Circulation

ORIGINAL RESEARCH ARTICLE

Impact of Socioeconomic Status, Race and Ethnicity, and Geography on Prenatal Detection of Hypoplastic Left Heart Syndrome and Transposition of the Great Arteries

BACKGROUND: Prenatal detection (PND) has benefits for infants with hypoplastic left heart syndrome (HLHS) and transposition of the great arteries (TGA), but associations between sociodemographic and geographic factors with PND have not been sufficiently explored. This study evaluated whether socioeconomic quartile (SEQ), public insurance, race and ethnicity, rural residence, and distance of residence (distance and driving time from a cardiac surgical center) are associated with the PND or timing of PND, with a secondary aim to analyze differences between the United States and Canada.

METHODS: In this retrospective cohort study, fetuses and infants <2 months of age with HLHS or TGA admitted between 2012 and 2016 to participating Fetal Heart Society Research Collaborative institutions in the United States and Canada were included. SEQ, rural residence, and distance of residence were derived using maternal census tract from the maternal address at first visit. Subjects were assigned a SEQ z score using the neighborhood summary score or Canadian Chan index and separated into quartiles. Insurance type and self-reported race and ethnicity were obtained from medical charts. We evaluated associations among SEQ, insurance type, race and ethnicity, rural residence, and distance of residence with PND of HLHS and TGA (aggregate and individually) using bivariate analysis with adjusted associations for confounding variables and cluster analysis for centers.

RESULTS: Data on 1862 subjects (HLHS: n=1171, 92% PND; TGA: n=691, 58% PND) were submitted by 21 centers (19 in the United States). In the United States, lower SEQ was associated with lower PND in HLHS and TGA, with the strongest association in the lower SEQ of pregnancies with fetal TGA (quartile 1, 0.78 [95% CI, 0.64–0.85], quartile 2, 0.77 [95% CI, 0.64–0.93], quartile 3, 0.83 [95% CI, 0.69–1.00], quartile 4, reference). Hispanic ethnicity (relative risk, 0.85 [95% CI, 0.72–0.99]) and rural residence (relative risk, 0.78 [95% CI, 0.64–0.95]) were also associated with lower PND in TGA. Lower SEQ was associated with later PND overall; in the United States, rural residence and public insurance were also associated with later PND.

CONCLUSIONS: We demonstrate that lower SEQ, Hispanic ethnicity, and rural residence are associated with decreased PND for TGA, with lower SEQ also being associated with lower SEQ also being associated with decreased PND for HLHS. Future work to increase PND should be considered in these specific populations.

Anita Krishnan, MD
⋮
Mary T. Donofrio, MD
On behalf of the Fetal Heart Society

© 2021 American Heart Association, Inc.

https://www.ahajournals.org/journal/circ

Clinical Perspective

What Is New?

- This is the largest multicenter study to our knowledge to identify socioeconomic, race or ethnic, and geographic barriers to the prenatal detection of critical congenital heart disease in North America.
- This study finds that lower socioeconomic position, Hispanic ethnicity, and rural residence are associated with decreased prenatal detection.

What Are the Clinical Implications?

- Clinicians can use the findings of this study to focus efforts on improving overall prenatal detection rates for congenital heart disease.
- Clinicians can specifically improve health equity in prenatal detection of congenital heart disease and timing of prenatal detection by improving linkages between the tertiary care center and the populations and regions identified in this study.

Prenatal diagnosis (PND) reduces morbidity and mortality in hypoplastic left heart syndrome (HLHS) and transposition of the great arteries (TGA), 2 of the most common critical neonatal cardiac defects.[1,2] The benefits of PND include perinatal stabilization, coordination of timely interventions such as catheterization,[3] and selection of a delivery center in proximity to the tertiary care center.[4] In HLHS, patients with PND are reported to have lower preoperative and postoperative mortality, shorter hospital stay, and lower rates of acidosis and multiorgan dysfunction.[2] PND is thought to be associated with improved longer-term outcomes, including better neurodevelopmental outcomes,[5] improvements in postnatal brain maturation, and decreased risk of postnatal brain injury.[6] Although the benefits of PND have been recognized for decades, it occurs in <60% of congenital heart disease (CHD) cases in many regions of the United States.[7,8] Understanding barriers to PND is critical for identifying effective strategies to improve holistic care and outcomes for patients with CHD.

Limited data exist that specifically explore the effect of social determinants of health on PND of CHD. In particular, limited previous studies have demonstrated that Hispanic ethnicity, lower maternal education, lower population density, public and governmental insurance, and lower socioeconomic status have been associated with lower rate of prenatal detection.[9–11] However, these data have largely been derived from single-center or regional investigations, making generalizability across multiple regions challenging.[9] In addition, the largest study to date on this topic grouped all CHDs together, not accounting for the clear variability in PND by lesion.[11]

The present study examined a large, multicenter retrospective cohort from 21 North American cardiology centers. Our primary aim was to evaluate whether socioeconomic, demographic, or geographic factors are associated with lower rates of PND or delayed gestational age at time of PND of HLHS or TGA in the United States. A secondary aim was to examine whether the effect (or lack thereof) of socioeconomic, demographic, or geographic factors is comparable between the United States and Canada, which have divergent health care systems.

METHODS

Study Design

The findings from this study are available from the corresponding author on reasonable request. We conducted a multicenter retrospective cohort study performed through the Fetal Heart Society Research Collaborative (FHSRC) to identify potential socioeconomic, demographic, and geographic barriers to PND of HLHS and TGA. Twenty-one sites in the United States (n=19) and Canada (n=2) participated. These sites represented all geographic regions in the United States defined by the US Department of Health and Human Services. Institutional review board approval was obtained for each participating site with a waiver of consent, and a data use agreement was established between each site and the University of Utah. Data were submitted through an Open Clinica Database managed by the Data Collection Center at the University of Utah.

