ORIGINAL ARTICLE

Neurodevelopmental outcomes of extreme-low-birth-weight infants born between 2001 and 2002

High Risk Follow-up Working Group (Kowloon Region)*

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Objective To report the neurodevelopmental outcomes of extreme-low-birth-weight survivors.

Design Multicentre cohort study.

Setting Three regional hospitals in Hong Kong.

Patients Surviving extreme-low-birth-weight infants born in 2001 and 2002 underwent neurodevelopmental, neurosensory, and functional assessment under the High Risk Follow-up Program in three Child Assessment Centres.

Main outcome measures Demographic characteristics, neonatal diagnoses and treatment given, as well as neurodevelopmental outcomes were prospectively collected, and possible maternal and neonatal risk factors for major disability evaluated.

Results Of 81 extreme-low-birth-weight infants, 49 had undergone evaluation under the High Risk Follow-up Program. Their mean gestational age was 26.2 (standard deviation, 1.8) weeks and mean birth weight was 789 g (standard deviation, 125 g). Seventeen infants were less than 750 g and 32 were between 751 and 999 g. The rates of cerebral palsy, intellectual impairment, hearing deficit, and visual impairment were 12%, 16%, 4%, and 6%, respectively. Fifteen (31%) infants had at least one major disability. There was no association between neurodevelopmental disability and low birth weight. For neurodevelopmental disabilities, postnatal use of steroids conferred a significant risk (relative risk=7.4; 95% confidence interval, 1.9-29.2). Corresponding figures for other significant risk factors were as follows: severe grades of intraventricular haemorrhage (2.7; 1.2-5.9), presence of periventricular leukomalacia (4.5; 2.1-9.3), patent ductus arteriosus requiring ligation (2.8; 1.3-6.1), severe grades of retinopathy of prematurity (2.4; 1.0-5.6), and severe grades of necrotising enterocolitis (3.2; 1.6-6.3).

Conclusion Extreme-low-birth-weight infants are at risk of major neurodevelopmental disability. Our rates of cerebral palsy, intellectual disability, and significant visual and hearing impairment were comparable to those reported in many western studies. Further longitudinal study to assess long-term neurodevelopmental outcomes in this group of children is needed.

Introduction

Extreme-low-birth-weight (ELBW) infants are defined as those with birth weight below 1000 g. Survival rate of ELBW infants has been increasing since the introduction of antenatal steroid therapy, postnatal surfactant replacement, and various types of advanced ventilator therapy.[1-3] The incidence of neurodevelopmental disabilities among these infants is substantial. This has implications on resource allocation to the health care system, though local data on this subject are scanty.

This multicentre prospective study aimed to explore the long-term (30-36 months) neurodevelopmental outcomes of a cohort of ELBW infants born in three regional hospitals during the 2-year period from 2001 to 2002, together with associated identifiable risk factors.

Key words
Developmental disabilities; Infant, premature; Infant, very low birth weight; Neurologic examination

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2001至2002年出生體重極低的嬰兒神經發育的情況

目的 報告出生體重極低的嬰兒神經發育的情況。

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患者 2001至2002年出生體重極低而存活下來的嬰兒，在三個兒童體能智力測驗中心接受高風險隨訪計劃(High Risk Follow-up Program)對神經發育、感應神經、功能三方面的評估。

主要結果測量 收集與人口有關的特點數據、對新生兒的診斷和施行的治療，以及神經發育結果的情況。此外，亦評估了與主要發育障礙有關、源自母系及新生兒本身的風險因素。

結果 在81名出生體重極低的嬰兒中，有49名接受高風險隨訪計劃評估。平均胎齡26.2星期（標準差：1.8星期），出生平均體重789克（標準差：125克），當中17個輕於750克，其餘32個在751至999克之間。出現腦癱、智能障礙、聾、視覺障礙的比率按序分別為12%、16%、4%、6%。15個嬰兒(31%)至少有一種主要發育障礙。神經發育障礙與出生體重低不相關，反而是出生後服用類固醇才是一個相當重要的風險因素（相對風險系數=7.4；95%置信區間，1.9-29.2）。其他重要的風險因素還包括嚴重腦室內出血（2.7；1.2-5.9），腦室周圍白質軟化（4.5；2.1-9.3），動脈導管末閉而須結紮（2.8；1.3-6.1），嚴重早產兒視網膜病（2.4；1.0-5.6），以及嚴重壞死性小腸結腸炎（3.2；1.6-6.3）。

