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ORIGINAL RESEARCH

Association of Number of Live Births With Electrocardiographic and Cardiac Structural Changes

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BACKGROUND: Pregnancy is a major life event unique to women and leads to significant hemodynamic, hormonal, and metabolic changes. The purpose of this study was to use the DHS (Dallas Heart Study), a multiethnic population-based cohort study of Dallas county adults, to evaluate the association between number of live births and cardiac magnetic resonance imaging and ECG parameters later in life.

METHODS AND RESULTS: Women were included if they had data on self-reported live births and ECG or cardiac magnetic resonance imaging measurements. The 3014 women were stratified by number of live births: 0, 1, 2, 3, 4, and ≥5. Higher number of live births was associated with larger left ventricular (LV) end-diastolic volume (β, 1.31±0.41; $P<0.01$), LV end-systolic volume (β, 0.83±0.24; $P<0.01$), and LV mass (β, 1.13±0.49; $P=0.02$) and lower LV ejection fraction (β, −0.004±0.0014; $P<0.01$). Increasing parity was associated with longer PR intervals (β, 1.07±0.38; $P<0.01$). Subgroup analysis by race demonstrated that the association between number of live births and magnetic resonance imaging parameters (LV end-diastolic volume, LV end-systolic volume, and LV ejection fraction) only remained significant in Black women (P value for interaction <0.05).

CONCLUSIONS: Increasing number of live births was associated with electrocardiographic and cardiac structural changes in a multiethnic population. When stratified by race and ethnicity, magnetic resonance imaging structural changes only remained significant in Black participants. Whether these changes are pathologic and increase the risk of heart failure or arrhythmias in multiparous women warrants further investigation.

Key Words: cardiac magnetic resonance imaging ∎ cardiovascular risk factors ∎ ECG ∎ parity ∎ women's health

Cardiovascular disease remains the leading cause of death for women in the United States.[1] Although coronary heart disease makes up the majority of events, hypertension, heart failure, and stroke remain significant causes of mortality in women.[1,2] In addition, arrhythmias, such as atrial fibrillation, are associated with increased morbidity and mortality in women compared with men.[3] The importance of considering sex-specific risk factors and risk enhancers in coronary artery disease is gaining awareness.[3–5] The role of sex-specific risk factors in other cardiovascular diseases, such as arrhythmias or heart failure, is still being understood and requires additional research.[6]

Pregnancy is a major life event unique to women and leads to significant hemodynamic, physiologic, and cardiac structural changes.[7] Higher number of pregnancies and live births have been associated with increased subclinical atherosclerosis[8] and with future maternal cardiovascular events, including a higher risk of coronary artery disease,[9,10] heart failure,[10,11] and arrhythmias.[12] The underlying mechanism for these associations remains unclear. Cumulative cardiac structural and electrical changes over multiple pregnancies may play a role.

Using the DHS (Dallas Heart Study), a multiethnic population cohort study of Dallas county adults, we

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sought to evaluate whether there was an association between number of live births and cardiac structural and electrical conduction parameters. We used cardiac magnetic resonance imaging (MRI) and electrocardiographic parameters to study this association.

METHODS

The data, methods used in the analysis, and materials used to conduct the research will not be made available to any researcher for purposes of reproducing the results or replicating the procedure.

Study Population

The DHS is a multiethnic probability-based population cohort study of Dallas County adults, with intentional oversampling of Black adults. Phase 1 of the DHS (DHS1) was conducted between 2000 and 2002 and included 3 separate visits: visit 1, an initial home visit for collection of demographic data, medical history, blood pressure, and anthropometric data; visit 2, a second home visit for collection of fasting blood and urine samples; and visit 3, a final visit to the University of Texas Southwestern Medical Center for completion of detailed imaging studies. All participants who were available for this final visit underwent ECG and cardiac MRI to obtain cardiac structural data. Between 2007 and 2009, phase 2 of the DHS (DHS2) was performed and included prior DHS1 participants who had completed visit 2 as well as spouses and significant others of the DHS1 participants.

