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Short-term Outcome of Perinatal Care in a Swedish County

Mortality, neonatal intensive care and overall evaluation of neuromotor function at 0–10 months of corrected age in preterm and term infants

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Abstract

Improvements in obstetrical and neonatal care during the last decades have led to a marked increase in survival rate of preterm and term infants. In order to study the short- and long-term outcome in infants who survived neonatal intensive care (NIC) and were born in the county of Uppsala between January 1st 1986 and April 30th 1989, a prospective long-term follow-up study was conducted.

Epidemiological data on all infants born in the county during the study period and the short-term outcome, measured as overall neuromotor function at term and at 2, 4, 6 and 10 months of corrected age in 245 infants surviving NIC and 72 healthy control infants are presented. The infants' neuromotor function was evaluated with different clinical neurological methods.

In the study population of NIC infants 85.9% survived the neonatal period. The early infant mortality was high in this group 11.6% compared to that of all infants born in the county of Uppsala (0.30%). Only a minority of the infants showed abnormal neuromotor function. A comparison of the results of the overall evaluation of neuromotor function at 10 months of age with those of the examinations made at an earlier age showed poor correspondence in individual infants, especially in preterm and very preterm infants.

INTRODUCTION

In the last decades there has been a sharp decline in perinatal mortality, largely as a result of improved survival rates of low birth weight and preterm infants (10, 21, 48, 49, 50). During the same period new intensive care techniques have become available for the treatment of

neonatal diseases with a high neonatal mortality. Examples of these are new ventilatory techniques (25, 46, 47) and surfactant replacement therapy (14, 27, 28).

Improvements in obstetrical care have not yet reduced the incidence of preterm birth or intrauterine growth retardation and the stillbirth rate has been only marginally affected. On the other hand, better maternity care, monitoring of risk deliveries and timing of obstetrical interventions have resulted in lower morbidity in preterm infants and in infants of high risk mothers, and a reduction in the proportion of high risk deliveries (8, 30). Later, the use of antenatal steroids has lowered the incidence and severity of respiratory distress syndrome (6, 28, 34).

The marked rise in survival rates has led to increased concern regarding long-term morbidity among survivors (19, 21, 22, 23, 35, 45, 51, 57). Major handicaps such as severe CP syndromes are usually diagnosed within the first year of postnatal life (39, 51), whereas it is more difficult to diagnose moderate and minor problems in motor performance, perception, co-ordination, concentration, speech development and cognitive functions at an early stage (4, 31, 33, 38, 39).

Follow-up data have often been focused on outcome measures based on crude statistics, such as mortality and morbidity. These are important for follow-up studies, as the mortality rate and early morbidity have a great impact on the definition of a study population and the proportion of liveborn infants left for follow-up examinations. The main causes of bias in follow-up studies are retrospective study designs, hospital-based studies without an epidemiological description of the studied population, insufficient study samples and lack of control groups. Specific demands should be placed concerning infants entering a follow-up study, so that it is known from which population they are recruited, that they meat certain entry criteria and that specific information about their perinatal intensive care is documented prospectively (15, 36).

The aim of the present study was to record the perinatal mortality among all births in the county of Uppsala, Sweden, during a defined period of time and to evaluate the short-term outcome in infants surviving neonatal intensive care (NIC). Collection of data in these infants was started before the introduction of antenatal steroids and the use of surfactant replacement therapy during NIC. Together with a control group of neonatally healthy infants, the surviving infants were included in a follow-up study, which is planned to continue until the age of 10 years. The study population is described in detail and the short-term outcome is presented in terms of an overall evaluation of neuromotor function at a corrected postnatal age of 10 months. In addition, the grading of the infant's neuromotor function at 0, 2, 4 and 6 months, as normal, possibly abnormal or abnormal was compared with that at 10 months.

MATERIAL

The county of Uppsala has 280,000 inhabitants and its population is slightly younger and has a slightly higher mean educational level than the Swedish population as a whole. There is only one delivery unit and one neonatal unit in the county. Of all deliveries, 99.9% take place in the University Hospital. To cover the whole infant population of the county of Uppsala, women living in the county but who had delivered a child in a hospital outside this county were traced and their infants (n=3) were included in the study population.

During the study period January 1st 1986 to April 30th 1989, 12,187 infants were delivered of women in the county of Uppsala; of these infants 12,141 were liveborn and 46 stillborn. A total of 311 liveborn infants fulfilled one or more of the criteria of NIC.

These criteria were as follows: 1) Infants born at less than 32 completed weeks of gestation (c.w) irrespective of the remaining criteria; 2) treatment with a respirator; 3) treatment with continuous positive airway pressure (CPAP); 4) perinatal asphyxia with an Apgar score ≤4 at 5 minutes; 5) neonatal convulsions treated with continuous intravenous anticonvulsive drugs; 6) total parental nutrition in the neonatal period.

The infants who fulfilled the criteria of NIC were divided into three groups:

Group I - very preterm infants born at 23-31 c.w.

