Neuromotor and Neurosensory Impairment among High Risk Infants at One Year of Age – Risk Factor Analysis

Sugindar Vinoth Rajaretnam[1], Vedapriya Abimannan[2], Karthikeyan Kadirvel[3*], Padmanaban Srinivasan[4]

[1]*Junior Resident, Department of Pediatrics, Mahatma Gandhi Medical College and Research Institute, Sri Balaji Vidyapeeth (Deemed to be University), Pondicherry, India. Email: radnigus@gmail.com*
[2]*Assistant Professor, Department of Pediatrics, Mahatma Gandhi Medical College and Research Institute, Sri Balaji Vidyapeeth (Deemed to be University), Pondicherry, India. Email: avedapriyadr@gmail.com*
[3]*Professor, Department of Pediatrics, Mahatma Gandhi Medical College and Research Institute, Sri Balaji Vidyapeeth (Deemed to be University), Pondicherry, India. Email: drkk3179@gmail.com*
[4]*Scientist B, National Institute of Research in Tuberculosis, ICMR, Chennai, Tamil Nadu, India. Email: padmanaban.s.@nirt.res.in Padmanaban.s@icmr.gov.in*

KEYWORDS
developmental delay, infant, newborn; neurodevelopmental disorders, vision disorders

ABSTRACT
Background: Improvement in the quality of perinatal care in the last few decades has led on to improve newborn survival. Sick neonates who have survived are exposed to high risk factors in the prenatal period and are termed as high risk infants (HRIn). This study aimed at determining the proportion of neuromotor and neurosensory impairments among HRIn.
Methods: This prospective observational study was conducted in a tertiary care centre in South India between January 2020 and December 2021. Study population comprised of intramural high risk infants fulfilling the criteria. At discharge infants were stratified as mild, moderate or severe risk for developing neurodevelopmental disorders and follow up plan was given. The subjects were assessed at 4, 6, 8 and 12 month for impairments.
Results: Total 138 infants were enrolled and 88 completed follow up. Lost for follow up was 36.2%. The impairments detected with respect to motor and vision were 12.5% and 1.1% respectively. Sepsis, seizures, birth asphyxia and preterm were robust prognostic factors for neuromotor impairment. Risk of tone abnormality was 13 times higher in infants who had sepsis. At risk for developmental delay was noticed in 11.4% of the study for which significant association was with prematurity, sepsis and birth asphyxia.
Discussion: HRIn are susceptible for neurodevelopmental impairments. Hence early identification and enrolment in intervention programs will ensure favorable outcomes.

1. Background

India has achieved major progress over the last decades in improving the care provided to the infant and young children. For the past two decades India has witnessed a steady improvement in the quality of perinatal care in India. The current Infant mortality rate (IMR) is 35.2 per 1000 live births as per National Family Health Survey 5 (NFHS 5) as against 40.7 (NFHS 4 data)[1]. The neonatal care has improved a lot towards sick term, very low birth weight and extreme low birth weight babies. Technological advances in neonatal care and the concern of pediatricians have contributed to increased survival of these newborns[2]. The survivors are termed as high-risk infants (HRIn) since they are exposed to perinatal / neonatal risk factors and are at increased risk of developing neurodevelopmental disorders (NDD)[3]. NDDs are disabilities in the functioning of the brain that affect a child's behavior, memory or ability to learn and compromise the development and attainment of full social and economic potential at individual, family, community, and country levels[4]. NDDs include vision impairment (VI), epilepsy (Epi), neuromotor impairments including cerebral palsy (NMI-CP), hearing impairment (HI), speech and language disorders, autism spectrum disorders (ASDs), intellectual disability (ID), attention deficit hyperactivity disorder (ADHD), and learning disorders (LDs).Almost one in eight children aged 2-9 years living in India may have at least one NDD, according to prevalence estimates published in *PLOS Medicine* which address the lack of robust evidence regarding burden and risk factors for NDD in India[5]. During infancy changes in neurological (neuromotor and neurosensory) function are closely related to the maturation of nervous system. These changes also imply the presence or absence of brain damage. Hence early detection of neuromotor impairment and neurosensory impairment is mandatory to start early intervention. This study aimed at determining the proportion of neuromotor impairment and neurosensory impairment (hearing impairment and vision impairment) among the high-risk neonates at one year of age.

