duration of hospital stay (15.61+/- 6.77 days) as compared to ESNS score ≥13 (6.33+/- 2.99 days) which is statistically significant (p<0.001). In terms of death and discharge also we have observed that 48.2 % patients died in <13 ESNS group as compared to only 1.5% in ≥13 ESNS group.

Similarly from previous studies done by Richard et al CRIB score, gestation, and birth weight were significant univariate predictors of hospital mortality (P<0.0001). When compared with gestation and birth weight, CRIB was good in predicting mortality and predicting morbidity, but was less good in predicting length of stay and it did not follow that CRIB can predict neuro-developmental outcome(10). This study differs from the present study in terms of use of different variables.

When it came to using these mortality scores for predicting neuro disability Fowlie et al combined CRIB with cranial ultrasonography in 297 infants from cohort surviving beyond 72 hours. CRIB scoring was performed at 72 hours, with ultrasound appearances from around 72 hours. A CRIB score greater than 4 with a grade 3 or 4 intraventricular haemorrhage was predictive of severe disability (11). Calame et al reported that the prevalence of developmental delay is found to be quite high in SNCU graduates (31.6%). (12). Similarly study by Lefebvre et al used nursery neurobiologic risk score(NBRS) to predict developmental outcome at 18 months in very premature infants. 121 infants were followed up at 18 months of age and NBRS score was correlated to developmental quotient(13). In the present study ESNS has measured the morbidity in terms of neuro developmental delay by using gold standard test which is also confirmatory for development i.e. Bayley 4 scale.

In present study for neuro developmental assessment on 82 participants, 76.8%(n=63) participants were developmentally normal and among delay, 23% (n=19) participants were delayed in all cognitive, language, motor, socio-emotional and adaptive behavioural domain. In comparison with study done by Logan et al using SNAP II, higher score was associated

with increased risk of neurological impairment in preterm neonates when assessed at 10 year of age (14).
In this study, ESNS of <13 had the best sensitivity 95% and best specificity 88% in terms of predicting neuro-developmental morbidity.
As among <13 ESNS group, when assessed for cognitive, language and motor domain 75% (n=15) were found delayed & 25% (n=5) were developmentally normal. In socio-emotional and adaptive behavioural domain 85% (n=17) were found delayed & 15% (n=3) were developmentally normal. The p value (<0.001) was significant for each observation when comparing the outcome with gold standard tool i.e., Bayley 4 scale.

Study limitations – Less number of follow up because of constraints due to COVID-19 pandemic.

5. CONCLUSION & RECOMMENDATIONS

ESNS can be applied rapidly and reliably to newborns in resource constrained settings to predict immediate outcome. Not only ESNS is highly sensitive and specific score in predicting immediate outcome, its sensitivity and specificity for predicting long term neuro developmental outcome in term neonates is remarkable.

Acknowledgement
The authors are grateful for all the participants of the study

Declaration of Conflicting Interests
The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding
The authors received no financial support for the research, authorship, and/or publication of this article.

Conflict of interest: None stated.

6. REFERENCES:

[1] Mwaniki MK, Atieno M, Lawn JE, Newton CR. Long-term neuro-developmental outcomes after intrauterine and neonatal insults: a systematic review. Lancet. 2012 Feb 4;379(9814):445-52
[2] WHO. The global burden of disease: a comprehensive assessment of mortality and disability from diseases, injuries and risk factors in 1990 and projected to 2020. Cambridge, MA: Harvard University Press, 2001
[3] Fleisher BE, Murthy L, Lee S, Constantinou JC, Benitz WE, Stevenson DK. Neonatal severity of illness scoring systems: a comparison. Clin Pediatr (Phila). 1997 Apr;36(4):223-7.
[4] Richardson DK, Corcoran JD, Escobar GJ, Lee SK. SNAP II and SNAPPE II: Simplified newborn illness severity and mortality risk scores J Pediatr. 2001;138(1):92-100.
[5] Rachuri S, Paul S, Jaidev MD. SNAPPE II score: predictor of mortality in NICU. Int J Contemp Pediatr. 2019;6:422-6.

[6] Rathod D. Adhisivam B, Bhat BV. Sick Neonate Score - a simple clinical score for predicting mortality of sick neonates in predicting mortality of sick neonates in resource limited settings. Indian J Pediatr. 2016;83;103-6.
[7] Ray S, Mondal R, Chatterjee K, Samanta M, Hazra A, Sabui TK. Extended Sick Neonate Score (ESNS) for Clinical Assessment and Mortality Prediction in Sick Newborns referred to Tertiary Care. Indian Pediatr. 2019 Feb 15;56(2):130-133.
[8] Sundaram V, Dutta S, Ahluwalia J, Narang A. Score for neonatal acute physiology II predicts mortality and persistent organ dysfunction in neonates with severe septicemia. Indian Pediatr. 2009 Sep;46(9):775-80. Epub 2009 Apr 1. PMID: 19430085.
[9] Modified Sick Neonatal Score (MSNS): A Novel Neonatal Disease Severity Scoring System for Resource-Limited Settings K. P. Mansoor,1 S. R. Ravikiran , 1 Vaman Kulkarni , 2 Kiran Baliga,1 Suchetha Rao , 1 Kamalakshi G. Bhat,1 B. Shantharam Baliga,1 and Nutan Kamath.
[10] Use of the CRIB (clinical risk index for babies) score in prediction of neonatal mortality and morbidity Richard H B de Courcy-Wheeler, Charles D A Wolfe, Anthony Fitzgerald, Maxine Spencer, Jonathan D S Goodman, Harold R Gamsu.
[11] Fowlie PW, Tarnow-Mordi WO, Gould CR, *et al.* Predicting outcome in very low birthweight infants using an objective measure of illness severity and cranial ultrasound scanning. *Arch Dis Child Fetal Neonatal Ed*1998;**78**:F175–8.
[12] Calame A, Reymond-Goni I, Maherzi M, Roulet M, Marchand C, Prod'hom LS. Psychological and neuro-developmental outcome of high risk newborn infants Helv Paediatr Acta. 1976;31:287-97
[13] Lefebvre F , Gregoire MC, Dubois J, et al. Nursery Neurobiologic Risk Score and outcome at 18 months. Acta Paediatr1998;87:751–7.
[14] Logan JW, Dammann O, Allred EN, et al. Early postnatal illness severity scores predict neurodevelopmental impairments at 10 years of age in children born extremely preterm. J Perinatol. 2017;37(5):606-614. doi:10.1038/jp.2016.242