Racial and Temporal Variations in the Prevalence of Heart Defects

Lorenzo D. Botto, MD; Adolfo Correa, MD, PhD; and J. David Erickson, DDS, PhD

ABSTRACT. Background. Documenting the prevalence and trends of congenital heart defects provides useful data for pediatric practice, health-care planning, and causal research. Yet, most population-based studies use data from the 1970s and 1980s. We sought to extend into more recent years the study of temporal and racial variations of heart defects occurrence in a well-defined population.

Methods. We used data from the Metropolitan Atlanta Congenital Defects Program, a population-based registry with active case ascertainment from multiple sources. Heart defects were identified among liveborn infants up to 1 year old, among stillborn infants, and among pregnancy terminations to mothers residing in metropolitan Atlanta.

Results. From 1968 through 1997, the registry ascertained 5813 major congenital heart defects among 937 195 infants, for a prevalence of 6.2 per 1000. The prevalence increased to 9.0 per 1000 births in 1995 through 1997. The prevalence of ventricular septal defects, tetralogy of Fallot, atrioventricular septal defects, and pulmonary stenosis increased, whereas that of transposition of the great arteries decreased. For some defects, prevalence and trends varied by race.

Conclusions. The prevalence of congenital heart defects is increasing. Whereas most findings likely result from improved case ascertainment and reporting, others might be because of changes in the distribution of risk factors in the population. The basis of the racial variations is incompletely understood. Pediatrics 2001;107(3). URL: http://www.pediatrics.org/cgi/content/full/107/3/e32; heart defects, whites, blacks, epidemiology, prevalence.


Congenital heart defects are frequent and serious anomalies that have a major impact on pediatric morbidity, mortality, and health care costs.1–4 Knowing the expected prevalence and distribution of these serious anomalies can help pediatricians and public health professionals better assess health care needs, evaluate potential clusters, and conduct causal research.

Current prevalence estimates are often based on population-based studies conducted between the 1960s and 1980s.5–7 In such studies, the prevalence at birth of congenital heart defects varied from 2.0 to 5.5 per 1000 births, with higher rates usually associated with later studies or with the use of broader diagnostic criteria.5–7 Such figures, however, may underestimate the current impact at birth of heart defects because some of these studies,5,8 as well as later studies,9–11 documented an increase over time in the occurrence of some heart defects. For example, an increased occurrence rate of ventricular septal defects was reported in some areas of the United States during the 1970s9 and 1980s.8 A similar increase was reported for pulmonic stenosis during the 1980s.8 In some cases, temporal trends seemed to vary with race.12

We assessed the temporal and racial variations in heart defect occurrence during a 30-year period in a well-defined population. Our objectives were to: 1) provide a more recent estimate of the impact of major heart defects than is currently available; 2) evaluate past temporal trends and assess whether such trends are still occurring; and 3) assess whether such trends differed by race.

To decrease bias and enhance generalizability, we based our study on a population-based monitoring system with active case ascertainment from multiple sources.

METHODS

Case Ascertainment

We used data from the Metropolitan Atlanta Congenital Defects Program (MACDP). MACDP is a population-based registry that actively monitors birth defects among infants born to mothers residing in the 5-county metropolitan Atlanta area. Trained abstractors from the registry actively ascertain structural birth defects among liveborn infants up to 1 year old, among stillborn infants, and among pregnancies terminated at or after 20 weeks of gestation. The abstractors regularly visit hospitals, pediatric and specialty wards, cytogenetic laboratories, and the vital records office in the 5-county area. Data sources include medical records, hospital logs, and birth and death certificates. The abstracted information is reviewed by the medical staff of MACDP, which includes geneticists and pediatricians. Congenital defects are coded in accordance with a modified International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) coding scheme.

Case Classification

We selected all cases for which a major cardiac defect was recorded in MACDP (ICD-9-CM codes 745.00 to 747.49). Each case participant received a principal cardiac diagnosis, according to a hierarchical classification system13 (Table 1). In such system, defects placed toward the top of the list are postulated to occur earlier in embryogenesis than those placed further down the list (the exception being the group of “other major defects,” which,
TABLE 1. Prevalence and Distribution of Major Congenital Heart Defects by Birth Status and During Specified Time Periods, Metropolitan Atlanta, 1968–1997

