

# Birth asphyxia in a Danish hospital uptake area was reduced after centralisation of deliveries

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## ABSTRACT

**INTRODUCTION:** Severe birth asphyxia is a major cause of neonatal morbidity and long-term disability and may be prevented. However, the consequences of organisational changes are rarely evaluated.

**METHODS:** A cohort study comparing morbidity and mortality for term-born infants born with severe birth asphyxia, defined as an Apgar score  $\leq 5$  at 5 min., before and after major changes in the organisation of births in a Danish district.

**RESULTS:** The study included 77 infants born in 1997-2004 and 40 infants born in 2009-2013 who were admitted to a neonatal intensive care unit with an Apgar score  $\leq 5$  at 5 min. The rate of severe birth asphyxia was 1.9 per 1,000 births in the early years and 2.5 per 1,000 births for the 2009-2013 period ( $p = 0.16$ ). Mortality in the first three years of life with severe birth asphyxia was 0.24 per 1,000 births in 1997-2004 (ten deaths) and 0.06 per 1,000 births in 2009-2013 (one death) ( $p = 0.20$ ). We observed a highly significant difference between the two periods in the proportion of infants with neonatal seizures and age at discharge after birth. The outcome of death or cerebral palsy was present in 17/77 (22%) in the early period and 3/40 (7.5%) in the more recent period ( $p < 0.05$ ).

**CONCLUSIONS:** Over a relative short time period, death and disability due to severe birth asphyxia at term decreased significantly. This improvement is most likely explained by changes in the organisation of births in the hospital uptake area, as well as in treatment

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Birth asphyxia is a medical condition resulting from deprivation of oxygen to the foetus and the newborn infant lasting long enough to cause physical harm, usually to the brain. The process of the brain injury begins with the initial insult, but may continue after resuscitation, lasting hours or days. Changes in the cerebral metabolism and resulting energy failure are observed and may persist for up to 72 hours [1, 2]. Severe birth asphyxia is a major cause of neonatal hypoxic-ischaemic encephalopathy, a condition associated with a high mortality and severe developmental disorders such as cerebral palsy [3]. A new treatment of severe birth asphyxia in term-born infants is induced hypothermia immediately after

birth or at least within six hours postnatally. The first study on neonatal cooling was published in 2005 [4]; and in 2013, a Cochrane Review based on 11 trials concluded: "Cooling reduces mortality without increasing major disability in survivors and the benefits of cooling on survival and neurodevelopment outweigh the short-term adverse effects" [5]. In conclusion, hypothermia treatment can prevent or reduce cell death (apoptosis) in the brain by changing the cerebral metabolism.

There is no commonly agreed definition of birth asphyxia, and its clinical presentation may differ. Therefore, it is difficult to compare the frequencies reported in the literature. The most commonly used definitions are based on Apgar scores and umbilical cord measurements [6, 7]. The validity of the Apgar score has been questioned, but the association between a low Apgar score and cerebral palsy and school performance has been documented in population-based studies in Norway and Sweden [8, 9].

Focussing on prevention of birth asphyxia is important for healthcare systems. In Denmark, two initiatives have been in place over the past ten years: centralisation of births including the closure of a number of small delivery units, and implementation of the initiative "Sikker Fødsel" (Safe Births) [10] at all delivery units including training exercises for staff and standardised care across hospitals. Hypothermia treatment for neonates with severe birth asphyxia was introduced in 2006 at Rigshospitalet, Copenhagen, and subsequently, in 2008, at Odense University Hospital, the referral hospital for Kolding Hospital for hypothermia treatment [11].

In the former Vejle County, there were four maternity units up to 2003 one of which was located at a hospital (Kolding) that had a neonatal intensive care unit (NICU). Infants born outside Kolding with immediate need of specialised neonatal care had to be transported for up to 45 min. In 2003-2006, two maternity units were closed and one maternity unit was moved administratively to another region. In the same period, a specialised transport system for severely ill neonates was implemented.

Surveillance of the consequences following structural changes in the healthcare system is very important, but is only conducted infrequently. The aim of the present study was to compare the prevalence of severe

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 TABLE 1

Background data for the two groups of infants with severe birth asphyxia, i.e. an Apgar score  $\leq 5$  at 5 min.

