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Risk factors in term children for visual impairment without a known prenatal or postnatal cause

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Summary

Risk factors were studied for visual impairment in children without known pre- or postnatal cause, for a decrease of visual acuity. Children born at term 1979–98 and with a visual impairment were identified from the Swedish Register of Visually Impaired Children and data were linked with the Swedish Medical Birth Registry. Maternal characteristics such as maternal age, parity, maternal smoking habits in early pregnancy, maternal education, nationality, and subfertility were studied as well as maternal diagnoses such as pre-eclampsia, prolonged second stage of labour, abruptio placentae, and placenta praevia. Mode of delivery was analysed as well as birthweight, and birthweight in relation to gestational age.

Abruptio placentae turned out to be the strongest risk factor (OR = 8.24 [95% CI 5.01, 13.51]). Smoking did not give a statistically significant increased risk. There is an increased risk with breech delivery (OR = 2.01 [95% CI 1.28, 3.17]). Pre-eclampsia was associated with an increased risk (OR = 2.22 [95% CI 1.46, 3.38]). There is also an increase in risk at low birthweight and small-for-gestational-age as well as birthweight >4 kg and large-for-gestational-age.

In this study we found that risk factors particularly worth noticing in term children with a presumed perinatal cause of visual impairment are abruptio placentae, pre-eclampsia, excessively low as well as excessively high birthweight, and breech delivery, a fact worth noticing in current discussion on risks, advantages or excessive exploitation of caesarean section.

Introduction

The prevalence of visual impairment among children in the industrialised part of the world is 12/10 000.[1–3] A predominance of various prenatal aetiological factors is seen[4] but also peri-/neonatal complications play an important role and are seen in 20% of all children with visual impairment. For a number of years much interest has been focused on peri-/neonatal complications in preterm infants. Nevertheless children born at term are of no less interest as 45% of children with visual impairment resulting from peri-/neonatal complications are born full-term. In addition, the majority (94%) has multiple impairments.[4] Thus, this is a group which is of considerable clinical importance not least in the light of their multiple impairments. Little is found in the literature about possible causes or risk factors; we therefore thought it important to analyse this problem further in a search for possible preventive measures.

Materials and methods

Data sources

Children born at term and with visual impairment resulting from peri-/neonatal complications were identified by an inventory of the Swedish Register of Visually Impaired Children.[1] The analysis was restricted to individuals born in 1979–98. At the time of analysis, 1998 was the last complete year of the Medical Birth Registry which was used as background material.

The Swedish Register of Visually Impaired Children

This database includes information on all visually impaired children in the country, 0–19 years of age, and with a visual acuity of ≤0.3 and/or a simultaneous visual field defect. It was originally obtained by orga-

nising data obtained by reviewing medical records on Low Vision Clinics and Departments of Ophthalmology throughout Sweden and is now continuously updated. Data obtained on each child is recorded on a standardised form and subsequently entered and organised into a database. Each record contains information on name, sex, date of birth, patient's ophthalmologist and low vision clinic, county, ophthalmological diagnosis, systemic diagnosis, aetiological factors, additional impairments, classification of visual impairment, visual field defects, refraction, near vision, and family history.

Suggested aetiological factors are divided into four main categories: (1) prenatal; (2) peri-/neonatal; (3) infantile/juvenile; and (4) unknown, according to the system in previous Nordic studies.[4,5]

A classification of visual impairment is made according to the WHO (World Health Organisation) definitions, and ophthalmological diagnoses are classified according to a Californian version of ICD-9 (International Classification of Diseases, 9th version).[2,6,7]

On 31 December 1999, the database included data on 2774 individuals, 0–19 years of age. The total Swedish population at that date was 8.86 million and the age-specific population at that point was 2.25 million.

Records from this register were linked with the Medical Birth Register for the years 1979–98[8] (see also http://www.sos.se/fulltext/112/2003-112-3/2003-112-3.pdf). Matching was possible only for cases with a complete personal identification number and who were born in Sweden. A total of 2293 records matched (83%).

