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Characteristics, Adverse Events, and Racial Differences Among Delivering Mothers With Peripartum Cardiomyopathy

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Objectives The aim of this study was to identify clinical features associated with peripartum cardiomyopathy (PPCM) and possible racial differences and to quantify in-hospital outcomes in delivering mothers with PPCM.

Background Investigation of patient characteristics and outcomes in PPCM has been limited to small cohorts. Hospital discharge data allow assembly of the largest number of PPCM cases to date.

Methods Hospital records from 6 states were screened for PPCM. Clinical profiles, maternal, and fetal outcomes in delivering mothers with and without PPCM were compared and stratified by race. A maternal major adverse event (MAE) was defined as death, cardiac arrest, heart transplantation, or mechanical circulatory support. Logistic regression was used to identify variables associated with PPCM.

Results In total, 535 of 4,003,914 records of delivering mothers specified a diagnosis of PPCM. Prevalence of PPCM was highest among African Americans and similar in Caucasians and Hispanics. Established risk factors including age $\geq$30 years, African- American race, hypertension, preeclampsia/eclampsia, and multigestational status were associated with PPCM, and novel associations such as anemia and asthma were identified. Autoimmune disease and substance abuse, which can cause cardiomyopathy independently, were also associated with PPCM. Maternal MAE (odds ratio: 436, $p < 0.0001$) and stillbirth (odds ratio: 3.8, $p < 0.0001$) occurred more frequently among women with PPCM.

Conclusions The prevalence of PPCM at the time of delivery in Hispanics was similar to Caucasians and lower than African Americans. Autoimmune disease, substance abuse, anemia and asthma were conditions associated with PPCM not consistently identified in smaller cohorts. Peripartum cardiomyopathy was also associated with increased risk of stillbirth and maternal MAEs at delivery. (J Am Coll Cardiol HF 2013;1:409–16) © 2013 by the American College of Cardiology Foundation

Peripartum cardiomyopathy (PPCM) is an idiopathic cardiomyopathy presenting with heart failure secondary to left ventricular systolic dysfunction toward the end of pregnancy or in the months after delivery. It is a diagnosis of exclusion when no other cause of heart failure is found (1). Prognosis of PPCM is variable and might range from full recovery to death or need for heart transplantation in up to 10% of cases (2). Peripartum cardiomyopathy has a low incidence in the United States, estimated at 1 of 3,000 to 1 of 4,000 births, making epidemiologic studies to investigate comorbidities associated with PPCM and PPCM-related adverse events challenging. It is known that the incidence of PPCM varies in different racial backgrounds (3–5), but the reason remains unclear in part due to small sample sizes. Currently accepted factors associated with development of PPCM include advanced maternal age, preeclampsia, hypertension, multiple gestations, African-American race, and prolonged use of tocolytics (6). Identification of additional risk factors would be important in development of a model to identify those at highest risk.

To better determine the clinical profiles and rates of adverse events in PPCM patients hospitalized for delivery, we used regional hospital discharge data to assemble the largest number of PPCM cases to date. We compared clinical profiles and outcomes in PPCM patients and stratified them on the basis of their racial backgrounds.

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Abbreviations and Acronyms

CI = confidence interval

ICD-9-CM = International Classification of Diseases-9-Clinical Modification

MAE = major adverse event

OR = odds ratio

PPCM = peripartum cardiomyopathy

Methods

Data source. The study was approved by our local institutional review board, and because all data are publicly available, the requirement for informed consent was waived. Data sources were administrative databases containing all inpatient hospital stays from all hospitals in each state during the study period. De-identified hospital records were obtained from state agencies in California, New Hampshire, New Jersey, New York, Vermont, and West Virginia (7–12), and all records after the 2003 introduction of PPCM International Classification of Diseases-9 Clinical Modification (ICD-9-CM) codes (674.5x) were screened. Demographic data, comorbid conditions, procedures, and outcomes were quantified using dataset documentation and ICD-9-CM codes (Online Appendix). Records were classified as reporting autoimmune disease if diagnosis codes for systemic lupus erythematosus, rheumatoid arthritis, dermatomyositis, polymyositis, Wegener's granulomatosis, Takayasu's arteritis, ulcerative colitis, or Crohn's disease were present. Records were classified as reporting substance abuse if abuse of alcohol, cocaine, opioids, sedatives/hypnotics, cannabis, amphetamines, hallucinogens, inhalants, or phencyclidine was reported. Population estimates were generated with 2000 and 2010 U.S. Census data (13). Data harmonization was performed with MySQL Server (version 5.5.18, Oracle Corporation, Redwood Shores, California).

