Cardiology in the Young (2011), **21**, 281–285
doi:10.1017/S1047951110001940

Original Article

The changing occurrences of tetralogy of Fallot and simple transposition of the great arteries in Southern Nevada

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Abstract We analysed the occurrence of tetralogy of Fallot and simple transposition in the Hispanic and non-Hispanic populations of Clark County, Nevada, in the United States of America over a 30-year period from 1980 to 2009. We found a downward trend in the incidence of simple transposition of the great arteries in the non-Hispanic population but an upward trend in the incidence in the Hispanic population. For tetralogy of Fallot, we found an upward trend in the incidence in both populations; the trend, however, was more dramatic in the Hispanic population. We also noted differences in the male to female ratios in the different groups. Even though we make no definitive conclusions regarding the causes of these incidence curves or the differences in occurrence between males or females, the data suggest an interplay of genetics and the environment.

Keywords: Congenital cardiac disease; Hispanics; incidence; infant sex

Received: 5 April 2010; Accepted: 1 December 2010; First published online: 28 January 2011

Tetralogy of Fallot and transposition of the great arteries together constitute the majority of the cyanotic cardiac malformations, and they are among the most easily recognised and earliest diagnosed forms of congenital cardiac disease. Previous works have determined the occurrences of these two conditions in large population studies. On average, tetralogy of Fallot occurs in about 30–40 infants and transposition of the great arteries in about 20–30 infants out of a 100,000 live births. Even though population studies show detection rates to have gone up for congenital cardiac disease in general, most of the same studies demonstrate consistent occurrence rates for tetralogy of Fallot and transposition regardless of the era of study or the geography of the population.[1–11]

Few studies show temporal changes in the occurrences of specific cardiac malformations, especially the more significant forms. In 2001, however, Botto and colleagues reported temporal and racial differences in the incidences of congenital cardiac disease between blacks and whites in the metropolitan Atlanta region that occurred between 1968 and 1997.[12] The authors concluded that the increased incidences in most forms of congenital cardiac disease resulted primarily from improved detection that occurred over time. They did note, however, a small decrease in the rate of transposition and an increase in the rate of tetralogy of Fallot, which they concluded lacked solid explanation. In this study, we report changing incidences of simple transposition and tetralogy of Fallot over a 30-year period in the Hispanic and non-Hispanic populations of Clark County.

Methods

We inquired our congenital cardiac database for the period from July, 1980 to December, 2009 to identify patients born in Clark County with tetralogy of Fallot or tetralogy of Fallot with pulmonary atresia (we use the term tetralogy of Fallot for both variations) and simple transposition

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of the great arteries (or simple transposition), and those with pregnancy terminations for the two conditions. We also inquired our foetal database for the period from March, 2002 (database initiation date) to December, 2009 for identifying prenatally detected simple transpositions, tetralogy of Fallots, and pregnancy terminations for the two conditions. We analysed the identified patients by the six 5-year periods. We further compared the data between the Hispanic and non-Hispanic populations. Hispanic patients were identified by their surname and parental self-reporting based on the fact that the US Bureau of the Census used self-report as a standard to assign people to a particular race/ethnicity and it has used Spanish surnames to identify the Hispanic population when self-identification is not attainable.[13] Besides, there are some studies that show that using a Spanish surname is an accurate identifier of the Hispanic population.[14,15] As the database information was incomplete, we did not subdivide our non-Hispanic population into additional ethnic groups. For data analysis, we used SPSS version 13.0 (SPSS Inc., Chicago, Illinois, United States of America). Statistical methods included chi-squared test for the analysis of proportion of gender, simple linear regression analysis for the trends in incidence, and Student's *t*-test to compare slopes. We set a p-value of less than 0.05 as significant.

We obtained the number of births per year in Clark County from data available on the State of Nevada website and we calculated the incidence for tetralogy of Fallot and transposition of the great arteries by quinquennia. The population of Southern Nevada is more than 95% concentrated around Clark County. The United States census data provided the estimates for the percent of population figures for Hispanics and non-Hispanics in Clark County. We have no data on maternal cormorbidities or use of folic acid supplementation. There is no governmental database for pregnancy termination. Since 1980, the Clark Country Coroner's Office and the Clark County Child Death Review Committee have consulted us to review deaths in children with conditions not suspected premortem, and there are no enquiries from these organisations regarding deaths from tetralogy of Fallot or simple transposition in previously undiagnosed patients.

Results

We identified 249 patients born in Clark County with tetralogy of Fallot, and 78 patients born in Clark County with simple transposition. Our foetal database inquiry listed only two terminations for tetralogy of Fallot and none for simple transposition.

Of the 249 patients with tetralogy of Fallot, 152 were males with a male:female ratio of 1.6:1.0, 63 (25%) were Hispanics, and 186 (75%) were non-Hispanics. Of the 63 Hispanic patients, 33 were females with a female:male ratio of 1.1:1.0. Of the 186 non-Hispanic patients, 122 were males with a male:female ratio of 1.9:1.0.