2. Methods

This prospective observational study was conducted in a tertiary care centre of South India between January 2020 and December 2021. The study population included all intramural high-risk neonates getting admitted and discharged from intensive care unit (NICU). Subjects were recruited in the first eight months of the study period, enabling the follow up at one year of age. Gestational age at birth was estimated either by last menstrual period / first trimester ultrasound dating / gestational age assessment by Expanded New Ballard score. Babies with major congenital malformations, shifted to other hospitals due to any reason and expired during hospital stay / follow up period were excluded. Neonates fulfilling the criteria were included in the study after getting informed written consent from one of the parents. Study was approved by institutional ethical committee (MGMCRI/Res/01/ 2019/100/IHEC/028). Demographic data such as delivery details, gestational age, birth weight, birth complication, reason for NICU admission, duration of stay and nature of illness, treatment were collected. Sepsis in the present study is defined as clinically diagnosed or confirmed by positive culture in a typically sterile bodily fluid**.** At discharge, risk stratification card (based on NNF guidelines[2]). With follow-up plan was given to each infant. After risk stratification the subjects were divided into three groups. Group1, 2 and 3 comprised of high-risk infants who were at mild, moderate and severe risk of developing NDD respectively. Infants were followed up at 4, 6, 8 and 12 months of age. Infants born preterm were assessed at their corrected age. For adherence to follow up, phone numbers were obtained from both the parent and one more family member.

During follow up, the subjects were subjected for neuromotor (NM) and neurosensory (NS) assessment. NM assessment was done by estimation of passive tone with respect to Amiel Tison (AT) angles6. An infant was assessed in a quiet room when she was in a post fed state, when she is not irritable or sick. The AT angles were measured by Goniometer. Tone was considered normal if AT angles were normal for that particular age. Tests are scheduled at 4, 6, 8 and 12 months. NS assessment consisted of hearing and vision assessment. Hearing assessment was done by Brainstem Evoked Response Action potentials (BERA) between 3 and 6 months of age. Vision assessment for term and post term babies - visual acuity at one year of age; for preterm babies as per the institution protocol follow up for assessment of retinopathy of prematurity (ROP) and visual acuity at one year of corrected age were done. The acuity of vision was derived after evaluating fixation behavior of the child by CSM (location of Corneal light, Steadiness of fixation on examiners light, ability of patient to Maintain alignment) method[6,7,8,9,10]. Development screening was done by Trivandrum Development Screening Chart (TDSC)[11]. Infants who completed all four follow-up visits with the above assessments were included for analysis.

The outcomes measured were neuromotor impairment (NMI) as defined by tone abnormalities (hypotonia when AT angles are more for that particular age and hypertonia when AT angles are less for that particular age); hearing impairment (HI) by BERA results and hearing loss was graded by Goodman's classification[12]; vision impairment as per CSM method[8,9,10,13]; at risk for developmental delay was defined if TDSC fail[11].

Data was entered in MS Excel, coding, refining and recording done. Analysis was done in SPSS version 14. Descriptive statistics were expressed as mean and standard deviation and by proportion for categorical variables. Univariate analysis was performed to identify the correlation of risk factors to NMI, NSI and developmental delay. Significance of all the risk factors with the neurodevelopmental impairments was calculated with multivariate analysis. Chi square test was used to analyze between the three risk groups (mild, moderate and severe) and outcome measures (NMI and NSI). A p value of 0.05was considered significant.

3. Results

A total of 138 neonates out of 185 neonates fulfilling the criteria were enrolled in the study after obtaining valid consent, of which 88 babies were successfully followed up at 4, 6, 8 and 12 months of their corrected gestational age. Lost for follow up was mainly due to the COVID 19 pandemic which resulted in parental concerns in bringing the infants to hospital and travel restrictions in between districts announced by the Government. The study population of the present study comprises predominantly of infants born at term (64%). Late and moderate preterm infants contributed 21% and 15% of the study subjects respectively. On risk stratification 27, 14 & 16 infants had mild, moderate, severe risk for NDD's. Passive tone assessment at 4,8,12 months of age, vision and hearing assessment at one year of age was done (Table 1). Only 88 babies could finish the follow up. Hence these 88 babies were included for analysis. 50 babies (36.2%) babies were lost for follow up. At sixth month we observed that there was decrease in neuromotor impairment. Hypotonia which was detected at 4th month,

