Long-term offspring epilepsy outcomes following planned assisted homebirth versus hospital birth

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SUMMARY

Background. Planned homebirth is an option available to a small minority of expecting mothers. Compared with hospital births, long-term risks of homebirths are poorly known.

Aim. To study very long-term outcome for death, seizure remission, and other neurological long-term comorbidities

Material and Methods. A cohort of virtually all children (n = 230) in a geographically defined area with onset of epilepsy in or active epilepsy diagnosed prior to 1961–1964, and prospectively followed-up for 50 years.

Results. The proportion of homebirths was 16% in blue collar families and 2% in white collar families ($p = 0.007$). No significant differences between homebirths and hospital births were found in the frequencies of either abnormal pregnancy (27% vs 27%, $p > 0.99$) or abnormal birth (32% vs 35%, $p = 0.82$). Premature mortality following homebirths was non-significantly higher than that following hospital births (41% vs 27%, $p = 0.13$). Homebirth did not significantly affect 5-year (38% vs 40%) or 10-year (38% vs 37%) remission. Neither was homebirth alone associated with neurological morbidity (2.1, 0.82–6.1, $p = 0.137$).

Conclusion. Homebirth is an observable but non-significant risk factor of offspring mortality and neurological morbidity of an offspring with epilepsy. Blue collar families preferred homebirth to hospital birth for reasons which are not fully understood. Further research is needed in a prospective setting by applying modern standards of early identification of risk pregnancies and deliveries, carefully monitoring the health of expecting mothers, and anticipating referral to specialist services according to medical needs.

Key words: home birth • epilepsy • long-term study • mortality • seizure outcome

BACKGROUND

Planned homebirth rates and trends vary over time in developed countries. The incidence of births outside obstetric units is mostly less than 2% (Chervenak et al., 2013) but, consequent to various national legislations and cultures, there is a wide variation in the incidence, from 0.04% in Sweden (Hildingsson et al., 2010) to 23.4% in the Netherlands (Central Bureau voor de Statistiek, Den Haag, 2012). In Finland, planned home birth rates were 0.082% in 2015 and 0.085% in 2016 (THL, 2017). The country wise variation is due, among other things, to aspects of safety of mother and child, mother's satisfaction, respect for women's rights, and cost-effectiveness. Previous studies from several countries including Canada (Janssen et al., 2009), Den-

mark (Jensen et al., 2017), The Netherlands (Bolten et al., 2016; de Jonge et al., 2013), and Switzerland (Ackermann-Liebrich et al., 1996) showed no significant differences between homebirths and hospital births in deaths or short-term morbidity. According to Bolten et al. (2016), spontaneous deliveries were more likely and medical interventions fewer in homebirths than in hospital births. The existing literature on the risks for mother and offspring of planned homebirth vs hospital birth is limited to perinatal events.

AIM

Our aim was to study the long-term outcomes of offspring after planned homebirth in a cohort of patients with childhood-onset epilepsy, with special reference to mortality, cognitive disability, and seizure outcome. Our hypothesis was that homebirth is a risk factor of offspring death and impaired neurological long-term outcome.

MATERIALS AND METHODS

The study subjects included all children aged < 16 years, resident in the catchment area of the Turku University Hospital, Turku, Finland who, during 1961–1964, met the criteria for epilepsy (two unprovoked seizures). Subjects were identified on the basis of hospital, institution and primary health care records, and a review of the National Health Service records, a register of all patients residing in Finland. In Finland, as a rule, all children with an epileptic seizure were hospitalized for evaluation. Altogether, 245 patients were identified, 91% of them from the Turku University Hospital and the remaining 9% from other hospitals, institutions, and public or private offices. An ongoing surveillance for five years revealed three relevant patients, who were lost to identification. Thus, our study subjects represent virtually all children with epilepsy in the area in the years 1961–1964.

