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ORIGINAL RESEARCH

CARDIO-OBSTETRICS

Cardiovascular Severe Maternal Morbidity and Mortality at Delivery in the United States

A Population-Based Study

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ABSTRACT

BACKGROUND Cardiovascular conditions are the leading cause of maternal mortality in North America.

OBJECTIVES The purpose of this study was to examine the relationship between cardiovascular severe maternal morbidity (CSMM) and mortality during delivery hospitalization.

METHODS We performed a cohort study using the Health Care Cost and Utilization Project, Nationwide Inpatient Sample, and identified delivery hospitalizations with CSMM from 1999 to 2015. We described temporal trends in the incidence of CSMM and its associated case-fatality. Among individuals with CSMM, we evaluated the association between participant characteristics and mortality using logistic regression analyses.

RESULTS Of 13,791,605 delivery hospitalizations, 11,152 were complicated by CSMM. Of those, 495 resulted in mortality. The overall incidence of CSMM was 8.09 per 10,000 delivery hospitalizations (95% CI: 7.94-8.24), increasing from 7.76 to 8.38 per 10,000 delivery hospitalizations over 15 years ($P < 0.001$). The overall case-fatality for CSMM was 4.44 per 100 CSMM (95% CI: 4.06-4.85), decreasing from 6.55 to 2.50 per 100 CSMM events over the study period ($P = 0.035$). Among participants with CSMM, Black (adjusted odds ratio [aOR]: 1.80; 95% CI: 1.39-2.32) and Hispanic (aOR: 1.44; 95% CI: 1.09-1.90) women and those with Medicaid insurance (aOR: 1.52; 95% CI: 1.22-1.88), postpartum hemorrhage (aOR: 4.06; 95% CI: 3.05-5.41), or systemic lupus erythematosus (aOR: 2.50; 95% CI: 1.31-4.78) were at increased risk of mortality.

CONCLUSIONS The incidence of CSMM increased over 15 years, reflecting transformations within the obstetric population. Although it decreased during the study period, case-fatality from CSMM remained elevated. Several factors associated with mortality from CSMM were identified. (JACC Adv 2022;1:100121) © 2022 Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Cardiovascular diseases have become the leading causes of maternal mortality in the U.S. and other high-income countries.[1-3] Maternal mortality is in a continuum of maternal health—from wellness to morbidity, to severe morbidity, to death.[4] Severe maternal morbidity designates a group of critical conditions associated with increased health care utilization, long-term

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ABBREVIATIONS AND ACRONYMS

CSMM = cardiovascular severe maternal morbidity

HCUP-NIS = Health Care Cost and Utilization Project, Nationwide Inpatient Sample

ICD-9 = 9th edition of the International Classification of Diseases diagnosis and procedure

OR = odds ratio

SLE = systemic lupus erythematosus

disability, and high case-fatality.[5-7] Given its significant impact on maternal health, monitoring severe maternal morbidity in addition to maternal mortality has been recommended by the World Health Organization to improve the quality of obstetric care.[8] Assessment of trends in cardiovascular severe maternal morbidity (CSMM) and its associated mortality is needed to better characterize the epidemiology of maternal cardiovascular deaths. Moreover, since most maternal deaths can be prevented,[2,9] identifying factors associated with mortality in CSMM may lead to the future development of targeted mitigation strategies.

Using a large and representative sample of the US population, we sought to better characterize CSMM and describe temporal trends in its incidence and case-fatality. Moreover, we aimed to examine factors associated with mortality in the setting of CSMM. We hypothesized that the incidence of CSMM may have increased and that several risk factors for maternal mortality would be identified.