Group II - moderately preterm infants born at 32-36 c.w.

Group III - infants born at term, i.e. 37 c.w., who needed NIC.

To fulfil the criteria of a prospective follow-up study, a control group of neonatally healthy fullterm infants, group IV, was included. These control infants were matched to the infants in group I for sex and birth order (first born/later born). Characteristics of these four groups are given in Table 1. A small group of infants with congenital malformations or disorders that could have an influence on their neuromotor development survived NIC. These infants were studied as a separate group of infants with congenital malformations (IWCM).

Another 3 infants were born with Down's syndrome during the study period. These infants were excluded from the study although for a short time they needed CPAP.

Of the 311 infants who fulfilled criteria for NIC, 19 belonged to the IWCM group (table 4 and 5), which is reported separately. As 44 of the remaining infants died and the parents of three infants refused to let their infants participate, 245 infants were left for further investigations. Together with the 72 infants in the control group, altogether 317 infants were included in the follow-up study. All parents gave their informed consent and the study was approved by the Ethics Committee of the Medical Faculty of Uppsala University.

METHODS AND ASSESSMENT PROCEDURE

Data on perinatal epidemiology

From the Epidemiology Unit at the Swedish National Board of Health and Welfare, which is responsible for the Swedish Medical Birth Register, information on liveborn and stillborn infants, including their gestational age, birth weight and day of death within the first year of life, was retrieved. This register covers more than 99% of all births in Sweden (16).

From the patient records on the mother and infant at the Department of Obstetrics and Gynaecology, Uppsala University Hospital, data were collected concerning the delivery, whether the infant was liveborn or stillborn, gestational age, birth weight, birth length and Apgar score at 1 and 5 min.

From the patient records in the Neonatal Intensive Care Unit at the University Children's Hospital, data on assisted ventilation, i.e. duration on a respirator and/or of treatment with CPAP, duration of supplementary oxygen therapy and duration of hospital care until the infant was discharged home or died, were collected (Tables 1, 3 and 5).

From these data calculations were made of the perinatal mortality, early neonatal mortality, late neonatal mortality, neonatal mortality and postneonatal infant mortality.

Evaluation of gestational age

At birth the gestational age was estimated in all infants. The maturity of the infants in group I was assessed according to the method proposed by Dubowitz (13) and that of the other infants according to external criteria as described by Finnström (18). The infant's gestational age at birth was calculated from pregnancy data and/or an ultrasound examination of the foetus during pregnancy. When there was a discrepancy of more than one week concerning the date of expected birth between the two methods, the ultrasound estimation was chosen as correct, otherwise the date according to pregnancy data. In a few cases where pregnancy data and the ultrasound examination were unreliable or missing, an estimation of gestational age according to Dubowitz (13) and/or Finnström (18) was used together with the infant's birth weight and birth length, in order to assess the gestational age at birth as reliably as possible.

Methods used at the clinical examination

All infants were assessed at term or corrected term and at a corrected age of 2, 4, 6 and 10 months ± 1 week. In the following, the word 'age' always refers to corrected age, i.e. the age from the estimated due date of delivery. At every examination the protocol for Structured Observation of Motor Performance, SOMP-I (41, 42, 43), was followed together with

assessment of passive tone (44), postural reactions (55), joint extensibility (1) and motor-perception (26). At the end of each assessment an overall evaluation of the infant's neuromotor function was made and the results of this are presented in this paper. The findings at the other assessments will be reported separately.

Overall evaluation of neuromotor function

The overall evaluation of the infant's neuromotor function is based on the examiners' subjective clinical judgement of all examinations of the infant. This judgement was made in consensus by two examiners immediately after each examination. The combined results of the examinations of the infant's motor performance, muscle tone, postural reactions, joint extensibility and motor-perceptual development comprised, together with the examiners' clinical experience, the basis of the overall evaluation of the neuromotor function, which was then assessed as normal, possibly abnormal or abnormal.

Assessment procedure

All examinations were made by two investigators, one physiotherapist and one out of eight neonatologists. The main observers were one of the neonatalogists, who is also a paediatric-neurologist (BS), and the physiotherapist (KP). One of these two was always present and in most cases they performed the examinations together. All examinations took place in a warm and comfortable room either in the neonatal ward, as long as the infants needed hospital care, or in the outpatient clinic when the infants had been discharged from the hospital. The examinations were always made in a given order, which only occasionally was changed to meet the needs of the infant. Procedures that could be unpleasant were left to the end and every effort was made to keep the infant calm and co-operative. The state of the infant as described by Brazelton (9) was noted for each examination at term. At 2, 4, 6 and 10 months the infant's co-operation was graded subjectively as good, partial or none (41). The whole examination did not last more than 30 min, with a few exceptions.

Table 1. Infant data, Apgar score and ventilatory care in infants (n=245) from the county of Uppsala who survived neonatal intensive care, January 1986 – April 1989, at Uppsala University Children's hospital, Uppsala, Sweden (groups I-III) and neonatally healthy controls in the follow-up study (n=72, group IV).