The current study includes women who participated in either DHS1 or DHS2, who had reported number of live births, and who had ECG or cardiac MRI data recorded (total, n=3014; DHS1, n=2535; and DHS2, n=479). For women with both DHS1 and DHS2 data available, only DHS2 data were included. Of the 2535 DHS1 participants, 1535 completed an ECG for analysis, and 1004 completed a cardiac MRI. Of the 479 DHS2 participants, 476 completed an ECG for analysis, and 223 completed a cardiac MRI.

The study protocol was approved by the Institutional Review Board of the University of Texas Southwestern Medical Center, and all participants provided written informed consent.

Variable Definitions

Number of live births was self-reported on a questionnaire administered at study entry to DHS1 and again for DHS2 (DHS1 questionnaire asked for number of live births, whereas DHS2 questionnaire asked for number of children). There were 118 women who had children between DHS1 and DHS2. Demographic data, including age, race, socioeconomic status, and education level, were obtained by participant self-report. Race/ethnicity was self-identified by participants as non-Hispanic Black, non-Hispanic White, Hispanic, and other. Education was categorized into 4 groups (less than high school, high school, some college, and college or more), and income was categorized into quartiles based on annual income (<$16000, $16 000–30000, $30 000–50000, and >$50 000). Diabetes was defined by one of the following: self-report accompanied by use of antihyperglycemic medication or by elevated serum glucose (fasting >126 mg/dL [7.0 mmol/L]) or by nonfasting glucose >200 mg/dL (11.1 mmol/L). In DHS2, hemoglobin A1C was measured, so the DHS2 criteria for diabetes also included an A1C ≥6.5%. Plasma lipids were collected during the clinical visit after a 12-hour fast. The Friedewald equation was used to calculate low-density lipoprotein cholesterol from total cholesterol, triglyceride, and high-density lipoprotein cholesterol measurements. Smoking status was treated as a binary variable and determined by self-report (current smoker versus not current smoker). Blood pressure was measured a total of 5 times during each visit, with the average of the last 3 readings representing the blood pressure for that visit. Hypertension was defined as average systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, or use of antihypertensive medications. Body mass index (BMI) was calculated on the basis of measured height and weight. Waist circumference was measured 1 cm above the iliac crest, and hip circumference was measured at the widest circumference of the buttocks at the area of the greater trochanters.

Cardiac MRI

Cardiac imaging was performed using short-axis, breath-hold, ECG-gated cine sequence, 1.5-T MRI (Phillips Medical Systems) in DHS1 and 3.0 T (Phillips Medical Systems) in DHS2. Endocardial and epicardial borders at end diastole and end systole were manually traced in each short-axis image from apex to base using QMass software (Dallas, TX) to calculate left ventricular (LV) volume and LV mass. Measurements from each slice were summed by the method of disks (Simpson rule). Papillary muscles were included in myocardial LV mass and excluded from LV volume measurement. LV wall thickness was obtained from short-axis images, as previously described.[13] LV concentricity was defined as LV mass/LV end-diastolic volume (LVEDV). In DHS1, left atrial (LA) images were acquired using prospective electrocardiographic gating and turbo field echo sequencing. In DHS2, LA images were acquired using retrospective ECG gating and balanced fast field echo sequencing. Maximum LA volume was measured using the biplane area-length method.[14]

Several cardiac structural and functional measurements were assessed, including LVEDV (mL), LV end-systolic volume (LVESV; mL), LA end-diastolic volume (mL), LV mass (g), LV wall thickness (mm), LV concentricity (g/mL), and LV ejection fraction (LVEF; %).

Measurement of ECG Parameters

Twelve-lead ECG was performed at the same visit as the cardiac MRI using a Marquette Medical System (General Electric) with MAC 5000 hardware and software configuration, which measured rate, rhythm, intervals (PR, QRS, and QT), and voltages. ECG parameters included in the analysis included the PR interval (ms), QRS interval (ms), QT interval (ms), and rate (beats per minute). ECGs were interpreted by Marquette Universal System for Electrocardiography and overread by a board-certified cardiologist.