Of the 245 patients, 150 (61%) were incident cases, i.e., they were first evaluated for epilepsy in 1961–1964. The remaining 95 patients (39%) were prevalent cases, that is, they had been seen for epilepsy before 1961, and had had at least one seizure in three years prior to or during the years 1961–1964. All 245 patients were examined at baseline by the same child neurologist (Sillanpää, 1973) and enrolled for prospective follow-up of medical and social outcomes. Follow-up included ongoing review of the medical records and a comprehensive evaluation with structured questionnaires in five-year intervals. The study design and some earlier results have been reported earlier (Sillanpää et al., 1998; Sillanpää et al., 2004; Sillanpää and Shinnar, 2002; Sillanpää et al., 1999; Sillanpää and Schmidt, 2006).

Place of birth was explicitly known in 230 (94%) patients who comprised the present study population. They were born in 1948–1964. For the present study, the data on the course of pregnancy and delivery were re-evaluated for abnormalities and subsequent risks.

Definitions

Planned homebirth was defined as planned birth at home guided by a registered midwife. Hospital births included public tertiary care or secondary care hospitals, other obstetric units led by trained obstetrician or, in fewer cases, primary care (municipal) hospitals led by general practitioner. The general practitioners of primary care hospitals were by rule experienced clinicians and well aware of the health status of the population of their catchment area. Whether home or other birthing, all pregnant mothers were followed and supervised by a public midwife throughout the pregnancy.

Seizure outcome was evaluated using two definitions: 5-year terminal remission with last two years without medication (5YTR), and 10-year terminal remission with 5 last years without medication (10YTR). In addition to seizures, neurological morbidity included cognitive disability, cerebral palsy, hyperkinesia, and autism. Cognitive disability was defined as lowered ability to plan, comprehend and reason, and to apply social and practical skills in everyday life or, when formal intelligence test results were available, a full-scale IQ of less than 85. Socioeconomic status (SES) was defined and reclassified according to the classification of Statistics Finland (Statistics Finland, 2013).

Statistical analysis

Fisher's exact tests were used for the association of home vs hospital birth with 1) prenatal factors related to family or conditions during pregnancy and birth: family provider's socioeconomic status, family history of epilepsy or cognitive function, and complications during pregnancy and/or birth; 2) postnatal epilepsy-related factors: clustering of seizures, early effect of seizure therapy, early treatment seizure frequency, epilepsy syndrome, etiology of seizures, pre-treatment seizure frequency, status epilepticus, time to first 5-year remission, and time to first 10-year remission; and 3) factors representing long-term social outcomes: achieved ba-

sic or vocational education, employability, marital status, number of offspring, and premature retirement.

The main outcome variables included mortality and seizure outcome. The analyses were carried out with univariate and multivariable Cox regression models, using age as the time scale for mortality and number of follow-up years since the diagnosis of epilepsy for 5YTR and 10YTR. The proportionality of the hazards was checked using supremum tests and –log-hazard plots. Place of birth was included in all multivariable models, together with all prenatal or epilepsy-related factors associated to home birth with $p < 0.1$ in the Fisher's exact tests. Due to assumed independent effect on the outcomes, reported abnormalities during pregnancy or birth were also included as potential covariates. To evaluate the modifying effect of homebirth on the behavior of other risk factors, bivariate interactions of homebirth and the selected covariates were checked on all outcomes. The model inclusion criteria for interactions was $p < 0.05$. A backward selection process was used to reduce the number of covariates in the final models, with a cut-off value of $p > 0.1$ for exclusion for the main effects and $p > 0.05$ for interaction effects. The results of the Cox regression models are given as hazard ratios (HR) with 95% confidence intervals (95% CIs). A similar process, fitting exact logistic regression models, was used for the neurological outcomes other than epilepsy. The analyzed outcomes were cognitive disability alone, and neurological morbidity defined as any or several of the following: cognitive disability, cerebral palsy, hyperkinesia, and autism. The results of the logistic models are given as odds ratios (OR) with 95% CIs.

P-values < 0.05 were considered as significant. All tests were two-sided. Statistical computations were done using SAS System for Windows, release 9.4 (SAS Institute, Cary, NC, U.S.A.).

ETHICAL COMMITTEE

The study design was approved by the Institutional Review Board (ETMK 120/180/2008).

