Developmental problems in very prematurely born children

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ABSTRACT

INTRODUCTION: The aim of the present study was to describe the developmental outcome of routine follow-up assessments at the age of five years in a regional cohort of children born at a gestational age < 32 weeks and to investigate neonatal risk factors associated with developmental problems.

MATERIAL AND METHODS: The cohort consisted of 237 infants with a gestational age ≥ 24 and < 32 weeks born in the 1996-2000 period. The children were assessed using the Movement Assessment Battery for Children and Miller Assessment for Preschoolers. The presenting clinical and demographic features were investigated for their association with developmental problems at five years of age by determining odds ratios in univariate analysis. The results are given with 95% confidence intervals.

RESULTS: 14% died. 86% of the surviving children were routinely assessed at five years of age. 40% of the children had a normal developmental outcome, 41% were to be observed for developmental deficiencies and 19% had developmental deficiencies. Male gender, low social group, a gestational age < 28 weeks, sepsis, persistent ductus arteriosus, bronchopulmonary dysplasia and abnormal cerebral ultrasound were significantly associated with an unfavourable developmental outcome.

CONCLUSION: More than half of the assessed very prematurely born children had developmental problems at five years of age. Children who were to be observed for developmental deficiencies outnumbered children with deficiencies at a two to one ratio. Follow-up assessments of very prematurely born children are still needed to evaluate changes in neonatal practise and developmental outcome in the future.

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In Denmark, figures from the Danish National Birth Registry show a rise in prematurely born infants from 5.1% in 1990 to 7.2% in 2004. In the same period, studies have shown that the mortality rate has fallen while morbidity has remained largely unchanged [1]. Studies of very prematurely born children, i.e. at a gestational age < 32 weeks, show that 20-50% of these children develop some form of developmental deficiency [2]. Other studies have shown a need for follow-up on these children well into their primary school years [3]. Several studies have focused on different risk factors in order to understand developmental problems in prematurely born children: gestational age (GA) [4], gender [5], abnormal cerebral ultrasound [4], bronchopulmonary dysplasia (BPD) [2, 6], sepsis [7] and the parents' social status [8, 9]. At Aalborg Hospital, we have made routine follow-up assessments of very prematurely born children with a gestational age < 32 weeks from discharge until five years of age since 1996. The aim of the present study was to describe the developmental outcome at five years of age in a regional cohort of very prematurely born children and to identify neonatal risk factors associated with developmental problems.

MATERIAL AND METHODS

Participants

The cohort consists of all live births with a GA ≥ 24 and < 32 weeks in the County of North Jutland, Denmark within the catchment area of Aalborg Hospital during the period from 1 January 1996 to 31 December 2000. The study was approved by the Danish Data Registration Committee.

Procedures

At five years of age, the children were assessed at the outpatient clinic of Aalborg Hospital according to the routine follow-up assessment program for very prematurely born children. Assessment was carried out by experienced physiotherapists and occupational therapists who are trained in the use of the test manuals available for even and precise assessment . After all the children in the birth cohort for a given year had been assessed at five years of age, they were categorized by the same physiotherapist and occupational therapist according to their developmental outcome within the following areas: gross motor function, fine motor function, perception, cognition and behaviour. They were divided into three categories. Category 1 contained children with a normal developmental outcome corresponding to their age. Category 2 contained children under observation for developmental deficiencies, i.e. children with slight deficiencies in 1-3 areas compared with a normal

