Trend of Prenatal Invasive Testing and Down's Syndrome Screening in a Tertiary Referral Centre in Hong Kong

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Objectives:
To determine (1) the trend of amniocentesis and chorionic villus sampling (CVS), and (2) the number of women aged 35 years or more who underwent Down's syndrome screening from 1997 to 2005.

Methods:
A retrospective review from the clinical database of the Prenatal Diagnosis and Counselling Department was performed. All the data were entered by nurse specialists working in the department. The number and indications of amniocentesis and CVS performed from 1997 to 2005 were retrieved. In addition, the number of such women who underwent Down's syndrome screening tests was also retrieved.

Results:
From 1997 to 2005, the total number of referrals increased from 1680 to 2010, the number of amniocentesis undertaken decreased from 708 (42%) to 390 (19%). Although chromosome study remained as the main indication for amniocentesis (88% to 96%), the numbers performed for that purpose decreased by almost half. In addition, the numbers performed to test for genetic diseases decreased markedly from 38 (6%) to 8 (2%). From 1997 to 2002, the number of CVS procedures decreased from 84 (5%) to 33 (2%), with a decrease in numbers undertaken for chromosome study from 46 to 5. Later, there was an increase in the number of CVS chromosome studies from 8 in 2004 to 22 in 2005. The proportion of women aged 35 years or more who underwent a Down's syndrome screening test increased from 31% to 65%, while the proportion who underwent an invasive test (amniocentesis or CVS) decreased from 76% in 1997 to 40% in 2005. In 2000, 38% of women aged 35 years or more underwent a second-trimester Down's syndrome screening test. After the introduction of nuchal translucency scanning in 2001, 41% of women underwent an integrated screening test in 2002, while the proportion who underwent second-trimester Down's syndrome screening decreased to 11%. With the introduction of first-trimester serum markers for Down's syndrome in mid-2005, 11% and 1% of women underwent first-trimester combined screening tests and fully integrated screening tests, respectively. Compared to 2004, the proportion of women who underwent the integrated test for Down's syndrome decreased by 10% and the total proportion of those who underwent such screening increased by 3%.

Conclusion:
From 1997 to 2005, the proportion of women aged 35 years or more who underwent a Down's syndrome screening test increased from about one-third to two-thirds while the proportion who underwent invasive testing decreased by about one half.

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Introduction

Conventionally, prenatal diagnosis is performed by invasive testing, which is associated with 0.5 to 2% miscarriage rate. With the introduction of second- and then first-trimester Down's syndrome screening and ultrasound exclusion of haemoglobin Bart's disease, the need for a prenatal invasive testing for Down's syndrome or alpha thalassaemia has decreased. The objective of the present study was to determine (1) the trend of amniocentesis and chorionic villus sampling (CVS), and (2) the number of women of age 35 years or more who underwent Down's syndrome screening from 1997 to 2005.

Methods

This was a retrospective review. Data were collected from the database of the Prenatal Diagnosis and Counselling Department at Tsan Yuk Hospital, Hong Kong. This was a clinical database that had been entered by nurse specialists working in the department. From 1997 to 2005, the number of amniocentesis and CVSs performed and their indications were retrieved. The number of women aged 35 years or more who underwent a Down's syndrome screening test was also retrieved. The following Down's syndrome screening tests were available:

1. Second-trimester serum screening: alpha fetal protein and human chorionic gonadotropin (hCG) from 16 to 19 weeks and 6 days;
2. Integrated screening: nuchal translucency (NT) + pregnancy-associated plasma protein A (PAPP-A) and hCG from 16 to 19 weeks and 6 days;
3. First-trimester combined screening: NT + PAPP-A and free β-hCG from 11 to 13 weeks and 6 days; and
4. Fully integrated test: NT + PAPP-A (from 11 to 13 weeks and 6 days) + alpha fetal protein and hCG from 16 to 19 weeks and 6 days.

Statistical Analysis

The Statistical Package for the Social Sciences (Windows version 15.0; SPSS Inc, Chicago [IL], US) was used for statistical analysis. The Chi-square test was used to test the trend of linearity between years.

