European Society for Paediatric Research
Society for Pediatric Research
www.nature.com/pr

POPULATION STUDY ARTICLE

Association of social determinants with the severity of congenital heart disease

Mario J. Forero-Manzano[1,2,3], Eddy Triana-Palencia[2], Jenny A. Figueroa-Rueda[2], Claudia X. Flórez-Rodríguez[1,2,3], Javier M. Castro-Monsalve[1,2], Doris C. Quintero-Lesmes[4]✉ and Edna M. Gamboa-Delgado[5]

BACKGROUND: Congenital heart diseases are the most prevalent congenital malformations and cause greater morbi-mortality in newborns and infants. The aim of this study was to analyze the social determinants in families with children with the severity of congenital heart disease.
METHODS: Analytical cross-sectional study in 140 families of children with congenital heart disease to whom a structured survey was applied addressing topics related to family structure, health, economic conditions, exposure factors, and other social conditions relevant to the study, during 1 year.
RESULTS: In all, 53.7% of the studied population belonged to low socioeconomic levels. No association was found between the severity of the heart disease and the presence of pathological antecedents in the parents. The families resided in urban areas. Also, 28.3% of the mothers had four or fewer prenatal controls during pregnancy. Only 22% of heart diseases were diagnosed during pregnancy. It was found that exposure to cigarette and wood smoke during pregnancy, in addition to low socioeconomic status, was associated with greater severity of heart disease (RACHS-1 and STS-Score), when evaluated by pathophysiological groups (cyanotic/non-cyanotic/single ventricle).
CONCLUSIONS: Exposure to cigarette smoke, wood smoke during pregnancy, and low socioeconomic status turned out to be social determinants associated with the severity of heart disease analyzed by pathophysiological groups.

Pediatric Research (2023) 93:1391–1398; https://doi.org/10.1038/s41390-022-02205-6

IMPACT:

- The social component has not been well characterized as a cause of congenital heart disease, especially in countries like ours, where the existence of gaps and social inequities have a high impact.
- The findings of this study could have an impact on public health to the extent that policies are implemented to reduce exposure to cigarettes, especially during pregnancy.
- Knowledge of these changes and their measurement in this type of pathology could open the door to the creation of policies aimed at their prevention, focusing on the local risk factors found, which can impact the disease.

INTRODUCTION

Congenital heart disease (CHD) represents the most common form of congenital malformations, with an estimated incidence of 8–12 cases per 1000 live births, being the first cause of death within this group, explaining 6–10% of the overall mortality and up to 40% of deaths from congenital defects.[1] Although the proposed etiology is multifactorial,[2] the studies reported to date show variable results, noting ethnic, racial, demographic, socioeconomic, and exposure differences, among others. These variations can also be explained by the availability of diagnostic methods and the type of study used.[3–5] Approximately 25% of CHDs have a known genetic cause, 10% have associated environmental factors, and the remaining 65% remain of unknown cause, possibly of a multifactorial and epigenetic nature.[4,6]

On the other hand, the World Health Organization (WHO) defines the Social Determinants of Health, DSS, as "the circumstances in which people are born, grow, work, live and age, including the broader set of forces and systems that influence the conditions of everyday life."[6] Through the different conferences and declarations made on this topic, a consensus has been reached in which the key to dealing with the profound inequities that exist today between various groups of the population, both globally and within each country, is to generate a growing collective awareness of the need to intervene in such determinants.[6]

[1]Neumología Pediátrica, Hospital Internacional de Colombia HIC – Instituto Cardiovascular, Fundación Cardiovascular de Colombia, Piedecuesta, Santander, Colombia. [2]Servicio de Cardiocirugía Pediátrica, Hospital Internacional de Colombia HIC – Instituto Cardiovascular, Fundación Cardiovascular de Colombia, Piedecuesta, Santander, Colombia. [3]Fundación Universitaria FCV, Floridablanca, Santander, Colombia. [4]Centro de Investigaciones, Fundación Cardiovascular de Colombia FCV, Floridablanca, Santander, Colombia. [5]Escuela de Nutrición y Dietética, Universidad Industrial de Santander, Bucaramanga, Santander, Colombia. ✉email: dorisquintero@fcv.org

Received: 1 March 2022 Revised: 3 June 2022 Accepted: 22 June 2022
Published online: 19 August 2022

It is of great importance for society to clarify how inequalities in the distribution of social goods such as income, wealth, stable employment, healthy eating, healthy lifestyles, access to health services, education, and recreation, among others, are manifested by generating differences unfair in the health status of social groups.[7] Few studies have analyzed CHD from the perspective of the social determinants of health. Findings from these studies have found that low socioeconomic status, low income, and low parental education represent a higher risk for the development of heart disease.[1,8,9] However, these associations are not enough to explain most CHDs, so this study aimed to analyze the social determinants in a group of families with children affected by CHD, performing an analysis based on the severity of the disease and their association with such determinants.

METHODS

Design

This is an analytical cross-sectional study.