<table>
<thead>
<tr>
<th>Defect Type</th>
<th>Liveborn</th>
<th>Stillborn</th>
<th>Total 1968–1997</th>
<th>Change During Study</th>
<th>Trend† (P Value)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. %</td>
<td>No. %</td>
<td>Rate‡</td>
<td>Rate in 1995–1997‡</td>
<td>Contribution to Total Change (%)</td>
</tr>
<tr>
<td>Heterotaxias</td>
<td>78 1.4</td>
<td>2 1.5</td>
<td>81 1.4 0.9</td>
<td>0.9 0.5</td>
<td>0.8</td>
</tr>
<tr>
<td>Corrected (L) transposition</td>
<td>39 0.7</td>
<td>0 0.0</td>
<td>39 0.7 0.4</td>
<td>0.7 0.4</td>
<td>0.6</td>
</tr>
<tr>
<td>Outflow tract defects</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tetralogy of Fallot</td>
<td>345 6.1</td>
<td>6 4.5</td>
<td>353 6.1 3.8</td>
<td>4.7 2.2</td>
<td>3.7</td>
</tr>
<tr>
<td>D-transposition of the great arteries</td>
<td>226 4.0</td>
<td>4 3.0</td>
<td>231 4.0 2.5</td>
<td>2.4 −0.4</td>
<td>−0.4</td>
</tr>
<tr>
<td>Double outle right ventricle</td>
<td>96 1.7</td>
<td>3 2.2</td>
<td>101 1.7 1.1</td>
<td>2.2 2.0</td>
<td>3.4</td>
</tr>
<tr>
<td>Truncus arteriosus</td>
<td>54 1.0</td>
<td>4 3.0</td>
<td>60 1.0 0.6</td>
<td>0.6 0.2</td>
<td>0.3</td>
</tr>
<tr>
<td>Atrioventricular septal defect</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>With Down syndrome</td>
<td>138 2.4</td>
<td>2 1.5</td>
<td>140 2.4 1.5</td>
<td>2.4 1.7</td>
<td>3.0</td>
</tr>
<tr>
<td>Without Down syndrome</td>
<td>104 1.8</td>
<td>7 5.2</td>
<td>111 1.9 1.2</td>
<td>1.0 0.6</td>
<td>1.1</td>
</tr>
<tr>
<td>Total anomalous pulmonary venous return</td>
<td>66 1.2</td>
<td>0 0.0</td>
<td>66 1.1 0.7</td>
<td>0.7 0.1</td>
<td>0.2</td>
</tr>
<tr>
<td>Ebstein anomaly</td>
<td>36 0.6</td>
<td>4 3.0</td>
<td>40 0.7 0.4</td>
<td>0.6 0.5</td>
<td>0.8</td>
</tr>
<tr>
<td>Right obstructive defects</td>
<td>27 0.5</td>
<td>3 2.2</td>
<td>31 0.5 0.3</td>
<td>0.3 0.0</td>
<td>−0.1</td>
</tr>
<tr>
<td>Tricuspid atresia</td>
<td>48 0.8</td>
<td>2 1.5</td>
<td>50 0.9 0.5</td>
<td>0.7 0.2</td>
<td>0.4</td>
</tr>
<tr>
<td>Pulmonary atresia, intact septum</td>
<td>357 6.3</td>
<td>0 0.0</td>
<td>358 6.2 3.8</td>
<td>6.0 4.3</td>
<td>7.4</td>
</tr>
<tr>
<td>Pulmonic stenosis</td>
<td>333 5.9</td>
<td>0 0.0</td>
<td>333 5.7 3.6</td>
<td>7.0 6.9</td>
<td>11.7</td>
</tr>
<tr>
<td>Peripheral pulmonary stenosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left obstructive defects</td>
<td>189 3.3</td>
<td>5 3.7</td>
<td>196 3.4 2.1</td>
<td>2.1 0.5</td>
<td>0.8</td>
</tr>
<tr>
<td>Hypoplastic left heart</td>
<td>267 4.7</td>
<td>1 0.7</td>
<td>268 4.6 2.9</td>
<td>3.5 0.7</td>
<td>1.2</td>
</tr>
<tr>
<td>Coarctation of the aorta</td>
<td>57 1.0</td>
<td>1 0.7</td>
<td>58 1.0 0.6</td>
<td>0.6 0.3</td>
<td>0.4</td>
</tr>
<tr>
<td>Aortic arch atresia or hypoplasia</td>
<td>90 1.6</td>
<td>0 0.0</td>
<td>90 1.5 1.0</td>
<td>0.8 0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Aortic valve stenosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septal defects</td>
<td>1514 26.8 39 29.1</td>
<td>1559 26.8 16.6</td>
<td>25.0 17.1 29.2</td>
<td>***</td>
<td></td>
</tr>
<tr>
<td>Ventricular septal defect</td>
<td>395 7.0</td>
<td>34 25.4 431 7.4 4.6</td>
<td>10.0 8.8 15.0</td>
<td>***</td>
<td></td>
</tr>
<tr>
<td>Atrial septal defect</td>
<td>617 10.9</td>
<td>0 0.0</td>
<td>617 10.6 6.6</td>
<td>8.1 5.3 9.0</td>
<td>***</td>
</tr>
<tr>
<td>Patent ductus arteriosus</td>
<td>580 10.3</td>
<td>17 12.7</td>
<td>598 10.3 6.4</td>
<td>9.7 6.8 11.7</td>
<td>***</td>
</tr>
<tr>
<td>Other major heart defects</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>5656 134</td>
<td>3813 62.0</td>
<td>5813 60.2 58.7</td>
<td>100.0 ***</td>
<td></td>
</tr>
</tbody>
</table>