MATERIALS AND METHODS

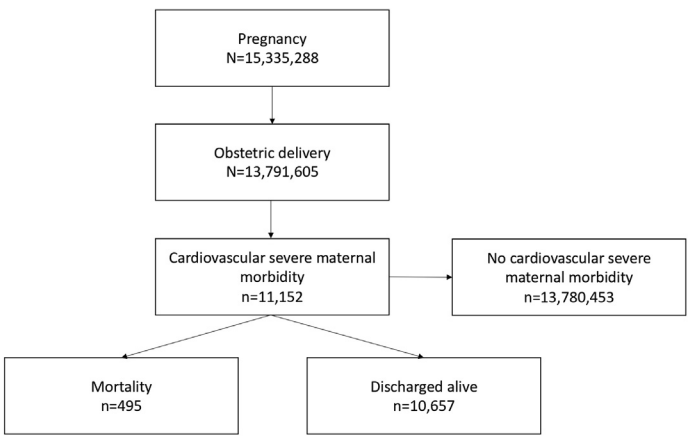
DATA SOURCE AND STUDY POPULATION. The Health Care Cost and Utilization Project, Nationwide Inpatient Sample, (HCUP-NIS) was utilized to perform a retrospective cohort study.[10] The HCUP-NIS is the largest publicly available database in the U.S., capturing a large and representative sample of all hospital discharges from US nonfederal community hospitals (excluding rehabilitation and long-term acute care hospitals).[11] The database is coded with the 9th edition of the International Classification of Diseases diagnosis and procedure (ICD-9), patient demographic characteristics, hospital characteristics, and expected payment source.[11,12] Hospitalizations with pregnancy-related codes (procedure 72.xx-75.xx or diagnosis 634.xx-679.xx or V22.xx, V23.xx, and V27.xx) and delivery-related codes (procedure 72.xx, 73.xx, 74.0x, 74.1x, 74.2x, 74.4x, 74.99 or diagnosis 650.xx, 677.xx, 651.xy-676.xy [y = 0, 1, or 2]) from January 1, 1999, to September 30, 2015, were identified to build the study sample of delivery hospitalizations. Hospitalizations with abortive outcomes were excluded (diagnosis 63x.xx). Since our data did not allow us to identify individuals with multiple deliveries during the study period, the unit of analysis was delivery hospitalization.

CARDIOVASCULAR SEVERE MATERNAL MORBIDITY AT DELIVERY. We used a composite measure regrouping a subset of cardiovascular indicators of severe maternal morbidity, as defined by the Centers for Disease Control and Prevention.[7] The validity of this composite measure has previously been found to be comparable to the validity of the larger Centers for Disease Control and Prevention coding algorithm for severe maternal morbidity.[13,14] According to the coding algorithm's version associated with the highest positive predictive value,[14] hospitalizations with at least one of the following indicators were considered as complicated by CSMM: acute myocardial infarction (410.xx), aneurysm (ie, aortic aneurysm and dissections; 441.xx), ventricular fibrillation (427.41, 427.42), puerperal cerebrovascular disorders (including ischemic and hemorrhagic strokes, transient ischemic attack, and central venous thrombosis; 430, 431, 432.x, 433.xx, 434.xx, 436, 437.x, 674.0x, 997.02), pulmonary edema/acute heart failure (518.4, 428.1, 428.0, 428. 21, 428.23, 428.31, 428.33, 428.41, 428.43), conversion of cardiac rhythm (ie, any cardioversion; procedure 99.6x), and cardiogenic shock (785.51).[14] Indicators for possibly noncardiogenic types of shock (785.50, 785.59) and for cardiac arrest (427.5), comprised in the original composite measure, were not used to identify CSMM since these indicators alone may have represented noncardiovascular adverse events (eg, sepsis, amniotic fluid embolism, or postpartum hemorrhage).[14] Women with these indicators were, however, not excluded.

MATERNAL MORTALITY. Maternal deaths were identified with the ICD-9 code for maternal mortality (761.6x) or the HCUP-NIS indicator for patients who died during hospitalization.

BASELINE CHARACTERISTICS. Factors potentially associated with mortality in patients with CSMM

FIGURE 1 Flowchart of the Study Population



Of a total of 13,791,605 delivery hospitalizations, 11,152 were complicated by cardiovascular severe maternal morbidity, of which 495 resulted in mortality.

