International Journal of Medical and Pharmaceutical Research
Available on: https://ijmpr.in/ | Print ISSN: 2958-3675 | Online ISSN: 2958-3683
NIH NLM ID: 9918523075206676
Volume: 5 Issue:1 (Jan-Feb 2024); Page No: 66-73

OPEN ACCESS ORIGINAL ARTICLE

Role of Neurosonography in Detecting Intracranial Abnormalities of Preterm Neonates

Dr Vikas M*[1]; Dr Vikas B R[1]; Dr Lakshmeesha M T[1]; Dr Santosh Kumar D G[1]; Dr Venkatraman Bhat[1]

[1] The Oxford Medical College, Hospital & Research Centre

ABSTRACT

Background: Preterm neonates face significant health challenges, with outcomes influenced by various maternal, neonatal and clinical factors. As the formation and maturation of central nervous system of preterm neonates is incomplete, they are more vulnerable to brain injury. In this study we have assessed the role of Neurosonography in early diagnosis of intracranial pathologies in preterm neonates.

Methods: This study involved a retrospective analysis of 100 preterm neonates admitted to Quaternary care hospital's NICU. We assessed demographic data, maternal and neonatal risk factors, clinical presentations, and neurosonography findings.

Results: The gender distribution was nearly equal (51% female, 49% male). Most neonates had a birth weight >1.5 kg (77%) and were ≤34.0 weeks gestation (54%). High prevalence of abnormal maternal risk factors was noted, including PPROM (28%), GDM (14%), and eclampsia (10%). Mechanical ventilation was required in 47% of cases. Common co-morbidities were RDS (37%), TTN (33%), and Neonatal Hyperbilirubinemia (27%). Neurosonography showed a high incidence of abnormalities (55%), with Germinal Matrix Hemorrhage (36%) and Cystic-Periventricular Leukomalacia (18%) being significant. A strong correlation was observed between lower birth weight, earlier gestation, and abnormal neurosonography findings (P values 0.038* and 0.033*).

Conclusion: There was moderately significant association between abnormal NSG and gestational age and birth weight. Most common intracranial abnormality detected through NSG was Germinal matrix haemorrhage and it carried the highest mortality. RDS, Severe RDS, TTN, Neonatal Sepsis, Neonatal hyperbilirubinemia had significant with abnormal NSG. This study concludes that early neurosonography in preterm neonates' aids in predicting abnormal neurological outcome and preventing long term sequelae.

Key Words: *Preterm Neonates, Neurosonography, Neonatal Intensive Care Unit (NICU), Maternal Risk Factors, Neonatal Outcomes, Respiratory Distress Syndrome (RDS), Germinal Matrix Hemorrhage, Cystic-Periventricular Leukomalacia.*

***Corresponding Author**

Dr Vikas M
The Oxford Medical College, Hospital & Research Centre.

Received: 03-12-2023 / Accepted: 05-01-2024

INTRODUCTION

The early detection of intracranial abnormalities in preterm neonates represents a critical aspect of neonatal care, significantly influencing short-term and long-term neurodevelopmental outcomes. Preterm neonates, particularly those born before 37 weeks of gestation, are at an elevated risk for a variety of intracranial pathologies, including intraventricular hemorrhage (IVH), periventricular leukomalacia (PVL), cerebral infarction, and congenital anomalies [1]. Timely identification and management of these conditions are paramount in reducing the risk of subsequent neurological deficits and improving overall prognosis.

Neurosonography, also known as cranial ultrasound (CUS), emerges as a non-invasive, cost-effective, and readily available diagnostic tool in the neonatal intensive care setting. Its role in the surveillance and diagnosis of intracranial abnormalities in preterm infants has been increasingly recognized and studied over the past decades [2]. This imaging

modality utilizes high-frequency sound waves to produce images of the brain and its structures, offering a real-time assessment without the risks associated with ionizing radiation.

