Hypertension

ORIGINAL ARTICLE

Cardiac Abnormalities in Hispanic/Latina Women With Prior De Novo Hypertensive Disorders of Pregnancy

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BACKGROUND: Hypertensive disorders of pregnancy (HDP) are associated with long-term maternal risks for cardiovascular disease for reasons that remain incompletely understood.

METHODS: The HCHS/SOL (Hispanic Community Health Study/Study of Latinos), a multi-center community-based cohort of Hispanic/Latino adults recruited 2008 to 2011, was used to evaluate the associations of history of de novo HDP (gestational hypertension, preeclampsia, eclampsia) with echocardiographic measures of cardiac structure and function in Hispanic/Latina women with ≥1 prior pregnancy and the proportion of association mediated by current hypertension (>140/90 mm Hg or antihypertensive therapy).

RESULTS. The study cohort included 5168 Hispanic/Latina women with an average age (SD) of 58.7 (9.7) years at time of echocardiogram. Prior de novo HDP was reported by 724 (14%) of the women studied and was associated with lower left ventricle (LV) ejection fraction −0.66 (95% confidence interval [CI], −1.21 to −0.11), higher LV relative wall thickness 0.09 (95% CI, 0–0.18), and 1.39 (95% CI, 1.02–1.89) higher risk of abnormal LV geometry after adjusting for blood pressure and other confounders. The proportion of the association mediated by current hypertension between HDP and LV ejection fraction was 0.09 (95% CI, 0.03–0.45), LV relative wall thickness was 0.28 (95% CI, 0.16–0.51), abnormal LV geometry was 0.14 (95% CI, 0.12–0.48), concentric left ventricular hypertrophy was 0.31 (95% CI, 0.19–0.86), and abnormal LV diastolic dysfunction was 0.58 (95% CI, 0.26–0.79).

CONCLUSIONS. In a large cohort of Hispanic/Latina women those with history of de novo HDP had detectable and measurable subclinical alterations in cardiac structure and both systolic and diastolic dysfunction that were only partially mediated by current hypertension. ***(Hypertension.* 2024;81:255–263. DOI: 10.1161/HYPERTENSIONAHA.123.21248.)** • **Supplement Material**.

Key Words: blood pressure ■ cardiovascular disease ■ cardiovascular pregnancy complication ■ Hispanic ■ hypertension ■ ventricular cardiac remodeling

The rates of hypertensive disorders of pregnancy (HDP), including preeclampsia and gestational hypertension, more than doubled from 2007 to 2019 in the United States with highest rates in Non-Hispanic Black and Hispanic/Latina women.[1,2] Growing evidence demonstrates that history of HDP is associated with higher maternal risk for long-term cardiovascular disease (CVD) and CVD-related death;[3,4] resulting in the addition of HDP as a risk-modifier in the 2019 American College of Cardiology/American Heart Association primary prevention guidelines.[5]

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ORIGINAL ARTICLE

NOVELTY AND RELEVANCE

What Is New?

First study to evaluate the cardiac sequelae of de novo hypertensive disorder of pregnancy in a cohort of 5168 Hispanic/Latina women.

What Is Relevant?

Women with de novo hypertensive disorders of pregnancy had detectable and measurable subclinical alterations in cardiac structure and both systolic and diastolic dysfunction, above and beyond the effects of current hypertension.

Clinical/Pathophysiological Implications?

Our findings suggest that women with de novo hypertensive disorders of pregnancy have pathophysiologic cardiac sequelae decades later that likely play a role in modulating long-term cardiovascular risk in women.