TABLE 1 Distribution of Individual Cardiovascular Severe Maternal Morbidity Subtypes

Acute myocardial infarction	314 (2.8)
Aneurysm	206 (1.9)
Ventricular fibrillation	151 (1.4)
Puerperal cerebrovascular disorders	2,713 (24.3)
Pulmonary edema/acute heart failure	7,182 (64.4)
Conversion of cardiac rhythm	915 (8.2)
Cardiogenic shock	163 (1.5)

Values are n (%).

included demographic characteristics, pregnancy-related conditions, and pre-existing medical comorbidities at delivery hospitalization. Demographic characteristics comprised maternal age, race/ethnicity, income quartile, and insurance type. Hospitals were characterized as rural, urban nonteaching, or urban teaching. Pregnancy-related conditions evaluated were multiple pregnancy, postpartum hemorrhage, gestational hypertension, preeclampsia, eclampsia, and gestational diabetes. Since peripartum cardiomyopathy captured at delivery could have developed during the index pregnancy, it was classified as a pregnancy-related condition. Pre-existing cardiac disease assessed included the following conditions considered to be present prior to pregnancy: congenital heart disease (including severe congenital heart disease, shunts, valvular disease, or other congenital heart disease identified using a previously validated algorithm[15-17]), noncongenital valvular heart disease (including rheumatic and nonrheumatic valvular heart disease), cardiomyopathy (except peripartum cardiomyopathy), aortic dilatation, and diseases of the pulmonary circulation. Other comorbidities examined were obesity, chronic hypertension, chronic kidney disease, type 1 and 2 diabetes, hypothyroidism, hyperthyroidism, systemic lupus erythematosus (SLE), anemia, asthma, tobacco use, alcohol, and substance use disorders. In addition, length of stay was described. Detailed ICD-9 codes can be found in Supplemental Table 1.

ETHICAL CONSIDERATIONS. According to the Tri-Council Policy Statement (2018), this study was exempt from institutional review board approval since it was based solely on publicly available data. Cells from tables comprising fewer than 11 individuals were not reported to protect confidentiality.

STATISTICAL ANALYSIS. Baseline characteristics at delivery hospitalizations with and without CSMM were described and compared using 2-way chi-square test. We examined the incidence of CSMM and its temporal trend. We then assessed the case-fatality rate of CSMM and its trend over the study period.

TABLE 2 Baseline Demographic Characteristics of the Study Population

	No CSMM (n = 13,780,453)	CSMM (n = 11,152)	*P* Value
Age (in y)			
<25	4,650,726 (33.8)	2,708 (24.3)	<0.0001
25-34	7,127,683 (51.7)	5,340 (47.9)	
≥35	2,002,044 (14.5)	3,104 (27.8)	
Race/ethnicity			
White	5,877,813 (55.7)	4,026 (46.9)	<0.0001
Black	1,516,770 (14.4)	2,325 (27.1)	
Hispanic	2,531,461 (24.0)	1,663 (19.4)	
Asian, Pacific Islander, Native American	633,144 (6.0)	568 (6.6)	
Income quartile			
Q1	2,808,252 (27.3)	2,806 (32.9)	<0.0001
Q2	2,588,403 (25.2)	2,147 (25.2)	
Q3	2,530,669 (24.6)	1,935 (22.7)	
Q4	2,365,764 (23.0)	1,637 (19.2)	
Insurance type			
Medicare	74,453 (0.5)	385 (3.5)	<0.0001
Medicaid	5,590,994 (40.7)	4,862 (43.7)	
Private	7,259,512 (52.8)	5,218 (46.9)	
Other	827,794 (6.0)	664 (6.0)	
Hospital type			
Rural	1,589,263 (11.6)	698 (6.3)	<0.0001
Urban nonteaching	5,644,196 (41.1)	3,363 (30.3)	
Urban teaching	6,498,147 (47.3)	7,039 (63.4)	

Values are n (%).
CSMM = cardiovascular severe maternal morbidity.

The incidence of CSMM was expressed in number of delivery hospitalizations complicated by CSMM per 10,000 delivery hospitalizations, with 95% CI. The case-fatality rate for CSMM was expressed in number of deaths per 100 delivery hospitalizations with CSMM, with 95% CI. Trend chi-square test was performed to evaluate trends in the incidence of CSMM and its associated case-fatality rate in the calendar years 1999 to 2015.[18] The mortality rate associated with each CSMM subtype and the frequency of each CSMM subtype among individuals who died were described in percentages.