The Swedish Medical Birth Registry

The Medical Birth Register contains data on antenatal care, delivery, and the paediatric examination of the newborn. Since 1982 it has been based on copies of the original medical records, computerised by the National Board of Health in Stockholm.

Exclusions

Cases were selected with a gestational duration (in most cases based on second trimester ultrasound) of at least 37 completed weeks ($n = 1770$). In 13 instances, no information existed on pregnancy duration – the majority of these infants had a birthweight <2500 g and were probably preterm. Children with a known genetic ($n = 563$) or chromosomal ($n = 135$) anomaly were excluded and also infants whose visual impairment was the result of a post-neonatal event ($n = 118$). The risk factor study was restricted to infants ($n = 715$) without a genetic or chromosomal anomaly, a postnatal cause of the visual impairment, a central nervous system malformation ($n = 175$) or a multiple malformation syndrome ($n = 51$).

Risk factors studied

Maternal characteristics: maternal age (5-year categories), parity (0–3+), maternal smoking habits in early pregnancy (recorded since 1983, none, <10 cigarettes/day, 10+ cigarettes/day and known for about 93% of cases), maternal education on 1 January 1996 (up to and including 1995, a 6-step scale), maternal nationality, subfertility in mother (recorded since 1983 as the number of years of involuntary childlessness).

Information on maternal smoking and subfertility was obtained by midwife interview at the first antenatal care visit (usually in weeks 10–12). Information on education and nationality was linked from the registers of Statistics Sweden.

Maternal diagnoses: pre-eclampsia, prolonged second stage of labour, abruptio placentae, placenta praevia. These were based on ICD-codes (International Classification of Diseases) given in the delivery records.

Delivery: pregnancy duration in completed weeks, breech delivery and instrumental delivery. Information was obtained from the delivery records.

Infant characteristics: birthweight and standard deviation scores (SDS) from normal birthweight in that gestational week based on data from the register[9]), low Apgar score (<7 at 5 min). Information obtained from the records of the paediatric examination of the newborn.

Analysis of gestational duration, birthweight, SDS, and instrumental delivery were limited to singleton births. Other variables were studied in all infants.

Comparisons were made with data for all term births with exclusion of infants who died before the age of 1 year, sometimes restricted to singleton births (see above).

The statistical analysis was made using Mantel-Haenszel procedure with various adjustments. Risk estimates were expressed as odds ratios (OR) with

95% confidence intervals [95% CI], the latter determined with Miettinen's test-based method. When no natural reference group existed (maternal education, gestational duration, birthweight), comparisons were made between each exposure group and all other groups.

Results

Maternal characteristics

Table 1 shows some maternal characteristics as risk factors for visual impairment in term infants. Maternal

Table 1. Maternal characteristics as risk factors for visual impairment in term infants

Risk factor	Stratification	N[a]	N1[b]	OR	[95% CI]
Maternal age (years)	Year of birth, parity, smoking				
–19		30	62 082	1.18	[0.78, 1.77]
20–24		167	455 218	0.99	[0.81, 1.21]
25–29		264	750 797	1.00	Reference
30–34		172	529 104	0.95	[0.78, 1.15]
35–39		72	200 769	1.05	[0.80, 1.38]
40+		10	36 016	0.75	[0.38, 1.50]
Total		715	2 033 986		
Parity	Year of birth, age, smoking				
0		312	844 485	1.15	[0.97, 1.37]
1		232	733 726	1.00	Reference
2		113	321 613	1.10	[0.87, 1.39]
3+		58	134 162	1.48	[1.08, 2.02]
Total		715	2 033 986		
Smoking	Year of birth, age, parity				
Unknown		44	103 277	–	
None		357	1 190 590	1.00	Reference
<10 cigs/day		84	227 047	1.08	[0.84, 1.39]
10+ cigs/day		59	137 810	1.27	[0.95, 1.69]
Total		544	1 658 724		
Nationality	Year of birth, parity, smoking, education				
Swedish		638	1 180 213	1.00	Reference
Non-Swedish		53	135 065	0.78	[0.57, 1.07]
Total		691	1 315 278		
Education	Year of birth, parity, smoking, nationality				
Unknown		17	40 355	0.21	[0.16, 0.28]
<9 years compulsory school		21	31 220	0.96	[0.61, 1.52]
9–10 years compulsory school		137	189 367	1.49	[1.24, 1.80]
1–2 years of gymnasium		299	542 531	1.23	[1.06, 1.42]
3–4 years of gymnasium		71	151 531	1.08	[0.85, 1.39]
1–2 years postgymnasium		86	216 497	0.80	[0.63, 1.00]
3+ years postgymnasium		60	143 777	0.79	[0.61, 1.03]
Total		691	1 315 278		
Subfertility	Year of birth, parity, smoking, education				
No subfertility		643	1 240 022	1.00	Reference
1+ years of involuntary childlessness		48	75 256	1.11	[0.79, 1.58]
Total		691	1 315 278		

