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Socioeconomic Mediators of Racial and Ethnic Disparities in Congenital Heart Disease Outcomes: A Population-Based Study in California

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**Background**—Racial/ethnic and socioeconomic disparities exist in outcomes for children with congenital heart disease. We sought to determine the influence of race/ethnicity and mediating socioeconomic factors on 1-year outcomes for live-born infants with hypoplastic left heart syndrome and dextro-Transposition of the great arteries.

**Methods and Results**—The authors performed a population-based cohort study using the California Office of Statewide Health Planning and Development database. Live-born infants without chromosomal anomalies were included. The outcome was a composite measure of mortality or unexpected hospital readmissions within the first year of life defined as >3 (hypoplastic left heart syndrome) or >1 readmissions (dextro-Transposition of the great arteries). Hispanic ethnicity was compared with non-Hispanic white ethnicity. Mediation analyses determined the percent contribution to outcome for each mediator on the pathway between race/ethnicity and outcome. A total of 1796 patients comprised the cohort (n=964 [hypoplastic left heart syndrome], n=832 [dextro-Transposition of the great arteries]) and 1315 were included in the analysis (n=477 non-Hispanic white, n=838 Hispanic). Hispanic ethnicity was associated with a poor outcome (crude odds ratio, 1.72; 95% confidence interval [CI], 1.37–2.17). Higher maternal education (crude odds ratio 0.5; 95% CI, 0.38–0.65) and private insurance (crude odds ratio, 0.65; 95% CI, 0.45–0.71) were protective. In the mediation analysis, maternal education and insurance status explained 33.2% (95% CI, 7.66–66.4) and 27.6% (95% CI, 6.5–63.1) of the relationship between race/ethnicity and poor outcome, while infant characteristics played a minimal role.

**Conclusions**—Socioeconomic factors explain a significant portion of the association between Hispanic ethnicity and poor outcome in neonates with critical congenital heart disease. These findings identify vulnerable populations that would benefit from resources to lessen health disparities. *(J Am Heart Assoc. 2018;7:e010342. DOI: 10.1161/JAHA.118.010342.)*

**Key Words:** congenital heart disease • outcomes research • socioeconomic position

Congenital heart disease (CHD) is the most common birth defect, with an incidence of $\approx 0.8\%$. In the recent era, advances in perioperative care have led to improved survival of newborns with critical CHD. Despite improvements, these children continue to face significant morbidities and mortality. Among other factors, race and ethnicity have been previously shown to be associated with mortality in children undergoing surgery for various types of CHD. In particular, vulnerable racial/ethnic groups such as Hispanic and black patients have an increased risk of mortality as seen in large population-based studies.

The cause of racial/ethnic disparity in CHD outcomes is largely unknown. Race and ethnicity are mainly regarded as...
social constructs, thus healthcare disparities are likely mediated through various socioeconomic factors rather than through biological differences between groups. Few studies have assessed the role of socioeconomic factors as primary predictors of outcome, such as parental education levels, insurance status, and income, which are known to be important contributors to health and healthcare disparities. The few studies in the CHD literature that have accounted for these factors have conducted analyses that have not taken into account the intimate relationship between race/ethnicity and various socioeconomic factors as a conceptual model for healthcare disparity. For example, studies utilizing the Texas Birth Defects Registry have suggested that access to care (by virtue of residing in high poverty areas) more than race/ethnicity plays a major role in 1-year mortality for patients with severe CHD. Still, it is unclear whether certain racial/ethnic groups within these regions are at proportionately higher risk. Similarly, several other studies have identified regional differences in outcome in the United States within racial/ethnic groups without a clear identification of specific factors that may be responsible for the disparities within that state or region.

Understanding the socioeconomic factors that may then mediate the relationship between race/ethnicity and outcome in CHD would be helpful for developing target intervention strategies for specific vulnerable populations. Our primary aim in the current study was to determine whether socioeconomic factors mediate racial/ethnic disparities in 1-year outcomes for live-born infants with 2 forms of complex CHD requiring a neonatal intervention, hypoplastic left heart syndrome (HLHS) and dextro-Transposition of the great arteries (d-TGA), in the current era. We hypothesized that socioeconomic factors may explain a large percentage of the racial/ethnic disparities seen in this population.

Methods

The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure. The California Office of Statewide Health Planning and Development maintains a birth cohort database containing 3 160 268 live births from the years 2007–2012. This database includes detailed information on infant and maternal clinical and demographic characteristics derived from hospital discharge records (maternal hospitalization, birth hospitalization, and readmissions), linked to birth and death certificates, from birth to 1 year of age. The file provides diagnosis and procedure codes based on the International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM). The same database has been used by our group to report on a variety of neonatal outcomes. Informed consent was waived for this study.

Patients

We included all live-born infants with gestational age 22 to 42 completed weeks and excluded newborns with known chromosomal abnormalities or major structural birth defects other than the cardiac lesions of interest. Structural birth defects were considered “major” if determined by clinical review to result in mortality or major morbidity and likely to be identified at birth or lead to hospitalization during the first year of life.

Infants with HLHS or d-TGA were identified by ICD-9-CM diagnostic and procedure codes present in the birth, transfer, or readmission records. Two experts including a cardiologist and a cardiac intensivist (A.M.G. and M.A.S.) reviewed all cases according to a proposed framework based on morphogenetically similar developmental mechanisms to ensure correct classification of infants with multiple ICD-9-CM codes. Final diagnosis was reached by consensus.