The strength of the association between baseline characteristics and mortality in CSMM was estimated using simple and multivariable logistic regression models. We measured unadjusted odds ratio (OR) with 95% CI for the association between risk factors and mortality in CSMM. We developed a multivariable logistic regression model using stepwise selection with $P = 0.25$ for entry into the model and $P = 0.05$ for remaining in the model. We estimated adjusted ORs using all covariates remaining in the model. We considered a 2-sided P value ≤0.05 as statistically significant for all analyses. Statistical analyses were performed using SAS Enterprise Guide v7.1. This study was conducted in accordance with

TABLE 3 Baseline Clinical Characteristics of the Study Population

	No CSMM (n = 13,780,453)	CSMM (n = 11,152)	*P* Value
Length of stay (in days)	2.6 ± 2.3	7.8 ± 10.7	<0.0001
Pregnancy-related conditions			
Gestational hypertension	440,360 (3.2)	541 (4.9)	<0.0001
Preeclampsia	537,808 (3.9)	3,561 (31.9)	<0.0001
Eclampsia	10,591 (0.1)	474 (4.3)	<0.0001
Gestational diabetes	726,099 (5.3)	821 (7.4)	<0.0001
Multiple pregnancy	225,640 (1.6)	651 (5.8)	<0.0001
Postpartum hemorrhage with transfusion	44,047 (0.3)	554 (45.0)	<0.0001
Peripartum cardiomyopathy	1,218 (0.01)	1,037 (9.3)	<0.0001
Pre-existing cardiac conditions	80,114 (0.6)	2,711 (24.3)	<0.0001
Cardiomyopathy[a]	2,599 (0.02)	1,579 (14.2)	<0.0001
Congenital heart disease	8,698 (0.1)	227 (2.0)	<0.0001
Valvular heart disease	68,860 (0.5)	1,112 (10.0)	<0.0001
Diseases of the pulmonary circulation	1,998 (0.01)	456 (4.1)	<0.0001
Aortic dilatation	59 (0.00)	-[b]	-
Medical comorbidities			
Obesity	388,721 (2.8)	1,077 (9.7)	<0.0001
Chronic hypertension	235,856 (1.7)	1,942 (17.4)	<0.0001
Chronic kidney disease	4,053 (0.03)	197 (1.8)	<0.0001
Type 1 diabetes	34,381 (0.3)	183 (1.6)	<0.0001
Type 2 diabetes	71,150 (0.5)	358 (3.2)	<0.0001
Hypothyroidism	243,073 (1.8)	378 (3.4)	<0.0001
Hyperthyroidism	23,103 (0.2)	104 (0.9)	<0.0001
SLE	16,510 (0.1)	116 (1.0)	<0.0001
Asthma	364,984 (2.7)	801 (7.2)	<0.0001
Anemia	1,315,948 (9.6)	3,259 (29.2)	<0.0001
Tobacco use	709,262 (5.2)	955 (8.6)	<0.0001
Alcohol use	2,168 (0.02)	-[b]	-
Substance use	38,554 (0.3)	97 (0.9)	<0.0001

Values are mean ± SD or n (%). [a]Excluding peripartum cardiomyopathy. [b]Cells with counts <11 are not reported.
CSMM = cardiovascular severe maternal morbidity; SLE = systemic lupus erythematosus.

the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement guidelines.[19]

RESULTS

Of 13,791,605 delivery hospitalizations, 11,152 were complicated by CSMM, including 495 deaths (Figure 1). Pulmonary edema (n = 7,182, 64.40%) and cerebrovascular disease (n = 2,713, 24.33%) were the most common CSMM subtypes to occur (Table 1). Individuals with CSMM were older, with less private insurance, and delivered more commonly in urban teaching hospitals than those without CSMM (Table 2). At least a quarter of women with CSMM had concomitant preeclampsia and/or pre-existing cardiac disease, and almost one-half experienced postpartum hemorrhage with transfusion (Table 3). Gestational hypertension, gestational diabetes, multiple pregnancies, postpartum hemorrhage with transfusion, and peripartum cardiomyopathy were more prevalent in individuals with CSMM than among those without CSMM (Table 3). In addition, women with CSMM had more comorbidities, including pre-existing cardiac conditions, obesity, chronic hypertension, chronic kidney disease, type 1 and 2 diabetes, SLE, asthma, and anemia than women without CSMM (Table 3).

