Placental Abruption and Child Mortality

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abstract

BACKGROUND AND OBJECTIVES: Placental abruption causes asphyxia and leads to high perinatal mortality. Our objective was to study the overall mortality and causes of death among children born after placental abruption.

METHODS: Data on children born from singleton pregnancies complicated by placental abruption between 1987 and 2005 were collected from the Finnish Medical Birth Register, the Hospital Discharge Register, and the Cause-of-Death Register. A reference group consisted of children born from pregnancies without placental abruption. After excluding stillbirths, the final study sample comprised 3888 children born after placental abruption (index children) and 12 530 referent children. The main outcome measure was overall mortality.

RESULTS: By the end of 2013, there were 280 deaths among the index children and 107 deaths among the referent children. Compared with the referent children, the overall mortality among the index children was significantly increased (hazard ratio: 8.70; 95% confidence interval 6.96–10.90). During the neonatal period (0–27 days) the mortality was nearly 15-fold (14.8; 10.9–20.0), birth-related asphyxia being the leading cause of death (108; 34–341). The mortality remained high during days 28 to 365 (10.3; 4.83–21.8) and beyond 365 days (1.70; 1.03–2.79). Furthermore, the overall mortality was increased among the index children born at 32 to 36 + 6 gestational weeks (2.77; 1.54–4.98) and at ≥37 weeks (4.98; 3.54–6.99) and among children with a birth weight of 2500 g or more (5.94; 4.33–8.14).

CONCLUSIONS: The impact of abruption on offspring mortality extends far beyond the perinatal period. This is mainly due to birth-related asphyxia and prematurity-related consequences.

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WHAT'S KNOWN ON THIS SUBJECT: Placental abruption is associated with high perinatal mortality and increased morbidity of infants born after abruption. Prematurity and birth-related asphyxia are the main causes of adverse outcome among these children.

WHAT THIS STUDY ADDS: Placental abruption increases overall mortality in children who primarily survive after abruption. The impact of abruption on offspring mortality extends far beyond the perinatal period. Birth-related asphyxia and prematurity-related causes continue to explain the increase in mortality.

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Placental abruption, the premature separation of the placenta before delivery, is often a life-threatening obstetric emergency to the fetus,[1] associated with prematurity, stillbirth, hypoxia, and major congenital anomalies.[2,3] Perinatal mortality is ~10%.[4,5] Fetal and newborn survival is determined mainly by gestational age and severity of the abruption.[6]

Increased morbidity of infants born after placental abruption is established.[7–13] Adverse outcome related to prematurity and birth-related asphyxia may compromise neurodevelopmental outcome of these children.[7] Data reveal that children who survive after placental abruption have a higher risk for conditions such as cerebral palsy,[8–10] cystic periventricular leukomalacia, intraventricular hemorrhage,[8,11] respiratory distress syndrome (RDS),[13] and neonatal apnea.[12] This may increase the overall mortality. In addition to increased morbidity, the impact of abruption on perinatal mortality has been demonstrated in several studies and populations.[4,5,7,14] Nevertheless, systematic studies on overall and cause-specific mortality of these children do not exist. Our aim was to more thoroughly evaluate the overall and cause-specific mortality of children born after placental abruption. To this end, we used the nationwide comprehensive health care registers of Finland.

METHODS

We conducted a population-based case-control study using linked data from population-based birth and cause-of-death registers from Finland. All singleton births in Finland from 1987 to 2005 were included in the study. We used the medical birth register (MBR) and the hospital discharge register (HDR) maintained by the National Institute for Health and Welfare to identify all women with a diagnosis of placental abruption by using codes from the *International Classification of Diseases, Ninth Revision* (codes 641.20, 641.21, and 641.23 for 1987–1995) and the *International Classification of Diseases, 10th Revision* (codes O45.0, O45.8, and O45.9 from 1996 onward) in the HDR and a check mark for placental abruption (yes or no) in the MBR (October 1990–2005).
A reference group originated from the same registers (HDR and MBR) and consisted of 3 women without placental abruption for each abruption, matched by maternal age, parity, multiplicity, year of birth, and hospital district area. If all controls were not found, the age criteria were loosened by ±1 year to achieve 3 controls for each case. The hospital discharge data were then linked to the MBR by using the mother's unique personal identification number to identify all births with placental abruption. Multiple pregnancies were excluded from the final study sample. We identified 4190 women with a singleton birth and placental abruption and 12 570 matched referent women with a singleton birth without placental abruption. After excluding stillbirths, the final study population comprised 3888 children born after placental abruption (later referred to as index children) and 12 530 referent children.

The proportion of immigrants in the Finnish population is relatively small. Although data on the native country of the parturient are currently included in the MBR from 2000 onward, these data were not available for the whole study period (1987–2005).

Baseline data on interventions that mothers receive during pregnancy and delivery and on the newborn's outcome during the first 7 days are collected in the MBR from all delivery units (since 1987). All live births and stillbirths involving infants who are either gestational age of at least 22 completed weeks (≥155 days) or have a birth weight ≥500 g are registered in the MBR. The data are compiled at the time of birth by using the mother's maternity records. Less than 0.1% of all births are missing from the MBR. The data have been validated and correspond well with data available from hospital records.[15,16] In the HDR, data are collected on all inpatient episodes in all hospitals (since 1967), all outpatient surgical procedures in public hospitals (since 1994), and all outpatient visits in public hospitals (since 1998). The register contains information on admission and discharge date and diagnosis.

Both index and referent children were linked to the cause-of-death register (maintained by Statistics Finland) by their unique personal identification number to identify all deaths recorded up to the end of 2013. Causes of death were obtained from death certificates. The determination of the cause of death is based on medical or forensic evidence required for the death certificate. Forensic determination of the cause of death may be necessary if the death is not the result of an illness, if it is accidental or violent, or if it is caused by a treatment procedure or an occupational disease.[17] In other cases, the death certificate is based on medical evidence. Data on underlying causes of death since 1969 have been collected in a computerized database. The coverage of cause-of-death statistics is 99.9%, and coding is based on *International Classification of Diseases, Ninth Revision* codes (used during 1987–1995) and *International Classification of Diseases, 10th Revision* codes (used since 1996). The causes of death were grouped by taking into account both the main and underlying causes of death. External causes of death included accidents, homicides, and suicides. All deaths of index and referent children were manually

double-checked by 2 authors (O.R. and M.T.) to confirm the accurate cause of death.

The duration of gestation calculated from the last menstrual period was confirmed or corrected by ultrasound screening examinations at 11 to 13 or 18 to 20 weeks' gestation. Recorded in the MBR is the best clinical estimate for gestational age at birth. Smoking habits were recorded during antenatal clinic visits. Women who smoked at least 1 cigarette per day through the pregnancy were defined as smokers. Birth weight and gestational age were used to study the outcome of newborns. Newborns who were small for gestational age (SGA) were defined as having a birth weight ≤−2 SD, and newborns who were large for gestational age (LGA) were defined as having a birth weight ≥+ 2 SD of the national sex-specific standard.[18] Extremely preterm newborns were born before 28 weeks' gestation, very preterm newborns were born from 28 0/7 to 31 6/7 weeks' gestation, and moderately preterm newborns were born from 32 0/7 to 36 6/7 weeks' gestation.

An interaction analysis was performed if a compound effect between variables was suspected. Cox proportional hazard regression method was used to compare the index children to the referent children. Age-adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated. *P* values <.05 were considered statistically significant. The analyses were performed by IBM SPSS Statistics version 23 (IBM SPSS Statistics, IBM Corporation). The trend of infant mortality during the follow-up was tested as 2-sided by the Cochran-Armitage trend test by using StatXact version 4.0.1.

The study was approved by the National Institute for Health and Welfare (the register keeper), which also authorized the use of health register data in scientific research (permission: 1202/5.05.00/2013; date of amendment: June 7, 2017), as required by national data protection legislation. Statistics Finland authorized the use of cause-of-death register data (permission: TK-53-1035-13).

The protocol for this study was approved by the ethics committee of Helsinki University Hospital (permission: 334/13/03/03/2013; date of amendment: June 15, 2017). Because we used routinely collected anonymized electronic health records, no formal patient consent was required for this study.