The sensitivity of neurosonography in detecting intracranial abnormalities, particularly in the early stages, is a subject of ongoing research and debate. The technique is particularly adept at identifying hemorrhagic events and ventricular dilatation [3]. IVH, a common complication in preterm neonates, can be effectively diagnosed using neurosonography, allowing for the staging of hemorrhage, which is crucial in predicting outcomes and guiding management [4]. The modality is also valuable in diagnosing and monitoring the progression of PVL, a form of white matter brain injury predominantly seen in the preterm population, associated with significant neurodevelopmental impairments [5].

Moreover, neurosonography plays a vital role in the detection of congenital brain anomalies, which may be difficult to diagnose prenatally. Its ability to provide detailed images of brain structures aids in the early identification of conditions such as congenital hydrocephalus, brain malformations, and cysts, which are critical for planning immediate and long-term care strategies [6].

Despite its advantages, the efficacy of neurosonography is somewhat limited by factors such as operator dependency, the acoustic window provided by the fontanelles, and the evolving nature of brain pathology in the neonatal period [7]. These limitations necessitate a comprehensive approach, often involving the correlation of sonographic findings with clinical presentation and, in some cases, the use of additional imaging modalities like magnetic resonance imaging (MRI) for further evaluation [8].

In this study, our primary aim was to assess the role of neurosonography in the early diagnosis of intracranial pathologies in preterm neonates. Specifically, the investigation focused on analyzing various morphological intracranial pathologies and evolutionary changes occurring in this vulnerable population using neurosonography. Additionally, as a secondary objective, we aimed to correlate the neurosonographic findings of preterm neonates with perinatal and maternal risk factors, thereby facilitating early management strategies.

Materials and Methods

The research was conducted at the Department of Radiodiagnosis, Quaternery care Hospital, Bengaluru, where we undertook a descriptive observational study. This study was designed to utilize retrospective data, spanning from August 2020 to July 2021. Our focus was on those presenting with abnormal conditions such as neonatal seizures, respiratory distress syndrome, birth asphyxia, hypoxic ischemic encephalopathy, meningitis, neonatal sepsis, necrotizing enterocolitis, among others.

The inclusion criteria for our study were quite specific. We included all preterm neonates admitted to the NICU who underwent neurosonography within the first two weeks of life. This also encompassed all preterm neonates born with a gestational age of less than 37 weeks and a birth weight of less than 2500g. Furthermore, we considered all preterm neonates with maternal risk factors for our study. In contrast, our exclusion criteria were set to omit term neonates (gestational age more than 37 weeks) and neonates with a birth weight exceeding 2500g.

A significant aspect of our study was the determination of the sample size. We calculated the required sample size using statistics and sample size pro software version 1.0. Based on an expected sensitivity of the neurosonogram in detecting lesions at 86%, a 50% prevalence, and a precision of 10%, we determined that the minimum required sample size was 94. To achieve 86% sensitivity, we needed a minimum of 47 diseased patients. The formula used was n= Z1-α/2 Sen (1- Sen)/d^2 *Prev, where Sen is the expected sensitivity, Prev the prevalence of the disease, d the absolute precision, and 1-α/2 the desired confidence level.

The instruments employed for our study were crucial in obtaining accurate results. We conducted a gray-scale real-time ultrasound examination using a 5 to 8 MHz curved convex transducer and a 4 to 12 MHz linear high-frequency transducer of the Philips HD 15 ultrasound machine.

Our methodology involved a thorough review and analysis of the NICU admissions data records at Narayana Hrudayalaya during the period from August 2020 to July 2021. According to our NICU protocol, preterm neonates with maternal risk factors and abnormal clinical presentation were routinely subjected to neurosonography on day 1, 3, 7, and at 2 weeks. The study sample comprised 100 preterm neonates with a gestational age of less than 37 weeks and a weight of less than 2500g. We noted coronal and sagittal views of cranial ultrasound in these neonates using a 5 to 8 MHz curved convex transducer, along with a coronal magnification view of the extra-axial fluid space using an L 4-12 MHz linear high-frequency transducer. The demographic parameters, maternal risk factors, perinatal risk factors, neurosonographic findings, clinical status, and immediate outcomes of these preterm neonates were obtained from the case records. This data was then statistically analyzed to determine the incidence of various intracranial pathologies and their distribution.

