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Trends and Outcomes After Prenatal Diagnosis of Congenital Cardiac Malformations by Fetal Echocardiography in a Well Defined Birth Population, Atlanta, Georgia, 1990–1994

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Objectives. **In this study we used a population-based approach to assess the impact of fetal echocardiography on a well defined birth population with nearly complete ascertainment of cardiac defects.**

Background. **Although fetal echocardiography is being used more frequently in the prenatal diagnosis of congenital cardiac malformations, its impact on the diagnosis and surveillance of cardiac defects has not been described in defined populations.**

Methods. **All stillborn and live-born infants with diagnosed cardiac defects and whose mothers resided in the metropolitan Atlanta area from January 1990 through December 1994 were ascertained through an established birth defects surveillance system. All fetuses with cardiac defects diagnosed prenatally by a pediatric cardiologist were identified from clinical records. The spectrum of cardiac defects, diagnostic trends and adverse fetal outcomes were described.**

Results. **We identified 1,589 infants with congenital cardiac malformations, for a live-birth prevalence rate of 8.1/1,000 (95% confidence interval [CI] 7.8 to 8.6). Overall, 97 (6.1%) of these cases of cardiac malformations were diagnosed prenatally. The proportion of cardiac defects diagnosed prenatally rose from 2.6% in 1990 to 12.7% in 1994, a nearly fivefold increase. The proportion of cardiac defects diagnosed prenatally during the study varied by the type of defect, from a low of 4.7% for atrial septal defects to a high of 28% for hypoplastic left heart syndrome. Prenatally diagnosed cardiac malformations were associated with a high incidence of infant mortality (30.9%, 95% CI 2.4 to 5.4) and fetal wastage (17.5%, 95% CI 6.2 to 11.3).**

Conclusions. **These data show that fetal echocardiography is being used increasingly in the prenatal diagnosis of congenital cardiac malformations in metropolitan Atlanta. Few pregnancy terminations were reported as a result of such diagnoses. However, the study had limited power (10%) to detect a meaningful decrease in birth prevalence rates for congenital heart disease. In addition, survival of infants was not improved after prenatal diagnosis with fetal echocardiography.**

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The use of fetal echocardiography to diagnose congenital cardiac malformations prenatally is rapidly becoming the standard of care in most large pediatric cardiology centers (1,2). Centers routinely performing fetal echocardiography are making earlier diagnoses of more complex cardiac malformations, associated extracardiac anomalies and intrauterine cardiac failure, all of which lead to poor fetal outcomes (1–3). Multispecialty teams consisting of pediatric cardiologists, perinatologists and obstetricians are rapidly evolving to manage these more frequently identified high risk pregnancies with hemodynamically significant congenital cardiac malformations.

Fetal echocardiography resulting from referral after screening obstetrical ultrasound is being used increasingly to diagnose the complete prenatal spectrum of congenital cardiac malformations and to predict fetal outcomes. Nevertheless, the impact of fetal echocardiography on the prenatal diagnosis of congenital cardiac malformations has not been described in well defined birth populations.

The purpose of this study was to use a population-based approach to assess the proportion of pregnancies in which a prenatal diagnosis of congenital cardiac malformations was made by fetal echocardiography. We did this to evaluate the impact of this technology on the measured birth prevalence of cardiac malformations. We also compared the frequencies of cardiac malformations, associated noncardiac malformations and fetal outcomes among pregnant women who had a prenatal diagnosis by fetal echocardiography with those who did not.

Methods

Patient population. All infants born from January 1990 through December 1994 and diagnosed with a congenital cardiac malformation were registered by the Metropolitan Atlanta Congenital Defects Program (MACDP). Since 1967,

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MACDP has been an ongoing, population-based surveillance system for birth defects, with active case ascertainment. Details of the program have been described elsewhere (4,5).

The following criteria must be fulfilled to meet the MACDP case definition of a congenital defect: 1) the mother must be a resident of the five-county metropolitan Atlanta area (Cobb, Clayton, Decatur, Fulton and Gwinnett) at the time of birth; 2) the baby must have a gestational age of at least 20 weeks or a birth weight of at least 500 g; 3) the baby must have a structural or chromosomal defect that can adversely affect his or her health or development; 4) the diagnosis must be made or symptoms must be present in the child's first year of life; and 5) the case must be abstracted by the child's sixth birthday. Although MACDP may not detect minor birth defects among infants not requiring hospital care, we believe it does provide near complete ascertainment for most congenital cardiac defects.