結論 出生體重極低的嬰兒易於出現主要神經發育障礙。本研究中嬰兒出現腦癱、智能障礙，以及嚴重聽覺、視覺障礙的比率與許多西方研究報告的結果相若。我們認為有需要進一步進行追蹤研究，以評估這類嬰兒神經發育的長遠情況。

Methods

Patient selection and definitions

All surviving ELBW infants with birth weight below 1000 g and born between 1 January 2001 and 31 December 2002, under the neonatal care of the three major hospitals (Queen Elizabeth, Kwong Wah, and United Christian hospitals) in the Kowloon Cluster were recruited to this cohort. Upon discharge for follow-up developmental assessment under the High Risk Follow-up Program, these babies were referred to either the Central Kowloon Child Assessment Centre, the Arran Street Child Assessment Centre, or the Pamela Youde Child Assessment Centre (Kwun Tong). Data about their respective demographic characteristics, neonatal diagnoses and treatments were prospectively collected.

The High Risk Follow-Up Program was named as "小樹苗成長計劃". Pamphlets about the programme were available for the parents in both English and Chinese.

Neurodevelopmental assessments

Developmental assessment at the three Child Assessment Centres included close monitoring of sensori-motor development by physiotherapists: at corrected chronological age (CCA) of 4 months, 8 months, and 12 months; and at chronological age (CA) of 24 to 36 months. Audiological and visual assessments were performed at 8 months (CCA) and around 24 to 36 months (CA). Developmental paediatricians performed neurodevelopmental evaluation at around 24 to 36 months (CA). For babies diagnosed to have delay in development during follow-up, neurodevelopmental evaluation was accordingly arranged at an earlier age.

During the first year of life, the Infant Neurological International Battery (INFANIB) and Alberta Infant Motor Scale (AIMS) were used. When the children reached 24 to 36 months of age, the Peabody Developmental Motor Scale 2 (PDMS-2) was used for early detection of motor problems and monitoring of the gross motor skills. The INFANIB is an instrument to assess the neurological integrity of infants from birth to the age of 18 months.[4] The 20-item instrument assesses five areas: spasticity, vestibular function, the head and trunk, French angles, and the legs. Cut-off points were set that separate infants by age into three categories: normal, transiently abnormal, and abnormal neurological development. The AIMS is an observational scale measuring gross motor maturation from term to independent walking.[5] It focuses on evaluation of sequential development of postural control and consists of four subscales: prone, supine, sitting, and standing. Three aspects of motor performance were observed for each test item: weight bearing, posture, and antigravity movement. In our surveillance, the cut-off scores of the 5th and 10th percentiles at CCAs of 4 and 8 months respectively were taken as reference scores for therapy training referrals, because they were found predictive of gross motor delay at 18 months.[6] The PDMS-2 is a norm-referenced test designed to assess motor development in children from birth to the age of 71 months.[7] The PDMS-2 has six subtests: reflexes, stationary, locomotion, object manipulation (Gross Motor Composite), grasping, and visual-motor integration (Fine Motor Composite). Both PDMS and PDMS-2 have been used to measure the motor development of very-low-birth-weight infants overseas and locally.[8,9]

Neurodevelopmental evaluation was based on the Griffiths Mental Development Scale (GMDS) and the Reynell Developmental Language Scale (RDLS), history from parents, and clinical observation of

behaviour. The GMDS is a developmental test for children from birth to 8 years old, with six subscales: locomotor, personal-social, hearing and speech, eye and hand coordination, performance, and practical reasoning.[10] The subscale on hearing and speech was omitted. For the language aspect, we used the Chinese version of the RDLS (雷妮氏語言發展量表1987粵語版),[11] the only Cantonese language test available with local Hong Kong norms. Neurological examination included evaluation of tone, strength, reflexes, and posture.

