Maternal age at child birth, birth order and suicide at a young age – a sibling comparison

Authors

Johan Håkon Bjørngaard, PhD[*,1,2] postdoctoral fellow
Ottar Bjerkeset, MD, PhD[3,4]
Lars Vatten, MD, PhD[1] , professor
Imre Janszky, MD, PhD [1,5]
David Gunnell, MD, PhD[6], professor
Pål Romundstad, PhD[1] , professor

[*]**Corresponding author**: johan.h.bjorngaard@ntnu.no

[1]Department of Public Health, Faculty of Medicine, Norwegian University of Science and Technology, 7491 Trondheim, Norway

[2]Forensic Department and Research Centre Bröset St. Olav's University Hospital Trondheim, Trondheim, Norway

[3]Institute of Neuromedicine, Faculty of Medicine, Norwegian University of Science and Technology, Trondheim, Norway

[4]Department of Research and Development, Levanger Hospital, Nord-Trøndelag Health Trust, Levanger, Norway

[5]Karolinska Institutet, Stockholm, Sweden

[6]School of Social and Community Medicine, Bristol University, Bristol, UK

Abstract

Previous studies have reported strong associations between birth order, maternal age and suicide, but these may be confounded by socioeconomic and other factors. To control for such factors, we compared suicide risk between siblings and studied how maternal age at child birth and birth order influenced risk in a cohort study of 1,690,306 Norwegians born 1967-1996 that were followed up until 2008. Using stratified Cox regression, we compared suicide risk within families with two or more children where one sibling died from suicide. Altogether, 3,005 suicides occurred over a mean follow-up period of 15 years; 2,458 of these suicides occurred among 6,741 siblings within families of two or more siblings. Among siblings, birth order was positively associated with risk: each increase in birth order was associated with 46% (adjusted hazard ratio, aHR, 1.46, 95% CI 1.29-1.66) higher risk of suicide. For each 10-year increase in maternal age at child birth, the offspring's suicide risk was reduced by 57% (aHR 0.43, 95% CI 0.30-0.62). Our study suggests that confounding due to familial factors is not likely to explain the associations of birth order and maternal age at child birth with suicide risk.

Introduction

Suicide is one of the most common causes of death among young adults in western societies, and for each completed suicide ~~twenty or more~~ several people attempt to end their lives(1, 2). While mental illness and substance misuse contribute to a high proportion of suicides, impulsive behavior in moments of crisis, as well as poverty and serious physical illness are also important risk factors(3, 4).

Recent studies indicate that birth order is associated with suicide risk, with later born children experiencing an increased risk of suicide, whereas maternal age at child birth may be inversely related to risk among the offspring(5-9). It has been estimated that more than 20% of suicides may be attributable to the combined effects of maternal age at child birth and birth order(9). If these estimates are correct, a better understanding of their underlying causal nature may provide important information about the family's role in the complex etiology of suicide.

The relationship between siblings and the relations of siblings with their parents are unique for each individual within a family and these inter-individual differences may have profoundly different effects on a child's development(10) and later suicide risk. Thus, it has been suggested that older siblings benefit from more parental attention than younger siblings(11). Furthermore, it has been speculated that short intervals between births may be associated with poorer mental health because of fetal under-nutrition due to depletion of maternal nutritional reserves during the preceding pregnancy, and this impacts on neurodevelopment(12). Such effects are likely to be stronger in third born than second born children and fourth born than third born and so on. In relation to maternal age, the offspring of young mothers are at higher risk of several adverse psychosocial outcomes; this may be due to the limited social, psychological and economic resources available to them(13, 14). Confounding due to familial socioeconomic

position, genetic and environmental factors could also contribute to the observed associations. The birth order effect could for example be confounded by family size(15) and young mothers themselves have an increased risk of psychiatric illness and low socioeconomic position(14). It is difficult to adequately control for the possible confounding effect of socioeconomic position and genetic influences on mental health with the limited data available in large record linkage studies. Previous studies have compared individuals from population samples, where information on family characteristics and possible confounders is often not available. One way to overcome this limitation is by carrying out a sibling comparison – comparing risk in relation to maternal age and birth order *within* families because a family design will in itself control for shared factors that could have confounded the results of other studies(16).