Referrals for fetal echocardiography. All referrals for prenatal diagnoses of congenital cardiac malformations made by using fetal echocardiography were identified by a retrospective review of the clinical records of The Children's Heart Center at the Emory University School of Medicine. Because this center is the only pediatric cardiology center in the Atlanta area, providing services for infants born with serious cardiac malformations, the records were considered complete. Previously, Emory University School of Medicine has contributed clinical information on other congenital malformations to the MACDP surveillance system.

Fetal outcomes. After a prenatal diagnosis by fetal echocardiography was made, outcome data, including all live-births, stillbirths, spontaneous and induced abortions at >20 weeks' gestation and at least 500 g birth weight and death before 5 years of age, were obtained from the MACDP surveillance system. Pregnancy terminations before 20 weeks were not actively ascertained in the MACDP surveillance data; however, an incomplete and passive recording system of induced abortions is maintained. Therefore, unrecognized pregnancy terminations were actively sought from available hospital perinatology and cardiology records. These data were used to test the hypothesis that early prenatal diagnosis of cardiac defects does not favorably affect fetal outcome.

Statistical analysis. We compared available demographic and clinical data of the subjects known to have had a prenatal diagnosis using fetal echocardiography at The Children's Heart Center and all subjects identified in MACDP as having cardiac malformations. Comparison groups were created from existing surveillance data using SAS Systems software (SAS Institute Inc.), and univariate analysis was performed. Subjects were compared with respect to demographics, cardiac malformations, noncardiac malformations, syndromes and fetal outcomes. We compared the frequency of diagnoses and yearly trends with and without prenatal diagnosis. Cardiac malformations were grouped by presumed pathogenetic mechanisms using the classification of Clark (6), a developmental approach to classifying cardiac malformations. We performed the chi-square test for linear trends using the extended Mantel-Haenszel method that accompanies Epi Info Software 6.0 (Centers for Disease Control and Prevention).

Table 1. Selected Sociodemographic Characteristics of All Subjects With a Congenital Cardiac Malformation and Those With Prenatally Diagnosed Malformations, Atlanta, Georgia, 1990–1994

Characteristic	All Subjects [no. (%)]	Prenatally Diagnosed Subjects [no. (%)]
Total	1,589 (100)	97 (6.1)
Race		
White	807 (50.9)	37* (38.1)
Black	667 (41.9)	42 (43.3)
Other	115 (7.2)	18† (18.6)
Gender		
Male	865 (54.4)	60 (61.8)
Female	724 (45.6)	37 (38.2)
Maternal age (yr)		
<20	156 (9.8)	8 (8.21)
20–29	811 (51.1)	47 (48.5)
30–34	388 (24.4)	23 (23.7)
35+	234 (14.7)	19 (19.6)

*$p < 0.05$ (95% confidence interval [CI] 0.62 to 0.92). †$p < 0.001$ (95% CI 2.92 to 5.19).

Results

Patient demographics. During the 5-year study period, 1,589 infants registered in MACDP had a diagnosis of congenital cardiac malformation. During this same period, there were 194,754 total live births in the Atlanta area, resulting in a birth prevalence of 8.1 cases/1,000 live births (95% confidence interval [CI] 7.8 to 8.6). Of the 1,589 infants with congenital cardiac malformations, 97 (6.1%) had their malformation diagnosed prenatally with fetal echocardiography (Table 1).

Overall, when classified by race, subjects with a congenital cardiac malformation diagnosed prenatally were significantly less likely to be classified as "white" and more likely to be classified as "other race" when compared with all subjects with cardiac defects. There were no significant gender differences between the subjects diagnosed prenatally and those who were not.

The proportion of subjects with a congenital cardiac malformation diagnosed prenatally increased from 2.6% in 1990 to 12.7% in 1994 (Fig. 1).

The average estimated gestational age at the time of prenatal diagnosis by fetal echocardiography was shown to decrease during the study period, from 28.7 weeks in 1990 to a low of 24.6 weeks in 1993 ($p > 0.05$) (Fig. 2).