Cerebral palsy was defined as a non-progressive central nervous system disorder characterised by abnormal muscle tone in at least one extremity and abnormal control of movement and posture. Developmental delay was defined as developmental levels substantially behind the average expectations of preschool children of the same age in two or more domains. These domains included cognitive and intellectual, gross motor, fine motor, language, social, and adaptive development. Significant developmental delay was inferred if scores were 1.5 to 2.0 standard deviations (SDs) below the mean on norm-referenced age-appropriate developmental tests. Significant hearing impairment was defined as moderate hearing loss or worse in both ears, requiring a hearing aid or cochlear implant. Significant visual impairment was defined as loss of visual acuity and/or loss of visual field that made it difficult or impossible for the affected person to complete daily tasks without specialised adaptations. These included low vision with residual vision to total blindness in the better eye. Neurodevelopmental impairment was defined by having one of the following: cerebral palsy, significant developmental delay, significant hearing impairment, or significant visual impairment.

Statistical analyses

Chi squared or, when appropriate, Fisher's exact test were used to analyse categorical measures such as cohort features, hospital interventions, risk factors, and their associations with birth weight, neurological and sensory outcomes. The *t* test was used to analyse the difference between means, such as birth weight and gestational age. A P value of less than 0.05 was considered statistically significant. For factors showing a significant association with disability, relative risks (RRs) and associated 95% confidence intervals (CIs) were calculated to estimate the magnitude of the effect size and precision. An RR of greater than 1 indicates risk of having disability among subjects with exposure to the risk factor. Moreover, the wider the CI, the less precise must be the effect. Because of the limited sample size and its impact on estimation of stability, a multivariate approach was not used to investigate potential confounding from identified significant risk factors. Statistical analysis was conducted using the statistical application software SAS Enterprise Guide 2.0.[12,13]

Results

A total of 81 ELBW infants were born in the three hospitals during the year of 2001 and 2002, of which 21 died before the age of 2 years and 60 (74%) survived longer. Among the latter, a total of 49 underwent neurodevelopmental follow-up in Child Assessment Centres till the age of 30 to 36 months; 11 defaulted attending the above High Risk Follow-up Program.

Demographic characteristics, in-hospital treatments and diagnoses of the 49 ELBW infants are summarised in Table 1. Their mean gestational age was 26.2 (SD, 1.8; range, 24.5-28.0) weeks; 49% were male. The mean birth weight of the babies was 789 g (SD, 125 g; range, 664-914 g); 17 weighed 750 g or less, and 32 weighed 751 to 999 g. More babies in the former group received the postnatal steroids and developed retinopathy of prematurity (ROP) grades 3 to 4, while more in the latter group were born to mothers experiencing premature rupture of membranes (>18 hours).

With respect to major developmental outcomes in these 49 infants (Table 2), there were no significant differences between the two groups. Six (12%) had cerebral palsy, eight (16%) significant developmental delay, two (4%) significant hearing impairment, and three (6%) visual impairment. Approximately one third of these ELBW infants had at least one major neurodevelopmental disability. Regarding 15 (31%) of the infants with major neurodevelopmental disability (Table 3), six had cerebral palsy, among whom one had spastic quadriplegia with significant developmental delay, one had dyskinetic cerebral palsy with significant intellectual impairment, one had mixed spastic-dyskinetic cerebral palsy with mild intellectual impairment, and one had left monoplegia (lower limb) with borderline intellectual impairment and moderate-to-severe hearing loss (using hearing aids). Two with normal intellectual functioning had spastic diplegia and right hemiplegia, respectively, two had severe low vision (of the better eye) due to bilateral ROP stages 3 and 4, respectively, and one had bilateral blindness due to ROP stage 4, as well as bilateral severe hearing loss treated by cochlear implants. Three had significant developmental delay while three had mild developmental delay. There were seven with bilateral ROP stage 3, only one of whom developed severe low vision. Outcomes for the two with bilateral ROP stage 4 were less favourable; one developed severe low vision and the other became blind.