Statistical Analysis

Continuous data are presented as median values with interquartile ranges, and categorical variables are presented as proportions. Women were stratified on the basis of the reported number of live births (0, 1, 2, 3, 4, or ≥5). Differences in baseline characteristics were analyzed using the Jonckheere-Terpstra trend test across categories. Sequential multivariable linear regression models with ECG and MRI parameters as the outcomes were used to assess independent associations of the number of live births and measures of cardiac and structural parameters. Model 1 adjusted for age, race and ethnicity, education level, income, and either BMI (ECG parameters) or body surface area (cardiac MRI parameters). Model 2 included the variables in model 1 plus hypertension, smoking, waist/

hip ratio, and diabetes. Given the racial and ethnic diversity in the population, structural MRI and ECG findings were also analyzed using formal interaction terms (Black/non-Black) race×number of live births; $P<0.05$ considered statistically significant) as well as in race- and ethnicity-specific models.

Sensitivity analyses dichotomizing the data using 3 live births also was performed using fully adjusted model 2.

Least square means for the statistically significant LV and ECG measures are presented, adjusting for model 2 covariates. All statistical analyses were performed using SAS version 9.2.

For all statistical testing, a 2-sided $P<0.05$ was considered statistically significant.

RESULTS

Baseline Characteristics

The baseline characteristics of the women, stratified by number of live births, are shown in Table 1. Women with higher number of live births were older, had a higher BMI, and were more likely to have hypertension compared with women with fewer live births. They were also less likely to have a college education and were of lower socioeconomic status based on income level. White women had fewer live births, whereas Hispanic women had more live births. Black women were equally represented in each category of live births. Low-density lipoprotein and total cholesterol levels were not associated with number of live births. Higher number of live births was inversely associated with high-density lipoprotein levels and directly associated with triglyceride levels. The Figure shows the adjusted means for cardiac LV parameters and PR interval measurements and the P values for trend across categories of live births. There was a trend toward increasing PR interval, LVEDV, LVESV, and LV mass for each live birth.

Cardiac MRI Parameters

In adjusted linear regression analyses, increasing number of live births was associated with increased LVEDV (β, 1.22±0.41; $P<0.01$), LVESV (β, 0.78±0.24; $P<0.01$), LV mass (β, 0.98±0.50; $P=0.05$), and decreased LVEF (β, −0.004±0.0014; $P<0.01$) (Table 2). The association between live births and LVEDV, LVESV, LV mass, and LVEF remained significant after adjusting for hypertension, smoking, waist/hip ratio, and diabetes. The findings were unchanged when these MRI parameters were indexed to body surface area (Table 2). No significant association was found between number of live births and LA end-diastolic volume, LV wall thickness, or LV concentricity. In an additional analysis by LV hypertrophy subtypes (eccentric, concentric, or

