Down's syndrome in South Africa — incidence, maternal age and utilisation of prenatal diagnosis

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Summary

Down's syndrome (DS) is the most common chromosomal cause of mental retardation, and amniocentesis is the most significant factor affecting its prevalence.

In South Africa, prenatal cytogenetic diagnoses have been available for just over a decade and the utilisation and effect of this procedure in the white population born between 1980 and 1984 was evaluated.

On the basis of pooled data involving 4 939 640 births, an overall world mean rate for DS of 1,34/1 000 live births (mainly Caucasian) for single-year maternal ages was calculated. Accordingly, 58 cases of DS were expected in the 40-year and older maternal age group in South Africa. Only 34 cases (59%) were detected prenatally, and a further 3 cases were identified by the notification system during the same period and in the same maternal age group.

Another 24 DS cases in the maternal age group of 40 years and over could thus potentially have been detected prenatally and prevented, while 21 cases in this age group (36%) could not be accounted for at all. Cost-benefit analyses are shown and the number of amniocenteses required for various maternal age groups to affect the prevention of DS is calculated.

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Several factors affect the prevalence of Down's syndrome (DS) in the general population, such as the increased mortality rate — especially for DS babies born to mothers 35 years and older, compared with those born to younger mothers.[1] However, the most significant factor affecting this prevalence has been the introduction of amniocentesis, a procedure considered to be safe, accurate and reliable for the prenatal diagnosis of DS. This test has made the prenatal diagnosis of some 200 genetic conditions possible in most industrialised countries.

In South Africa, prenatal diagnoses have been available for just over a decade.[2] The Genetic Services (GS) Division within the Department of National Health and Population Development (DNHPD) since 1979 enhanced the use of prenatal diagnostics for the prevention of genetic abnormalities in this country.

Owing to the increased risk of DS associated with advanced maternal age and since amniocentesis involves only a small risk of spontaneous abortion,[3] a routine prenatal test was made available by the DNHPD to all women aged 40 years and over. This age group is considered a practical and 'safe' cut-off point for the prenatal test and should not burden the available cytogenetic units to the point where the required laboratory standards cannot be maintained.

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This report examines the ascertainment of individuals with DS born between 1980 and 1984 in the white population of South Africa. These data are compared with a calculated world incidence of DS. It was also one of the objectives of this study to calculate how many individuals with DS were born to mothers aged 40 years and older, so that the utilisation of prenatal cytogenetic diagnosis of DS in this age group during the period 1980 - 1984 could be evaluated.

Material and methods

Ascertainment of DS by the GS Division of the DNHPD is attempted for surveillance purposes and to ensure that a comprehensive genetic service is or has been provided to the families concerned. This ascertainment rate is not considered an incidence rate since the ascertainment is incomplete.

Notifications for the surveillance of families with DS are provided by all agencies concerned with this syndrome, such as special schools, training centres, care and rehabilitation centres (CRCs), clinics and DS parent groups. Such notifications are voluntary and maintained in a central data bank.[4]

Genetic services are rendered to all population groups in South Africa. However, only DS cases in the white population born between 1980 and 1984 were included in this analysis, since the majority (± 90%) of requests for prenatal diagnosis had come from members of the white population.

The number of live births among whites, with 1-year intervals of maternal age from 1980 to 1984, was obtained from the State Central Statistical Services (Table I). The total number of DS cases in South Africa, detected prenatally by cytogenetic investigations from 1980 to 1984, could be calculated from the central cytogenetic database kept by the GS Division. This information was contributed by laboratories of the Department of Human Genetics at Groote Schuur, Tygerberg and Bloemfontein Hospitals, the cytogenetic laboratories at the University of Pretoria and at MEDUNSA, the Blood Transfusion Service of Natal, the South African Institute for Medical Research (SAIMR) in Johannesburg and the DNHPD laboratory at Potchefstroom.

For purposes of comparison, a mean rate of DS per 1 000 live births for single-year maternal age intervals was calculated from pooled data from six large studies, i.e. upstate New York,[5] Ohio,[6] British Columbia,[7] Massachusetts,[8] Sweden[9] and Clanmorgan,[10] representing 4 939 640 live births. Data from the large European collaborative study[11] and other large studies such as the Atlanta study[12] were not included, since these rates were based on prenatal diagnoses. The other studies from which the mean rate was calculated apparently reflect rates calculated before the advent of active prenatal diagnosis.

The DS rate obtained from the amniocentesis figures in the European collaborative study was compared with the world DS rate in births, calculated in this study.

The observed rate of DS per 1 000 live births is based on notified, as well as prenatally detected, DS cases. This rate is compared with an expected DS rate calculated from the pooled data of 4 939 640 live births, as well as from the number of DS cases not ascertained according to the expected number.