Factors significantly associated with increased major neurodevelopmental disability included use of steroids postnatally (RR=7.4; 95% CI, 1.9-29.2),

TABLE 1. Characteristics of the study cohort (n=49)

Characteristic*	≤750 g† (n=17)	751-999 g† (n=32)	Total† (n=49)	Chi squared	*t*	P value
Mother's education level‡				4.530		0.30
Unknown	4 (24)	7 (22)	11 (22)			
Primary	1 (6)	2 (6)	3 (6)			
Lower secondary	6 (35)	6 (19)	12 (24)			
Higher secondary	5 (29)	17 (53)	22 (45)			
Tertiary	1 (6)	0 (0)	1 (2)			
Birth weight (g)	649±81	863±66	789±125		-10.01	<0.001
Gestational age (weeks)	25.3±1.7	26.8±1.7	26.2±1.8		-2.94	0.005
Antenatal steroids‡	15 (88)	28 (88)	43 (88)	0.006		1.00
Postnatal steroids	13 (76)	10 (31)	23 (47)	9.115		0.003
IVH grade						
Grade 0	5 (30)	17 (53)	22 (45)	2.523		0.11
Grades 1-2	6 (35)	9 (28)	15 (31)	0.269		0.60
Grades 3-4‡	6 (35)	6 (19)	12 (24)	1.643		0.30
PVL‡	2 (12)	8 (25)	10 (20)	1.197		0.46
Male gender	9 (53)	15 (47)	24 (49)	0.164		0.69
Multiple births‡	0 (0)	7 (22)	7 (14)	4.339		0.08
Drug use‡	0 (0)	1 (3)	1 (2)	0.542		1.00
Mat PET‡	3 (18)	4 (13)	7 (14)	0.240		0.68
PROM >18 hours‡	1 (6)	11 (34)	12 (24)	4.874		0.04
BPD‡	15 (88)	25 (78)	40 (82)	0.757		0.47
Mode of delivery (C/S)	4 (24)	13 (41)	17 (35)	1.432		0.23
PDA present	13 (76)	17 (53)	30 (61)	2.549		0.11
PDA treatment type						
Conservative‡	2 (15)	4 (24)	6 (20)	0.305		0.67
Indocid	7 (54)	9 (53)	16 (53)	0.002		0.96
Ligation	4 (31)	4 (24)	8 (27)	0.197		0.70
Worst ROP staging						
Grade 0‡	1 (6)	4 (13)	5 (10)	0.531		0.65
Grades 1-2	6 (35)	19 (59)	25 (51)	2.576		0.11
Grades 3-4	10 (59)	9 (28)	19 (39)	4.407		0.04
Meningitis‡	0 (0)	2 (6)	2 (4)	1.108		0.54
NEC max stage						
Grade 0‡	13 (76)	28 (88)	41 (84)	0.989		0.42
Grades 1-2‡	2 (12)	1 (3)	3 (6)	1.442		0.27
Grade 3‡	2 (12)	3 (9)	5 (10)	0.069		1.00
Small for gestational age	6 (35)	9 (28)	15 (31)	0.269		0.60
VP shunt‡	0 (0)	2 (6)	2 (4)	1.108		0.54

* IVH denotes intraventricular haemorrhage, PVL periventricular leukomalacia, Mat PET maternal pre-eclampsia, PROM premature rupture of membranes, BPD bronchopulmonary dysplasia, C/S caesarian section, PDA patent ductus arteriosus, ROP retinopathy of prematurity, NEC necrotising enterocolitis, and VP ventriculoperitoneal

† Data are shown in No. (%) or as mean±standard deviation

‡ Fisher's exact test was used

intraventricular haemorrhage (IVH) grade 3 or 4 (RR=2.7; 95% CI, 1.2-5.9), periventricular leukomalacia (PVL) [RR=4.5; 95% CI, 2.1-9.3], presence of patent ductus arteriosus (PDA) treated by ligation (RR=2.8; 95% CI, 1.3-6.1), ROP grade 3 or 4 (RR=2.4; 95% CI, 1.0-5.6), and presence of necrotising enterocolitis (NEC) grade 3 (RR=3.2; 95% CI, 1.6-6.3). Delivery by caesarean section was associated with a lower percentage of major disabilities (RR=0.3; 95% CI, 0.1-1.1) [Tables 4 and 5].