Group	GA w	Birth weight g	Birth length cm	Apgar score 1 min	Apgar score 5 min	Resp. therapy (d)	CPAP (d)	Oxygen therapy (d)	Total days until discharge (d)
Group I (23-31 w)									
(n=71)	*n=71*	*n=71*	*n=65*	*n=70*	*n=66*	*n=40*	*n=65*	*n=55*	*n=71*
Mean	29	1300	39	7	8	9	22	30	77
SD	2	383	4	2	2	12	26	56	43
Median	29	1256	39	7	8	4	10	6	69
Group II (32-36 w)									
(n=86)	*n=86*	*n=86*	*n=82*	*n=86*	*n=80*	*n=14*	*n=84*	*n=52*	*n=86*
Mean	34	2379	46	7	9	2	3	2	28
SD	1	545	3	2	2	1	3	2	17
Median	34	2408	46	8	9	2	2	2	26
Group III (37-42 w)									
(n=88)	*n=88*	*n=88*	*n=81*	*n=86*	*n=82*	*n=30*	*n=78*	*n=59*	*n=88*
Mean	40	3708	52	6	7	2	2	3	14
SD	1	632	3	3	3	2	2	6	15
Median	40	3739	53	6	8	1	1	1	9
Group IV (37-42 w)									
(n=72)	*n=72*	*n=72*	*n=72*	*n=72*	*n=70*				
Mean	40	3557	51	9	10				
SD	1	408	2	0	0				
Median	40	3460	51	9	10				

GA=gestational age at birth, n=numbers of infants, d=days, CPAP=continuous positive airway pressure

Missing data

If an infant at term or at corrected term was too sick to allow a full assessment, this assessment was cancelled. A few infants were missed from the scheduled examinations at 2, 4, 6 and 10 months because of illness or inconvenience. The number of infants assessed and

the number of infants lost to examinations at the different assessment ages are shown in Table 2.

In a few cases one part of an examination was missed, mostly because of the infant's lack of co-operation or the parent's refusal, while the rest of the examination was completed. In these cases just the missing part was cancelled, but the completed parts of an examination were included in the evaluation.

Table 2. Total numbers of assessed infants at the different examination ages and numbers of lost infants at the different examination ages.

Groups		term	2 months	4 months	6 months	10 months	Total
Group I	(n=68)	2	0	0	1	1	4
Group II	(n=81)	6	4	3	3	2	18
Group III	(n=77)	31	3	7	5	7	53
Group IV	(n=72)	0	1	0	0	0	1
Total loss		39	8	10	9	10	76
Totally assessed		259	290	288	289	288	

RESULTS

Perinatal epidemiology

Of all infants born alive in the county of Uppsala between January 1st 1986 and April 30th 1989, 311 (2.6%) needed NIC as defined previously. As the parents of three infants refused to let their infant participate in the study, 308 infants were left for follow-up. Ninety infants belonged to group I, 104 to group II and 114 to group III. Of these 311 infants 44 died, resulting in a survival rate after intensive care of 85.9 %.

The number of infants born in the county of Uppsala during the study period was 12,187. Of these, 82 infants were either stillborn (46 or 3.8 ‰) or died in the early neonatal period (36 or 3.0 ‰), giving a perinatal mortality of 6.7 ‰. Of the 36 infants who died during their first week of life, 13 infants or 36% belonged to group I, 10 or 28% to group II and 13 or 36% to group III. Late neonatal death occurred in 8 infants (0.7 ‰). Of these, there were 2

each in groups II and III. The other 4 infants died from cardiac defects and were never treated in the neonatal unit.

Postneonatal death occurred in 4 infants treated in the NIC unit. Three of these belonged to group I and one to group II. Another 23 cases were reported from the Swedish National Board of Health and Welfare Epidemiology Unit as infant deaths in infants not transferred postnatally to the neonatal unit. Twelve of these infants died of sudden infant death syndrome (SIDS). In 5 cases the cause of death could not be found in the available records. Among the remaining 6 cases, the cause was a chromosomal aberration combined with a congenital heart defect in 3 cases, septicaemia in 2 and trauma in 1. Thus the infant mortality 0-365 days after birth was 5.7‰.

The study population of 311 infants fulfilling the criteria for NIC had an early neonatal mortality of 115.8 ‰ or 36 out of 311. The infants who died were distributed almost equally between the different gestational age groups, with 16, 13 and 15 in groups I, II and III respectively (Table 3). Of the deceased infants, 22 had different severe malformations or chromosomal aberrations either alone or in combination with prematurity or asphyxia. The deaths of the remaining 22 were the result of neonatal problems caused by severe asphyxia and or immaturity.