Nonstandard Abbreviations and Acronyms

BP	blood pressure
CVD	cardiovascular disease
EF	ejection fraction
HCHS/SOL	Hispanic Community Health Study/ Study of Latinos
HDL	high-density lipoprotein
HDP	hypertensive disorders of pregnancy
LV	left ventricle
LVH	left ventricular hypertrophy
RWT	relative wall thickness
TTE	transthoracic echocardiography

Prior investigations have found evidence of structural cardiac abnormalities during the antepartum and immediate postpartum period, attributable in part to the short-term hemodynamic effects of excess afterload in pregnancies complicated by HDP.[6–8] These cardiac structural changes, including increased left ventricle (LV) wall thickness, mass index, diastolic dysfunction, and abnormalities in strain, have been shown to persist postpartum in pregnancies complicated by HDP.[9–11] Up to 20% of women with pregnancies complicated by HDP remain hypertensive after 6 months postpartum and have a 3- to 10-fold lifetime risk of chronic hypertension.[12,13] However, the role of chronic hypertension on adverse cardiac remodeling in women with history of HDP remains debatable. This is due to the mixed findings in studies to date, from some showing adverse cardiac remodeling driven by chronic hypertension regardless of HDP-history, to evidence that adverse remodeling is independent of the development of chronic hypertension, to reports on the cumulative effects of history of HDP and chronic hypertension on adverse remodeling.[9–11] Yet, very little is known about the effects of HDP on cardiac abnormalities and the role of chronic hypertension in Hispanic/Latina women, one of the fastest-growing ethnic minority group in the United States with a diverse genetic architecture.[14]

The degree to which cardiac abnormalities occur well beyond the early postpartum period before the development of CVD decades later—notwithstanding the effects of postpartum or age-related chronic hypertension—has remained unclear. We hypothesize that history of de novo HDP is associated with pathological alterations in cardiac structure and function that are only partially mediated by current hypertension. We aimed to examine this hypothesis in a diverse cohort of Hispanic/Latina women in the United States.

METHODS

Study Sample

We studied participants of the HCHS/SOL (Hispanic Community Health Study/Study of Latinos), a multi-center community-based cohort of all Hispanic/Latino adults representing diverse backgrounds (Central American, Cuban, Dominican, Mexican, Puerto Rican, and South American).[14] The HCHS/SOL sampling methods and design have been detailed previously.[15,16] In brief, self-identified Hispanic/Latino men and women were recruited between March 2008 to June 2011 from 4 communities in the United States (Bronx, NY; Chicago, IL; Miami, FL; and San Diego, CA) using a multi-stage area probability sample design. At each stage of sampling, oversampling occurred, and sampling weights were generated to reflect the probabilities of selection. The institutional review board at each study site approved all protocols, and all study participants provided written informed consent. Data from the HCHS/SOL cohort is publicly available to researchers upon application to NHLBI BIOLINCC.

Of the 16 415 HCHS/SOL participants who enrolled in this study, we included women age ≥45 years who completed visit 2 and transthoracic echocardiography (TTE) and reported at least 1 prior pregnancy at baseline visit (2008–2011) or visit 2 (2014–2017). We excluded men (n=4281), participants that did not complete visit 2 (n=4792), did not complete TTE (n=1663), participants that were never pregnant or missing data on pregnancy

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history (n=405), and participants with missing data on HDP history (n=109). The final sample for this analysis included 5168 women (724 with HDP and 4444 without HDP; Figure).

Clinical and Echocardiographic Data Collection

At each study visit, all study participants underwent a standardized assessment of demographic and clinical characteristics including questionnaires regarding medical and pregnancy history along with standardized measurements of blood pressure (BP), as previously described.[16,17] Visit 2 questionnaire collected self-reported data on the history of gestational hypertension (collected as high BP or hypertension first diagnosed during pregnancy), preeclampsia (collected as preeclampsia or toxemia) and eclampsia (collected as seizures, convulsions, or eclampsia) for all their pregnancies. We defined composite de novo HDP status as any history of gestational hypertension, preeclampsia, or eclampsia.