Predictors and Primary Outcome

The main predictors included maternal race/ethnicity and socioeconomic variables available in the California Office of Statewide Health Planning and Development data set. Race and ethnicity of the mother was self-reported and obtained from the infant’s birth certificate record. Race/ethnicity was classified as non-Hispanic white, non-Hispanic black, any Hispanic ethnicity, Asian, and Other (reported as American Indian, Hawaiian/Pacific Islander, other race, >1 race or unknown). Similarly, available socioeconomic predictors were largely recorded based on self-report. Maternal education was obtained from the birth certificate record of
the infant and categorized by years of education (12, <12, and >12 years). Community dwelling was determined by the county of birth reported on the infant birth certificate record and categorized by the Federal Information Processing Standards code as 1 to 2: urban; 3 to 4: intermediate; and 5 to 6: rural. Insurance status was obtained from the hospital discharge records and categorized as public, private, or self-pay/other. Other predictors included birth hospital neonatal intensive care unit (NICU) level (classified as no NICU, intermediate, community, or regional) based on the California Department of Health Care Services (http://www.dhcs.ca.gov). Finally, infant clinical characteristics were assessed including gestational age at birth (classified as >38, 37–38, 34–36, or <34 weeks) and birth weight (classified as small for gestational age, birth weight <10th percentile), large for gestational age (birth weight >90th percentile), and adequate for gestational age.19 The remainder of the analysis was performed comparing non-Hispanic white with Hispanic patients given the large sample size in each group in California. The smaller sample size in the other racial/ethnic categories did not allow for meaningful comparisons and thus were excluded from the main analysis. Missing data were rare in this cohort; however, if a patient was missing data in any variable of interest they were excluded from the analysis.

The primary outcome was intended a priori as a composite outcome of 1-year mortality and unanticipated hospital readmissions. The composite outcome necessarily differed based on cardiac lesion. For patients with HLHS, the primary outcome was death (determined by death certificate or hospital discharge status) or >3 readmissions (hospitalizations not including the birth hospitalization) within the first year of life. This cutoff was chosen for HLHS given the need for at least 2 hospitalizations within the first year of life for additional diagnostic or surgical procedures. An additional hospitalization was added to account for minor illnesses that may lead to hospitalization due to a lower threshold for inpatient care. Similarly, for patients with d-TGA, the primary outcome was death or >1 readmission within the first year of life. Readmissions to any hospital were captured in this database.

Statistical Analysis
The analysis was performed for the entire cohort together while maintaining the primary outcome definitions for each lesion (HLHS and d-TGA). First, descriptive statistics were used to display baseline characteristics of the cohort by racial/ethnic group (non-Hispanic white and Hispanic). Then, we used a traditional approach by assessing the relationship between the predictors and our composite outcome as defined above in a univariable and multivariable logistic regression analysis. All factors in the univariable model (regardless of statistical significance) were included in the multivariable model. The results were presented as odds ratios (ORs) and 95% confidence intervals (CIs). To limit the data to the time period that socioeconomic factors may have the biggest impact, a sensitivity analysis was performed excluding patients who died before their neonatal hospital discharge (ie, only included patients who were discharged alive from their initial neonatal hospitalization).

We then performed a formal mediation analysis. The conceptual model is demonstrated in the Figure. A mediator is defined as a variable that is on the causal pathway between the predictor and outcome of interest. In other words, a predictor can influence a mediator, which then influences the outcome. In traditional analyses, mediators are often adjusted for when assessing the relationship between a predictor and primary outcome. However, this approach may abolish meaningful relationships between the predictor and outcome and falsely conclude a lack of association. Thus, performing formal mediation analyses allows the identification of factors that may explain the relationship between a predictor and an outcome. First, a set of potential mediators was determined a priori based on available data. Factors may mediate the relationship between racial/ethnic group and outcomes if the following 4 conditions are met: (1) race/ethnicity is associated with the outcome of interest; (2) racial/ethnic group is associated with a set of potential mediating socioeconomic factors; (3) a set of potential mediating factors are associated with the outcome of interest; and (4) including both racial/ethnic group and the set of mediating factors in a model changes the association between the outcome of interest and racial/ethnic group observed in condition 1. To test condition 1 and 3, we built univariable logistic regression models with the respective predictors and the composite outcome. To test condition 2, we used chi-square tests to assess the association between racial/ethnic group and each set of potential mediating factors.

To conduct the final condition, we used the derived mediation analysis method based on the counterfactual framework proposed by Yu and Li.20,21,22 The method was implemented using the mma package in the statistics software R (version 3.5.0) and explained in detail elsewhere.22 We used multiple additive regression trees to calculate the total direct effect, total indirect effect, and the individual effect of each mediator in the relationship of Hispanic ethnicity and poor outcome.22 The study was approved by the Committee for the Protection of Human Subjects within the California Health and Human Services Agency. All analyses were performed with software R (see above) and with STATA version 14.2 (StataCorp).
Results

Of the 3,160,268 live births, the prevalence of live-born infants with HLHS or d-TGA without chromosomal anomalies was 1,796 (0.05%) (d-TGA=832, HLHS=964). Baseline demographics of the entire population are listed in Table 1. There was a large proportion of non-Hispanic white and Hispanic patients in the population (46.7% Hispanic and 26.6% non-Hispanic white). Other racial/ethnic groups were less well represented (non-Hispanic black, n=93; Asian, n=188; other, n=200). Thus, the remainder of the analysis was performed comparing Hispanic patients (n=838) with non-Hispanic white patients (n=477). Demographics of this subpopulation are listed in Table 2. In general, Hispanic patients had fewer years of maternal education, higher rates of public insurance, younger maternal age, lived in urban communities, and their infants were born in community hospitals and were small for gestational age as compared with non-Hispanic white patients. There was no difference in mortality alone when comparing the 2 groups.

