PAPERS AND ORIGINALS

Perinatal mortality by birth order within cohorts based on sibship size*

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Summary and conclusions

Cross-sectional surveys of perinatal mortality show a U-shaped curve when plotted against parity, implying that fourth and subsequent babies are at increased risk. Our study of a large, population-based longitudinal data set shows that this result is an artefact and that perinatal mortality falls with increasing parity. Within cohorts of mothers based on attained sibship size the perinatal mortality decreases with increasing parity and increases with sibship size. These associations, which are not noticeably affected by maternal age, seem in part to operate through an association between parity, sibship size, and birth weight.

This analysis shows the importance of using longitudinal data in analysing such relations.

Introduction

Studies of fetal and perinatal mortality give contrasting results when analyses of longitudinal data are compared with results from cross-sectional studies.¹⁻³ Billewicz¹ has shown that the rate of unsuccessful pregnancies (miscarriages and perinatal deaths) declines as birth order increases within cohorts of women having a given number of pregnancies. These findings were based on about 5000 married women in their first pregnancies in Aberdeen during 1949-54 whose reproductive

histories were followed up for 10-15 years. A recent study by Roman *et al*³ was based on a questionnaire on reproductive histories answered by about 3000 women doctors in England and Wales. It showed that within cohorts of women having the same gravidity rates of fetal loss decrease with each succeeding pregnancy. These findings seem to contradict those obtained from analyses of cross-sectional data.^{4 5} Longitudinal data sets have been indispensable to demographers interested in studying the distribution of intervals between consecutive births,^{6 7} but the lack of appropriate population-based data sets giving information on birth weight, gestational age, and adverse outcomes of pregnancy have effectively limited research to cross-sectional studies of perinatal mortality.

This study is based on a large, population-based data set using information available on all births that occurred in Norway during 1967-73. For this seven-year period we have analysed perinatal mortality by birth order and maternal age for cohorts of women with an attained sibship size. The results of the analyses within these cohorts are strikingly different from those obtained by pooling the data, as in a cross-sectional study.

Subjects and methods

In Norway information on births has been collected since 1967 through a notification system known as "medical registration of births." This system includes all live births and fetal deaths in which the gestational age is 16 weeks or more.^{8 9} During 1967-73, 464 067 births were recorded. For the seven years under study we were able to identify and link the information on successive births to each mother. This is because all people in Norway are assigned unique identification numbers, which are recorded for both parents when a birth is registered.

The data in this report are based on a total of 294 534 mothers who during 1967-73 gave birth to one or more of their first four single babies. Mothers who delivered their fifth or higher-order child or who had any multiple births were excluded from the analysis. Given these restrictions, 417 086 births were available for study. The analysis of mortality was based on perinatal deaths. We defined perinatal mortality as the number of deaths of fetuses with a gestational age of 16 weeks or more plus the number of deaths occurring during the first week of life per 1000 births. The denominator includes all live births and deaths of fetuses of gestational age 16 weeks or more.

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Results

Table I shows the distribution of mothers and births by parity. Ten parity combinations were possible for mothers who gave birth to one or more of their first four babies within the seven-year study period. Nearly one-third of the mothers delivered their first and only child during the seven years, while the proportion of mothers who gave birth to their first three children during these seven years comprised 4% of the total. This proportion, however, represented 11 828 mothers, which was sufficiently large for us to compare the perinatal mortality.

Table II shows the number of perinatal deaths and the rate per 1000 births for each of the 10 parity combinations as a function of birth order. The perinatal mortalities for the total number of mothers studied confirm the well-known relation between parity and perinatal mortality derived from numerous cross-sectional studies.^{1,5,10-12} The U-shaped relation between parity and perinatal mortality indicates a relatively higher mortality for first compared with second births, and an increasing mortality for third and fourth births compared with second births. These perinatal mortalities based on cross-sectional analysis are plotted as the solid bold line in fig 1. This figure shows that, by using the data from table II and focusing on cohorts of mothers with an attained sibship size, quite a different pattern of associations between parity and perinatal mortality emerges. Two principal features are now apparent. Firstly, within each of the parity combinations there is a significant decrease in mortality as birth order (or rank in sibship) increases. For example, for mothers with their first, second, and third babies the perinatal mortality drops from 55.3 to 36.1 to 15.5 respectively per 1000 births. The magnitude of the drop in perinatal mortality from one parity to the next is on average 40%. Secondly, as the attained size of sibship increases the mortality generally increases.