At visit 2, participants age ≥45 years underwent comprehensive 2-dimensional TTE performed according to a previously detailed standardized protocol.[18] In brief, TTE examination was performed with the participant in the partial left decubitus position with image acquisition techniques and measurements of cardiac structure and function performed according to American Society of Echocardiography guidelines.[19,20] All image acquisition was performed by centrally trained and certified research sonographers and all imaging measurements were conducted by imaging technical specialists at the core HCHS/SOL Echocardiography Reading Center at Brigham and Women's Hospital.[18]

As previously described, we defined concentric remodeling as LV mass index ≤95 gm/m^2 and relative wall thickness (RWT) >0.42, concentric LV hypertrophy (LVH) as LV mass index >95 gm/m^2 and RWT >0.42, and eccentric LVH as LV mass index >95 gm/m^2 and RWT ≤0.42.[19] Abnormal LV geometry was defined as presence of concentric remodeling, concentric LVH, or eccentric LVH. Diastolic function was graded according to an algorithm that integrates American Society of Echocardiography guidelines with Redfield criteria as previously described.[17] In the analysis, LV diastolic dysfunction was dichotomized and grade I–IV diastolic dysfunction was compared with normal diastolic function.

Statistical Analyses

We compared demographic, clinical, and echocardiographic traits in Hispanic/Latina women with and without prior HDP using the Student *t* test for continuous variables and χ^2 test for categorical variables. Holm-Bonferroni method was used to adjust for multiple comparisons.

We then used multivariable-adjusted regression models to examine the association of prior HDP status with established measures of cardiac structure and function: LV ejection fraction (EF), LV stroke volume, LV mass index, LV end-diastolic diameter, LV mass/end-diastolic volume ratio, LV RWT, peak tricuspid regurgitation velocity, lateral E/e′ ratio, concentric remodeling, concentric LVH, eccentric LVH, abnormal LV geometry, and abnormal LV diastolic function. We constructed linear and logistic regression models for continuous and categorical variables, respectively. For all echocardiographic traits, model 1 adjusted for age, study field center, and Hispanic/Latino background. Model 2 adjusted for the covariates in model 1, in addition to SBP and treatment with antihypertensive therapy at visit 2. Model 3 adjusted for the covariates in model 2, in addition to body mass index, diabetes, smoking, total number of prior pregnancies, total cholesterol/HDL (high-density lipoprotein) ratio, and urine albumin-to-creatinine ratio all assessed at visit 2. Covariates were selected based on prior studies demonstrating association with HDP and LV measures of structure and function.[9–11] No adjustments were made for multiple testing. Stratified analyses were performed by type of HDP for gestational hypertension and preeclampsia, however, the sample size was too small to perform adjusted models for eclampsia.

In secondary analyses, we examined the extent to which current hypertension (defined as BP >140/90 mm Hg or antihypertensive therapy at visit 2) mediated the associations of HDP with echocardiography traits. Models are adjusted for age, field center, Hispanic/Latino background, and current hypertension. These analyses test the extent to which current

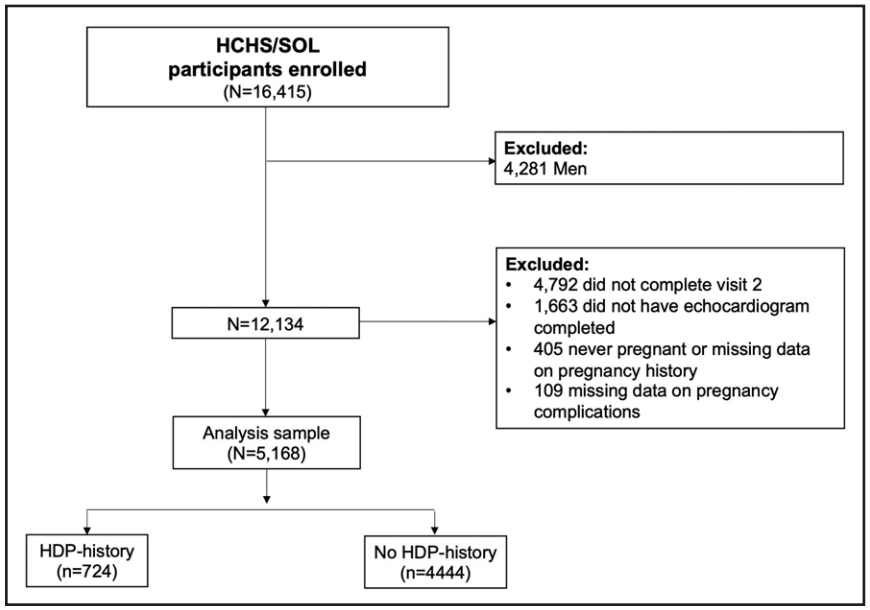

Figure. Sampling strategy and study design.
Central illustration. Proportion of association between hypertensive disorders of pregnancy and measures of left ventricular structure and function mediated by current hypertension in Hispanic/Latina women. Figure created using BioRender. HCHS/SOL indicates Hispanic Community Health Study/Study of Latinos; and HDP, hypertensive disorders of pregnancy.

