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Intraventricular Hemorrhage and Related Hydrocephalus Patients Demographics in a University Hospital NICU: Single-Center Data

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ABSTRACT

AIM: To analyze the demographic and clinical data of preterm or low birth weight newborns with periventricular hemorrhage.

MATERIAL and METHODS: This retrospective study analyzed patients admitted to the neonatal intensive care unit of a Bahçeşehir University School of Medicine-Affiliated Hospital due to preterm birth or low birth weight between June 1, 2012, and April 30, 2021. Categorical values were evaluated by Pearson chi-square or Fisher's exact test. The Mann-Whitney U test compared continuous values between the groups. Logistic regression was used to evaluate the factors that affected permanent Cerebrospinal fluid (CSF) diversion.

RESULTS: The study finally evaluated 180 newborns. Ninety-one newborns (50.5%) had grade I, 18 (10%) had grade II, 22 (12.2%) had grade III, and 49 (27.2%) had grade IV hemorrhage. One hundred and forty-nine patients (82.8%) were delivered by cesarean section, and 31 (17.2%) were delivered vaginally. All patients with low-grade hemorrhage who needed temporary CSF diversion eventually required permanent CSF diversion. For high-grade hemorrhage, 15 (grade III, 1; grade IV, 14) of 51 (29.4%) patients with ventricular access device (VAD) insertion required permanent CSF diversion. Fifteen (grade III, 6; grade IV, 9) of these 51 (29.4%) patients did not need permanent CSF diversion; thus, their VADs were removed.

CONCLUSION: The permanent CSF diversion rate was significantly higher in the high-grade hemorrhage group, which had significantly lower weight and gestational age at birth. Moreover, only weight at VAD insertion had minimal effect on the need for permanent CSF diversion.

KEYWORDS: Germinal matrix hemorrhage, Posthemorrhagic hydrocephalus, Ventricular access device, Permanent CSF diversion

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INTRODUCTION

Periventricular hemorrhage can occur in the fragile germinal matrix of preterm and low birth weight newborns (13) and can be complicated by hemorrhagic infarctions and posthemorrhagic ventricular dilatation (PHVD) (14,21,22). A devastating long-term complication of intraventricular hemorrhage (IVH) is posthemorrhagic hydrocephalus, which affects 30% of preterm or low birth weight infants and requires lifelong treatment (5).

IVH severity is characterized by the Papile grading scale, ranging from I to IV (14). Despite the decline in IVH incidence and related mortality over the last decades (11,18), higher degrees of hemorrhage (grade III and IV) are more commonly related to neurodevelopmental delay and cerebral palsy (1, 3).

This article analyzes the demographic and clinical data of preterm or low birth weight newborns treated in a university hospital.

MATERIAL and METHODS

This retrospective study included all patients admitted to the neonatal intensive care unit of Bahçeşehir University School of Medicine–Göztepe Medical Park Hospital due to preterm birth or low birth weight between June 1, 2012, and April 30, 2021. These patients were initially assessed. Specific International Classification of Diseases (ICD-10) codes were defined, including I62 (Other and unspecified nontraumatic intracranial hemorrhage), P52 (Intracranial nontraumatic hemorrhage of the newborn), and G91 (Hydrocephalus). All patients with these codes were further analyzed. Patients with underlying pathologies other than IVH with the G91 or I62 code were excluded from the study. The study was approved by the local ethics committee of Bahçeşehir University School of Medicine (approval number: 2021-12/04).

The study recruited 3938 patients at the end of the first database search. Of these patients, 207 constituted the target patient population, but 27 were excluded due to hydrocephalus unrelated to IVH. Thus, the final evaluation included 180 newborns who fulfilled the previously mentioned criteria.