Study population. From January 2003 through December 2007, there were 39,829,857 hospital records from 620 hospitals. All records that specified the outcome of a delivery (V27.x) were included in the analysis. A record was classified as indicating PPCM if it included any of the ICD-9 CM codes 674.50 to 55. Records were excluded if the patient was male or if the hospital record did not include an outcome of a delivery (n = 35,827,402). Among those excluded were 1,459 PPCM records without a delivery outcome.

Outcome Measures. The primary outcome was a composite of major adverse events (MAEs): death, cardiac arrest, heart transplantation, and/or mechanical circulatory support. Secondary outcomes included individual components of the primary endpoint, length of hospital stay, Cesarean delivery, and stillbirth.

Statistics. Comparisons of demographic data and comorbidities between the PPCM and control cohorts were first performed with the chi-square test for categorical variables, and Welch's t-test was performed for comparisons of length of stay. Odds ratios (ORs) for PPCM and corresponding confidence intervals (CIs) associated with demographic data and comorbid conditions were determined with univariate and multivariate logistic regression. Characteristics significantly associated with PPCM were then counted for each record. Association between the number of characteristics and PPCM was assessed with logistic regression. Demographic data, outcomes, and features associated with PPCM were also quantified according to 3 racial backgrounds: non-Hispanic Caucasian (Caucasian), non-Hispanic African-American (African-American), or Hispanic for all hospital stays in California, New York, and New Jersey where race and ethnicity were reported (n = 448 of 511). Race was not reported in Vermont, New Hampshire, or West Virginia (n = 24). Three-way chi-square testing was used to evaluate differences in categorical variables between all 3 groups collectively, and 2-way chi-square testing was used to compare PPCM and non-PPCM patients within each group. Logistic regression was used to identify significant interactions between demographic data, comorbidities, race, and presence of PPCM at the time of delivery. A p value <0.05 was considered significant. All statistical analyses were performed with the R statistical package (version 2.15.0; R Foundation for Statistical Computing, Vienna, Austria).

Results

Prevalence of PPCM present at delivery. A total of 535 hospital records from 243 different hospitals specified a diagnosis of PPCM and a delivery outcome during the study period. The PPCM records were compared with 4,003,379 records that included a delivery outcome without a diagnosis of PPCM (approximately 1 in 7,500).

Characteristics of the patients. Characteristics of all patients are shown in Table 1. The PPCM patients were more likely to be older and African-American and to have multiple gestations, preeclampsia, and eclampsia than the control group ($p < 0.0001$ for all). The PPCM patients were also more likely than control patients to have diabetes mellitus, hypertension, tobacco use, anemia, substance abuse, obesity ($p < 0.0001$ for all), and autoimmune disease ($p = 0.001$).

Patient characteristics associated with PPCM. Baseline characteristics of delivering mothers with PPCM were compared with delivering mothers without PPCM with logistic regression. Univariate and multivariate ORs for PPCM associated with all demographic features are shown in Table 2. Age ≥30 years old, African-American race, hypertension, anemia, substance abuse, asthma, multiple gestational status, preeclampsia, and eclampsia were significantly associated with PPCM in multivariate analysis. Among the characteristics identified via multivariate analysis, 87.1% of non-PPCM deliveries had 1 characteristic or less, whereas 66.5% of PPCM deliveries had at least 2 characteristics. The rate of PPCM present at the time of delivery increased exponentially with each additional characteristic associated with PPCM (Fig. 1) and was approximately 800× greater in patients with ≥6 characteristics than in those with none ($p < 0.0001$).