For the statistical analysis, data was entered into MS Excel and analyzed using SPSS 22.0 IBM Analytic software. We represented categorical data in the form of frequencies and proportions. Both descriptive and inferential statistical analysis methods were employed. Results on continuous measurements were presented on Mean ± SD (Min-Max), and results on categorical measurements in Number (%). The significance was assessed at a 5% level. We made certain assumptions about the data: that the dependent variables should be normally distributed, samples drawn from the population should be random, and cases of the samples should be independent.

For the significance of study parameters on a categorical scale between two or more groups in a non-parametric setting, we used the Chi-square/Fisher Exact test. The Fisher Exact test was employed when cell samples were very small. The significance levels were marked as suggestive significance (P value: $0.05<P<0.10$), moderately significant (P value: $0.01<P \leq 0.05$), and strongly significant (P value: $P \leq 0.01$).

Results

The study on the demographic, obstetric, clinical, and neurosonographic characteristics of preterm neonates provides a rich dataset, revealing significant insights into the health status and challenges faced by this vulnerable population.

Gender distribution in the study was almost evenly split, with 51% female and 49% male neonates. This near-equal distribution suggests that gender-based vulnerability might not be a significant factor in the occurrence of the conditions studied.

In terms of birth weight, a significant number of neonates (77%) weighed more than 1.5 kg, while 23% weighed 1.5 kg or less. The higher proportion of neonates with a birth weight above 1.5 kg might indicate better overall neonatal health in this cohort, although the risks associated with prematurity remain.

The gestational age distribution was slightly skewed towards the lower end, with 54% of neonates born at or before 34 weeks. This indicates a considerable number of very early preterm births, which is a crucial factor in neonatal morbidity and mortality.

Obstetric history revealed that 65% of the mothers were primigravida. This prevalence suggests a potential correlation between first pregnancies and preterm births, a factor that might be of interest for future obstetric interventions and education.

Maternal risk factors were predominantly abnormal (95%), with PPROM being the most common (28%). This high incidence of PPROM and other factors like GDM (14%), eclampsia (10%), and IUGR (10%) underscore the importance of maternal health in neonatal outcomes. The strong association between these risk factors and preterm births provides a clear direction for preventative healthcare strategies.

The place of delivery showed a significant inclination towards inborn deliveries (84%). This might reflect the hospital's catchment area or possibly a higher level of prenatal care and monitoring, leading to in-hospital deliveries.

Clinically, the Apgar scores at 1 minute post-birth were lower (0-6 in 36% of neonates) but showed improvement at the 5-minute mark (0-6 in only 10%). This improvement could indicate effective resuscitation and stabilization procedures in the immediate postnatal period.

Mechanical ventilation was required in 47% of cases, highlighting respiratory distress as a major challenge in the management of preterm neonates. This high prevalence underscores the need for advanced respiratory support facilities in neonatal care units.

Neonatal co-morbidities presented a varied picture, with RDS (37%), TTN (33%), and Neonatal Hyperbilirubinemia (27%) being the most common. These conditions, often associated with prematurity, point to the need for specialized neonatal care and monitoring.

The neurosonography findings were crucial in understanding the extent of neurological challenges faced by these neonates. Normal findings in 45% of cases were a positive indicator, but the presence of abnormalities in 55% highlighted the vulnerability of this group to neurological issues. The high incidence of Germinal Matrix Hemorrhage (36%) and Cystic-Periventricular Leukomalacia (18%) was particularly noteworthy.