Cardiac lesions diagnosed prenatally. The proportion of cardiac malformation cases that were prenatally diagnosed is shown by the developmental and anatomic groups (according to the Clark classification [6]) in Table 2. Of 57 cases of hypoplastic left heart syndrome diagnosed during the study period, 28% were diagnosed prenatally. The proportion of other major cardiac malformations that were diagnosed prenatally included atrioventricular septal defects (16.3%), trun-

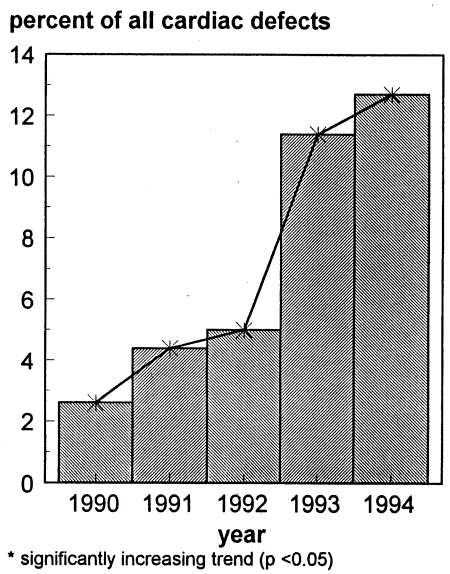

Figure 1. Proportion of all cardiac defects diagnosed prenatally by fetal echocardiography, Atlanta, Georgia, 1990–1994.

cus arteriosus (15%), single ventricle (14.2%), tetralogy of Fallot (13.6%), anomalous systemic veins (11%) and tricuspid valve anomalies (9.1%). Ventricular septal defects and atrial septal defects, with postnatal prevalence rates, as reported by MACDP, of 2.7 (95% CI 2.3 to 2.8) and 3.91 (95% CI 3.6 to 4.2) cases per 1,000 live births, respectively, were each diagnosed prenatally in <5% of cases with malformations.

Trends in diagnosis by year. An analysis of trends in the referrals for fetal echocardiographic prenatal diagnosis of selected cardiac malformations is shown in Figure 3. Over the 5-year study period, increasing percentages of major congenital cardiac malformations were diagnosed by fetal echocardiography. During 1990, only 18.8% of all subjects with hypoplastic left heart syndrome had the syndrome diagnosed prenatally. This proportion increased to 40% during 1994 ($p < 0.05$). Similar increasing trends in prenatal diagnosis were shown for all types of cardiac malformations: tricuspid valve

Figure 2. Average estimated gestational age at prenatal diagnosis by year, Atlanta, Georgia, 1990–1994.

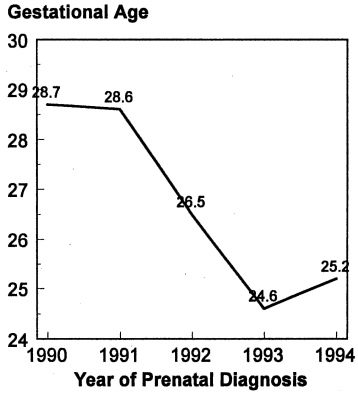

Table 2. Subjects With Specific Types of Congenital Cardiac Malformations Who Were Diagnosed Prenatally, Atlanta, Georgia 1990–1994

Developmental Category	All Subjects (n = 1,589) (no.)	Prenatally Diagnosed Subjects (n = 97) [no. (%)]*
Ectomesenchymal tissue migration defects		
Tetralogy of Fallot	66	9 (13.6)
Transposition of great arteries	80	5 (6.3)
Truncus arteriosus	13	2 (15.0)
Targeted growth defects		
Anomalous systemic veins	164	18 (11.0)
Hemodynamic defects, right sided		
Pulmonary artery stenosis/atresias	180	9 (5.0)
Hemodynamic defects, left sided		
Hypoplastic left heart syndrome	57	16 (28.0)
Aortic arch hypoplasia/atresias	146	11 (7.5)
Aortic valve stenosis/atresias	92	8 (8.7)
Mitral valve stenosis/atresias	123	11 (8.9)
Extracellualar matrix/cell death defects		
Atrioventricular septal defects†	80	13 (16.3)
Tricuspid valve stenosis/atresias‡	404	37 (9.1)
Single ventricle§	12	2 (14.2)
Atrial septal defects	761	36 (4.7)
Ventricular septal defects	486	24 (4.9)
Congenital heart block	43	3 (7.0)