hypertension mediate the associations of HDP with the given echocardiographic trait, whereby a mediation effect of 0 would indicate that current hypertension does not mediate the association and a mediation effect of 1 would indicate that current hypertension mediates all of the association (range of possible effect is from 0 to 1). We also assessed for potential interaction of current hypertension on HDP associations with each of the echocardiographic traits.

Reported values were survey-weighted, to account for the complex study design and the nonresponses for visit 2.[15] Weights were trimmed and calibrated to the 2010 Census characteristics by age, sex, and Hispanic/Latino background. We considered statistical significance as a 2-tailed *P* value and Holm-Bonferroni adjusted *P* value of <0.05. All statistical analysis were conducted using R (v4.0.4).

RESULTS

Of the total study sample including 5168 Hispanic/Latina women with prior pregnancy, 724 (14%) reported a history of de novo HDP including 439 (61%) gestational hypertension, 219 (30%) preeclampsia, and 66 (9%) eclampsia. The mean age (SD) at visit 2 was 58.7 (9.7) years. The demographic and clinical characteristics of the study sample at visit 2 are shown in Table 1. Hispanic/Latina women with a history of de novo HDP, compared with those without HDP were younger, had a higher level of education, greater body mass index, and more frequent history of dyslipidemia. After the Holm-Bonferroni adjustment, dyslipidemia and HDL-cholesterol levels were no longer statistically different between the groups. With respect to echocardiographic LV characteristics (Table S1), Hispanic/Latina women with prior HDP had lower LV EF, and higher LV stroke volume, LV mass index, LV RWT, and peak tricuspid regurgitation velocity. After the Holm-Bonferroni adjustment, LV mass index and peak tricuspid regurgitation velocity were not significantly different between the groups. HDP was associated with higher rates of concentric LVH, abnormal LV geometry, and abnormal LV diastolic function.

In multivariable-adjusted analyses, prior de novo HDP was associated with lower LV EF in all models after adjustment for systolic BP, antihypertensive therapy and confounders ($P \leq 0.02$; Table 2). Prior HDP was also associated with higher LV RWT in all models ($P \leq 0.04$). Prior HDP was associated with a 1.92-fold higher odds of LV stroke volume, LV mass index, LV relative wall thickness, peak tricuspid regurgitation velocity, and lateral E/e′ ratio after adjustment for age and demographic factors (model 1) but the associations were attenuated in subsequent models. Notably, prior HDP was significantly associated with higher risk of abnormal LV geometry in all models ($P \leq 0.04$). Prior HDP was associated with higher risk of concentric LVH and abnormal LV diastolic function after adjustment for age and demographic factors (model 1; $P = 0.001$ and $P = 0.01$, respectively); these associations were attenuated when adjusted for systolic BP and antihypertensive therapy. All other measures of cardiac structure and function were not significantly associated with history of HDP.

In secondary analyses, we examined the extent to which current hypertension mediated the associations of de novo HDP with echocardiography traits. Current hypertension at visit 2 was seen in 459 (63.4%) of Hispanic/Latina women with HDP-history and 1830 (41.2%) with normotensive pregnancies. We found that the proportion of the association between HDP and LV EF mediated by current hypertension was modest at 0.09 (95% confidence interval [CI], 0.03–0.45), with similar results seen for abnormal LV geometry (0.14 [95% CI, 0.12–0.48]); Table 3). The proportion of the association between HDP and other traits mediated by postpartum hypertension were higher for LV RWT (0.28 [95% CI, 0.16–0.51]), concentric LVH (0.31 [95% CI, 0.19–0.86]), and abnormal LV diastolic dysfunction (0.58 [95% CI, 0.26–0.79]). We also assessed for potential interaction of current hypertension on the associations of HDP with each of the echocardiographic traits and found no significant interactions ($P > 0.30$ for all). We observed no material difference in any results of analyzing data using survey-weighted versus unweighted values.