TABLE 2. Neurological and sensory outcomes according to birth weight category

Findings*	No. (%) of patients			Chi squared	P value
	≤750 g (n=17)	751-999 g (n=32)	Total (n=49)		
Cerebral palsy	1 (6)	5 (16)	6 (12)	0.9807	0.65
Hearing impairment	0 (0)	2 (6)	2 (4)	1.1077	0.54
Intellectual impairment	4 (24)	4 (13)	8 (16)	0.9886	0.42
Vision impairment	2 (12)	1 (3)	3 (6)	1.4418	0.27

* Fisher's exact test was used

TABLE 3. Birth weight and outcomes in patients with major neurodevelopmental disability (n=15)

Birth weight (g)	Sex	Hearing	Vision	Cerebral palsy	Intellectual impairment
830	M	N*	N	N	Mild delay
680	F	N	N	N	Mild delay
787	F	N	N	Spastic quadriplegia	Significant delay
860	M	Significant hearing loss	Blindness	N	Borderline delay
760	F	Moderate-to-severe hearing loss	N	Left lower limb monoplegia	Borderline delay
720	M	Mild hearing loss	N	Mixed spastic-dyskinetic	Mild delay
905	F	N	N	Spastic diplegia	N
652	M	N	Severe low vision	N	Borderline delay
750	M	N	Severe low vision	N	N
613	F	Mild hearing loss	N	N	Mild delay
900	M	N	N	Dyskinetic	Significant delay
824	M	N	N	N	Significant delay
550	M	N	N	N	Significant delay
540	F	N	N	N	Significant delay
950	F	N	N	Right hemiplegia	N

* N denotes normal

Regarding the 11 infants who had defaulted from the High Risk Follow-up Program, four had migrated overseas and four had defaulted completely without hospital follow-up. Thus, no outcome data were available for these patients. The remaining three were being regularly followed up at the hospital neonatal subspecialty out-patient clinics, and had no major neurodevelopmental disability.

Regarding the 21 infants who died before reaching the age of 2 years, 15 (71%) had birth weights of 750 g or lower (<600 g [n=8], 600-700 g [5], 701-750 g [2]), while six (29%) weighed between 751 and 999 g. Among the 17 (81%) infants who died before discharge, 14 had birth weights of 750 g or lower, and three between 751 and 999 g. One of these (weighing 660 g) had multiple congenital anomalies including an encephalocele and the other (weighing 913 g) had an encephalocele. Of the four infants who died after discharge, one (weighing 910 g) had spastic quadriplegic cerebral palsy, hydrocephalus, and chronic lung disease, one (weighing 790 g) had short gut syndrome resulting from NEC, one (weighing 730 g) had sepsis, and one (weighing 550 g) had sudden infant death.

Discussion

This was a multicentre, prospective study of the outcome at 30 to 36 months in a cohort of 49 ELBW infants born between 2001 and 2002 in three major hospitals in Kowloon. Analysis was carried out by dividing the children into two subgroups according to birth weights: 750 g or lower versus between 751 and 999 g.

A total of 69% of the babies in our cohort were assessed to have normal neurological (including neurosensory) development. The overall incidence of cerebral palsy was 12%, which is similar to figures ranging from about 7 to 15% described by others,[14,15] but superior to Vohr et al's study[16] that reported an incidence of 17%.

Our incidence of significant visual impairment (6% blind) and hearing impairment for which hearing aids were provided (4%) was higher than those described in other studies (3% blind and 3% requiring hearing aids).[14,15]

In our cohort, 16% of the children had significant developmental delay compared to 37% reported by Vohr et al.[16] We have noted that postnatal

TABLE 4. Major disability according to prevailing demographic features and risk factors