*Percentages do not equal 100% because some subjects have multiple defects. †Includes ostium primum atrial septal defects. ‡Includes Ebstein's anomaly, stenosis and atresias; anomalies of tricuspid valve not differentiated in surveillance data. §Excludes tricuspid valve atresia with dominant ventricle; may include other functionally single ventricles where a rudimentary or hypoplastic ventricle exists.

stenosis/atresia (3.5% to 14%), great vein anomalies (1% to 13.6%), pulmonary valve stenosis/atresia (2.4% to 12.5%), aortic arch stenosis/atresia (1.8% to 16.3%), atrial septal

Figure 3. Major trends in prenatal diagnosis of total and selected congenital cardiac malformations, Atlanta, Georgia, 1990–1994. ASD = atrial septal defect; HLHS = hypoplastic left heart syndrome; VSD = ventricular septal defect.

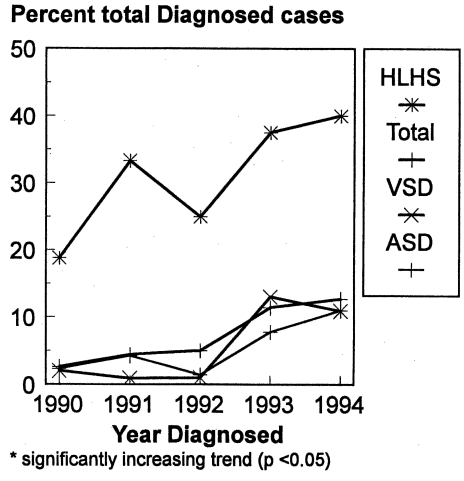

Table 3. Subjects With Congenital Cardiac Malformations Who Were Diagnosed Prenatally and Classified by the Presence of Associated Anomalies and Syndromes, Atlanta, Georgia, 1990–1994

Defect Group	All Subjects (n = 1,589) [no. (%)]	Prenatally Diagnosed (n = 97) [no. (%)]
Isolated cardiac anomalies	823 (51.8)	46 (47.4)
Multiple major anomalies	560 (35.2)	34 (35.1)
Chromosomal syndromes*	206 (13)	17 (17.5)

*Included six cases of trisomy 21, six of trisomy 18 and five of other autosomal disorders.

defects (2.3% to 11%) and ventricular septal defects (2% to 10.9%).

Noncardiac malformations. Subjects with and without cardiac malformations diagnosed prenatally were grouped according to the presence of noncardiac malformations and syndromes (Table 3). The majority in both groups presented with isolated cardiac anomalies. Furthermore, the two groups did not differ significantly with respect to other associated anomalies. The most common noncardiac malformations among the prenatally diagnosed group were musculoskeletal anomalies (10.9%), central nervous system anomalies (10%) and esophageal/upper gastrointestinal atresia (11.8%). However, most types of major noncardiac malformations were represented. Major chromosomal anomalies were also seen among the prenatally diagnosed infant group, with frequent diagnoses of trisomy 18 and 21 (six cases each) and autosomal deletions (five cases) reported.

Fetal outcomes. Outcomes, as assessed from the surveillance reporting system after prenatal diagnosis of congenital cardiac malformation, are shown in Table 4. Most fetuses (82.5%) with a prenatal diagnosis of cardiac malformation developed and survived birth. Among fetuses with diagnosed cardiac malformations, 32.9% were born premature and 59.8% were born small for their gestational age ($p < 0.01$). Of the infants whose defect was diagnosed prenatally, 30.9% ($p < 0.01$) died before 5 years of age, and almost 10% were stillborn, reflecting the severity of the conditions. In the total study population, only 10% of infants with a cardiac malformation died before age 5 years, and only 2% were stillborn. In 8.2% of the prenatally diagnosed cases of cardiac malformations, the women involved chose to have induced abortions.

Table 4. Pregnancy Outcomes of Subjects With Congenital Cardiac Malformation Prenatally Diagnosed With Fetal Echocardiography, Atlanta, Georgia, 1990–1994

Outcome	No. (%)	RR (95% CI)
Live-born	80 (82.5)	NS
Premature*	32 (32.9)	NS
SGA†	58 (59.8)	NS
Died in <5 yr	30 (30.9)‡	3.6 (2.4–5.4)
Induced abortion§	8 (8.2)‡	8.4 (6.2–11.3)
Stillborn¶	9 (9.3)‡	5.1 (2.8–9.3)
Total	97 (100)	

*Born before 36 weeks' gestation. †Small for gestational age. ‡$p < 0.05$ versus total group of subjects with heart defects. §Termination before 20 weeks' gestation. ¶Stillborn after 20 weeks' gestation or birth weight >500 g. CI = confidence interval; RR = relative risk; SGA = small for gestational age.