The overall incidence of CSMM was 8.09 per 10,000 delivery hospitalizations (95% CI: 7.94-8.24). From 1999 to 2015, the incidence of CSMM increased from 7.76 to 8.38 per 10,000 delivery hospitalizations (8% increase, $P < 0.001$) (Central Illustration). The overall case-fatality rate for CSMM was 4.44 per 100 deliveries with CSMM (95% CI: 4.06-4.85). From 1999 to 2015, the case-fatality for CSMM decreased from 6.55 to 2.50 per 100 CSMM events (62% decrease, $P = 0.035$) (Central Illustration). Among all CSMM subtypes, mortality was highest for conversion of cardiac rhythm, ventricular fibrillation, and cardiogenic shock and lowest for pulmonary edema (Figure 2). Conversion of cardiac rhythm, puerperal cerebrovascular disease, and pulmonary edema were the most common CSMM subtypes to occur among women who died (Figure 3).

Crude OR for the association between each baseline characteristics and mortality in participants with CSMM is shown in Supplemental Table 2. In the multivariable analysis of patients with CSMM, Black and Hispanic women, as well as those with Medicaid insurance coverage, were more likely to experience mortality (Table 4). In addition, postpartum hemorrhage with transfusion and SLE were associated with mortality in CSMM (Table 4). In contrast, individuals with CSMM who were younger than 25 years, with anemia, and tobacco use were at lower risk of mortality (Table 4). Moreover, patients who developed CSMM at delivery without previously being known for hypertensive disorders, cardiomyopathy (including peripartum cardiomyopathy), or valvular heart disease were at increased risk of mortality (Table 4).

DISCUSSION

We described temporal trends in the incidence of CSMM and its associated case-fatality during delivery hospitalization in the U.S. Over the 15-year study period, we observed an increase in the incidence of CSMM. While its case-fatality decreased over time, it remained unacceptably high. Cardioversion, ventricular fibrillation, and cardiogenic shock were the CSMM subtypes with the highest mortality rates. Cardioversion, cerebrovascular disease, and

pulmonary edema were the most frequent CSMM subtypes to occur among individuals who died. Insurance type, race/ethnicity, postpartum hemorrhage with transfusion, and SLE were associated with an increased risk of mortality in CSMM. In addition, individuals without a known hypertensive disorder, cardiomyopathy, or valvular heart disease who developed CSMM during delivery hospitalization were more likely to die.

Overall, severe maternal morbidity events complicated 144 per 10,000 delivery hospitalizations in the U.S. in 2014.[7] As such, CSMM, affecting ~8 per 10,000 delivery hospitalizations, represented a substantial burden of severe maternal morbidity. We observed a rise in the incidence of CSMM over time. This temporal trend may be a result of the growing proportion of persons with structural heart disease being pregnant, as previously reported,[20] possibly due to improvements in surgical correction of maternal congenital heart defects and greater access to assisted reproductive technologies.[15,21,22] Moreover, the prevalence of risk factors for CSMM in the pregnant population, including chronic and gestational hypertension and maternal age ≥35 years, increased during the study period.[23-25] Although it remained elevated, the case-fatality from CSMM decreased over time. Since most women with CSMM had pulmonary edema (ie, the CSMM subtype with the lowest mortality rate), future research would be required to assess whether a decrease in case-fatality of CSMM may have been due to a rising incidence of heart failure, including in the context of phenotypes associated with a lower mortality (eg, heart failure with preserved ejection fraction or hypertrophic cardiomyopathy).[26-28] In addition, whether improved access to specialized cardiovascular care across the pregnancy continuum contributed to reducing maternal mortality should be evaluated.[29]

We found that CSMM subtypes were associated with varying mortality rates. Cardioversion, ventricular fibrillation, and cardiogenic shock—events at the extreme end of the spectrum of maternal health—were associated with the highest mortality rates. Although the cause for cardioversion was not specified, cardioversion during delivery hospitalization was likely to have represented a nonelective, emergent cardioversion for unstable arrhythmia, including ventricular fibrillation. Interventions to reduce mortality once these CSMM subtypes are established should focus on improving resuscitative measures in pregnancy.[30] While pulmonary edema was associated with a lower mortality than other CSMM subtypes, it was the most frequent CSMM subtype to occur and one of the most common CSMM subtypes found in patients who died (ie, ~1 in 10). As such, pulmonary edema in pregnancy should be systematically investigated to identify specific causes of heart failure and prevent future maternal deaths.