	1997-2004	2009-2013	p-value <sup>a</sup>
Total live births, n	40,222	15,876	-
Infants with an Apgar score $\leq 5/5$ min., n	77	40	-
Rate, n/1,000 births	1.9	2.5	0.16
Maternal age, yrs, mean ( $\pm$ SD)	29.6 ( $\pm$ 4.4)	30.6 ( $\pm$ 6.1)	0.40
Gestational age at birth, days, mean ( $\pm$ SD)	282.6 ( $\pm$ 10.8)	279.4 ( $\pm$ 10.9)	0.13
Born with a GA $\geq 42$ wks, n (%)	12 (16)	3 (8)	0.26
Birth weight, g, mean/median ( $\pm$ SD)	3,498 ( $\pm$ 692)	3,413 ( $\pm$ 614)	0.51
Born in Kolding, n (%)	32 (42)	40 (100)	-
Mode of delivery, n (%)			0.14
Vaginal delivery	48 (62)	31 (78)	
Caesarean section	27 (35)	9 (23)	
Unknown	2 (3)	-	
Apgar score, n (%)			0.93
0-2	12 (16)	6 (15)	
3-5	65 (84)	34 (85)	

GA = gestational age; SD = standard deviation.

a) Calculated where relevant, tests for categorical variables are chi-squared tests, tests for continuous variables are t-tests.

birth asphyxia defined by a low Apgar score and the outcome for these infants born in two different periods, before and after the centralisation of births.

## METHODS

The study included all new-born infants admitted to the neonatal ward at Kolding Hospital, born at term (gestational age (GA)  $\geq 37$  weeks) with severe birth asphyxia defined as an Apgar score  $\leq 5$  after 5 min. in two time periods: 1997-2004 and 2009-2013. In the first period, the uptake area for the neonatal unit was the four hospitals in Vejle, Horsens, Fredericia and Kolding. In the second period, all deliveries occurred at Kolding Hospital, as the maternity ward in Vejle and Fredericia were closed in 2003 and 2006, respectively, and infants born at Horsens Hospital from 2006 and onwards were transferred to Aarhus University Hospital, Skejby, if they needed neonatal observation or treatment. The number of delivery room deaths for the two periods were investigated using different data sources.

Data used for the study were obtained from a neonatal database for quality treatment and care (Neobase). All infants admitted to the neonatal unit are included in this database. The database consists of a data sheet for every infant which is completed at discharge or at referral to another hospital. The sheet contains information about mode of delivery, GA, birth weight and the Apgar score after 1 and 5 min., etc. Follow-up data after discharge were obtained from the paediatric medical records linked to vital statistics up to the age of three years. Data for the years 1997-2004 were collected and

analysed in 2005, but were not published and later anonymised (the historical group). The data source for this time period also included information about delivery room deaths from the Perinatal Audit Committee for Vejle County with evaluation and classification of all deaths before, during and after birth. For the period 2009-2013, all Neobase data sheets were double-checked with the neonatal discharge diagnosis of severe birth asphyxia (ICD10 code P210). Furthermore, the birth protocol and the discharge database with maternal diagnosis for the births were checked for codes for death during delivery and in the delivery room. Infants who were born in other hospitals with birth asphyxia and later transferred to Kolding Hospital were not included in the second-time period. Infants with severe or lethal congenital anomalies were excluded.

The data variables for this follow-up study were defined in 2004 and included information about symptoms after birth and health status at one and three years of age. The symptoms recorded in the first days of life were: changes in alertness, depression of sucking reflex, depression of other reflexes, seizures and impaired renal function. In order to ensure a uniform data collection, it was decided to use the same questionnaire for collection of the follow-up data for the more recent time period, although the questionnaire did not mention all symptoms included in the criteria of encephalopathy for cooling.

Statistics: Tests for categorical variables are chi-squared tests, except for deaths in the first year or first three years of life, cerebral palsy and developmental delay (Fisher's exact test). Tests for continuous variables are t-tests. The analyses on cerebral palsy and developmental delay at three years of age were restricted to children who remained alive at three years of age.

*Trial registration:* not relevant.