RESULTS

There were 1 121 244 singleton deliveries in Finland during the study period, with the incidence of placental abruption being 374 out of 100 000 (0.4%). A total of 280 deaths among index children and 107 deaths among referent children were recorded by the end of 2013. The median follow-up time was 18 years (interquartile range: 13–22; range: 0–27).

Baseline characteristics of the mothers with and without placental abruption in relation to offspring mortality are presented in Table 1. The results reveal that despite the mother's age at delivery, marital status, socioeconomic status, or parity, the overall mortality was increased among children born after placental abruption (HR: 8.70; 95% CI 6.96–10.9). With Figure 1, we show that the cumulative hazard of death among the index children was higher compared with the referent children. The difference is evident already in the early postnatal period and increases toward the end of the follow-up. With Figure 2, we present the infant mortality as a 2-year moving average by year of birth among the index and referent children during the study period. The trend of infant mortality among the index children was decreasing ($P < .001$).

Detailed data of the interaction of placental abruption, maternal smoking, and offspring mortality in 4 different subgroups are presented in Table 2. Nonabruption, nonsmoking mothers were set as the reference group. Overall offspring mortality and mortality in all age groups were increased not only among smoking mothers with abruption, but also among smoking nonabruption mothers. However, although the point estimate for offspring mortality was higher among smoking women with abruption compared with nonsmoking women with abruption, the CIs were overlapping.

The mortality after placental abruption was increased during the neonatal period (<28 days), at the age of 28 to 365 days, and at the age of over 1 year. The major causes of death in both groups are listed in Table 3. By cause, the strongest increase in neonatal mortality was observed for birth-related asphyxia (HR: 108; 95% CI 34–341). Mortality was also increased because of prematurity, intracerebral hemorrhage, RDS or other respiratory disorders, anomaly, infection, and other causes. A list of causes of deaths that counted as anomaly or other cause is presented in the Supplemental Information. At the age of 28 to 365 days, there were 27 deaths among the index children and 9 deaths among the referent children. The mortality difference in this age category was significant (HR: 10.3; 95% CI 4.83–21.8). Among index children, there were 4 deaths due to sudden infant death syndrome (SIDS) and none among the referent children. Beyond the age of 365 days, a total of 23 deaths occurred among the index children and 47 among the referent children. Mortality of the index children was increased (HR: 1.7; 95% CI 1.03–2.79) compared with the referent children. For the index children,

TABLE 1 Selected Baseline Characteristics Among Singleton Births of Women With Placental Abruption and Controls

Characteristic	Abruption		No Abruption		Adjusted Mortality
	All, *N* = 3888	Offspring Death (*n* = 280), *n* (%)	All, *N* = 12 530	Offspring Death (*n* = 107), *n* (%)	Overall, *n* = 387
					HR (95% CI)
Offspring death	3888	280 (7.2)	12 530	107 (0.9)	8.70 (6.96–10.9)
Age, y					
<25	661	42 (6.4)	2150	17 (0.8)	8.25 (4.70–14.5)
25–34	2329	159 (6.8)	7519	58 (0.8)	9.15 (6.77–12.4)
≥35	898	79 (8.8)	2861	32 (1.1)	8.06 (5.34–12.2)
Marital status					
Married	2450	167 (6.8)	8377	69 (0.8)	8.48 (6.40–11.2)
Cohabiting	968	67 (6.9)	2886	21 (0.7)	9.88 (6.05–16.1)
Single	422	34 (8.1)	1127	11 (1.0)	8.61 (4.36–17.0)
Unknown	48	12 (25.0)	140	6 (4.3)	5.96 (2.22–15.9)
Socioeconomic status					
Upper white-collar worker	442	36 (8.1)	1609	6 (0.4)	22.4 (9.43–53.2)
Lower white-collar worker	1284	73 (5.7)	4178	30 (0.7)	8.13 (5.31–12.4)
Blue-collar worker	639	35 (5.5)	1704	11 (0.6)	8.49 (4.31–16.7)
Other	509	43 (8.4)	1689	21 (1.2)	7.00 (4.15–11.8)
Unknown	1014	93 (9.2)	3350	39 (1.2)	8.23 (5.66–12.0)
Parity					
0	117	66 (5.8)	3628	29 (0.8)	7.46 (4.82–11.5)
1–2	1717	116 (6.8)	5555	39 (0.7)	9.91 (6.89–14.2)
≥3	1004	93 (9.3)	3225	34 (1.1)	9.14 (6.17–13.5)
Unknown	30	5 (16.7)	122	5 (4.1)	4.26 (1.23–14.8)

Differences between groups were analyzed by Cox proportional hazard regression analyses showing results by HRs with 95% CIs. Births between 1987 and 2005, with follow-up to the end of 2013. Mortality models were adjusted by mothers' age. Note: The data only allow the comparison of index and reference groups within each variable. The data do not allow comparison between variables. *N*, number of total population in the group; *n*, number of deaths in the group; %, percentage of deaths in the group.

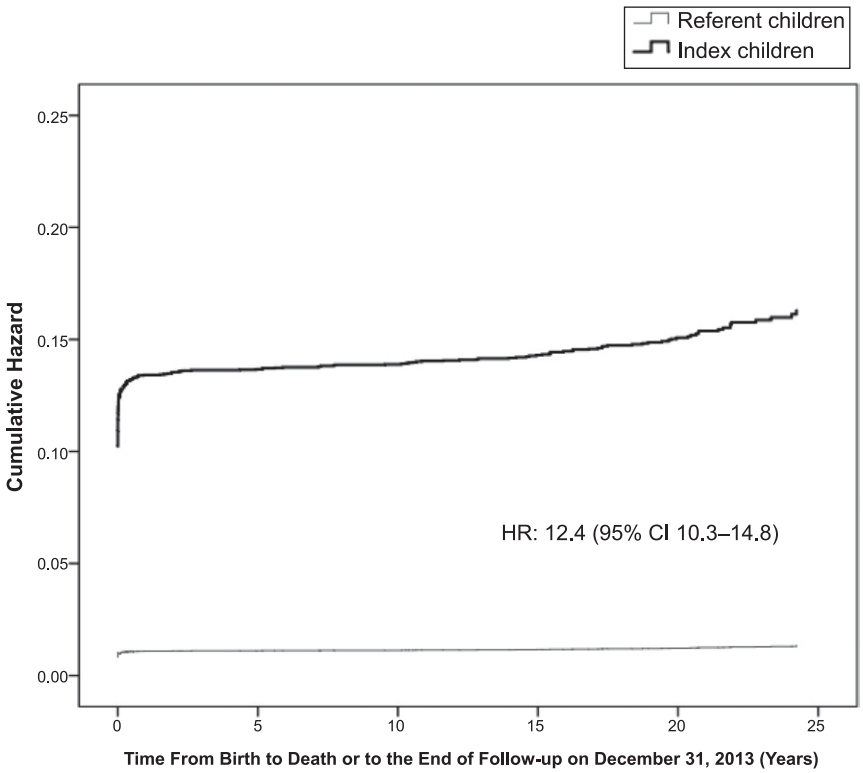

FIGURE 1
Cumulative hazard for all-cause mortality of children born after placental abruption (index children) and referent children born after nonabruption deliveries during 1987–2013.

the median was 12.86 years (range: 1.64–24.05), and for the referent children, the median was 15.13 years (range: 1.50–24.23). Nearly half of all deaths of the referent children were due to external causes, whereas for the index children, these causes covered only one-fourth of all deaths. Deaths due to cancer were also more common among referent children than among index children.

