IMPACT OF SECOND-TRIMESTER MATERNAL SERUM SCREENING ON PRENATAL DIAGNOSIS OF DOWN SYNDROME AND THE USE OF AMNIOCENTESIS IN THE TAIWANESE POPULATION

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SUMMARY

Objective: To investigate the impact of second-trimester maternal serum screening on prenatal diagnosis of Down syndrome and the use of amniocentesis in the Taiwanese population.

Materials and Methods: From 1990 to 2000, 166,419 amniocenteses were analyzed cytogenetically in the Taiwanese population. Among these, 58.85% were for advanced maternal age, 4.5% for abnormal ultrasound findings, 26.17% for abnormal maternal serum screening results, 1.82% for a previous child with congenital anomaly, 1.02% for a family history of chromosome aberrations, and 7.63% for other purposes. Chromosome aberrations were detected in 4,217 cases (2.53%), of which 1,277 (30.28%) were Down syndrome. Of the Down syndrome cases, 65.86% were detected by amniocentesis for advanced maternal age, 5.95% for abnormal ultrasound findings, 21.14% for abnormal maternal serum screening results, 1.25% for a previous child with congenital anomaly, 1.18% for a family history of chromosome aberrations, and 4.62% for other purposes.

Results: There was a prominent increase in the number of women undergoing amniocentesis in the Taiwanese population between 1990 and 2000. There was an 8.9-fold increase in the number undergoing amniocentesis for advanced maternal age, a 6.3-fold increase in that for abnormal ultrasound findings, a 46.2-fold increase in that for abnormal maternal serum screening results, a 2.9-fold increase in that for a previous child with congenital anomaly, a 5.6-fold increase in that for a family history of chromosome aberrations, and a 4.4-fold increase in that for other purposes. There was also a 35.7-fold increase in the number of prenatally detected Down syndrome cases, from seven in 1990 to 250 in 2000. The highest rates of Down syndrome were found in cases with abnormal ultrasound findings (1/99 tests). Down syndrome was 0.72-fold as common in amniocenteses performed because of positive serum screening results (1/161 tests) compared with the rate seen in the advanced maternal age group (1/116 tests). The detection rates increased from 1/449 tests in 1990, through 1/198 tests, 1/203 tests, 1/215 tests, 1/229 tests, 1/169 tests, 1/143 tests, 1/90 tests, 1/92 tests, to 1/123 tests in 2000.

Conclusion: Both the number of women undergoing amniocentesis and the number of detected cases of Down syndrome increased during these years. Amniocentesis in this population no longer led to a significant improvement in the detection rate of Down syndrome. In view of the effective use of amniocentesis as a diagnostic procedure for Down syndrome, efforts should be made to use more efficient prenatal screening programs and to reduce the number of unnecessary amniocenteses. [Taiwanese J Obstet Gynecol 2005;44(1):31-35]

Key Words: amniocentesis, Down syndrome, maternal serum screening

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Introduction

Genetic amniocentesis is the most common invasive diagnostic procedure for prenatal diagnosis of fetal aneuploidy. Although advanced maternal age remains the most common indication for genetic amniocentesis, the introduction of maternal serum biochemistry screening has led to a growing number of amniocenteses. The impact of second-trimester maternal serum screening on prenatal diagnosis of Down syndrome and on the use of amniocentesis in Asian populations has rarely been described. Here, we document an 11-year (1990–2000) experience of prenatal diagnosis of Down syndrome by amniocentesis in the Taiwanese population.

Materials and Methods

Data were compiled in a database for 26 cytogenetic laboratories (Appendix) in Taiwan and covered the cytogenetic analyses of amniocytes from second-trimester amniocenteses between 1990 and 2000. The data provided a detailed account of the amniocentesis results following the main indications of a family history of chromosome aberrations, advanced maternal age, abnormal maternal serum screening results, abnormal ultrasound findings, a previous child with a congenital anomaly, and other purposes. In some instances, there were multiple indications. For investigative simplicity, multiple indications were reduced to a single indication using the priority order above. A family history of chromosome aberrations included a family history of aneuploidy, translocation, inversion, or marker chromosome. Advanced maternal age was defined as more than 35 years old at delivery. Abnormal maternal serum screening results included patients who were screen-positive for Down syndrome and trisomy 18. Taiwan began an active national policy of offering amniocentesis to women aged at least 35 years and those with indications other than age in 1990. A large-scale, second-trimester maternal serum screening double-marker testing program for Down syndrome using the maternal serum markers alpha-fetoprotein (AFP), human chorionic gonadotropin (hCG), or its variant free beta-hCG was implemented in 1994. Prior to 1994, only maternal serum AFP was used for prenatal screening. Abnormal ultrasound findings included anomalies and ultrasound markers suggesting chromosomal abnormalities. Other purposes included an abnormally high level of maternal serum AFP, prenatal biochemical or molecular referrals, a history of spontaneous abortion, and elective purposes such as anxiety, normal maternal serum screening results close to a Down syndrome risk cut-off level of 1/270, maternal age close to 35 years, etc. Chromosome aberrations included autosomal trisomies, triploidy, tetraploidy, mosaicism, ring chromosomes, deletion, duplication, inversion, balanced translocation, unbalanced translocation, and marker chromosomes. Chromosome variants such as inversion of chromosomes 9 and Y, double satellites or marked satellite on acrocentric chromosomes, and hyperchromatin on chromosomes 1, 9, and 16 were categorized as normal. The Chi-squared test was used to compare rates. A p value of less than 0.05 was considered significant.