In stratified analysis by type of HDP, there was a significant trend towards lowest EF and LV stroke volume and highest LV RWT in women with eclampsia history (Table S2). The proportion of concentric LVH was highest in women with history of gestational hypertension and the proportion of abnormal LV geometry was highest in those with history of eclampsia and gestational hypertension. In multivariable-adjusted analyses, gestational hypertension was associated with LV RWT and 1.79-fold higher risk of abnormal LV geometry across all models, whereas there was no association between preeclampsia and any of the measures of LV structure and function (Table S3).

DISCUSSION

In our study of over 5100 Hispanic/Latina women with prior pregnancy, 14% reported de novo HDP. Women with history of de novo HDP were significantly more likely to have measurable abnormalities in cardiac structure and function, including lower LV systolic function and higher rates of abnormal LV geometry than women without history of HDP. These cardiac alterations were in part mediated by the effects of current hypertension (Central Illustration).

The rate of de novo HDP in this study is consistent with the 12.5% (95% CI, 12.2–12.8) reported in the United States National Inpatient Sample between 2017 and 2019.[21] To date, a scant number of studies have examined longer-term cardiac phenotypes following delivery before development of clinical CVD; these

Table 1. Demographics and Clinical Characteristics by De Novo Hypertensive Disorders of Pregnancy History

Characteristics at visit 2	Overall, N=5168	De novo HDP history		*P* value	Adjusted *P* value
		No	Yes		
		N=4444	N=724		
Demographics					
Age, y, mean (SD)	58.7 (9.7)	59.2 (9.7)	56.3 (8.8)	<0.001	<0.001
Hispanic/latino background, %				0.1	0.7
Dominican	11	11	13		
Central/South American	12	12	12		
Cuban	22	22	23		
Mexican	34	36	28		
Puerto-Rican	18	17	21		
Other or >1 heritage	3	2	4		
Participant's field center, %				0.1	0.9
Bronx	29	28	33		
Chicago	13	13	11		
Miami	32	32	34		
San Diego	26	27	23		
Years living in United States, y, mean (SD)	29.3 (16.6)	29.3 (16.5)	28.9 (16.7)	0.7	1.0
Annual family income ≥$30 000, %	62	62	62	1.0	1.0
Health insurance coverage, %	81	81	82	0.5	1.0
Clinical characteristics					
Blood pressure based on ACC/AHA, %				<0.001	<0.001
Normal	27	30	18		
Elevated BP	9	10	6		
Stage 1 hypertension	43	41	58		
Stage 2 hypertension	11	11	10		
Antihypertensive therapy, %	43	41	58	<0.001	<0.001
Diabetes, %	31	30	39	<0.001	<0.001
Dyslipidemia, %	30	29	35	0.02	0.3
Metabolic syndrome, %	53	51	63	<0.001	<0.001
Current smoker, %	13	13	14	0.7	1.0
Number of pregnancy, mean (SD)	4 (2)	4 (2)	4 (2)	0.6	1.0
HDP type, %	14				
Gestational hypertension	9	…	61		
Preeclampsia	4	…	30		
Eclampsia	1	…	9		
Clinical measures					
Systolic blood pressure, mm Hg, mean (SD)	127 (20)	127 (20)	129 (19)	0.05	0.5
Diastolic blood pressure, mm Hg, mean (SD)	73 (11)	72 (10)	76 (12)	<0.001	<0.001
Body mass index, kg/m^2, mean (SD)	31 (6)	30 (6)	32 (7)	<0.001	<0.001
Cholesterol, total, mg/dL, mean (SD)	201 (40)	200 (40)	203 (41)	0.3	1.0
LDL cholesterol, mg/dL, mean (SD)	121 (36)	121 (36)	121 (37)	0.8	1.0
HDL cholesterol, mg/dL, mean (SD)	54 (15)	55 (15)	53 (15)	0.03	0.4
Triglycerides, mg/dL, mean (SD)	130 (80)	127 (72)	144 (116)	0.003	0.05
Urine albumin/creatinine ratio, mean (SD)	46 (330)	40 (318)	77 (404)	0.1	0.9