Fig 1 also shows that perinatal mortality was higher in babies born to mothers who had all of their children during the seven-year period compared with babies born to mothers who had the same number of children by the end of the study period, but not all concentrated within the seven years. For example, second, third, and fourth babies born to mothers having all four babies within the seven-year period had higher perinatal mortalities than the corresponding babies of

FIG 1—Perinatal mortality by parity and sibship size. Based on 294 534 mothers and their 417 086 single births in Norway, 1967-73.

mothers who during the study period had only their second, third, and fourth or third and fourth babies. This tendency appeared also for sibships of three, though not for sibships of two. This suggests that babies born to mothers who have had three or four children within a seven-year period are at a higher risk of dying in the perinatal period than those born to mothers whose deliveries occurred over a period exceeding seven years.

The associations between parity and perinatal mortality for births within cohorts of mothers having different sizes of sibships were analysed separately for mothers grouped according to their age at the time of their first delivery. For example, fig 2 shows the perinatal mortalities of babies born to mothers whose first three children were born within the seven-year study period. Significant differences in the perinatal mortalities of the first babies existed only between the youngest and oldest mothers. The differences in mortality were minor between second and third babies for any of the maternal age groups. The slope (decline) of the perinatal mortality curves by parity, however, is steeper the higher the maternal age at the time of the first birth.

Fig 3 shows the proportion of low-weight births (2500 g or less) by parity and sibship size. Low-birth-weight deliveries become less common as parity increases. Thus for mothers with their first, second, and third babies the proportion of low-weight births dropped from 7.4% among first births to 5.1% and 3.4% among second and third births respectively. For mothers with their first four babies the proportions of low-weight births were 9.0%, 7.0%, 5.8%, and 3.9% for the first, second, third, and fourth babies respectively. This drop in the frequency of low birth weight reflects a general tendency for

TABLE I—Numbers of mothers and births by parity combinations, based on singleton births in Norway, 1967-73

Parity combination	No of mothers	Para			
		0	1	2	3
0	96 705	96 705			
0,1	67 297	67 297	67 297		
0,1,2	11 828	11 828	11 828	11 828	
0,1,2,3	1 050	1 050	1 050	1 050	1 050
1	39 919		39 919		
1,2	16 473		16 473	16 473	
1,2,3	2 456		2 456	2 456	2 456
2	34 473			34 473	
2,3	7 064			7 064	7 064
3	17 269				17 269
Total	294 534	176 880	139 023	73 344	27 839

TABLE II—Perinatal mortality (number of perinatal deaths/1000 births) by parity for births to Norwegian mothers grouped according to parity combinations during seven years 1967-73

Parity combinations	No of mothers	Para							
		0		1		2		3	
		No of deaths	Perinatal mortality	No of deaths	Perinatal mortality	No of deaths	Perinatal mortality	No of deaths	Perinatal mortality
0	96 705	1511	15.6						
0,1	67 297	1206	17.9	663	9.9				
0,1,2	11 828	654	55.3	427	36.1	183	15.5		
0,1,2,3	1 050	65	61.9	66	62.9	44	41.9	21	20.0
1	39 919			407	10.2				
1,2	16 473			389	23.6	216	13.1		
1,2,3	2 456			111	45.2	82	33.4	32	13.0
2	34 473					487	14.1		
2,3	7 064					233	33.0	124	17.6
3	17 269							367	21.3
Total	294 534	3434	19.4*	2063	14.8*	1245	17.0*	544	19.5*

*Based on corresponding denominators in table I.

birth weight to increase with increasing parity.¹³⁻¹⁵ This could account for a major part of the association between declining perinatal mortality and increasing parity within sibships of a given size.