Table 1. Baseline Characteristics

Characteristic	No. of live births						
	0	1	2	3	4	≥5	
Total No.	148	632	1043	649	304	238	*P*-trend
Age, y	41 (27–54)	41 (28.5–52)	44 (34–54)	44 (37–54)	45 (36–59)	55 (43–62)	<0.01
Body composition							
BMI, kg/m^2	28.2 (24.3–33.3)	28.9 (24.5–35.0)	29.4 (24.9–35.3)	29.64 (25.4–34.9)	30.4 (26.3–36.0)	31.4 (26.5–36.3)	<0.01
WHR	0.84 (0.8–0.9)	0.85 (0.81–0.91)	0.85 (0.81–0.9)	0.86 (0.81–0.91)	0.86 (0.82–0.91)	0.87 (0.84–0.92)	0.01
Race or ethnicity							
White	39 (26)	153 (24)	262 (25)	136 (21)	40 (13)	27 (11)	<0.01
Black	87 (59)	356 (56)	578 (56)	371 (57)	171 (56)	138 (58)	0.83
Hispanic	22 (15)	107 (17)	176 (17)	125 (19)	90 (30)	67 (28)	<0.01
Other*	4 (3)	8 (1)	19 (2)	5 (1)	4 (1)	4 (2)	0.39
Income, $							
<16 000	35 (25)	143 (25)	220 (23)	156 (27)	91 (31)	86 (40)	<0.01
16 000–30 000	27 (19)	135 (23)	198 (20)	145 (25)	82 (28)	59 (27)	0.02
30 000–50 000	34 (24)	154 (27)	218 (22)	151 (26)	63 (21)	35 (16)	0.04
>50 000	36 (26)	118 (21)	278 (29)	108 (18)	46 (16)	26 (12)	<0.01
Education							
Less than high school	27 (18)	97 (15)	177 (17)	170 (26)	115 (38)	110 (46)	<0.01
High school	28 (19)	206 (33)	345 (33)	227 (35)	101 (33)	77 (32)	0.07
Some college	72 (49)	268 (42)	426 (41)	224 (35)	78 (26)	42 (18)	<0.01
College or more	21 (14)	59 (9)	95 (9)	27 (4)	10 (3)	8 (3)	<0.01
Risk factors							
Diabetes	19 (20)	69 (17)	81 (11)	75 (15)	34 (14)	38 (21)	0.76
Smoking	38 (26)	134 (21)	207 (20)	162 (25)	60 (20)	49 (21)	0.89
Hypertension	58 (39)	216 (35)	401 (39)	255 (40)	141 (47)	129 (55)	<0.01
SBP, mmHg	119.67 (107–134.67)	122.67 (111.33–136)	123.67 (112.33–137)	124.5 (114–139)	126.33 (112.6–143)	133.67 (118.67–148.83)	<0.01
DBP, mmHg	76 (68–84.67)	77.67 (71–84.67)	78.33 (72–85)	78.67 (73.33–86)	79.33 (72–86.67)	79.33 (73–86.17)	<0.01
TC, mg/dL	193 (169–217)	189 (168–215)	188 (164–216)	185 (161–209)	187.5 (166–214)	185 (161.5–219.5)	0.23
LDL-C, mg/dL	106 (83–127)	109 (91–134)	112 (90–135)	108 (87–132)	112 (91–134)	109 (90–138)	0.79
HDL-C, mg/dL	57 (46–72)	53 (46–63)	53 (45–63)	51 (45–61)	50 (43–60)	50 (43–59.5)	<0.01
Triglycerides, mg/dL	86.5 (62–139)	91 (69–140)	94 (68.5–134)	96 (69–130)	99 (74–143)	112.5 (77–162)	<0.01

Data are given as median (interquartile range) or number (percentage). BMI indicates body mass index; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; TC, total cholesterol; and WHR, waist/hip ratio.

*Race/ethnicity was self-identified by participants as non-Hispanic Black, non-Hispanic White, Hispanic, and other.

indeterminate), no association was noted with parity or race (data not shown).
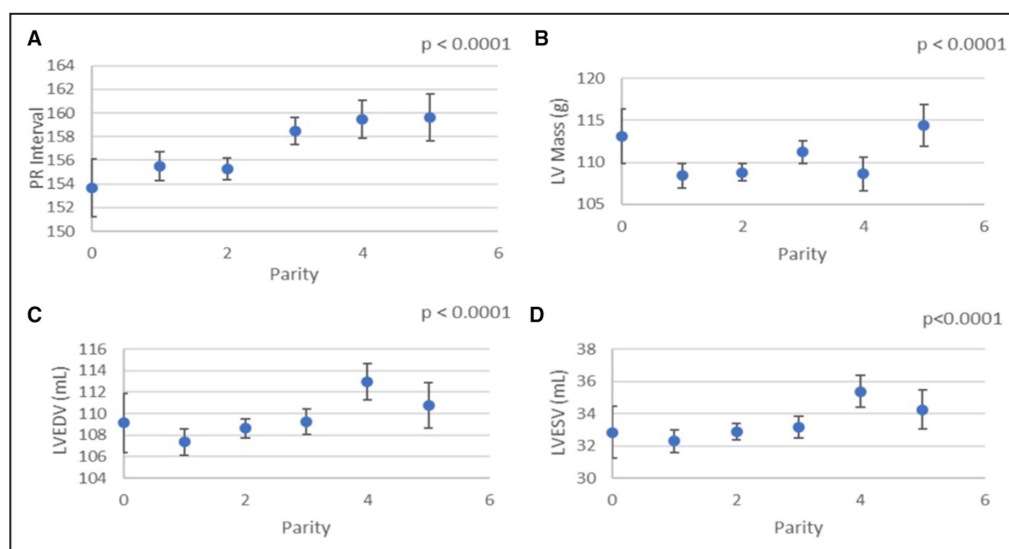
ECG Parameters

Increasing number of live births was associated with a longer PR interval (β, 1.12±0.38; *P*<0.01). There was no association between number of live births and QRS interval, QT interval, or ventricular rate. The association with PR interval remained statistically significant after adjusting for hypertension, smoking, waist/hip ratio, and diabetes (Table 3).