[a,b]Numbers of infants with visual impairment (N), number of infants in comparison group (N1). Stratification as stated. Note that total numbers differ between groups because of lack of data or restriction of study period.

age had no effect and parity only a weak and uncertain U-shaped effect. Smoking increased the risk but statistical significance was not reached. Non-Swedish nationality is slightly protective while maternal education had an effect with a moderately increased risk if the mother had only completed compulsory school. Involuntary childlessness did not show up as a risk factor.

Maternal diagnoses and mode of delivery

A diagnosis of pre-eclampsia was present in 22 instances, giving an OR = 2.22 [95% CI 1.46, 3.38] after stratification for year of birth, parity, maternal smoking, and education. In a similar analysis, there was no increased risk after prolonged second stage of labour ($n = 39$, OR = 0.92 [95% CI 0.66, 1.29]) but the risk after abruptio placentae ($n = 12$) was strong and statistically significant: OR = 8.24 [95% CI 5.01, 13.5].

Three modes of delivery were compared. Using non-instrumental vaginal delivery ($n = 515$) as a reference (1.0), the OR for instrumental vaginal delivery ($n = 52$) was 1.36 [95% CI 1.01, 1.84] and for caesarean section ($n = 125$) 2.06 [95% CI 1.70, 2.51].

Breech presentation ($n = 19$) compared with head presentation at vaginal delivery gave an OR = 2.01 [95% CI 1.28, 3.17). No significant differences were found in a comparison between the different delivery units in Sweden (data not shown).

Table 2. Infant characteristics as risk factors for visual impairment in term infants

Risk factor	N[a]	N1[b]	OR	[95% CI]
Gestational duration (weeks)				
37	55	99 468	1.49	[1.12, 1.99]
38	120	260 410	1.29	[1.06, 1.57]
39	146	459 445	0.82	[0.69, 0.99]
40	177	560 696	0.81	[0.68, 0.96]
41	129	359 450	0.97	[0.80, 1.18]
42	64	136 193	1.32	[1.02, 1.71]
43	10	16 119	1.61	[0.87, 2.99]
44	0	1 888	–	
Total	701	1 893 669		
Birthweight (g)				
1500–1999	8	1 625	4.52	[1.54, 13.3]
2000–2499	37	20 155	3.96	[2.81, 5.59]
2500–2999	117	175 514	1.35	[1.07, 1.71]
3000–3499	231	626 166	0.91	[0.76, 1.09]
3500–3999	182	698 227	0.72	[0.59, 0.87]
4000–4499	89	297 682	0.98	[0.75, 1.27]
4500–4999	19	59 657	1.36	[0.83, 2.24]
5000–5499	5	7 080	1.58	[0.40, 6.26]
5500+	0	685	–	
Total	688	1 886 791		
Standard deviation score (SDS[c])				
<–3SD	17	4 687	7.85	[5.76, 10.7]
≥–3SD–<–2SD	20	11 290	4.19	[3.23, 5.81]
≥–2SD–<2SD	612	840 545	1.00	Reference
≥2SD–<3SD	8	12 177	1.85	[1.12, 3.06]
≥3SD	10	7 791	3.63	[2.36, 5.59]
Total	667	1 876 490		

Only singleton births. [a,b]Number of infants with visual impairment (N), number of infants in comparison group (N1). Stratification for year of birth, maternal age, parity, education, and smoking habits. Note that total numbers differ because of lack of data. For gestational duration and birthweight, each category is compared with all other categories.