Results

From 1997 to 2005, the total number of referrals increased from 1680 to 2010, while the number of amniocentesis procedures performed decreased from 708 (42%) to 390 (19%). Although chromosome study remained the main indication for amniocentesis (88 to 96%), the number of procedures for that purpose decreased by almost one half. The number performed for genetic diseases decreased markedly from 38 (6%) to 8 (2%) [Table 1].

From 1997 to 2002, the number of CVS procedures decreased from 84 (5%) to 33 (2%). Whilst those performed for chromosome study increased from 8 in 2004 to 22 in 2005 (Table 2).

From 1997 to 2005, the overall proportion of women aged 35 years or more who underwent a Down's syndrome screening test increased from 31% to 65% while the proportion who underwent an invasive test (amniocentesis or CVS) decreased from 76% to 40% (Table 3 and Figure).

In 2000, 38% of women aged 35 years or more underwent second-trimester Down's syndrome screening (Table 3). After the introduction of NT scans in our department in 2001, 41% of women underwent the integrated screening test in 2002, while the proportion undergoing second-trimester testing decreased to 11%.

With the introduction of first-trimester serum markers for Down's syndrome in our laboratory in mid-2005, 11% and 1% of women underwent first-trimester combined screening and fully integrated screening, respectively (Table 3). Compared to 2004, the proportion of women who underwent the integrated test for Down's syndrome decreased by 10% and the proportion who underwent Down's syndrome screening increased by 3%.

Discussion

From 1997 to 2005, the proportion of women who underwent an invasive test (amniocentesis or CVS) for karyotyping and DNA study decreased by 32% and 4%, respectively. The decrease was probably due to the introduction of NT scanning and integrated testing in 2001, and the first-trimester combined screening test in 2005. The proportion of women who underwent a Down's syndrome screening increased by 34% over the same period. Women preferred a non-invasive approach with a lower risk, rather than an invasive test with a 0.5

Table 1. Comparative statistics: indications for and numbers of amniocentesis from 1997 to 2005

Year	Chromosome study No. (%)	Genetic diseases No.(%)	Fetal abnormality No. (%)	Alpha thalassaemia No. (%)	Total No. of amniocentesis No. (%)
1997	635 (90)	38 (6)	35 (5)	0	708 (42)
1998	597 (94)	26 (4)	12 (2)	0	635 (36)
1999	629 (93)	21 (3)	28 (4)	6 (1)	678 (36)
2000	702 (96)	14 (2)	15 (2)	0	731 (37)
2001	581 (91)	15 (2)	40 (6)	5 (1)	636 (35)
2002	422 (89)	20 (4)	35 (7)	1 (0.2)	477 (29)
2003	416 (89)	10 (2)	40 (9)	0	466 (28)
2004	401 (88)	11 (2)	42 (9)	0	454 (25)
2005	345 (89)	8 (2)	37 (10)	0	390 (19)

* CVS = chorionic villus sampling

Table 2. Comparative statistics: indications for and total numbers of chorionic villus samplings (CVSs) per year

Year	Chromosome study No. (%)	Genetic diseases No. (%)	Fetal abnormality No. (%)	Total No. of CVS No. (%)	Total No. of referrals	Detection rate (%)	False positive rate (%)
1997	46 (55)	33 (39)	5 (6)	84 (5)	1680	100	6.8
1998	55 (70)	16 (20)	8 (10)	79 (5)	1749	83	5.6
1999	29 (56)	22 (42)	1 (2)	52 (3)	1846	76	6.5
2000	24 (46)	19 (37)	9 (17)	52 (3)	1974	73	6.5
2001	17 (36)	25 (53)	5 (11)	47 (3)	1836	80	6.2
2002	5 (15)	20 (61)	8 (24)	33 (2)	1648	82	5.4
2003	11 (24)	17 (38)	17 (38)	45 (3)	1630	100	8.1
2004	8 (16)	28 (55)	15 (29)	51 (3)	1796	93	5.7
2005	22 (48)	12 (26)	12 (26)	46 (2)	2010	100	3.7

Table 3. Statistics of women aged 35 years or more presenting before 20 weeks of gestation who underwent screening between 1997 and 2005