Selected baseline characteristics of the children of both groups are listed in Table 4. In very preterm and extremely preterm children, the groups did not differ in terms of mortality. However, both moderately preterm and term infants in the index group had increased overall mortality (HR: 2.77; 95% CI 1.54–4.98 and HR: 4.98; 95% CI 3.54–6.99, respectively). Among term infants in the index group, the mortality remained increased up to the age of 1 year compared with the referent children. For birth weight, significant

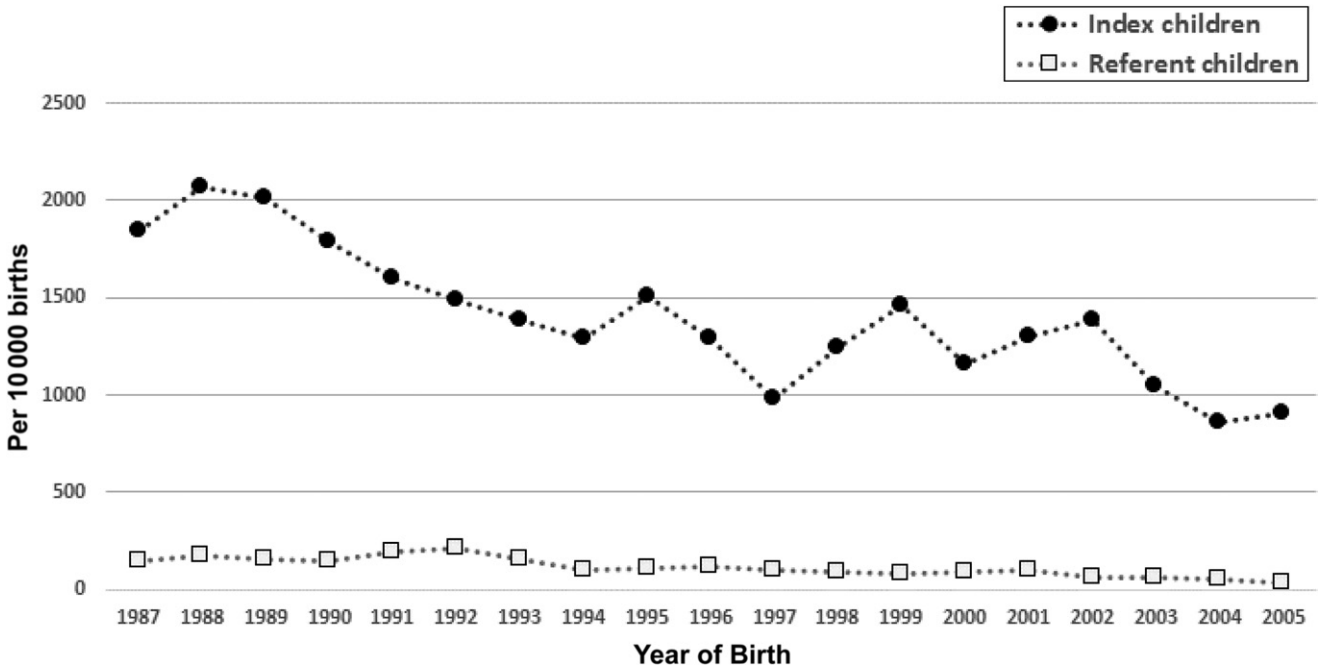

FIGURE 2
Infant mortality as a 2-year moving average by year of birth among the index children and referent children during 1987–2005. The trend of infant mortality was tested as 2-sided by the Cochran-Armitage trend test by using StatXact version 4.0.1.

TABLE 2 Interaction Between Placental Abruption, Maternal Smoking, and Offspring Mortality

	Overall Mortality, *n* = 387			Mortality at 0–27 d, *n* = 281			Mortality at 28–365 d, *n* = 36			Mortality at >365 d, *n* = 70		
	P	HR	95% CI	*P*	HR	95% CI	*P*	HR	95% CI	*P*	HR	95% CI
Nonabruption. Nonsmoking	<.001	1.000	—	<.001	1.000	—	<.001	1.000	—	.003	1.000	—
Nonabruption. Smoking	<.001	2.549	1.664–3.907	.019	2.232	1.142–4.364	.026	4.460	1.193–16.672	.005	2.432	1.310–4.513
Abruption. Nonsmoking	<.001	9.531	7.188–12.636	<.001	17.329	11.691–25.688	<.001	13.599	5.049–36.628	.273	1.449	0.746–2.814
Abruption. Smoking	<.001	14.898	10.738–20.670	<.001	26.488	17.112–41.000	<.001	21.578	7.037–66.167	.004	3.099	1.425–6.739

Differences between groups were analyzed by Cox proportional hazard regression analyses showing results by HRs with 95% CIs. Altogether, 856 (22.0%) mothers of index children and 1946 (15.5%) mothers of referent children smoked during pregnancy. Nonsmokers included women who had stopped smoking during pregnancy. Smoking data were not available for 199 mothers of index children and 396 mothers of referent children. The reference group was adjusted by maternal age. —, not applicable.

difference in mortality was observed only in index infants weighing 2500 g or more (HR: 5.94; 95% CI 4.33–8.14). The mortality remained increased up to the age of 1 year. For infants in the index group who were SGA, the mortality was increased during the neonatal period, whereas for infants in the index group who were LGA, both the neonatal and overall mortality were increased compared with the referent children. After placental abruption, boys had an increased overall mortality relative to girls (HR: 1.39; 95% CI 1.09–1.77; data not shown).

DISCUSSION

In this population-based case-control study of over 1 million births, we showed that children surviving after placental abruption had increased overall mortality compared with the referent children. Mortality was higher not only during the neonatal period but throughout the follow-up, and it was further increased by maternal smoking. Birth-related asphyxia was the leading cause of death.

Our study has several strengths and limitations. The study was based on national data obtained from validated and comprehensive health registers. The index and reference groups were large. However, the actual number of deaths in both groups was relatively small, which is a limitation concerning the conclusions to be drawn. For children who had died as neonates or infants, the numbers of deaths were small for several cause-of-death categories; this is another limitation. Moreover, we did not have information on the severity of the abruption. Finally, although the data were population-based and of high quality, this is a single-country study,

TABLE 3 Observed Numbers and Major Causes of Death Among Singleton Children Born Alive After Placental Abruption (Index Children) and Singleton Referent Children Born Alive After Nonabruption Deliveries

	Index Children, *n* = 3888	Referent Children, *n* = 12 530	Age-Adjusted
	Deaths	Deaths	HR (95% CI)
All deaths	280	107	8.70 (6.96–10.9)
Cause of death at age of 0–27 d	230	51	14.8 (10.9–20.0)
Birth-related asphyxia	100	3	108 (34–341)
Prematurity	32	6	17.5 (7.21–41.8)
Intracerebral hemorrhage	11	1	36.9 (4.76–286)
RDS or breathing problem	35	4	29.0 (10.3–81.7)
Anomaly	28	24	3.83 (2.22–6.61)
Infection	15	7	7.04 (2.87–17.3)
Other cause	9	6	4.90 (1.74–13.8)
Cause of death at age of 28–365 d	27	9	10.3 (4.83–21.8)
Cerebral palsy	3	0	—
Birth-related asphyxia	3	0	—
Prematurity	5	0	—
Intracerebral hemorrhage	0	1	—
RDS or breathing problem	4	0	—
Anomaly	3	4	—
Infection	1	1	—
SIDS	4	0	—
External cause	0	2	—
Other cause	4	1	—
Cause of death at age of >365 d	23	47	1.70 (1.03–2.79)
Cerebral palsy	6	0	—
Birth-related asphyxia	2	1	—
Cancer	1	11	—
External cause	6	24	—
Anomaly	3	1	—
Infection	2	5	—
Other cause	3	5	—

Differences between groups were analyzed by Cox proportional hazard regression analyses showing results by HRs with 95% CIs. Births are between 1987 and 2005, with follow-up to the end of 2013. For age groups 28–365 d and >365 d, there were too few deaths for the HRs of the specific cause-of-death categories to be computed. —, not applicable.

limiting the generalizability of the results.

We have previously demonstrated that maternal smoking is an independent risk factor for perinatal mortality among infants born after placental abruption.[4] In the current study, maternal smoking increased offspring mortality in both abruption-related and non–abruption-related births. As expected, the highest overall offspring mortality was found after placental abruption and maternal smoking. Our data can be used to suggest an additive effect with the combination of placental abruption and maternal smoking. However, the underlying mechanism for this additive effect is difficult to explain.

Children born after abruption are certainly vulnerable even beyond the immediate perinatal time period and thus remain more susceptible to neonatal morbidity and mortality compared with children without abruption.[12] Maternal smoking may further increase this and simply make things worse.