Study Population

This study population included prenatally diagnosed fetuses with HLHS or TGA and postnatally diagnosed liveborn infants of <2 months of age with HLHS or TGA with at least 1 visit recorded in the institutional database of the participating FHSRC center with a first hospital encounter in the system between January 1, 2012, and December 31, 2016. These 2 specific CHD lesions were chosen because they represent 2 of the most common critical newborn CHDs. They also represent both single and biventricular forms of CHD that require urgent and, in some cases, emergent intervention. Furthermore, although HLHS is identifiable through 4-chamber imaging, detection of TGA requires additional fetal outflow tract views on prenatal ultrasound screening and may be more difficult to detect prenatally than HLHS.[10,11]

HLHS was defined as classic forms of this diagnosis (mitral and aortic stenosis, mitral stenosis and aortic atresia, and mitral and aortic atresia) with an intact ventricular septum or double outlet right ventricle with mitral atresia and intact ventricular septum, amenable to a stage I palliation or hybrid procedure. TGA was defined as D-transposed great arteries with D-looped ventricles and concordant ventricular size with intact ventricular septum or small muscular ventricular septal defect. When possible, the cardiac diagnosis was confirmed postnatally or at autopsy.

Exclusion criteria included any of the following: lack of confirmation regarding the diagnosis in liveborn patients,

missing maternal address either because of lack of documentation or patient being homeless, or absent documentation of whether a case was diagnosed prenatally or postnatally. Subjects with anatomic variants of HLHS including critical aortic stenosis without evolution to HLHS or Shones complex, or TGA variants with tricuspid atresia, heterotaxy, double outlet right ventricle, Taussig-Bing anomaly, or hypoplasia of 1 ventricle or atrioventricular septal defect were also excluded, given that their presence may increase or decrease the likelihood of PND. With respect to TGA, we excluded fetuses and newborns with (1) a ventricular septal defect larger than a small muscular ventricular septal defect, (2) more than mild pulmonary stenosis, or (3) coarctation of the aorta.

Study Variables

The primary independent variables were neighborhood socioeconomic quartile (SEQ), neighborhood poverty level >20%, neighborhood race or ethnicity distribution, rural residence, at-risk geographic location (United States–Mexico border, Native American reservation, or island home), driving distance to cardiac surgical center, driving time to cardiac surgical center, maternal insurance, and maternal race or ethnicity. Maternal age, maternal primary language, presence of extracardiac defects, and multiple-gestation pregnancy were treated as covariates.

SEQ Calculation

For US patients, the SEQ was determined using the neighborhood summary score derived from the maternal census tract as described previously by Diez Roux et al.[12] For each patient, z scores of the neighborhood summary score were calculated. The neighborhood summary score was calculated by summing 6 elements extracted from each census tract: (1) log of median household income, (2) log of median housing value, (3) percentage of high school graduates (percentage whose highest educational attainment was graduation from high school or equivalent for the population ≥25 years of age), (4) percentage of college graduates (percentage whose highest educational attainment was a bachelor's degree or advanced degree for the population ≥25 years of age), (5) percentage of persons ≥16 years of age in executive, managerial, or professional specialty occupations, and (6) percentage of households receiving interest, dividend, or net rental income for each patient census tract. A z score was calculated for each of these elements on the basis of distribution within the data set, and z scores were then summed for each subject. Subjects were grouped into 4 quartiles on the basis of total neighborhood socioeconomic status score, with quartile 4 being the wealthiest. The maternal census tract was determined using the first address available in the maternal or infant medical chart. Relevant variables for each census tract were derived from the 2015 American Community Survey data using a CDX Zipstream software package (CDX Technologies, Randolph, NJ).

For the Canadian cohort, patients came from the 2 largest centralized fetal cardiology and surgical centers in 2 provinces, Alberta and Ontario. The postal code for the mother during pregnancy or the first postal code for the infant on record was recorded. The Chan index[13] was derived by investigators at the Canadian centers by extracting variables from the Canadian census. These included 22 variables related to cultural identities, environmental pollutants, environmental injustice studies, and the Pampalon deprivation index. A principal component analysis was performed on the 22 variables, and then the factor scores were averaged to generate the score. These scores were then converted to z scores and categorized into quartiles to be comparable to the US data.

Additional Neighborhood Characteristics

Neighborhood poverty level, race and ethnic distribution, rural designation, and at-risk geographic location were based on maternal census tract data derived from the 2015 American Community Survey and extracted using the CDX Zipstream software. A neighborhood in poverty was designated using a cutoff of ≥20%, in accordance with the US Census Bureau.[14] Given that maternal race and ethnicity data were not available for all subjects, the neighborhood variable of >50% Hispanic, non-Hispanic Black, or Native American inhabitants was examined as an independent variable. Rural versus urban status was based on the US Department of Agriculture 1 to 9 classification.[15] Rural residence was defined as categories 4 to 9. These variables were not available for Canadian subjects.

Geographic Distance From Maternal Residence to Care Center

Distance from maternal address to the surgical center in minutes and miles for the US population was calculated using the CDX Zipstream software and was provided by the Canadian centers and expressed in quartiles. Cases where patients were transferred from a surgical hospital near their homes to another surgical center were not included in the distance analysis.

Determination of Insurance Status

Presence or absence of public insurance was used by the maternal or infant insurance type from the medical chart, using the earliest available documentation for either the fetal or neonatal record. Public insurance was defined as Medicare, Medicaid, or a military or government insurance plan. For the Canadian provinces of Alberta and Ontario, provincial government health services are publicly funded and available for the population. Therefore, insurance status was not examined in the Canadian subcohort, and patients without insurance were not examined in the US cohort. Self-pay patients in the United States were not included in the analysis. Patients with unknown or undocumented insurance in the chart or missing insurance type in the chart were not included in the analysis.

Maternal and Fetal and Infant Characteristics

Maternal age at delivery, race, ethnicity, and primary language were derived from individual maternal and infant medical charts. Maternal race or ethnicity was not reliably available for Canadian subjects. Presence of a multiple gestation pregnancy and extracardiac defects were also extracted from medical charts.

Determination of Primary and Secondary Outcomes

The primary outcome of interest was PND. This was defined by at least 1 fetal echocardiogram report or clinic visit (performed by a pediatric cardiologist) in the participating center carrying the fetal diagnosis of TGA or HLHS. When

possible, a PND was confirmed postnatally. The secondary outcome studied was gestational age at PND (limited to prenatally diagnosed patients), as determined by the gestational age in weeks of the first fetal echocardiogram at the participating institution.

