Prevalence of neural tube defects in South Australia, 1966-91: effectiveness and impact of prenatal diagnosis

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Abstract

Objective—To determine trends in total prevalence of neural tube defects in South Australia during 1966-91, the impact of prenatal diagnosis on birth prevalence, and the effectiveness of prenatal screening for neural tube defects in 1986-91.

Design—All births and terminations of pregnancy affected by neural tube defects and information on prenatal screening were ascertained from multiple sources including the South Australian perinatal and abortion statistics collections, birth defects register, and state maternal serum α fetoprotein screening programme.

Setting—Southern Australia.

Subjects—All 1058 births and terminations of pregnancy affected by neural tube defects in 1966-91.

Main outcome measures—Total prevalence and birth prevalence of individual and all neural tube defects. The proportion of screened cases detected prenatally.

Results—Total prevalence of neural tube defects during 1966-91 was 2.01/1000 births with no upward or downward trend. However, birth prevalence fell significantly (by 5.1% a year), with an 84% reduction from 2.29/1000 births in 1966 to 0.35/1000 in 1991 (relative risk=0.16, 95% confidence interval 0.07 to 0.34). The fall was 96% for anencephaly and 82% for spina bifida. 85% of defects, both open and closed, were detected before 28 weeks' gestation in women screened by serum α fetoprotein or mid-trimester ultrasonography, or both, in 1986-91 (99.0% for anencephaly and 75.7% for spina bifida).

Conclusions—While the total prevalence of neural tube defects in South Australia remained stable, prenatal diagnosis and termination of pregnancy resulted in an 84% fall in birth prevalence during 1966-91. Screening detected over four fifths of cases in 1986-91.

Introduction

Neural tube defects, which include anencephaly, spina bifida, and encephalocele, are an important group of severe birth defects whose prevalence has fallen over the past six decades in many countries. The fall has been attributed to natural causes in some countries—for example, in the Republic of Ireland, where screening programmes and terminations of pregnancy are not available^{1,2} and in the United Kingdom, the Netherlands, Sweden, Hungary, and the United States before screening programmes were established in the 1980s.^{1,3-7} In Australia the natural fall in prevalence initially reported in three states from 1976 to 1981⁸ was not sustained after 1981.⁹

The introduction of antenatal ultrasonography and population based maternal serum α fetoprotein screening programmes in the late 1970s has enhanced the

natural fall in prevalence.^{2,10-12} The impact of prenatal diagnosis cannot be assessed when statistics on terminations of pregnancy are lacking,^{10,13} but where these statistics are available stable prevalence or fluctuations in prevalence with no time trends have been reported.²

We conducted this study to determine the total prevalence of neural tube defects in South Australia for the years 1966-91, the impact of prenatal diagnosis on birth prevalence (excluding terminations) during this period, and the effectiveness of prenatal screening for neural tube defects in 1986-91. South Australia has a population of 1.4 million, with one million living in the capital city, Adelaide. There are about 20 000 babies born of at least 400 g birth weight or 20 weeks' gestation annually. Details of pregnancy and birth, including congenital abnormalities, are notified by midwives to the perinatal statistics collection. Termination of pregnancy before 28 weeks' gestation has been legal in South Australia since 1970 and about 4500 terminations are notified annually under regulations. The South Australian birth defects register obtains further notifications of congenital abnormalities from several other sources for children whose abnormalities are identified after the early neonatal period and before the age of 5.

The chemical pathology department at Adelaide Children's Hospital established a pilot maternal serum α fetoprotein screening programme for neural tube defects in 1977-82, which included about a quarter of women who gave birth in South Australia in that period. A full state-wide programme has been operating since May 1982, and this has included an increasing proportion of women who have given birth, from 52% in 1983 to 81% in 1986-91. Doctors notify to the programme fetuses or babies with neural tube defects in women screened. Antenatal ultrasonography has been used in South Australia since the 1970s, and data from the perinatal statistics collection show that the proportion of women giving birth who had had at least one antenatal ultrasound examination was 64% in 1981 and 92% in 1991.