Outcomes. There were 36 MAEs (6.7%) in the PPCM cohort compared with 655 (0.02%) in the non-PPCM

Table 1 Characteristics of PPCM and Control Cohorts

	PPCM (n = 535)	Non-PPCM (n = 4,003,379)
Age, yrs*		
<18	15 (2.8%)	114,037 (2.8%)
18–29	185 (34.6%)	1,851,517 (46.2%)
30–39	246 (46.0%)	1,506,278 (37.6%)
>40	30 (5.6%)	134,621 (3.4%)
Not available	59 (11.0%)	396,927 (9.9%)
Race*		
Caucasian	173 (32.3%)	1,441,657 (36.0%)
African American	105 (19.6%)	324,430 (8.1%)
Hispanic	123 (23.0%)	1,183,438 (29.6%)
Other	37 (6.9%)	428,459 (10.7%)
Not available	97 (18.1%)	625,395 (15.6%)
Payor*		
Medicare	14 (2.6%)	10,963 (0.3%)
Medicaid	225 (42.1%)	1,622,410 (40.5%)
Private	271 (50.7%)	2,157,220 (53.9%)
Self-pay	15 (2.8%)	133,425 (3.3%)
Other	9 (1.7%)	66,038 (1.7%)
Not available	1 (0.0%)	10,963 (0.3%)
Comorbid conditions		
Diabetes mellitus*	15 (2.8%)	30,405 (0.8%)
Hypertension*	251 (46.9%)	254,863 (6.4%)
Tobacco use*	33 (6.2%)	85,826 (2.1%)
Anemia*	182 (34.0%)	255,747 (6.4%)
Substance abuse*	37 (6.9%)	45,006 (1.1%)
Asthma*	43 (8.0%)	88,023 (2.2%)
Obesity*	29 (5.4%)	43,084 (1.1%)
Autoimmune disease†	6 (1.1%)	8,344 (0.2%)
Pregnancy characteristics		
Multiple gestation*	60 (11.2%)	73,955 (1.8%)
Preeclampsia*	157 (29.3%)	119,165 (3.0%)
Eclampsia*	11 (2.1%)	3,020 (0.1%)

Values are n (%). *p < 0.0001. †p = 0.001.
PPCM = peripartum cardiomyopathy.

cohort. As shown in Table 3, the presence of PPCM was associated with a higher rate of MAEs compared with the control group (OR: 436.0, 95% CI: 303.1 to 607.7, p < 0.0001). Compared with non-PPCM deliveries, PPCM at the time of delivery was also associated with higher in-hospital mortality (OR: 175.2, 95% CI: 74.5 to 344.6, p < 0.0001), longer length of hospital stay (Δ 5.5 days, 95% CI: 5.33 to 5.74, p < 0.0001), higher likelihood of Cesarean section (OR: 5.49, 95% CI: 4.56 to 6.64, p < 0.0001) and stillbirth (OR: 3.74, 95% CI: 1.69 to 5.64, p < 0.0001). No heart transplantations or mechanical circulatory support were reported among PPCM patients hospitalized during delivery.