Statistical Analysis

Bivariate analyses were performed first overall and then stratified by country and diagnosis to determine whether there were associations between the primary independent variables, covariates, and the primary outcome using χ^2 for categorical variables and t test or Wilcoxon rank-sum test for continuous variables, as appropriate. Adjusted analyses using log-binomial regression with robust SEs were then performed for each independent variable, stratified by country and diagnosis, adjusting for covariates with $P \leq 0.1$ in bivariate analysis and clustering by site using generalized estimating equations. Subanalyses were then performed evaluating associations between the primary independent variables and the secondary outcome of gestational age at PND, limiting to those with a PND. These analyses were performed for each variable, stratified by country and diagnosis, adjusting for covariates with $P \leq 0.1$ in bivariate analysis and clustering by site using generalized linear models. All analyses were performed using SAS software, version 9.4 (SAS Institute Inc, Cary, NC).

RESULTS

The study included 1862 patients: 1171 patients with HLHS (91.8% prenatally diagnosed) and 691 with TGA (58% prenatally diagnosed). Of these, 1582 (85%) were from US centers. Of the Canadian patients, 133 had HLHS (n=120, 90.2% prenatally diagnosed) and 147 had TGA (n=84, 57% prenatally diagnosed). Postnatal confirmation was not available for 209 of the 1862 patients. One hundred thirty-eight did not survive to birth (1 miscarriage, 21 intrauterine fetal demise, 114 termination of pregnancy, 2 unknown). Thirty moved from the area before delivery and had unknown birth outcomes, and 41 were lost to follow-up. PND was significantly more common among those with HLHS compared with TGA (91.8% versus 58%; $P<0.0001$; Table 1).

Of the maternal patients in the US cohort, 43% had public insurance. We did not include 356 patients in the analysis: 339 had an unknown status (260 were from 1 center without information in the database), 2 were unable to be classified, 1 was missing, and 14 were self-pay). The racial distribution of our cohort was similar to that of the US Census distribution.[16] Of the US patients, 13% lived in a rural location as defined by US Department of Agriculture classifications 4 to 9.[15] A very small number of patients were living in an at-risk geographic location (n=7). Given this, this variable was not examined in stratified analyses.

Associations With PND

In unadjusted analyses evaluating the entire cohort, socioeconomic variables associated with a lack of PND were lower SEQ, rural address, further distance in miles or time to a care center, and public insurance (Table 1). Younger maternal age was also associated with lack of PND, as was singleton pregnancy compared with multiple-gestation pregnancy. When stratifying by country and lesion in unadjusted analyses, lower SEQ was only associated with lack of PND for TGA in the United States (relative risk [RR] for SEQ 1 versus 4, 0.69 [95% CI, 0.57–0.84]; Table 2). Additional distance from a care center was associated with lack of PND of TGA in the United States, which was most significant in the third quartile of distance (RR, 0.71 [95% CI, 0.58–0.88]; Table 2). Although no association between further distance and lack of PND of HLHS was noted in the US cohort, an association was noted in the Canadian cohort; however, given the small numbers, further study is needed.

Adjusted analyses were then performed adjusting for maternal age and accounting for hospital clustering. Stratified analyses could not be stably adjusted for multiple gestation pregnancies given the infrequency overall, with only 3 patients in the no-PND group. Within the United States, adjusted analyses demonstrated that PND was 6% less likely (RR, 0.94 [95% CI, 0.9–0.99]) among HLHS subjects in the lowest SEQ compared with those in the highest SEQ and up to 22% less likely (RR, 0.78 [95% CI, 0.64–0.85]) among TGA subjects in the lowest SEQ (1) compared with the highest SEQ (Table 3). This trend was not observed in the Canadian population. In the United States, PND was less common among Hispanic mothers compared with non-Hispanic White mothers (HLHS: RR, 0.97 [95% CI, 0.94–1.00]; TGA: RR, 0.85 [95% CI, 0.72–0.99]) and in those who lived in a rural location compared with an urban location (RR, 0.78 [95% CI, 0.64–0.95]) in the TGA group. In the United States, insurance, Black race, driving distance, and time to surgical center were not associated with prenatal detection in the adjusted analysis. In the unadjusted analyses of the Canadian cohort, further distance from a care center was associated with a lack of PND in HLHS in quartile 3 but not in TGA. For quartile 4, patients in the United States and Canada may have traveled for second opinions after initial fetal diagnosis at a site in their region. We queried 5 US centers, and of the 181 patients in quartile 4 in those centers, 87.8% were second opinions.

Associations With Gestational Age at Time of PND

When examining associations between independent variables and gestational age at PND, lower SEQ was

Table 1. Socioeconomic, Demographic, and Clinical Characteristics of the Cohort, by Prenatal Diagnosis

Demographic and clinical characteristics	Prenatal diagnosis, n (%)			P value
	Overall	No	Yes	
No. of participants (%)	1862	386 (20.8)	1473 (79.2)	
Diagnosis				<0.0001*
HLHS	1171 (62.9)	96 (8.2)	1072 (91.8)	
TGA	691 (37.1)	290 (42.0)	401 (58.0)	
Socioeconomic characteristics				
Socioeconomic status quartile				0.03*
1 (lowest)	454 (25.0)	98 (21.6)	355 (78.4)	
2	454 (25.0)	102 (22.5)	352 (77.5)	
3	450 (25.0)	99 (22.1)	349 (77.9)	
4 (highest)	459 (25.0)	72 (15.7)	387 (84.3)	
Poverty (>20% of census block)†				0.89
No	1226 (77.8)	243 (19.8)	983 (80.2)	
Yes	349 (22.2)	68 (19.5)	281 (80.5)	
Neighborhood population >50% Black or Hispanic†				0.34
No	1226 (77.9)	236 (19.3)	990 (80.7)	
Yes	348 (22.1)	75 (21.5)	273 (78.5)	
Rural location (4–9)†‡				0.02*
No	1368 (86.8)	257 (18.8)	1111 (81.2)	
Yes	208 (13.2)	54 (26.0)	154 (74.0)	
At-risk geographic location†				1.00
No	1226 (99.4)	258 (21.0)	968 (79.0)	
Yes	7 (0.6)	1 (14.3)	6 (85.7)	
Driving distance to care center, miles				0.002*
1 (<20)	479 (25.9)	80 (16.7)	398 (83.3)	
2 (20–49)	448 (24.3)	98 (22.0)	348 (78.0)	
3 (50–134)	458 (24.8)	120 (26.2)	338 (73.8)	
4 (≥135)	462 (25.0)	86 (18.6)	376 (81.4)	
Driving time to care center, min				0.004*
1 (<30)	422 (24.4)	66 (15.6)	356 (84.4)	
2 (30–59)	466 (26.9)	94 (20.2)	371 (79.8)	
3 (60–119)	362 (20.9)	95 (26.2)	267 (73.8)	
4 (≥120)	481 (27.8)	100 (20.8)	381 (79.2)	
Maternal insurance†				0.01*
Private	702 (57.3)	121 (17.2)	581 (82.8)	
Public§	524 (42.7)	106 (20.2)	418 (79.8)	
Maternal characteristics				
Maternal race/ethnicity				0.33
White, non-Hispanic	986 (68.0)	149 (16.1)	776 (83.9)	
Black, non-Hispanic	165 (11.8)	30 (18.7)	130 (81.3)	
Hispanic/Latino	210 (15.3)	43 (20.7)	165 (79.3)	
Asian	58 (3.7)	11 (22.0)	39 (78.0)	
Native American/Alaskan/Pacific Islander	25 (1.3)	5 (27.8)	13 (72.2)	
Maternal age, y, mean (SD)	29.1 (5.9)	28.2 (5.7)	29.3 (5.9)	0.008*
English as primary language				0.33
No	139 (8.0)	30 (21.6)	109 (78.4)	
Yes	1597 (92.0)	291 (18.2)	1305 (81.8)	