The association between the PR interval and parity remained significant even when including LV mass or LVEDV in the multivariate model, suggesting an independent association that is not mediated by these parameters (data not shown).

Subgroup Analyses by Race and Ethnicity

Subgroup analysis by race demonstrated that the association between number of live births and the MRI parameters listed above only remained significant in Black women (LVEF: β, −0.00645, *P*<0.01; LVEDV: β, 2.06, *P*<0.01; LVESV: β, 1.32, *P*<0.01; LV mass: β, 1.77, *P*=0.02), with significant *P* value for interaction (*P*<0.05) for LVEF, LVEDV, and LVESV but not LV mass (Table 4).

Figure. Least square means for the association of PR interval and cardiac MRI variables with number of live births.

Least square means for ECG and cardiac MRI parameters and their association with increasing levels of parity in fully adjusted models for age, race, income, education level, hypertension, smoking, and either body mass index (ECG parameters) or body surface area (cardiac MRI parameters). **A**, PR interval with increasing levels of parity. **B**, Left ventricular (LV) mass with increasing levels of parity. **C**, LV end-diastolic volume (LVEDV) with increasing levels of parity. **D**, LV end-systolic volume (LVESV) with increasing levels of parity. MRI indicates magnetic resonance imaging.

The correlation between number of live births and longer PR interval was not modified by race (P interaction=0.73) (Table 4).

Sensitivity Analyses

Sensitivity analyses dichotomizing higher parity and lower parity demonstrated that >3 live births were associated with increased LVEDV (β, 2.37±1.15; P=0.04) and a trend toward increased LVESV (β, 1.3±0.67; P=0.058) but no change in LV wall thickness or LVEF. This association remained significant only in Black participants (LVEDV: β, 3.77±1.76, P=0.032; LVESV: β, 2.2±0.98, P=0.0238).

Dichotomizing the cohort at 3 live births also demonstrated that >3 live births was associated with a significantly longer PR interval (β, 3.65±1.12; P=0.012) with no significant difference in QRS interval, QT interval, or ventricular rate. This association was similar for Black (β, 3.8±1.56; P=0.015), White (β, 4.65±2.17; P=0.032), and Hispanic (β, 4.7±2.5; P=0.06) participants.

DISCUSSION

In a large, multiethnic population of women, increasing number of live births was associated with a small, but statistically significant, change in cardiac structure and electrical conduction. Increasing number of live births was associated with increased LVEDV, LVESV, and LV mass, longer PR interval, and lower LVEF. When analyzed by race, these findings were only significant in Black women for LVEF, LVEDV, and LVESV, but not for LV mass or PR interval. Sensitivity analyses dichotomizing the data at 3 live births support the overall findings, except LV mass and LVEF were no longer significantly associated with parity.

Data from the MESA (Multi-Ethnic Study of Atherosclerosis) cohort (average age, 62 years; n=2234) found that each increase in live birth was associated with increased LVEDV, LVESV, and LV mass, and a decrease in LVEF, as assessed by cardiac MRI.[15] Another study evaluating echocardiographic data from

Table 2. Association of LV Structure and Function Measures by MRI per Number of Live Births

Model	LVEDV	LVESV	LAEDV	LVEF	LV mass	LV wall thickness	Concentricity
1	1.22±0.41 (<0.01)	0.78±0.24 (<0.01)	0.12±0.38 (0.76)	−0.004±0.0014 (<0.01)	0.98±0.50 (0.05)	0.0063±0.027 (0.82)	0.004±0.005 (0.47)
2	1.31±0.41 (<0.01)	0.83±0.24 (<0.01)	0.17±0.38 (0.68)	−0.004±0.0014 (<0.01)	1.13±0.49 (0.02)	0.013±0.026 (0.61)	−0.003±0.004 (0.55)

Data are given as β coefficient±SE (P value). Model 1 covariates: age, race, income, education level, and body surface area. Model 2 covariates: model 1 covariates+hypertension, smoking, waist/hip ratio, and diabetes. LAEDV indicates left atrial end-diastolic volume; LV, left ventricular; LVEDV, LV end-diastolic volume; LVEF, LV ejection fraction; LVESV, LV end-systolic volume; and MRI, magnetic resonance imaging.