The univariable analysis assessing the composite primary outcome of 1-year mortality or unanticipated readmissions revealed several important associations as seen in Table 3. Patients of Hispanic ethnicity had significantly higher odds of a poor outcome as compared with non-Hispanic whites (crude OR, 1.72; 95% CI, 1.37–2.17). Several socioeconomic factors were associated with the composite outcome. In particular, maternal education >12 years and private insurance status were both associated with a significantly decreased odds of a poor outcome as compared with those with <12 years of education and public insurance status, respectively (education >12 years: crude OR, 0.5 [95% CI, 0.38–0.65]; private insurance: crude OR, 0.65; [95% CI, 0.45–0.71]). There was no significant association between Federal Information Processing Standards code and outcome or hospital NICU level and outcome. As expected, infants with a lower gestational age at birth and lower birth weight (ie, small for gestational age) had increased odds of a poor composite outcome. In addition, older maternal age (age >34 years) appeared to be associated with decreased odds of a poor outcome as compared with those who were younger than 18 years. Other infant and maternal characteristics were not associated with the primary composite outcome.

In the multivariable analysis, the protective effects of higher maternal education and private insurance status remained significant (maternal education >12 years: adjusted OR, 0.70 [95% CI, 0.49–0.98]; private insurance: adjusted OR, 0.73 [95% CI, 0.55–0.97]), while the effect of race/ethnicity became nonsignificant after adjusting for all variables in the univariable analysis (Table 3). Furthermore, prematurity remained a poor predictor of outcome (Table 3).

A sensitivity analysis was performed by excluding all patients who died before neonatal hospital discharge (n=1133, Table 4). In this analysis the primary outcome was
Table 1. Baseline Characteristics of the Entire Population

| Sociodemographic factors | White (n=477) | Hispanic (n=838) | Non-Hispanic Black (n=93) | Asian (n=188) | Other (n=200) |
|--------------------------|--------------|-----------------|---------------------------|--------------|--------------|
| Maternal education, y    |              |                 |                           |              |              |
| <12                      | 28 (5.9)     | 359 (42.8)      | 16 (17.2)                 | 16 (8.5)     | 28 (14.0)    |
| 12                       | 99 (20.8)    | 275 (32.8)      | 33 (35.5)                 | 32 (17.0)    | 48 (24.0)    |
| >12                      | 333 (70.0)   | 184 (22.0)      | 41 (44.1)                 | 133 (70.4)   | 61 (30.5)    |
| Missing                  | 17 (3.6)     | 20 (2.4)        | 3 (3.2)                   | 7 (3.7)      | 63 (31.5)    |
| Insurance status         |              |                 |                           |              |              |
| Public                   | 127 (26.6)   | 610 (72.8)      | 64 (68.8)                 | 51 (27.1)    | 95 (47.5)    |
| Private                  | 329 (69.0)   | 197 (23.5)      | 25 (26.9)                 | 131 (69.7)   | 97 (48.5)    |
| Self-pay/other           | 20 (4.2)     | 30 (3.6)        | 4 (4.3)                   | 6 (3.2)      | 8 (4.0)      |
| Missing                  | 1 (0.2)      | 1 (0.1)         | NA                        | NA           | NA           |
| Maternal age, y          |              |                 |                           |              |              |
| <18                      | 4 (0.8)      | 28 (3.3)        | 2 (2.2)                   | 2 (1.1)      | 8 (4.0)      |
| 18–34                    | 358 (75.1)   | 688 (82.1)      | 79 (85.0)                 | 146 (77.7)   | 158 (79.0)   |
| >34                      | 115 (24.1)   | 122 (14.6)      | 12 (12.9)                 | 40 (21.3)    | 34 (17.0)    |
| FIPS code                |              |                 |                           |              |              |
| Urban                    | 323 (67.7)   | 637 (76.0)      | 75 (80.6)                 | 143 (76.1)   | 145 (72.5)   |
| Intermediate             | 131 (27.5)   | 193 (23.0)      | 18 (19.4)                 | 36 (19.2)    | 33 (16.5)    |
| Rural                    | 13 (2.7)     | 4 (0.5)         | NA                        | NA           | 4 (2.0)      |
| Missing                  | 10 (2.1)     | 4 (0.5)         | NA                        | 9 (4.8)      | 18 (9)       |
| Birth hospital NICU level|              |                 |                           |              |              |
| No NICU                  | 131 (27.5)   | 211 (25.2)      | 13 (13.9)                 | 51 (27.1)    | 30 (15)      |
| Intermediate             | 22 (4.6)     | 35 (4.2)        | 4 (4.3)                   | 5 (2.6)      | 4 (2)        |
| Community                | 176 (36.9)   | 393 (46.9)      | 44 (47.3)                 | 86 (45.7)    | 84 (42)      |
| Regional                 | 148 (31.0)   | 199 (23.8)      | 32 (34.5)                 | 46 (24.6)    | 82 (41)      |
| Infant factors           |              |                 |                           |              |              |
| Gestational age, wk      |              |                 |                           |              |              |
| >38                      | 250 (52.4)   | 442 (52.7)      | 52 (55.9)                 | 91 (48.4)    | 94 (47)      |
| 37–38                    | 156 (32.7)   | 260 (31.0)      | 28 (30.1)                 | 74 (39.4)    | 77 (38.5)    |
| 34–36                    | 48 (10.1)    | 94 (11.2)       | 7 (7.5)                   | 15 (8)       | 19 (9.5)     |
| <34                      | 23 (4.8)     | 42 (5.0)        | 6 (6.5)                   | 8 (4.3)      | 10 (5)       |
| Birth weight             |              |                 |                           |              |              |
| SGA                      | 42 (8.8)     | 120 (14.3)      | 64 (68.8)                 | 150 (79.8)   | 157 (78.5)   |
| AGA                      | 400 (83.9)   | 649 (77.5)      | 21 (22.6)                 | 33 (17.5)    | 30 (15)      |
| LGA                      | 35 (7.3)     | 69 (8.2)        | 8 (8.6)                   | 5 (2.7)      | 13 (6.5)     |
| Female sex               | 164 (34.4)   | 284 (33.9)      | 42 (45.2)                 | 73 (38.8)    | 69 (34.5)    |
| Outcomes                 |              |                 |                           |              |              |
| LOS, median (IQR)        | 17 (2–50)    | 17 (2–62)       | 14 (2–64)                 | 14 (2–31)    | 20 (4–42)    |
| 1-y Mortality            | 80 (16.7)    | 171 (20.4)      | 19 (20.4)                 | 30 (16.0)    | 37 (18.5)    |
| Mortality before discharge| 52 (10.9)    | 130 (15.5)      | 11 (11.8)                 | 20 (11.7)    | 28 (14.0)    |
| Mortality after discharge| 28 (5.8)     | 41 (4.9)        | 8 (8.6)                   | 10 (5.3)     | 9 (4.5)      |