(*Continued*)

Table 1. Continued

Demographic and clinical characteristics	Prenatal diagnosis, n (%)			P value
	Overall	No	Yes	
Fetal/infant characteristics				
Extracardiac birth defect				0.29
No	1594 (89.8)	318 (19.9)	1276 (80.1)	
Yes	180 (10.2)	30 (16.7)	150 (83.3)	
Multiple gestation pregnancy				0.0002*
No	1765 (95.3)	378 (21.4)	1386 (78.6)	
Yes	87 (4.7)	4 (4.6)	83 (95.4)	

The P values are based on a t test (continuous) or a χ^2 test (categorical); numbers in bold are significant at P<0.05. HLHS indicates hypoplastic left heart syndrome; and TGA, transposition of the great arteries.

*Indicates P values significant at <0.05.

†US only.

‡US Department of Agriculture 1–9 classification.[15]

§All Canadian records except 3 are publicly insured.

associated with later gestational age at PND for both HLHS and TGA in both the United States and Canada (Table 4). In the United States, public insurance, rural residence, and further distance of residence were all associated with a later gestational age at PND for both HLHS and TGA. In quartile 4, this may reflect second opinions. In the United States, Hispanic ethnicity was associated with later gestational age at diagnosis for HLHS. In Canada, further distance of residence in quartile 3 was associated with later gestational age at diagnosis for TGA.

DISCUSSION

Our study evaluated a large, geographically diverse group of patients to determine associations between social determinants of health and rates of PND. We found that, in the United States, lower SEQ was associated with lower PND of HLHS and TGA; for TGA, Hispanic ethnicity and rural location were also associated with decreased PND. Among Canadian patients, only further distance to a cardiac surgical center was associated with lower PND rates of HLHS, demonstrating differences between 2 countries with different health care systems. Our study adds more granular detail to earlier work showing that demographic and socioeconomic factors have a relationship with PND of CHD on a large scale with data from a large cohort of North American patients.

Previous studies in North America on the influences of race or ethnicity, insurance, and socioeconomic position on PND have been obtained from single-center or regional studies and are conflicting or evaluate different parameters.[9,10,17] A study by Peiris et al[9] evaluated all critical CHD in Boston between 2003 and 2006 and found that higher socioeconomic position and private insurance were associated with increased rates of PND. In contrast, in our US cohort, public insurance

(Medicare, Medicaid, or other government insurance such as military insurance) was not associated with decreased PND. This may be because of differences in eras or differences in regional influences versus national influences. Hill et al[10] studied children with critical CHD in Wisconsin and found that barriers to prenatal detection included the need for outflow tract visualization, poverty, low population density area, and absence of an extracardiac abnormality. In our study, decreased PND was associated with Hispanic ethnicity among children with TGA, supporting previous studies.[18] Given the limitations of collecting self-reported race and ethnicity from retrospective data, we also used census tract data to assess the proportion of families in a given tract who were non-Hispanic Black, Hispanic, or Native American. For both the HLHS and TGA analyses, the effect estimates for those living in a census tract with >50% of those minorities mirrored those of Hispanic mothers, although they were not statistically significant. Whereas the distribution of race and ethnicity in the US cohort generally mirrors the country's racial and ethnic distribution, the conclusions may not be representative in individual areas with higher percentages of minority populations.

In the present study, we found overall prenatal detection rates of 92% for fetal HLHS and 58% for fetal TGA to be higher than reported previously, both before and after the publication of fetal echocardiography guidelines, which include outflow tract evaluation.[11,19] After the initial publication of universal screening guidelines, nationwide PND rates were estimated to be ≈67% for HLHS and 28% for TGA.[11] Following the most recent American Institute of Ultrasound in Medicine recommendations[19] for inclusion of outflow tract views in the evaluation of the fetal heart, diagnostic rates for DTGA have been reported at 30% to 41% in recent US regional studies,[20,21] while showing more of an improvement in Canadian studies.[22] Hence, whereas there has

Table 2. Unadjusted Associations Between Socioeconomic Variables and Prenatal Diagnosis, by Diagnosis and Country