Discussion

In this study we showed that the spectrum of defects diagnosed by fetal echocardiography differs markedly from that diagnosed postnatally, and that prenatal diagnoses are being made earlier every year (average 24.6 weeks' gestation). These diagnoses tended to be more severe and complex and were associated with a higher frequency of prematurity, low birth weight and adverse pregnancy outcomes, including fetal wastage and early childhood mortality, than were cardiac malformations diagnosed postnatally in the birth population.

Prenatal referrals for fetal echocardiography. During the study period, the Atlanta area, as reported by the MACDP surveillance system and the regional cardiology center, experienced a rapid rise in the proportion of infants with congenital cardiac malformations who were referred for prenatal diagnosis. This was attributable mostly to an expanding pediatric cardiology, obstetric and perinatology provider network in Atlanta during the study period. In addition, increased education and awareness by the obstetric community may have increased early referrals for fetal cardiovascular assessment.

Many centers where fetal echocardiography is the established standard of care cite active training of community obstetric ultrasonographers in basic fetal cardiac imaging techniques as the main reason for increased early recognition of fetal congenital cardiac malformations (1,5).

Associated noncardiac malformations. The finding of frequent associated noncardiac defects and syndromes among infants with congenital cardiac malformations diagnosed prenatally has been reported previously by several centers (2,3). In addition, it is recognized that the presence of both extra cardiac anomalies and prenatal cardiac failure substantially increases prenatal and postnatal mortality among these infants (6). This study further supports the notion that prenatally diagnosed congenital heart disease carries a poor prognosis.

Study limitations. The true incidence of congenital cardiac malformations within a birth population can only be determined with the complete ascertainment of all fetal outcomes (i.e., live births, stillbirths, spontaneous abortions and induced abortions); this ascertainment process should include the inspection of all products of fetal wastage. We were unable to completely ascertain all fetal outcomes in the present study, primarily because spontaneous and induced abortions <20 weeks' gestation were not regularly documented by the surveillance system.

Although we found that a small proportion of pregnancies involving prenatally diagnosed congenital cardiac malformations were terminated, the total number of induced abortions with cardiac defects captured by the surveillance system was probably underestimated because not all products of conception were examined. In addition, some pregnancies with fetal

cardiac malformations may have been recognized and, if severe, terminated by obstetricians without referral to a pediatric cardiologist for fetal echocardiography.

Nevertheless, because the birth prevalence of congenital cardiac malformations has remained relatively stable, at ~8 cases/1,000 live births throughout the study period, the impact of pregnancy terminations after prenatal diagnosis of congenital cardiac malformations is probably small. The study had limited power (10%) to detect a meaningful decrease in birth prevalence rates for congenital heart disease; even if all women prenatally diagnosed (6.1% of total) chose pregnancy termination, prevalence rates would only decrease minimally to 7.6 cases/1,000 live births.

Study strengths. The data for this study came from a well-established birth defects surveillance system (MACDP), which ascertains all congenital cardiac malformations within a well-defined birth population, and from a single primary pediatric cardiology provider, The Children's Heart Center. Because of this concentration of data in only two sources, the collection of information regarding prenatal diagnosis was facilitated. These two data sources allowed reliable and almost complete linkage of all congenital cardiac malformations during the study.

Conclusions. This study documents the increasing role of fetal echocardiography in the prenatal diagnosis of congenital cardiac malformations in a well defined population. It also shows that the prenatal diagnosis of congenital cardiac malformations has led to only a small number of pregnancy terminations and thus has had no effect on the birth prevalence or ultimate outcomes after diagnosis of these birth defects. Finally, it shows that the rate of prenatal diagnosis varies considerably by the type of cardiac defect.

Prenatal diagnosis by fetal echocardiography will continue to have a greater impact on the practice of pediatric cardiology and the surveillance of congenital cardiac malformations in large, well defined birth populations. As earlier fetal diagnosis of congenital cardiac malformations becomes the norm, pediatric cardiologists, perinatologists and obstetricians must work together closely to provide both mother and fetus optimal care and support during the difficult transition toward birth.

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