We have studied the associations of maternal age at child birth and birth order with the offspring's risk of suicide before the age of 42 years in Norway. Our main aim was to assess suicide risk among siblings within families where a suicide occurred during follow-up. For comparison, we also studied suicide risk in the population as a whole.

Method

The study is based on a linkage between data from the Medical Birth Registry of Norway (www.fhi.no/mbrn) and information on suicide obtained from the Norwegian Cause of Death Registry. The Medical Birth Registry was established in 1967, and information on virtually all births that have taken place in the country since then, is registered. The registry includes health and demographic information on the mother and her offspring at the time of birth.

Follow-up for suicide was conducted among participants who were born between 1 January, 1967 and 31 December, 1996 and were alive at 12 years of age; a total of 1,690,306

people were eligible for follow-up from the age of 12 years because suicides prior to the age of 12 are rare(17). Our analyses were based on two samples. The first sample consisted of the population as a whole, and the second sample ("sibling cohort") consisted of siblings within families with at least two siblings where at least one sibling committed suicides. The exposure variables of interest were maternal age at child birth and birth order of siblings, and we also included information on the offspring's sex, year of birth, time interval between births, maternal marital status, and maternal and paternal education at the time of birth (Table 1).

Suicides from the age of 12 years until the end of follow-up (31 December, 2008) were identified through individual linkage with the Cause of Death Registry in Norway (http://www.ssb.no/english/dodsarsak). From the International Classification of Disease 9th edition (ICD-9), we used suicide codes E950–E959, and from ICD-10, we used codes X60–84 (suicide) to indicate suicide. In most cases of sudden unexpected deaths forensic autopsies are conducted to determine cause of death.

Siblings of the deceased were identified using the unique identification number of each mother; this enabled linkage of information between siblings within families with at least two siblings. The present study was approved by the Regional Committee for Medical Research Ethics in Central Norway.

Statistical analysis

Both in the population as a whole and in the sibling cohort we assessed suicide risk using Cox proportional hazards models with age as the time axis. The participants were followed from the age of 12 years until death caused by suicide, deaths from other causes, emigration or until the end of follow-up (31 December 2008), whichever event occurred first. The oldest participants in the cohort were born in 1967 and were 41 years of age at the end of follow-up.

Both in the population as a whole and in the sibling cohort, we studied suicide risk related to birth order and maternal age at delivery. In multivariable analyses, we controlled for offspring sex, year of birth (1967-1976 vs. 1977-1999), maternal marital status (married/cohabiting or other) and maternal and paternal level of education (recorded in three categories); in the analysis of maternal age at child birth, we also adjusted for birth order, and in the analysis of birth order, we also adjusted for maternal age at child birth. In the analysis of the population as a whole, we used a standard Cox regression approach, but in the sibling cohort, we used stratified Cox models to control for factors that are shared within families(18). This approach enabled us to compare associations with maternal age and birth order within sibships. In such an analysis, characteristics that are shared by siblings (e.g. socioeconomic position, parental history of mental illness) cannot have confounding effects on the estimated associations. We also carried out a test to investigate the possibility of effect measure differences of maternal age and birth order between sons and daughters.

In a separate analysis of the sibling cohort, we assessed whether the association of birth order with suicide risk differed depending on the time-interval since the prior birth (<2 years, 2-3 years, >3 years). In additional analyses, we studied whether maternal age at child birth, and sibship size, could influence the association of birth order with suicide risk among siblings.

The proportional hazards assumptions were assessed on the basis of Schoenfeld residuals and there was no evidence against the proportionality assumption. Stata version 11 (www.stata.com) was used for the statistical analyses.

Results

Characteristics of the study population and the sibling cohort are presented in Table 1. In the population as a whole, 3,005 suicides occurred during more than 25 million person-years of

follow-up (25,407,240 person years during a mean follow-up of 15 years). Among these suicides, 2,458 occurred within the cohort of 6,741 siblings (111,472 person years; mean follow-up, 17 years). Eighteen families experienced two suicides. The risk of suicide was over three times higher in males than females and was increased in offspring of mothers who were not married or cohabiting and amongst those with less educated fathers (see Web Table 1). The crude Hazard Ratio of those being an only child vs. sibships with two or more siblings was 0.99 (95% CI 0.86-1.15).