## RESULTS

The total number of infants born at the four hospitals in 1997-2004 were 40,222, and 15,876 infants were born at Kolding Hospital in 2009-2013. Two infants born in 1997-2004 were excluded due to lethal congenital anomalies. The study included 77 infants born in 1997-2004, and 40 infants born in 2009-2013 admitted to the NICU with an Apgar score  $\leq 5$  at 5 min. Background data for the two populations are presented in **Table 1**. The two groups were comparable with respect to maternal age, GA, birth weight, mode of delivery and distribution of Apgar score. The median GA for infants in the recent time period was 3.2 days younger than in the historical time period ( $p = 0.13$ ). There was no significant difference in the proportion of infants born with GA  $\geq 42$  weeks (16% and 8%, respectively). The rate of severe birth asphyxia was 1.9 per 1,000 births in the early years

and 2.5 per 1,000 births for the years 2009-2013 ( $p = 0.16$ ). The mortality in the first three years of life after severe birth asphyxia in the two populations was 0.24 per 1,000 births in 1997-2004 (ten deaths) and 0.06 per 1,000 births in 2009-2013 (one death) ( $p = 0.20$ ).

### Neonatal morbidity

There was a highly significant difference between the two periods in the proportion of study infants with neonatal seizures and age at discharge after birth (Table 2).

### Mortality and disability

There were seven deaths within the first year of life in the early period and a further three severely disabled children died between one and three years of age ( $10/77 = 13\%$ ). There was only one death in the more recent period ( $1/40 = 2.5\%$ ).

Follow-up data for surviving children at one and three years of age was available for 39/67 (58%) and 25/67 (37%) in the historical period, and 38/39 (97%) and 23/39 (59%) respectively, in the more recent time period. Cerebral palsy at three years of age was present in seven surviving children from the early period and in two survivors from the more recent period ( $7/67 = 10\%$  and  $2/39 = 5.1\%$ , respectively) (Table 3). The outcome death or cerebral palsy was present in 17/77 (22%) in the early period and 3/40 (7.5%) in the more recent period ( $p < 0.05$ ). The rate of death or cerebral palsy after Apgar score  $\leq 5$  at 5 min. in the population of newborn infants was 0.42 per 1,000 births in 1997-2004 and 0.18 per 1,000 births in 2009-2013.

### Deaths during labour and in the delivery room

In the historical period 1997-2004, 11 term born foetuses were classified by the perinatal audit committee as having died during labour. All had Apgar scores of 0 at 1, 5 and 10 min. GA at birth was 38 + 0 to 42 + 1 and the median birth weight was 3,350 g (range: 2,980-4,100 g). Nine of the births were spontaneous labour.

We found no deaths during labour or deaths in the delivery room for term births using several data sources including the birth protocol and the lists of discharge diagnoses for the more recent period 2009-2013.

### DISCUSSION

In the present study, we have documented a significant improvement in the health of term-born babies with severe birth asphyxia in our area. Even though a higher rate of infants was born with an Apgar score  $\leq 5$  at 5 min. after birth, mortality and morbidity have decreased. Applying the mortality for the early period (0.24/1,000 births) to the more recent time period with 15,876 births, the lives of three newborn infants were saved. This improvement may have several explan-

TABLE 2

Neonatal morbidity and infant mortality for infants with an Apgar score  $\leq 5$  at 5 min.

	1997-2004	2009-2013	p-value <sup>a</sup>
Infants with an Apgar score $\leq 5/5$ min., n (%)	77 (100)	40 (100)	-
Death in 1st year of life, n (%)	7 (9)	1 (3)	0.26
Cooling/hypothermia, n (%)	0	6 (15)	-
Neonatal seizures, n (%)	28 (36)	4 (10)	0.002
Age at 1st discharge: survivors, days ( $\pm$ SD)	13 ( $\pm$ 16)	7 ( $\pm$ 8)	0.015

SD = standard deviation.

a) Tests for categorical variables are chi-squared tests except for deaths in the 1st year of life (Fisher's exact test), tests for continuous variables are t-tests.

TABLE 3

Outcomes at one and three years for infants with birth asphyxia.

	1997-2004	2009-2013	p-value
Infants with an Apgar score $\leq 5$ , n	77	40	-
Status, 1 year old, n (%)			0.05 <sup>a</sup>
Normal + unknown	32 + 28 = 60 (78)	36 + 1 = 37 (93)	
Abnormal + dead	7 + 10 = 17 (22)	2 + 1 = 3 (8)	
Status, 3 yrs old, n (%)			0.02 <sup>a</sup>
Normal + unknown	3 + 52 = 55 (71)	20 + 16 = 36 (90)	
Abnormal + dead	12 + 10 = 22 (29)	3 + 1 = 4 (10)	
Died before 1 yr of age, n (%)	7 (9)	1 (3)	0.26 <sup>b</sup>
Died before 3 yrs of age, n (%)	10 (13)	1 (3)	0.10 <sup>b</sup>
Cerebral palsy at 3 yrs, n (%)	7 (9)	2 (5)	0.48 <sup>b, c</sup>
Developmental delay at 3 yrs, n (%)	10 (13)	2 (5)	0.20 <sup>b, c</sup>
Death or cerebral palsy, n/1,000 births	0.42	0.18	0.22 <sup>b</sup>

a) Chi-squared tests.