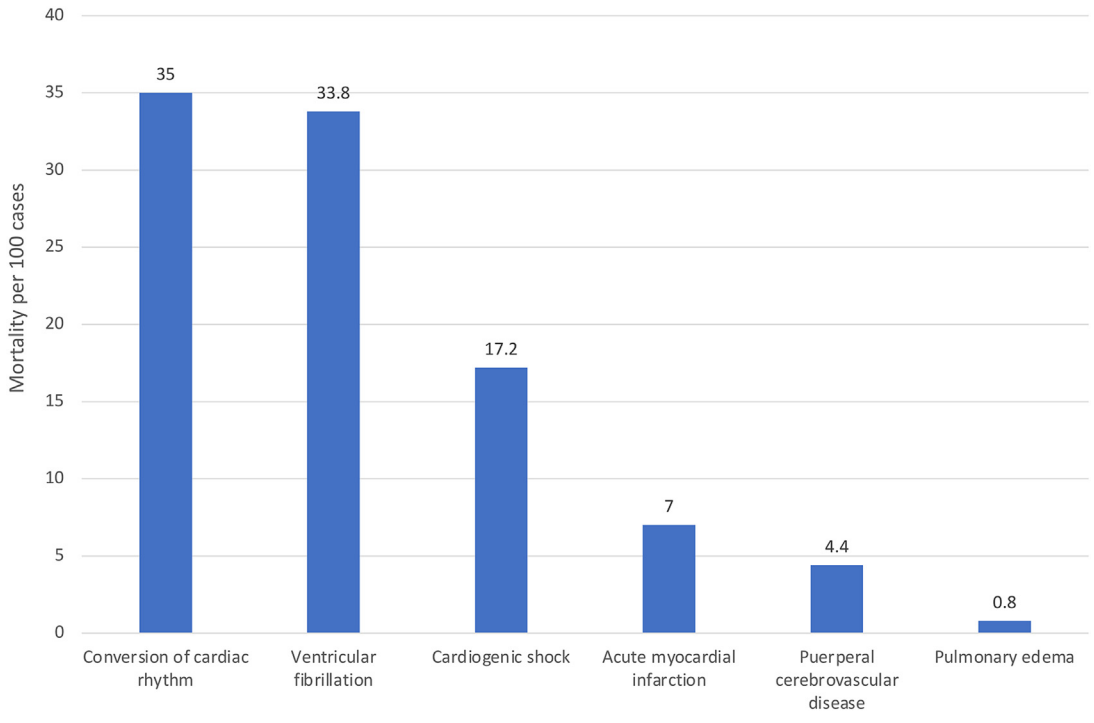
Demographic characteristics associated with maternal mortality in women with CSMM included race/ethnicity independent of income quartile, hospital type, or comorbidities. This is in keeping with previously described racial and ethnic disparities in severe maternal morbidity and mortality.[9,31] Thus, examining and addressing interpersonal and

TABLE 4 Association Between Baseline Characteristics and Mortality Among Patients With Cardiovascular Severe Maternal Morbidity