The adjusted *P* value represents the Holm-Bonferroni adjustment for multiple comparisons (alpha set at <0.05). ACC/AHA indicates American College of Cardiology/American Heart Association; BP, blood pressure; HDL, high-density lipoprotein; HDP, hypertensive disorders of pregnancy; and LDL, low-density lipoprotein.

Table 2. Associations Between De Novo Hypertensive Disorders of Pregnancy History and Measures of Left Ventricle Structure and Function.

Echocardiographic measures	Model 1		Model 2		Model 3	
	Coefficient (95% CI)	*P* value	Coefficient (95% CI)	*P* value	Coefficient (95% CI)	*P* value
Continuous measures						
LV ejection fraction, %	−0.90 (−1.45 to −0.04)	0.001	−0.75 (−1.30 to −0.21)	0.01	−0.66 (−1.21 to −0.11)	0.02
LV stroke volume, mL	1.72 (0.32 to 3.12)	0.02	0.94 (−0.41 to 2.29)	0.2	0.32 (−0.96 to 1.61)	0.6
LV mass index, g/m^2	3.70 (1.46 to 5.94)	0.001	1.57 (−0.50 to 3.64)	0.1	1.05 (−1.01 to 3.10)	0.3
LV end-diastolic diameter, cm	0.01 (−0.49 to 0.52)	1.0	−0.12 (−0.62 to 0.38)	0.7	−0.29 (−0.75 to 0.18)	0.2
LVMI/EDV ratio	0.01 (−0.03 to 0.04)	0.7	−0.01 (−0.04 to 0.03)	0.7	0 (−0.04 to 0.03)	0.9
LV relative wall thickness, cm	0.22 (0.13 to 0.31)	<0.001	0.14 (0.05 to 0.23)	0.003	0.09 (0 to 0.18)	0.04
PTRV, cm/s	7.37 (2.50 to 12.25)	0.003	4.0 (−0.92 to 8.92)	0.1	2.22 (−2.65 to 7.09)	0.4
Lateral E/e′ ratio	0.58 (0.19 to 0.96)	0.004	0.19 (−0.19 to 0.58)	0.3	0 (−0.37 to 0.38)	0.1
Categorical measures						
Concentric LV remodeling	1.33 (1.01 to 1.75)	0.05	1.25 (0.94 to 1.67)	0.1	1.16 (0.87 to 1.55)	0.3
Concentric LVH	1.92 (1.32 to 2.79)	0.001	1.45 (0.97 to 2.16)	0.1	1.30 (0.85 to 1.99)	0.2
Eccentric LVH	1.60 (0.80 to 3.21)	0.2	1.32 (0.64 to 2.75)	0.4	1.38 (0.63 to 3.0)	0.4
Abnormal LV geometry	1.86 (1.39 to 2.49)	<0.001	1.51 (1.12 to 2.03)	0.01	1.39 (1.02 to 1.89)	0.04
Abnormal LV diastolic function	1.52 (1.13 to 2.05)	0.01	1.14 (0.83 to 1.57)	0.4	1.02 (0.73 to 1.42)	0.9

Model 1 is adjusted for age, field center, Hispanic background; model 2 is adjusted for all variables in model 1, in addition to systolic blood pressure and antihypertensive therapy at visit 2; model 3 is adjusted for all variables in model 2, in addition to diabetes status, smoking, total cholesterol HDL ratio, number of pregnancies, BMI, urine albumin-to-creatinine ratio. BMI indicates body mass index; EDV, end-diastolic volume; HDL, high-density lipoprotein; LV, left ventricle; LVH, left ventricular hypertrophy; LVMI, LV mass index; and PTRV, peak tricuspid regurgitation velocity.