RESULTS

Mean age of the participants at the end of follow-up was 46.7 years (median 51.1, range 1–63) for the total group, 30.2 years (median 31, range 1–60) for deceased and 53.4 years (median 53.0, range 46–63) for surviving participants. Mean follow-up for seizure outcome was 38.2 years (median 46, range 5–60) for homebirths and 39.0 years (median 44, range 2–59) for hospital births. Birthplace of 61 (27%) children was tertiary care hospital, 126 (55%) secondary care hospital, 14 (6%) non-specialist hospital, and the remaining 29 (13%) home.

Pregnancy and birth characteristics

The course of pregnancy was considered as normal in 167 (73%) and abnormal in 63 (27%) pregnancies with the presenting abnormality being preeclampsia/high blood pressure (in 37 patients), birth weight of less than 2500 g (13), twin pregnancy (4), external abdominal blow (3), and infection, threatening spontaneous abortion, edema, continuous slight bleeding throughout pregnancy, severe bronchial asthma, and potentially harmful medication, one each. The course of delivery was regarded as normal in 153 (67%) and abnormal in 77 (33%) patients. The abnormalities included asphyxia ($n = 27$), breech presentation (11), cesarean section (11), prolonged delivery (9), "difficult delivery" (4), twin (4), weak fetal heart sounds (3), pre-term (3), forceps (2), and post-term delivery, umbilical strangulation, and green amnion fluid plus partial ablation of placenta, one each. In 31 patients, both the course of pregnancy and delivery were abnormal.

Factors related to homebirth

The proportion of homebirths was 16% in blue collar families and 2% in white collar families ($p = 0.007$). Homebirths, compared to hospital births, were not associated with cognitive disability in 1st degree relative (32% vs 17%, $p = 0.074$), epilepsy in 1st degree relative (44% vs 27%, $p = 0.10$) or frequencies of abnormal pregnancy or abnormal birth (27% vs 27%, $p > 0.99$ and 32% vs 35%, $p = 0.82$, respectively). Of the postnatal medical and social factors, clustering of seizures was associated with homebirth vs hospital birth, with a doubled frequency in homebirths (34% vs 17%, $p = 0.040$).

While SES strongly overlapped with homebirth – all but one of the 29 home-born offspring were from blue collar families – it was not associated with any of the outcome variables in univariate models ($p > 0.25$ in all analyses). To avoid computational problems, SES was excluded and cognitive disability in 1st degree relatives and clustering of seizures remained as homebirth-related covariates in the multivariable models.

Mortality

At the end of follow-up, 163 (71%) of 230 participants were surviving and 67 (29%) had deceased. Median

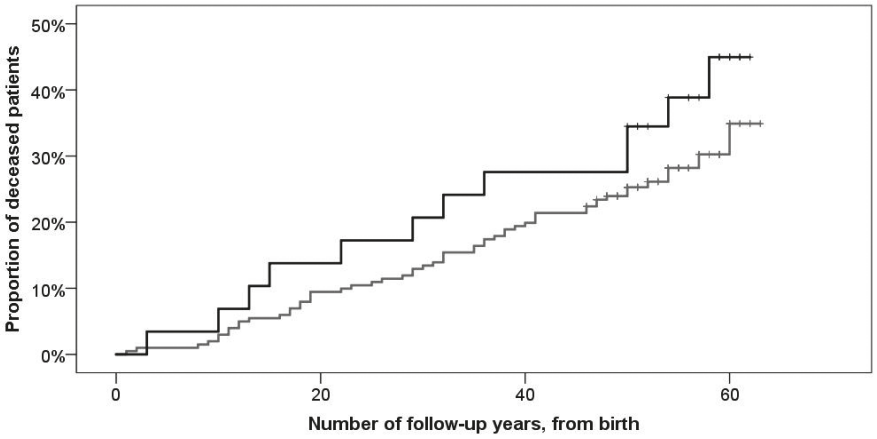

Figure 1. Death rates of 230 patients with childhood onset epilepsy. Black line: homebirths (n = 29); grey line: hospital births (n = 201).