Racial differences. According to census data, 52.3% of women 18 to 65 years of age were Caucasian, 9.9% were African American, and 24.3% were Hispanic in California, New Jersey, and New York combined, whereas 38.6% of PPCM cases were Caucasian, 23.4% were African-American, and 27.5% were Hispanic. Of note, Hispanics had a significantly higher rate of hospital stay for delivery (5,647 of 100,000) compared with Caucasians (3,122 of 100,000) and African Americans (3,409 of 100,000) during the study period (p < 0.0001). The prevalence of PPCM at the time of delivery varied significantly between the 3 races (Caucasian = 1 of 8,333 deliveries, African American = 1 of 3,120 deliveries, Hispanic = 1 of 9,700 deliveries, p < 0.0001). Characteristics of Caucasian, African American, and Hispanic PPCM versus non-PPCM patients are shown in Table 4. All characteristics were significantly different between non-PPCM delivering mothers alone from the 3 groups (p < 0.0001 for all). Among patients with PPCM, age, payor status, and presence of hypertension varied significantly between the 3 groups (p = 0.02, p < 0.0001, and p = 0.01, respectively), although these differences were primarily between Caucasians and the other racial groups. The PPCM was associated with a higher rate of private insurance in Caucasian PPCM patients compared with African American or Hispanic PPCM patients but a lower rate of private insurance in Caucasian PPCM patients than in non-PPCM Caucasian patients. We found significant interactions favoring the presence of PPCM in Hispanic women with hypertension (interaction OR: 1.7, 95% CI: 1.07 to 2.7, p = 0.03), tobacco usage (interaction OR: 5.7, 95% CI: 2.1 to 15.0, p < 0.001), asthma (interaction OR: 2.5, 95% CI: 1.03 to 6.0, p = 0.04), and age >40 years (interaction OR: 3.1, 95% CI: 1.01 to 9.8, p = 0.04). Among Caucasians and African Americans, the only significant interaction was between African Americans and preeclampsia (interaction OR: 0.53, 95% CI: 0.3 to 0.9, p = 0.02).

The rate of maternal MAE was higher in PPCM compared with non-PPCM patients in all 3 racial groups, whereas the rate of stillbirth was significantly different in Hispanics only (p = 0.04) when comparing PPCM and non-PPCM patients.

Discussion

With a large, multi-regional hospital database we report several new observations with regard to PPCM. We confirm associations between previously identified risk factors and PPCM, including age ≥30 years, African-American race, hypertension, multiple gestational status, preeclampsia, and eclampsia, and we quantify their prevalence in 3 racial groups, including for the first time a large Hispanic cohort. We also identify new clinical features associated with PPCM at the time of delivery, including anemia, substance abuse, asthma, and autoimmune disease. The likelihood of PPCM increased exponentially with the addition of each of the 7 features identified on multivariate analysis. We also showed that the prevalence of PPCM at delivery in Hispanics was similar to Caucasians and much lower than in African Americans. Finally, we report the increased risk of adverse maternal events and stillbirth when PPCM is present at the time of delivery compared with delivering women without PPCM.

Comorbidities previously associated with PPCM such as advanced maternal age, African-American race, hypertension, and preeclampsia/eclampsia were significantly

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Table 2 Clinical Features Associated With PPCM Compared With Non-PPCM Delivering Mothers

	Univariate		Multivariate	
	OR (95% CI)	p Value	OR (95% CI)	p Value
Age				
<18	1.30 (0.74–2.15)	0.31	0.82 (0.37–1.56)	0.58
18–29	Reference	—	Reference	—
30–39	1.63 (1.45–1.97)	<0.0001	1.82 (1.48–2.24)	<0.0001
40–49	2.23 (1.49–3.23)	<0.0001	1.71 (1.09–2.58)	0.01
Race				
Caucasian	Reference	—	Reference	—
African American	2.67 (2.09–3.40)	<0.0001	1.79 (1.37–2.31)	<0.0001
Hispanic	0.86 (0.68–1.08)	0.20	1.00 (0.78–1.28)	0.99
Other	0.72 (0.50–1.01)	0.07	0.77 (0.53–1.11)	0.19
Comorbid conditions				
Diabetes mellitus	3.52 (1.97–5.75)	<0.0001	1.42 (0.73–2.49)	0.26
Hypertension	13.1 (11.0–15.5)	<0.0001	6.41 (4.81–8.44)	<0.0001
Tobacco use	3.01 (2.08–4.21)	<0.0001	1.43 (0.89–2.22)	0.12
Anemia	7.60 (6.34–9.07)	<0.0001	4.89 (3.95–6.03)	<0.0001
Substance abuse	6.56 (4.62–9.03)	<0.0001	4.12 (2.71–6.04)	<0.0001
Asthma	3.90 (2.82–5.26)	<0.0001	2.23 (1.53–3.15)	<0.0001
Obesity	5.29 (3.56–7.54)	<0.0001	1.42 (0.84–2.24)	0.16
Autoimmune disease	5.45 (2.16–11.1)	<0.0001	3.61 (1.42–7.43)	0.002
Pregnancy characteristics				
Multiple gestation	6.74 (5.10–8.74)	<0.0001	2.88 (2.07–3.92)	<0.0001
Preeclampsia	13.60 (11.3–16.4)	<0.0001	1.99 (1.78–2.69)	<0.0001
Eclampsia	27.90 (14.4–48.2)	<0.0001	5.93 (2.88–10.9)	<0.0001