The follow-up protocol for preterm newborns in our institute is as follows. Transcranial ultrasonography (USG) is performed routinely on postnatal days 1, 7, 15, and 30 during the first month. Cranial computed tomography (CT) is routinely performed for grade III and IV hemorrhage to evaluate the accompanying ventricular dilatation and parenchymal pathologies. For grade I and II hemorrhages, cranial CT is performed if the transcranial USG is not conclusive for evaluating the accompanying ventricular dilatation and parenchymal pathology. In the newborns' clinical follow-up, if any undefined condition becomes evident (new-onset seizure, increased head circumference exceeding normal limits, unexplained increase in C-reactive protein (CRP) levels, and unexplained hemoglobin decline), additional transcranial USG is performed besides the routine follow-up. Cerebrospinal fluid (CSF) is diverted temporarily by inserting a ventricular access device (VAD) with a reservoir under general anesthesia. The need of CSF drainage is defined according to the patient's daily evaluation (head circumference and fontanel status). The CSF amount drained is 20 mL/kg/day. When the newborn exceeds 2500 g in weight, with a persistent need for CSF drainage but without infection, permanent CSF diversion (ventriculoperitoneal [VP] shunt insertion) is performed.

During the follow-up, if the newborn does not need CSF drainage for more than seven days, control CT scans are performed (at least five days apart). According to the CT scans, if the Evan index (8) is stable, the patient can be discharged with the VAD in situ or removed. In our clinic, we decide with the parents when to remove the VAD.

The parameters we assessed regarding their effect on IVH severity and need for a permanent VP shunt included sex of the newborns, birth routes, maternal age, gestational week, birth weight, weight at VAD insertion, CSF parameters at VAD insertion, postnatal age and weight at VAD insertion, CSF parameters at VP shunt insertion, and weight at VP shunt insertion.

Statistical Analysis

The patient data were analyzed with SPSS for Windows 23.0 (IBM Corp., Armonk, NY). Categorical data are presented as frequency and percentage, and continuous descriptive data are presented as median and range. Categorical values were evaluated with the Pearson chi-square or Fisher's exact test, whereas the Mann-Whitney U test compared continuous data. Logistic regression was used to evaluate the factors affecting the need for permanent CSF diversion. $P<0.05$ was considered statistically significant, and $p<0.001$ was considered highly significant.

RESULTS

There were 180 newborns (69 females [38.3%] and 111 males [61.7%]) in the final evaluation. Ninety-one (50.5%) had grade I, 18 (10%) had grade II, 22 (12.2%) had grade III, and 49 (27.2%) had grade IV hemorrhage. One hundred and forty-nine patients (82.8%) were delivered by cesarean section, and 31 (17.2%) were delivered vaginally. No significant difference was found between the severity of hemorrhage and delivery routes ($p=0.243$).

The median maternal age was 30 (range: 15–44) years. Four subgroups based on age (<20; 20–30; 30–40; >40) were defined, and there was no significant between hemorrhage grade and maternal age ($p=0.853$).

The median gestational age at birth was 28 weeks (range: 24–42) when all patient data were considered. The median gestational age at birth was 30 weeks (range: 24–42) for grade I, 27 weeks (range:24–38) for grade II, 28 weeks (range: 24–35) for grade III, and 27 weeks (range: 24–38) for grade IV hemorrhage; the differences were statistically significant ($p<0.001$).

The median birth weight was 1140 g (range: 435–4100). The median birth weight was 1280 g (range: 435–4100) for grade

I, 1055 g (range: 540–2540) for grade II, 1030 g (range: 620–2700) for grade III, and 980 g (range: 540–3290) for grade IV hemorrhage; the differences were statistically significant (p=0.005).

Sixty-four patients (35.6%) had PHVD at IVH diagnosis or during the follow-up period as follows: 3.3% of grade I, 11.1% of grade II, 72.7% of grade III, and 87.8% of the grade IV hemorrhage group had or developed PHVD, with significant between-group differences (p<0.001) (Table I).

Fifty-three patients (29.4%) underwent temporary CSF diversion during the follow-up period; 1.1% of grade I, 5.5% of grade II, 50% of grade III, and 81.6% of the grade IV hemorrhage group, with significant between-group differences (p<0.001).

The median weight of those who required CSF diversion on the day of the surgery, was 1260 g (range: 830–3010); 1530 g for grade I, 1460 g (range: 840–1580) for grade II, 1250 g (range: 895–1900) for grade III, and 1270 g (range: 830–3010) for grade IV hemorrhage. There was no significant difference between the groups (p=0.876).