Intervention/risk factor*	Major disability not found† (n=34)	Major disability found† (n=15)	Total† (n=49)	Chi squared	*t*	P value
Mother's educational level‡				7.022		0.13
Unknown	5 (15)	6 (40)	11 (22)			
Primary	3 (9)	0 (0)	3 (6)			
Lower secondary	7 (21)	5 (33)	12 (24)			
Higher secondary	18 (53)	4 (27)	22 (45)			
Tertiary	1 (3)	0 (0)	1 (2)			
Birth weight (g)	804±122	755±128	789±125		1.29	0.20
Gestational age (weeks)	26.4±1.6	25.8±2.0	26.2±1.8		1.17	0.25
Antenatal steroids‡	30 (88)	13 (87)	43 (88)	0.024		1.00
Postnatal steroids	10 (29)	13 (87)	23 (47)	13.699		<0.001
IVH grade‡				5.749		0.03
Grades 3-4	5 (15)	7 (47)	12 (24)			
PVL‡	2 (6)	8 (53)	10 (20)	14.428		<0.001
Male gender	16 (47)	8 (53)	24 (49)	0.164		0.69
Multiple births‡	6 (18)	1 (7)	7 (14)	1.025		0.41
Drug use‡	0 (0)	1 (7)	1 (2)	2.314		0.31
Mat PET‡	6 (18)	1 (7)	7 (14)	1.025		0.41
PROM >18 hours‡	8 (24)	4 (27)	12 (24)	0.055		1.00
BPD‡	26 (76)	14 (93)	40 (82)	1.974		0.24
Mode of delivery (C/S)	15 (44)	2 (13)	17 (35)	4.353		0.04
PDA present	18 (53)	12 (80)	30 (61)	3.210		0.07
PDA treatment type‡				5.568		0.03
Ligation	2 (11)	6 (50)	8 (27)			
Worst ROP staging				4.104		0.04
Grades 3-4	10 (29)	9 (60)	19 (39)			
Meningitis‡	0 (0)	2 (13)	2 (4)	4.726		0.09
NEC max stage‡				6.394		0.03
Grade 3	1 (3)	4 (27)	5 (10)			
Small for gestational age‡	13 (38)	2 (13)	15 (31)	3.039		0.10
VP shunt‡	1 (3)	1 (7)	2 (4)	0.369		0.52

* IVH denotes intraventricular haemorrhage, PVL periventricular leukomalacia, Mat PET maternal pre-eclampsia, PROM premature rupture of membranes, BPD bronchopulmonary dysplasia, C/S caesarian section, PDA patent ductus arteriosus, ROP retinopathy of prematurity, NEC necrotising enterocolitis, and VP ventriculoperitoneal

† Data are shown as No. (%) or mean±standard deviation

‡ Fisher's exact test was used

TABLE 5. Relative risk of major disability according to interventions and risk factors

Intervention/risk factor	Relative risk	95% Confidence interval
Postnatal steroids	7.4	1.9-29.2
IVH grades 3-4	2.7	1.2-5.9
PVL	4.5	2.1-9.3
PDA ligated	2.8	1.3-6.1
ROP grades 3-4	2.4	1.0-5.6
NEC grade 3	3.2	1.6-6.3
Mode of delivery (C/S)	0.3	0.1-1.1

* IVH denotes intraventricular haemorrhage, PVL periventricular leukomalacia, PDA patent ductus arteriosus, ROP retinopathy of prematurity, NEC necrotising enterocolitis, and C/S caesarian section

steroid treatment, grades 3 to 4 IVH, PVL, PDA treated by ligation, stages 3 to 4 ROP, and grade 3 NEC were associated with increased risks for major disabilities. These findings are in accord with the study by Vohr et al.[16] In that study, bronchopulmonary dysplasia (BPD) was associated with major disability but this was not evident in our cohort in which 40 (82%) of the babies had BPD. The mechanism by which postnatal steroid use affects neurodevelopment remains unclear. Animal models suggest a direct toxic effect.[17,18] Postnatal steroids have been associated with impaired cerebral cortical growth, a higher risk for cerebral palsy, and adverse neurodevelopmental outcomes.[19,20]

The study by Yeh et al[21] indicated that postnatal steroids had adverse effects on the physical and neurodevelopmental outcomes of preterm infants at school age. The dexamethasone-treated group had significantly smaller head circumferences, poorer visual-motor integration as well as motor skills and coordination. The full IQ scores, verbal IQ scores, and performance IQ scores were also significantly lower in the dexamethasone-treated group. As postnatal steroid treatment is associated with significant short- and long-term adversity, the American Academy of Pediatrics has offered recommendations on such use in the treatment and prevention of BPD.[22] Thus, routine use of dexamethasone for the prevention and treatment of BPD is not recommended; treatment should be limited to exceptional clinical circumstances (eg infants with BPD in receipt of maximal ventilatory and oxygen support).