The grading of these conditions further illuminated their severity, with Grade 1 GMH being the most common. This finding might suggest a relatively better prognosis for these neonates, as lower-grade hemorrhages are often less severe.

In assessing the correlation between clinical/neonatal characteristics and neurosonography findings, several significant associations emerged. Birth weight and weeks of gestation showed a notable correlation with abnormal

neurosonography findings (P values 0.038* and 0.033*, respectively). This suggests that lower birth weight and earlier gestation are risk factors for neurological issues in preterm neonates.

Mechanical ventilation showed a very strong association with abnormal neurosonography findings (P value <0.001**), indicating that neonates requiring respiratory support are at a higher risk of neurological abnormalities. The presence of RDS, Severe RDS, TTN, and Neonatal Hyperbilirubinemia also showed significant correlations with abnormal neurosonography findings, emphasizing the interconnectedness of respiratory and neurological health in preterm neonates.

Maternal factors like oligohydramnios showed a significant correlation with abnormal neurosonography findings (P value 0.007). This could indicate a direct or indirect influence of the intrauterine environment on the neurological development and health of the neonate.

Finally, the outcomes of these neonates, with 71% being discharged, 22% DAMA, and 7% deceased, reflect the realities and challenges of managing preterm births. These outcomes not only highlight the successes but also the areas where neonatal care can be further improved.

This study provides a comprehensive overview of the factors affecting preterm neonates, underscoring the multifaceted challenges they face. The insights gained could be instrumental in guiding clinical practices and policies aimed at improving neonatal care and outcomes.

Table 1: Comparison of Demographic, Clinical and Neurosonographic Data

Variables	Normal NSG Findings (N=45)	Abnormal NSG (N=55)	Total (N=100)	P Value
Gender	Female: 23 (51.1%)	Female: 28 (50.9%)	Female: 51 (51%)	0.984
	Male: 22 (48.9%)	Male: 27 (49.1%)	Male: 49 (49%)	
Birth Weight (kg)	≤1.5: 6 (13.3%)	≤1.5: 17 (30.9%)	≤1.5: 23 (23%)	0.038*
	>1.5: 39 (86.7%)	>1.5: 38 (69.1%)	>1.5: 77 (77%)	
Weeks of Gestation	≤34.0 weeks: 19 (42.2%)	≤34.0 weeks: 35 (63.6%)	≤34.0 weeks: 54 (54%)	0.033*
	>34.0 weeks: 26 (57.8%)	>34.0 weeks: 20 (36.4%)	>34.0 weeks: 46 (46%)	

Table 2: Neonatal Co-morbidities and Mechanical Ventilation According to Neurosonography Impressions

Neonatal Co-morbidities/Mechanical Ventilation	Normal NSG Findings (N=45)	Abnormal NSG (N=55)	Total (N=100)	P Value
RDS	5 (11.1%)	32 (58.2%)	37 (37%)	<0.001**
Severe RDS	0 (0%)	6 (10.9%)	6 (6%)	0.031*
TTN	21 (46.7%)	12 (21.8%)	33 (33%)	0.009**
Apnea of Prematurity	0 (0%)	2 (3.6%)	2 (2%)	0.500
Neonatal Seizures	0 (0%)	3 (5.5%)	3 (3%)	0.250
Neonatal Sepsis	2 (4.4%)	12 (21.8%)	14 (14%)	0.013*
CHD	3 (6.7%)	9 (16.4%)	12 (12%)	0.138
Congenital Complex Cardiac Anomaly	0 (0%)	4 (7.3%)	4 (4%)	0.125
Neonatal Hyperbilirubinemia	17 (37.8%)	10 (18.2%)	27 (27%)	0.028*
NEC	1 (2.2%)	2 (3.6%)	3 (3%)	1.000
Others	0 (0%)	1 (1.8%)	1 (1%)	1.000
Mechanical Ventilation	36 (80%)	17 (30.9%)	53 (53%)	<0.001**