* Includes cases of pregnancy terminations and of unknown birth status.
‡ Rate per 10 000 births.
§ Values, by Cochrane-Armitage test: * .01 < P < .05; ** .001 < P < .01; *** P < .001.

Although listed last, precedes in coding the category of patent ductus arteriosus. In practice, this system assigns to each infant only one cardiac diagnosis; an infant with multiple cardiac defects is assigned to the defect group that is listed closer to the top of the list. For example, an infant with tetralogy of Fallot, atrial septal defect, and patent ductus arteriosus is counted as (and only as) a case of tetralogy of Fallot.

In this study, ventricular septal defects included perimembranous, muscular, or unspecified defects. We did not analyze these subgroups separately because the ability to distinguish such subgroups depends on available technology and likely changed over the study. Atrioventricular septal defects also included cases of primum atrial septal defects and primum ventricular septal defects. Atrial septal defects included all atrial septal defects, including the generic atrial septal defects, but excluded primum defects.

Inclusions and Exclusions

We included cases of confirmed heart defects as documented by the medical records and notes. Not all cases, particularly in the earlier years of the study, were necessarily verified by echocardiography, catherization, surgery, or autopsy. This approach reduced the differences caused by changes in technology over the years and provides data that closely reflect the clinical burden of disease.

We excluded cases of heart defects that were noted in the medical records as being possible or probable cases and those for which a specific diagnosis was not made (eg, cases of murmur, congenital heart defect not otherwise specified, cyanotic heart defect not otherwise specified). We also excluded the following cases: 1) those based on fetal ultrasound examination alone, without postnatal confirmation; 2) isolated patent ductus arteriosus among stillborn infants, pregnancy terminations, and among infants whose birth weight was below 2500 g or whose gestational age was <37 weeks; 3) anomalies of the peripheral vascular system (ICD-9-CM codes 747.50–747.99), such as an aberrant subclavian artery or a peripheral arteriovenous malformation, unaccompanied by defects of the heart or the great vessels.

Statistical Analysis

We used the number of liveborn infants for the appropriate time and racial/ethnic group as the denominator of the rates. Because most newborns were white or black, we restricted our assessment of racial variation to these 2 groups.

We used SAS Software (SAS, Cary, NC) for the statistical analyses. We used the Cochran-Armitage test\textsuperscript{14,15} to analyze time trends and generate the associated \( P \) values. The time trends figures are based on 5-year moving averages. Time trend statistics were computed on actual yearly data.

RESULTS

Overall Findings

From 1968 through 1997, MACDP registered 5813 cases of major congenital heart defects among 937 195 infants (Table 1), for an overall prevalence of 62.0 per 10 000 births (6%). Of these cases, 97% were among liveborn infants and 2% were among stillborn infants. The total count also included 21 pregnancy terminations and 2 cases of unknown pregnancy outcome.

Most defect types were reported in similar propor-
tions among liveborn and stillborn infants, although atrial septal defects seemed to be more common in the latter group (Table 1). Overall, ventricular septal defects accounted for 27% of all cases, and atrial septal defects and patent ductus arteriosus for an additional 18%. Among the more severe defects, tetralogy of Fallot and transposition of the great arteries accounted for ~10% of cases.

Atrioventricular septal defects associated with Down syndrome accounted for 2.4% of all cases. Conversely, over half of all cases of atrioventricular septal defects (56%) occurred in infants with Down syndrome. Among these infants, atrioventricular septal defects accounted for ~40% of all cases (140/359) of heart defects (data not shown).