Data on infants who died during neonatal intensive care

As expected, the highest neonatal mortality was found among the infants of group I. Sixteen or 36% of the 44 who died belonged to group I. These infants also had the lowest mean birth weight, 850 ± 371 (SD) g, and the lowest mean Apgar scores, 2 at 1 min and 5 at 5 min (Table 3). Of the 44 infants who died in their first month of life, 13 or 29.5% belonged to group II. Their mean gestational age at birth was 35 ±1 (SD) c.w. and their mean birth weight 2,103 ±459 (SD) g, which meant that their mean birth weight was -1 SD from the mean of normal Swedish infants of corresponding gestational age (29). Fifteen infants or 34.1% belonging to group III died in the neonatal period. They had a mean gestational age at birth of 39 ±1 (SD) c.w. and a mean birth weight of 2,921 ±766 (SD) g. Thus, the infants in group III also had a mean birth weight of 1 SD below the mean of normal term infants (29). No difference in Apgar scores was found between the deceased moderately preterm infants and the deceased fullterm infants. However, the infants of groups I, II and III who died had a lower Apgar score at 5 min than the infants who survived NIC (Tables 1-3). The mean duration of treatment before death was much longer in group I than in groups II and III, while the median duration was one in all three groups.

Table 3. Infant data, Apgar score and ventilatory care in infants (n=44) from the county of Uppsala who died during neonatal intensive care, born January 1986 – April 1989, at Uppsala University Children's Hospital, Uppsala Sweden.

Group	GA w	Birth weight g	Birth length cm	Apgar score 1 min	Apgar score 5 min	Resp. therapy (d)	CPAP (d)	Oxygen therapy (d)	Days of treatment (d)
Group I (23-31 w)									
(n=16)	*n=16*	*n=16*	*n=9*	*n=16*	*n=15*	*n=16*	*n=2*	*n=15*	*n=12*
Mean	26	850	34	2	5	22	32	28	34
SD	2	371	2	2	2	63	42	80	88
Median	26	692	33	2	6	1	32	1	1
Mode	23			1	6	1		1	1
Group II (32-36 w)									
(n=13)	*n=13*	*n=13*	*n=12*	*n=12*	*n=12*	*n=13*	*n=13*	*n=13*	*n=13*
Mean	35	2103	45	4	6	1	0	1	8
SD	1	450	4	3	3	1	1	0	21
Median	35	2000	46	5	6	1	0	1	1
Mode	35			7	9	1	0	1	0
Group III (37-42 w)									
(n=15)	*n=15*	*n=14*	*n=11*	*n=14*	*n=14*	*n=15*	*n=15*	*n=15*	*n=15*
Mean	39	2921	49	5	5	2	1	2	3
SD	2	766	4	4	4	4	2	2	5
Median	38	2800	50	5	5	1	0	1	1
Mode	37			9	2	1	0	1	1

GA=gestational age at birth, n=numbers of infants, d=days, CPAP=continuous positive airway pressure

Data on infants surviving neonatal intensive care

Of all infants that needed treatment in the NIC unit, 245 infants without obvious congenital malformations survived, i.e. 71, 86 and 88 infants in groups I, II and III, respectively. As seen in Table 1, the mean birth weight and birth length of these 245 infants were appropriate for gestational age according to Swedish standards (29). The Apgar scores were almost the same in all groups and the mean Apgar score at 5 min did not indicate any sign of perinatal asphyxia. Almost all infants had some kind of respiratory treatment with a respirator, CPAP or supplementary oxygen and the duration of this treatment was longer in group I. As expected, the infants of group I had a longer total stay in the neonatal ward until discharge as compared with the other two groups (Table 1).

Table 4. Different malformations in the group of infants with congenital malformations (IWCM) distributed between the gestational age groups.

	Group I	Group II	Group III
Diagnose	n	n	n
Cardiac defects	1	3	
Diaphragmatic hernia			4
Cerebral malformation		2	1
Gastroschisis	1		1
Oesophageal atresia			1
Myotonic dystrophy			1
VATER syndrome			1
Renal malformation			1
Congenital hypothyroidism			1
Bilateral clubfoot	1		

Table 5. Infant data, Apgar score and ventilatory care in infants (n=19) from the county of Uppsala who had congenital malformation and survived neonatal intensive care (IWCM), January 1986 - April 1989 at Uppsala University Children's Hospital, Uppsala, Sweden

	GA	Birth weight	Birth Length	Apgar score	Apgar score	Resp. therapy	CPAP	Oxygen therapy	Total days until discharge
Group	w	g	cm	1 min	5 min	(d)	(d)	(d)	(d)
Group I (23-31 w) (n=3)	*n=3*	*n=3*	*n=2*	*n=3*	*n=3*	*n=3*	*n=3*	*n=3*	*n=3*
Mean	29	1398	38	5	7	5	26	30	78
SD	3	630	8	3	3	2	17	22	41
Median	29	1572	38	4	7	4	29	31	91
Group II (32-36 w) (n=5)	*n=5*	*n=5*	*n=4*	*n=5*	*n=5*	*n=1*	*n=5*	*n=2*	*n=5*
Mean	34	2021	44	6	8	1	1	2	58
SD	2	842	6	1	1		1	1	38
Median	33	1840	44	6	8	1	1	2	55
Group III (37-42 w) (n=11)	*n=11*	*n=11*	*n=9*	*n=10*	*n=10*	*n=8*	*n=10*	*n=9*	n=11
Mean	40	3578	53	6	8	2	4	6	28
SD	1	852	3	3	2	1	5	13	24
Median	40	3590	53	5	8	2	2	2	22