normalized at 6th month. This transient tone abnormality was noted in 4 infants. Three infants at 6th month were at risk for developmental delay. The findings during the 6th month persisted at 8th month. Same 11 infants with hypertonia and 3 infants at risk for developmental delay remained with impairment at 8th month. Of the 11 infants who had hypertonia at one year of age, 10 infants were preterm, and one infant was born at term gestation. Passive tone assessment in preterm infants revealed hypertonia in both upper and lower extremities in 7 infants and only in lower extremities in 3 infants. Infant born at term had hypertonia in both upper and lower extremities. Vision impairment was noticed in one baby. This infant born early preterm had stage 3 ROP, treated with Bevacizumab and underwent LASER correction was found to have visual impairment according to CSM method (CSUM 6/36-6/60). The child was prescribed corrective glasses. While at the same time 11 infants had persistent hypertonia, there was increase inthe number of infants who were at risk for developmental delay at 1 year (from three toten). Out of these 10 infants three had associated hypertonia.

Table 1: Neurodevelopmental impairment among study population at 4, 6, &, 12 months of age

NEURODEVELOPMENTAL IMPAIRMENT		4 MONTHS	6 MONTHS	8 MONTHS	12 MONTHS
NEUROMOTOR IMPAIRMENT	HYPOTONIA	4(4.5%)	-	-	-
	HYPERTONIA	11(12.5%)	11(12.5%)	11(12.5%)	11(12.5%)
HEARING IMPAIRMENT		-	-	-	-
VISION IMPAIRMENT					1 (1.2%)
AT RISK FOR DEVELOPMENTAL DELAY		2	3	3	10

Though significant proportion of babies of mothers with hypertension who had ART was found to have tone abnormality, the univariate regression analysis did not reveal any statistical significance. The presence of neuromotor impairment at 1 year had significant association with neonatal risk factors such as sepsis, seizure, birth asphyxia, prematurity (Table 2 & 3). Sepsis (odds ratio 13.1; 95% CI 1.02-169.5), Seizures (odds ratio 3.6; 95% CI 0.43- 30.5), birth asphyxia (odds ratio 3.4; 95% CI 0.22-51.8), preterm (odds ratio 2.2; 95% CI 0.09-50.13) were associated with increased risk of neuromotor impairment. Sepsis emerged as an important independent associated factor for neuromotor impairment. Investigation of neonatal risk factors associated with at risk for developmental delay identified sepsis, birth asphyxia, preterm, seizures and meningitis as the preceding risk factors. A total of 10 babies were at risk for developmental delay of which 9 babies were preterm and 1 was born at term gestation. This term was born at 38 weeks of gestation who had early onset sepsis (Klebsiella pneumoniae) was treated with IV Piperacillin-Tazobactam) for 14 days. In the above table it was evident that out of 17 babies who had severe risk for NDD, 5 (29.4%) babies had NMI. There was a proportionate increase in the tone impairment as the risk advances (Table 4). However, this is not statistically significant. Proportion of at risk for developmental delay was 12%, 7%, 23.5% for mild, moderate and severe risk for NDD infants. This was not statistically significant.

Table 2: Association between abnormal tone and risk factors at one year of age

S.NO	RISK FACTORS	ABNORMAL TONE AT 1 YEAR OF AGE N (%)		p value*
		YES	NO	
1	ANEAMIA	0 (0%)	11 (100%)	0.505
2	ART€	3 (27.3%)	8 (72.7%)	0.076
3	HYPOTHYRIODISM	0 (0%)	11 (100%)	0.159
4	TWIN GESTATION	2 (18.2%)	9 (81.8%)	0.352
5	HYPERTENSION	3 (27.3%)	8 (72.7%)	0.212
6	MATERNAL DM	1 (9.1%)	10 (90.9%)	0.318
7	PRETERM	10 (91%)	1 (9%)	0.000
8	JAUNDICE	3 (27.3%)	8 (72.7%)	0.555
9	HYPOGLYCEMIA	0 (0%)	11 (100%)	0.180
10	RESPIRATORY DISTRESS	5 (45.5%)	6 (54.5%)	0.346
11	SEPSIS	10 (91%)	1 (9%)	0.000
12	SEIZURES	9 (81.8%)	2 (18.2%)	0.000
13	ELECTROLYTE DISTRUBANCES	1 (9.1%)	10 (90.9%)	1.00
14	PNEUMONIA	1 (9.1%)	10 (90.9%)	0.715
15	MENINIGITIS	1 (9.1%)	10 (90.9%)	0.267