Continued
Socioeconomic Factors and Outcome in Congenital Heart Disease

Peyvandi et al

Mediation Analysis

To perform the mediation analysis for the primary outcome, 3 conditions were assessed and met for the entire cohort. In particular, Table 3 demonstrates that Hispanic ethnicity is associated with the primary outcome (condition 1). Table 2 demonstrates that a set of potential mediating factors (maternal education, insurance status, maternal age, Federal Information Processing Standards score, NICU level, and birth weight) is associated with maternal race/ethnicity (condition 2). Finally, Table 3 demonstrates the mediating factors (maternal education, insurance status, maternal age, and birth weight) that are associated with the primary outcome (condition 3). Table 5 demonstrates the final step of the mediation analysis. The total direct effect of race/ethnicity on outcome was 37.8% (95% CI, 1.3–69.6), while the total indirect effect (all mediators included) was 62.2% (95% CI, 30.4–101.3). In other words, as compared with non-Hispanic white ethnicity, Hispanic ethnicity explains 37.8% of the poor outcome, while the remainder (62.2%) is explained by mediating or indirect factors. Maternal education accounted for 33.2% of the relationship between Hispanic ethnicity and outcome (95% CI, 7.0–66.4), while insurance status explained 27.6% of the relationship (95% CI, 6.5–63.1). In contrast, birth weight and maternal age did not appear to be statistically significant mediators (birth weight: 1.5% [95% CI, −2.5 to 5.7]; maternal age: 1.9% [95% CI, −0.8 to 6.2]).

The mediation analysis was then repeated for the outcome excluding patients who died before neonatal hospital discharge (ie, death after discharge from neonatal hospitalization or unexpected readmissions). In this analysis, only maternal education and insurance status were included as possible mediators that fulfilled conditions 1 to 3 (Table 5). The total direct effect of Hispanic ethnicity on outcome was 28.5% (95% CI, −4.4 to 77.5), while the total indirect effect (all mediators included) was 71.4% (95% CI, 5–102). Maternal education accounted for 42% of the relationship between Hispanic ethnicity and outcome, while insurance status explained 38.3% of the relationship.

Discussion

In this large population-based sample from the state of California, we demonstrate the influence of specific socioeconomic mediators on the relationship between race/ethnicity and postnatal outcomes in HLHS and d-TGA. In particular, maternal education explains almost half of the association seen between Hispanic ethnicity and mortality or unexpected hospital readmissions in the first year of life in this population. Interestingly, infant characteristics themselves play a non-significant role. Our results identify socioeconomic factors within racial/ethnic groups that can influence 1-year outcomes in a CHD population in a large, homogeneous sample of patients and provides targets for intervention.