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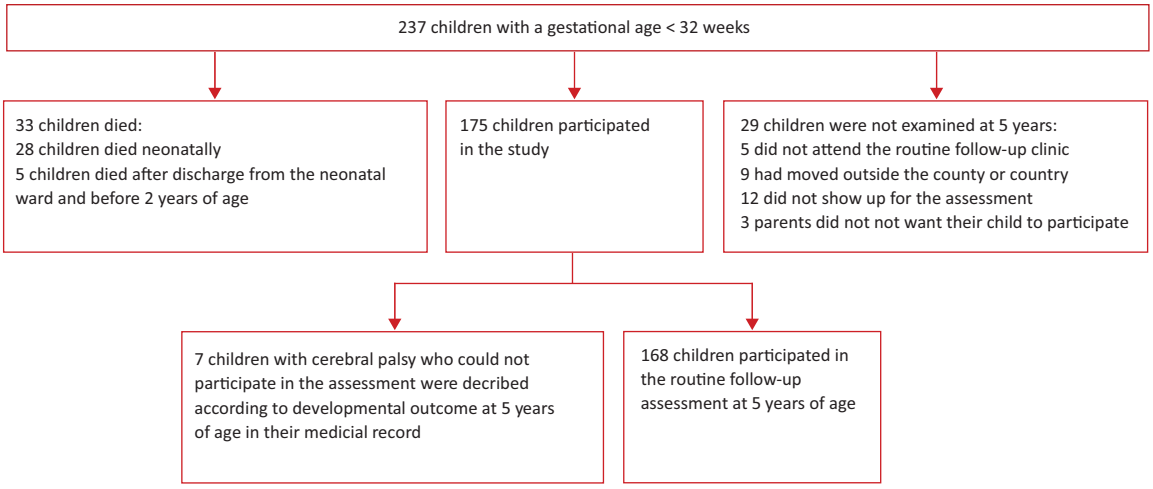
FIGURE 1

Cohort of very prematurely born children, i.e. gestational age < 32 weeks.



developmental outcome and who needed suggestions for stimulation, but otherwise had no further need for supportive measures. Category 3 contained children with developmental deficiencies, i.e. moderate to severe developmental deficiencies in more than two areas compared with a normal developmental outcome and in need of extra or extensive supportive measures. The developmental categories were defined in connection with a quality assessment project in 2002.

This project involved children born very prematurely in the County of North Jutland from 1995-1997 [10]. The categorization from the quality assessment project has since been used to define subsequent birth cohorts. Children with cerebral palsy (CP) who could not be candidates for assessment were categorised according to the assessment in their medical charts at five years of age. In order to distinguish between children who had a normal developmental outcome corresponding to their age and those who had not, we use the term developmental problems which refer to children placed in categories 2 and 3.

Measures

Motor function was examined using the Movement Assessment Battery for Children (MABC) [11]. MABC measures three items in the area of manual dexterity, two items in the area of ball skills and three items in the area of balance.

The items were scored from zero to five, where zero was the optimum score. The test is standardized and the scores are presented in relation to the 5th and the 15th percentile in the reference group. A score above the 15th percentile shows normal motor skills. A score between the 5th and the 15th percentile indicates need for observation for motor function deficit, and a score under the 5th percentile indicates a motor function deficit. MABC is a validated method [11].

Preschool skills were assessed using the cognitive parts of the Miller Assessment for Preschoolers (MAP) [12] with four items in the cognitive verbal area, five items in the cognitive non-verbal area and four items in the combined motor and cognitive area.

MAP is standardized and the scores are presented in relation to two different percentiles within the three areas and administered by colours according to the manual: green shows normal preschool skills, yellow indicates observation for deficit in preschool skills and red indicates a deficit in preschool skills. The MAP is a validated method [12].

Neonatal data and data on the parents' social group were obtained from Neobase forms and medical records. Neobase forms contain neonatal data on all newborn infants who are admitted to neonatal units in Denmark. BPD was defined as oxygen dependency 36

ABBREVIATIONS

BPD = bronchopulmonary dysplasia
BW = birth weight
CP = cerebral palsy
CI = confidence intervals
DISCO-88 = Danish International Standard Classification of Occupation
GA = gestational age
ISCED = International Standard Classification of Education
ISCO-88 = International Standard Classification of Occupation
IVH = intraventricular haemorrhage
MABC = Movement Assessment Battery for Children
MAP = Miller Assessment for Preschoolers
NEC = Necrotic enterocolitis
OR = odds ratio
PDA = persistent ductus arteriosus
PVL = periventricular leucomalacia
SGA = small for gestational age

weeks postmenstrually. Necrotic enterocolitis (NEC) was verified by X-ray and/or surgery. Infants with persistent ductus arteriosus (PDA) had clinical symptoms and were verified by echocardiography. Sepsis was verified by positive blood culture or defined as symptoms plus C-reactive protein > 50 mg/l.

The parents' social group were recorded according to the Danish International Standard Classification of Occupation (DISCO-88) , which is the official Danish version of the International Standard Classification of Occupation (ISCO-88) [13]. DISCO-88 uses ten main groups, which can be classified into four levels of education in relation to the International Standard Classification of Education (ISCED) [14]. Social group four has the highest level of education and social group one the lowest level.