Pulmonary hypertension in the newborn was reported in a small fraction of cases of heart defects, including atrial septal defects (1.9%) and patent ductus arteriosus (2.5%). Diaphragmatic hernia accounted for ~<10% of cases of pulmonary hypertension associated with either atrial septal defects or patent ductus arteriosus.

Temporal Variations

The overall occurrence rate of heart defects in the last 3 years of the study (1995–1997) was 90.2 per 10 000 (0.9%), an increase of 58.7 per 10 000 above the rate at the beginning of the study (1968–1972; Table 1). Ventricular septal defects, atrial septal defects, and peripheral pulmonic stenosis accounted for approximately half of such increase (Table 1). However, the rate of severe defects, such as tetralogy of Fallot, double-outlet right ventricle, and atrioventricular septal defects also increased significantly and accounted for ~11% of the overall increase. Among infants with Down syndrome, we noted an increase in the rate of both atrioventricular septal defects (from 0.7 to 2.4 per 10 000; Table 1) and of other heart defects (from 1.7 to 4.1 per 10 000; data not shown).

For some defects (eg, atrial and ventricular septal defects, valvular and peripheral pulmonic stenosis) the increase seemed to be continuing through the end of the study (Fig 1). For others (eg, atrioventricular septal defects) the increase seems to have been mostly confined to the 1970s. Other severe defects such as pulmonary atresia with intact ventricular septum and hypoplastic left heart syndrome did not vary appreciably during the study.

Anomalies often thought to share a common origin also showed evidence of heterogeneity (Fig 1). For example, tetralogy of Fallot increased, whereas transposition of the great arteries decreased. This distinction is acknowledged in a proposed pathogenetic classification of heart defects. Moreover, among the defects of the pulmonary outflow, the rate of pulmonic atresia with intact ventricular septum did not increase, whereas the rate of pulmonic stenosis increased 3-fold, and that of peripheral pulmonic stenosis increased >10-fold (Fig 1).

Racial Variations

The occurrence rate and distribution of heart defects varied between blacks and whites (Table 2). The higher overall occurrence rate for blacks than for whites was primarily driven by a higher occurrence of peripheral pulmonic stenosis and atrial septal defects. Other defects, however, occurred more often among whites; these included some outflow tract defects (transposition of the great arteries, truncus arteriosus) and some left obstructive defects (coarctation of the aorta, aortic stenosis). Racial differences were seen also within some broad defect categories (Table 2). For example, transposition of the great arteries, but not tetralogy of Fallot, was more common among whites. Similarly, among the left-side obstructive defects, coarctation of the aorta, but not hypoplastic left heart, was more common among whites.

Temporal trends also showed racial variations (Fig 2), although the overall rate of heart defects increased among both blacks and whites. However, ventricular septal defects increased more rapidly among whites than among blacks, whereas the reverse was true for peripheral pulmonary stenosis (Fig 2). The rate of coarctation of the aorta was stable among whites, but increased among blacks (P for increase = .036), whereas the rate of Ebstein anomaly was stable among blacks but increased among whites (P = .015).

Pregnancy Terminations

Pregnancy terminations accounted for a small proportion of heart defects in this study and such proportion changed over time. For example, pregnancy terminations accounted for .03% of cases overall but for 1.3% of cases in 1995 to 1997. This proportion did not vary appreciably by race.

DISCUSSION

The occurrence rate of major heart defects nearly tripled in metropolitan Atlanta from 1968 to 1997, when major heart defects were reported in 0.9% or 1 in 110 infants. This figure, although higher than previous estimates, is probably conservative because it excludes common conditions such as patent ductus arteriosus in preterm infants as well as some cases occurring among pregnancy terminations. The increase in prevalence does not seem to have ceased yet.

Although the increase can be attributed primarily to a few common defects (eg, ventricular and atrial septal defects, peripheral pulmonic stenosis), severe defects such as tetralogy of Fallot and double-outlet right ventricle also seem to be increasing.