Population and sample

The study population comprises 140 families of children with CHD treated in a high complexity institution, specializing in cardiovascular diseases, in the city of Bucaramanga.

Study variables

The main dependent variables were the presence of CHD classified according to Mortality risk defined by the RACHS-1 Score (Risk Adjustment in Congenital Heart Surgery) and Complexity defined by the STS Score (Society of Thoracic Surgeons score). The independent variables considered were: sex, age (months), birth weight (g), socioeconomic level, parents' education, parents' occupation and age, family income, displacement status, place of residence, prenatal maternal nutritional status. birth control, nutritional status of the child, maternal prenatal exposures (smoking, insecticides, herbicides, alcohol, psychoactive substances), maternal and paternal diseases, access to health services, participation in programs and public policies, number of children, time of onset of symptoms and attendance at medical centers, and history of congenital malformations in relatives up to the second degree (history of CHD in relatives).

Data collection

This process was carried out for 12 months, in which a survey was conducted on the mother, father, or main caregiver who was able to answer it. The data collection activity was carried out by two professional nurses who are part of the pediatric heart surgery service, previously trained by the study researchers. All parents or caregivers of the participants who agreed to participate in the study signed an informed consent form. Families were selected from hospital and outpatient services.

Data quality

Data quality was checked to ensure data completeness. The survey was conducted digitally using tablets to capture the information. The questionnaire was created on the Commcare mobile platform and the data were recorded in a database in the Excel program.

Statistical analysis

A descriptive analysis was performed in which the categorical variables were expressed as proportions and the continuous variables as arithmetic means and their corresponding standard deviation (SD) if they had a normal distribution. Otherwise, these variables were described as medians and their interquartile range (IR). Chi^2 test was used to determine whether there were statistically significant differences between the categorical variables and the Student's *t* test or the Mann–Whitney *U*-test for the continuous variables, according to their distribution. The analyses were performed in Stata version 15.

RESULTS

Characteristics of the participants

The sample consisted of 140 families, most of them (82.8%) belonging to low socio-economic levels (taking into account the socioeconomic stratum defined by the National Administrative Department of Statistics, DANE, and the Beneficiary Selection System for Programs Social -SISBEN-). Family income (in terms of current legal monthly minimum wages) was also taken into account.[10] There was no sex predominance. In all, 22% of children were diagnosed with heart disease during pregnancy. The median age of the child population included was 8.7 months (IR: 30 months). Most families lived in urban areas (73.5%), with a predominant percentage from the Colombian Andean area (53.7%), 28.2% from the Caribbean area, 7.5% from the Orinoquía, and 2.0% were international patients (Aruba, Venezuela, and Ecuador). No significant differences were found in the evaluation of social determinants regarding the severity of heart disease (based on the analysis of the RACHS-1 (from the English: Risk Adjustment in Congenital Heart Surgery) and the STS (from the English, Society of Thoracic Surgeons score).[11,12] No statistically significant differences were found either for the severity and mortality from CHD according to the age of the parents, the number of children, origin, religion, belonging to minority population groups, schooling, and occupation of the parents, and their family income. Table 1 summarizes the main variables included.

The families were made up of both parents and between one and three children (93%). Three couples (2.1%) were consanguinity. Most of the mothers were housewives (67.1%) with a median age of 24 years, while for the fathers it was 30 years. Thirty-eight (27.1%) of them had a formal employment relationship in different professions, the main profession being agriculture (18.6%), followed by jobs related to construction (12.4%). Eleven couples (7.6%) belonged to some indigenous ethnic group. The mothers had completed 11 academic years on average and the men 10 years. Regarding the personal pathological history, 10.3% of the mothers and 8.9% of the fathers had a history of diseases, such as asthma, diabetes, and hypertension, among others. Only one of the mothers had a history of CHD (tetralogy of Fallot). In all, 75.6% of the mothers had a normal preconception nutritional status.

Of the total, 26.9% of the women had started prenatal control after the fourth month of gestation and 28.3% managed to perform four or fewer prenatal controls. About 5% of the women stated that they had used psychoactive drugs during pregnancy, 12.4% alcoholic beverages, 11.7% smoked cigarettes, 36% of the mothers reported frequently sharing spaces with cigarette smokers, 48.5% reported contact with substances for agricultural use, and 34.2% daily exposure to wood smoke.

Seventeen women (12.1%) were diagnosed with micronutrient deficiency during pregnancy, 13 of them due to anemia. Twenty-three (15.9%) received some type of antibiotic (especially beta-lactams) at some point during pregnancy. Only 32 (22.0%) had in utero heart disease suspected by prenatal ultrasound.

The frequencies of CHD in children were divided into general pathophysiological groups for analytical purposes, as shown in Table 2. Eleven of the children had Down syndrome, two of them heterotaxy and one Noonan syndrome.