The difference in the gender ratios between the Hispanic and non-Hispanic populations was statistically significant ($p = 0.01$). Of the 249 patients, 22 (9%) had Down's syndrome, and 44 (18%) had tetralogy of Fallot with pulmonary atresia. There were no significant differences between Hispanics and non-Hispanics regarding the prevalence of Down's syndrome or tetralogy of Fallot with pulmonary atresia. Chromosome 22q11 deletion data were incomplete and not analysed. The average age at diagnosis for tetralogy of Fallot was 4 ± 3 weeks, with a trend towards prenatal detection after 2007. Before 2007, prenatal detection was sporadic with an overall rate of less than 5%. For the years 2007–2009, 14 of 51 (28%) tetralogy of Fallots were detected prenatally: 6 of 26 (23%) in the Hispanic population and 8 of 25 (32%) in the non-Hispanic population.

Of the 78 patients with simple transposition, 50 were male with a male:female ratio of 1.8:1.0, 28 (36%) were Hispanics, and 50 (64%) were non-Hispanics. Of the 28 Hispanic patients, 19 were male with a male:female ratio of 2.1:1.0. Of the 50 non-Hispanic patients, 31 were male with a male:female ratio of 1.6:1.0. There was no statistically significant gender difference between the Hispanic and non-Hispanic populations. No patient had Down's syndrome or confirmed chromosome 22q11 deletion. All patients with simple transposition were diagnosed as newborns with no variation by decade of diagnosis, other than a trend towards increased prenatal detection after 2007. Similar to tetralogy of Fallot, before 2007 prenatal diagnosis was sporadic. For the years 2008–2009, 4 of 12 (33%) simple transpositions were detected prenatally: 3 of 5 (60%) in the non-Hispanic population and 1 of 7 (14%) in the Hispanic population.

Figure 1 shows the incidence figures and trends for tetralogy of Fallot patients per 100,000 live births for each 5-year interval for both the Hispanic and non-Hispanic populations. We found statistical significance in the upward trend of the incidence of tetralogy of Fallot in the Hispanic population. Although the non-Hispanic population's incidence of tetralogy of Fallot trended upwards, it did not reach statistical significance. Figure 2 shows the incidence figures and trends for simple transposition patients per 100,000 live births for each 5-year interval for both the Hispanic and non-Hispanic

https://doi.org/10.1017/S1047951110001940 Published online by Cambridge University Press

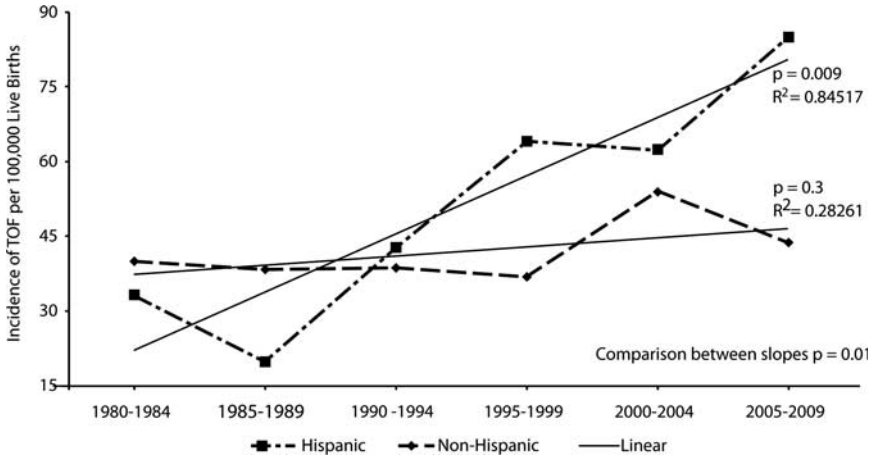

Figure 1.
Incidence rates for tetralogy of Fallot per 100,000 live births for the Hispanic and non-Hispanic populations in Clark County. Solid lines represent the linear regression curve for each population.

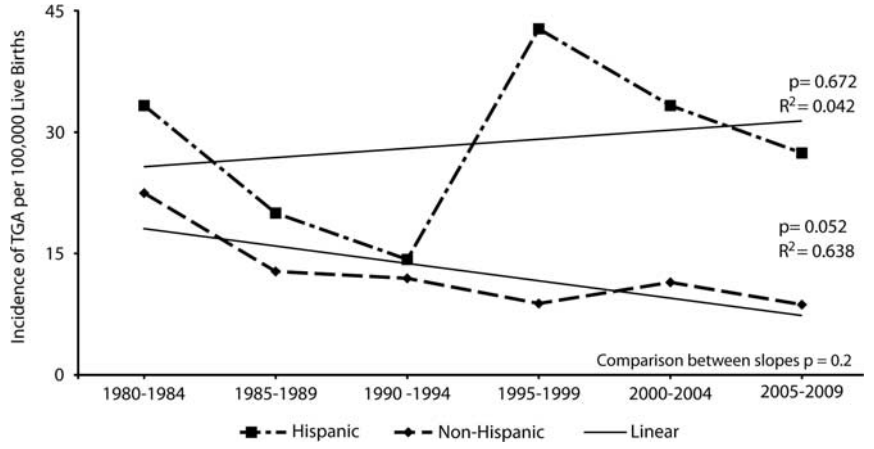

Figure 2.
Incidence rates for transposition of the great arteries per 100,000 live births for the Hispanic and non-Hispanic populations in Clark County. Solid lines represent the linear regression curve for each population.

populations. The incidence of simple transposition in the Hispanic population shows a slight upward trend that was not statistically significant. The incidence of simple transposition in the non-Hispanic population shows a downward trend that just fell short of statistical significance at $p = 0.052$.