Table 2 shows that birth order was positively associated with suicide risk in the population as a whole. In the unadjusted analysis, suicide risk increased by 11% (HR 1.11, 95% CI, 1.08-1.15) for each increase in birth order category, and after adjustment for maternal age at delivery, offspring sex, time period of birth, maternal marital status and parental education, the corresponding risk increase was 26% (aHR 1.26, 95% CI 1.20-1.31). In relation to maternal age at child birth, there was an inverse association with suicide risk among the offspring. For each 10-year increase in maternal age, the unadjusted risk reduction was 14% (HR 0.86, 95% CI 0.80-0.93), and after adjustment for birth order, offspring sex, time period of birth, maternal marital status and parental education, the corresponding risk reduction was 30% (aHR 0.70, CI 0.64-0.77).

In the sibling cohort (Table 3), the unadjusted HRs for birth order and suicide risk were similar to those observed for the total population, but for maternal age at child birth we found no clear association. However, after adjustment for maternal age at child birth and birth order in the same model, the associations among siblings were substantially stronger than those observed in the total population. For each increase in birth order category, the adjusted risk increase among siblings was 46% (aHR 1.46, 95% CI 1.29-1.66). In relation to maternal age at child birth and

offspring suicide risk, there was a risk reduction of 57% (aHR 0.43, 95% CI 0.30-0.62) for each 10 year increase in maternal age.

There was no strong evidence that associations with birth order differed in males and female siblings (p interaction =0.41). For each increase in birth order category, the adjusted risk increase among brothers was 44% (aHR 1.44, 95% CI 1.26-1.64) and 51% (aHR 1.51, 95% CI 1.30-1.76) among sisters. There was some statistical evidence (p interaction =0.06) that associations with maternal age differed in sons and daughters. Among brothers, risk declined by 60% (aHR 0.40, 95% CI 0.27-0.58) with each 10 year increase in maternal age; the corresponding estimate for sisters was 49% (aHR 0.51, 95% CI 0.34-0.76).

In Table 4, we stratified the analysis of birth order by time interval between births. The results showed that the positive association with suicide risk was strongest if the time interval between births was relatively short (p interaction=0.001). Thus, the crude hazard ratio per birth order category was 1.40 (95% CI 1.17-1.69) if the time interval was less than two years, compared to 1.20 (95% CI 1.08-1.34) if the interval was between 2 and 3 years, and 1.02 (95% CI 0.89-1.17) if the interval was 3 years or more. The effect measure modification was attenuated after adjustment for maternal age (p interaction=0.03). In separate analyses (Web Table 2), we stratified the association of birth order by sibship size. The positive association of birth order with suicide risk did not substantially differ by size of the sibship. A model excluding the 175 twins from the sibling cohort gave almost identical results as those shown in table 3.

Discussion

In this large prospective study of suicide before 42 years of age, we found a strong increase in suicide risk with increasing birth order, and a strongly reduced risk with increasing maternal age at child birth.

Strengths and limitations

The main strength of these analyses is the large sample size (2,458 suicides in the analysis of siblings within affected families) that makes chance an unlikely explanation for our findings. Another important strength is that we could assess suicide risk among siblings within families; and thereby, important factors that are shared between siblings will be taken into account by the study design. Among others, these factors include parental education, the socioeconomic situation of the household, parental mental illness and other shared factors that could be relevant for suicide risk[3].

However, we cannot exclude the possibility that comparisons within families may be vulnerable to time-dependent factors that could influence the internal family environment, and have different effects on the siblings. Relevant examples include parental divorce, placement into foster care, the onset of serious mental illness in a parent, domestic violence or other events that have occurred at different stages of the siblings' lives when age is important for the effects of such factors[19, 20]. However, these factors could also be considered as possible mediating factors, rather than confounders, because they can be neither causes of maternal age at child birth nor determinants of birth order.