CI = confidence interval; OR = odds ratio; PPCM = peripartum cardiomyopathy.

associated with PPCM in our analysis as well (3–6,14,15). We also identified new comorbidities that were independently associated with PPCM, including substance abuse, anemia, asthma, and autoimmune disease. Substance abuse was strongly associated with PPCM in our cohort (OR: 6.56, 95% CI: 4.62 to 9.03) and was present in 6.9% of PPCM cases hospitalized during delivery. Of the 37 cases where substance abuse was reported, opioid, alcohol, and cocaine/amphetamine abuse were reported in 0, 3 (8.1%), and 23 (62.2%) cases, respectively. Before our study, only cocaine abuse had been reported a possible risk factor for PPCM in a total of 3 women (16). Anemia is not commonly accepted as a risk factor but was associated with PPCM in 1 study that included 110 patients (3). In our cohort, anemia was

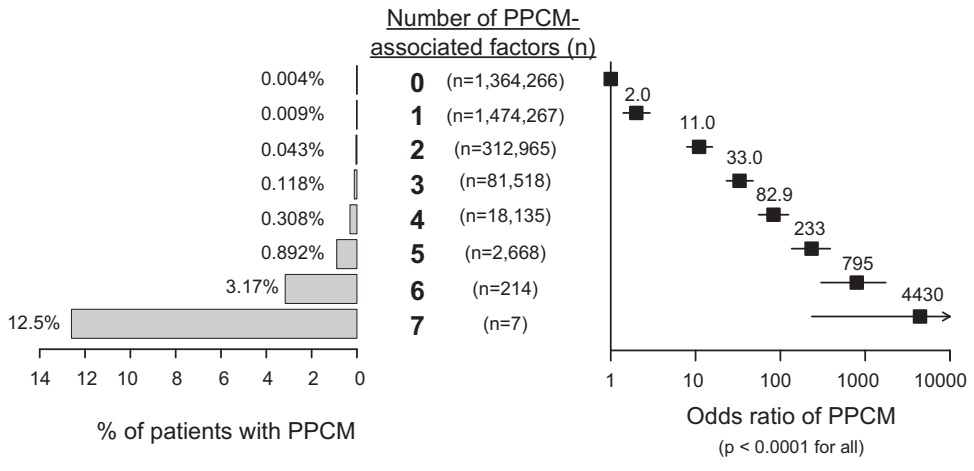

Figure 1 Rate and Odds Ratios of PPCM

Rate and odds ratios of peripartum cardiomyopathy (PPCM) at delivery according to presence of age ≥30 years, African-American race, hypertension, anemia, substance abuse, asthma, autoimmune disease, multiple gestations, and/or preeclampsia/eclampsia.

Table 3 Outcomes for PPCM and Non-PPCM Cohorts

	PPCM		PPCM Delivery vs. Non-PPCM Delivery	
	Delivery (n = 535)	Non-PPCM (n = 4,003,379)	OR (95% CI)	p Value
Primary outcome	36 (6.7%)	665 (0.02%)	436.0 (303.1–607.7)	<0.0001
Death	7 (1.3%)	304 (0.008%)	175.2 (74.5–344.6)	<0.0001
Mechanical circulatory support	0 (0%)	9 (0.0002%)	NA	
Transplant	0 (0%)	0 (0%)	NA	
Cardiac arrest	31 (5.8%)	459 (0.01%)	538.5 (363.3–769.7)	<0.0001
Length of stay, days	7.0 (4–9)	2.0 (2–3)	Δ = 5.5 (5.3–5.7)	<0.0001
Shock	10 (1.9%)	195 (0.005%)	392.5 (193.3–706.6)	<0.0001
Cesarean-section	481 (71.2%)	1,254,514 (31.3%)	5.49 (4.56–6.65)	<0.0001
Stillbirth	11 (2.3%)	458 (0.6%)	3.74 (1.69–5.64)	<0.0001