Fig 3 also shows the perinatal mortality for babies weighing 2500 g or less at birth. For fixed size of sibship these death rates do not change much as a function of birth order. There was an overall doubling, however, in the perinatal mortality of low-weight babies of mothers of three or four babies compared with mothers of only two babies (from about 200 to 400 deaths/1000 births). Such a large difference in mortality of low-weight babies suggests that there may be differences in the distribution of birth weights below 2500 g in

babies of mothers with two children compared with those of mothers with three or more children. To explore this hypothesis we calculated the birth-weight-specific perinatal mortality for each 250-g birth-weight category between 1000 and 3000 g. In each of these categories the perinatal mortality in mothers who had had two babies in the seven years was about only half that in mothers who had had their first three babies. No substantial differences were found after comparing the birth-weight-specific perinatal mortality between mothers who had had their first three and those who had had their first four babies. Hence the different levels of low-birth-weight-specific mortality shown in fig 3 do not result from an artefact operating through an unequal distribution of birth weights less than 2500 g. Instead there remains a significant difference, as yet unaccounted for, between the cohort of mothers with only their first two babies and those cohorts of mothers having more than their first two babies.

Discussion

The association between perinatal mortality and parity shown in this study using cohorts based on attained sibship size is strikingly different from the standard cross-sectional relation found by pooling births to mothers with unequal sibship sizes. Within cohorts based on sibship size the perinatal mortality decreases steadily as parity increases, moreover, the perinatal mortality is high for cohorts of larger sibships. These effects on perinatal mortality operate, in part, through birth-weight distributions. Thus the proportion of low-weight births decreases as parity increases within sibships and is higher in larger sibships. Birth-weight distributions, however, cannot account for all of the observed differences, since the birth-weight-specific perinatal mortality is twice as high for mothers of more than two babies than for mothers of only two babies.

The clustering of perinatal deaths within sibships was investigated for mothers who had had their first two, three, and four consecutive babies. When at least one of the first two babies had died, in only 2.6% of mothers had both children died. When at least one of the first three children had died, however, 7% of the mothers had experienced more than one perinatal death. Out of the mothers who had their first four children, of whom at least one died, 18.8% experienced more than one death. If exactly one death occurred within each sibship then the proportions of deaths accounted for at para 0 were 0.63, 0.53, and 0.32 for mothers having two, three, and four babies respectively. These results are consistent with the known tendency to become pregnant again after a pregnancy with an early adverse outcome and the higher probability of stopping childbearing after a successful outcome of pregnancy.²¹⁶⁻¹⁹ These factors should contribute to the decline in perinatal mortality with increasing parity within cohorts based on sibship size. They also help to explain the increased perinatal mortality in babies in larger compared with smaller sibships.

Socioeconomic differences probably exist between mothers who have several babies and those who have fewer babies in a seven-year period. Since socioeconomic conditions have been related to perinatal mortality,²⁰⁻²³ this factor may also partly account for our findings. Socioeconomic or educational differences, or both, may be related to the difference in birth-weight-specific perinatal mortality rates for mothers of more than two babies as compared with mothers of only two babies. So far we have not attempted to measure any relation with educational or socioeconomic variables. This will be done, however, in a larger data set based on a 10-year study.

Roman *et al*³ recently published findings similar to ours. Their study was concerned with fetal loss (including early fetal loss), gravidity, and pregnancy order in 3068 women doctors from England and Wales. The study showed that the risk of fetal loss at a given parity varied with the woman's gravidity (total sibship size) such that within each gravidity group the rates of fetal loss decreased with each successive pregnancy. Other workers^{1-3 23 24} have suggested that the established relationships between variables like maternal age and parity and the measures of pregnancy outcome such as perinatal mortality may have been artificially constructed owing to the

FIG 2—Perinatal mortality by parity and maternal age at time of birth of first baby. Based on mothers delivering first, second, and third single babies in Norway, 1967-73.

FIG 3—Proportions of low-birth-weight (LBW) births and perinatal mortality of LBW births by parity and sibship size.

cross-sectional approach to the data analysis. The present study has shown using a cohort approach in an analysis based on sibships that associations between parity and mortality exist that could not be inferred from cross-sectional data.

Thus, the findings indicate that perinatal mortality decreases with increasing parity, within sibships, at least until the fourth baby is born. The familiar U-shaped relation is not present when the data are analysed within cohorts based on attained sibship size. The association between perinatal mortality and parity seems partly to operate through an association between parity and birth weight, and is basically the same regardless of maternal age. Maternal age does seem to have an appreciable influence on the perinatal mortality of the first baby, although the effect of maternal age on perinatal mortality in higher parities is minor.