Table 3. Association of ECG Parameters per Number of Live Births

Model	PR interval	QRS duration	QT interval	Ventricular rate
1	1.14±0.38 (<0.01)	0.04±0.18 (0.84)	−0.02±0.53 (0.97)	−0.06±0.18 (0.73)
2	1.07±0.38 (<0.01)	−0.009±0.19 (0.96)	−0.05±0.52 (0.92)	−0.01±0.17 (0.94)

Data are given as β coefficient±SE (*P* value). Model 1 covariates: age, race, income, and education level. Model 2 covariates: model 1 covariates+hypertension, smoking, body mass index, waist/hip ratio, and diabetes.

Hispanic women (aged >45 years; n=1172) in 4 different US cities found that grand parity was positively associated with increased LVEDV, LVESV, LA volume indexed, and the presence of diastolic dysfunction.[16] This study demonstrates similar findings using a diverse cohort of women from the DHS. Moreover, we report novel findings of an effect modification of the associations of parity with cardiac structural abnormalities by race and an association of parity with ECG parameters.

The hemodynamic changes associated with pregnancy are one possible explanation for these findings. Pregnancy is associated with a significant increase in circulating plasma volume, with almost 50% above baseline.[7] With this augmentation in preload, there are small but significant increases in all 4 chamber dimensions during pregnancy without a significant change in LV thickness, resulting in eccentric hypertrophy.[17] Concentric hypertrophy has also been reported with late gestational age and higher maternal weight.[18] Some of these changes persist 1 year postpartum and are accentuated by subsequent pregnancies.[19] Whether these changes persist long-term and whether small physiologic changes during pregnancy can result in pathologic changes with accumulated exposure are unclear. This study demonstrates long-term increases in LV chamber volumes and LV mass, without a significant change in concentricity.

Although some studies report no significant change in LVEF during pregnancy,[20] others demonstrate a small, but statistically significant, decrease in LVEF in the third trimester and a decrease in all strain parameters at the end of pregnancy.[21] LVEF and strain parameters improve in the immediate postpartum state;

however, whether there are longer-term sequelae of these small functional changes with recurrent pregnancies is unknown. In the present study, parity is inversely associated with LVEF, suggesting an additive effect of each pregnancy. Although statistically significant, clinical relevance of such small changes is unclear.

Cardiometabolic changes or accumulated cardiometabolic risk factors may be an alternate mechanism for the noted changes. Multiparity has been associated with cardiovascular risk factors, including midlife BMI, waist and hip circumference, and weight gain,[22] that partially attenuate the association with long-term cardiovascular risk. Obesity causes increased blood volume with associated increased preload. Studies have shown that obesity is associated with larger LA size and both eccentric and concentric patterns of LV hypertrophy: the degree of cardiac remodeling correlates with the severity and duration of obesity. Cardiac structural changes associated with obesity have been shown to be only partially reversible with significant weight loss after bariatric surgery.[23,24] Obesity may also augment the normal physiologic structural changes seen in pregnancy.[18]

Age and cardiometabolic risk factors can affect cardiac structure and function. However, the association between parity and LVEDV, LVESV, LV mass, and LVEF remained significant after adjustment for age, hypertension, BMI, waist/hip ratio, and diabetes, suggesting an independent association of parity on the observed cardiac structural changes.

Lower socioeconomic status is also correlated with a higher burden of cardiometabolic risk factors and higher parity; however, adjustment for education and income as surrogates for socioeconomic status did not attenuate the association.