Socioeconomic risk characteristics	United States, RR (95% CI)*		Canada, RR (95% CI)†	
	HLHS	TGA	HLHS	TGA
Socioeconomic status quartile				
1 (lowest)	0.95 (0.81–1.00)	0.69 (0.57–0.84)‡	1.08 (0.97–1.19)	1.05 (0.72–1.53)
2	0.98 (0.93–1.02)	0.71 (0.59–0.86)‡	0.97 (0.82–1.13)	0.88 (0.59–1.32)
3	0.96 (0.92–1.01)	0.75 (0.63–0.91)‡	0.99 (0.83–1.16)	0.80 (0.52–1.23)
4 (highest)	Ref.	Ref.	Ref.	Ref.
Poverty (>20% of census block)				
No	Ref.	Ref.	—	—
Yes	1.00 (0.96–1.04)	0.87 (0.71–1.07)		
Neighborhood population >50% Black or Hispanic				
No	Ref.	Ref.	—	—
Yes	0.98 (0.93–1.02)	0.81 (0.66–1.01)		
Rural location (4–9)				
No	Ref.	Ref.	—	—
Yes	0.96 (0.90–1.02)	0.77 (0.60–1.00)		
Driving distance to care center, miles				
1 (<20)	Ref.	Ref.	Ref.	Ref.
2 (20–49)	0.99 (0.94–1.04)	0.84 (0.70–1.00)	1.02 (0.98–1.07)	1.09 (0.74–1.59)
3 (50–134)	0.97 (0.92–1.02)	0.71 (0.58–0.88)‡	0.80 (0.66–0.97)‡	0.70 (0.43–1.13)
4 (≥135)	0.98 (0.94–1.03)	0.87 (0.71–1.04)	0.95 (0.84–1.06)	1.16 (0.82–1.64)
Driving time to care center, min				
1 (<30)	Ref.	Ref.	Ref.	Ref.
2 (30–59)	0.99 (0.94–1.04)	0.91 (0.77–1.08)	0.95 (0.86–1.05)	1.07 (0.67–1.70)
3 (60–119)	0.97 (0.92–1.02)	0.66 (0.53–0.83)	0.88 (0.73–1.05)	0.65 (0.34–1.26)
4 (≥120 min)	0.98 (0.94–1.03)	0.87 (0.72–1.05)	0.80 (0.62–1.03)	0.78 (0.44–1.39)
Maternal insurance				
Private	Ref.	Ref.	–	–
Public	0.97 (0.93–1.01)	0.88 (0.75–1.04)		
Maternal race/ethnicity				
White, non-Hispanic	Ref.	Ref.	–	–
Black, non-Hispanic	0.98 (0.93–1.04)	0.75 (0.54–1.03)		
Hispanic/Latino	0.97 (0.92–1.03)	0.78 (0.60–1.01)		
Asian	0.95 (0.83–1.08)	1.00 (0.73–1.36)		
Native American/Alaskan/Pacific Islander	0.89 (0.69–1.14)	0.77 (0.34–1.71)		

Numbers in bold are significant at *P*<0.05.

HLHS indicates hypoplastic left heart syndrome; Ref., reference; RR, relative risk; and TGA, transposition of the great arteries.

*Estimates are based on log-binomial regression.

†Estimates are based on log-binomial regression or log-Poisson regression with robust SEs.

‡Indicates *P* values significant at <0.05.

been a slow and steady trend toward increased PND, there continue to be clear discrepancies between detection rates of lesions such as HLHS that are readily identified on fetal 4-chamber views and TGA with intact ventricular septum that are frequently missed if outflow tract views are not systematically obtained.[11,17] There also continues to be regional variation in PND of both of these critical lesions. PND rates reported in different state registry-based studies have varied from 60%

to 77% for HLHS and 17% to 36% for TGA.[7,11,17,23–25] Initial screening begins with obstetricians or radiologists who obtain cardiology or maternal fetal medicine consultation for screening indications or concerns of abnormality. Barriers to communication between these specialists may exist,[26] so further effort is needed to study providers in the areas outlined in this article.

It is interesting that despite universalized health care in Canada, the prenatal detection rates in the

Table 3. Adjusted Associations Between Socioeconomic Variables and Prenatal Diagnosis, by Diagnosis and Country

Socioeconomic risk characteristics	United States, aRR (95% CI)*		Canada, aRR (95% CI)†	
	HLHS	TGA	HLHS	TGA
Socioeconomic status quartile				
1 (lowest)	0.94 (0.90–0.99)‡	0.78 (0.64–0.85)‡	1.00 (1.00–1.00)	1.17 (0.95–1.44)
2	0.97 (0.91–1.02)	0.77 (0.64–0.93)‡	0.96 (0.89–1.04)	0.90 (0.69–1.18)
3	0.96 (0.91–1.01)	0.83 (0.69–1.00)	0.95 (0.86–1.05)	0.86 (0.76–0.97)‡
4 (highest)	Ref.	Ref.	Ref.	Ref.
Poverty (>20% of census block)				
No	Ref.	Ref.	–	–
Yes	1.00 (0.97–1.03)	0.97 (0.83–1.13)		
Neighborhood population >50% Black or Hispanic				
No	Ref.	Ref.	–	–
Yes	0.97 (0.94–1.00)	0.85 (0.70–1.04)		
Rural location (4–9)				
No	Ref.	Ref.	–	–
Yes	0.97 (0.92–1.02)	0.78 (0.64–0.95)‡		
Driving distance to care center, miles				
1 (<20)	Ref.	Ref.	Ref.	Ref.
2 (20–49)	1.00 (0.95–1.05)	0.88 (0.76–1.02)	1.00 (1.00–1.00)	1.09 (1.04–1.15)‡
3 (50–134)	0.99 (0.95–1.02)	0.82 (0.67–1.01)	0.96 (0.89–1.04)	0.91 (0.67–1.24)
4 (≥135)	1.00 (0.96–1.03)	0.94 (0.75–1.17)	0.96 (0.93–1.00)	1.24 (1.03–1.51)‡
Driving time to care center, min				
1 (<30)	Ref.	Ref.	–	–
2 (30–59)	1.00 (0.95–1.04)	0.93 (0.83–1.04)		
3 (60–119)	1.00 (0.96–1.04)	0.83 (0.65–1.06)		
4 (≥120)	0.99 (0.95–1.03)	0.88 (0.71–1.09)		
Maternal insurance				
Private	Ref.	Ref.	–	–
Public	0.98 (0.94–1.02)	0.95 (0.81–1.13)		
Maternal race/ethnicity				
White, non-Hispanic	Ref.	Ref.	–	–
Black, non-Hispanic	0.98 (0.94–1.01)	0.87 (0.66–1.16)		
Hispanic/Latino	0.97 (0.94–1.00)	0.85 (0.72–0.99)‡		
Asian	0.97 (0.84–1.11)	0.97 (0.72–1.29)		
Native American/Alaskan/Pacific Islander	0.88 (0.69–1.12)	0.83 (0.34–2.03)		

Numbers in bold are significant at *P*<0.05. aRR indicates adjusted relative risk; HLHS, hypoplastic left heart syndrome; Ref., reference; and TGA, transposition of the great arteries.