Social determinants associated with severity of heart disease

Bivariate and multivariate analyses were performed to evaluate the social determinants and their relationship with the severity of CHD. Thus, 16 children (11.5%) were found to have a RACHS-1 greater than 3 and 37 (26.8%) and an STS score greater than 3. No statistical differences were found between heart disease and its severity based on these scales. In aspects such as sex, genetic syndrome, age of the parents, history of exposure or consumption of tobacco or psychostimulant substances during pregnancy, number of children, religion, belonging to minority population groups, education, and occupation of the parents, as well as the area of origin, no statistically significant differences were found either.

After grouping the heart diseases according to their physiology into cyanotic, non-cyanotic, and single ventricle, an analysis based

Table 1. Sociodemographic and clinical characteristics of the study population according to the risk of mortality measured by Score Rachs and Complexity measured by Score STS.

Characteristics of the patients	$n = 140$	Mortality risk (Rachs Score)			Complexity (STS score)		
		Score < 3	Score > 3	p^a	Score < 3	Score > 3	p^a
General socio-demographic conditions of the child and his family							
Age (months), median (IR)	8.7 (30.8)	8.8 (28.9)	8.7 (35.6)	0.6098	8.5 (26.7)	9.0 (37.4)	0.7750
Sex, *n* (%)							
Women	70 (50.0)	63 (51.2)	7 (41.1)	0.438	53 (51.9)	17 (44.7)	0.447
Men	70 (50.0)	60 (48.7)	10 (58.8)		49 (48.0)	21 (55.2)	
Area, *n* (%)							
Urban	103 (73.5)	89 (72.3)	14 (82.3)	0.381	74 (72.5)	29 (76.3)	0.683
Rural	37 (26.4)	34 (27.6)	3 (17.6)		28 (27.4)	9 (23.6)	
Low socioeconomic level, *n* (%)							
No	24 (17.1)	21 (17.0)	3 (17.6)	0.953	18 (17.6)	6 (15.7)	0.795
Yes	116 (82.8)	102 (82.9)	14 (82.3)		84 (82.3)	32 (84.2)	
Health security system, *n* (%)							
Subsidized	3 (2.1)	3 (2.4)	0 (0.0)	0.382	3 (2.9)	0 (0.0)	0.298
Contributory	107 (76.4)	92 (74.8)	15 (88.2)		74 (72.5)	33 (86.8)	
Other	30 (21.4)	28 (22.7)	2 (11.7)		25 (24.5)	5 (13.1)	
Garbage collection, *n* (%)							
No	44 (31.4)	40 (32.5)	4 (23.5)	0.454	32 (31.3)	12 (31.5)	0.981
Yes	96 (68.5)	83 (67.4)	13 (76.4)		70 (68.6)	26 (68.4)	
Sewer network, *n* (%)							
No	41 (29.2)	34 (27.6)	7 (41.1)	0.250	30 (29.4)	11 (28.9)	0.957
Yes	99 (70.7)	89 (72.3)	10 (70.7)		72 (70.5)	27 (71.0)	
Family information							
Mother's age (years), median (IR)	24 (11.5)	24 (12)	25 (7)	0.4743	24 (11)	25.5 (13)	0.2333
Mother's education (years), median (IR)	11 (6)	11 (6)	11 (5)	0.7379	11 (6)	11 (5)	0.9698
Mother's occupation, *n* (%)							
Housewife	94 (67.1)	81 (65.8)	13 (76.4)	0.382	68 (66.6)	26 (68.4)	0.844
Other	46 (32.8)	42 (34.1)	4 (23.5)		34 (33.3)	12 (31.5)	
Father's age (years), median (IR)	30 (13)	30 (13)	29 (12)	0.9847	30 (12)	29 (14)	0.9869
Father's education (years), median (IR)	11 (6)	10 (6)	11 (3)	0.2851	11 (6)	10 (6)	0.2346
Father's occupation, *n* (%)							
No	1 (0.71)	1 (0.8)	0 (0.0)	0.709	0 (0.0)	1 (2.6)	0.100
Yes	139 (99.2)	122 (99.1)	17 (100)		102 (100.0)	37 (97.3)	
Number of children in the household, median (min–max)	2 (1–9)	2 (1–9)	2 (1–4)	0.6159	2 (1–9)	2 (1–7)	0.2472
Family income (monthly), *n* (%)							
Less than one SMMLV	76 (54.2)	67 (54.4)	9 (52.9)	0.741	55 (53.9)	21 (55.2)	0.352
Between 1 and 2 SMMLV	46 (32.8)	39 (31.7)	7 (41.1)		31 (30.3)	15 (39.4)	
Between 2.1 and 4 SMMLV	15 (10.7)	14 (11.3)	1 (5.8)		13 (12.7)	2 (5.2)	
More than 4 SMMLV	3 (2.1)	3 (2.4)	0 (0.0)		3 (2.9)	0 (0.0)	
Benefit social programs, *n* (%)							
No	88 (62.8)	78 (63.4)	10 (58.0)	0.713	63 (61.7)	25 (65.7)	0.661
Yes	52 (37.1)	45 (36.5)	7 (41.1)		39 (38.2)	13 (34.2)	
Blood relationship of the father of your child with you, *n* (%)							
No	137 (97.8)	120 (97.6)	17 (100)	0.515	100 (98.0)	37 (97.3)	0.807
Yes	3 (2.1)	3 (2.4)	0 (0.0)		2 (1.9)	1 (2.6)	
Smoking during pregnancy, *n* (%)							
No	126 (89.9)	106 (88.5)	17 (100)	0.263	88 (86.2)	35 (92.1)	0.483
Yes	14 (10.0)	14 (11.3)	0 (0.0)		11 (10.7)	3 (7.8)	