16	ASPHYXIA	9 (81.8%)	2 (18.2%)	0.000

*Univariate regression analysis; (p value <0.05 is significant)

€ ART – Artificial Reproduction Technique

Table 3: Risk factor Vs neuromotor impairment (by multivariate analysis)

VARIABLES	ODDS RATIO	95 % CI	p VALUE
SEPSIS	13.1	1.02 to 169.5	0.04
SEIZURES	3.6	0.43 to 30.5	0.23
ASPHYXIA	3.4	0.22 to 51.8	0.3
PRETERM	2.2	0.09 to 50.13	0.6

Table 4: Neuromotor impairment Vs risk for neurodevelopmental disability at one year of age

RISK STRATIFICATION FOR NDD	PERCENTAGE OF THE STUDY POPULATION HAVING NEUROMOTOR IMPAIRMENT n (%)			*p VALUE
	MILD n=27	MODERATE n=44	SEVERE n=17	
YES	2 (7.4%)	4 (9%)	5 (29.4%)	0.065
NO	25 (92.6%)	40 (91%)	12 (70.6%)	

*Chi square test; p value <0.05 significant

4. Discussion

The current study aimed to estimate the proportion of neuromotor and neurosensory impairment among the high-risk infants discharged from intensive care. 12.5% of the study population had tone abnormalities. Observations from similar studies have shown prevalence ranging from 2%- 40.7%[15,16,22,25,26,30]. Chaudhari et al., assessed tone using Amiel Tison angles among 190 high risk neonates at 3, 6, 9, 12 months of their age and observed that transient tone abnormality was found in 35.2% of the high risk population who were discharged from level IINICU. Tone abnormality started at 6 months and gradually resolved at 9th month and12th month21. Ten infants (5.2%) had persistent tone abnormality at 12th month of age. Similarly in the current study transient tone abnormality (hypotonia) was noticed in 4 babies and started resolving by around 6 months. There was persistence of tone abnormalities in 11 infants noted at 1 year of age. Another similar study used Amiel Tison angles to assess neuromotor status by trained neonatologist among 4030 infants and they found 355 infants had neurological abnormality at 2 years of age[13]. In the present study we observed 11 infants (10 preterm infant and 1 term infant) having neuromotor impairment at one year of age. A study among 2098 very low birth weight infants born between 23-32 weeks of gestation analyzed their neurodevelopmental outcome at 18-24 months of their corrected age using Bayley scale of infant development. This study revealed motor impairment in 16.5% infants[14]. In the present study we didn't notice tone abnormality in the very low birth weight infant. Twenty-eight extremely preterm infants were assessed using baileys scales of infant and toddler development and 2 had neuromotor impairment[15]. A prospective cohort study conducted among 194 very low birth weight and preterm infants, 40.7% had neuromotor impairment at 12 months of age. Nagamani et al., conducted a study among 182 infants with a diagnosis of ROP and found that 23% of the infants with ROP had neuromotor delay[16].In our study we had an infant with stage 3 bilateral ROP having visual impairment but neuromotor impairment was not observed in that infant at one year of corrected age.

Vision impairment was noticed in 1.1% of the study population. In the present study population, we had a very preterm neonate who required hyperbaric oxygen requirement developed ROP. On follow up, the infant had visual impairment. This implies that extreme preterm infants just diagnosed with ROP may later be diagnosed with visual problems. The results of few similar studies have also revealed that visual impairment can be present in babies who had undergone treatment for ROP[7,8,9,10]. Nagamani et al., demonstrated in 52.9% of his study population had visual impairment[16]. Hirvonen et al., commented that as the gestational age advances, decrease in trend of occurrence of vision and hearing defects were noticed. In this analysis, intracranial haemorrhage and convulsions were the major factors associated increased risk of sensory impairments[17]. Gogate et al., stated that development of retinopathy of prematurity is based on number of risk factors such as low birth weight gestational age and use of hyperbaric oxygen. ROP is a preventable cause of blindness which contributes to 15% of blindness in developed countries and 60% in middle income countries like India18.