TABLE I. RATE OF BIRTHS OF DS INFANTS TO WHITE MOTHERS AND EXPECTED RATE ACCORDING TO MATERNAL AGE, 1980 - 1985

Maternal age	No. of births	Cases notified	Detected prenatally	Observed rate* per 1 000 births	Expected rate per 1 000 births	Expected No. of cases	No. of cases observed minus expected
15	590	—		—	0,613	0	
16	1 817	1		0,55	0,524	1	0
17	4 972	—		—	0,750	4	−4
18	9 503	3		0,32	0,785	7	−4
19	14 421	6		0,42	0,657	9	−3
20	19 163	5		0,26	0,658	13	−8
21	22 684	3		0,13	0,795	16	−13
22	26 266	6		0,23	0,633	17	−11
23	28 673	12	1	0,42	0,678	19	−6
24	30 718	6		0,20	0,821	25	−19
25	30 827	10		0,32	0,795	25	−15
26	30 780	10		0,32	0,850	26	−16
27	28 992	6		0,21	1,027	30	−24
28	26 236	8		0,30	0,912	24	−16
29	23 024	12		0,52	0,92	21	−9
30	19 549	9	2	0,46	1,247	24	−13
31	16 773	9		0,54	1,372	23	−14
32	13 534	7		0,52	1,667	23	−15
33	11 290	2		0,18	1,936	22	−20
34	8 894	6		0,67	2,22	20	−14
35	7 131	5	2	0,70	3,104	22	−15
36	5 548	5	1	0,90	3,554	20	−14
37	4 148	4	3	0,96	4,531	19	−12
38	2 913	5	6	1,72	6,079	18	−7
39	2 044	3	5	1,47	7,881	16	−8
40	1 406	2	4	1,42	10,506	15	−9
41	953	1	4	1,05	11,419	11	−6
42	581		13		15,149	9	+4
43	364		4		19,198	7	−3
44	188		1		29,634	6	−5
45	94		5		34,072	3	+2
46	46		1		52,779	3	−2
47	29		2		51,095	2	−0
48	16				68,313	1	−1
49	8				87,953	1	−1
50	7						
51	6						
52	4						
53	1						
54	4						
>55	—						
Total	**394 197**	**146**	**54**		**1,34**	**502**	**−299**
DS cases detected by amniocentesis	**54**	**54**					
Corrected total	**394 251**	**200**		**0,51**	**1,34**	**528†**	**−328‡**

* Calculated from pooled data for single maternal age groups (see text) based on 4 939 640 live births.
† Expected number of DS cases corrected.
‡ DS observed minus expected corrected.

Results

The total number of births according to single-year maternal age groups in the white population for the 5-year period 1982 - 1984 is given in Table I.

In Table II the total number of births for all maternal age groups, the number of live DS cases notified, the number of DS cases diagnosed prenatally, the number of amniocenteses done, and the calculated expected DS rate for age are given on an annual basis for 1980 - 1984. A total of 200 cases of DS out of 384 197 live births were identified. In Table III age-specific rates for DS in the advanced maternal age group (> 35 years) (crude rate) compared with rates in live births are presented.

TABLE II. DS CASES NOTIFIED AFTER BIRTH AND DETECTED BY AMNIOCENTESIS COMPARED WITH EXPECTED RATE

Year	Births	Live-born cases notified	Prenatally diagnosed	Total amniocenteses done	Expected No.*	Cases observed minus cases expected
1980	74 777	30	7	1 235	100	-63
1981	79 061	36	13	1 355	106	-57
1982	77 686	26	7	1 759	104	-71
1983	81 139	23	6	1 920	109	-80
1984	81 534	31	21	2 193	109	-57
Terminations	54					
Total	394 261	146	54	8 462	528	-328

* Based on overall mean rate of 1,34/1 000 live births.

TABLE III. AGE-SPECIFIC RATES FOR DS IN ADVANCED MATERNAL AGE GROUP (>35 YEARS) (CRUDE RATE), RATES IN LIVE BIRTHS (/1 000)

Maternal age (yrs)	Rate in pregnancy*	Fractional	Rate in live births†	Fraction
35	3,5	1/286	3,1	1/323
36	5,7	1/175	3,7	1/270
37	6,8	1/147	4,5	1/222
38	8,1	1/123	6,1	1/164
39	10,9	1/92	7,9	1/127
40	12,3	1/81	10,5	1/95
41	14,7	1/68	12,0	1/83
42	21,9	1/45	15,1	1/66
43	32,4	1/31	19,2	1/52
44	29,5	1/33	29,6	1/34
45	45,3	1/22	34,1	1/29
46	81,9	1/12	52,8	1/18

* Figures obtained from the European Collaborative Study.
† Figures calculated from pooled data (Table I).

The expected reduced rates in live births compared with rates during pregnancy are clearly evident.

Discussion

An overall world mean rate of DS per 1 000 live births (mainly among whites) for single-year maternal ages is 1,34, based on pooled data involving 4 939 640 births. According to this rate, the overall mean fractional rate is 1/746 live births, which is somewhat lower than the rate of 1/600 or 1/650 often cited in genetic counselling.[13,14]

Genetic counsellors mostly consult the rate (risk) for DS in live births between the maternal age groups over 35 years, and often the fractional rates are preferred to the decimal rates. These rates are derived from Table I and are presented in Table III for the sake of convenience for counsellors. As expected, rates for DS in pregnancies are somewhat higher than in live-borns and have been included in Table III (derived from the European Collaborative Study) for easy reference.