Racial and Ethnic Disparities in CHD

Several studies have suggested a relationship between race/ethnicity and various outcomes in CHD. This disparity dates back to older eras and continues to be seen in more contemporary cohorts.6,7,9,14,23 Although survival has increased over time in general for various subtypes of CHD,24 the disparity in outcome between those who are non-Hispanic white versus non-Hispanic black or Hispanic remains in the United States. Boneva et al25 demonstrated

Table 1. Continued

| Condition | White (n=477) | Hispanic (n=838) | Non-Hispanic Black (n=93) | Asian (n=188) | Other (n=200) |
|-----------|--------------|-----------------|--------------------------|--------------|--------------|
| 1-y Mortality or unexpected readmission | 213 (44.6) | 448 (58.2) | 49 (52.7) | 79 (42.0) | 92 (46.0) |
| Mortality after discharge or unexpected admission | 161 (37.9) | 358 (50.6) | 38 (46.3) | 59 (35.1) | 64 (37.2) |

Values are expressed as number (percentage). AGA indicates adequate for gestational age; FIPS, Federal Information Processing Standards (code 1 to 2: urban; code 3 to 4: intermediate; and code 5 to 6: rural); IQR, interquartile range; LGA, large for gestational age (<90th percentile); LOS, length of stay (duration of initial hospitalization for infants who survived to discharge); NA, not available; NICU, neonatal intensive care unit; SGA, small for gestational age (<10th percentile).
### Table 2. Baseline Characteristics of the Patient Subpopulation Included in the Analysis

| Characteristics                      | Non-Hispanic White (n=477) | Hispanic (n=838) | P Value* |
|--------------------------------------|-----------------------------|------------------|----------|
| **Sociodemographic factors**         |                             |                  |          |
| Maternal education, y                |                             |                  | <0.001   |
| <12                                  | 28 (5.9)                    | 359 (42.8)       |          |
| 12                                   | 99 (20.8)                   | 275 (32.8)       |          |
| >12                                  | 333 (70.0)                  | 184 (22.0)       |          |
| Missing†                             | 17 (3.6)                    | 20 (2.4)         |          |
| Insurance status                     |                             |                  | <0.001   |
| Public                               | 127 (26.6)                  | 610 (72.8)       |          |
| Private                              | 329 (69.0)                  | 197 (23.5)       |          |
| Self-pay/other                       | 20 (4.2)                    | 30 (3.6)         |          |
| Missing                              | 1 (0.2)                     | 1 (0.1)          |          |
| Maternal age, y                      |                             |                  | <0.001   |
| <18                                  | 4 (0.8)                     | 28 (3.3)         |          |
| 18–34                                | 358 (75.1)                  | 688 (82.1)       |          |
| >34                                  | 115 (24.1)                  | 122 (14.6)       |          |
| FIPS code                            |                             |                  | <0.001   |
| Urban                                | 323 (67.7)                  | 637 (76.0)       |          |
| Intermediate                         | 131 (27.5)                  | 193 (23.0)       |          |
| Rural                                | 13 (2.7)                    | 4 (0.5)          |          |
| Missing                              | 10 (2.1)                    | 4 (0.5)          |          |
| Birth hospital NICU level            |                             |                  | <0.003   |
| No NICU                              | 131 (27.5)                  | 211 (25.2)       |          |
| Intermediate                         | 22 (4.6)                    | 35 (4.2)         |          |
| Community                            | 176 (36.9)                  | 393 (46.9)       |          |
| Regional                             | 148 (31.0)                  | 199 (23.8)       |          |
| **Infant factors**                   |                             |                  | 0.879    |
| Gestational age, wk                  |                             |                  |          |
| >38                                  | 250 (52.4)                  | 442 (52.7)       |          |
| 37 to 38                             | 156 (32.7)                  | 260 (31.0)       |          |
| 34 to 36                             | 48 (10.1)                   | 94 (11.2)        |          |
| <34                                  | 23 (4.8)                    | 42 (5.01)        |          |
| Birth weight                         |                             |                  | 0.009    |
| SGA                                  | 42 (8.8)                    | 120 (14.3)       |          |
| AGA                                  | 400 (83.9)                  | 649 (77.5)       |          |
| LGA                                  | 35 (7.3)                    | 69 (8.2)         |          |
| Female sex                           | 164 (34.4)                  | 284 (33.9)       | 0.857    |
| **Outcomes**                         |                             |                  |          |
| LOS, median (IQR)                    | 17 (2–50)                   | 17 (2–62)        | 0.66     |
| 1-y Mortality                        | 80 (16.7)                   | 171 (20.4)       | 0.107    |
| Mortality before discharge           | 52 (10.9)                   | 130 (15.5)       | 0.068    |
| Mortality after discharge            | 28 (5.8)                    | 41 (4.9)         | 0.068    |

Continued
these trends in overall survival with no change in racial disparities over a period of 30 years. In particular, non-Hispanic black patients with CHD continued to have at least a 19% disparity in death over this prolonged time period as compared with non-Hispanic white patients. These trends have also been seen in more contemporary cohorts.\(^8,26\) In our study, we were unable to make any meaningful conclusions about the effect of black race on outcome as compared with non-Hispanic white patients because of the relatively low percentage of black infants in this cohort, although our data suggested a trend towards increased 1-year mortality and a poor composite outcome for black patients compared with non-Hispanic white patients (Table 1). However, there was a large number of Hispanic patients in the cohort allowing for meaningful comparisons with the reference group (non-Hispanic white patients). Although there did not appear to be a difference by race/ethnicity when assessing mortality alone in our cohort, we found that in a univariable analysis, Hispanic ethnicity was associated with a poor outcome (1-year mortality or hospital readmissions) as compared with non-Hispanic white patients. Interestingly, this effect of Hispanic ethnicity disappeared in the multivariable model after adjusting for various socioeconomic factors and maternal and infant characteristics. This suggests that these other factors may play a stronger role in outcome since they are controlled for in multivariable analysis. This traditional analytic approach only allows for assumptions based on hypothesized mechanisms (ie, confounders and mediators) explaining the relationship between predictor and outcome. Thus, the formal mediation analysis performed in this study allows for a stronger conclusion regarding the effects of race/ethnicity and socioeconomic factors on outcome in this population.