In our study, grades 3 to 4 IVH and PVL were associated with an increased risk for major disability outcome. Infants with grades 3 to 4 IVH and PVL were 1.7 and 3.5 times more likely to suffer major disability, respectively. This observation was consistent with findings from other studies.[16,23,24] Significant IVH and onset of subsequent PVL indicate a profound cerebral insult with neurodevelopmental sequelae. In these extremely premature infants whose cerebral autoregulation is not yet well developed, measures to avoid abrupt alterations in cerebral blood flow and pressure are recommended, so as to minimise the risk of IVH. Such measures include avoidance of asynchrony in mechanical and spontaneous breathing, prevention of rapid infusion of colloids, and prompt correction of metabolic derangements like hypoxia, hypercarbia, and hypocarbia. Endotracheal suctioning should also be gentle. Moreover, regular bedside ultrasound scanning of the brain since early postnatal age is essential in the screening and follow-up of the ELBW babies.

Babies with PDAs requiring ligation were also associated with worse neurodevelopmental outcomes. These babies were usually more haemodynamically disturbed in the early neonatal period and underwent more prolonged periods of ventilation with suboptimal nutrition due to the use of fluid restriction. Thus, they may have been at higher risk of brain insult and hence poorer neurodevelopmental outcomes.

Our study showed that infants with stages 3 to 4 ROP were 1.4 times more likely to endure major disability than those without. Two infants with stage 4 ROP subsequently developed severe low vision and blindness. Among the eight with stage 3 ROP, seven had normal visual function on follow-up. Thus, even most infants with stage 3 ROP appeared to have a good visual prognosis. Lately, laser treatment has been recommended at earlier stages of ROP.[25] Ongoing high-risk follow-up studies of ELBW infants born after 2003 may help to confirm whether significant visual impairment is reduced after early use of laser therapy in those with severe ROP.

As in our study, Vohr et al[16] showed that NEC was one of the risk factors associated with abnormal neurological development and a low Bayley Psychomotor Developmental Index. Though the pathophysiology of NEC is not yet clearly understood, it appears that inflammatory mediators associated with bacterial invasion lead to vasoconstriction, and that the resulting ischaemic events may play a role.[26] Surgical intervention, longer hospital stay, and prolonged parenteral nutritional requirement could be contributing factors.[26]

In our study, babies delivered by caesarean section had a lower risk for major neurodevelopmental disability, but the significance of this observation is doubtful, because the 95% CI overlapped unity. Obstetricians have to balance the benefits and risks to the mother and foetus before deciding the mode of delivery. For babies with no major neurodevelopmental disabilities, only longer-term follow-up can reveal whether minor co-morbidities develop when they reach primary school age.

A limitation of this study was the relatively small number of ELBW infants in our sample. Although we were able to identify risk factors for major disability, we were unable to infer causative relationship due to the small cohort size. Moreover, owing to the wide 95% CIs we encountered, our estimates of effect size for each potential risk factor lacked precision. However, our information was useful in that it served as an example of how collaborative research could be conducted among teams from different hospitals and child assessment centres. Further collaborative ELBW outcome studies involving all the neonatal units in the hospitals of Hong Kong are worth pursuing. These could provide representative local statistics for Hong Kong, and facilitate comparison of relevant findings with other Asian countries and elsewhere.

Conclusion

Despite the small size of our cohort, our findings are quite similar to those reported in overseas studies involving much larger numbers of ELBW babies. As the survival of these babies has improved, health care providers must become aware that these children are at increased risk of neurological (including sensory), developmental, and functional morbidity. All ELBW babies must be carefully monitored for developmental outcome after discharge, so as to ensure early detection of any disabilities and recourse to appropriate early interventions.

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