Trends in prenatal screening for and diagnosis of Down's syndrome: England and Wales, 1989-97

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The National Down Syndrome Cytogenetic Register holds data on 10651 cases of prenatally or postnatally diagnosed Down's syndrome occurring in England and Wales from 1 January 1989 to 31 December 1997 (93% of all eligible cases) (J Morris, personal communication). We used these data to investigate the trends in prenatal diagnosis of Down's syndrome between 1989 and 1997.

Subjects, methods, and results

All clinical cytogenetic laboratories in England and Wales notify the register anonymously of trisomy 21 or related karyotypes, together with the date, place of and indications for referral, parental age, and family history. Most send a copy of the notification to the referring physician for confirmation and completion.¹ The outcome of the pregnancy is requested for all cases diagnosed prenatally (but may not be known for several months) and is known for 91% of registered prenatal diagnoses overall.

In 1989 registrations numbered 1081; in 1993, 1144; and in 1997, 1336 (table). In contrast, births nationally dropped from 688 000 in 1989 to 642 000 in 1997.² The proportion diagnosed prenatally at all maternal ages rose from 30% to 53% between 1989 and 1997. In 1989 only 9% of affected pregnancies were diagnosed prenatally in mothers under 35, rising to 45% in 1997. For mothers aged 35 and over prenatal diagnosis of affected pregnancies rose from 60% in 1989 to 72.2% in 1996 (table). However, the percentage diagnosed prenatally levelled out from 1994 onwards.

Maternal age was the first indication for 78% of all prenatal diagnostic tests in 1989 but only 16% in 1997. Maternal serum screening results as an indication increased from 6% in 1989 to 37% in 1996 and fetal ultrasound findings from 13% to 43%. Around a fifth (8/43) of ultrasound referrals for diagnosis concerned

the nuchal zone in 1989, but this was 55% (191/350) in 1997.

Amniocentesis accounted for 78% (246/316) of prenatal diagnoses in 1989 and 61% (431/701) at a mean gestational age of 17.2 weeks in 1997. Between 1989 and 1992, 37% of all prenatal diagnoses followed amniocentesis before 16 weeks' gestation; between 1993 and 1996 this fell to 31%. Prenatal diagnosis by chorionic villus sampling or placental biopsy decreased from 18% (58/316) (mean gestation 11.5 weeks) in 1989 to 10% in 1992 following reports of limb defects after biopsy before week 12, increasing to 37% in 1997 at a mean gestation of 13.7 weeks.

From 1989 to 1997, 92% of cases diagnosed prenatally and with known outcome were terminated, 1.9% were miscarried, 1.5% were recorded as a stillbirth or neonatal death, and nearly 5% were live births surviving to discharge from hospital. In some of these an offer to terminate the pregnancy had been declined. When diagnosis occurred after 23 weeks, usually on the basis of ultrasound findings, only a quarter of affected pregnancies were terminated, while 23% were miscarried, stillborn, or died in the neonatal period.

Comment

A previous report provided evidence of the validity of these data.³ This showed that after adjustment for the number of terminations and the fetal losses that would have occurred naturally, the maternal age specific risks of Down's syndrome remained similar to those before the availability of prenatal diagnosis. The rise in registrations is due to the demographic trend towards starting families later in life; the high proportion of older mothers from the postwar births bulge⁴; and the increase in early prenatal diagnoses of trisomy 21 in fetuses leading to terminations of pregnancy that would previously have aborted spontaneously.⁵ All of these would tend to stabilise the annual number of

Numbers (percentages) of prenatal and postnatal diagnoses of trisomy 21 by maternal age and reason for referral for cytogenetic diagnosis*