The median age at temporary CSF diversion was 19 days (range: 3–142); 35 days for grade I (only one patient), 25 days (range: 20–71) for grade II, 14 days (range: 11–34) for grade III, and 19 days (range: 3–142) for grade IV hemorrhage. There was no significant difference between the groups (p=0.391).

The median age at permanent CSF diversion was 77 days (range: 30–225), 138 for grade I, 116 for grade II, 43 for grade III, and 77 days (range: 30–225) for grade IV hemorrhage (Table II).

All patients with low-grade hemorrhage (grade I and grade II) who needed temporary CSF diversion eventually required permanent CSF diversion. For high-grade hemorrhage (grade III and grade IV), 15 (grade III, 1; grade IV, 14) of the 51 patients (29.4%) with VAD insertion required permanent CSF diversion. Fifteen patients (grade III, 6; grade IV, 9) of these 51 (29.4%) patients did not need permanent CSF diversion surgery; thus, their VADs were removed (Figure 1).

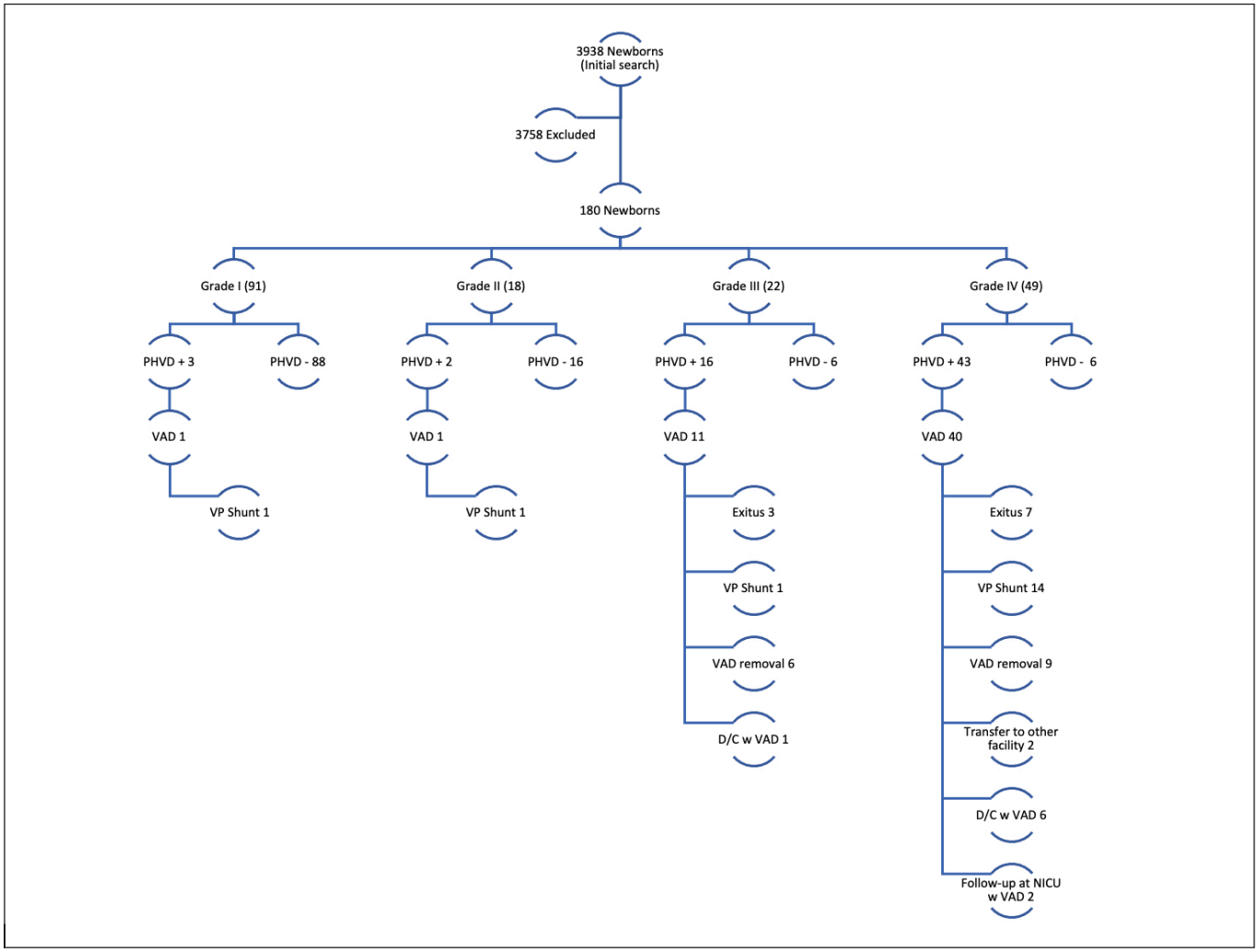

Figure 1: Summary of patient data and interventions.

Table I: Characteristics of the Patients

Characteristics (n=180)	Total (n=180)	Grade I (n=91)	Grade II (n=18)	Grade III (n=22)	Grade IV (n=49)	p-value
	n (%) / Median (range)	n (%) / Median (range)	n (%) / Median (range)	n (%) / Median (range)	n (%) / Median (range)	
Sex						0.778
Male	111 (61.7)	54 (59.3)	13 (72.2)	14 (63.6)	30 (61.2)	
Female	69 (38.3)	37 (40.7)	5 (27.8)	8 (36.4)	19 (38.8)	
Birth route						0.243
C/S	149 (82.8)	76 (83.5)	12 (66.7)	18 (81.8)	43 (87.8)	
NSV	31 (17.2)	15 (16.5)	6 (33.3)	4 (18.2)	6 (12.2)	
Maternal age, years	30 (15–44)	30 (15–38)	29 (19–44)	30.5 (15–39)	30 (19–44)	0.853
<20	9 (5.0)	3 (3.3)	1 (5.69	2 (9.1)	3 (6.1)	0.383
20–30	87 (48.3)	45 (49.5)	10 (55.6)	9 (40.9)	23 (46.9)	
30–40	80 (44.4)	43 (47.3)	6 (33.3)	11 (50.0)	20 (40.8)	
> 40	4 (2.2)	0 (0)	1 (5.6)	0 (0)	3 (6.1)	