Placental abruption is strongly associated with preterm delivery.[5] In the analysis of cause-specific mortality, we observed that children born after placental abruption had an increased mortality because of prematurity and also because of intracerebral hemorrhage, RDS or other respiratory disorders, and infections, all entities closely associated with prematurity. There were no statistically significant differences in mortality between the index and referent children born extremely preterm or very preterm. However, referent children probably had other health problems that led to prematurity. Thus, the causal effect of placental abruption on increased mortality among premature children should be interpreted with caution.[19]

We have shown earlier that ~15% of newborns with abruption are born with asphyxia (pH 7.05 or less) compared with 1.5% of newborns without abruption.[20] In this study, the role of birth-related asphyxia as a cause of death among children born after placental abruption was remarkable. The largest number of asphyxia-related deaths of the index children was recorded in the neonatal period, with an over 100-fold increase in mortality relative to the referent children. With this observation, we highlight the fact that birth-related asphyxia is a strong negative marker even if the child primarily survives. In this study, birth-related asphyxia remained a cause of death also in the older age groups. In addition, it may play a role in deaths due to intracerebral hemorrhage, cerebral palsy, and SIDS. Placental abruption has been linked to SIDS.[21,22] This was also found in our study. Deaths due to SIDS were more common among children born after placental abruption compared with the expected number of cases in the general population.[17] It might be useful to counsel parents of newborns with asphyxia to follow the recommended safe sleep practice guidelines to reduce the risk of sleep-related infant deaths.[23]

Nine index children died of cerebral palsy after the neonatal period. There were no such deaths among the referent children. However, some causes of death, such as cancer and external causes, were more common

TABLE 4 Selected Baseline Characteristics and Mortality of Singleton Children Born After Placental Abruption (Index Children) and Referent Children Born After Nonabruption Deliveries

	Index Children		Referent Children		Adjusted Mortality			
	Deaths, *n*	Total (%)	Deaths, *n*	Total (%)	Overall	At Age of 0–27 d Age-Adjusted	At Age of 28–365 d	At Age of >365 d
					HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Sex								
Boys	175	2127 (8.2)	61	6483 (0.9)	9.07 (6.77–12.1)	13.4 (9.17–19.6)	8.70 (3.40–22.2)	2.56 (1.36–4.82)
Girls	105	1761 (6.0)	46	6047 (0.8)	8.03 (5.68–11.4)	16.9 (10.2–28.1)	13.2 (3.69–47.5)	0.88 (0.36–2.14)
Gestational age, wk								
<28	97	187 (51.9)	15	32 (46.9)	1.12 (0.64–1.93)	1.08 (0.61–1.90)	[a]	[b]
28–31 + 6	38	348 (10.9)	8	48 (16.7)	0.66 (0.31–1.43)	0.55 (0.25–1.20)	[a]	[a]
32–36 + 6	80	1172 (6.8)	13	514 (2.5)	2.77 (1.54–4.98)	3.48 (1.66–7.27)	3.28 (0.40–26.7)	1.29 (0.41–2.06)
≥37	63	2138 (2.9)	71	11 801 (0.6)	4.98 (3.54–6.99)	12.4 (7.41–20.7)	4.95 (1.79–13.6)	1.22 (0.59–2.50)
Birth wt, g								
<1500	127	434 (29.3)	22	72 (30.6)	0.97 (0.61–1.52)	0.91 (0.57–1.44)	[a]	0.18 (0.01–2.94)
1500–2499	65	882 (7.4)	15	307 (4.9)	1.55 (0.88–2.71)	1.57 (0.81–3.03)	2.89 (0.36–23.1)	1.09 (0.29–4.02)
≥2500	86	2536 (3.4)	70	12 042 (0.6)	5.94 (4.33–8.14)	16.8 (10.1–28.0)	4.26 (1.54–11.7)	1.37 (0.72–2.61)
Standardized birth wt								
SGA (≤–2 SD)	41	334 (12.3)	18	243 (7.4)	1.72 (0.98–2.99)	2.02 (1.07–3.82)	[c]	0.64 (0.17–2.40)
LGA (≥+2 SD)	9	109 (8.3)	5	459 (1.1)	7.78 (2.61–23.2)	8.57 (2.58–28.5)	[c]	4.50 (0.28–72.2)

Differences between index and referent children were analyzed by Cox proportional hazard regression analyses showing results by HRs with 95% CIs. Results of missing cases were not shown.

[a] No deaths among referent children.

[b] No deaths among the index children.

[c] Nine deaths among referent children, all appropriate for gestational age.

among the referent children relative to the index children at the age of 1 year or more. This observation may merely be a chance finding or result from the small number of observed cases.

We have previously shown that major congenital anomalies are twice as common among infants born after placental abruption than among referent infants.[3] In this study, the neonatal mortality due to anomalies was nearly fourfold among the index children relative to the referent children.

To the best of our knowledge, there are no earlier studies in which researchers focus on placental abruption and subsequent offspring mortality, although the impact of abruption on perinatal mortality is well known.[4,5] Moreover, in a recent US study,[12] abruption was associated with a more than sevenfold increased risk of neonatal mortality. In our study, the HR for neonatal mortality was nearly twice as high. This difference can probably be explained by our study period being longer and starting earlier (1987–2005) than in the American study, in which the children were born more recently (2002–2008). Our study also allowed evaluation of mortality trends; a decreasing trend was observed for infant mortality over time. This observation is in line with our previous study revealing a decreasing trend in perinatal mortality.[4]

CONCLUSIONS

Both overall and cause-specific mortality in Finnish children born after placental abruption are increased. The impact of placental abruption on offspring mortality clearly extends far beyond the perinatal period.

ABBREVIATIONS

CI: confidence interval
HDR: hospital discharge register
HR: hazard ratio
LGA: large for gestational age
MBR: medical birth register
RDS: respiratory distress syndrome
SGA: small for gestational age
SIDS: sudden infant death syndrome

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Supplemental Information

LIST OF CAUSES OF DEATH COUNTED AS EITHER ANOMALY OR OTHER CAUSE

"Anomaly": anencephalus; anomalies of abdominal wall; anomalies of diaphragm; atresia of pulmonary artery; atrioventricular septal defect; chondrodystrophy; coarctation of the aorta; congenital cystic lung; congenital diaphragmatic hernia; congenital hydrocephalus; congenital malformation syndromes predominantly associated with short stature; cystic kidney disease; congenital stenosis of aortic valve; double inlet ventricle; Down syndrome; exomphalos; hypoplastic left heart syndrome; encephalocele; hereditary progressive muscular dystrophy; multiple congenital anomalies, so described; other bulbus cordis anomalies and anomalies of cardiac septal closure; other conditions due to autosomal anomalies; other congenital malformations of great veins; other specified anomalies; other specified anomalies of the heart; other specified anomalies of kidney; other specified anomalies of nervous system; other specified anomalies of unspecified limb; Patau syndrome; Potter syndrome; reduction deformities of brain; renal agenesis and dysgenesis; stenosis of pulmonary artery; tracheoesophageal fistula, esophageal atresia and stenosis; trisomy 18; unspecified anomaly of brain, spinal cord, and nervous system; vertebral defects-anal atresia-tracheoesophageal fistula with esophageal atresia-radial and renal dysplasia–association; ventricular septal defect.

"Other cause": birth injury to spine and spinal cord; cardiomyopathy, unspecified; cerebral edema due to birth injury; condition originating in the perinatal period, unspecified; congenital anemia; death certificate missing; disorders of glycine metabolism; disorders of tyrosine metabolism; fetal adrenal hemorrhage; hydrops fetalis not due to isoimmunization; massive aspiration syndrome; metabolism disorders, unspecified; neuronal ceroid lipofuscinosis; other and unspecified cirrhosis of liver; other cardiovascular disorders originating in the perinatal period.

Placental Abruption and Child Mortality

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abstract

BACKGROUND AND OBJECTIVES: Placental abruption causes asphyxia and leads to high perinatal mortality. Our objective was to study the overall mortality and causes of death among children born after placental abruption.