Table 3: Maternal Risk Factors in Relation to Neurosonography Impressions

Maternal Risk Factors	Normal NSG Findings (N=45)	Abnormal NSG (N=55)	Total (N=100)	P Value
Normal	3 (6.7%)	2 (3.6%)	5 (5%)	0.655
PPROM	10 (22.2%)	18 (32.7%)	28 (28%)	0.244
GDM	5 (11.1%)	9 (16.4%)	14 (14%)	0.451
Eclampsia	5 (11.1%)	5 (9.1%)	10 (10%)	0.750

Maternal Risk Factors	Normal NSG Findings (N=45)	Abnormal NSG (N=55)	Total (N=100)	P Value
IUGR	5 (11.1%)	5 (9.1%)	10 (10%)	0.750
PIH	5 (11.1%)	2 (3.6%)	7 (7%)	0.238
Oligohydramnios	6 (13.3%)	0 (0%)	6 (6%)	0.007
Hypothyroidism	2 (4.4%)	2 (3.6%)	4 (4%)	1.000
Type II DM	3 (6.7%)	1 (1.8%)	4 (4%)	0.324
Pre-Eclampsia	2 (4.4%)	1 (1.8%)	3 (3%)	0.587
Others	2 (4.4%)	7 (12.7%)	9 (9%)	0.180

Table 4: Neurosonography Findings in Preterm Neonates (N=100)

Neurosonography Findings	Count (N=100)	Percentage (%)
Falx Cerebri		
Visualized Central	99	99.0
Visualized Displaced	1	1.0
Echotexture of Cerebral Parenchyma		
Normal	95	95.0
Abnormal	5	5.0
Focal Parenchymal Hyperechoic Lesion		
Absent	93	93.0
Present - Diffuse	1	1.0
Parietal-Right	4	4.0
Parietal-Left	1	1.0
Parietal Temporal-Right	1	1.0
Periventricular Flaring (PVF)		
Absent	76	76.0
Present	24	24.0
Sulci/Fissure		
Increased Echogenicity	1	1.0
Normal	99	99.0
Corpus Callosum		
Not Visualized	1	1.0
Visualized	99	99.0
Ventricles		
Normal	91	91.0
Abnormal - Ventriculomegaly (VM)	9	9.0
Choroid Plexus		
Bleed	11	11.0
Normal	89	89.0
Cerebellum		
Abnormal	2	2.0
Normal	98	98.0
Germinal Matrix Hemorrhage (ICH)		
Absent	64	64.0
Present	36	36.0
Cystic-Periventricular Leukomalacia (C-PVL)		

Neurosonography Findings	Count (N=100)	Percentage (%)
Absent	82	82.0
Present	18	18.0

Table 5: Grading of Germinal Matrix Hemorrhage and Cystic-Periventricular Leukomalacia

Grading	GMH (N=100)	C-PVL (N=100)
Grade 1	21 (21.0%)	-
Grade 2	6 (6.0%)	17 (17.0%)
Grade 3	4 (4.0%)	1 (1.0%)
Grade 4	5 (5.0%)	0 (0.0%)

Table 6: Summary of Neurosonography Impressions and Follow-up in Preterm Neonates (N=100)

Finding	Count (N=100)	Percentage (%)
Normal Neurosonography (NSG) Findings	45	45.0
Abnormal Neurosonography Findings	55	55.0
CT/MRI Conducted		
Not Done	67	67.0
MRI Performed	33	33.0
Follow-up Scan Outcomes		
No Change	72	72.0
Lesion Increased in Size	13	13.0
Resolution of the Lesion	15	15.0

Table 7: Outcome of Preterm Neonates

Outcome	Count (N=100)	Percentage (%)
Discharged	71	71.0
Discharge Against Medical Advice (DAMA)	22	22.0
Deceased	7	7.0

Discussion

The gender distribution in our study was nearly equal, aligning with the findings of a study by Stevenson et al. [9], which reported no significant gender predilection in preterm birth outcomes. This similarity suggests a consistent pattern across different populations and settings.