Table 1. Univariate and multivariable analyses for predictors of long-term survival in homebirths vs hospital births

	Univariate[a]			Multivariable[b]		
	HR	(95% CI)	p-value	HR	(95% CI)	
Death						
Home birth	1.5	(0.8–2.7)	0.235	1.3	(0.7–2.5)	0.391
Clustering of seizures	2.0	(1.2–3.5)	0.011	2.0	(1.1–3.3)	0.014
Abnormal birth	1.3	(0.8–2.1)	0.382	–		
Abnormal pregnancy	1.3	(0.7–2.1)	0.466	–		
Cognitive disability in 1st degree relatives	0.8	(0.4–1.6)	0.576	–		

[a] – Cox regression models; HRs calculated for home vs hospital births, abnormal vs normal pregnancies or births, any vs none cognitive disability in 1st degree relatives, or clustered vs non-clustered seizures.

[b] – Homebirth as the main predictor was included in all final multivariable models; covariates with p > 0.1 were excluded in a backward selection process. None of the pairwise interactions of homebirth and the covariates reached the inclusion criteria of p < 0.05.

HR – hazard rate

age at death was 30.5 (interquartile range [IQR] 14–50) years in homebirth and 31 (17–41) years in hospital births (p = 0.86) Premature mortality following homebirths was non-significantly higher than that following hospital births (41% vs 27%, p = 0.13). Figure 1 shows the mortality rates that were, throughout the observation period, steadily but non-significantly higher in homebirths than in hospital births (HR = 1.5, 95% CI 0.8–2.7, p = 0.23) (Table 1). Home birth did not modify the effect of the covariates on mortality (p > 0.10 in all bivariate interaction analyses). The only independent predictor for premature death was clustering of seizures (p = 0.014) (Table 1).

Seizure outcome

Both poor 5YTR (Figure 2) and poor 10YTR (Figure 3) were predicted by an abnormal course of birth, but the association was not modified by birthplace (homebirth* abnormal birth interaction[1] p > 0.28 for both 5YTR and 10YTR). Thirty-eight per cent of homebirths and 40% of hospital births ended up in 5YTR. Ten-year terminal remission was attained by 38% and 37%, respectively. The median follow-up time for achieving 5YTR was 10 years (IQR 7–19 years) in homebirths and 11.5 years (IQR 7.5–17.5 years) in hospital births. The corre-

[1] Bivariate interaction of homebirth and abnormal birth, please see *Statistical methods* section in p. 8.

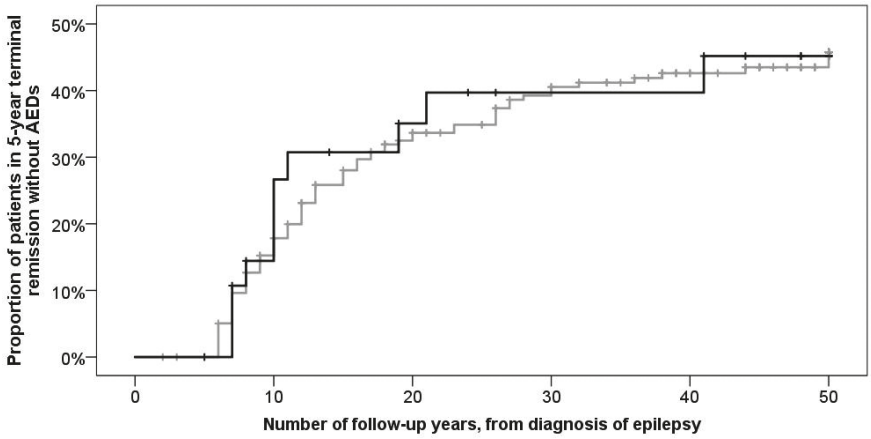

Figure 2. Five-year terminal remission rates of 230 patients with childhood-onset epilepsy by birthplace. Black line: homebirths (n = 29); grey line: hospital births (n = 201).