Values are n (%).
Abbreviations as in Table 2.

present in 34% of PPCM patients and was associated with a nearly 5-fold likelihood of PPCM (OR: 4.89, 95% CI: 3.95 to 6.03). Finally, asthma and autoimmune disease (systemic lupus erythematosus, rheumatoid arthritis, dermatomyositis, polymyositis, Wegener's granulomatosis, Takayasu's arteritis, ulcerative colitis, and/or Crohn's disease) are comorbidities associated with PPCM in our cohort that have not previously been described in the published data.

Hypertension, anemia, substance abuse, and autoimmune disease have all been associated with nonischemic dilated cardiomyopathy through a variety of mechanisms (17,18). It is possible that the simultaneous presence of these and other factors might reflect complementary myocardial insults resulting in development of PPCM. These factors might also interact with other proposed mechanisms of PPCM, such as transient autoimmunity related to pregnancy due to fetal cells in maternal blood during and after pregnancy or increased myocardial apoptosis due to increased cleavage of prolactin into its anti-angiogenic, pro-apoptotic 16-kDa form (19–21). The exponential increase in rate of PPCM associated with the presence of additional factors supports this "multi-hit" hypothesis. However, the relationships between PPCM and comorbidities observed in this study are associations only, and it is not possible to determine directly whether the comorbidities identified (i.e., asthma) contribute to the development of PPCM or are diagnostic confounders. Consequently, novel associations must be validated in independent datasets.

The risk of PPCM in Hispanic women has not been clearly defined. Two previous studies observed a lower rate of PPCM in Hispanics compared with Caucasians and African Americans (3,4). However, the number of Hispanics with PPCM was small (n = 21 of 178,864), and further demographic data according to race were not presented. With a much larger Hispanic cohort (n = 1,183,560) with 122 Hispanic PPCM patients, we found that the rate of PPCM at delivery was lower in Hispanics than in African Americans but not significantly different than Caucasians. Because our study was limited to cases where PPCM was present at the time of delivery, it is possible that the relative rates of PPCM might be different when considering cases presented post-partum.

We quantified the prevalence of key demographic features according to racial group to determine whether differences in the prevalence of risk factors explained the racial variability in PPCM incidence. Delivering mothers with PPCM were significantly older than non-PPCM mothers in all 3 groups, suggesting that advancing age is a risk factor in all racial groups. We also identified significant interactions between Hispanic race and tobacco usage, hypertension, age >40, and asthma, suggesting that the presence of these features was associated with PPCM in Hispanics more strongly than in Caucasian or African-American patients, although the cumulative rate of PPCM in African Americans was higher. Our findings support the hypothesis that PPCM might have different environmental and acquired contributors in different races, but these findings should be considered exploratory. Association between PPCM and poor socioeconomic status has been postulated but remains unclear (22,23). In our study, lack of private insurance was associated with PPCM in Caucasians but not Hispanics or African Americans. Payor status might be an imperfect surrogate for socioeconomic status, but our findings suggest the impact of socioeconomic status on rate of PPCM, if any, is complex and might be affected by competing factors.

Maternal in-hospital mortality in PPCM patients observed in our study was higher than non-PPCM delivering mothers. Mortality was similar to the findings of another published PPCM study (14) and less than in-hospital rate for all-cause acute decompensated heart failure (24,25). The increased rate of stillbirth associated with PPCM has not been described previously but has been reported in pregnant women with pre-existing dilated cardiomyopathy (26). One small study involving 35 women with a history of PPCM who had a subsequent pregnancy reported no stillbirths but had insufficient power to study this outcome (27). Other studies have noted that babies born to mothers with PPCM were more likely to be premature, underweight, small for gestational age, and have lower Apgar scores (3).