Naturally, birth order is highly correlated with maternal age, and in the analyses of each factor, careful adjustment for the other factor is essential. This is particularly important since the

results of birth order and maternal age show opposite effects on suicide risk. Thus, without adjustment for maternal age the positive association of birth order would be much weaker than the adjusted association due to the underlying inverse effect of maternal age at child birth.

It is possible that suicide is underreported in the Cause of Death Registry, but this would only bias our results if the underreporting were associated with maternal age at child birth or with birth order. However, the prospective approach of the study makes such a bias unlikely.

Previous studies

The results of a few previous studies have suggested that maternal age at child birth is inversely associated with suicide risk in the offspring(5, 6, 9), and that birth order is positively associated with the risk of suicide(5-9). It has also been suggested that low maternal age at child birth is associated with increased risk of suicide attempts(21). The association of maternal age at child birth in our study was both stronger and displayed a linear relation with suicide risk, whereas the results of other studies(6, 9) suggest that the increased risk may be restricted to the offspring of very young mothers (<20 years). Family designs with comparisons of siblings have not been previously used in relation to suicide risk, and the advantage of controlling for shared family factors provided by the sibling design of our study may have contributed to the stronger associations. Furthermore, more than 80% of the suicides in our study were included in the sibling cohort – making the results fairly representative for families being exposed to a suicide.

Possible mechanisms

The results from the present study indicate that the associations of maternal age and birth order with suicide are not confounded by socioeconomic or genetic factors. There are several possible mechanisms for the observed associations.

The linear reduction in suicide risk associated with increasing maternal age at child birth may seem surprising, since both maternal and paternal age are positively associated with the offspring's risk of serious psychiatric morbidity, including schizophrenia, conditions that are associated with increased risk of suicide(22-24). Although serious mental illness is an important risk factor for suicide, these conditions may be too rare to compete with the impact of low social, psychological and economic resources faced by many young mothers.

The inverse association of maternal age with the offspring's risk of suicide may also be related to the possible stressful situation for younger mothers, as young mothers are more likely to have mental health problems, family problems – as well as problems at school, education, employment and housing(14). Furthermore, it has been suggested that stressful pregnancies may influence fetal brain development, and possibly influence the psychological development and mental health of the child(25).

The results from the present study support the view that family relationships and bonds made in early childhood may have an influence on psychiatric morbidity and suicide risk later in life(26-28). Many studies have suggested that first born children have a more prominent position in the family than subsequently born siblings, and it has been consistently reported that birth order is inversely associated with intelligence(11, 29). Possibly, our findings related to birth order may be relevant within a similar context, suggesting that the older siblings may profit from this position by a higher degree of stimulation and support during their early years. It is also possible that younger siblings are more easily bullied by older siblings, and it has been repeatedly reported that bullying is a strong risk factor for suicide(30). The strong positive unadjusted association of birth order with suicide was stronger in families with short intervals between births, are supporting the possible impact of nutrition on the developing brain(12). However, this finding could partly be explained by the protective effect of increasing maternal age.

Implications

While several twin studies have found only marginal effects of shared family environmental factors on mental health(10), the results of our study strongly indicate that family factors that are not shared by siblings may operate from an early age and influence suicide risk. Furthermore, early motherhood, especially teenage pregnancy, is associated with several adverse psychosocial outcomes in their offspring(14). The incidence of early motherhood varies considerably worldwide(31) and the results of the present study underscore the potential importance of ~~reducing teenage pregnancy and~~ offering support to young mothers and their offspring.

Conclusion

The inverse association of maternal age at childbirth and the positive association of birth order with suicide risk among siblings strongly indicate that family factors that are not shared by siblings may operate from an early age and influence suicide risk. Our study suggests that confounding due to familial factors is not likely to explain the associations of birth order and maternal age at child birth with suicide risk.