*Estimates are based on log-binomial regression with clustering by site, adjusted for maternal age.

†Estimates are based on log-Poisson regression with robust SEs with clustering by site, adjusted for maternal age.

‡Indicates *P* values significant at <0.05.

United States and Canada were almost identical in this study. There is regional variability of detection rates in Canada; and in this study only 2 centers, Alberta and Ontario, were studied. This may have been 1 reason for the lack of differences between the United States and Canada. The Canadian centers included were limited to those participating in the FHSRC and had limitations in power to detect differences, but the authors believed that it was important to include the positive findings, which did highlight differences in the health care systems. Factors related to where and who performs the scan likely play a role and will require further investigation. Overall, the Canadian patients accounted for 20% of TGA patients and 10% of HLHS patients. Although we cannot determine definitively why this is the case, it may reflect higher termination for

Table 4. Association of Sociodemographic Variables With Gestational Age at Time of Prenatal Diagnosis of Hypoplastic Left Heart Syndrome and D-Transposition of the Great Arteries in the United States and Canada

Socioeconomic risk characteristics	United States, mean (95% CI)		Canada, mean (95% CI)	
	HLHS	TGA	HLHS	TGA
Socioeconomic status quartile (1 is lowest)				
1	25.4 (23.7–27.0)*	27.8 (26.7–29.0)*	24.4 (22.6–26.1)*	25.4 (23.0–27.8)*
2	24.9 (24.0–25.9)*	26.7 (25.8–27.7)*	22.0 (21.0–23.0)*	25.5 (25.4–25.6)*
3	24.4 (23.3–25.4)*	25.1 (24.2–26.0)*	22.7 (21.9–23.5)	23.2 (22.4–24.0)*
4 (reference)	22.3 (21.5–23.2)	23.6 (22.7–24.6)	22.4 (21.1–23.7)	22.0 (20.4–23.7)
Neighborhood population >50% Black or Hispanic				
No	24.2 (23.2–25.1)	25.5 (23.9–27.1)		
Yes	24.7 (23.3–26.0)	25.5 (24.5–26.5)		
Rural location (4–9)				
No (reference)	24.2 (23.2–25.2)	25.3 (24.4–26.1)		
Yes	25.0 (24.2–25.9)*	27.4 (25.8–29.0)*		
Driving distance to care center, miles				
1 (<20, reference)	23.5 (22.6–24.4)	24.8 (23.6–26.0)	22.8 (20.5–25.1)	24.4 (22.4–26.5)
2 (20–49)	23.7 (22.6–24.8)	24.3 (22.9–25.7)	22.4 (22.0–22.9)	23.8 (22.3–25.4)
3 (50–134)	24.0 (22.8–25.1)	25.0 (24.1–25.9)	23.9 (22.9–24.9)	25.1 (22.6–27.6)*
4 (≥135)	26.2 (24.3–28.1)*	28.3 (26.9–29.7)*	22.5 (21.2–23.9)	23.3 (20.1–26.5)*
Driving time to care center, min†				
1 (<30, reference)	23.3 (22.5–24.2)	24.5 (23.3–25.7)	24.4 (22.4–26.4)	25.2 (22.3–28.1)
2 (30–59)	23.9 (22.8–25.1)	24.6 (23.5–25.7)	22.3 (20.1–24.4)	22.9 (20.6–25.3)
3 (60–119)	23.8 (22.5–25.1)	24.9 (23.9–26.0)	21.9 (19.5–24.4)	26.1 (22.7–29.5)
4 (≥120)	26.1 (24.2–27.9)*	28.3 (26.9–29.6)*	25.6 (22.9–28.2)	27.2 (24.2–30.2)
Maternal insurance				
Private (reference)	24.0 (23.2–24.8)	25.2 (24.1–26.2)		
Public	25.3 (24.2–26.4)*	26.7 (25.8–27.7)*		
Maternal race/ethnicity				
White, non-Hispanic (reference)	24.0 (23.1–24.9)	25.2 (24.1–26.4)		
Black, non-Hispanic	25.0 (23.2–26.8)	26.1 (22.8–29.3)		
Hispanic/Latino	25.3 (24.0–26.7)*	25.9 (24.3–27.6)		
Other	25.1 (23.2–27.0)	24.2 (23.2–25.2)		

Least-squares means estimates from generalized linear models controlling for maternal age with clustering by site. HLHS indicates hypoplastic left heart syndrome; and TGA, transposition of the great arteries.

*Indicates P values significant at <0.05.

†Unable to control for site and maternal age; information provided for 1 Canadian site only.

HLHS; termination rates for prenatally diagnosed CHD in Canada are reported at 50% before 24 weeks[27] and would reasonably be expected to be higher for single ventricle disease. Typically, at the Alberta and Calgary centers, the patients with HLHS would have still been included in the study because of a confirmatory fetal echocardiogram being performed by a pediatric cardiologist. However, it is possible that some patients in Toronto may have been seen by a pediatric cardiologist in the community and terminated before being seen by a provider at the Hospital for Sick Children. This may have accounted for the lower overall percentage of Canadian patients with HLHS compared with the total.

Some factors associated with lack of PND (low SEQ, rural location) may have collinearity. The association of these factors with lack of PND could be related to access to specialized health care services, which has been previously related to area deprivation.[28] The association of lower SEQ with lower PND was only seen in the United States, although patients with lower SEQ had later gestational age of diagnosis in both US and Canadian subjects. Although the total number of subjects was lower in the Canadian group, the inverse trend suggests that the differences are valid. This could suggest that universal health care may mitigate the effect of socioeconomic status on prenatal care and thus PND. There is precedent for this in neurodevelopmental

ORIGINAL RESEARCH ARTICLE

MD; Nelangi M. Pinto, MD; Rachel Schwartz, MD; Kenan W.D. Stern, MD; Carolyn Taylor, MD; Varsha Thakur, MD; Wayne Tworetzky, MD; Carol Wittlieb-Weber, MD; Kris Woldu, MD; Mary T. Donofrio, MD; On behalf of the Fetal Heart Society

Correspondence

Anita Krishnan, MD, Children's National Medical Center, 3rd Floor, Cardiology, 111 North Michigan Ave NW, Washington, DC 20010. Email akrishna@childrensnational.org