Table 4 Characteristics of PPCM vs. Non-PPCM Delivering Mothers According to Reported Race

	Caucasian			African American			Hispanic		
	PPCM (n = 173)	Non-PPCM (n = 1,441,657)	p Value	PPCM (n = 104)	Non-PPCM (n = 324,430)	p Value	PPCM (n = 122)	Non-PPCM (n = 1,183,438)	p Value
Age, yrs*			0.007			0.006			<0.001
<18	2 (1.2%)	22,933 (1.6%)		2 (1.9%)	9,584 (3.0%)		3 (2.5%)	47,145 (4.0%)	
18–29	51 (29.5%)	589,092 (40.9%)		44 (42.3%)	183,087 (56.4%)		55 (45.1%)	727,842 (61.5%)	
30–39	106 (61.3%)	691,014 (47.9%)		41 (39.4%)	98,025 (30.2%)		53 (43.4%)	352,664 (29.8%)	
>40	7 (4.0%)	65,837 (4.6%)		8 (7.7%)	11,231 (3.5%)		7 (5.7%)	24,027 (2.0%)	
Not available	7 (4.0%)	72,781 (4.6%)		9 (8.7%)	22,503 (6.9%)		4 (3.3%)	31,760 (2.7%)	
Payor†			<0.001			<0.0001			0.01
Medicare	4 (2.3%)	6,622 (0.5%)		6 (5.8%)	2,249 (0.7%)		1 (0.8%)	1,704 (0.1%)	
Medicaid	49 (28.3%)	314,411 (21.8%)		54 (51.9%)	172,355 (53.1%)		67 (54.9%)	746,190 (63.1%)	
Private	114 (65.9%)	1,061,739 (73.6%)		40 (38.5%)	127,675 (39.4%)		46 (37.7%)	368,190 (31.1%)	
Self-pay	4 (2.3%)	23,352 (1.6%)		4 (3.8%)	16,055 (4.9%)		4 (3.3%)	52,867 (4.5%)	
Other	1 (0.6%)	29,314 (2.0%)		0 (0%)	5,079 (1.6%)		4 (3.3%)	12,221 (1.0%)	
Not available	1 (0.6%)	6,219 (0.4%)		0 (0%)	1,017 (0.3%)		0 (0%)	2,266 (0.2%)	
Comorbid conditions									
Diabetes mellitus	2 (1.2%)	9,025 (0.6%)	NS	4 (3.8%)	3,535 (1.1%)	NS	3 (2.5%)	9,636 (0.8%)	NS
Hypertension*	70 (40.5%)	89,735 (6.2%)	<0.0001	58 (55.8%)	33,320 (10.3%)	<0.0001	62 (50.8%)	66,250 (5.6%)	<0.0001
Tobacco use	10 (5.8%)	46,257 (3.2%)	NS	5 (4.8%)	9,232 (2.8%)	NS	8 (6.6%)	7,790 (0.7%)	<0.0001
Anemia	52 (30.1%)	76,790 (5.3%)	<0.0001	42 (40.4%)	36,008 (11.1%)	<0.0001	42 (34.4%)	78,763 (6.7%)	<0.0001
Substance abuse	14 (8.1%)	16,746 (1.2%)	<0.0001	11 (10.6%)	9,212 (2.8%)	<0.0001	8 (6.6%)	9,307 (0.8%)	<0.0001
Asthma	11 (6.4%)	36,836 (2.6%)	0.003	12 (11.5%)	13,803 (4.3%)	<0.001	11 (9.0%)	17,935 (1.5%)	<0.0001
Obesity	6 (3.5%)	15,807 (1.1%)	0.009	4 (3.8%)	5,631 (1.7%)	NS	8 (6.6%)	11,954 (1.0%)	<0.0001
Autoimmune disease	2 (1.2%)	4,355 (0.3%)	NS	3 (2.9%)	719 (0.2%)	<0.0001	0 (0%)	1,399 (0.1%)	NS
Pregnancy characteristics									
Multiple gestation	24 (13.9%)	34,217 (2.4%)	<0.0001	10 (9.6%)	6,792 (2.1%)	<0.0001	9 (7.4%)	14,501 (1.2%)	<0.0001
Preeclampsia	48 (27.7%)	37,716 (2.6%)	<0.0001	28 (26.9%)	1,5180 (4.7%)	<0.0001	43 (35.2%)	34,940 (3.0%)	<0.0001
Eclampsia	3 (1.7%)	784 (0.1%)	<0.0001	2 (1.9%)	390 (0.1%)	0.0001	4 (3.3%)	1,054 (0.1%)	<0.0001
Outcomes									
Primary outcome	12 (6.9%)	238 (0.0%)	<0.0001	4 (3.8%)	98 (0.0%)	<0.0001	7 (5.7%)	145 (0.0%)	<0.0001
Length of stay, days	6 (4–9)	2 (2–3)	<0.0001	7.5 (6–11)	3 (2–3)	<0.0001	7 (4.25–9)	2 (2–3)	<0.0001
Cesarean-section	122 (70.5%)	459,151 (31.8%)	<0.0001	76 (73.1%)	109,156 (33.6%)	<0.0001	88 (72.1%)	354,023 (29.9%)	<0.0001
Stillborn	2 (1.2%)	7,542 (0.5%)	NS	3 (2.9%)	4,078 (1.3%)	NS	3 (2.5%)	7,218 (0.6%)	0.04