Table 1. continued

Characteristics of the patients	$n = 140$	Mortality risk (Rachs Score)			Complexity (STS score)		
		Score < 3	Score > 3	p^a	Score < 3	Score > 3	p^a
Sharing spaces with smokers during pregnancy, *n* (%)							
No	89 (63.5)	80 (65.0)	9 (52.9)	0.331	67 (65.6)	22 (57.8)	0.394
Yes	53 (36.4)	43 (34.9)	8 (47.0)		35 (34.3)	16 (42.1)	
Alcohol during pregnancy, *n* (%)							
No	124 (88.5)	109 (88.6)	15 (88.2)	0,963	90 (88.2)	34 (89.4)	0.838
Yes	16 (11.4)	14 (11.3)	2 (11.7)		12 (11.7)	4 (10.5)	
Psychoactive substances in pregnancy, *n* (%)							
No	134 (95.7)	118 (95.9)	16 (94.1)	0.729	98 (96.0)	36 (94.7)	0.727
Yes	6 (4.2)	5 (4.0)	1 (5.8)		4 (3.9)	2 (5.2)	
Cooking with firewood during pregnancy, *n* (%)							
No	92 (65.7)	81 (65.8)	11 (64.7)	0.926	65 (63.7)	27 (71.0)	0.417
Yes	48 (34.2)	42 (34.1)	6 (35.2)		37 (36.2)	11 (28.9)	
Diagnosis of micronutrient deficiency during pregnancy, *n* (%)							
No	123 (87.8)	108 (87.8)	15 (88.2)	0.959	92 (90.2)	31 (81.5)	0.165
Yes	17 (12.1)	15 (12.2)	2 (11.7)		10 (9.8)	7 (18.4)	
Drug use during pregnancy, *n* (%)							
None	6 (4.2)	5 (4.0)	1 (5.8)	0.984	6 (5.8)	0 (0.0)	0.397
Folic acid	20 (14.2)	18 (14.6)	2 (11.7)		14 (13.7)	6 (15.7)	
Vitamins	63 (45.0)	56 (45.5)	7 (41.8)		45 (44.1)	18 (47.3)	
Minerals	29 (20.7)	25 (20.3)	4 (23.5)		19 (18.6)	10 (26.3)	
Others	22 (15.7)	19 (15.4)	3 (17.5)		18 (17.6)	4 (10.5)	
Use of agricultural substances during pregnancy, *n* (%)							
No	72 (51.4)	63 (51,2)	9 (52.9)	0.894	50 (40.0)	22 (57.8)	0.350
Yes	68 (48.5)	60 (48,7)	8 (47.0)		52 (50.9)	16 (42.1)	
Family history of congenital heart disease, *n* (%)							
No	99 (70.7)	90 (73.1)	9 (52.9)	0.171	69 (67.5)	30 (78.9)	0.364
Yes	38 (27.1)	31 (25.2)	7 (41.1)		31 (30.3)	7 (18.4)	
Diagnosis of congenital heart disease was during pregnancy, *n* (%)							
No	108 (77.1)	94 (76.4)	14 (82.3)	0.585	79 (77.4)	29 (76.3)	0.887
Yes	32 (22.8)	29 (22.5)	3 (17.6)		23 (22.5)	9 (23.6)	
Conditions related to the infant with heart disease							
Birth weight (g), median (IR)	2850 (823)	3950 (803)	3200 (802)	0.1151	3772 (5969)	4015 (6683)	0.9477
Weight (g) (min–max)	6410 [2500–68,000]	6500 [2500–68,000]	6000 [3070–56,000]	0.7814	6115 [2500–60,000]	7650 [3000–68,000]	0.3720
Height (cm) (min–max)	66.5 (42–170)	66 (42–170)	69 (48–165)	0.7375	66 (42–160)	69.5 (48–170)	0.4363
Main heart disease, *n* (%)							
Cyanosants	73 (52.9)	65 (53,2)	8 (50.0)	0.166	60 (59.4)	13 (35.1)	0.023
No cyanosants	35 (25.3)	33 (27,0)	2 (12.5)		22 (21.7)	13 (35.1)	
Single ventricles	26 (18.8)	20 (16,3)	6 (37.5)		15 (14.8)	11 (29.7)	
Others	4 (2.9)	4 (3.2)	0 (0.0)		4 (3.9)	0 (0.0)	
Time elapsed between symptoms and medical consultation (months), median (min–max)	0 [0–16]	0 [0–204]	0 [0–15]	0.2673	1 [0–204]	0 [0–15]	0.005