GA=gestational age at birth, n=numbers of infants, d=days, CPAP=continuous positive airway pressure

A small group of infants (n=19) born with obvious congenital malformations or diseases that could have influenced the infants' neurological development survived NIC. As seen in Table 4 this was a very heterogeneous group regarding the different congenital malformations or diseases. Data on these infants are shown in Table 5. None of them was small for gestational age according to Swedish standards (29) and all of them needed ventilatory treatment with either a respirator or CPAP, or both and most of them also received supplementary oxygen. The duration of treatment was longer in infants with a shorter gestation, as might be expected.

MORBIDITY AND COMPLICATIONS IN THE NEONATAL PERIOD

Cranial ultrasound findings in surviving infants

Ultrasound examinations of the infants' brains were performed on clinical grounds in 124 NIC infants during their first week after birth. Fifty (40%) of these infants belonged to group I, 29 (23%) to group II, 35 (28%) to group III and 10 (8%) to the IWCM group. None of the infants in group IV underwent a cranial ultrasound examination. In 22 of these early ultrasound examinations there were pathological findings of different kinds. Intraventricular haemorrhages were found in 7 infants, hydrocephalus in 3 and parenchymal echodensities in 6. In 6 further infants unspecified changes were found. Of the infants with haemorrhages, there were 3 in each of groups I and II and 1 in group III. All 3 infants with early diagnosed hydrocephalus were in group II. Five of the infants with parenchymal echodensities were in group I, and 1 in group II. The changes of uncertain aetiology were found in four infants of group I and in one infant each in group III and the IWCM group. In another 8 infants serial ultrasound examinations during the neonatal period revealed intracranial haemorrhages.

Respiratory treatment and duration of NIC

Most of the infants that needed NIC, i.e. the infants of groups I-III, required ventilatory support. In group I all but one infant needed treatment with either a respirator, CPAP or supplementary oxygen. In infants requiring assisted ventilation (n=84) this was provided with a Baby Bird respirator with a frequency of 60 breaths/min and in some cases superimposed oscillations, but antenatal steroids were not used and endotracheal instillation of surfactant was not given, as no surfactant preparation was licensed in Sweden at that time. Infants treated with CPAP (n=227) received this through nasal prongs connected to the Baby Bird respirator. The mean duration of any kind of ventilatory support was longest in infants with

the shortest gestation, as seen in Table 1, where it is shown that in group I the mean time on a respirator was 9 days ±12 SD and the mean duration of CPAP 22 days ±26 SD. As expected, the total stay until discharge from the ward was also much longer in the infants of group I than in the other two NIC groups (mean ±SD: 77 ±43 days, 28 days ±17 days and 14 ±15 days in groups I, II and III respectively).

Data on pneumothorax, extra-alveolar air leaks and bronchopulmonary dysplasia (BPD).

Of the infants given assisted ventilation (n=84), 22 or 26% had a pneumothorax. Eight of these infants belonged to group I, 2 to group II and 12 to group III. A clinical and radiological diagnosis of BPD was noted in only two respirator-treated infants, both of group I, i.e.2 out of 40 infants or 5%. The number of infants with pulmonary interstitial emphysema was low. This complication occurred in a total of 18 (21%) infants, 15 in group I, 1 in group II and 2 in group III. Nine infants born at a gestation of < 32 c.w. were oxygen-dependent at a time corresponding to 36 weeks of gestation. Only one infant needed oxygen therapy at discharge.

SHORT-TERM OUTCOME IN THE FOLLOW-UP STUDY

Overall evaluation of neuromotor function

At follow-up at 2, 4, 6 and 10 months a significantly larger proportion of neonatally healthy infants were judged to be normal compared with the infants of the three groups requiring NIC (Table 6). At term, 96% of the control group (group IV) were considered to be normal, as against 85%, 89% and 87% of groups I, II and III respectively but the difference between the control group and these groups was not significant (χ^2 =4.94; df=3; p=0.176). In group III however, 50 % of the examinations were lost at term as the infants were still in NIC, which made an assessment impossible. At 2 months, the proportion of infants judged to be normal was decreased in all groups compared with that at term. At 10 months 83% of the neonatally healthy infants in group IV were judged to be normal, compared with 55%, 62% and 74% of the NIC groups I, II and III respectively (χ^2 =15.49; df=3; p=0.001).