Year	Total No. of women	Second-trimester blood test No. (%)	Nuchal translucency No. (%)	Integrated screening No. (%)
1997	1049	321 (31)	0	0
1998	1041	596 (57)	0	0
1999	1118	421 (38)	0	0
2000	1185	447 (38)	0	0
2001	1071	244 (23)	1 (0.1)	194 (18)
2002	951	101 (11)	37 (4)	390 (41)
2003	988	80 (8)	51 (5)	456 (46)
2004	1064	80 (8)	46 (4)	529 (50)
2005	1075	90 (8)	47 (4)	431 (40)

* CVS = chorionic villus sampling

Total No. of Down's syndrome detected	No. of Down's syndrome / No. of invasive procedures (amniocentesis + CVS*)	Total No. of Down's syndrome missed	Total No. of referrals	Total No. of Down's syndrome missed per referral
2	2/824	1	1680	1/1680
3	3/841	2	1749	2/1749
2	2/762	0	1846	0/1846
3	3/810	1	1974	1/1974
2	2/707	1	1836	1/1836
5	5/516	0	1648	0/1648
1	1/515	0	1630	0/1630
3	3/521	0	1796	0/1796
5	5/458	0	2010	0/2010

to 1% risk of miscarriage.

These results were comparable to those reported by Muller et al[1]. In their study, there was a significant decrease in the use of second-trimester Down's syndrome maternal serum screening (from 75% in 1995 to 25% in 2005; p<0.001) and a corresponding significant increase in first-trimester combined screening (from 0.8% in 2000 to 49% in 2005; p<0.001). The proportion of all confinements that involved invasive prenatal testing fell (from 9% in 1995 to 8% in 2005; p<0.001). There was a significant decrease in the number of invasive prenatal tests needed to detect a Down's syndrome fetus (from 86 in 1995 to 40 in 2005; p<0.001), with no significant change in the proportion of cases detected prenatally.

This trend was consistent with current recommendations by the American and Royal Colleges of Obstetricians and Gynecologists, such screening being offered to women aged 35 years or more[2,3]. It needs time for the public and doctors to absorb such a new idea[4].

There was an increase in the number of CVS procedures for chromosome study from 8 in 2004 to 22 in 2005, which was probably due to the introduction in 2005 of the first-trimester combined screening for Down's syndrome with the option of CVS. In that year, 11% of women underwent first-trimester combined screening. First-trimester screening has been shown to be an effective and reliable for detecting Down's syndrome[2]. Besides, implementation of early second-trimester

Full integrated screening No. (%)	First-trimester combined screening No. (%)	Total No. of women undergoing a Down's syndrome screening test, No. (%)	Amniocentesis for karyotype No. (%)	CVS* for karyotype No. (%)
0	0	321 (31)	708 (68)	84 (8)
0	0	596 (57)	635 (61)	79 (8)
0	0	421 (38)	678 (61)	52 (5)
0	0	447 (38)	731 (62)	52 (4)
0	0	439 (41)	636 (59)	47 (4)
0	0	528 (56)	477 (50)	33 (3)
0	0	587 (59)	466 (47)	45 (5)
0	0	655 (62)	454 (43)	51 (5)
12 (1)	123 (11)	703 (65)	390 (36)	46 (4)