The data show *n* (%), median, interquartile ranges, and [min–max] (minimum–maximum).
RACHS-1 Risk Adjustment in Congenital Heart Surgery, *STS* Society of Thoracic Surgeons score.
[a]*p* values of the *t* test or rank sum for normally and non-normally distributed continuous variables and chi-square test for discrete variables.

on severity was performed for both the RACHS-1 and STS scores, in which statistically significant differences were found in the three groups in relationship with low socioeconomic status, exposure to cigarette smoke and wood smoke during pregnancy, as shown in Tables 3 and 4. There was a greater strength of association between the variables of interest in the group of single ventricles in these aspects when compared to the other pathophysiological groups. For some other variables, significant associations were found, but not consistently in the two models based on the evaluated score.

DISCUSSION

Establishing the etiology of CHD continues to be a challenge. Several studies have warned of the possible association between social determinants and the presence of heart disease.[1,2,6,7] These

Table 2. Frequency of congenital heart disease by pathophysiological groups.

No cyanosants	*n*	%	Cyanosants	*n*	%	Single ventricle	*n*	%
	77	**55.0**		**54**	**38.6**		**9**	**6.4**
Interventricular defect	30	39.0	pulmonary atresia	10	18.5	Single ventricle	9	100.0
Associated with atrial septal defect (ASD)	8	10.4	With interventricular defect	7	13.0	Pulmonary stenosis	3	33.3
Associated with patent ductus arteriosus (PDA)	5	6.5	Complete interventricular septum	3	5.6	Pulmonary free flow	3	33.3
			Additional severe tricuspid valve hypoplasia	1	1.9	Tricuspid atresia	3	33.3
Atrioventricular canal	13	16.9	Tetralogy of Fallot	10	18.5			
Type A	7	9.1						
Type B	3	3.9						
Transitional	2	2.6						
Partial	1	1.3						
Atrial communication	12	15.6	Double outflow tract of the right ventricle	10	18.5			
Associated with PDA	2	2.6	—Transposed vessels	4	7.4			
			—Fallot physiology	3	5.6			
			—Ventricular septal defect (VSD) related	3	5.6			
Coarctation of the aorta	7	9.1	Transposition of the great arteries	9	16.7			
			D transposition	8	14.8			
			L transposition	1	1.9			
Hypoplasia—interruption of the aortic arch	6	7.8	Tricuspid atresia	5	9.3			
			IIB	1	1.9			
			IIC	1	1.9			
			IIIC	1	1.9			
			Normorelated vessels without obstruction	1	1.9			
			Transposed vessels	1	1.9			
Patent ductus arteriosus	2	2.6	Total anomalous venous drainage	4	7.4			
			Supracardiac	2	3.7			
			Heart failure	1	1.9			
			Intracardiac	1	1.9			
Double aortic arch	2	2.6	Hypoplastic left heart syndrome	3	5.6			
			Mitral aortic atresia	2	3.7			
			Mitral aortic stenosis	1	1.9			
Congenital mitral valve dysplasia	2	2.6	Ebstein anomaly	1	1.9			
			Type C	2	3.7			
			Type D	1	1.9			
Congenital aortic valve stenosis	1	1.3						
Anomalous left coronary artery from the pulmonary artery	1	1.3						
Shone's syndrome	1	1.3						

factors could play an important role in epigenetic events, which would explain the geographical differences in the incidence and type of heart disease.[2] The present study found a relationship between certain social determinants, potentially modifiable, with the type of heart disease and its complexity, an aspect not described so far in the reported series.

Different studies have studied the relationship between low socioeconomic status and its impact on children with CHD. The study by Pace et al. demonstrated, for example, how low economic status and sociodemographic factors related to it affected the survival of children with CHD regardless of the pathology group studied, with some differences when taking into account the type of heart defect.[13] Nembhard et al., for their part, also found differences in the mortality of children with this condition when the maternal ethnic group was analyzed in a study based on the Texas Birth Defect Registry, of children born with CHD from 1996 to 2003.[14] The relationship of factors associated with low socioeconomic status would cause a gap to exist in the social determinants, still unclear, when they are compared with the most favored families. On the other hand, but from an etiological point of view, Aghan et al. found that low socioeconomic status favored the presence of severe and non-severe heart defects, with

Table 3. Association between social determinants and congenital heart disease adjusted by the RACHS-1.