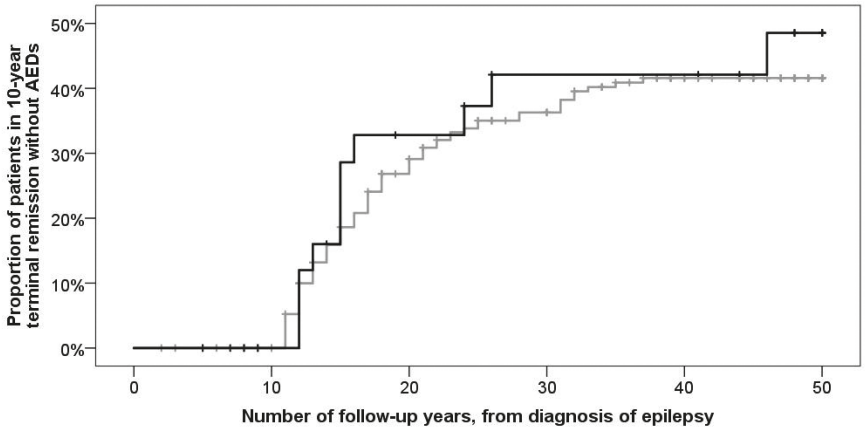

Figure 3. Ten-year terminal remission rates of 230 patients with childhood-onset epilepsy by birthplace. Black line: homebirths (n = 29); grey line: hospital births (n = 201).

sponding proportions for 10YTR were 38% in homebirths (median 15, IQR 12–24 years) and 37% in hospital births (median 16, IQR 12–21 years). Abnormal birth reduced the hazard of achieving 5YTR by 54% and 10YTR by 57% (Table 2).

Other neurological outcomes

Neurological morbidity other than epilepsy was found in 76% of homebirths and in 60% of hospital births. None of the bivariate interactions of homebirth and the covariates was significant, but abnormal pregnancy and abnormal birth were associated with neurological morbidity on univariate models (OR 2.2, 95% CI 1.1–4.7, p = 0.022 for abnormal pregnancy and 2.9, 1.5–5.9, p = 0.001, for abnormal birth). Homebirth alone was not associated with neurological morbidity (2.1, 0.82–6.1, p = 0.137). The results remained virtually the same in the multivariable models, except for abnormal pregnancy which lost the significance.

Cognitive disability was found in 66% of homebirths and in 48% of hospital births. On univariate analysis, abnormal pregnancy (2.0, 1.03–3.9, p = 0.040) and abnormal birth (2.9, 1.6–5.6, p < 0.001) – but not homebirth (2.0, 0.9–5.1, p = 0.123) – predicted cognitive disability. On multivariable analysis, abnormal birth, irrespective of birthplace, predicted cognitive disability (2.9, 1.6–5.7, p < 0.001).

Table 2. Univariate and multivariable analyses for predictors of seizure outcome in homebirths vs hospital births

	Univariate[a]			Multivariable[b]		
	HR	(95% CI)	p-value	HR	(95% CI)	
5YTR, 2 years off-AEDs						
Home birth	1.1	(0.6–2.0)	0.854	1.4	(0.8–2.5)	0.269
Abnormal birth	0.5	(0.3–0.8)	0.002	0.5	(0.3–0.7)	0.002
Abnormal pregnancy	0.8	(0.5–1.3)	0.432	–		
Cognitive disability in 1st degree relatives	1.0	(0.6–1.6)	0.993	–		
Clustering of seizures	0.8	(0.5–1.5)	0.510	–		
10YTR, 5years off-AEDs						
Home birth	1.2	(0.6–2.2)	0.588	1.6	(0.9–2.9)	0.123
Abnormal birth	0.4	(0.3–0.7)	0.002	0.4	(0.3–0.7)	0.001
Abnormal pregnancy	0.8	(0.5–1.4)	0.497	–		
Cognitive disability in 1st degree relatives	1.0	(0.6–1.6)	0.939	–		
Clustering of seizures	1.0	(0.5–1.7)	0.880	–		

[a] – Cox regression models; HRs calculated for home vs hospital births, abnormal vs normal pregnancies or births, any vs none cognitive disability in 1st degree relatives, or clustered vs non-clustered seizures.

[b] – Homebirth as the main predictor was included in all final multivariable models; covariates with $p > 0.1$ were excluded in a backward selection process. None of the pairwise interactions of homebirth and the covariates reached the inclusion criteria of $p < 0.05$.