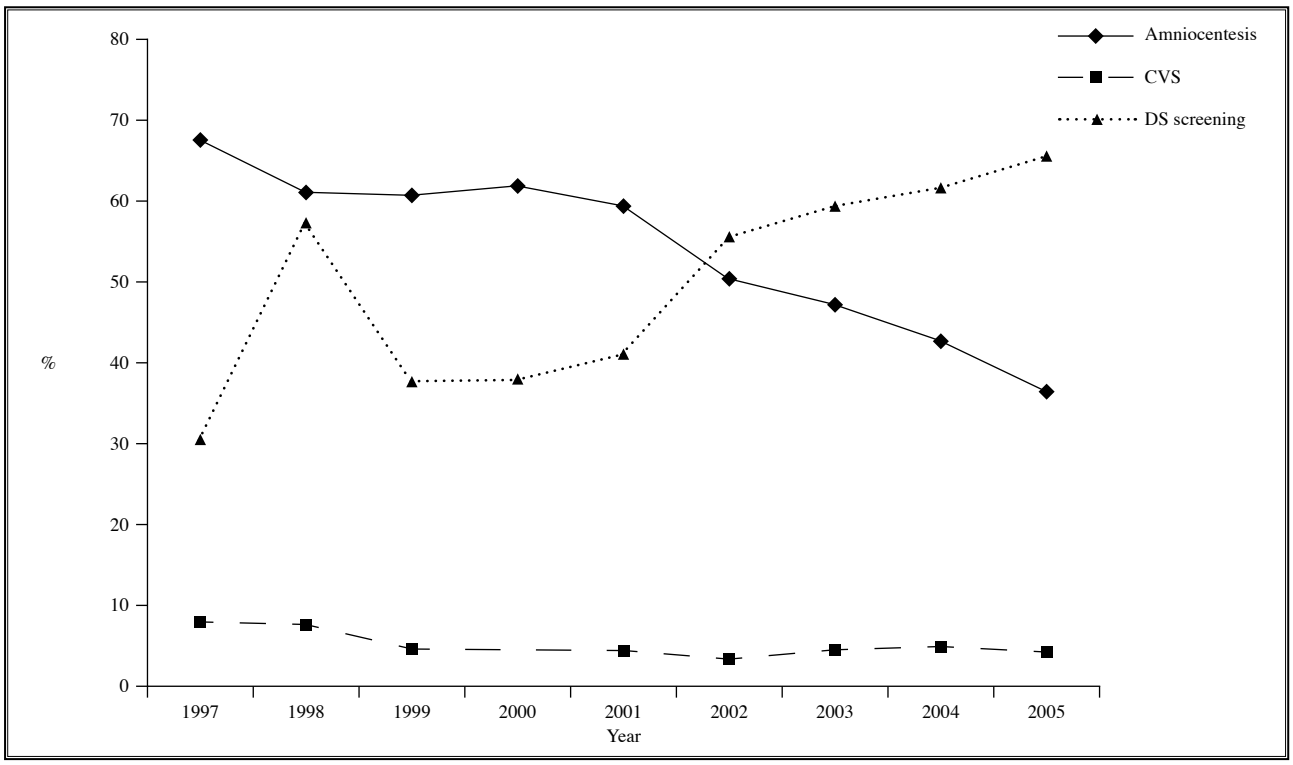

Figure. Percentage of uptake of amniocentesis, chorionic villus sampling (CVS), and Down's syndrome (DS) screening among women aged 35 years or more from 1997 to 2005

scanning allowed early detection of fetal abnormalities and an option of CVS if abnormalities were present[5,6]. Jenkins and Wapner[7] in their review concluded that first-trimester CVS is both safe and effective for the diagnosis of fetal chromosomal, biochemical, and molecular disorders, with risks comparable to those of second-trimester amniocentesis. The lower risk associated with first-trimester abortions may be an important influence on prospective parents deciding between CVS and amniocentesis[8].

From 1997 to 2005, there was a decrease in the number and proportion of women who underwent an invasive test (amniocentesis or CVS) for genetic diseases. In Hong Kong, the commonest genetic disorder is thalassaemia. In our centre, we offer couples a non-invasive approach for the diagnosis of alpha-thalassaemia[9]. Serial ultrasound examinations were performed on at-risk women starting from 12 weeks' gestation, with a view to identifying pregnancies affected by homozygous alpha^0-thalassaemia. This approach is well-accepted by women[9].

There were some limitations of the present study. Firstly, the first-trimester combined screening test for Down's syndrome was introduced in our Department in 2005, a long-term study is required to examine the trend in terms of uptake of this screening test by women. Secondly, we did not study the sensitivities and false positive rates for the Down's syndrome screening tests.

In conclusion, from 1997 to 2005, the proportion of women aged 35 years or more who underwent Down's syndrome screening increased from about one-third to two-thirds, while the proportion who underwent an invasive test decreased.

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