Statistical analysis

All data were related to the developmental categories at five years of age. Considering the size of the study material, we reduced the data to 11 clinical and demographic features according to the following considerations: birth weight (BW) correlates with the gestational age (GA) and small for gestational age (SGA), so by choosing GA and SGA, we considered BW to be represented. Intraventricular haemorrhage (IVH) grades III & IV, and periventricular leucomalacia (PVL) have been combined under the term "abnormal cerebral ultrasound". As the only child with NEC also had sepsis, NEC was included in the term sepsis. BPD, PDA, gender, birth, Apgar score after five minutes and social group were selected as representative data. The children were divided into two groups: "normal" = category 1 and "developmental problems" = categories 2 and 3.

The presenting clinical and demographic features were investigated for association with developmental problems at five years of age by determining odds ratios (OR) in univariate analysis of 175 children. The results are given as OR with 95% confidence intervals (95% CI).

Trial registration: not relevant.

RESULTS

From 1 January 1996 to 31 December 2000, a total of 18,809 children were born in the County of North Jutland. In all 237 children with a GA ≥ 24 and < 32 weeks were born within the catchment area of Aalborg Hospital. Among these, 14% died. Twenty-eight infants died before discharge from the neonatal ward for the following reasons (number of infants): congenital malformations (4), asphyxia (2), RDS (4), pulmonary haemorrhage (5), BPD (1), IVH (1), sepsis (5), NEC (3), hydrops (1), haemorrhagic disorder (1) and immaturity (1). Five children died after discharge from the neonatal ward and before the age of 2 years: congenital malformations (1), BPD (1), pneumonia (1), sudden infant death syndrome (1) and neuroblastoma (1). A total of 204 children survived, of whom 86% were routinely assessed at five years of age. The cohort is shown in **Figure 1**.

The average GA was 29 weeks (range 24-31) and the average BW was 1,298 g (range 534-2,490). Further clinical and demographic data were: number (%): GA < 28 weeks: 37 (21); multiple birth: 52 (30); SGA: 38 (22); male gender: 99 (57); Apgar score ≤ 7/5 min: 17 (10); sepsis: 31 (18); RDS: 67 (38); IVH III+IV/PVL: 15 (9); IVH 0-II: 160 (91); BPD: 19 (11); PDA: 18 (10); social group 4: 24 (14); social group 3: 19 (11); social group 2: 94 (51); social group 1: 29 (17); missing social group: 8 (5).

Table 1 features the distribution of the 168 children at the age of five years in the MABC test. According to the MABC, there were more children with problems in the area of ball skills than in the areas of manual dexterity and balance. According to the MAP test, more children had problems in their cognitive verbal area than in

TABLE 1

Distribution of 168 children according to Movement Assessment Battery for Children and Miller Assessment for Preschoolers at five years of age. The values are n (%).

	Normal[a]		Observation[b]		Deficits[c]	
Test/developmental skills	> 15 percentile	green	> 5 and ≤ 15 percentile	yellow	≤ 5 percentile	red
MABC (motor function)						
Total	107 (64)	–	31 (18)	–	30 (17)	–
Manual dexterity	135 (80)	–	15 (9)	–	18 (11)	–
Ball skills	86 (51)	–	59 (35)	–	23 (14)	–
Balance	118 (70)	–	33 (20)	–	17 (10)	–
MAP (preschool skills)						
Cognitive verbal skills	–	127 (76)	–	23 (14)	–	18 (11)
Cognitive non verbal skills		151 (90)	–	11 (7)	–	6 (3)
Combined cognitive and motor skills	–	135 (80)	–	21 (13)	–	12 (7)

MABC = Movement Assessment Battery for Children; MAP = Miller Assessment for Preschoolers.
a) Children with normal motor function and preschool skills according to their age; b) Children with uncertain motor function and preschool skills according to their age; c) Children with deficit within motor function and preschool skills according to their age.

Out into the world.

TABLE 2

Clinical factors and events associated with developmental problems at five years of age in 175 children (univariate analysis).