b) Fisher's exact test.

c) Restricted to children who remained alive at 3 yrs of age, as those who had died were not at risk of cerebral palsy/developmental delay.

ations: centralisation of births with neonatal care available in the delivery room for all new-born infants, cooling of the infants with the most severe birth asphyxia, implementation of specialised transport for referral of severely ill neonates and implementation of the quality of care project "Sikker fødsel" at the Maternity Unit. During the more recent period, the guidelines for treatment of prolonged pregnancy changed from recommending induction of birth at GA 42 weeks to more frequent monitoring of the pregnancy from GA 41 weeks and recommendation of birth before GA 42 weeks. This may also have had an impact on the results in our study although the changes were not implemented in all five years, with 8% of infants with severe birth asphyxia in the recent period being born at GA  $\geq 42$  weeks.

We cannot explain why the prevalence of severe birth asphyxia (Apgar score  $\leq 5$  at 5 min.) was higher in the more recent period despite a lower morbidity and mortality. It has been shown that there are large international differences in the distribution of Apgar scores [12]. The prevalence of severe birth asphyxia in our

study was calculated based on the number of infants admitted to the NICU. In the historical period, some infants with a low Apgar score at 5 min. may have recovered so fast that they stayed at the hospital of birth without being transferred to Kolding for neonatal care. Another explanation may be an increased focus on Apgar score and birth asphyxia owing to the quality of care projects. Furthermore, there may be a true increase over time, but better postnatal treatment was given due to immediate neonatal care from trained paediatricians with direct access to the NICU and hypothermia treatment was offered to the most severely affected new-borns.

There was a non-significant decrease in the proportion of infants with a low Apgar score who were born by Caesarian section: from 35% in the historical period to 23% in the more recent time period. This may be a random finding. It may also be explained by better monitoring during labour that makes the staff more confident with continuing vaginal delivery.

A study from Denmark found that the small labour units had the highest rates of approval for submitted claims [13]. Another study by Milland et al concluded that the labour units with the lowest annual delivery volume had higher incidence rates of approved injury claims in total and of approved fatal injuries as a subgroup, when compared with units with higher delivery volumes [14]. These findings are in line with our results, revealing a significant decrease in morbidity after severe birth asphyxia following the centralisation of births.

Over the past decade, many organisational changes have occurred in the Danish hospital system: some changes have been evidence-based and others based on political decisions. A number of small maternity units has been closed and most maternity units are now located in hospitals with neonatal intensive care units. When major changes are implemented, they should be followed by an audit of the results before and after their implementation. This is only done infrequently, and historical comparisons may be biased by several concomitant organisational changes and changes in clinical treatment.

### Strengths and limitations

A strength of our study is the detailed population-based data that were available from two different periods for the same geographical area. Data on outcomes were collected in the same way using the same questionnaires. It is a limitation that the data sources could not be exactly the same in the two periods as the Perinatal Audit Committee was not in place during the more recent time, and only perinatal deaths in the early period were classified by the Committee. In theory, there may have been deaths during labour in the more recent period that were misclassified as deaths before birth

and therefore missed. If mortality during labour was the same in the two periods, we should have been able to find 3-4 deaths during labour in our data sources for 2009-2013. However, despite using several data sources, we found no deaths after birth and before admission to the NICU in the more recent period.

For the historical period, follow-up information at and three years was available for a limited number of infants, and the true rate of cerebral palsy could have been higher. However, in a Danish context, it is very unlikely that infants and children without contact to the hospital have cerebral palsy or other severe disability as treatment is free of charge. Despite the lower follow-up rate, death and disability were much more frequent in the historical period.

### CONCLUSIONS

Over a relatively short period, death and disability due to severe birth asphyxia at term decreased significantly. This improvement is likely explained by changes in the organisation of births in our uptake area as well as changes in the treatment.

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