These findings must be interpreted in the context of the limitations and strengths of the study. Diagnostic and reporting practices may have changed during the study, improving ascertainment and reducing the average age at diagnosis. Conversely, some cases may have been missed if diagnosed in outpatient clinics or outside the study area. Although the registry collects data on pregnancy terminations, their ascertainment is likely incomplete. For example, we only had data on pregnancy terminations that occurred at 20 gestational weeks or later, and, of these, only diagnoses confirmed after delivery were included. The impact of prenatal diagnosis on heart
defect rates in Atlanta is difficult to estimate. A special study on prenatal diagnosis of heart defects in this same Atlanta population between 1990 and 1994 reported a rapid increase in the fraction of cases of heart defects diagnosed prenatally, so that by 1994 an estimated 12% of heart defects were diagnosed in utero. However, that study also reported that only few such affected pregnancies (8%) were
The main strength of the study is its use of the MACDP, a registry with active ascertainment of cases from a geographically well-defined population. Moreover, ascertainment relied on multiple sources of information and extended through the first year of life. Such an intensive population-based approach is likely to have minimized underascertainment of cases and improved the representativeness of the findings.

Our findings complement and extend those from previous reports. Investigators in North America and elsewhere noted an increase in specific heart defects, including pulmonic stenosis and ventricular, atrial, and atrioventricular septal defects, during the 1970s and 1980s.7–9,11,19,21–23 Our findings document a continuation of such trends well into the 1990s.

The underlying causes of these increases are unclear. Increased availability of 2-dimensional and color-Doppler echocardiography services in the community has often been cited as the main reason for such time trends. In fact, investigators of the Baltimore-Washington Infant Study directly documented an increased reporting of heart defects diagnosed by echocardiography but not of those diagnosed by invasive methods.8 Although we could not conduct a similar analysis, we found that increases were more-Washington Infant Study directly documented an increased reporting of heart defects diagnosed by echocardiography but not of those diagnosed by invasive methods.8 Although we could not conduct a similar analysis, we found that increases were more...
increasing trends is also consistent with improved diagnosis and reporting, a finding that others have noted as well. Muscular ventricular defects, in particular, tend to be clinically mild or even asymptomatic and have been detected in as many as 5% of newborns screened by color-Doppler echocardiography. The increased rate of atrioventricular septal defect among infants with Down syndrome in our study is consistent with previous reports and also may reflect a more intensive or earlier cardiologic
evaluation of affected pregnancies, newborns, or young infants.

The racial variations in this study offer additional, if indirect, clues to understanding such time trends. Racial and ethnic differences in the prevalence of specific heart defects are well-documented.12 Their interpretation in terms of genetic and environmental causation, however, is not straightforward. For example, racial and ethnic variations are often associated with socioeconomic differences, lifestyle variation, cultural factors, and other factors that indicate environmental exposures. We noted an excess of white infants among certain heart defects (eg, transposition of the great arteries, aortic stenosis, coarctation of the aorta). These findings are similar to those reported in a different geographic area12 and may indicate differences in background risk or genetic susceptibility. In contrast, the similar temporal trends in the overall rate of heart defects among black and white infants (Fig 2, first panel) are consistent with improved reporting.

It is, however, difficult to explain all instances of increased occurrence with improvement in diagnosis and reporting. For example, the timing of the trends is not identical across heart defect types (Fig 1). For ventricular septal defects an increasing trend is evident from the beginning of the study, whereas for atrial septal defects the increase seems to begin later. Likewise, it is also difficult to ascribe solely to diagnostic improvements the increase in severe defects, such as tetralogy of Fallot, or the racial variations in temporal trends (eg, for coarctation of the aorta and ventricular septal defects).

The reason for the possible decrease of transposition of the great arteries is also unclear. Selective pregnancy termination is unlikely to have played a major role.17 In the study previously discussed from metropolitan Atlanta, only 6% of cases of transposition of the great arteries were diagnosed prenatally, and only 8% of women carrying a fetus with a prenatally diagnosed heart defect terminated the pregnancy.17

The findings from this study have some practical implications. First, even if these trends exclusively reflect diagnostic improvements, a high and increasing rate of heart defects among young children and their parents increases the burden on families and health care providers, both in terms of parental anxiety and of the direct costs of diagnostic examinations, follow-up, and possibly treatment. Second, the trends in heart defects magnify the challenge of detecting teratogen-induced epidemics of birth defects. The small increases in rates that are often associated with teratogenic exposures may go undetected if confounded by the larger background trend. Close collaboration between clinical and public health professionals is needed to face this challenge. Finally, much of the temporal and racial variations in heart defect occurrence remain unexplained and underscore the need to study further the genetic and environmental determinants of heart defects. Population-based studies of trends that account for prenatal diagnosis, method of diagnosis, and severity of the lesion may help elucidate the extent to which artifactual and causal factors contribute to the temporal and racial variations in the occurrence of cardiac defects.

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