Ascertainment

One hundred and forty-six of the 200 individuals with DS out of 384 197 live births (white population group; 1980 -1984) were ascertained by the notification system of the GS Division of the DNHPD. The rest (54) were diagnosed prenatally by amniocentesis and the pregnancies were terminated. The total of 200 cases give a rate for DS of 0,51/1 000 live births, only 38% of the calculated rate of 1,34/1 000 live births, which leaves a total of 328 cases of DS unaccounted for and indicates an under-reporting of 62%. Under-reporting and under-ascertainment are, however, also experienced in many other countries, although to a lesser extent.[5] As expected, the majority of prenatally undetected DS cases in the white population of SA occurred in the 21 - 36-year age groups (Table I). This is probably due to the fact that mothers in this age range do not qualify for a prenatal test, since they are not considered to be at high risk of having a baby with DS. However, most babies are born to mothers in this age group, because it is considered to be the most fertile period. Although the majority of DS cases therefore occur in this lower age group, the incidence per 1 000 live births is relatively low.

The method(s) of ascertainment of DS in SA, as is the case in many other countries, will have to be improved dramatically for practical prevention purposes.

Utilisation of prenatal diagnosis

A total of 8 462 amniocenteses were done in South Africa (1980 - 1983) specifically for the prenatal detection of fetuses with chromosomal abnormalities (Table II).

A total of 54 DS fetuses (mothers of all ages) were diagnosed prenatally, and with a few exceptions the pregnancies were terminated. Advanced maternal age, i.e. 40 years and older, was the most common (± 40%) indication for amniocentesis. As expected, the most common abnormality detected was DS.

In the 40-year and older maternal age group only 34 (59%) of the expected 58 DS fetuses were detected prenatally. Only a further 3 DS cases were identified by the notification system during the same period and in the same maternal age group. Another 24 cases could therefore potentially have been detected prenatally and prevented, while 21 (36%) of cases in this age group could not be accounted for at all. This trend is also being experienced in other countries, e.g. in Australia, where the utilisation rate for high-risk pregnant women aged 40 years and over was only 38,8% in 1982.[15]

According to the expected occurrences rate shown in Table I, about 11,5% of the expected number of DS cases for all age groups occurred in maternal age group of 40 years and over. It is thus estimated that only 5% of the expected number (528) of DS births in SA from 1980 to 1984 were therefore prevented as a result of prenatal cytogenetic diagnoses.

According to the expected number of DS cases (Table I), 31% of all cases of this syndrome should have occurred in the maternal age group of 35 years and over, i.e. 19,5% in the 35 - 39 years group. Approximately a further 21 000 prenatal diagnoses in the 35 - 39 years group would have had to be done during the 5-year period to detect and prevent the births of another expected 95 individuals with DS.

Cost-benefit

The cost to the State of a prenatal cytogenic investigation was R84, whereas the cost of caring for a child with DS in a CRC is conservatively calculated at R5 000 per year (excluding approximately R8 000 per year for special education). The care-cost per patient according to the most recent figures obtained from the Mitchell's Plain CRC in Cape Town is calculated at roughly R10 000 per year per patient (excluding special education). With a life expectancy of at least 30 years[16] and basic expenses of at least R5 000 - R10 000 per year, the total care-cost per individual amounts to between R150 000 and R300 000 (excluding special education).

The cost of prenatal detection of a DS fetus in the maternal age group of 40 years and over currently amounts to approximately R3 360, based on an estimated 1/40 occurrence rate of DS in this age group. A national prenatal screening programme for DS in this age group would therefore undoubtedly be very cost-effective. It is also indicated that the cost benefit derived from prenatal screening for DS would still be greater than the cost of caring for an affected individual even if the maternal age limit was lowered to 32 years.[5]

In the maternal age group of 36 - 40 years, the risk of having a child with DS is approximately 1/175. At R84 per test it would cost approximately R23 000 to detect one fetus with DS prenatally in this age interval. However, a screening programme would still be cost-effective if the financial implications of such a programme are compared with those of caring for an affected individual. It must be mentioned that a price increase to approximately R100 per chromosome test is expected for the State cytogenetic investigations, which would affect the cost-benefit accordingly.

A 100% utilisation rate of amniocentesis by all mothers aged 35 years and older requires laboratory and clinical facilities for some 24 000 amniocenteses per year. To accommodate all population groups in South Africa, facilities for at least 145 000 amniocenteses per year would have to be provided. To accommodate only women aged 40 years and older, facilities for about 18 000 amniocenteses would be necessary.

Conclusion

The results presented here show that only approximately 60% of pregnant women in the age group 40 years and older were subject to amniocentesis and in fact had the benefit of primary prevention. This indicates the scope that remains for a further 40% of mothers in this age group (white) to be reached.

It is expected that the utilisation rate in other population groups will be much lower owing to limited awareness and acceptance of prenatal diagnosis and primary prevention.

With existing cytogenetic laboratories operating at capacity and with only 2612 amniocenteses being performed in 1986, the urgent need for appropriate facilities for prenatal cytogenetic investigations in South Africa, with approximately 1 million births per year, is evident.

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