Subjects and methods

We included all neural tube defects, open and closed, whether occurring in isolation or with only secondary or minor defects (singles) or together with other serious abnormalities or as part of syndromes (multiples). When a case of spina bifida was associated with anencephaly it was classified as anencephaly, and when an encephalocele was associated with spina bifida, it was classified as spina bifida.¹⁴

We ascertained all births and terminations of pregnancy affected by neural tube defects from notifications to the perinatal statistics and abortion statistics collections, the South Australian birth defects register, and the chemical pathology department. We also used perinatal and paediatric death certificates, necropsy

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reports on perinatal deaths, post-neonatal deaths, and terminations of pregnancy for congenital abnormalities; reports from doctors; and hospital case records, including those of the department of neurosurgery at Adelaide Children's Hospital (the only paediatric neurosurgical unit in South Australia).

For 1966-73, data on children born with anencephaly and spina bifida were collected by the department of neurosurgery from stillbirth and death records, from the hospital's case records, and through postal inquiry to all obstetric hospitals in South Australia.⁸ For 1974-80, before the establishment of the perinatal statistics collection, the reports of the Australian Bureau of Statistics on perinatal deaths due to neural tube defects were also used.

STATISTICAL ANALYSIS

Total prevalence was calculated by dividing the total number of live births, stillbirths, and terminations of pregnancy affected by a neural tube defect by the total number of live births and stillbirths for each year, and expressing this as a rate per 1000 births. Birth prevalences excluded terminations of pregnancy and were based on only live births and spontaneous stillbirths with neural tube defects.

We analysed time trends for total prevalence of all neural tube defects and individual defects for 1966-91 using Poisson regression analysis,¹⁵ where the dependent variable was the number of defects and the predictor variable was year. We repeated the analysis for birth prevalence, excluding terminations of pregnancy. In view of the aetiological heterogeneity of neural tube defects^{7,16} and the suggestion that they should be analysed separately as single and multiple defects,⁷ we repeated analyses for encephalocele for single defects only. Analyses for single defects only for anencephaly and spina bifida could not be done as detailed information on these defects was not available in all the earlier years.

Comparisons of birth prevalences between 1966 and 1991 were made for all neural tube defects and individually for anencephaly, spina bifida, and encephalocele by calculating relative risks (and 95% confidence intervals) for the defects with the Epi Info program.¹⁷

FIG 1—Total prevalence of neural tube defects, South Australia, 1966-91

Results

Table 1 shows the total prevalence and birth prevalence of neural tube defects in South Australia for 1966-91. Figures 1 and 2 show the total prevalence and birth prevalence for all neural tube defects and for individual defects. As there were no terminations for neural tube defects until 1978, total prevalence and birth prevalence were the same for 1966-77.

The annual total prevalence of neural tube defects in South Australia in 1966-91 fluctuated between 1.49 and 2.37/1000 births with no upward or downward

TABLE 1—Total prevalence and birth prevalence of neural tube defects, South Australia, 1966-1991

Year of birth or termination	Total births*	No with anencephaly		No with spina bifida		No with encephalocele		All neural tube defects				
		Births and terminations of pregnancy	Births	Births and terminations of pregnancy	Births	Births and terminations of pregnancy	Births	Births and terminations of pregnancy	Rate/1000 births	Births	Rate/1000 births	
1966	20 556	24	24	23	23	0	0	47	2.29	47	2.29	
1967	20 597	8	8	23	23	2	2	33	1.60	33	1.60	
1968	21 424	27	27	17	17	0	0	44	2.05	44	2.05	
1969	22 185	25	25	21	21	1	1	47	2.12	47	2.12	
1970	22 817	13	13	19	19	4	4	36	1.58	36	1.58	
1971	23 246	27	27	23	23	0	0	50	2.15	50	2.15	
1972	22 073	25	25	23	23	4	4	52	2.36	52	2.36	
1973	20 651	22	22	21	21	2	2	45	2.18	45	2.18	
1974	20 417	22	22	19	19	1	1	42	2.06	42	2.06	
1975	20 175	17	17	10	10	3	3	30	1.49	30	1.49	
1976	19 157	15	15	14	14	3	3	32	1.67	32	1.67	
1977	19 438	15	15	17	17	4	4	36	1.85	36	1.85	
1978	18 736	17	13	16	16	3	3	36	1.92	32	1.71	
1979	18 641	19	12	11	11	1	1	31	1.66	24	1.29	
1980	18 638	20	11	19	19	1	1	40	2.15	31	1.66	
1981	19 052	12	3	24	18	7	6	43	2.26	27	1.42	
1982	19 128	19	7	15	12	4	4	38	1.99	23	1.20	
1983	19 800	15	7	27	20	5	3	47	2.37	30	1.52	
1984	20 281	17	4	23	11	5	3	45	2.22	18	0.89	
1985	19 833	14	5	24	12	3	2	41	2.07	19	0.96	
1986	19 800	16	3	20	8	2	2	38	1.92	13	0.66	
1987	19 395	16	2	20	10	1	1	37	1.91	13	0.67	
1988	19 530	14	1	22	9	3	3	39	2.00	13	0.67	
1989	19 823	17	1	26	12	0	0	43	2.17	13	0.66	
1990	19 988	23	0	19	6	4	0	46	2.30	6	0.30	
1991	19 749	20	1	15	4	5	2	40	2.03	7	0.35	
Total	525 130	479	310	511	398	68	55	1058	2.01	763	1.45	