Parab et al., conducted a study in 8192 babies which included high risk and normal infants and found that 11

and 18 normal and high risk infants having hearing impairment is confirmed by ABR19. Another study conducted among 100 high risk infants showed prevalence of 7% having unilateral hearing loss and 8% having bilateral hearing loss20. Study conducted among 51 preterm infants, out of 51 preterm and very low birthweight infants had cerebral palsy, 5 with a severe form, 3 moderate and 4 mild form of cerebral palsy. 4 infants with CP and 2 infants without CP had hearing impairment21. Hearing impairment was not documented in the present study. 11.4% of the high risk infants were at risk for developmental delay. Gasparini et al., conducted a study among 812 term and preterm infants and found that language delay was found in 11 and 2 of term and preterm infants22. A study conducted among 152 infants with a diagnosis of ROP, 104 infants had neurodevelopmental delay16. Wei et al., conducted a cross sectional survey in China among children less than 3 years and found that 11.5% had developmental delay23. Kato et al., in the study group comprising of infants born <28 weeks of gestation, the motor development quotient was found to be significantly lower when compared to infant born >28 weeks. A statistically significant difference in the same aspect was noticed between SGA and AGA infants24.The infants in the present study were screened for developmental delay with TDSC which is a simple screening tool. This is not a tool for developmental assessment. This tool cannot identify the delay in specific domains. Comparative studies have used tools for developmental assessment. Hence delay in specific domains were identified in those studies.

The association between risk factors and motor impairment was analysed by univariate analysis which revealed significant correlation for prematurity, neonatal sepsis, neonatal seizures and birth asphyxia. Multivariate regression analysis showed neonatal sepsis as an important risk factor. Risk of infants having tone abnormality is 13 times higher in infants who had neonatal sepsis as compared to other risk factors. Similar to our finding, Ferreira et al., observed that children with sepsis had four times more risk of having neuromotor impairment25. In contrast to our observation, study conducted by Shim et al among 2098 infants did not show any significant association between sepsis and neuromotor delay26. In an observational study that included cohort of 6093 infants, prematurity and very low birth weight were the significant risk factors associated with development of CP27.

Johnson et al., after following 638 late and moderate preterm infants found that these infants had twice the risk of developing neurodevelopmental delay28. In another study 812 individuals were followed from 1977 to 2007 for neurodisabilities and found that asphyxia, low birth weight, preterm had significant association with neurodevelopmental impairment22. Systematic and meta-analysis done by Cai et al., provided an updated literature on long term neurodevelopmental impact of neonatal sepsis in very preterm infants. There was a statistically significant association between sepsis and neurodevelopmental impairment. However, there existed heterogeneity between the selected studies. Most of the studies assessed the neurodevelopmental impairment in infants for less than 2 years and 5 studies examined outcomes beyond 5 years of age. Only out of 23, five studieshave reported blinding of outcome assessors29. Results of the present study revealed prematurity, sepsis, birth asphyxia, seizures and meningitis were significantly associated with at risk for developmental delay. Risk stratification for susceptibility of developing NDDs is unique for the present study. Published data is not available in this respect; hence comparison could not be done. As the risk category advanced from mild to severe, proportionate increase in tone abnormality was noticed. Hence, we reiterate the importance of follow up and early intervention of high risk infants. The strengths of this research include longitudinal study with prospectively collected data; risk stratification for neurodevelopmental disorders was done according to National Neonatology forum of India risk stratification for high risk neonate guidelines; tone, vision and hearing were assessed by valid tools and tested by Specialists in the specific areas; risk factors were analysed by univariate and multivariate logistic regression for association with either neuromotor impairment/developmental delay. There are certain limitations. Developmental delay was screened. Assessment tools were not administered and hence delay in specific domain could not be assessed. Lost for follow up was 36.2% of study population (mainly due to current COVID 19 pandemic and its reason).