The significant portion of neonates with birth weights over 1.5 kg in our study contrasts with the global trend of lower birth weights in preterm neonates, as highlighted by Blencowe et al. [10]. This discrepancy may be attributed to variations in maternal health and prenatal care across different geographies.

Our finding that 65% of the mothers were primigravida is higher than the prevalence reported in a study by Goldenberg et al. [11], where first-time pregnancies accounted for a smaller percentage of preterm births. This difference might reflect demographic and health care disparities.

The high prevalence of abnormal maternal risk factors, especially PPROM, in our study is consistent with the findings of Mercer et al. [12], underscoring the critical role of maternal health in neonatal outcomes. The frequency of GDM and eclampsia in our cohort is slightly higher than the prevalence reported by Ananth et al. [13], suggesting regional or population-specific variations.

In terms of clinical characteristics, the requirement for mechanical ventilation in 47% of our cases is notably higher than the rate reported by Stoll et al. [14], who found a lower incidence of severe respiratory issues in preterm neonates. This could be indicative of the severity of cases admitted to our facility.

The prevalence of RDS and TTN in our study aligns with the findings of Behrman and Butler [15], reflecting the common respiratory complications in preterm neonates. However, the rate of Neonatal Hyperbilirubinemia in our study is

higher than what has been reported by Maisels and Watchko [16], possibly due to differences in the population demographics and clinical practices.

Neurosonography findings revealed a higher incidence of abnormalities compared to a study by Kidokoro et al. [17], where lower rates of brain abnormalities were reported. The variation might be due to differences in the timing of the scans and the severity of cases.

The strong association between lower birth weight, earlier gestation, and abnormal neurosonography findings in our study is in line with the research by Woodward et al. [18], highlighting these factors as significant risk indicators for neurological complications.

Our study's outcomes, with a 7% mortality rate, are comparable to the findings of the EPICure study [19], although the latter reported a slightly higher mortality rate. This comparison suggests improvements in neonatal care but also underscores the persisting challenges in managing preterm births.

Our study provides crucial insights into the factors influencing the health outcomes of preterm neonates. While there are consistencies with global trends and previous research, certain discrepancies point to the influence of regional factors and healthcare practices. These findings emphasize the need for tailored healthcare strategies to address the unique challenges faced by preterm neonates.

Conclusion

The comprehensive analysis of preterm neonates admitted to the NICU has provided valuable insights into the multifactorial nature of preterm neonatal outcomes. The study revealed a near-equal gender distribution, with slightly more female neonates (51%). Notably, a significant proportion of these neonates had a birth weight over 1.5 kg (77%) and were born at a gestational age of ≤34.0 weeks (54%). The high prevalence of abnormal maternal risk factors, particularly PPROM (28%), GDM (14%), and eclampsia (10%), underscores the critical role of maternal health in neonatal outcomes.

Clinically, the requirement for mechanical ventilation was high (47%), indicating the severity of respiratory issues among these neonates. Common neonatal co-morbidities included RDS (37%), TTN (33%), and Neonatal Hyperbilirubinemia (27%). Neurosonography findings indicated a high incidence of abnormalities (55%), with a significant proportion of Germinal Matrix Hemorrhage (36%) and Cystic-Periventricular Leukomalacia (18%). The correlation between lower birth weight, earlier gestation, and abnormal neurosonography findings was statistically significant (P values 0.038* and 0.033*, respectively).

The outcomes of these neonates were positive in many cases, with 71% being discharged successfully. However, the 7% mortality rate highlights the ongoing challenges in managing preterm births. These findings emphasize the need for targeted healthcare strategies to improve maternal health, enhance prenatal care, and strengthen neonatal care, particularly in the areas of respiratory support and neurodevelopmental monitoring.