### Socioeconomic Factors

Although race and ethnicity are critical in understanding health disparities in CHD outcomes, understanding socioeconomic factors within racial/ethnic groups that contribute to poor outcomes is crucial to identify targets for intervention.\(^10\)\(^–\)\(^12\) As a conceptual model, we used mediation analysis to better identify these other factors without removing race/ethnicity from the equation as an influence on outcomes. The importance of other socioeconomic factors as mediators of the relationship between race/ethnicity and outcome has been explored in other patient populations, although not often in the CHD literature. For example, in a large population-based study assessing causes of fetal death, maternal, fetal, and socioeconomic factors mediated a large percentage of fetal death seen in black and Hispanic patients compared with non-Hispanic white patients.\(^27\)

Various socioeconomic factors (ie, poverty, access to care, and insurance status) have been shown to play a role in outcomes of CHD utilizing traditional analyses.\(^26,28–30\) Conducting mediation analysis led us to find that maternal education explains a large percentage of the poor outcome seen in Hispanic patients as compared with non-Hispanic whites with HLHS and d-TGA. Education levels have been shown to be a strong indicator of socioeconomic disparity in health-related outcomes.\(^11\) Educational status reflects a range of social characteristics that can influence ones’ health such as general and health-related knowledge and literacy and problem-solving skills. In addition to level of education, quality of education and access to material resources can influence health outcomes. Importantly, given our research in the pediatric population, maternal education is thought to play a significant role in children’s health outcomes not only in childhood but also across the lifespan. For example, parental education levels can have downstream effects on their children’s earnings, occupation, and health in adult years.\(^31,32\) Maternal education has repeatedly been shown to be significantly associated with neurodevelopmental outcomes in children born prematurely\(^33,34\) and even in children with complex CHD.\(^35\) Therefore, not only can maternal education influence shorter-term outcomes in the CHD population, we would expect it to continue influencing longer-term outcomes including neurodevelopment, successful transition to independence in adulthood, and quality of life. Further studies should address the question of whether specific educational interventions can alter outcomes in these high-risk infants.
Table 3. Crude and Adjusted Analyses of Factors Associated With Poor Outcome (Defined as 1-Year Mortality or >1 Readmission for Dextro-Transposition of the Great Arteries and Mortality or >3 Readmissions for Hypoplastic Left Heart Syndrome)

| Characteristics               | Crude OR (95% CI) | Adjusted OR* (95% CI) |
|-------------------------------|------------------|-----------------------|
| **Sociodemographic factors**  |                  |                       |
| Maternal race                 |                  |                       |
| White                         | Reference        | Reference             |
| Hispanic                      | 1.72 (1.37–2.17) | 1.21 (0.92–1.62)      |
| **Maternal education, y**     |                  |                       |
| <12                           | Reference        | Reference             |
| 12                            | 0.78 (0.58–1.04) | 0.90 (0.66–1.23)      |
| >12                           | 0.50 (0.38–0.65) | 0.70 (0.49–0.98)      |
| **Insurance status**          |                  |                       |
| Public                        | Reference        | Reference             |
| Private                       | 0.65 (0.45–0.71) | 0.73 (0.55–0.97)      |
| Self-pay/other                | 0.74 (0.42–1.32) | 0.84 (0.46–1.52)      |
| **Maternal age, y**           |                  |                       |
| <18                           | Reference        | Reference             |
| 18–34                         | 0.63 (0.30–1.31) | 0.78 (0.35–1.73)      |
| >34                           | 0.45 (0.21–0.98) | 0.65 (0.28–1.51)      |
| **FIPS code**                 |                  |                       |
| Urban                         | Reference        | Reference             |
| Intermediate                  | 0.83 (0.64–1.07) | 0.84 (0.64–1.09)      |
| Rural                         | 0.74 (0.28–1.93) | 1.06 (0.38–3.0)       |
| **Birth hospital NICU level** |                  |                       |
| No NICU                       | Reference        | Reference             |
| Intermediate                  | 1.63 (0.92–2.90) | 1.72 (0.94–3.15)      |
| Community                     | 1.20 (0.92–1.57) | 1.07 (0.80–1.42)      |
| Regional                      | 1.24 (0.92–1.67) | 1.12 (0.81–1.55)      |
| **Infant factors**            |                  |                       |
| Gestational age, wk           |                  |                       |
| >38                           | Reference        | Reference             |
| 37–38                         | 1.21 (0.95–1.55) | 1.26 (0.97–1.63)      |
| 34–36                         | 1.37 (0.95–1.97) | 1.30 (0.89–1.91)      |
| <34                           | 2.25 (1.30–3.89) | 2.16 (1.22–13.84)     |
| Birth weight                  |                  |                       |
| SGA                           | 1.41 (1.01–1.98) | 1.27 (0.89–1.81)      |
| AGA                           | Reference        | Reference             |
| LGA                           | 0.83 (0.56–1.25) | 0.83 (0.55–1.26)      |
| Female sex                    | 1.04 (0.83–1.31) | 0.98 (0.77–1.25)      |

AGA indicates adequate for gestational age; CI, confidence interval; FIPS, Federal Information Processing Standards (code 1 to 2: urban; code 3 to 4: intermediate; and code 5 to 6: rural); LGA, large for gestational age (>90th percentile); NICU, neonatal intensive care unit; OR, odds ratio; SGA, small for gestational age (<10th percentile). *Adjusted for all variables listed in the table. †Denotes statistical significance at the P < 0.05 level.