Characteristics	Cyanosants			No cyanosants			Single ventricle		
	OR	95% CI	*p*	OR	95% CI	*p*	OR	95% CI	*p*
Rural zone	0.86	0.35–2.01	0.735	1.27	1.03–3.01	0.047	0.86	0.24–3.08	0.813
Low socioeconomic level	1.79	1.29–2.01	0.036	1.56	1.16–4.67	0.031	3.68	1.67–19.87	0.012
Low monthly income	0.86	0.48–1.54	0.6310	0.94	0.46–1.82	0.881	1.23	0.55–2.75	0.562
Benefit from social programs (yes)	1.37	0.65–2.89	0.375	0.35	0.14–0.88	0.045	1.42	0.54–3.74	0.449
Share spaces with smokers (yes)	**2.40**	**2.15–5.83**	**0.033**	**1.54**	**1.33–3.68**	**0.031**	**1.80**	**1.62–4.85**	**0.023**
Use of agricultural substances during pregnancy (yes)	1.96	1.46–2.02	0.022	1.17	1.04–2.83	0.02	0.90	0.33–2.37	0.845
Consumption of psychoactive substances during pregnancy (yes)	0.91	0.17–4.74	0.911	0.42	0.04–4.34	0.466	2.88	1.48–17.89	0.03
Cooked with firewood during pregnancy (yes)	**1.45**	**1.05–3.25**	**0.037**	**1.46**	**1.36–3.66**	**0.043**	**1.33**	**1.04–1.95**	**0.046**
Drug use during pregnancy	1.10	0.80–1.54	0.541	0.99	0.69–1.43	0.952	0.86	0.55–1.36	0.585

95% CI confidence interval of 95%.
The values indicated in bold correspond to associated variables that were statistically significant.

Table 4. Association between social determinants and congenital heart disease adjusted for Complexity (Score STS).

Characteristics	Cyanosants			No cyanosants			Single ventricle		
	OR	95% CI	*p*	OR	95% CI	*p*	OR	95% CI	*p*
Rural zone	0.85	0.34–2.16	0.756	1.10	0.37–3.10	0.831	0.80	0.22–2.90	0.752
Low socioeconomic level	**1.73**	**1.25–2.05**	**0.044**	**1.63**	**1.19–1.88**	**0.039**	**3.65**	**1.67–19.53**	**0.012**
Low monthly income	**0.76**	**0.41–1.40**	**0.385**	**1.08**	**1.06–2.13**	**0.040**	**1.27**	**1.06–2.83**	**0.036**
Benefit from social programs (yes)	1.31	1.26–2.81	0.045	0.41	0.14–1.00	0.057	1.53	0.60–3.98	0.379
Share spaces with smokers (yes)	1.43	1.20–2.98	0.038	1.40	1.07–3.36	0.042	1.78	1.65–4.81	0.027
Use of agricultural substances during pregnancy (yes)	0.91	0.43–1.93	0.809	1.32	1.07–3.18	0.045	0.88	0.33–2.33	0.805
Consumption of psychoactive substances during pregnancy (yes)	0.94	0.15–5.07	0.950	0.40	0.09–4.34	0.459	2.81	0.46–17.51	0.270
Cooked with firewood during pregnancy (yes)	**1.27**	**1.05–2.91**	**0.046**	**1.61**	**1.08–4.24**	**0.034**	**1.37**	**1.09–2.25**	**0.009**
Drug use during pregnancy	1.10	0.79–1.54	0.549	0.98	0.65–1.41	0.948	0.90	0.60–1.42	0.669

95% CI confidence interval of 95%.
The values indicated in bold correspond to associated variables that were statistically significant.

the low educational level being the only significant factor in severe cases, thus proposing that this factor could influence this difference, allowing, for example, greater access to therapeutic abortion in the group with a better educational level.[1]

However, one of the latent difficulties when evaluating the social determinants of a population and its impact on health status could be related to the way in which low socioeconomic status has been established in the different studies since this would include not only monthly monetary income, but also aspects related to the geographic area of residence, the sociopolitical structure of the country or jurisdiction evaluated, or even access to quality health and education services, among others, for which precise definitions are required to better define the real social level of a family. In the present study, families with a low economic level (determined by social stratum according to DANE criteria),[10] exposure to cigarette smoke and wood smoke during pregnancy, turned out to be social determinants associated with the severity of heart diseases analyzed by physiological groups. Although these could be related, as previously mentioned, to epigenetic changes, which would partly explain the regional differences described, there are no studies that investigate such changes at the population level.

There is growing evidence of the association of cigarette exposure, either as a previous active or passive smoker and during pregnancy (even after stopping) with the development of several congenital malformations in the child.[15–19] Several of the components of tobacco and tobacco smoke have been associated with teratogenic or embryogenic phenomena in animal models, with nicotine and carbon monoxide being the most studied given their ability to cross the placenta and therefore reach the fetal circulation.[20] The mechanisms involved in the development of these conditions are not yet completely clear, nor can they be considered as an independent factor, although some studies have shown their association mainly with septal and left ventricular outflow tract defects, being more significant when exposure occurred before and after conception.[17] Probably the phenomenon of fetal hypoxia related to tobacco, determined by the vasoconstrictor effect of nicotine on the uterine arteries and the increase in the concentration of carboxyhemoglobin in the fetus due to carbon monoxide, contributes to the development of embryopathy.[20] The rest of the components of tobacco have not been analyzed in-depth and unfortunately, most of the studies have been carried out establishing exposure through surveys (qualitative evaluation), which could favor the presence of various biases, since the existence of a dose-effect relationship would be likely (after measurement of blood or urine concentrations of nicotine in the pregnant mother, to mention one example). The

findings of this study could have an impact on public health to the extent that policies are implemented to reduce exposure to cigarettes, especially during pregnancy.