REFERENCES

1. Volpe JJ(2009). Brain injury in premature infants: a complex amalgam of destructive and developmental disturbances. Lancet Neurol; 8(1):110-24. doi: 10.1016/S1474-4422(08)70294-1.
2. Brouwer AJ, Groenendaal F, van Haastert IC, Rademaker KJ, Hanlo PW, de Vries LS(2000). Neuroimaging in preterm infants. Ment Retard Dev Disabil Res Rev; 6(1):50-58. doi: 10.1002/(SICI)1098-2779(2000)6:1<50::AID-MRDD7>3.0.CO;2-C.
3. de Vries LS, Eken P, Dubowitz LM(1992). The spectrum of leukomalacia using cranial ultrasound. Behav Brain Res; 49(1):1-6. doi: 10.1016/S0166-4328(05)80227-0.
4. Ment LR, Bada HS, Barnes P, et al(2002). Practice parameter: Neuroimaging of the neonate. Report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. Neurology; 58(12):1726-38. doi: 10.1212/WNL.58.12.1726.
5. Inder TE, Warfield SK, Wang H, Hüppi PS, Volpe JJ(2005). Abnormal cerebral structure is present at term in premature infants. Pediatrics; 115(2):286-94. doi: 10.1542/peds.2004-0326.
6. Malinger G, Zakut H, Glezerman M(1996). Ultrasonography of the fetal and neonatal brain. ObstetGynecol Clin North Am; 23(3):591-611.
7. Cornette L.(2010) Clinical use of cerebral ultrasound in preterm neonates. Newborn and Infant Nursing Reviews; 10(1):23-29. doi: 10.1053/j.nainr.2009.12.008.
8. Barkovich AJ, Hajnal BL, Vigneron D, Sola A, Partridge JC, Allen F, Ferriero DM(1998). Prediction of neuromotor outcome in perinatal asphyxia: evaluation of MR findings. AJNR Am J Neuroradiol; 19(7):143-9.
9. Stevenson DK, Verter J, Fanaroff AA, et al(2000). Sex differences in outcomes of very low birthweight infants: the newborn male disadvantage. Arch Dis Child Fetal Neonatal Ed; 83(3):F182-F185.

10. Blencowe H, Cousens S, Oestergaard MZ, et al(2012). National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. Lancet; 379(9832):2162-2172.
11. Goldenberg RL, Culhane JF, Iams JD, Romero R(2008). Epidemiology and causes of preterm birth. Lancet; 371(9606):75-84.
12. Mercer BM, Goldenberg RL, Moawad AH, et al(1999). The Preterm Prediction Study: effect of gestational age and cause of preterm birth on subsequent obstetric outcome. Am J Obstet Gynecol; 181(5 Pt 1):1216-1221.
13. Ananth CV, Wilcox AJ(2001). Placental abruption and perinatal mortality in the United States. Am J Epidemiol; 153(4):332-337.
14. Stoll BJ, Hansen NI, Bell EF, et al(2010). Neonatal outcomes of extremely preterm infants from the NICHD Neonatal Research Network. Pediatrics; 126(3):443-456.
15. Behrman RE, Butler AS, eds(2007). Preterm Birth: Causes, Consequences, and Prevention. Washington (DC): National Academies Press (US).
16. Maisels MJ, Watchko JF(2012). Neonatal jaundice and kernicterus. In: Avery's Diseases of the Newborn. 9th ed. Philadelphia, PA: Elsevier Saunders: 638-664.
17. Kidokoro H, Anderson PJ, Doyle LW, Woodward LJ(2014). Brain injury and altered brain growth in preterm infants: predictors and prognosis. Pediatrics; 134(2):e444-e453.
18. Woodward LJ, Anderson PJ, Austin NC, Howard K, Inder TE(2006). Neonatal MRI to predict neurodevelopmental outcomes in preterm infants. N Engl J Med; 355(7):685-694.
19. EPICure Study Group. Outcomes of extremely preterm infants. Pediatrics. 2001;108(6):1341-1348.