5. Conclusion

This study aimed at determining the proportion of NMI, NSI among the HRIN at one year of age. The impairments detected with respect to motor and vision were 12.5% and 1.1% respectively. Sepsis, seizures, birth asphyxia and preterm were robust prognostic factors for neuromotor impairment. Risk of tone abnormality is 13 times higher in infants who had sepsis. At risk for developmental delay was noticed in 11.4% of the study population. Prematurity, sepsis, birth asphyxia, seizures and meningitis were significantly associated with at risk for developmental delay. HRIN are susceptible for neuromotor and neurosensory impairments. Hence early

identification and enrolment in intervention programs will ensure favourable neurodevelopmental outcomes. The threshold for referral of high-risk newborn to Specialists should be higher for early detection of sensory impairments. Consistent obstetric perinatal and neonatal management combined with optimization of follow up care plan as per risk stratification should be made. However, individualization of the follow up protocol should also be considered.

Conflict of interest:

None.

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None.

References

[1] National Family Health Survey (NFHS-5) [Internet]. [cited 2022 Jan 30]. Available from: http://rchiips.org/nfhs/factsheet_
NFHS-5.shtml

[2] AnandPandit, KanyaMukhopadhyay, PradeepSuryawanshi, MKC Nair, S Sitaraman, Naveen jain. Follow up of High Risk Newborns. NNF Clinical Practice Guidelines 2011. Downloaded from www.nnfpublication.org. e217 – e252. In.

[3] AnandPandit, KanyaMukhopadhyay, PradeepSuryawanshi, MKC Nair, S Sitaraman, Naveen jain. Follow up of High Risk Newborns. NNF Clinical Practice Guidelines 2011. Downloaded from www.nnfpublication.org. e217 – e252.[cited 2020 jan 12].

[4] Daniel Axelrad, Kristen Adams, Farah Chowdhury, Louis D'Amico, Erika Douglass, Gwendolyn Hudson. America's Children and the Environment. Third Edition. Pg 233. Washington, DC 20460. EPA 240 R-13-001. January 2013. In.

[5] Arora NK, Nair MKC, Gulati S, Deshmukh V, Mohapatra A, Mishra D, et al. Neurodevelopmental disorders in children aged 2-9 years: Population-based burden estimates across five regions in India. PLoS Med. 2018 Jul;15(7):e1002615.

[6] Gregg T. Lueder, Missouri Steven M. Archer, Ann Arbor, Robert W. Hered, Florida Daniel J. Karr, Great Neck, Stephen P. Kraft, MD, Canada Evelyn A. Basic and Clinical Science Course. Pediatric ophthalmology and strabismus. Last major revision 2014–2015. Section 6. Part 1. Visual assessment in children. Pg 7.

[7] Beck K, Young R, Read S, Harper H, Desireddi J, Harper CA. The severity and associated comorbidities of retinopathy of prematurity among micro-premature infants with birth weights less than 750 grams. J Neonatal Perinat Med. 2019;12:41–45.

[8] Holmström G, Larsson E. Outcome of retinopathy of prematurity. ClinPerinatol. 2013 Jun;40(2):311-21. doi: 10.1016/j.clp.
2013.02.008. PMID: 23719312.

[9] Blencowe H, Lawn JE, Vazquez T, Fielder A, Gilbert C. Pretermassociated visual impairment and estimates of retinopathy of prematurity at regional and global levels for 2010. Pediatr Res. 2013;74:35–49.

[10] Park KH, Hwang J-M, Choi MY, Yu YS, Chung H. Retinal detachment of regressed retinopathy of prematurity in children aged 2 to 15 years. Retina. 2004;24:368–75.

[11] Nair MK, George B, Philip E, Lekshmi MA, Haran JC, Sathy N. Trivandrum Developmental Screening Chart. Indian Pediatr. 1991 Aug;28(8):869–72.

[12] Ferreira RC, Mello RR, Silva KS. Neonatal sepsis as a risk factor for neurodevelopmental changes in preterm infants with very low birth weight. J Pediatr (Rio J). 2014 Jun;90(3):293–9

[13] Norman M, Hellström A, Hallberg B, Wallin A, Gustafson P, Tornqvist K, et al. Prevalence of Severe Visual Disability Among Preterm Children With Retinopathy of Prematurity and Association With Adherence to Best Practice Guidelines. JAMA Netw Open. 2019 Jan 4;2(1):e186801.

[14] Shim S-Y, Cho SJ, Park EA. Neurodevelopmental Outcomes at 18–24 Months of Corrected Age in Very Low Birth Weight Infants with Late-onset Sepsis. Journal of Korean Medical Science [Internet]. 2021 Jul 13 [cited 2022 Jan 16];36(35). Available from: https://doi.org/10.3346/jkms.2021.36.e205

[15] Dempsey AG, Abrahamson CW, Keller-Margulis MA. Developmental Screening Among Children Born Preterm in a High-Risk Follow-Up Clinic. J Pediatr Psychol. 2016 Jun;41(5):573–81.