Affiliations

Divisions of Cardiology (A.K., M.T.D.) and Biostatistics (M.B.J.), Children's National Hospital, Washington, DC. Department of Obstetrics, Gynecology, and Reproductive Sciences, University of California, San Diego (M.B.J.). Division of Pediatric Cardiology, Baylor College of Medicine, Houston, TX (S.A.M., K.N.L.). Division of Cardiology, Department of Pediatrics, University of California, San Francisco (S.P.). Division of Cardiology, Seattle Children's Hospital, University of Washington (A.H.B.). Division of Pediatric Cardiology, Columbia University Irving Medical Center, New York (A.C.). Division of Pediatric Cardiology, Johns Hopkins University, Baltimore, MD (J.S.C., S.K.). Division of Cardiology, Department of Pediatrics, Massachusetts General Hospital, Boston (J.S.C.). Division of Cardiology, Children's Hospital of Colorado/University of Colorado, Aurora (B.F.C., L.H.). Division of Cardiology, Johns Hopkins University All Children's Hospital, St. Petersburg, FL (G.F.). Division of Pediatric Cardiology, University of Alberta, Edmonton, Canada (L.K.H., A.M.). Division of Cardiology, The Children's Heart Clinic/Children's Minnesota, Minneapolis (L.H.). Division of Cardiology, Ann and Robert H. Lurie Children's Hospital of Chicago, IL (N.H.). Division of Cardiology, Department of Pediatrics, University of Texas Southwestern Medical Center, Dallas (C.I., K.W.). Division of Pediatric Cardiology, Monroe Carell Jr. Children's Hospital at Vanderbilt, Nashville, TN (A.K.-M.). University of Nebraska Medical Center, Omaha (S.K.). Division of Cardiology, Department of Pediatrics, Washington University School of Medicine, St. Louis, MO (C.L.). Emory University School of Medicine, Children's Healthcare of Atlanta/Sibley Heart Center, GA (E.C.M.). Division of Pediatric Cardiology, University of Utah, Salt Lake City (N.M.P.). Division of Cardiology, Boston Children's Hospital, MA (R.S., W.T.). The George Washington School of Medicine, Washington, DC (R.S.). Division of Pediatric Cardiology, Albert Einstein College of Medicine, Children's Hospital at Montefiore, New York (K.W.D.S.). Division of Pediatric Cardiology, Icahn School of Medicine at Mount Sinai, Kravis Children's Hospital, New York (K.W.D.S.). Division of Pediatric Cardiology, Medical University of South Carolina, Charleston (C.T.). Division of Cardiology, University of Toronto, Ontario, Canada (V.T.). Division of Pediatric Cardiology, University of Rochester, NY (C.W.-W.). Division of Cardiology, Children's Hospital of Philadelphia, PA (C.W.-W.). Division of Cardiology, Cook Children's Heart Center, Ft. Worth, TX (K.W.).

Disclosures

None.

APPENDIX

Collaborators include Mary Craft, RDCS (University of Nebraska Medical Center, Omaha), Heather Gramse, BSc (University of Utah School of Medicine, Salt Lake City), Anita Moon-Grady, MD (Division of Cardiology, Department of Pediatrics, University of California, San Francisco), Wesley Lee, MD (Department of Obstetrics and Gynecology, Baylor College of Medicine, Houston, TX), Dawn Park, RDCS (Division of Cardiology, Children's Hospital of Colorado/University of Colorado, Aurora), and Alysia Wiener, MD (George Washington School of Medicine, Washington, DC, and Department of Obstetrics and Gynecology, University of Pittsburgh Medical Center).

REFERENCES

1. Bonnet D, Coltri A, Butera G, Fermont L, Le Bidois J, Aggoun Y, Acar P, Villain E, Kachaner J, Sidi D. Prenatal diagnosis of transposition of great vessels reduces neonatal morbidity and mortality [in French]. *Arch Mal Coeur Vaiss*. 1999;92:637–640.

2. Tworetzky W, McElhinney DB, Reddy VM, Brook MM, Hanley FL, Silverman NH. Improved surgical outcome after fetal diagnosis of hypoplastic left heart syndrome. *Circulation*. 2001;103:1269–1273. doi: 10.1161/01.cir.103.9.1269

3. Donofrio MT, Levy RJ, Schuette JJ, Skurow-Todd K, Sten MB, Stallings C, Pike JI, Krishnan A, Ratnayaka K, Sinha P, et al. Specialized delivery room planning for fetuses with critical congenital heart disease. *Am J Cardiol*. 2013;111:737–747. doi: 10.1016/j.amjcard.2012.11.029

4. Morris SA, Ethen MK, Penny DJ, Canfield MA, Minard CG, Fixler DE, Nembhard WN. Prenatal diagnosis, birth location, surgical center, and neonatal mortality in infants with hypoplastic left heart syndrome. *Circulation*. 2014;129:285–292. doi: 10.1161/CIRCULATIONAHA.113.003711

5. Calderon J, Angeard N, Moutier S, Plumet MH, Jambaqué I, Bonnet D. Impact of prenatal diagnosis on neurocognitive outcomes in children with transposition of the great arteries. *J Pediatr*. 2012;161:94–8.e1. doi: 10.1016/j.jpeds.2011.12.036

6. Peyvandi S, De Santiago V, Chakkarapani E, Chau V, Campbell A, Poskitt KJ, Xu D, Barkovich AJ, Miller S, McQuillen P. Association of prenatal diagnosis of critical congenital heart disease with postnatal brain development and the risk of brain injury. *JAMA Pediatr*. 2016;170:e154450. doi: 10.1001/jamapediatrics.2015.4450

7. Friedberg MK, Silverman NH, Moon-Grady AJ, Tong E, Nourse J, Sorenson B, Lee J, Hornberger LK. Prenatal detection of congenital heart disease. *J Pediatr*. 2009;155:26–31, 31.e1. doi: 10.1016/j.jpeds.2009.01.050

8. van Velzen CL, Ket JCF, van de Ven PM, Blom NA, Haak MC. Systematic review and meta-analysis of the performance of second-trimester screening for prenatal detection of congenital heart defects. *Int J Gynaecol Obstet*. 2018;140:137–145. doi: 10.1002/ijgo.12373