Higher parity was more common among Hispanic women and less common among White women, with no association with Black race. When stratified by race, the association between parity and LVEDV, LVESV, LV mass, and LVEF was only significant in Black women. Although not statistically significant, these LV parameters showed similar trends in White and Hispanic women (except for LV mass in White women). Baseline LV structural differences by race are likely present[23–25] and may affect a woman's ability to adapt to the hemodynamic stress of pregnancy. In this study, a higher

Table 4. Association of MRI Parameters and PR Interval per Number of Live Births, Stratified by Race or Ethnicity

Variable	LVEDV	LVESV	LVEF	LV mass	PR interval
Black race	2.07±0.60 (<0.01)*	1.32±0.33 (<0.01)*	−0.0066±0.002 (<0.01)*	1.77±0.75 (0.02)	1.19±0.51 (0.02)
White race	0.27±0.81 (0.74)	0.17±0.45 (0.71)	−0.0001±0.003 (0.97)	−0.83±0.75 (0.27)	1.09±0.82 (0.18)
Hispanic ethnicity	0.46±0.73 (0.53)	0.32±0.40 (0.42)	−0.0015±0.0026 (0.56)	0.66±0.80 (0.41)	1.26±0.76 (0.097)

Data are given as β coefficient±SE (*P* value). Covariates: age, race, income, education level, hypertension, smoking, and body mass index for ECG parameter or body surface area for MRI parameters. LV indicates left ventricular; LVEDV, LV end-diastolic volume; LVEF, LV ejection fraction; LVESV, LV end-systolic volume; and MRI, magnetic resonance imaging.

P interaction for race or ethnicity×number of live births <0.05.

percentage of Black participants had hypertension and diabetes (Table 5), which may contribute to the reported association. The hemodynamic stress of pregnancy may lead to more adverse cardiac remodeling in populations with higher risk factor burden. It remains to be determined whether these findings may partially explain observed differences in pregnancy outcomes between races.[26]

This study also demonstrated an association between increasing number of live births and a longer PR interval. There was no association with any other ECG intervals. There has only been 1 other study to show an association between parity and electrocardiographic parameters.[27] The authors reported that grand multiparity (≥5 live births) was associated with a 1.32-ms increase in PR interval, supporting the plausibility of our findings. Pregnancy has been associated with increase in P-wave parameters (P-wave duration and P-wave dispersion) when compared with controls,[28] with exaggerated changes in pathologic states, such as preeclampsia.[29,30] The mechanism for the increased PR interval with higher parity may be related to the cardiac structural changes that occur with higher parity. A study from the MESA cohort demonstrated an association between a prolonged PR interval and LV parameters, including LV mass, LVESV, and LVEDV.[31] In the current study, the association between parity and the PR prolongation was independent of increased LV mass, LVESV, and LVEDV.

Another possible mechanism is prolonged exposure to the hormonal milieu of pregnancy, resulting in electrical conduction changes. A large-scale study reported that prolonged reproductive duration (age from menarche to menopause) is associated with a prolonged PR interval, suggesting a hormonal effect on cardiac conduction.[27]

PR prolongation has also been associated with adverse clinical outcomes. A subanalysis of the CARE-HF (Cardiac Resynchronization-Heart Failure) trial demonstrated that a prolonged PR interval was associated with increased heart failure hospitalizations and all-cause mortality in a multivariate analysis.[32] A prolonged PR interval has also been associated with advanced LA remodeling in atrial fibrillation and may be a predictor of atrial fibrillation incidence and recurrence, although the data are mixed.[33,34] Whether PR prolongation is a marker of underlying disease or a mediator of disease is unclear and requires additional research.

Our findings support and add to the limited data in this field on the association between parity and long-term cardiac structural and electrical changes. The addition of electrical conduction parameters in our study allows for a more comprehensive assessment of pregnancy-associated cardiovascular changes. This study is also unique in that it includes a population with a large representation of Black women.

The association between increasing number of live births and cardiac structural and electrical conduction parameters later in life suggests that there may be long-term legacy effects of pregnancy. Whether these accumulative changes are pathologic and are mediators of the increased risk of heart failure and arrhythmias, including atrial fibrillation, that is seen in multiparous women requires additional investigation.

This study adds to the growing body of literature that pregnancy can have a significant impact on future cardiovascular risk. A pregnancy history including number of children, gestational ages, number of miscarriages, and adverse pregnancy outcomes should be included as part of comprehensive risk assessment in women. The additive role of parity in cardiovascular risk assessment is still to be determined.