Sample year	Mothers under 35							Mothers 35 and over										Missing maternal age			Total of all diagnoses
	Reason for referral						Reason for referral						Postnatal diagnoses, births, stillbirths, neonatal deaths								
	Prenatal diagnoses with reason					Postnatal diagnoses, births, stillbirths, neonatal deaths	Prenatal diagnoses with reason					Total									
	Maternal age	Maternal serum	Ultrasound	Other	Total		Maternal age	Maternal serum	Ultrasound	Other	Total										
1989	0	12 (1.9)	33 (5.3)	8 (1.3)	53 (8.6)	566 (91.4)	619	249 (56.0)	6 (0.1)	9 (2.0)	4 (0.9)	268 (60.2)	177 (39.8)	445	0	17	1 081				
1990	4 (0.7)	23 (3.8)	42 (7.0)	9 (1.5)	78 (13.0)	524 (87.0)	602	242 (50.0)	31 (6.4)	18 (3.7)	5 (1.0)	296 (61.2)	188 (38.8)	484	0	7	1 093				
1991	3 (0.5)	44 (7.2)	52 (8.5)	7 (1.1)	106 (17.2)	509 (82.8)	615	223 (43.3)	50 (9.7)	38 (7.4)	10 (1.9)	321 (62.3)	194 (37.7)	515	1	13	1 144				
1992	0	82 (13.9)	78 (13.2)	7 (1.2)	167 (28.3)	424 (71.7)	591	183 (36.9)	94 (19.0)	37 (7.5)	5 (1.0)	319 (64.3)	177 (35.7)	496	3	45	1 135				
1993	1 (0.2)	93 (15.6)	80 (13.4)	12 (2.0)	186 (31.1)	412 (68.9)	598	177 (34.6)	114 (22.3)	68 (13.3)	8 (1.6)	367 (71.8)	144 (28.2)	511	0	35	1 144				
1994	2 (0.3)	123 (19.8)	94 (15.1)	16 (2.6)	235 (37.8)	387 (62.2)	622	168 (30.7)	119 (21.7)	77 (14.1)	9 (1.6)	373 (68.2)	174 (31.8)	547	2	51	1 222				
1995	1 (0.2)	118 (20.4)	112 (19.4)	13 (2.2)	244 (42.2)	334 (57.8)	578	153 (26.3)	109 (18.7)	125 (21.5)	16 (2.7)	403 (69.2)	179 (30.8)	582	3	38	1 201				
1996	1 (0.2)	134 (20.8)	144 (22.4)	12 (1.9)	291 (45.3)	352 (54.7)	643	155 (26.1)	129 (21.7)	128 (21.5)	9 (1.5)	421 (70.8)	174 (29.2)	595	3	54	1 295				
1997†	2 (0.3)	112 (19.0)	142 (24.1)	5 (1.0)	261 (44.4)	327 (55.6)	588	110 (17.6)	149 (23.9)	166 (26.6)	10 (1.6)	435 (69.7)	189 (30.3)	624	14	110	1 336				
Total	14	741	777	89	1621	3835	5456	1660	801	666	76	3203	1596	4799	26	370	10 651				

*Data are drawn from year of referral and exclude spontaneous miscarriage not prenatally diagnosed and residents from outside England and Wales. Fifteen cases in which reason for referral was not given are also excluded. Of all prenatal diagnoses, 224 resulted in a liveborn infant with Down's syndrome and 67 in a still birth or neonatal death. These are among the prenatal diagnoses above.
†Provisional data.

affected births, in spite of the increase in the numbers diagnosed prenatally.

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Effect of parity, gravidity, previous miscarriage, and age on risk of Down's syndrome: population based study

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The increased risk of Down's syndrome with maternal age underlies the recommendation for older pregnant women to be offered screening by amniocentesis or chorionic villus sampling. Recently Schimmel et al suggested that increased parity was an independent risk factor for Down's syndrome, but their study was not population based and did not include terminations of pregnancy.¹

Using statewide statistics on births and terminations of pregnancy we investigated whether the risk of Down's syndrome is increased independently of maternal age by maternal parity, gravidity, or previous miscarriage.

Subjects, methods, and results

South Australia has around 20 000 births annually. The state collects data on birth defects that include maternal characteristics in both its perinatal and abortion statistics. These statutory collections are complemented by notifications from health professionals to the South Australian Birth Defects Register of defects in children detected within the first 5 years of life and by cytogenetic and necropsy reports. Each case of Down's syndrome included in these collections has been cytogenetically confirmed.

The effects of parity, gravidity, number of previous miscarriages, and mother's age (by single year of age) on risk of having a fetus with Down's syndrome were modelled separately using Poisson regression; then the effects of parity, gravidity, and previous miscarriage were modelled separately after adjustment for the effect of mother's age. Overdispersion was detected in all the Poisson models constructed, and an overdispersion factor was estimated using the square root of Pearson's χ^2 divided by the number of degrees of freedom.² The analysis was performed using PROC GENMOD in SAS.³ Analyses were undertaken for 1986-95 and 1986-90, which was similar to the period of study of Schimmel et al (1981-9) and preceded the gradually increasing use of maternal serum screening for Down's syndrome.

Analysis using births and terminations of pregnancy showed no significant increase in risk for increase in parity or gravidity (table). When only births were analysed for 1986-95, the increased risks with increase in parity ($P < 0.001$) and gravidity ($P < 0.01$) were not significant after adjustment for age ($P = 0.46$ and $P = 0.75$ respectively); similar results were obtained for 1986-90 for increase in parity. The risk was not increased with the number of previous miscarriages, but the increase in risk with age was constant ($P < 0.001$).

Comment

Schimmel et al studied live births alone among women of high parity attending one hospital. Their analysis of maternal age by five year age groups might have contributed to spurious results through truncation.¹

The low risk found in women of low parity may have resulted from the inadvertent exclusion of women of low parity who had had Down's syndrome diagnosed in their fetus prenatally elsewhere and spontaneously miscarried or terminated the pregnancy.¹ Another Australian population based study found that older pregnant women who had had three or more previous births were less likely than those of lower parity to undergo amniocentesis or chorionic villus sampling, although all were eligible for a medical service rebate.⁴ We found a similar differential use of prenatal diagnosis in univariate analysis among South Australian women who were pregnant in 1991-6 (odds ratio 0.55 (95% confidence interval 0.51 to 0.61)) and also found a similar higher use of these tests among women who had had a previous termination of pregnancy. These and other differences identified may reflect different degrees of knowledge about the availability of tests, concern about the possibility of having a disabled child, or attitudes towards termination of pregnancy.⁴

With the operation of selection factors and increasing use of prenatal diagnosis, risk estimates of Down's

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