Similarly, more than 250 organic compounds generated from the combustion of wood have been identified, some volatilized with the ability to recondense into fine particles and other pyrolysis products secondary to the reactions of said process, noting in addition to particulate material, aromatic hydrocarbons, levoglucosan, carbon monoxide, and nitrogen dioxide. These will vary according to the type of wood studied.[21] There are studies that associate indoor pollution due to products of biomass combustion (including wood) and different pathological conditions. In the pediatric population, most of them are related to respiratory disease, low birth weight, excess perinatal mortality, and sudden infant death syndrome.[22] Although there are controversial studies in which the presence of various congenital malformations is associated with proximity or direct exposure to incinerators, as an example of the emission of biomass products,[23–26] the association after exposure to wood smoke does not has been systematically reported. Oxidative stress with subsequent recruitment of inflammatory cells and generation of reactive oxygen species after entry into the respiratory system and even the bloodstream of particulate matter and high concentrations of toxic gases such as carbon monoxide have been implicated as reasonable mechanisms. in the generation of these pathologies,[22,27] and that could also explain cardiac embryopathy. This study found significant statistical differences related between potentially modifiable factors and the pathophysiological group of heart disease, which could explain the geographical differences in the incidence of its different types according to the region studied. Unfortunately, given the selection of the sample, the number of participants, the varied type of heart disease included, and the risk of data loss affected by recall bias could influence the results obtained in the long run.

Finally, it is important to highlight that a total of 530,000 households in a situation of extreme poverty, where 2.1 million Colombians live, face the risk factor (use of fossil fuels in the home).[28]

In Colombia, there is a guideline from the National Council for Economic and Social Policy (CONPES), Document CONPES 3550 of 2008, which in the formulation of its action plan considered the control of the use of traditional fuels and previously, since 2007, a study commissioned by the World Bank had made indoor pollution visible as one of the environmental priorities for reducing poverty in the country.[29]

Perhaps, as has been mentioned, the development of CHD has a multifactorial origin, where, without a doubt, social determinants play an important role. There is of course the influence of confounding factors that would further complicate the establishment of these relationships. Perhaps the combination and potentiation between some of them favor the presentation and its severity. The detection of such determinants could support interventions from the field of public health that truly impact child health. Population-based studies that include quantitative exposure assessment are required to clearly define which are the most relevant and which could be modifiable.

The conclusions were that exposure to cigarette smoke, wood smoke during pregnancy, and low socioeconomic status were found to be social determinants associated with the severity of heart disease analyzed by physiological groups. The detection of such determinants could support interventions from the field of public health that have an impact on the incidence and severity of this type of congenital defect.

DATA AVAILABILITY

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request. The data can be requested from the following email address dorisquintero@fcv.org, given that internally in the institution where the project was developed, permission must be requested from the research ethics committee for the delivery of data.

