OBSTETRICS

Trends in timing of prenatal diagnosis and abortion for fetal chromosomal abnormalities

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OBJECTIVE: Our objective was to evaluate changes in the timing of prenatal diagnosis and abortion for chromosomal abnormalities over the past 10 years.

STUDY DESIGN: This retrospective review identified singleton pregnancies with fetal chromosomal abnormalities that were diagnosed from 2005-2014 and included Down syndrome, Trisomy 18, and Trisomy 13. The study period was divided into 3 intervals: 2005-2006; 2007-2011; and 2012-2014. Gestational ages at prenatal diagnosis and abortion were compared over these intervals.

RESULTS: The 213 cases included 142 cases of Down syndrome (66.7%), 47 cases of Trisomy 18 (22.1%), and 24 cases of Trisomy 13 (11.3%). Two hundred one women (94.4%) chose to undergo abortion. The median gestational ages at prenatal diagnosis and abortion for Trisomy 18 or 13 were 12 weeks (interquartile range, 12—13 weeks) and 13 weeks (interquartile range, 12—15.5 weeks) and did not change over the study period. In contrast, in pregnancies with Down syndrome, the median gestational age at prenatal diagnosis (16, 13, and 12 weeks; $P < .001$) and abortion (17, 14, and 13 weeks; $P < .001$) both decreased significantly over the study intervals. In Down syndrome pregnancies, the proportion of women who underwent chorionic villus sampling significantly increased over the 3 study intervals (36%, 63%, and 86%; $P < .001$).

CONCLUSION: Since 2005, the gestational ages at prenatal diagnosis and abortion for Down syndrome have declined significantly. These changes are likely attributable to improvements in early screening that leads to higher rates of chorionic villus sampling.

Key words: abortion, Down syndrome, noninvasive prenatal testing (NIPT), prenatal diagnosis

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Prenatal testing for chromosomal abnormalities has been enhanced by risk assessment that is available earlier in pregnancy and has greater screening performance. Our ability to provide better information to women who are considering invasive prenatal diagnosis has also enhanced patient autonomy. Major changes in the United States over the past decade include recommendations from the American College of Obstetricians and Gynecologists (ACOG) to remove age-based criteria for invasive testing and to offer first-trimester risk assessment to all patients in 2007[1,2] and for the availability of cell-free fetal DNA or noninvasive prenatal testing (NIPT), which is reportedly the most sensitive and specific screen for Down syndrome, in 2012.[3]

In our medical center, we started first-trimester screening for chromosomal abnormalities by measuring nuchal translucency in 2000[4] and added first-trimester biochemistry in 2003.[5] We subsequently described a significant reduction in gestational ages at prenatal diagnosis and abortion for chromosomal abnormalities from 1999-2005. Although an increasing proportion of cases were detected in the first-trimester throughout the study period, most cases of Down syndrome were still diagnosed in the second trimester, with a median gestational age of abortion of 17 weeks.[6]

Our objective was to evaluate the changes in the timing of prenatal diagnosis and abortion for chromosomal abnormalities over the past 10 years in our patient population.

Materials and Methods

We identified all singleton pregnancies with fetal chromosomal abnormalities that were diagnosed from 2005-2014. Those pregnancies with a diagnosis of Down syndrome, Trisomy 18, and Trisomy 13 were included. Medical records were reviewed to determine the tests that were used to assess a risk for chromosomal abnormalities, the timing and technique of prenatal diagnosis, and the timing of abortion. The study period was divided into 3 intervals to coincide with revised ACOG recommendations for first-trimester screening and prenatal diagnosis (2007)[1,2] and the availability of cell-free fetal DNA assessment (2012)[3]: 2005-2006, 2007-2011, and 2012-2014.