Gestational age, weeks	**28 (24–38)**	**30 (24–38)**	**27 (24–38)**	**28 (24–35)**	**27(24–38)**	**<0.001**
Birth weight, g	**1140 (435–3560)**	**1280 (435–3560)**	**1055 (540–2540)**	**1030 (620–2700)**	**980 (540–3290)**	**0.005**
Post-hemorrhagic ventricular dilatation	**64 (35.6)**	**3 (3.3)**	**2 (11.1)**	**16 (72.7)**	**43 (87.8)**	**<0.001**
Exitus	**42 (23.3)**	**14 (15.4)**	**7 (38.9)**	**9 (40.9)**	**12 (24.5)**	**<0.001**

C/S: *Cesarean section,* ***NSV:*** *Normal spontaneous vaginal.*

Table II: Summary of All Interventions and Related Parameters

	Total (n=180)	Grade I (n=91)	Grade II (n=18)	Grade III (n=22)	Grade IV (n=49)	p-value
	n (%)/Median (Min-Max)	n (%)/Median (Min-Max)	n (%)/Median (Min-Max)	n (%)/Median (Min-Max)	n (%)/Median (Min-Max)	
VAD insertion	**53 (29.4)**	**1 (1.1)**	**1 (5.5)**	**11 (50)**	**40 (81.6)**	**<0.001**
Weight at VAD insertion, g	1260 (830–3010)	1530 (1530–1530)	1460 (840–1580)	1250 (895–1900)	1270 (830–3010)	0.876
Age at VAD insertion, days	19 (3–142)	35 (35–35)	25 (20–71)	14 (11–34)	19 (3–142)	0.236
CSF protein at VAD insertion	266.5 (28–2909)	155 (155–155)	401 (279–531)	177 (97–365)	300 (28–2909)	0.095
CSF glucose at VAD insertion	18 (5–85)	14 (14–14)	33 (30–85)	16 (5–28)	18 (5–60)	0.059
Age at VAD removal, days	60 (24–225)	62 (62–62)	60 (50–116)	48 (30–79)	62 (24–225)	0.445
Permanent CSF diversion	**17**	**1**	**1**	**1**	**14**	**<0.001**
Age at VP shunt insertion, days	77 (30–225)	138 (138–138)	116 (116–116)	43 (43–43)	77 (30–225)	0.391
Weight at VP shunt insertion, g	2670 (2120–4178)	4178 (4178–4178)	2680 (2680–2680)	2895 (2895–2895)	2520 (2120–3700)	0.380
CSF protein at VP shunt insertion, mg/dL	192.5 (88–503)	367 (367–367)	308 (308–308)	172 (172–172)	190 (88–503)	0.410
CSF glucose at VP shunt insertion, mg/dL	27 (5–48)	14 (14–14)	42 (42–42)	16 (16–16)	27(5–48)	