Table 5. Risk Factors by Race or Ethnicity

Variable	White race (n=657)	Black race (n=1656)	Hispanic ethnicity (n=587)	Other (n=44)	*P* value
Age, y	50.0 (40.0–59.0)	45.0 (35.0–54.0)	38.0 (29.0–47.0)	41.5 (31.0–51.0)	<0.0001
BMI, kg/m^2	27.4 (24.1–32.7)	30.7 (25.9–36.5)	28.8 (24.9–33.6)	30.0 (22.7–28.8)	<0.0001
WHR	0.84 (0.80–0.89)	0.86 (0.82–0.91)	0.87 (0.82–0.91)	0.87 (0.82–0.92)	<0.0001
Hyperlipidemia	156 (28.0)	249 (22.3)	59 (14.7)	6 (20.7)	<0.0001
Diabetes	48 (8.6)	196 (17.4)	54 (13.4)	3 (10.3)	<0.0001
Smoking	166 (25.4)	395 (24.0)	64 (10.9)	6 (13.6)	<0.0001
Hypertension	236 (36.3)	785 (48.3)	123 (21.1)	10 (23.3)	<0.0001
SBP, mmHg	123.0 (111.8–135.3)	128.0 (115.7–142.7)	116.2 (107.3–127.3)	121.3 (107.7–134.3)	<0.0001
DBP, mmHg	77.3 (71.3–83.0)	80.0 (74.0–87.7)	74.3 (68.3–81.0)	73.7 (70.0–84.0)	<0.0001
TC, mg/dL	196.0 (172.0–223.0)	186.0 (162.0–211.0)	183.0 (160.0–209.0)	182.0 (164.0–218.0)	<0.0001
LDL-C, mg/dL	113.0 (93.0–137.0)	111.0 (89.0–134.0)	106.5 (87.0–128.0)	107.0 (94.0–138.0)	0.02
HDL-C, mg/dL	54.0 (45.0–66.0)	53.0 (45.0–62.0)	48.0 (40.0–56.0)	54.0 (48.0–63.0)	<0.0001
Triglycerides, mg/dL	107.0 (75.0–157.0)	86.0 (65.0–117.0)	122.5 (84.0–171.0)	103.0 (88.0–132.0)	<0.0001

Data are given as median (interquartile range) or number (percentage). BMI indicates body mass index; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; TC, total cholesterol; and WHR, waist/hip ratio.

Limitations

The limitations of our study include a retrospective cohort design that limits our ability to assess for causality. Given the prior link between lower socioeconomic status and higher live births, we have adjusted for surrogate markers of socioeconomic status (eg, race, income, and education). However, we acknowledge there may be additional biological or socioeconomic confounders that are not accounted for in our multivariable models and recognize that race is a social construct and a proxy for structural racism, rather than a proxy for genetics. Structural racism influences social determinants of health, which, in turn, influence cardiac risk factors. We did not evaluate associations between number of live births in men and cardiac structural findings because of incomplete data: such analyses represent another approach to account for confounding by socioeconomic factors.[35] Pregnancy history obtained in the DHS was limited. Information on miscarriages, abortions, adverse pregnancy outcomes, maternal age at delivery, and delivery dates is not available. Thus, time elapsed from dates of delivery to date of MRI is unknown and unable to be adjusted for. We were unable to adjust for preeclampsia, gestational diabetes, and other pregnancy complications that are known to be associated with increased cardiovascular risk. However, prior studies have shown that the association of parity with cardiovascular disease is independent of pregnancy complications.[36] The DHS questionnaire asked participants to report total number of live births in DHS1 and total number of children in DHS2. Although the questions are worded differently, there was a strong correlation ($r=0.92$) between the responses for these 2 questions for women who responded in both DHS1 and DH2. Our study did not adjust for medications, such as antidepressants, which can affect electrocardiographic parameters. However, changes in other electrocardiographic parameters (eg, QRS interval and QT interval) were not observed, which are more likely to be affected by antidepressants. Because of low event rates in this study population, we were unable to correlate the electrocardiographic and structural findings with clinical outcomes.

CONCLUSIONS

Increasing number of live births was associated with prolongation of the PR interval, an increase in LVEDV, LVESV, and LV mass, and lower LVEF in a multiethnic population. This is one of the first studies to correlate ECG parameters with number of live births. Whether these changes are pathologic and increase the risk of heart failure or arrhythmias in women warrants further investigation. When stratified by race, the association between MRI structural changes and parity were only significant in Black women, underscoring the racial differences noted in maternal morbidity and mortality.

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