Acknowledgements

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Table 1 Characteristics of the total population and the cohort of siblings within the total population

	Total cohort				Sibling cohort			
	Suicides		Non-suicides		Suicides		Non-suicides	
Sex (N, %)								
Men	2,330	78	864,873	51	1,894	77	2,129	50
Women	675	22	822,428	49	564	23	2,154	50
Birth period								
1967 – 1976	1,943	65	610,337	36	1,496	61	2,312	54
1977 – 1999	1,062	35	1,076,96	64	962	39	1,971	46
Birth order (N, %)								
First	1,057	35	698,861	41	859	35	1,160	27
Second	1,065	35	538,108	35	927	38	1,339	31
Third	539	18	273,730	16	430	17	1,003	23
Fourth or higher	344	12	131,602	8	242	10	781	18
Maternal age (Mean, SD)	25.6	5.5	26.6	5.2	25.1	5.0	26.4	5.7
Maternal marital status (N, %)								
Married, cohabitant	2,566	85	1,506,493	89	2,124	86	3,793	89
Other	439	15	180,808	11	334	14	490	11
Maternal educational level (N, %)								
Primary/lower secondary	1,028	34	451,153	27	819	34	1,503	35
Upper secondary	1,389	47	783,587	47	1,134	46	1,900	45
College/university	573	19	442,332	26	492	20	854	20
Paternal educational level (N, %)								
Primary/lower secondary	928	31	394,827	24	730	30	1,322	31
Upper secondary	1,490	51	847,553	51	1,241	51	2,124	50
College/university	525	18	416,642	25	443	18	766	18
Total	3,005		1,687,301		2,458		4,283	

N varies due to missing data on parental education. Due to rounding errors, percentages do not sum to 100.

Table 2. Hazard ratios for suicide according to maternal age and birth order in the total population.

	N	Crude[a]		Adjusted[b]	
	Suicides	HR	95% CI	HR	95% CI
Birth order					
1st child	1,057	1.00	Ref	1.00	Ref
2nd child	1,065	1.22	1.12, 1.33	1.50	1.37, 1.65
3rd child	539	1.28	1.15, 1.42	1.73	1.53, 1.95
4th child or more	344	1.42	1.26, 1.60	2.11	1.81, 2.47
Birth order – trend	3,005	1.11	1.08, 1.15	1.26	1.20, 1.31
Maternal age					
Maternal age <20 years	371	1.00	Ref.	1.00	Ref.
Maternal age 20 - 24 years	1,051	0.72	0.64, 0.81	0.74	0.65, 0.84
Maternal age 25-29 years	902	0.67	0.59, 0.75	0.63	0.55, 0.73
Maternal age 30-34 years	457	0.69	0.60, 0.79	0.57	0.48, 0.67
Maternal age >34 years	224	0.71	0.60, 0.84	0.50	0.41, 0.61
Maternal age in 10-years intervals[c]	3,005	0.86	0.80, 0.93	0.70	0.64, 0.77

[a] Adjusted for sex, age (time variable), birth period.
[b] Adjusted for sex, age (time variable), birth period, maternal age, birth order and parental education and marital status. N suicides=2,930 due to missing parental education.
[c] Maternal age at birth divided by 10

Table 3. Hazard ratios for suicide according to maternal age and birth order among siblings within families.

	N Suicides	Crude[a] HR	95% CI	Adjusted[b] HR	95% CI
Birth order					
1st child	859	1.00	Ref.	1.00	Ref.
2nd child	927	1.29	1.15, 1.46	1.60	1.37, 1.86
3rd child	430	1.36	1.14, 1.62	2.12	1.62, 2.76
4th child or more	242	1.55	1.18, 2.03	3.05	2.04, 4.58
Birth order – trend	2,458	1.16	1.08, 1.25	1.46	1.29, 1.66
Maternal age					
Maternal age <20 years	314	1.00	Ref.	1.00	Ref.
Maternal age 20-24 years	926	1.09	0.89, 1.34	0.87	0.69, 1.09
Maternal age 25-29 years	746	1.14	0.89, 1.46	0.72	0.52, 0.99
Maternal age 30-34 years	353	1.21	0.88, 1.67	0.62	0.40, 0.96
Maternal age >34 years	119	1.21	0.77, 1.89	0.53	0.30, 0.94
Maternal age in 10-years intervals[c]	2,458	1.05	0.85, 1.30	0.43	0.30, 0.62

[a] Adjusted for sex, age (time variable) and birth period
[b] Adjusted for sex, age (time variable), birth period, maternal age and birth order
[c] Maternal age at birth divided by 10

Table 4. Hazard ratios for suicide according to birth order among siblings within families, stratified by time interval from the birth of an older sibling.