*Births=livebirths plus spontaneous stillbirths.
There were no terminations for neural tube defects before 1978.

FIG 2—Birth prevalence of neural tube defects, South Australia, 1966-91

trend (Poisson regression, $p=0.46$). Total prevalence for the study period was 2.01/1000 births for all neural tube defects, 0.91/1000 for anencephaly, 0.97/1000 births for spina bifida. No time trends were seen for anencephaly ($p=0.4$) or spina bifida ($p=0.31$). The prevalence of encephalocele increased significantly ($p=0.02$), but the effect was lost when only single defects were analysed ($p=0.19$).

Termination of pregnancy for neural tube defects rose from 1978-91 as detection rates increased (fig 3). Birth prevalence fell by 5.1% a year, for all neural tube defects during 1966 to 1991 ($p<0.0001$); the fall was significant for anencephaly (8.6% a year, $p<0.0001$) and spina bifida (3.5% a year, $p<0.0001$) but not for encephalocele ($p=0.57$ for all encephaloceles and $p=0.97$ for single defects only).

Birth prevalence for all neural tube defects fell by 84%, from 2.29/1000 births in 1966 to 0.35/1000 in 1991 (relative risk=0.16, 95% confidence interval 0.07 to 0.34). The fall was 96% for anencephaly, from 1.17 to 0.05/1000 births (0.04, 0.01 to 0.32), and 82% for spina bifida, from 1.12 to 0.20/1000 births (0.18, 0.06 to 0.52). No significant change in birth prevalence was seen for encephalocele.

Table II shows the cases of neural tube defects detected before 28 weeks' gestation in 1986-91. In all 80% (95% confidence interval 75% to 85%) of cases were detected in the period. The percentage was higher for anencephaly (95%) than for spina bifida (69%) or for encephalocele (60%).

If only the women screened by maternal serum α fetoprotein at 16-20 weeks' gestation or mid-trimester

ultrasonography, or both, were included—that is, 227 women with affected babies in 1986-91—the percentage of cases detected prenatally before 28 weeks' gestation was 85% (81% to 90%). The corresponding percentages for individual defects were 99% for anencephaly, 76% for spina bifida, and 64% for encephalocele. Only five of the 194 cases detected before 28 weeks' gestation were detected after 20 weeks' gestation by ultrasound examination.

Discussion

The study has shown that the total prevalence of neural tube defects in South Australia was stable during 1966-91 but that the birth prevalence fell greatly because of effective prenatal diagnosis and termination of pregnancy.

As spontaneous loss of fetuses with neural tube defects occurs, prenatal detection and termination of affected fetuses before 20 weeks' gestation may have resulted in some cases being included in the total prevalence for 1978-91 that would have been excluded from the data collected before 1978 because they had aborted spontaneously. Creasy and Alberman have estimated that 17.4% of fetuses with neural tube defects are lost spontaneously at 12-15 weeks' gestation and 4.5% at 16-19 weeks.¹⁸ We applied the estimates to the number of terminations at those gestations in 1978-

FIG 3—Terminations of pregnancy for neural tube defects (top) and proportion of pregnancies affected by neural tube defects that were terminated (bottom), South Australia, 1977-91

91 to determine spontaneous losses for each year. This would have resulted in the exclusion of one fetus with a neural tube defect in each of the years 1983-7 and 1989 and of two fetuses in 1988, 1990, and 1991. Excluding these fetuses did not affect the conclusion of an absence of trend in the total prevalence of all neural tube defects for 1966-91 (Poisson regression analysis, $p=0.77$) or of anencephaly, the defect contributing the largest proportion of terminations ($p=0.21$).