VAD: *Ventricular access device,* ***CSF:*** *Cerebrospinal fluid,* ***VP:*** *Ventriculoperitoneal.*

Table III: Factors Affecting the Need for Permanent CSF Diversion

Characteristics	Univariate analysis		Multivariate analysis	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Weight at VAD insertion	**1.002 (1.001–1.004)**	**0.003**	**1.002 (1,000–1,004)**	**0.028**
Age at VAD insertion	**1.029 (1.000–1.058)**	**0.049**	1.017 (0.977–1.058)	0.406
CSF protein at VAD insertion	1.000 (0.999–1.001)	0.329	1.000 (0.999–1.001)	0.807
CSF glucose at VAD insertion	1.000 (0.961–1.038)	0.944	0.990 (0.937–1.045)	0.714

CSF: *Cerebrospinal fluid,* ***VAD:*** *Ventricular access device,* ***HR:*** *Hazard's Ratio,* ***CI:*** *Confidence interval.*

DISCUSSION

According to the gestational age at birth, preterm birth is from 20–37 weeks (10), and extremely preterm births have a gestational age of <28 weeks. Regarding birth weight, very low birth weight is defined as <1500 g, and extremely low birth weight (ELBW) is <1000 g (7). Recent data show that preterm birth constitutes nearly 11% of all live births (2). Mortality also increases with decreased gestational age, reaching 50% in preterm babies born before 28 weeks (9,12,19).

One of the most devastating long-term complications of preterm birth is neurodevelopmental impairment, which could require lifelong special treatment. Neurodevelopmental impairments include cerebral palsy, epilepsy, learning disabilities, attention deficiency, autism spectrum disorders, and psychiatric problems (6,15,20,23). One reason for neurodevelopmental impairment is germinal matrix hemorrhage and PHVD/posthemorrhagic hydrocephalus, which contribute to white matter loss in these patients (4,16).

Concerning factors that can influence hemorrhage grades specific to this cohort, there is no significant difference when the sex of the newborns, birth routes, maternal age, and maternal status (gravidity and parity) are considered.

There is an inverse proportion between the birth weight/gestational age and the grade of the germinal matrix hemorrhage. When the gestational age or weight at birth decreases, the incidence and grade of germinal matrix hemorrhage increase. In preterm newborns with grade III and IV hemorrhages, there is a significantly increased need for permanent CSF diversion (17). In our cohort, 130 newborns (72.2%) had a birth weight of <1500 g, 68 (37.7%) were in an ELBW group, and 89 (49.4%) were in the extremely preterm group.

In our study, the high-grade hemorrhage groups (grade III and grade IV) demonstrated significantly lower birth weight and gestational age at birth compared to the low-grade groups. Consistent with the previous literature, our study showed a significant association between high-grade hemorrhage and lower weight and gestational age at birth. Higher IVH grades were related to a significant increase in PHVD and the need for temporary CSF diversion. The need for temporary CSF diversion was significantly lower (1.83%) in the low-grade groups than in the high-grade groups (71.83%), consistent with the literature (Table II) (11,17).

Concerning factors influencing the need for permanent CSF diversion, we assessed weight at VAD insertion, age at VAD insertion, CSF protein and glucose levels at VAD insertion, age at VAD removal, age at VP shunt insertion, weight at VP shunt insertion, and CSF protein, and glucose levels at VP shunt insertion. None of these factors had a significant effect on the need for permanent CSF diversion need in our study (Table II).