REFERENCES

1. Agha, M. M., Glazier, R. H., Moineddin, R., Moore, A. M. & Guttmann, A. Socio-economic status and prevalence of congenital heart defects: does universal access to health care system eliminate the gap? *Birth Defects Res.* **91**, 1011–1018 (2011).
2. Wong, P. et al. Early life environment and social determinants of cardiac health in children with congenital heart disease. *Pediatr. Child Health* **23**, 92–95 (2018).
3. Hoffman, J. I. The global burden of congenital heart disease. *Cardiovasc. J. Afr.* **24**, 141 (2013).
4. Trevisan, P. et al. Cardiopatias congênitas e cromossomopatias detectadas por meio do cariótipo. *Rev. Paul. Pediatr.* **32**, 262–271 (2014).
5. Van der Linde, D. et al. Birth prevalence of congenital heart disease worldwide: a systematic review and meta-analysis. *J. Am. Coll. Cardiol.* **58**, 2241–2247 (2011).
6. Mejía, L. Los Determinantes Sociales de la Salud: base teórica de la salud pública. *Rev. Fac. Nac. Salud Pública* **31**, 28–36 (2013).
7. Álvarez, L. S. Los determinantes sociales de la salud: más allá de los factores de riesgo. *Rev. Gerenc. Polit. Salud* **8**, 69–79 (2009).
8. Yang, J. et al. Socioeconomic status in relation to selected birth defects in a large multicentered US case-control study. *Am. J. Epidemiol.* **167**, 145–154 (2008).
9. Carmichael, S. L., Ma, C. & Shaw, G. M. Socioeconomic measures, orofacial clefts, and conotruncal heart defects in California. *Birth Defects Res. A Clin. Mol. Teratol.* **85**, 850–857 (2009).
10. Departamento Administrativo Nacional de Estadística. Frequently Asked Questions document. https://www.dane.gov.co/files/geoestadistica/Preguntas_frecuentes_estratificacion.pdf (2020).
11. Jenkins, K. J. et al. Consensus-based method for risk adjustment for congenital heart surgery. *J. Thorac. Cardiovasc. Surg.* **123**, 110–118 (2002).
12. Gaynor, J. W. et al. International Congenital Heart Surgery justment in Congenital Heart Surgery (RACHS-1). Nomenclature Heart Surgery Committees of the Society of Thoracic Surgeons. European Association for Cardio-Thoracic Surgery. Congenital Heart Surgery Nomenclature and Database Project: update and proposed data harvest. *Ann. Thorac. Surg.* **73**, 1016–1018 (2002).
13. Pace, N. D. et al. Sociodemographic factors and survival of infants with congenital heart defects. *Pediatrics* **142**, e20180302 (2018).
14. Nembhard, W. N. et al. Racial/ethnic disparities in risk of early childhood mortality among children with congenital heart defects. *Pediatrics* **127**, e1128–e1138 (2011).
15. Perry, M. F., Mulcahy, H. & DeFranco, E. A. Influence of periconception smoking behavior on birth defect risk. *Am. J. Obstet. Gynecol.* **220**, 588.e1–588.e7 (2019).
16. Hackshaw, A., Rodeck, C. & Boniface, S. Maternal smoking in pregnancy and birth defects: a systematic review based on 173 687 malformed cases and 11.7 million controls. *Hum. Reprod. Update* **17**, 589–604 (2011).
17. Baldacci, S. et al. Environmental and individual exposure and the risk of congenital anomalies: a review of recent epidemiological evidence. *Epidemol. Prev.* **42**(3-4 Suppl 1), 1–34 (2018).
18. Malik, S. et al. Maternal smoking and congenital heart defects. *Pediatrics* **121**, e810–e816 (2008).
19. Zhang, D. et al. Is maternal smoking during pregnancy associated with an increased risk of congenital heart defects among offspring? A systematic review and meta-analysis of observational studies. *J. Matern Neonatal Med.* **30**, 645–57 (2017).
20. Karatza, A. A. et al. Periconceptional tobacco smoking and Xisolated congenital heart defects in the neonatal period. *Int. J. Cardiol.* **148**, 295–299 (2011).
21. Fine, P. M., Cass, G. R. & Simoneit, B. R. T. Chemical characterization of fine particle emissions from fireplace combustion of woods grown in the Northeastern United States. *Environ. Sci. Technol.* **35**, 2665–2675 (2001).
22. Bruce, N., Pérez-Padilla R. & Albalak, R. Indoor air pollution in developing countries: a major environmental and public health challenge. *Bull. World Health Organ.* **78**, 1078–1092 (2000).
23. Cordier, S. et al. Risk of congenital anomalies in the vicinity of municipal solid waste incinerators. *Occup. Environ. Med.* **61**, 8–15 (2004).
24. Cordier, S. et al. Maternal residence near municipal waste incinerators and the risk of urinary tract birth defects. *Occup. Environ. Med.* **67**, 493–499 (2010).
25. Vinceti, M. et al. Adverse pregnancy outcomes in a population exposed to the emissions of a municipal waste incinerator. *Sci. Total Environ.* **407**, 116–21 (2008).
26. Vinceti, M. et al. Risk of congenital anomalies around a municipal solid waste incinerator: a GIS-based case-control study. *Int. J. Health Geogr.* **8**, 8 (2009).
27. Corsini, E., Marinovich, M. & Vecchi, R. Ultrafine particles from residential biomass combustion: a review on experimental data and toxicological response. *Int. J. Mol. Sci.* **20**, 4992 (2019).

28. Soto-Moreno, J. A. & Ballester-Díez, F. Contaminación del aire de interiores en hogares en situación de pobreza extrema en Colombia. *Rev. Salud Pública* **15**, 80–89 (2013).
29. Sánchez-Triana, E. Ahmed, K. & Awe, Y. *Prioridades Ambientales para la Reducción de la Pobreza en Colombia: Un Análisis Ambiental del País para Colombia. Direcciones para el Desarrollo-Medio Ambiente y Desarrollo Sustentable 38610* (Banco Mundial-Mayol Ediciones, 2007).

ACKNOWLEDGEMENTS

To the parents and caregivers who participated in the study and to the Fundación Cardiovascular de Colombia for their support in this research.

AUTHOR CONTRIBUTIONS

Substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data: M.J.F.-M., E.T.-P., J.A.F.-R., D.C.Q.-L., E.M.G.-D. Drafting the article or revising it critically for important intellectual content. C.X.F.-R., J.M.C.-M., M.J.F.-M., D.C.Q.-L., E.M.G.-D. Final approval of the version to be published: all authors.

COMPETING INTERESTS

The authors declare no competing interests.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was reviewed and approved by the Research Ethics Committee (CEI) of the Fundación Cardiovascular de Colombia (Record No. 372). All participating parents or caregivers gave their informed consent. All participating parents or caregivers gave their informed consent.

ADDITIONAL INFORMATION

Correspondence and requests for materials should be addressed to Doris C. Quintero-Lesmes.