[c]SDS = birthweight in standard deviations (SD) from expected weight at that gestational week, standardised for parity (0, 1+) and infant sex.

Infant characteristics

Table 2 shows the ORs for various gestational duration categories, birthweight (500 g categories), and for SDS score. There is a U-formed risk according to gestational duration with a minimum at 39–40 completed weeks. There is a strong excess risk at low birthweight and an increasing risk at birthweights >4 kg which is mirrored in the data based on SDS values where there is an excess risk both for infants that are small-for-date (<2 SD) and for infants that are large for date (>2 SD). Among the 24 infants with a birthweight ≥4500 g, only one had a mother with a diagnosis of diabetes.

The OR for low Apgar score (<7 at 5 min) ($n = 109$) is 12.5 [95% CI 10.3, 15.1] after stratification for year of birth, smoking, maternal education, and infant SDS.

Discussion

We have analysed possible risk factors for visual impairment in term children with no definite prenatal or postnatal cause. Improved neonatal care during the last decades has significantly reduced both mortality and morbidity among term as well as preterm infants in industrialised countries. The increased survival rate in preterm infants is, however, resulting in an increased number of individuals with functional problems caused by their prematurity.[10] Much attention has been focused on their ophthalmological problems, notably retinopathy of prematurity (ROP), described already in 1942.[11] Other complications such as optic atrophy, refractive errors, strabismus, and cerebral damage have also been reported.[12–15] Recently, damage of the posterior visual pathways and associated problems have been described.[16,17] Risk factors for developing ROP and other complications have been much debated, yet no unfailing proof for the pathophysiological mechanisms has been found. Low gestational age, serious neonatal complications such as infections, intraventricular haemorrhage, or respiratory problems have been implicated. Recently IGF1 has been suggested to play an important role in the development of ROP.[18]

The eye problems of term children exposed to hypoxia or affected by cerebral damage have raised less interest. Yet this is a significant group considering their often very serious additional problems, best illustrated by the large proportion of children with both visual and additional impairments, 94%, as found, for example, in a Swedish study of 2373 visually impaired individuals, 0–19 years of age.[4] Virtually nothing is known about possible risk factors and this lack of information is addressed in this paper.

In our analysis abruptio placentae turned out to be the strongest risk factor. The risk for abruptio is influenced by maternal smoking habits. Even if smoking as such does not give statistical significance it cannot be ruled out as being of no importance due to its influence on the placenta.

Another interesting fact is the increased risk with breech delivery. It has been shown that breech delivery is associated with increased mortality and now also with serious visual problems and a high proportion of other impairments. This is noteworthy and should be considered in the current debate on caesarean section as an alternative to vaginal delivery at breech presentation.[19] Also caesarean section as such shows a significantly increased risk but this may be due to the fact that emergency section is chosen when the well-being of the infant is threatened.

Both low and high SDS values [i.e. birthweight expressed in standard deviations from the expected weight at that gestational age, standardised for parity (0, 1+) and infant sex] were associated with an increased risk for visual impairment in term children. The high risk for infants with low SDS is not surprising since the low birthweight indicates unfavourable prenatal conditions, making the infant more vulnerable to any strain during delivery and complications in the perinatal period and thus more prone to suffer from injury. The same explanation probably applies to the increased risk associated with pre-eclampsia.

It has been shown that children large-for-gestational-age have an increased mortality and are also over-represented among children with cerebral palsy.[20] In this study we find further evidence of the danger connected with high birthweight, apparently unrelated to a prolonged second stage of labour.

The increased risk in children with low Apgar scores at 5 min is not surprising as this is the indicator of an unfavourable event causing impairment.

From a clinical point of view the risk factors particularly worth noting are abruptio placentae (a condition linked to smoking mothers), pre-eclampsia, excessively low as well as excessively high birthweight and breech delivery. The last of these is worth noting in the current discussion on risks, advantages or excessive exploitation of caesarean section.

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