9. Peiris V, Singh TP, Tworetzky W, Chong EC, Gauvreau K, Brown DW. Association of socioeconomic position and medical insurance with fetal diagnosis of critical congenital heart disease. *Circ Cardiovasc Qual Outcomes*. 2009;2:354–360. doi: 10.1161/CIRCOUTCOMES.108.802868

10. Hill GD, Block JR, Tanem JB, Frommelt MA. Disparities in the prenatal detection of critical congenital heart disease. *Prenat Diagn*. 2015;35:859–863. doi: 10.1002/pd.4622

11. Quartermain MD, Pasquali SK, Hill KD, Goldberg DJ, Huhta JC, Jacobs JP, Jacobs ML, Kim S, Ungerleider RM. Variation in prenatal diagnosis of congenital heart disease in infants. *Pediatrics*. 2015;136:e378–e385. doi: 10.1542/peds.2014-3783

12. Diez Roux AV, Merkin SS, Arnett D, Chambless L, Massing M, Nieto FJ, Sorlie P, Szklo M, Tyroler HA, Watson RL. Neighborhood of residence and incidence of coronary heart disease. *N Engl J Med*. 2001;345:99–106. doi: 10.1056/NEJM200107123450205

13. Chan E, Serrano J, Chen L, Stieb DM, Jerrett M, Osornio-Vargas A. Development of a Canadian socioeconomic status index for the study of health outcomes related to environmental pollution. *BMC Public Health* 2015;. 15:714. doi: 10.1186/s12889-015-1992-y

14. United States Census Bureau. American Community Survey Reports 2010, changes in areas with concentrated poverty: 2000 to 2010. Accessed June 2014. https://www.census.gov/library/publications/2014/acs/acs-27.html

15. United States Department of Agriculture. Economic research service; rural-urban continuum codes. Accessed 2020. https://www.ers.usda.gov/data-products/rural-urban-continuum-codes.aspx

16. United States Census Bureau. American Community Survey 5-year data profiles, demographic and housing estimates, table DP05. Accessed 2020. https://data.census.gov/cedsci/table?q=DP05&tid=ACSDP5Y2015. DP05&hidePreview=false

17. Pinto NM, Keenan HT, Minich LL, Puchalski MD, Heywood M, Botto LD. Barriers to prenatal detection of congenital heart disease: a population-based study. *Ultrasound Obstet Gynecol*. 2012;40:418–425. doi: 10.1002/uog.10116

18. Ailes EC, Gilboa SM, Riehle-Colarusso T, Johnson CY, Hobbs CA, Correa A, Honein MA; National Birth Defects Prevention Study. Prenatal diagnosis of nonsyndromic congenital heart defects. *Prenat Diagn*. 2014;34:214–222. doi: 10.1002/pd.4282

19. American Institute of Ultrasound in Medicine. AIUM practice guideline for the performance of fetal echocardiography. *J Ultrasound Med*2013;. 32:1067–1082. doi:10.7863/ultra.32.6.1067

20. Sun HY, Proudfoot JA, McCandless RT. Prenatal detection of critical cardiac outflow tract anomalies remains suboptimal despite revised obstetrical imaging guidelines. *Congenit Heart Dis*. 2018;13:748–756. doi: 10.1111/chd.12648

21. Escobar-Diaz MC, Freud LR, Bueno A, Brown DW, Friedman KG, Schidlow D, Emani S, Del Nido PJ, Tworetzky W. Prenatal diagnosis of transposition of the great arteries over a 20-year period: improved but imperfect. *Ultrasound Obstet Gynecol*. 2015;45:678–682. doi: 10.1002/uog.14751

22. Ravi P, Mills L, Fruitman D, Savard W, Colen T, Khoo N, Serrano-Lomelin J, Hornberger LK. Population trends in prenatal detection of transposition of great arteries: impact of obstetric screening ultrasound guidelines. *Ultrasound Obstet Gynecol*. 2018;51:659–664. doi: 10.1002/uog.17496

23. Acherman RJ, Evans WN, Luna CF, Rollins R, Kip KT, Collazos JC, Restrepo H, Adasheck J, Iriye BK, Roberts D, et al. Prenatal detection of congenital heart disease in southern Nevada: the need for universal fetal cardiac evaluation. *J Ultrasound Med*. 2007;26:1715–1720. doi: 10.7863/jum.2007.26.12.1715

24. Sekar P, Heydarian HC, Cnota JF, Hornberger LK, Michelfelder EC. Diagnosis of congenital heart disease in an era of universal prenatal ultrasound screening in southwest Ohio. *Cardiol Young*. 2015;25:35–41. doi: 10.1017/S1047951113001467

25. Sklansky MS, Berman DP, Pruetz JD, Chang RK. Prenatal screening for major congenital heart disease: superiority of outflow tracts over the 4-chamber view. *J Ultrasound Med*. 2009;28:889–899. doi: 10.7863/jum. 2009.28.7.889

26. Pinto NM, Henry KA, Grobman WA, Ness A, Miller S, Ellestad S, Gotteiner N, Tacy T, Wei G, Minich LL, et al. Physician barriers and facilitators for screening for congenital heart disease with routine obstetric ultrasound: a national United States survey. *J Ultrasound Med*. 2020;39:1143–1153. doi: 10.1002/jum.15199

27. Trines J, Fruitman D, Zuo KJ, Smallhorn JF, Hornberger LK, Mackie AS. Effectiveness of prenatal screening for congenital heart disease: assessment in a jurisdiction with universal access to health care. *Can J Cardiol*. 2013;29:879–885. doi: 10.1016/j.cjca.2013.04.028

28. Vos AA, Posthumus AG, Bonsel GJ, Steegers EA, Denktaş S. Deprived neighborhoods and adverse perinatal outcome: a systematic review and meta-analysis. *Acta Obstet Gynecol Scand*. 2014;93:727–740. doi: 10.1111/aogs.12430

29. Peyvandi S, Chau V, Guo T, Xu D, Glass HC, Synnes A, Poskitt K, Barkovich AJ, Miller SP, McQuillen PS. Neonatal brain injury and timing of neurodevelopmental assessment in patients with congenital heart disease. *J Am Coll Cardiol*. 2018;71:1986–1996. doi: 10.1016/j. jacc.2018.02.068