Few infants were judged to be abnormal at term (10%; Table 6). With age, however, the proportion of infants judged to be abnormal increased in the groups of very preterm (group I) and moderately preterm (group II) infants and reached 19% and 14%, respectively, at 10 months of age. In the term infants (group III) there was an increase in the proportion of infants judged to be abnormal especially at 4 months, but this proportion decreased to 10% at

10 months of age. At that age only one control infant was considered to show abnormal neuromotor function (Table 6).

Table 6. Overall evaluation of neuromotor function at the clinical examinations at 0, 2, 4, 6 and 10 months of corrected postnatal age in very preterm (group I), moderately preterm (group II) and fullterm infants (group III) who needed neonatal intensive care together with a group of neonatally healthy fullterm infants (group IV). The overall evaluation was graded as normal (N), possibly abnormal (P) or abnormal (A).

Age at examination	0 month		2 months		4 months		6 months		10 months	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%
Group I (n=68)	*66*		*68*		*67*		*67*		*67*	
N		85		49		57		67		55
P		15		44		28		18		25
A				7		15		15		19
Group II (n=81)	*75*		*77*		*78*		*78*		*79*	
N		89		53		60		64		62
P		9		38		31		23		24
A		1		9		9		13		14
Group III (n=77)	*46*		*74*		*70*		*72*		*70*	
N		87		53		44		60		74
P		4		38		39		26		16
A		9		9		17		14		10
Group IV (n=72)	*72*		*71*		*72*		*72*		*72*	
N		96		72		76		85		83
P		4		25		19		15		15
A				3		4				1
Kruskal Wallis test; df=3 (N/PA);	*p=.173*		*p=.022*		*p=.001*		*p=.003*		*p=.001*	

The proportion of infants assessed as being possibly abnormal at term was larger among the very preterm and moderately preterm than among the fullterm infants. At 2 months, however, there was a large increase in the number of infants considered to be possibly abnormal in all groups. Over time the numbers varied, but there was a general decrease in the number of infants judged as abnormal at 10 months in comparison with the overall evaluation at the age of 2 months.

The stability in the overall evaluation of neuromotor function as normal or abnormal in the individual infant is shown in Tables 7 and 8 respectively. Only infants who participated in all examinations, i.e. at 2, 4, 6 and 10 months, are included in this comparison. The examination at term was excluded, as many examinations were lost in infants of group III. As seen in Table 6, the neuromotor function was judged to be normal in the majority of cases in all groups and very few were judged to be abnormal.

Forty-five per cent of the neonatally healthy fullterm infants (group IV) were found to display normal neuromotor function at four out of four examinations (Table 7). This was approximately twice as many as in the very preterm (22%) and the moderately preterm infants (26%). Moreover, in the three NIC groups, compared with the control group, a considerably higher proportion of infants were never found to have normal neuromotor function.

Table 7. Number of infants (%) judged to be normal at no, 1, 2, 3 or 4 examinations during the first 10 months of corrected postnatal age in the overall evaluation of the neuromotor function. Only infants who underwent all four clinical examinations are included in the table.

Number of examinations		0/4 exam.	1/4 exam	2/4 exam	3/4 exam	4/4 exam
	n	%	%	%	%	%
Group I (n=68)	65	11	20	22	26	22
Group II (n=81)	76	18	9	15	32	26
Group III (n=77)	68	12	16	22	29	21
Group IV (n=72)	71	1	7	10	37	45

Group I = very preterm infants; Group II = moderately preterm infants; Group III = fullterm infants; Group IV = neonatally healthy fullterm infants.

As seen in Table 8, only a small percentage of the very preterm (2%) and the moderately preterm infants (5%) were judged to be abnormal on all four occasions, and none in the other two groups. However, 10 % of the term infants that needed NIC (group III) were judged to be abnormal at three out of four examinations and in this group 11 infants, or 12%, were missed at one of the scheduled examinations and therefore not included in this analysis.

Table 8. Number of infants (%) judged to be abnormal at no, 1, 2, 3 or 4 examinations during the first 10 months of corrected postnatal age in the overall evaluation of the neuromotor function. Only infants who underwent all four clinical examinations are included in the table.

Number of examinations		0/4 exam.	1/4 exam	2/4 exam	3/4 exam	4/4 exam
	n	%	%	%	%	%
Group I	(n=68) 65	75	8	5	11	2
Group II	(n=81) 76	79	9	4	3	5
Group III	(n=77) 68	75	13	2	10	
Group IV	(n=72) 71	93	6	1		

Group I = very preterm infants; Group II=moderately preterm infants; Group III = fullterm infants; Group IV = neonatally healthy fullterm infants.

In Table 9 the overall evaluation of neuromotor function at 10 months is presented as a short-term outcome in the 216 NIC infants and the 72 control infants. These 288 infants are grouped according to the examiners' judgement as being normal (n=198), possibly abnormal (n=58) or abnormal (n=32) at this age. Irrespective of the judgement at 10 months the majority of the infants were found to be normal at term except for the fullterm infants who needed NIC. In this group (group III) only 33% were judged to be normal at term but later abnormal at 10 months.