Results

From 1990 to 2000, 166,419 amniocenteses were analyzed cytogenetically in the Taiwanese population (Table 1). Among these, 58.85% were done for advanced maternal age, 4.5% for abnormal ultrasound findings, 26.17% for abnormal maternal serum screening results, 1.82% for a previous child with a congenital anomaly, 1.02% for a family history of chromosome aberrations, and 7.63% for other purposes. Chromosome aberrations were detected in 4,217 cases (2.53%), of which 1,277 (30.28%) were Down syndrome. Of the Down syndrome cases, 65.86% were detected by amniocentesis for advanced maternal age, 5.95% for abnormal ultrasound findings, 21.14% for abnormal maternal serum screening results, 1.25% for a previous child with a congenital anomaly, 1.18% for a family history of chromosome aberrations, and 4.62% for other purposes (Table 2).

There was a prominent increase in the number of women undergoing amniocentesis in the Taiwanese population from 1990 to 2000. There was an 8.9-fold increase in the group undergoing amniocentesis for advanced maternal age (p < 0.01), a 6.3-fold increase in those for abnormal ultrasound findings (p < 0.01), a 46.2-fold increase in those for abnormal maternal serum screening results (p < 0.01), a 2.9-fold increase in those for a previous child with a congenital anomaly (p < 0.05), a 5.6-fold increase in those for a family history of chromosome aberrations (p < 0.01), and a 4.4-fold increase in those undergoing amniocentesis for other purposes (p < 0.05). There was also a 35.7-fold increase in the number of prenatally detected Down syndrome cases, from seven in 1990 to 250 in 2000 (p < 0.01).

The highest rates of Down syndrome were present in women undergoing amniocentesis for abnormal ultrasound findings (1/99 tests). Down syndrome was 0.72-fold as common in amniocenteses performed because of positive serum screening results (1/161 tests) compared with the rate seen in the advanced maternal
Second-trimester Maternal Serum Screening

This study showed a significant increase in the number of Down syndrome cases detected prenatally between 1990 and 2000 in the Taiwanese population. During this period, there was also an increase in the number of amniocenteses. The increase was especially prominent after 1994, when maternal serum screening double-marker testing was first applied in this population. The increases in both the number of detected cases of Down syndrome and the number of amniocenteses were attributed to the national policy of offering amniocentesis to women aged at least 35 years, the introduction of maternal serum biochemical double-marker testing, and the active application of prenatal ultrasonography. While both the number of women undergoing amniocentesis and the number of detected cases of Down syndrome increased during these years, the detection rates for Down syndrome remained constant after 1998. This suggests that amniocentesis in this population no longer led to a significant improvement in the detection rate of Down syndrome. Therefore, more powerful screening programs such as first-trimester maternal serum screening in conjunction with nuchal translucency and nasal bone measurement by early ultrasound examination are required.

On the other hand, in this population, a great number of non-recommended amniocenteses were performed for elective purposes such as anxiety, normal maternal serum screening results that were close to a Down syndrome risk cut-off level of 1/270, and a maternal age nearing 35 years. This was partly due to insufficient genetic counseling facilities and personnel and partly due to changing family values that emphasize the quality rather than quantity of children in this population. The impact of maternal serum screening on the birth prevalence of Down syndrome and on the use of invasive genetic tests has been described in different populations [1–6]. This 11-year Taiwanese experience of prenatal diagnosis of Down syndrome shows that the introduction of second-trimester maternal serum screening programs resulted in increased use of amniocentesis and an increased number of prenatally detected cases of Down syndrome but no improvement in the detection rate of Down syndrome by amniocentesis in the end of this period. In view of the effective use of amniocentesis as a diagnostic procedure for Down syndrome, efforts should be made using more efficient

**Table 1. All amniocentesis cases, cases with chromosome aberrations, and main indications between 1990 and 2000 in Taiwan**

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<tbody>
<tr>
<td>Total examined</td>
<td>2,073</td>
<td>2,149</td>
<td>2,707</td>
<td>3,152</td>
<td>3,559</td>
<td>4,848</td>
<td>10,484</td>
<td>13,764</td>
<td>16,952</td>
<td>18,484</td>
<td>97,936</td>
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<tr>
<td>Rate of chromosome aberrations*</td>
<td>2.47%</td>
<td>2.84%</td>
<td>3.07%</td>
<td>3.32%</td>
<td>2.53%</td>
<td>2.52%</td>
<td>2.53%</td>
<td>2.44%</td>
<td>2.29%</td>
<td>2.43%</td>
<td>2.53%</td>
</tr>
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*Rate of chromosome aberrations = Cases with chromosome aberrations/Total cases examined.
prenatal screening programs and reducing the number of unnecessary amniocenteses.

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References

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