METHODS: Data on children born from singleton pregnancies complicated by placental abruption between 1987 and 2005 were collected from the Finnish Medical Birth Register, the Hospital Discharge Register, and the Cause-of-Death Register. A reference group consisted of children born from pregnancies without placental abruption. After excluding stillbirths, the final study sample comprised 3888 children born after placental abruption (index children) and 12 530 referent children. The main outcome measure was overall mortality.

RESULTS: By the end of 2013, there were 280 deaths among the index children and 107 deaths among the referent children. Compared with the referent children, the overall mortality among the index children was significantly increased (hazard ratio: 8.70; 95% confidence interval 6.96–10.90). During the neonatal period (0–27 days) the mortality was nearly 15-fold (14.8; 10.9–20.0), birth-related asphyxia being the leading cause of death (108; 34–341). The mortality remained high during days 28 to 365 (10.3; 4.83–21.8) and beyond 365 days (1.70; 1.03–2.79). Furthermore, the overall mortality was increased among the index children born at 32 to 36 + 6 gestational weeks (2.77; 1.54–4.98) and at ≥37 weeks (4.98; 3.54–6.99) and among children with a birth weight of 2500 g or more (5.94; 4.33–8.14).

CONCLUSIONS: The impact of abruption on offspring mortality extends far beyond the perinatal period. This is mainly due to birth-related asphyxia and prematurity-related consequences.

WHAT'S KNOWN ON THIS SUBJECT: Placental abruption is associated with high perinatal mortality and increased morbidity of infants born after abruption. Prematurity and birth-related asphyxia are the main causes of adverse outcome among these children.

WHAT THIS STUDY ADDS: Placental abruption increases overall mortality in children who primarily survive after abruption. The impact of abruption on offspring mortality extends far beyond the perinatal period. Birth-related asphyxia and prematurity-related causes continue to explain the increase in mortality.

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Dr Riihimäki designed the study, collected and analyzed the data, interpreted the data, and drafted the initial manuscript; Dr Metsäranta analyzed and interpreted the data and critically reviewed and revised the manuscript; Ms Luukkaala analyzed and interpreted the data and reviewed and revised the manuscript; Dr Gissler interpreted the data and reviewed and revised the manuscript; Drs Andersson, Nuutila, and Paavonen reviewed and revised the manuscript; Dr Tikkanen designed the study, coordinated and supervised data analyses, interpreted the data, and critically reviewed and revised the manuscript; and all authors approved the final manuscript as submitted and are accountable for all aspects of the work.

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Placental abruption, the premature separation of the placenta before delivery, is often a life-threatening obstetric emergency to the fetus, [1] associated with prematurity, stillbirth, hypoxia, and major congenital anomalies.[2,3] Perinatal mortality is ~10%.[4,5] Fetal and newborn survival is determined mainly by gestational age and severity of the abruption.[6]

Increased morbidity of infants born after placental abruption is established.[7–13] Adverse outcome related to prematurity and birth-related asphyxia may compromise neurodevelopmental outcome of these children.[7] Data reveal that children who survive after placental abruption have a higher risk for conditions such as cerebral palsy,[8–10] cystic periventricular leukomalacia, intraventricular hemorrhage,[8,11] respiratory distress syndrome (RDS), [13] and neonatal apnea.[12] This may increase the overall mortality. In addition to increased morbidity, the impact of abruption on perinatal mortality has been demonstrated in several studies and populations.[4,5,7,14] Nevertheless, systematic studies on overall and cause-specific mortality of these children do not exist. Our aim was to more thoroughly evaluate the overall and cause-specific mortality of children born after placental abruption. To this end, we used the nationwide comprehensive health care registers of Finland.

METHODS

We conducted a population-based case-control study using linked data from population-based birth and cause-of-death registers from Finland. All singleton births in Finland from 1987 to 2005 were included in the study. We used the medical birth register (MBR) and the hospital discharge register (HDR) maintained by the National Institute for Health and Welfare to identify all women with a diagnosis of placental abruption by using codes from the *International Classification of Diseases, Ninth Revision* (codes 641.20, 641.21, and 641.23 for 1987–1995) and the *International Classification of Diseases, 10th Revision* (codes O45.0, O45.8, and O45.9 from 1996 onward) in the HDR and a check mark for placental abruption (yes or no) in the MBR (October 1990–2005). A reference group originated from the same registers (HDR and MBR) and consisted of 3 women without placental abruption for each abruption, matched by maternal age, parity, multiplicity, year of birth, and hospital district area. If all controls were not found, the age criteria were loosened by ±1 year to achieve 3 controls for each case. The hospital discharge data were then linked to the MBR by using the mother's unique personal identification number to identify all births with placental abruption. Multiple pregnancies were excluded from the final study sample. We identified 4190 women with a singleton birth and placental abruption and 12 570 matched referent women with a singleton birth without placental abruption. After excluding stillbirths, the final study population comprised 3888 children born after placental abruption (later referred to as index children) and 12 530 referent children.

The proportion of immigrants in the Finnish population is relatively small. Although data on the native country of the parturient are currently included in the MBR from 2000 onward, these data were not available for the whole study period (1987–2005).

Baseline data on interventions that mothers receive during pregnancy and delivery and on the newborn's outcome during the first 7 days are collected in the MBR from all delivery units (since 1987). All live births and stillbirths involving infants who are either gestational age of at least 22 completed weeks (≥155 days) or have a birth weight ≥500 g are registered in the MBR. The data are compiled at the time of birth by using the mother's maternity records. Less than 0.1% of all births are missing from the MBR. The data have been validated and correspond well with data available from hospital records.[15,16] In the HDR, data are collected on all inpatient episodes in all hospitals (since 1967), all outpatient surgical procedures in public hospitals (since 1994), and all outpatient visits in public hospitals (since 1998). The register contains information on admission and discharge date and diagnosis.

Both index and referent children were linked to the cause-of-death register (maintained by Statistics Finland) by their unique personal identification number to identify all deaths recorded up to the end of 2013. Causes of death were obtained from death certificates. The determination of the cause of death is based on medical or forensic evidence required for the death certificate. Forensic determination of the cause of death may be necessary if the death is not the result of an illness, if it is accidental or violent, or if it is caused by a treatment procedure or an occupational disease.[17] In other cases, the death certificate is based on medical evidence. Data on underlying causes of death since 1969 have been collected in a computerized database. The coverage of cause-of-death statistics is 99.9%, and coding is based on *International Classification of Diseases, Ninth Revision* codes (used during 1987–1995) and *International Classification of Diseases, 10th Revision* codes (used since 1996). The causes of death were grouped by taking into account both the main and underlying causes of death. External causes of death included accidents, homicides, and suicides. All deaths of index and referent children were manually

double-checked by 2 authors (O.R. and M.T.) to confirm the accurate cause of death.

The duration of gestation calculated from the last menstrual period was confirmed or corrected by ultrasound screening examinations at 11 to 13 or 18 to 20 weeks' gestation. Recorded in the MBR is the best clinical estimate for gestational age at birth. Smoking habits were recorded during antenatal clinic visits. Women who smoked at least 1 cigarette per day through the pregnancy were defined as smokers. Birth weight and gestational age were used to study the outcome of newborns. Newborns who were small for gestational age (SGA) were defined as having a birth weight ≤−2 SD, and newborns who were large for gestational age (LGA) were defined as having a birth weight ≥+ 2 SD of the national sex-specific standard.[18] Extremely preterm newborns were born before 28 weeks' gestation, very preterm newborns were born from 28 0/7 to 31 6/7 weeks' gestation, and moderately preterm newborns were born from 32 0/7 to 36 6/7 weeks' gestation.

An interaction analysis was performed if a compound effect between variables was suspected. Cox proportional hazard regression method was used to compare the index children to the referent children. Age-adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated. *P* values <.05 were considered statistically significant. The analyses were performed by IBM SPSS Statistics version 23 (IBM SPSS Statistics, IBM Corporation). The trend of infant mortality during the follow-up was tested as 2-sided by the Cochran-Armitage trend test by using StatXact version 4.0.1.

The study was approved by the National Institute for Health and Welfare (the register keeper), which also authorized the use of health register data in scientific research (permission: 1202/5.05.00/2013; date of amendment: June 7, 2017), as required by national data protection legislation. Statistics Finland authorized the use of cause-of-death register data (permission: TK-53-1035-13).