The greater fall in birth prevalence for anencephaly

TABLE II—Cases of neural tube defects detected before 28 weeks' gestation, 1986-91

Year of birth or termination	Anencephaly		Spina bifida		Encephalocele		All neural tube defects	
	Total No of defects	No (%) detected	Total No of defects	No (%) detected	Total No of defects	No (%) detected	Total No of defects	No (%) detected
1986	16	15 (94)	20	14 (70)	2	0	38	29 (76)
1987	16	14 (88)	20	11 (55)	1	0	37	25 (68)
1988	14	14 (100)	22	13 (59)	3	0	39	27 (69)
1989	17	16 (94)	26	19 (73)	0	0	43	35 (81)
1990	23	23 (100)	19	15 (79)	4	4 (100)	46	42 (91)
1991	20	19 (95)	15	12 (80)	5	5 (100)	40	36 (90)
Total	106	101 (95)	122	84 (69)	15	9 (60)	243	194 (80)

Public health implications

- Most women in developed countries are now offered screening for neural tube defects and affected babies are less common
- Ascertainment of all births and terminations of pregnancy affected by neural tube defects in South Australia shows that the total prevalence remained stable during 1966-91
- Birth prevalence, however, fell by 84% as a result of screening
- Serum α fetoprotein concentration and ultrasonography detected 85% of affected pregnancies before 28 weeks' gestation
- Coordinated population based screening programmes and registers of birth defects allow accurate assessment of effectiveness of prenatal diagnosis and preventive measures

than for spina bifida is to be expected as anencephaly is easier to diagnose by ultrasonography and it is usually associated with a high maternal serum α fetoprotein concentration. Serum α fetoprotein concentration is not often raised in closed spina bifida (which comprised 24.6% of the spina bifida cases in 1986-91). The fall in birth prevalence and the proportion of defects detected prenatally are consistent with the findings of other centres with a population based maternal serum α fetoprotein screening programme and wide access to ultrasound screening in pregnancy.^{2,10} Centres without a population based serum α fetoprotein screening programme have generally achieved a lower proportion of prenatal diagnoses.^{2,9}

The impact of prenatal diagnosis on birth prevalence is dependent not only on the sensitivity of the screening programme but also on the uptake of testing by doctors and pregnant women, presentation for antenatal care in time for screening and legal termination of pregnancy, and the attitude to termination of pregnancy of couples with affected fetuses.

Our results show the value of population based registers in accurate ascertainment of birth defects, which enables assessment of the effect of preventive strategies. The centralised maternal serum α fetoprotein screening programme facilitated ascertainment. Folate has been shown to reduce the rate of neural tube defects when taken before conception and in the early months of pregnancy.^{19,20} There is no formal policy on the use of folate before conception in South Australia, but the Australian National Health and Medical Research Council has recommended that women who have had an affected pregnancy or have a family history of neural tube defect should be offered genetic counselling and folic acid supplements around the time of conception (5 mg daily). The council has also recently recommended (115th session, Adelaide, June 1993) that women in low risk groups should take 0.5 mg of folic acid daily around the time of conception, that all women of childbearing age should be encouraged to increase their intake of folate rich foods, and that staple foods should be fortified with folic acid.

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Corrections

How frequently should basic cardiopulmonary resuscitation training be repeated to maintain adequate skill?

An editorial error occurred in this paper by Hubert J J M Berden and others (12 June, pp 1576-7). The figure suggests that resuscitation skills were measured only once in each group at time 0 whereas two measurements were made, immediately before and after training in resuscitation was given. Before training all three groups accrued about 38 penalty points, while after training they all accrued about 15 points.

Lifelong exercise and stroke

An editorial error occurred in this paper by Roger Shinton and Gian Sagar (24 July, pp 231-4). The first sentence in the second paragraph of the methods section should have read: "Between 1 October 1988 [not 1989] and 30 September 1990 we recruited men and women who had just had their first stroke and were aged 35-74."

Urinary microalbumin excretion in early pregnancy and gestational age at delivery

An editorial and an authors' error occurred in this paper by Ivan J Perry and others (14 August, pp 420-1). In the table the second quartile of distribution of albumin:creatinine ratio should be 0.35 to 0.62. In the first sentence of the second paragraph the study group was defined incorrectly; the group comprised 692 healthy nulliparous pregnant women and 11 women with chronic hypertension referred for antenatal care before 31 weeks' gestation.