few studies, with sample sizes of <200 women with history of HDP report an association with LVH and LV diastolic dysfunction.[22,23] In studies accounting for chronic hypertension, findings are mixed on whether or not the changes in cardiac structure and function associated with HDP history are present after adjusting for chronic hypertension —an obvious confounder of CVD risk.[9–11] We extend previous work and analyze one of the largest samples of de novo HDP in 724 women and compared their cardiac phenotypes with 4444 similarly aged clinical controls (ie, women with prior pregnancy but no HDP). Importantly, we found that prior HDP was associated with higher LV RWT and higher risk of abnormal LV geometry—even after adjusting for current hypertension and cardiovascular risk factors—consistent with a recent study by Countouris et al[11] in a cohort of non-Hispanic White and Black women. Our study extends these findings to Hispanic/Latina women who are underrepresented in research studies.

Table 3. Causal Mediation Analysis to Assess Mediation Effect of Current Hypertension for Observed Association Between De Novo Hypertensive Disorders of Pregnancy and Measures of Left Ventricle Structure and Function

Echocardiographic measures	Proportion of association with HDP mediated by current hypertension (95% CI)	*P* value
LV ejection fraction	0.09 (0.03 to 0.45)	0.01
LV relative wall thickness	0.28 (0.16 to 0.51)	<0.001
Concentric LVH	0.31 (0.19 to 0.86)	<0.001
Abnormal LV geometry	0.14 (0.12 to 0.48)	<0.001
Abnormal LV diastolic function	0.58 (0.26 to 0.79)	0.01

Models are adjusted for age, field center, Hispanic/Latino background, and current hypertension (defined as BP >140/90 or antihypertensive therapy). BP indicates blood pressure; HDP, hypertensive disorders of pregnancy; LV, left ventricle; and LVH, left ventricular hypertrophy.

History of pregnancy complicated by de novo HDP was associated with higher risk of abnormal LV geometry (defined as concentric LV remodeling, concentric LVH, or eccentric LVH as determined by LV mass index and RWT) after adjusting for important confounders. These findings are of clinical significance because abnormal LV geometry, particularly LVH, is an independent predictor of adverse cardiovascular events including heart failure, ischemic heart disease, and sudden cardiac death.[24] We also found an association between de novo HDP and abnormal LV diastolic function, which is linked to higher incidence of cardiovascular events in healthy cohorts and is a strong predictor of progression to heart failure.[25] Further, the individual measures of LV geometry (LV mass index, LV RWT) that we found to be associated with history of de novo HDP have also been shown to be associated with cardiovascular events. For instance, in the Framingham Heart Study of Offspring in a cohort of adults free of CVD, each 10 g/m^2 increment in LV mass index was associated with 33% increased risk of CVD and each 0.1 unit in LV RWT was associated with 59% increased risk of CVD.[26]

Further, this is the first known study to report de novo HDP history to be associated with decrements in LV systolic function. The finding of slightly lower LV EF despite greater concentric remodeling and higher stroke volume suggests a type of contractile inefficiency that is not typically seen in the setting of chronic hypertension alone, suggesting a pathophysiology distinct form of hypertensive heart disease. These findings and the LV diastolic dysfunction exhibited by these mothers all suggest a preheart failure with preserved EF remodeling phenotype, supported by the excess risk of heart failure with preserved EF in women with preeclampsia, that warrants further investigation.[27,28]

Hypertension results in chronic central pressure overload and myocardial ischemia that leads to the development of LVH and heart failure. Therefore, we evaluated the extent to which current hypertension mediated the association between history of de novo HDP and measures of cardiac structure and function. Hypertension is associated with significantly higher rates of concentric LVH and is a strong independent predictor of LV diastolic dysfunction, but the association with eccentric LVH and LV systolic dysfunction is less robust.[29,30] This helps explain why current hypertension was a moderate mediator in the association between HDP and concentric LVH and LV diastolic dysfunction but a weaker mediator of LV EF (a measure of LV systolic function). Our results are consistent with large epidemiological data indicating that the association of HDP with later-life CVD is only partially mediated by current hypertension.[4] These findings provide insights into HDP as a potential novel mechanism to explain the disproportionally higher risk of heart failure in women with a history of HDP.[31,32]