At 2 months the proportion of infants judged to show normal neuromotor function was lower in all groups regardless of the judgement at 10 months. This is most evident among the very preterm and moderately preterm infants especially in the infants who were judged to be possibly abnormal or abnormal at 10 months. In the control group the proportion of infants judged to be normal was high at all ages. Only one infant in this group was found to display abnormal neuromotor function at 10 months. In this infant the neuromotor function was judged to be possibly abnormal at term and at 4 and 6 months of age and abnormal at 2 months.

Among all NIC infants evaluated and found normal at 10 months, there was an increasing number that from 2 months onwards were evaluated as normal (Table 9). Accordingly, among those judged to be abnormal at 10 months the number of abnormal infants increased

with age. Among the infants judged to be possibly abnormal at 10 months, the results of the assessments varied between the different examination ages and there was no clear trend.

Table 9. The overall evaluation of neuromotor function at 0, 2, 4, and 6 months in very preterm (group I), moderately preterm (group II) and fullterm infants (group III) who needed neonatal intensive care and in a group of neonatally healthy infants (group IV) who were judged as normal, N (n=198), possibly abnormal, P (n=58) and abnormal, A (n=32) at 10 months of corrected age.

Age at examination		0 month				2 months				4 months				6 months				10 months
			%				%				%				%			%
Normal at 10 months																		
		n	N	P	A	*n*	N	P	A	*n*	N	P	A	*n*	N	P	A	*n*
Grupp	I	*37*	89	11		*37*	59	38	3	*36*	65	30	5	*37*	78	16	5	*37* 100
	II	*46*	91	7	2	*48*	65	33	2	*49*	82	18		*48*	85	15		*49* 100
	III	*33*	94	6		*51*	57	39	4	*51*	53	39	8	*51*	73	26	2	*52* 100
	IV	*60*	97	3		*59*	71	27	2	*60*	78	18	3	*60*	87	13		*60* 100
Possibly abnormal at 10 months																		
Grupp	I	*15*	93	7		*17*	47	53		*17*	59	35	6	*17*	65	29	6	*17* 100
	II	*19*	84	16		*18*	33	56	11	*18*	28	67	6	*19*	42	47	11	*19* 100
	III	*7*	71	29		*11*	55	27	18	*10*	30	60	10	*11*	36	46	18	*11* 100
	IV	*11*	100			*11*	82	18		*11*	73	18	9	*11*	82	18		*11* 100
Abnormal at 10 months																		
Grupp	I	*13*	62	39		*13*	15	54	31	*13*	23	23	54	*12*	33	8	54	*13* 100
	II	*10*	90	10		*11*	36	27	36	*11*	18	27	55	*11*	9	18	73	*11* 100
	III	*7*	33	67		*7*	14	71	14	*7*		14	86	*7*		14	86	*7* 100
	IV	*1*		100		*1*			100	*1*		100		*1*		100		*1* 100

DISCUSSION

Studies of mortality, morbidity and development in infants born before term and of low birth weight require clearly defined study populations, inclusion of relevant control groups and the use of well structured and standardised methods of assessment (4, 15, 17, 39). In the present ongoing follow-up study these requirements have been taken into account and the purpose of this paper is to report the perinatal mortality, the need for neonatal intensive care, the early morbidity and the short-term outcome at 10 months of age in a geographically defined population of preterm and fullterm infants who needed NIC, together with a group of neonatally healthy control infants. In addition, the evaluation of neuromotor function at 0, 2, 4 and 6 months was analysed with the infants grouped according to the judgement of this function at 10 months as normal, possibly abnormal or abnormal.

The perinatal mortality in the county of Uppsala is low, as has also been reported from the other Nordic countries (21). The figure for the county of Uppsala of 6.7 ‰ found in this study is well in accordance with the Swedish rate from 1983-86 of 6.3 ‰ presented by Hagberg in 1993 (22), but is a little higher than the figure of 5.9 ‰ from the period 1987-90 (23). The reason for this difference might be that none of the infants in this study received either prenatal steroids or inhaled surfactants. As expected, the highest neonatal mortality was found in the group of very preterm infants, in whom 37.2% died. On the other hand, this means that almost 2/3 of the infants in that gestational age group survived, which is a tremendous increase compared with reports from the early 1970s, when almost all infants in this gestational age group died (57). A great concern of neonatologists and researchers in this field however, is that little is known about the long term health condition and the incidence of sequelae in these infants.

Not all infants in this study underwent ultrasound examinations of the brain, and our figures should therefore be judged with caution. Only 15 out of 124 ultrasonically examined NIC infants, i.e. 12%, were diagnosed as having intracranial haemorrhages and in 30 of the same 124 infants pathological conditions were noted on ultrasound examination of the brain during the neonatal period.