When assessing factors (weight at VAD insertion, age at VAD insertion, CSF protein, and glucose levels) influencing the need for permanent CSF diversion via multivariate analysis, only weight at VAD insertion had a significant effect, with a hazard ratio of 1.002 (p=0.028) (Table III).

CONCLUSION

This study showed that the need for permanent CSF diversion was significantly higher in newborns with high-grade hemorrhage, who had a significantly lower weight and gestational age at birth. Regarding factors affecting permanent CSF diversion, only weight at VAD insertion was significant. Further multicenter studies are needed to develop better treatment protocols and clarify the factors that affect the need for permanent CSF diversion.

Statement of Ethics

This study protocol was reviewed and approved by Bahçeşehir University School of Medicine Clinical Research Ethics Board. Approval number: 2021-12/04. The study was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. We obtained written informed consent from the legal guardians of all patients.

AUTHORSHIP CONTRIBUTION

Study conception and design: SI, GDO
Data collection: GDO, BP
Analysis and interpretation of results: GDO, BP, BY
Draft manuscript preparation: GDO, TH
Critical revision of the article: SI, AA, ZOT, AHT
Other (study supervision, fundings, materials, etc...): OK, TH
All authors (GDO, SI, BP, OK, TH, AA, ZOT, BY, AHT) reviewed the results and approved the final version of the manuscript.