The mechanisms by which HDP may lead to abnormalities in cardiac structure and function beyond the effects of current hypertension remain to be elucidated.[33] Diabetes was found to be higher in Hispanic/Latina women with history of de novo HDP and although we included diabetes in our adjusted models it may have contributed to some of our findings. In fact, glucose intolerance, insulin resistance, and diabetes have been shown to be associated with increased LV mass and wall thickness and reduced end-diastolic volume, stroke volume, and EF.[34,35] Activation of pathways involving the antiangiogenic soluble fms-like tyrosine kinase 1 in preeclampsia can contribute to endothelial dysfunction and deranged lipid metabolism that can persist after delivery.[36,37] Dysregulations of the renin-angiotensin system may also contribute to persistent postpartum cardiac abnormalities. Additionally, shared upstream factors such as cardiovascular risk factors and genetics may predispose women to both HDPs and later in life pathological LV remodeling and function. Further investigations are needed to identify the potential mechanisms contributing to cardiac abnormalities in women with history of HDP and how these may be different by race and ethnicity.

Study Limitations

Several limitations of our study merit consideration. The cross-sectional design of our study precludes inference of causality, although timing of reported prior HDP consistently preceded timing of assessed cardiac traits. Prior HDP status was based on self-report, which is subject to recall bias and limits precision with respect to subtypes of HDP; nonetheless, self-report has been evaluated as valid and thus applied in the vast majority of cohort studies on HDP.[38,39] Data are not available on severity of preeclampsia, number of pregnancies complicated by HDP, or the exact timing of diagnosis of de novo HDP, or current hypertension. Therefore, we are unable to account for the time period between HDP pregnancy and development of hypertension, or performance of TTE at visit 2, or the length of time with hypertension diagnosis, which limits our understanding of how these important factors affect cardiac structure and function. Additionally, multiple echocardiographic measures were analyzed, which can lead to heightened type 1 error rate. Despite these limitations, our study offered several strengths including analyses from the largest study to date investigating the relations of prior HDP with cardiac traits in Hispanic/Latina women who represent a demographically important yet historically understudied population. In addition, all cardiac traits were assessed from echocardiographic protocols that involved standardized image acquisition and centralized measures performed at a core center with high interreader and intrareader reproducibility and BP was measured in a standardized method.

Conclusions

In a large cohort of previously pregnant Hispanic/Latina women, those with history of de novo HDP had detectable and measurable pathological alterations in cardiac structure and systolic and diastolic dysfunction. Our findings suggest that women with prior HDP have pathophysiologic cardiac sequelae decades later, not fully explained by hypertension postpartum, that likely play a role in modulating long-term cardiovascular risk. Notwithstanding the need for further investigations into the mechanisms driving HDP pathophysiology, our findings highlight the potential importance of targeted surveillance and interventions aimed at preventing later-life cardiovascular events in these at-risk understudied women.

Perspectives

Hispanic/Latina women are disproportionally affected by HDP, yet very little is known on how HDP affects cardiac structure and function in this growing population in the United States. In this study of a diverse cohort of Hispanic/Latina women, those with history of de novo HDP had higher rates of abnormal LV geometry, and alterations in cardiac structure (LV mass index, RWT) and function (LVEF, diastolic dysfunction), known

predictors of cardiovascular events and mortality. Notably, these findings appear to be in part mediated by current hypertension—underscoring the importance of screening for and managing hypertension. Hypertension alone did not account for all the associations between history of de novo HDP and morphological and functional cardiac alterations. With the higher rates of heart failure, particularly heart failure with preserved EF, in women and the alterations in cardiac structure and function identified in this study; we hypothesize HDP may be a sex-specific risk factor for heart failure that warrants further investigation.

ARTICLE INFORMATION

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Disclosures

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