These findings underline the importance of being able to study the effects of age and parity not in mixed samples of mothers and births but rather in longitudinal samples of women and with the analysis based on sibships. The implications of this study could be carried further and applied to various epidemiological observations using measures of pregnancy outcome other than perinatal mortality. Thus using cohort analysis unrecognised associations with either maternal age or parity might be discovered.

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ONE HUNDRED YEARS AGO A married woman, aged 21, seen on February 21st, 1879, always healthy until this illness, of good constitution and family, was under the care of Mr Todd, one of the resident medical officers of the dispensary. She had been confined of her second child four months previously. Soon after her confinement, the right breast inflamed; it suppurated, and was opened freely; but did not get well. It was now red and hard and swollen; pus also was escaping, though not freely, from the wound in it. Lately, albumen had been found in the urine, and she had begun to seem very ill altogether. I found her still fairly nourished, but with a pallid face, an eager, anxious, scared expression in her eyes; sitting upright in bed, unable to breathe in any other posture, and believing that the attempt to lie down would kill her. There was dropsy of the dependent parts (loins, lower abdomen, and thighs). There was scarcely any radial pulse. Upon inquiry, it was found that her legs had swollen much more during this second pregnancy than in her first; that, moreover, she had felt ailing the greater part of the time, and had had constant headache and vomiting—without, however, having asked for any advice or treatment. She was now purged several times a day; but passed a fair quantity of highly albuminous urine of specific gravity 1018. Though the breathing was rapid, there was no cough; there was free respiration over all the lungs, except at the base posteriorly, where moist râles were easily audible. On examining the heart, it was found to be beating rather rapidly and forcibly, but with a short snapping impulse, while, as already stated, the pulse at the wrist was so small as to be scarcely perceptible at all; there were no murmurs, but a very distinct reduplication of the second sound—the heart-sounds exactly resembling those caused by a galloping horse. It was therefore supposed that, in consequence of the abnormal state of the patient's blood, coupled with debility and a languid circulation, a thrombus was forming in one (or more) of the cardiac chambers, stretching through the aortic or pulmonary valve, thus causing the blood to leave the ventricles at an uneven speed, and so delaying the closure of one set of valves. In consequence of the (naturally) large size of the left and uninjured breast, together with the very nervous and prostrate state of the patient, it was not possible to define the diagnosis more accurately. Acting, however, upon the fact, ascertained by Dr B W Richardson, that (although it is not

the physiological solvent of fibrin, yet) ammonia in the blood does prevent the formation of fibrinous clots, fifteen minims of liquor ammoniac, BP, with five minims of tincture of digitalis, was given in an ounce of water, every three hours. She began to improve at once, and, continuing to take the medicine steadily until the fourth day, she could then lie down quite comfortably; the râles had disappeared from the bases of the lungs; her pulse was fairly full and regular; but the second heart-sound was still as distinctly doubled as before. There was less albumen in the urine; the diarrhoea persisted to the extent of six or seven loose offensive motions daily. During the pregnancy, she had suffered great constipation, occasionally going a week, and once even a whole fortnight (!), without any evacuation. However, nothing abnormal was now to be found in the abdomen beyond the dropsy already mentioned.

She continued to take ammonia and digitalis every three hours for fourteen days, when, as there had been no return of urgent symptoms and she seemed anaemic, fifteen minims of tincture of perchloride of iron and two drachms of liquor ammoniac acetatis, in water, was ordered to be taken three times daily. There was still some, though much less, albumen; and the breast had not much improved. She was up and walking about. The heart-sounds, something to my disappointment, remained as before. But, upon reflection, it seemed unreasonable to expect a clot, such as is seen *post mortem* in many a heart, strongly interlaced in the muscular bundles of the auricular or the ventricular walls, to be either absorbed or to be washed away, particle by particle, even by the swiftly but smoothly rushing blood-stream, in so short a time as a fortnight. I accordingly waited a month longer (until April 7th), and upon visiting the patient then, found that the reduplication was entirely gone and the heart-sounds were perfectly normal. A repeated examination, some days afterwards, showed the same result. The inflamed breast had in the meantime been thoroughly explored and opened up, under ether, by my colleague Mr McGill, and was healing fast. She was gaining flesh and strength very rapidly, and all trace of albuminuria had been lost, when she went into the country towards the end of April. She is now quite well. (*British Medical Journal*, 1879.)