The present study of the short-term outcome in the infants who needed NIC and in the control infants was restricted to an overall evaluation of neuromotor function, made at the end of each examination. This evaluation is primarily a clinical judgement based on the examiners' professional experience and is therefore subjective. During the examination however, both well known methods of assessment (1, 26, 44, 55) and a new method,

structured observation of motor performance (SOMP-I; 41, 42, 43) were used. Hence the overall evaluation of neuromotor function is a judgement based on a structured and detailed examination.

The results of examinations of neuromotor function during the first years of life should be interpreted with caution, in view of their uncertain predictive value (3, 12, 37, 54). In addition, at this early age, assessment methods have a limited ability to discriminate between normal and abnormal neuromotor function (20, 24, 32), especially in preterm infants (7). This was also the main reason for including a new method for assessment of motor performance in the follow-up study (42, 43). In the present study the overall judgement of neuromotor function as abnormal was made if a dysfunction was believed to be persistent, irrespective of its severity, and as possibly abnormal if a dysfunction was believed to be transient.

As expected, at 10 months of age significantly more infants in the control group were judged to be normal than in the other three groups of infants, who needed NIC. Only one of the control infants was judged to be abnormal, compared with 31 of the NIC infants. Among the latter, the highest proportion of infants with abnormal motor function was found in the very preterm group (19%) and the lowest in the fullterm group (9%). In many studies the numbers of abnormal infants have been found to be low during the first year of life but to increase with age (17, 39, 53). A follow-up study of a well defined population into school-age is therefore necessary in order to identify all kinds of impairments. At school-age, both minor and major handicaps can be more reliably assessed, but still the results vary between studies. From a review of studies of low birth weight and extremely low birth weight infants, Ornstein et al (39) reported that the increase of major handicaps varied between 6 and 12%, while minor motor impairments showed a much greater variation, with values between 20 and 69%. Hack et al (19) compared two groups of extremely low birth weight infants one born before the other after the introduction of surfactant therapy, and found a 20% increase in survival rate between the two groups but no difference in short term (20 months corrected age) neuro-developmental outcome.

The proportion of infants who were consistently judged to be abnormal was low, but it might be assumed that these infants will develop major handicaps. Only 2% and 5% of the very preterm and moderately preterm infants, respectively, were evaluated as abnormal in four out of four examinations. This is in accordance with the findings of van Zeben-van der Aa et al (56), who in a geographically defined population of infants born at a shorter gestation than 32 completed weeks found that 4.4% had major handicaps and 8.3% had minor handicaps at 2 years of age (56). In that study the handicap rate was not related to gestational

age. In our study no significant difference was found between the proportion of very preterm and moderately preterm infants judged to show abnormal neuromotor function at the different examinations. Surprisingly, none of the fullterm infants who needed NIC was judged to be abnormal at four out of four examinations but 10% of these infants were judged as abnormal at 3 out of 4 examinations. This might be due to the fact that many infants in group III were not examined at one of the five examinations performed in this study during the infants' first year of life.

A diagnosis of abnormal neuromotor function to a large degree remains unchanged with age, in contrast to early judgements of normality (5). As expected, in the present study we found that a higher proportion of healthy control infants (group IV) than of NIC infants (group I-III) were judged to be normal at term, regardless of the infant's gestational age. However, in all groups the proportion of children judged to be normal was lower at 10 months than at the examination at term (Table 9).

The differences in judgements of the performance of an individual infant between examinations at different ages might reflect two important aspects. First, the existence of transient abnormal neuromotor signs has been described in infants of different maturity, especially in preterm infants, by several authors (2, 11, 12, 37). According to Drillien (12), 60% of the studied low birth weight infants who showed transient signs normalised, 20% developed cerebral palsy and another 20% were found to have problems at a later age. This indicates that infants who show transient abnormal neuromotor signs should be followed up for several years. Secondly, knowledge about normal and abnormal development in preterm and especially very preterm infants is still limited, and many researchers have described differences in development between infants of different gestational ages (7). Because of this lack of knowledge as to normal development in these infants, there is uncertainty concerning the variability of normality, which might explain the difficulty in judging the development over time. In this study this is reflected by the fact that the majority of the preterm infants considered to be abnormal at 10 months were judged to be normal at term and none was considered abnormal.

CONCLUSIONS AND FINAL REMARKS

From this study it can be concluded that the perinatal mortality is low, and the level of neonatal morbidity seems to be in accordance with that at other regional hospitals with neonatal intensive care units. The presented results reveal that the majority of infants that need NIC survive even when born very preterm and that most of these infants show a normal

development according to an overall evaluation of neuromotor function at a corrected age of 10 months. Only a minority of the infants were considered to show abnormal neuromotor function at 2, 4, 6 and 10 months of age. A comparison of the overall evaluation of neuromotor function at 10 months with those of the earlier examinations showed a poor correspondence in each individual infant, especially in the preterm and very preterm infants. Further analysis of the data obtained with the separate methods of assessment, especially with the Structured Observation of Motor Performance in Infants (SOMP-I; 42), will be performed in order to allow a more objective and detailed description of the motor development in the studied preterm and fullterm infants.

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