The protocol for this study was approved by the ethics committee of Helsinki University Hospital (permission: 334/13/03/03/2013; date of amendment: June 15, 2017). Because we used routinely collected anonymized electronic health records, no formal patient consent was required for this study.

RESULTS

There were 1 121 244 singleton deliveries in Finland during the study period, with the incidence of placental abruption being 374 out of 100 000 (0.4%). A total of 280 deaths among index children and 107 deaths among referent children were recorded by the end of 2013. The median follow-up time was 18 years (interquartile range: 13–22; range: 0–27).

Baseline characteristics of the mothers with and without placental abruption in relation to offspring mortality are presented in Table 1. The results reveal that despite the mother's age at delivery, marital status, socioeconomic status, or parity, the overall mortality was increased among children born after placental abruption (HR: 8.70; 95% CI 6.96–10.9). With Figure 1, we show that the cumulative hazard of death among the index children was higher compared with the referent children. The difference is evident already in the early postnatal period and increases toward the end of the follow-up. With Figure 2, we present the infant mortality as a 2-year moving average by year of birth among the index and referent children during the study period. The trend of infant mortality among the index children was decreasing (*P* < .001).

Detailed data of the interaction of placental abruption, maternal smoking, and offspring mortality in 4 different subgroups are presented in Table 2. Nonabruption, nonsmoking mothers were set as the reference group. Overall offspring mortality and mortality in all age groups were increased not only among smoking mothers with abruption, but also among smoking nonabruption mothers. However, although the point estimate for offspring mortality was higher among smoking women with abruption compared with nonsmoking women with abruption, the CIs were overlapping.

The mortality after placental abruption was increased during the neonatal period (<28 days), at the age of 28 to 365 days, and at the age of over 1 year. The major causes of death in both groups are listed in Table 3. By cause, the strongest increase in neonatal mortality was observed for birth-related asphyxia (HR: 108; 95% CI 34–341). Mortality was also increased because of prematurity, intracerebral hemorrhage, RDS or other respiratory disorders, anomaly, infection, and other causes. A list of causes of deaths that counted as anomaly or other cause is presented in the Supplemental Information. At the age of 28 to 365 days, there were 27 deaths among the index children and 9 deaths among the referent children. The mortality difference in this age category was significant (HR: 10.3; 95% CI 4.83–21.8). Among index children, there were 4 deaths due to sudden infant death syndrome (SIDS) and none among the referent children. Beyond the age of 365 days, a total of 23 deaths occurred among the index children and 47 among the referent children. Mortality of the index children was increased (HR: 1.7; 95% CI 1.03–2.79) compared with the referent children. For the index children, the median was

TABLE 1 Selected Baseline Characteristics Among Singleton Births of Women With Placental Abruption and Controls

Characteristic	Abruption		No Abruption		Adjusted Mortality
	All, *N* = 3888	Offspring Death (*n* = 280), *n* (%)	All, *N* = 12 530	Offspring Death (*n* = 107), *n* (%)	Overall, *n* = 387
					HR (95% CI)
Offspring death	3888	280 (7.2)	12 530	107 (0.9)	8.70 (6.96–10.9)
Age, y					
<25	661	42 (6.4)	2150	17 (0.8)	8.25 (4.70–14.5)
25–34	2329	159 (6.8)	7519	58 (0.8)	9.15 (6.77–12.4)
≥35	898	79 (8.8)	2861	32 (1.1)	8.06 (5.34–12.2)
Marital status					
Married	2450	167 (6.8)	8377	69 (0.8)	8.48 (6.40–11.2)
Cohabiting	968	67 (6.9)	2886	21 (0.7)	9.88 (6.05–16.1)
Single	422	34 (8.1)	1127	11 (1.0)	8.61 (4.36–17.0)
Unknown	48	12 (25.0)	140	6 (4.3)	5.96 (2.22–15.9)
Socioeconomic status					
Upper white-collar worker	442	36 (8.1)	1609	6 (0.4)	22.4 (9.43–53.2)
Lower white-collar worker	1284	73 (5.7)	4178	30 (0.7)	8.13 (5.31–12.4)
Blue-collar worker	639	35 (5.5)	1704	11 (0.6)	8.49 (4.31–16.7)
Other	509	43 (8.4)	1689	21 (1.2)	7.00 (4.15–11.8)
Unknown	1014	93 (9.2)	3350	39 (1.2)	8.23 (5.66–12.0)
Parity					
0	117	66 (5.8)	3628	29 (0.8)	7.46 (4.82–11.5)
1–2	1717	116 (6.8)	5555	39 (0.7)	9.91 (6.89–14.2)
≥3	1004	93 (9.3)	3225	34 (1.1)	9.14 (6.17–13.5)
Unknown	30	5 (16.7)	122	5 (4.1)	4.26 (1.23–14.8)

Differences between groups were analyzed by Cox proportional hazard regression analyses showing results by HRs with 95% CIs. Births between 1987 and 2005, with follow-up to the end of 2013. Mortality models were adjusted by mothers' age. Note: The data only allow the comparison of index and reference groups within each variable. The data do not allow comparison between variables. *N*, number of total population in the group; *n*, number of deaths in the group; %, percentage of deaths in the group.

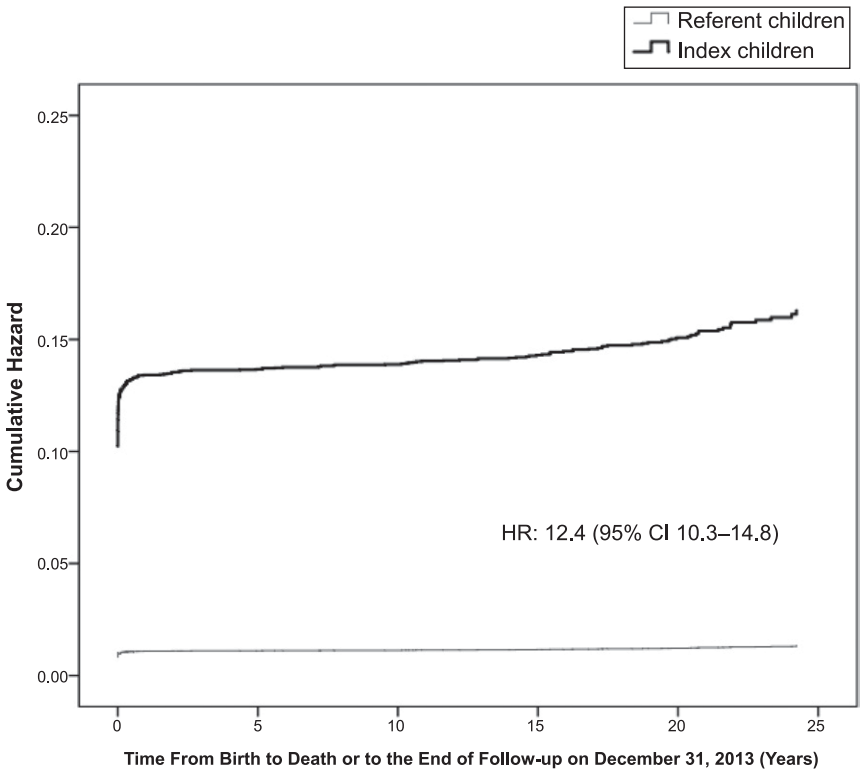

FIGURE 1
Cumulative hazard for all-cause mortality of children born after placental abruption (index children) and referent children born after nonabruption deliveries during 1987–2013.

12.86 years (range: 1.64–24.05), and for the referent children, the median was 15.13 years (range: 1.50–24.23). Nearly half of all deaths of the referent children were due to external causes, whereas for the index children, these causes covered only one-fourth of all deaths. Deaths due to cancer were also more common among referent children than among index children.