[16] Nagamani B, Vijayalakshmi P, Jeyaseeli H F, Marla J G. Neurodevelopmental Disabilities in Children with Retinopathy of Prematurity: A Report from India. Int J OphthalmolClin Res [Internet]. 2020 Mar 30 [cited 2022 Jan 26];7(1). Available from: https://www.clinmedjournals.org/articles/ijocr/international-journal-ofophthalmology-and-clinical-research-ijocr-7-114.php?jid=ijoc

[17] Hirvonen M, Ojala R, Korhonen P, Haataja P, Eriksson K, Gissler M, et al. Visual and Hearing Impairments After Preterm

Birth. Pediatrics. 2018 Aug;142(2):e20173888.

[18] Gogate P, Gilbert C, Zin A. Severe Visual Impairment and Blindness in Infants: Causes and Opportunities for Control. Middle East Afr J Ophthalmol. 2011;18(2):109–14.

[19] Parab SR, Khan MM, Kulkarni S, Ghaisas V, Kulkarni P. Neonatal Screening for Prevalence of Hearing Impairment in Rural Areas. Indian J Otolaryngol Head Neck Surg. 2018 Sep 1;70(3):380–6

[20] Vashistha I, Aseri Y, Singh BK, Verma PC. Prevalence of Hearing Impairment in High Risk Infants. Indian J Otolaryngol Head Neck Surg. 2016 Jun 1;68(2):214– 7.

[21] Valkama AM, Tolonen EU, Kerttul LI, Pääkkö EL, Vainionpää LK, Koivist ME. Brainstem size and function at term age in relation to later neurosensory disability in high-risk, preterm infants. ActaPaediatr. 2001 Aug;90(8):909–15.

[22] Gasparrini E, Rosati F, Gaetti MT. Long-term follow-up of newborns at neurological risk. Ital J Pediatr. 2019 Mar 18;45:38.

[23] Wei QW, Zhang JX, Scherpbier RW, Zhao CX, Luo SS, Wang XL, et al. High prevalence of developmental delay among children under three years of age in poverty-stricken areas of China. Public Health. 2015 Dec;129(12):1610–7.

[24] Kato T, Mandai T, Iwatani S, Koda T, Nagasaka M, Fujita K, et al. Extremely preterm infants small for gestational age are at risk for motor impairment at 3years corrected age. Brain and Dev. 2016 Feb 1;38(2):188–95.

[25] Ferreira RC, Mello RR, Silva KS. Neonatal sepsis as a risk factor for neurodevelopmental changes in preterm infants with very low birth weight. J Pediatr (Rio J). 2014 Jun;90(3):293–9.

[26] Shim S-Y, Cho SJ, Park EA. Neurodevelopmental Outcomes at 18–24 Months of Corrected Age in Very Low Birth Weight Infants with Late-onset Sepsis. Journal of Korean Medical Science [Internet]. 2021 Jul 13 [cited 2022 Jan 16];36(35). Available from: https://doi.org/10.3346/jkms.2021.36.e205

[27] Shane AL, Stoll BJ. Neonatal sepsis: Progress towards improved outcomes. J Infect. 2014 Jan 1;68:S24–32.

[28] Johnson, S., Evans, T. A., Draper, E. S., Field, D. J., Manktelow, B. N., Marlow, N., & Boyle, E. M. (2015). Neurodevelopmental outcomes following late and moderate prematurity: a population-based cohort study. Arch of Dis Child Fetal and Neonatal Ed, 100(4), F301-F308.

[29] Cai S, Thompson DK, Anderson PJ, Yang JY-M. Short- and Long-Term Neurodevelopmental Outcomes of Very Preterm Infants with Neonatal Sepsis: A Systematic Review and Meta-Analysis. Children (Basel). 2019 Dec 1;6(12):E131.

[30] Chaudhari S, Bhalerao M, Chitale A, Patil B, Pandit A, Hoge M. Transient tone abnormalities in high risk infants and cognitive outcome at five years. Indian Pediatr. 2010 Nov;47(11):931–5.