While maternal education mediated the largest percentage of ethnic/racial disparity in the current study, insurance status was also mediating a significant percentage of this disparity. This is consistent with the findings of Erickson et al, who demonstrated that children with CHD and private insurance were found to be cared for more often at lower mortality hospitals as compared with those with public insurance.

In our study, county of residence (rural versus urban) and the level of NICU care (none, intermediate, community, and regional) did not appear to influence the primary outcome and thus did not qualify as mediators. However, both of these factors are relatively weak surrogate markers for poverty or access to care and may not be sensitive enough to truly assess this important socioeconomic factor. Further studies are needed to investigate the impact of high-poverty regions and access to care (ie, prospective collection of more granular data such as home address and distance to treating hospitals) as mediators in the complex relationship between race/ethnicity and outcomes in infants with CHD. This limitation can also explain the fact that a direct effect of race/ethnicity on our primary outcome (37.8%) was noted in the mediation analysis (Table 3). This does not suggest that biologic influences of race/ethnicity can explain 37.8% of the relationship with the primary outcome, but may reflect the fact that other mediating socioeconomic factors such as access to care, income, and occupation were not included in the model.

**Study Limitations**

There are several notable limitations to our study. First, a challenge to using administrative data is the correct ascertainment of the diagnosis using ICD-9 codes. It is possible that cases were missed; however, cases were captured from multiple sources including birth hospitalization and transfer and readmission records during the first year of life. Misclassification is also possible. To minimize this risk, 2 physicians independently reviewed every case with multiple codes for CHD. Nonetheless, we cannot exclude the possibility of misclassification of infants with CHD based on ICD-9 codes. Despite this possibility, the incidence of CHD and these particular lesions is consistent with previous population-based studies. Infants with chromosomal abnormalities and other major congenital birth defects were excluded from the study given that these infants have a much higher risk of medical complications and poor outcomes as compared with those with isolated CHD. However, future studies should be powered to understand whether race/ethnicity and/or socioeconomic status influences outcomes in this subgroup of patients as well. Our decision to use a composite outcome of mortality or readmissions a priori was based on mortality...
Table 4. Crude and Adjusted Analyses Demonstrating the Sensitivity Analysis

| Characteristics                  | Crude OR (95% CI) | Adjusted OR* (95% CI) |
|----------------------------------|-------------------|-----------------------|
| **Sociodemographic factors**     |                   |                       |
| Maternal race                    | Reference         | Reference             |
| Hispanic                         | 1.67 (1.31–2.14)† | 1.13 (0.83–1.54)      |
| Maternal education, y            |                   |                       |
| <12                              | Reference         | Reference             |
| 12                               | 0.73 (0.53–0.99)† | 0.85 (0.61–1.20)      |
| >12                              | 0.48 (0.36–0.64)† | 0.65 (0.45–0.94)†     |
| Insurance status                 |                   |                       |
| Public                           | Reference         | Reference             |
| Private                          | 0.55 (0.43–0.70)† | 0.70 (0.52–0.96)†     |
| Self-pay/other                   | 0.85 (0.46–1.54)  | 0.92 (0.50–1.72)      |
| FIPS code                        |                   |                       |
| Urban                            | Reference         | Reference             |
| Intermediate                     | 0.84 (0.64–1.10)  | 0.82 (0.62–1.10)      |
| Rural                            | 1.0 (0.38–2.61)   | 1.33 (0.47–3.76)      |
| Birth hospital NICU level        |                   |                       |
| No NICU                          | Reference         | Reference             |
| Intermediate                     | 1.57 (0.85–2.90)  | 1.60 (0.84–3.04)      |
| Community                        | 1.19 (0.90–1.59)  | 1.11 (0.81–1.50)      |
| Regional                         | 1.08 (0.78–1.50)  | 1.03 (0.72–1.47)      |
| **Infant factors**               |                   |                       |
| Gestational age, wk              |                   |                       |
| >38                              | Reference         | Reference             |
| 37–38                            | 1.17 (0.90–1.51)  | 1.19 (0.90–1.56)      |
| 34–36                            | 1.07 (0.72–1.61)  | 1.0 (0.66–1.54)       |
| <34                              | 0.68 (0.32–1.45)  | 0.64 (0.29–1.43)      |
| Fetal growth                     |                   |                       |
| SGA                              | 1.19 (0.82–1.73)  | 1.14 (0.77–1.68)      |
| AGA                              | Reference         | Reference             |
| LGA                              | 0.86 (0.56–1.36)  | 0.85 (0.53–1.33)      |
| Female sex                       | 0.94 (0.73–1.21)  | 0.92 (0.71–1.20)      |

Factors associated with the outcome after excluding all patients who died before neonatal hospital discharge are listed (defined as mortality after discharge or ≥1 readmission for dextro-Transposition of the great arteries and mortality after discharge or ≥3 readmission for hypoplastic left heart syndrome). AGA indicates adequate for gestational age; CI, confidence interval; FIPS, Federal Information Processing Standards (code 1 to 2: urban; code 3 to 4: intermediate; and code 5 to 6: rural); LGA, large for gestational age (>90th percentile); NICU, neonatal intensive care unit; OR, odds ratio; SGA, small for gestational age (<10th percentile).†Adjusted for all variables listed in the table.