Selected baseline characteristics of the children of both groups are listed in Table 4. In very preterm and extremely preterm children, the groups did not differ in terms of mortality. However, both moderately preterm and term infants in the index group had increased overall mortality (HR: 2.77; 95% CI 1.54–4.98 and HR: 4.98; 95% CI 3.54–6.99, respectively). Among term infants in the index group, the mortality remained increased up to the age of 1 year compared with the referent children. For birth weight, significant difference in mortality was observed only in index infants weighing

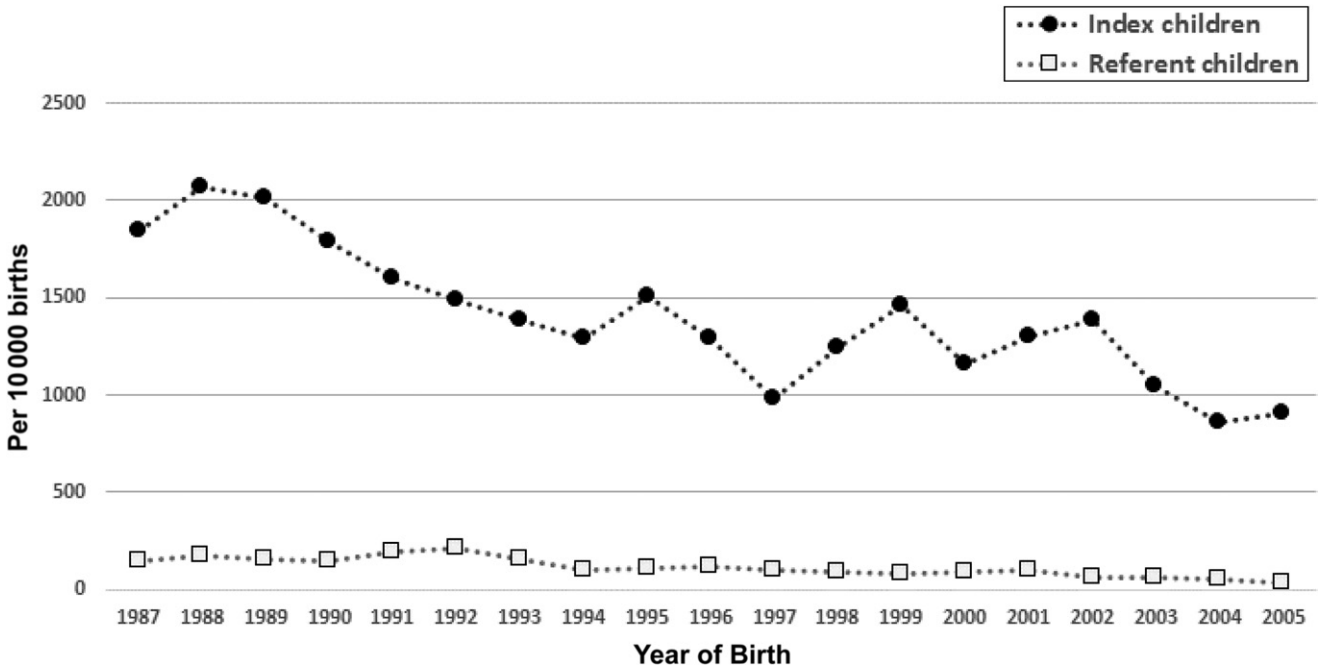

FIGURE 2
Infant mortality as a 2-year moving average by year of birth among the index children and referent children during 1987–2005. The trend of infant mortality was tested as 2-sided by the Cochran-Armitage trend test by using StatXact version 4.0.1.

TABLE 2 Interaction Between Placental Abruption, Maternal Smoking, and Offspring Mortality

	Overall Mortality, *n* = 387			Mortality at 0–27 d, *n* = 281			Mortality at 28–365 d, *n* = 36			Mortality at >365 d, *n* = 70		
	P	HR	95% CI	*P*	HR	95% CI	*P*	HR	95% CI	*P*	HR	95% CI
Nonabruption. Nonsmoking	<.001	1.000	—	<.001	1.000	—	<.001	1.000	—	.003	1.000	—
Nonabruption. Smoking	<.001	2.549	1.664–3.907	.019	2.232	1.142–4.364	.026	4.460	1.193–16.672	.005	2.432	1.310–4.513
Abruption. Nonsmoking	<.001	9.531	7.188–12.636	<.001	17.329	11.691–25.688	<.001	13.599	5.049–36.628	.273	1.449	0.746–2.814
Abruption. Smoking	<.001	14.898	10.738–20.670	<.001	26.488	17.112–41.000	<.001	21.578	7.037–66.167	.004	3.099	1.425–6.739

Differences between groups were analyzed by Cox proportional hazard regression analyses showing results by HRs with 95% CIs. Altogether, 856 (22.0%) mothers of index children and 1946 (15.5%) mothers of referent children smoked during pregnancy. Nonsmokers included women who had stopped smoking during pregnancy. Smoking data were not available for 199 mothers of index children and 396 mothers of referent children. The reference group was adjusted by maternal age. —, not applicable.

2500 g or more (HR: 5.94; 95% CI 4.33–8.14). The mortality remained increased up to the age of 1 year. For infants in the index group who were SGA, the mortality was increased during the neonatal period, whereas for infants in the index group who were LGA, both the neonatal and overall mortality were increased compared with the referent children. After placental abruption, boys had an increased overall mortality relative to girls (HR: 1.39; 95% CI 1.09–1.77; data not shown).

DISCUSSION

In this population-based case-control study of over 1 million births, we showed that children surviving after placental abruption had increased overall mortality compared with the referent children. Mortality was higher not only during the neonatal period but throughout the follow-up, and it was further increased by maternal smoking. Birth-related asphyxia was the leading cause of death.

Our study has several strengths and limitations. The study was based on national data obtained from validated and comprehensive health registers. The index and reference groups were large. However, the actual number of deaths in both groups was relatively small, which is a limitation concerning the conclusions to be drawn. For children who had died as neonates or infants, the numbers of deaths were small for several cause-of-death categories; this is another limitation. Moreover, we did not have information on the severity of the abruption. Finally, although the data were population-based and of high

TABLE 3 Observed Numbers and Major Causes of Death Among Singleton Children Born Alive After Placental Abruption (Index Children) and Singleton Referent Children Born Alive After Nonabruption Deliveries

	Index Children, *n* = 3888	Referent Children, *n* = 12 530	Age-Adjusted
	Deaths	Deaths	HR (95% CI)
All deaths	280	107	8.70 (6.96–10.9)
Cause of death at age of 0–27 d	230	51	14.8 (10.9–20.0)
Birth-related asphyxia	100	3	108 (34–341)
Prematurity	32	6	17.5 (7.21–41.8)
Intracerebral hemorrhage	11	1	36.9 (4.76–286)
RDS or breathing problem	35	4	29.0 (10.3–81.7)
Anomaly	28	24	3.83 (2.22–6.61)
Infection	15	7	7.04 (2.87–17.3)
Other cause	9	6	4.90 (1.74–13.8)
Cause of death at age of 28–365 d	27	9	10.3 (4.83–21.8)
Cerebral palsy	3	0	—
Birth-related asphyxia	3	0	—
Prematurity	5	0	—
Intracerebral hemorrhage	0	1	—
RDS or breathing problem	4	0	—
Anomaly	3	4	—
Infection	1	1	—
SIDS	4	0	—
External cause	0	2	—
Other cause	4	1	—
Cause of death at age of >365 d	23	47	1.70 (1.03–2.79)
Cerebral palsy	6	0	—
Birth-related asphyxia	2	1	—
Cancer	1	11	—
External cause	6	24	—
Anomaly	3	1	—
Infection	2	5	—
Other cause	3	5	—

Differences between groups were analyzed by Cox proportional hazard regression analyses showing results by HRs with 95% CIs. Births are between 1987 and 2005, with follow-up to the end of 2013. For age groups 28–365 d and >365 d, there were too few deaths for the HRs of the specific cause-of-death categories to be computed. —, not applicable.

quality, this is a single-country study, limiting the generalizability of the results.