REFERENCES

1. Beaino G, Khoshnood B, Kaminski M, Pierrat V, Marret S, Matis J, Ledesert B, Thiriez G, Fresson J, Roze JC, Zupan-Simunek V, Arnaud C, Burguet A, Larroque B, Breart G, Ancel PY, Group ES: Predictors of cerebral palsy in very preterm infants: The EPIPAGE prospective population-based cohort study. Dev Med Child Neurol 52:e119-125, 2010
2. Blencowe H, Cousens S, Oestergaard MZ, Chou D, Moller AB, Narwal R, Adler A, Vera Garcia C, Rohde S, Say L, Lawn JE: 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 379:2162-2172, 2012
3. Bolisetty S, Dhawan A, Abdel-Latif M, Bajuk B, Stack J, Lui K, New South W, Australian Capital Territory Neonatal Intensive Care Units' Data C: Intraventricular hemorrhage and neurodevelopmental outcomes in extreme preterm infants. Pediatrics 133:55-62, 2014
4. Brouwer MJ, de Vries LS, Kersbergen KJ, van der Aa NE, Brouwer AJ, Viergever MA, Isgum I, Han KS, Groenendaal F, Benders M: Effects of posthemorrhagic ventricular dilatation in the preterm infant on brain volumes and white matter diffusion variables at term-equivalent age. J Pediatr 168:41-49.e1, 2016
5. Christian EA, Jin DL, Attenello F, Wen T, Cen S, Mack WJ, Krieger MD, McComb JG: Trends in hospitalization of preterm infants with intraventricular hemorrhage and hydrocephalus in the United States, 2000-2010. J Neurosurg Pediatr 17:260-269, 2016
6. Dvir Y, Frazier JA, Joseph RM, Mokrova I, Moore PS, O'Shea TM, Hooper SR, Santos HP Jr, Kuban K, Investigators ES: Psychiatric symptoms: Prevalence, co-occurrence, and functioning among extremely low gestational age newborns at age 10 years. J Dev Behav Pediatr 40:725-734, 2019
7. Eichenwald EC, Stark AR: Management and outcomes of very low birth weight. N Engl J Med 358:1700-1711, 2008
8. Evans WA Jr: An encephalographic ratio for estimating ventricular enlargement and cerebral atrophy. Arch Neur Psych 47:931-937, 1942
9. Field DJ, Dorling JS, Manktelow BN, Draper ES: Survival of extremely premature babies in a geographically defined population: Prospective cohort study of 1994-9 compared with 2000-5. BMJ 336:1221-1223, 2008
10. Goldenberg RL, Culhane JF, Iams JD, Romero R: Epidemiology and causes of preterm birth. Lancet 371:75-84, 2008
11. Handley SC, Passarella M, Lee HC, Lorch SA: Incidence trends and risk factor variation in severe intraventricular hemorrhage across a population based cohort. J Pediatr 200:24-29.e3, 2018
12. Itabashi K, Horiuchi T, Kusuda S, Kabe K, Itani Y, Nakamura T, Fujimura M, Matsuo M: Mortality rates for extremely low birth weight infants born in Japan in 2005. Pediatrics 123:445-450, 2009
13. Novak CM, Ozen M, Burd I: Perinatal brain injury: Mechanisms, prevention, and outcomes. Clin Perinatol 45:357-375, 2018
14. Papile LA, Burstein J, Burstein R, Koffler H: Incidence and evolution of subependymal and intraventricular hemorrhage: A study of infants with birth weights less than 1,500 gm. J Pediatr 92:529-534, 1978
15. Pyhala R, Wolford E, Kautiainen H, Andersson S, Bartmann P, Baumann N, Brubakk AM, Evensen KAI, Hovi P, Kajantie E, Lahti M, Van Lieshout RJ, Saigal S, Schmidt LA, Indredavik MS, Wolke D, Raikkonen K: Self-reported mental health problems among adults born preterm: A meta-analysis. Pediatrics 139(4):e20162690, 2017
16. Sarkar S, Shankaran S, Barks J, Do BT, Laptook AR, Das A, Ambalavanan N, Van Meurs KP, Bell EF, Sanchez PJ, Hintz SR, Wyckoff MH, Stoll BJ, Carlo WA, Eunice Kennedy Shriver National Institute of Child H, Human Development Neonatal Research N: Outcome of preterm infants with transient cystic periventricular leukomalacia on serial cranial imaging up to term equivalent age. J Pediatr 195:59-65.e3, 2018
17. Shankaran S, Bajaj M, Natarajan G, Saha S, Pappas A, Davis AS, Hintz SR, Adams-Chapman I, Das A, Bell EF, Stoll BJ, Walsh MC, Laptook AR, Carlo WA, Van Meurs KP, Sanchez PJ, Ball MB, Hale EC, Seabrook R, Higgins RD, Eunice Kennedy Shriver National Institute of Child H, Human Development Neonatal Research N: Outcomes following posthemorrhagic ventricular dilatation among infants of extremely low gestational age. J Pediatr 226:36-44.e3, 2020
18. Stoll BJ, Hansen NI, Bell EF, Walsh MC, Carlo WA, Shankaran S, Laptook AR, Sanchez PJ, Van Meurs KP, Wyckoff M, Das A, Hale EC, Ball MB, Newman NS, Schibler K, Poindexter BB, Kennedy KA, Cotten CM, Watterberg KL, D'Angio CT, DeMauro SB, Truog WE, Devaskar U, Higgins RD, Eunice Kennedy Shriver National Institute of Child H, Human Development Neonatal Research N: Trends in care practices, morbidity, and mortality of extremely preterm neonates, 1993-2012. JAMA 314:1039-1051, 2015
19. Tyson JE, Parikh NA, Langer J, Green C, Higgins RD, National Institute of Child H, Human Development Neonatal Research N: Intensive care for extreme prematurity--moving beyond gestational age. N Engl J Med 358:1672-1681, 2008
20. Van Lieshout RJ, Boyle MH, Saigal S, Morrison K, Schmidt LA: Mental health of extremely low birth weight survivors in their 30s. Pediatrics 135:452-459, 2015
21. Volpe JJ: Intraventricular hemorrhage and brain injury in the premature infant. Diagnosis, prognosis, and prevention. Clin Perinatol 16:387-411, 1989
22. Volpe JJ: Intraventricular hemorrhage and brain injury in the premature infant. Neuropathology and pathogenesis. Clin Perinatol 16:361-386, 1989
23. Yates R, Treyvaud K, Doyle LW, Ure A, Cheong JLY, Lee KJ, Inder TE, Spencer-Smith M, Anderson PJ: Rates and stability of mental health disorders in children born very preterm at 7 and 13 years. Pediatrics 145(5):e20192699, 2020