Discussion

Population studies documenting the incidence of congenital cardiac disease frequently point out the limitation of malformation detection, which is dependent on, among other factors, the skill of healthcare providers, the presence or absence of significant positive physical findings, the source of the patient data, and the availability and use of technology, especially echocardiography. From 1980, infants and children with cardiac disease in Clark County have been evaluated by a continuous paediatric cardiology programme that has provided service to all children of the county with cardiac disease utilising echocardiography, which has been state-of-the art for each era. Cardiac malformation and limited patient information has been continuously entered into an electronic database since 1980. The population of Clark County has some characteristics not found in other large population centres. From 1980, the county has experienced rapid growth, at times the fastest in the United States. In addition, the percentage of Hispanic residents has risen from about 5% of the population in 1980 to 28% currently. Even though our database information did not allow us to subdivide our non-Hispanic population for data analysis, the racial make-up of the non-Hispanic population in Clark County has been stable over time: approximately 85% white, 10% black, and 5% Asian.

https://doi.org/10.1017/S1047951110001940 Published online by Cambridge University Press

Most epidemiological studies of congenital cardiac disease have noted consistent incidences for both tetralogy of Fallot and transposition from one era of investigation to the next and from one geographic location to the next. Recently, a few studies have suggested a possible relationship of maternal perinatal folic acid supplementation to the occurrence of congenital cardiac disease, especially conotruncal abnormalities. These studies have demonstrated conflicting results; thus, the effects of maternal folic acid supplementation on congenital malformations are not yet clear.[16–19]

Other studies have reported the relationship of sex, race, birthweight, socio-economic factors, or temporal changes in the diagnosis and incidence of congenital cardiac disease in general or with specific malformations.[11,20–26] Our data provide further observations regarding temporal changes in the incidence of tetralogy of Fallot and simple transposition. We found the incidence of simple transposition to be trending downwards in the non-Hispanic population from about 20 per 100,000 live births in the 1980s to about nine per 100,000 live births in the 2000s. The trend for simple transposition is up in the Hispanic population from about 20 per 100,000 live births in the 1980s to about 30 per 100,000 live births in the 2000s. The incidence of tetralogy of Fallot in the non-Hispanic population is trending upwards from about 40 per 100,000 live births in the 1980s to about 50 per 100,000 live births in the 2000s. However, the upward trend for tetralogy of Fallot in the Hispanic population is more dramatic, from about 30 per 100,000 live births in the 1980s to about 80 per 100,000 live births in the 2000s. We found significant differences in the male to female ratios for Hispanic versus non-Hispanic patients with tetralogy of Fallot. In contrast to most studies, we found more females than males with tetralogy of Fallot in the Hispanic population. We noted twice as many males as females with tetralogy of Fallot in the non-Hispanic population. For simple transposition, we found a higher male to female ratio in the Hispanic population versus the non-Hispanic population but noted no difference that was statistically significant.

Since 2007, the combined prenatal detection rate for simple transposition and tetralogy of Fallot has been about 30% for the entire Clark County population. These detection rates are similar to recent publications.[27,28] However, for the non-Hispanic population, the combined simple transposition and tetralogy of Fallot prenatal detection rate was 37%, but it was only 23% in the Hispanic population. Even though all patients referred for foetal echocardiography in Clark County undergo studies either by a paediatric cardiologist or supervised by a paediatric cardiologist, Hispanic patients may experience more limitations to access for screening obstetric ultrasounds than the non-Hispanic population. Regardless of access to care, both tetralogy of Fallot and simple transposition have normal four-chamber views on screening obstetric ultrasounds. Foetal echocardiography, however, can define these conditions prenatally. As our experience and that of others note that about two-thirds of serious foetal congenital cardiac disease can be missed on routine obstetric ultrasounds, our group has advocated universal foetal echocardiography as the best evidence-based method for the earliest detection of all significant cardiac malformations.[29]

This study is limited by being retrospective and by the smaller number of patients in earlier years. However, the strengths include the analysis of conditions that rarely miss detection and in which the data on specific patients were not dependent on third party acquisition, such as from hospital discharge information or state reporting agencies.

Similar to Botto et al, we conclude that the temporal trends in the occurrence rates of simple transposition and tetralogy of Fallot have no straightforward explanations. To the best of our knowledge, no other study has analysed temporal changes in the occurrences of simple transposition and tetralogy of Fallot in Hispanic populations versus non-Hispanic populations. Our findings suggest a complex interplay of environmental and genetic factors.

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