Adjusted first-trimester risk of Down syndrome and a composite risk for Trisomy 18 and Trisomy 13 were based on maternal age, nuchal translucency, and biochemistry. The higher of these adjusted risks in each pregnancy was considered for study purposes. If biochemistry was not performed because of extreme nuchal translucency or cystic hygroma,[7] the adjusted risk was

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TABLE 1
Trends in prenatal diagnosis and abortion for Down syndrome

Variable	Inclusive years 2005-2006	2007-2011	2012-2014	*P* value
Chorionic villus sampling, %	36	63	86	< .001[a]
Median gestational age at prenatal diagnosis, wk (interquartile range)	16 (12.5–17.0)	13 (12–16)	12 (11–13)	< .001[b]
Median gestational age at abortion, wk (interquartile range)	17 (14–19)	14 (13–17)	13 (12–14)	< .001[b]
Median interval from diagnosis to abortion, wk (interquartile range)	2 (1–3)	1 (1–2)	1 (1–2)	.047[b]
Abortion at <15 wk, %	30	59	81	< .001[a]

[a] χ^2 analysis; [b] Kruskal-Wallis test.

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considered to be >1 in 10. In those who underwent NIPT as the initial screen for chromosomal abnormalities, a positive screen was also considered to be consistent with a >1 in 10 risk.

First-trimester risk assessment with nuchal translucency and biochemistry were available to all patients throughout the study period, with referral of individual patients at the discretion of referring obstetricians. NIPT became available in 2012, with testing also at the discretion of referring providers and their patients. Both amniocentesis and chorionic villus sampling (CVS) have been available in our prenatal diagnosis unit and other local facilities and access did not change throughout the study period. First- and second-trimester abortion is available in our hospital and in other local facilities; patients generally are able to schedule procedures with minimal delays. Access to abortion did not change throughout the study period.

Changes in median gestational age at diagnosis and abortion over time were compared with Kruskal-Wallis Test. Categoric variables were compared with the use of χ^2 analysis and Fisher exact test. Continuous data are presented as median (interquartile range). Institutional review board approval was obtained to review medical records.

RESULTS

From 2005-2014, there were a total of 49,851 patients who underwent screening or diagnostic testing without screening for chromosomal abnormalities. Two hundred thirteen cases were identified and included 142 Down syndrome cases (66.7%), 47 Trisomy 18 cases (22.1%), and 24 Trisomy 13 cases (11.3%). The median maternal age was 37 years (interquartile range, 34-38 years) and did not differ over the 3 study periods. Two hundred one women (94.4%) chose to undergo abortion.

Chromosomal abnormalities were diagnosed by CVS in 129 cases (60.6%) and by amniocentesis in 61 cases (28.6%). There were 23 patients (10.8%) who underwent abortion because of ultrasound findings without invasive testing; abnormal karyotype was identified in tissue. Of these 23 pregnancies, 22 had fetal anomalies that were identified in the first trimester: cystic hygroma in 17 pregnancies, holoprosencephaly in 3 pregnancies, and generalized edema in 2 pregnancies. In the other pregnancy, multiple anomalies were noted at 20 weeks of gestation, including Dandy-Walker malformation and a cardiac abnormality. Trisomy 18 or Trisomy 13 was diagnosed in 15 of these 23 pregnancies (65.2%), with Down syndrome identified in 8 of them (34.8%).

Most patients (198; 93.0%) underwent first-trimester screening for chromosomal abnormalities, with no significant differences between study periods. Only 11 patients (5.2%) underwent CVS without screening, with a higher rate in 2012-2014 compared with 2005-2011 (12.5% vs 2.7%; $P = .02$).

Most patients who underwent first-trimester screening had high adjusted risk. The risk was ≥1 in 100 in 169 of 198 patients (85.4%), with no difference between study periods. There were 125 patients at a ≥1 in 10 risk (63.1%). The proportion of Down syndrome pregnancies with a ≥1 in 10 first-trimester risk did increase significantly over time, from 39.1% in 2005-2006, to 55.8% from 2007-2011, and 84.8% from 2012-2014 ($P < .001$). There was no such difference in pregnancies with Trisomy 18 or Trisomy 13. The rate of CVS was significantly higher in these patients who are at highest risk compared with those with a risk of <1 in 10 (85.8% vs 39.1%; $P < .001$).