Values are n (%) or median (range). Caucasian versus African American versus Hispanic peripartum cardiomyopathy (PPCM) cases: *$p < 0.05$. †$p < 0.0001$.
NS = not significant.

Therefore, it is not surprising that in a large cohort with over 500 PPCM patients, we were able to show that women with PPCM were more likely to have stillbirths compared with non-PPCM patients.

Study limitations. Our study has limitations inherent to retrospective studies using administrative data. Echocardiograms, laboratory tests, medications, and vital statistics on admission were not available, and there were no post-discharge data including long-term mortality and readmissions, because the hospital records were de-identified. In addition, we were unable to determine the number of unique patients in our cohorts, because of de-identification. Because healthcare providers often discourage subsequent pregnancies for PPCM patients due to concerns of possible poor outcomes, this limitation likely had a minimal effect on the cohort of delivering mothers (27,28). To establish a clear control group, this study also excluded PPCM patients hospitalized after delivery (n = 1,358). Others have shown that most PPCM patients are diagnosed after delivery (6), and the lower incidence of PPCM observed in this study compared with other U.S. studies (1 of 7,500 vs. 1 of 2,500 to 4,000) is due in part to the exclusion of those patients from the analysis. It is also possible that PPCM patients presenting postpartum have different clinical profiles and rates of adverse outcomes.

The current PPCM ICD-9 CM codes introduced in 2003 are more specific for PPCM than coding used in previous studies of administrative data (3,4,14), but they have not been validated systematically. Patient level data were not available to verify coding accuracy, because all data were de-identified. Furthermore, it is not clear that coding accuracy at high-volume institutions is generalizable to smaller community hospitals. Although diagnostic accuracy remains a concern, it is reassuring that our data are similar to others with regard to incidence, demographic data, and known risk factors for PPCM (3,4,14). Some of the factors associated with PPCM identified in this analysis are known to cause dilated cardiomyopathy in the absence of pregnancy, including hypertension and substance abuse, and it is not possible to determine whether subclinical disease might have been present before the onset of pregnancy. Finally, associations between comorbidities and outcomes were not assessed, due to the relatively small number of MAEs (n = 36) among delivering mothers with PPCM.

Conclusions

Peripartum cardiomyopathy is associated with a number of demographic and comorbid conditions, including advanced maternal age, African-American race, hypertension, anemia, substance abuse, asthma, autoimmune disease, multiple gestational status, preeclampsia, and eclampsia with some racial differences. PPCM patients had an increased risk of both MAEs and stillbirth at the time of delivery compared with women hospitalized for delivery without a diagnosis of PPCM.

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Key Words: cardiomyopathy ■ epidemiology ■ heart failure ■ peripartum ■ pregnancy.

APPENDIX

For a supplementary table, please see the online version of this article.