HR – hazard rate

DISCUSSION

Our data are from a unique, very long-term followed-up population study that gives information on life-circle of children with epilepsy. The proportion of abnormal pregnancies and deliveries were virtually the same in homebirths and hospital births and the two groups subsequently were comparable for risk estimations. The results showed that families with blue collar status highly preferred homebirth to hospital birth. The preference was not related to the costs of delivery because, according to the legislation, the services of public maternity and child health clinics were free of charge. Throughout the study period, risk for death was observably but non-significantly higher in homebirths than in hospital births. Clustering of seizures was two-fold as common in homebirths as in hospital births. Abnormal course of pregnancy and birth influenced on poor seizure outcome and neuro-comorbidity, but birthplace did not modify the effect. Neither had homebirth any significant effect on five-year or ten-year terminal remissions.

Our study is in line with the previous studies which showed no increased risks associated with homebirths in comparison with hospital births. A Swiss study (Ackermann-Liebrich et al., 1996) compared 489 healthy low-risk women opting for home delivery with 385 opting for hospital delivery for perinatal events, including need for medication, duration of labor, instrumentation births, occurrence of severe perineal lesions, maternal blood loss, and perinatal morbidity and mortality. Birth at home caused no increased maternal or offspring perinatal risk. In a Dutch study (Bolten et al., 2016), comparing planned home births with hospital births, 3495 low-risk nulliparous and parous women in midwife-guided care who gave planned homebirth, had less often medical or other interventions (episiotomy) during delivery. Another report (Janssen et al., 2009), based on 4752 planned homebirths and matched 5331 planned hospital births in Canada, reported parallel findings in women who gave homebirth to have fewer measures during pregnancy or delivery and their neonates being less often in need of resuscitation. Perinatal morbidity and mortality were similar or lower in a large Danish register study with 6395 planned homebirths and 266 604 planned hospital births, except for slight but significant increase in the number of early neonatal deaths among nulliparous women who gave birth at home (Jensen et al., 2017).

The previous literature does not show significant differences in short-term outcomes between homebirths and hospital births. Contrary to our hypothesis, even the long-term outcomes did not differ from each other to the extent we expected. Expected differences were absent despite an even distribution of risk factors both in the homebirth and hospital-birth groups. The thresh-

old for homebirths was obviously lower in the 1950s and 1960s than today. In countries where patients have to pay for the use of public health services, high expenses of hospital care may determine the choice of birth place. However, despite a strong overlapping of the socioeconomic status and homebirth, high costs could not have been a reason in our study, because public maternity clinic services were free for expecting mothers.

While today's advanced obstetric technology was not available in the 1950s and 1960s, one can only speculate about how the families might have opted between homebirth and hospital birth, if they had had access to modern facilities and how the technology might have impacted on the long-term outcomes. Availability of and accessibility to high-level services would not guarantee the usage of the services by the mothers. Trends in fashion and patient satisfaction, respects for women's rights and similar fully non-obstetrical issues may greatly contribute to the choices (Chervenak et al., 2013). Whatever the reasons for opting for homebirth are, planned and assisted homebirth does not meet current standards for mother and offspring safety (Chervenak et al., 2013). On obstetrical grounds, expecting mothers with a risk pregnancy or delivery or both should be advised against homebirth (Chervenak et al., 2013).

Our study has some limitations. The main problem is a small sample size. While the rates of death, poor seizure outcome and neurological comorbidity were higher in homebirths, the statistical power was insufficient to detect possible significances of the differences. The participants are, however, a representative sample of a geographic population. The prospective follow-up period is uniquely long and allows for disclosing any long-term effects. Childhood-onset epilepsy, the basic inclusion criterion in the study, is another limitation with regard to the generalizability of the results. However, this fact can also be considered as a strength, because epilepsy is known to be associated with several neurological and other comorbidities, thus increasing their incidence in the study sample, and providing larger number of events for analysis than would be expected in a random sample. Neither was the comparability between the homebirth and hospital birth groups affected by factors related to epilepsy, because the requirement of present epilepsy was the same in the both groups.

CONCLUSIONS

Homebirth is an observable but non-significant risk factor of the mortality and neurological morbidity of offspring with epilepsy. Blue collar families preferred homebirth to hospital birth for reasons which are not fully understood. Further research is needed in a prospective setting by applying modern standards of early identification of risk pregnancies and deliveries, carefully monitoring the health of expecting mothers, and anticipating referral to specialist services according to medical needs.

CONFLICT OF INTEREST DISCLOSURE

None of the authors have anything to disclose.

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