The gestational ages at prenatal diagnosis and abortion for Down syndrome declined significantly over the study period. The proportion of Down syndrome cases that were diagnosed in the first trimester increased significantly over the study period, with 86% of cases diagnosed by CVS from 2012-2014 (Table 1). In contrast, the median gestational ages at prenatal diagnosis and abortion for Trisomy 18 and Trisomy 13 were earlier than those for Down syndrome in the earlier study periods. There were no significant changes in timing of prenatal diagnosis or abortion for Trisomy 18 or Trisomy 13 over the study period (Table 2). The rates of invasive testing in our entire obstetric population declined significantly over the study intervals. Invasive testing was performed in 27.8% of pregnancies from 2005-2006, 22.8% from 2007-2011, and 13.5% from 2012-2014 ($P < .001$).

During the most recent study period (2012-2014), first-trimester NIPT was the initial screen for chromosomal

TABLE 2
Trends in prenatal diagnosis and abortion for Trisomy 18/13

Variable	Inclusive years 2005-2006	2007-2011	2012-2014	*P* value
Chorionic villus sampling, %	67	78	77	.64[a]
Gestational age at prenatal diagnosis, wk (interquartile range)	12 (12–17)	12 (12–13)	12 (11–13)	.15[b]
Gestational age at abortion, wk (interquartile range)	13 (13–17)	13 (12–16)	13 (12–14.5)	.45[b]
Interval from diagnosis to abortion, wk (interquartile range)	0.5 (0–1.25)	1 (0–1.5)	1 (1–1)	.44[b]
Abortion at <15 wk, %	71	74	73	.94[a]

[a] χ^2 analysis; [b] Kruskal-Wallis test.

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abnormalities in 31% of cases. In all of these cases, the specific trisomy suspected on NIPT was confirmed by invasive testing. All 19 of these patients underwent abortion at <15 weeks of gestation, compared with 30 of 43 of remaining patients (69.8%; $P = .006$).

Comment

In our obstetric population, most patients who pursue a prenatal diagnosis of chromosomal abnormalities choose to terminate pregnancies that are affected by autosomal trisomy. This is consistent with published data in other populations.[8] Over the past decade, the gestational ages at prenatal diagnosis and abortion for Down syndrome have declined significantly. In recent years, most diagnoses have been achieved with CVS, with abortion occurring before 15 weeks of gestation.

Earlier abortion has lower rates of complications compared with abortion later in the second trimester.[9,10] In some regions, second-trimester abortion is less available or unavailable, and patients may have to travel considerable distances for access to providers.[11,12] Thus, changes in timing and methods of screening that lead to earlier prenatal diagnosis can have a significant impact.

There has been no difference in the timing of prenatal diagnosis or abortion for Trisomy 18 or Trisomy 13, because most cases were identified in the first trimester in the early study period. The high rate of intrauterine death and miscarriage also makes the prevalence of these conditions much lower in the second trimester.[13]

The observed changes in timing of prenatal diagnosis of Down syndrome are likely, in part, due to the availability of first-trimester screening and, since 2012, NIPT. Although there was a high-rate of first-trimester screening even in the early study period, a higher proportion of pregnancies with Down syndrome were at highest adjusted risk in the later study periods, which suggests improved first-trimester risk assessment. As referring obstetricians become more comfortable with newer screening modalities, responses to abnormal testing may also become more consistent and lead to an earlier prenatal diagnosis. If NIPT, which can be performed as early as 9 weeks of gestation, becomes a primary screening modality, gestational age at prenatal diagnosis may decrease further.

A strength of this study was the longitudinal assessment of an obstetric population with high uptake of screening for chromosomal abnormalities and prenatal diagnosis. The single institution design enabled us to collect specific data about timing and method of prenatal diagnosis and timing of abortion. A limitation of the retrospective design was that, although enhancement in early screening did correspond with the observed changes, we could not determine what specific factors informed decisions of physicians and patients about their choices for screening and prenatal diagnosis. Thus, we could not assess directly the impact of ACOG recommendations and changing screening options. Another limitation was that retrospectively dividing any study period into intervals is arbitrary, because changes in guidelines and screening options do not have a clear or uniform effect. Because NIPT was available only in the most recent study period however, it is reasonable to conclude that its availability contributed to the observed trends towards earlier prenatal diagnosis and abortion.

In conclusion, we have seen the gestational ages of the prenatal diagnosis of Down syndrome decline significantly over the past decade, with a corresponding decline in gestational age at abortion. These changes, which may be related to earlier and better screening, have the potential to enhance significantly the autonomy of pregnant women. ■

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