	Development		
	normal, % (n = 70)	problems, % (n = 105)	OR (95% CI)
Gestational age < 28 weeks	13	27	2.46 (1.08-5.61)
Singleton birth	64	74	1.71 (0.89-3.28)
Small for gestational age	21	22	1.03 (0.49-2.14)
Gender: boy	40	68	3.13 (1.67-5.88)
Asphyxia (Apgar score ≤ 7/5 min)	7	11	1.68 (0.56-4.99)
Septicaemia	9	24	3.33 (1.29-8.62)
Respiratory distress syndrome	37	39	1.08 (0.58-2.02)
Bronchopulmonary dysplasia	3	16	6.57 (1.47-29.41)
Abnormal cerebral ultrasound	3	12	4.80 (1.05-22.00)
Persistent ductus arteriosus	1	16	13.33 (1.73-102.65)
Social class group 1 (lowest)	6	24	5.25 (1.73-15.89)

CI = confidence interval; OR = odds ratio.

their cognitive non-verbal area and the combined motor and cognitive area. The average age was 5.1 years (range 4.5-5.5).

At five years of age, 40% of the children (n = 70) had a normal, age-equivalent developmental outcome (category 1), 41% (n = 72) were to be observed for developmental deficiencies (category 2) and 19% (n = 33) had developmental deficiencies (category 3), i.e. 60% of the children had developmental problems (categories 2 and 3). Eleven out of 33 children in category 3 had CP.

The risk factors male gender, low parental social group, GA < 28 weeks, PDA, sepsis, BPD and abnormal cerebral ultrasound were statistically significantly associated with developmental problems. Odds ratios are shown in **Table 2**.

DISCUSSION

In our study, 14% of the very prematurely born children died. The causes of death before discharge from the neonatal ward, and death incidences were in the expected range [1, 2]. 60% of the assessed 175 very prematurely born children had developmental problems at the routine follow-up assessment at five years of age, with twice as many children under observation for developmental deficiencies (41%) as children with actual developmental deficiencies (19%). This is consistent with other studies which have found that 33-61% of the very prematurely born children have developmental problems [2, 8].

According to the MABC test, 64% of the children in our study had normal motor function, 18% were unsure in the area of motor function and 17% had a motor function deficit. These results are in agreement with other studies [2, 15]. The average score in the MABC test in our study corresponded to the 32nd percentile, while in three other studies using the MABC test, it corresponded to the 21st percentile [2] and to the 42nd percentile [16, 17]. In relation to the individual areas in the MABC test, we found more children with difficulties in the area of ball skills, while Johnson et al [17] found more children with difficulties in the area of balance, and Davis et al [16] more children in the area of manual dexterity. These differences may be due to national differences in the way children play, their activities and social status. According to the MAP test, cognitive deficits were evident in the cognitive verbal area.

A limitation of the study is that we had no control group. The MABC and MAP tests are not standardized for Danish children, and our study would have had a higher credibility if we had included a control group. This fact is supported by Marlow et al [18], who highlight the importance of a control group in the sense that they found a greater degree of developmental problems compared with a control group (41%) than with standard test values (21%). The physiotherapists and the occupational therapists did not have the children's medical records at the time of the assessments, but they were not blinded, which is another limitation.

Male gender, low parental social group, GA < 28 weeks, PDA, sepsis, BPD and abnormal cerebral US were identified as risk factors that negatively affected developmental outcome. Identical risk factors were found in other studies [2, 4-9].

Many different factors in a child's life influence their developmental outcome in terms of motor function and cognitive skills, both positively and negatively. We have explored neonatal clinical factors and the parents' social group, but we have not assessed family structure, the child's environment, or how the surroundings meet the child's needs. The surroundings appear to be more important for the child's development than the neonatal factors as the child grows older, and family factors are believed to have a greater influence on learning at school than perinatal complications [8, 9].

In conclusion, more than half of the assessed very prematurely born children had developmental problems, and children observed for developmental deficiencies outnumbered children with deficiencies two to one. Developmental problems were significantly associated with the risk factors male gender, low parental social group, GA < 28 weeks, PDA, sepsis, BPD and abnormal cerebral ultrasound at five years of age. It would be interesting to investigate how to improve developmental outcome and to examine if there are certain interventions that may shape the child's development, both in the long term and with regard to the child's schooling. It is relevant to continue with follow-up assessments of very prematurely born children in order to

evaluate their developmental outcome and their needs for intervention in the future and to evaluate the effect of changes in neonatal and obstetric practice over time.

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