*Denotes significance at the P < 0.05 level

being relatively rare in this cohort and the complex relationship between readmissions and mortality that could not be disentangled with this administrative database. A limitation of this approach is the fact that the underlying reason for the readmission was unknown; however, we attempted to mitigate this effect by choosing an appropriate cutoff for the number of readmissions for each lesion that would suggest readmission beyond what would be expected for routine clinical care. In addition, this database did not have information on cardiac transplantation as another component of outcome for these patients.

Finally, we lacked data on clinical variables that may have acted as effect modifiers or mediators such as surgical repair details and prenatal diagnosis of CHD, thus these variables were not included in the analysis. To minimize the influences of surgical and immediate postoperative complications on our primary outcome, we performed sensitivity analysis by excluding patients who died before discharge from their neonatal hospitalization. This analysis attempts to move beyond outcomes related solely to surgical repair and initial hospitalization and instead focuses on environmental and socioeconomic factors that these children are exposed to once they are discharged home. We found that even when excluding patients who died before hospital discharge, maternal education and insurance status continued to play a strong role in explaining the relationship between race/ethnicity and outcome. In fact, the effect of these mediators seemed stronger in the sensitivity analysis. In particular, the total indirect effect (ie, effect of mediators) was 9% higher when excluding patients who died before hospital discharge (Table 3).

**Study Strengths**

The strengths of our study include the large sample size, which included a large percentage of patients of Hispanic ethnicity, the focus on 2 homogeneous groups of complex CHD (HLHS and d-TGA) both requiring a neonatal operation, and the primary outcome chosen. By focusing on 2 forms of well-characterized complex CHD, we narrowed the focus of this analysis to infants who undergo a neonatal operation with typical surgical management strategies in the current era. We chose to assess the entire cohort in our analysis rather than each individual lesion for multiple reasons. First, the definition of having a poor outcome differed for HLHS and d-TGA, reflecting the inherent differences between these 2 lesions. Second, as mentioned above, the goal of this study was to understand the socioeconomic or environmental factors that these patients are exposed to once they are discharged home from the hospital. Thus, we would not expect that the specific cardiac lesion would influence socioeconomic factors such as maternal education and insurance status.
Table 5. Mediation Analysis

|                      | Primary Outcome: 1-y Mortality or Unexpected Readmissions (as Defined for Each Lesion) | Sensitivity Analysis: 1-y Mortality After Discharge From the Hospital or Unexpected Readmission (as Defined for Each Lesion) |
|----------------------|--------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------|
| Total direct effect, % | 37.8 (1.3–69.6)                                                                            | 28.5 (–4.4 to 77.5)                                                                                              |
| Total indirect effect, % | 62.2 (30.4–101.3)                                                                         | 71.4 (5–102)                                                                                                     |
| Maternal education, % | 33.2 (7.0–66.4)                                                                             | 42.0 (22.5–144)                                                                                                  |
| Insurance status, %   | 27.6 (6.5–63.1)                                                                             | 38.3 (5–102)                                                                                                     |
| Maternal age, %       | 1.9 (–0.8–6.2)                                                                             | NA                                                                                                               |
| Birth weight, %       | 1.5 (–2.5–5.7)                                                                             | NA                                                                                                               |

The impact of potential mediating factors that can explain racial/ethnic differences in outcome in Hispanic patients compared with non-Hispanic white patients. The percent explained is listed for the total direct and indirect effects of Hispanic ethnicity on outcome as compared with non-Hispanic whites and for each mediator included in the analysis. Only mediators that fulfilled each condition were included in the analysis as described in the methods. Condition 1: maternal race/ethnicity is associated with the primary outcome as well as the secondary outcome for the sensitivity analysis; condition 2: maternal race/ethnicity is associated with potential mediators as listed in Table 1 (maternal education, insurance status, maternal age, Federal Information Processing Standards score, neonatal intensive care unit level, and birth weight); condition 3: mediators are associated with the primary and secondary outcome as listed in Tables 3 and 4 (primary outcome: maternal education, insurance status, maternal age and birth weight; secondary outcome: maternal education, and insurance status). NA indicates not available.

*The sum of the percent explained effects of the individual mediators may not equal the total indirect effect because of correlation and overlapping mediation effects among mediators that is reflected in the total indirect effect but not the individual mediators.

Conclusions

Race/ethnicity continues to play an important role in 1-year outcomes among those with HLHS and d-TGA in a contemporary population-based cohort in California. Socioeconomic factors such as maternal education and insurance status seem to explain, in part, the poorer outcomes seen in Hispanic patients in California. These findings begin to identify specific factors within racial/ethnic groups that can be targeted for intervention. Community engagement and outreach to at-risk communities is a strategy that can identify specific barriers to healthcare access and in some cases has been shown to improve health outcomes in the pediatric population. For example, clinical-community collaborations have been shown to improve health-related outcomes by focusing on tailored provider training (increasing awareness of socioeconomic factors that influence health), optimal use of electronic health records (enhance awareness of available community resources), and innovate use of clinical space to enhance community engagement. Providing additional resources to these vulnerable populations has the potential to improve both short- and long-term outcomes, in addition to being cost-effective (ie, decreasing the number total hospital admissions). Further work is being performed to assess cost-effectiveness and to incorporate other measures of socioeconomic status.

Disclosures

None.

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