We have previously demonstrated that maternal smoking is an independent risk factor for perinatal mortality among infants born after placental abruption.[4] In the current study, maternal smoking increased offspring mortality in both abruption-related and non–abruption-related births. As expected, the highest overall offspring mortality was found after placental abruption and maternal smoking. Our data can be used to suggest an additive effect with the combination of placental abruption and maternal smoking. However, the underlying mechanism for this additive effect is difficult to explain. Children born after abruption are certainly vulnerable even beyond the immediate perinatal time period and thus remain more susceptible to neonatal morbidity and mortality compared with children without abruption.[12] Maternal smoking may further increase this and simply make things worse.

Placental abruption is strongly associated with preterm delivery.[5] In the analysis of cause-specific mortality, we observed that children born after placental abruption had an increased mortality because of prematurity and also because of intracerebral hemorrhage, RDS or other respiratory disorders, and infections, all entities closely associated with prematurity. There were no statistically significant differences in mortality between the index and referent children born extremely preterm or very preterm. However, referent children probably had other health problems that led to prematurity. Thus, the causal effect of placental abruption on increased mortality among premature children should be interpreted with caution.[19]

We have shown earlier that ∼15% of newborns with abruption are born with asphyxia (pH 7.05 or less) compared with 1.5% of newborns without abruption.[20] In this study, the role of birth-related asphyxia as a cause of death among children born after placental abruption was remarkable. The largest number of asphyxia-related deaths of the index children was recorded in the neonatal period, with an over 100-fold increase in mortality relative to the referent children. With this observation, we highlight the fact that birth-related asphyxia is a strong negative marker even if the child primarily survives. In this study, birth-related asphyxia remained a cause of death also in the older age groups. In addition, it may play a role in deaths due to intracerebral hemorrhage, cerebral palsy, and SIDS. Placental abruption has been linked to SIDS.[21,22] This was also found in our study. Deaths due to SIDS were more common among children born after placental abruption compared with the expected number of cases in the general population.[17] It might be useful to counsel parents of newborns with asphyxia to follow the recommended safe sleep practice guidelines to reduce the risk of sleep-related infant deaths.[23]

Nine index children died of cerebral palsy after the neonatal period. There were no such deaths among the referent children. However, some causes of death, such as cancer and external causes, were more common among the referent children relative to the index children at the age of 1 year or more. This observation may merely be a chance finding or result

TABLE 4 Selected Baseline Characteristics and Mortality of Singleton Children Born After Placental Abruption (Index Children) and Referent Children Born After Nonabruption Deliveries

	Index Children		Referent Children		Adjusted Mortality			
	Deaths, *n*	Total (%)	Deaths, *n*	Total (%)	Overall	At Age of 0–27 d Age-Adjusted	At Age of 28–365 d	At Age of >365 d
					HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Sex								
Boys	175	2127 (8.2)	61	6483 (0.9)	9.07 (6.77–12.1)	13.4 (9.17–19.6)	8.70 (3.40–22.2)	2.56 (1.36–4.82)
Girls	105	1761 (6.0)	46	6047 (0.8)	8.03 (5.68–11.4)	16.9 (10.2–28.1)	13.2 (3.69–47.5)	0.88 (0.36–2.14)
Gestational age, wk								
<28	97	187 (51.9)	15	32 (46.9)	1.12 (0.64–1.93)	1.08 (0.61–1.90)	[a]	[b]
28–31 + 6	38	348 (10.9)	8	48 (16.7)	0.66 (0.31–1.43)	0.55 (0.25–1.20)	[a]	[a]
32–36 + 6	80	1172 (6.8)	13	514 (2.5)	2.77 (1.54–4.98)	3.48 (1.66–7.27)	3.28 (0.40–26.7)	1.29 (0.41–2.06)
≥37	63	2138 (2.9)	71	11 801 (0.6)	4.98 (3.54–6.99)	12.4 (7.41–20.7)	4.95 (1.79–13.6)	1.22 (0.59–2.50)
Birth wt, g								
<1500	127	434 (29.3)	22	72 (30.6)	0.97 (0.61–1.52)	0.91 (0.57–1.44)	[a]	0.18 (0.01–2.94)
1500–2499	65	882 (7.4)	15	307 (4.9)	1.55 (0.88–2.71)	1.57 (0.81–3.03)	2.89 (0.36–23.1)	1.09 (0.29–4.02)
≥2500	86	2536 (3.4)	70	12 042 (0.6)	5.94 (4.33–8.14)	16.8 (10.1–28.0)	4.26 (1.54–11.7)	1.37 (0.72–2.61)
Standardized birth wt								
SGA (≤–2 SD)	41	334 (12.3)	18	243 (7.4)	1.72 (0.98–2.99)	2.02 (1.07–3.82)	[c]	0.64 (0.17–2.40)
LGA (≥+2 SD)	9	109 (8.3)	5	459 (1.1)	7.78 (2.61–23.2)	8.57 (2.58–28.5)	[c]	4.50 (0.28–72.2)

Differences between index and referent children were analyzed by Cox proportional hazard regression analyses showing results by HRs with 95% CIs. Results of missing cases were not shown.

[a] No deaths among referent children.

[b] No deaths among the index children.

[c] Nine deaths among referent children, all appropriate for gestational age.

from the small number of observed cases.

We have previously shown that major congenital anomalies are twice as common among infants born after placental abruption than among referent infants.[3] In this study, the neonatal mortality due to anomalies was nearly fourfold among the index children relative to the referent children.

To the best of our knowledge, there are no earlier studies in which researchers focus on placental abruption and subsequent offspring mortality, although the impact of abruption on perinatal mortality is well known.[4,5] Moreover, in a recent US study,[12] abruption was associated with a more than sevenfold increased risk of neonatal mortality. In our study, the HR for neonatal mortality was nearly twice as high. This difference can probably be explained by our study period being longer and starting earlier (1987–2005) than in the American study, in which the children were born more recently (2002–2008). Our study also allowed evaluation of mortality trends; a decreasing trend was observed for infant mortality over time. This observation is in line with our previous study revealing a decreasing trend in perinatal mortality.[4]

CONCLUSIONS

Both overall and cause-specific mortality in Finnish children born after placental abruption are increased. The impact of placental abruption on offspring mortality clearly extends far beyond the perinatal period.

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ABBREVIATIONS

CI: confidence interval
HDR: hospital discharge register
HR: hazard ratio
LGA: large for gestational age
MBR: medical birth register
RDS: respiratory distress syndrome
SGA: small for gestational age
SIDS: sudden infant death syndrome

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Supplemental Information

LIST OF CAUSES OF DEATH COUNTED AS EITHER ANOMALY OR OTHER CAUSE

"Anomaly": anencephalus; anomalies of abdominal wall; anomalies of diaphragm; atresia of pulmonary artery; atrioventricular septal defect; chondrodystrophy; coarctation of the aorta; congenital cystic lung; congenital diaphragmatic hernia; congenital hydrocephalus; congenital malformation syndromes predominantly associated with short stature; cystic kidney disease; congenital stenosis of aortic valve; double inlet ventricle; Down syndrome; exomphalos; hypoplastic left heart syndrome; encephalocele; hereditary progressive muscular dystrophy; multiple congenital anomalies, so described; other bulbus cordis anomalies and anomalies of cardiac septal closure; other conditions due to autosomal anomalies; other congenital malformations of great veins; other specified anomalies; other specified anomalies of the heart; other specified anomalies of kidney; other specified anomalies of nervous system; other specified anomalies of unspecified limb; Patau syndrome; Potter syndrome; reduction deformities of brain; renal agenesis and dysgenesis; stenosis of pulmonary artery; tracheoesophageal fistula, esophageal atresia and stenosis; trisomy 18; unspecified anomaly of brain, spinal cord, and nervous system; vertebral defects-anal atresia-tracheoesophageal fistula with esophageal atresia-radial and renal dysplasia–association; ventricular septal defect.

"Other cause": birth injury to spine and spinal cord; cardiomyopathy, unspecified; cerebral edema due to birth injury; condition originating in the perinatal period, unspecified; congenital anemia; death certificate missing; disorders of glycine metabolism; disorders of tyrosine metabolism; fetal adrenal hemorrhage; hydrops fetalis not due to isoimmunization; massive aspiration syndrome; metabolism disorders, unspecified; neuronal ceroid lipofuscinosis; other and unspecified cirrhosis of liver; other cardiovascular disorders originating in the perinatal period.