	N	Crude[a]		Adjusted[b]	
	Suicides	HR	95% CI	HR	95% CI
Time after preceding child < 2 yrs					
1st child[c]	859	1.00	Ref.	1.00	Ref.
2nd child	253	1.39	1.04, 1.85	1.40	0.99, 1.97
3rd child	109	1.95	1.22, 3.12	1.99	1.04, 3.83
4th child or more	69	3.34	1.59, 7.03	3.48	1.07, 11.35
Birth order – trend	1,290	1.40	1.17, 1.69	1.41	1.04, 1.91
Time after preceding child eq. 2-3 yrs					
1st child[c]	859	1.00	Ref.	1.00	Ref.
2nd child	436	1.34	1.14, 1.57	1.35	1.01, 1.81
3rd child	163	1.32	0.98, 1.77	1.34	0.75, 2.42
4th child or more	102	1.61	1.02, 2.55	1.66	0.63, 4.37
Birth order – trend	1,560	1.20	1.08, 1.34	1.24	0.93, 1.67
Time after preceding child > 3 yrs					
1st child[c]	859	1.00	Ref.	1.00	Ref.
2nd child	238	1.01	0.81, 1.27	1.75	1.20, 2.56
3rd child	158	1.10	0.79, 1.52	2.65	1.49, 4.72
4th child or more	71	1.06	0.58, 1.92	3.46	1.44, 8.37
Birth order – trend	1,326	1.02	0.89, 1.17	1.49	1.14, 1.95

[a] Adjusted for sex, age (time variable) and birth period

[b] Adjusted for sex, age (time variable), birth period, maternal age and birth order

[c] All analyses relative to the first child (n=859)

Web Table 1. Adjusted hazard ratios for suicide according to covariates included in Table 2 in the total population.

	N Suicides	HR[a]	95% CI
Women	656	1.00	Ref.
Men	2,274	3.31	3.03, 3.61
Birth period 1967 – 1976	1.902	1.00	Ref.
Birth period 1977 – 1999	1.028	1.07	0.98, 1.16
Maternal marital status			
Married, cohabitant	2,541	1.00	Ref.
Other	389	1.50	1.34, 1.68
Maternal education			
Primary/lower secondary	1,010	1.00	Ref.
Upper secondary	1,353	0.91	0.83, 0.99
College/university	567	1.07	0.95, 1.20
Paternal educational level			
Primary/lower secondary	921	1.00	Ref.
Upper secondary	1,485	0.88	0.80, 0.95
College/university	524	0.75	0.67, 0.85

[a] N suicides=2,930 due to missing parental education.

Web Table 2. Hazard ratios for suicide according to maternal age and birth order among siblings within families. Stratified on sib-ship size.

	N Suicides	Crude[a] HR	95% CI	Adjusted[b] HR	95% CI
Sibsize eq. 1[c]					
Maternal age in 10-years intervals[d]	198	0.71	0.54, 0.93		
Sibsize eq. 2					
Birth order – trend	919	1.24	1.04, 1.48	1.44	1.07, 1.94
Maternal age in 10-years intervals[d]	919	1.31	0.84, 2.02	0.63	0.31, 1.31
Sibsize eq. 3					
Birth order – trend	867	1.10	0.97, 1.24	1.58	1.26, 1.97
Maternal age in 10-years intervals[d]	867	0.81	0.57, 1.17	0.28	0.15, 0.53
Sibsize >3					
Birth order – trend	666	1.19	1.06, 1.33	1.43	1.19, 1.72
Maternal age in 10-years intervals[d]	666	1.18	0.83, 1.69	0.47	0.26, 0.85

[a] Adjusted for sex, age (time variable) and birth period
[b] Adjusted for sex, age (time variable), birth period, maternal age and birth order
[c] Stratified on those with no siblings. Analysed with ordinary cox regression
[d] Maternal age at birth divided by 10