	Total Death	N	OR (95% CI)	aOR[a] (95% CI)
Demographic characteristics				
Age (y)				
<25	113 (4.17)	2,708	0.93 (0.74-1.16)	0.78 (0.61-0.99)
25-34	240 (4.49)	5,340	1.00 (Ref)	1.00 (Ref)
≥35	142 (4.57)	3,104	1.02 (0.82-1.26)	1.13 (0.91-1.41)
Race/ethnicity				
White	144 (3.58)	4,026	1.00 (Ref)	1.00 (Ref)
Black	138 (5.94)	2,325	1.70 (1.34-2.16)	1.80 (1.39-2.32)
Hispanic	100 (6.01)	1,663	1.73 (1.33-2.24)	1.44 (1.09-1.90)
Asian, Pacific Islander, Native American	23 (4.05)	568	1.14 (0.73-1.78)	0.91 (0.57-1.44)
Other/missing	90 (3.50)	2,570	0.98 (0.75-1.28)	0.95 (0.72-1.24)
Income quartile				
Q1	112 (3.99)	2,806	1.00 (Ref)	1.00 (Ref)
Q2	98 (4.56)	2,147	1.15 (0.87-1.52)	1.22 (0.91-1.62)
Q3	88 (4.55)	1,935	1.15 (0.86-1.53)	1.29 (0.96-1.75)
Q4	53 (3.24)	1,637	0.81 (0.58-1.12)	0.93 (0.65-1.32)
Other/missing	144 (5.48)	2,627	1.40 (1.08-1.80)	1.51 (1.16-1.97)
Insurance type				
Medicare	12 (3.12)	385	0.86 (0.47-1.55)	0.92 (0.5-1.7)
Medicaid	255 (5.24)	4,862	1.47 (1.22-1.79)	1.52 (1.22-1.88)
Private	189 (3.62)	5,218	1.00 (Ref)	1.00 (Ref)
Other	37 (5.57)	664	1.57 (1.09-2.26)	1.52 (1.05-2.22)
Missing	-[b]	23	-	-
Pregnancy-related conditions				
Gestational hypertension	15 (2.77)	541	0.60 (0.36-1.01)	0.55 (0.32-0.93)
Preeclampsia	112 (3.15)	3,561	0.61 (0.49-0.76)	0.63 (0.51-0.79)
Multiple pregnancy	-[b]	651	-	-
Postpartum hemorrhage with transfusion	76 (13.72)	554	3.86 (2.98-5.02)	4.06 (3.05-5.41)
Peripartum cardiomyopathy	19 (1.83)	1,037	0.38 (0.24-0.60)	0.51 (0.32-0.82)
Pre-existing cardiac conditions				
Cardiomyopathy	32 (2.03)	1,579	0.41 (0.28-0.59)	0.43 (0.3-0.63)
Valvular heart disease	15 (1.35)	1,112	0.27 (0.16-0.46)	0.34 (0.2-0.58)
Medical comorbidities				
Chronic hypertension	47 (3.03)	1,550	0.56 (0.42-0.74)	0.58 (0.43-0.79)
SLE	11 (9.48)	116	2.28 (1.22-4.28)	2.5 (1.31-4.78)
Anemia	114 (3.50)	3,259	0.72 (0.58-0.89)	0.56 (0.45-0.71)
Tobacco use	23 (2.41)	955	0.51 (0.33-0.78)	0.64 (0.41-0.98)

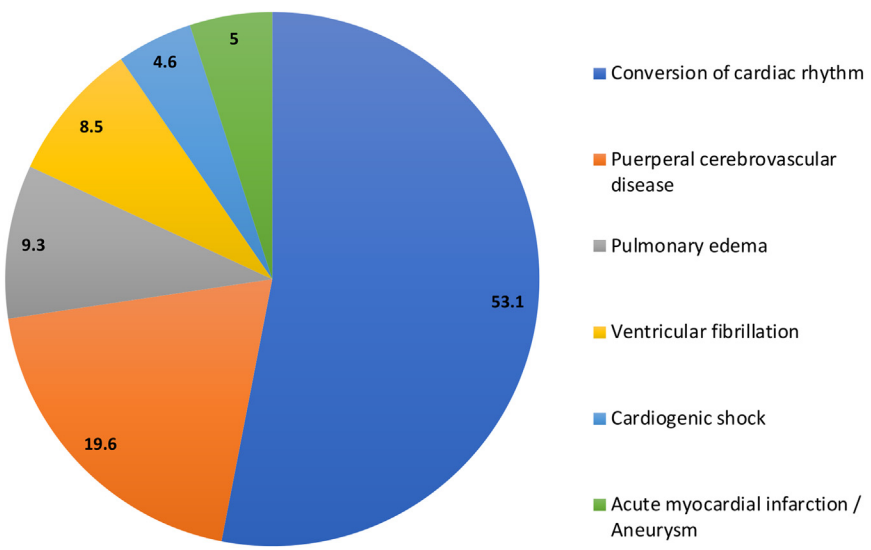
Values are n (%) unless otherwise indicated. [a]Adjusted for all covariates. [b]Cells with counts <11 are not reported.
aOR = adjusted odds ratio; Ref = reference category; SLE = systemic lupus erythematosus.

FIGURE 2 Mortality Rate Per Cardiovascular Severe Maternal Morbidity Subtype



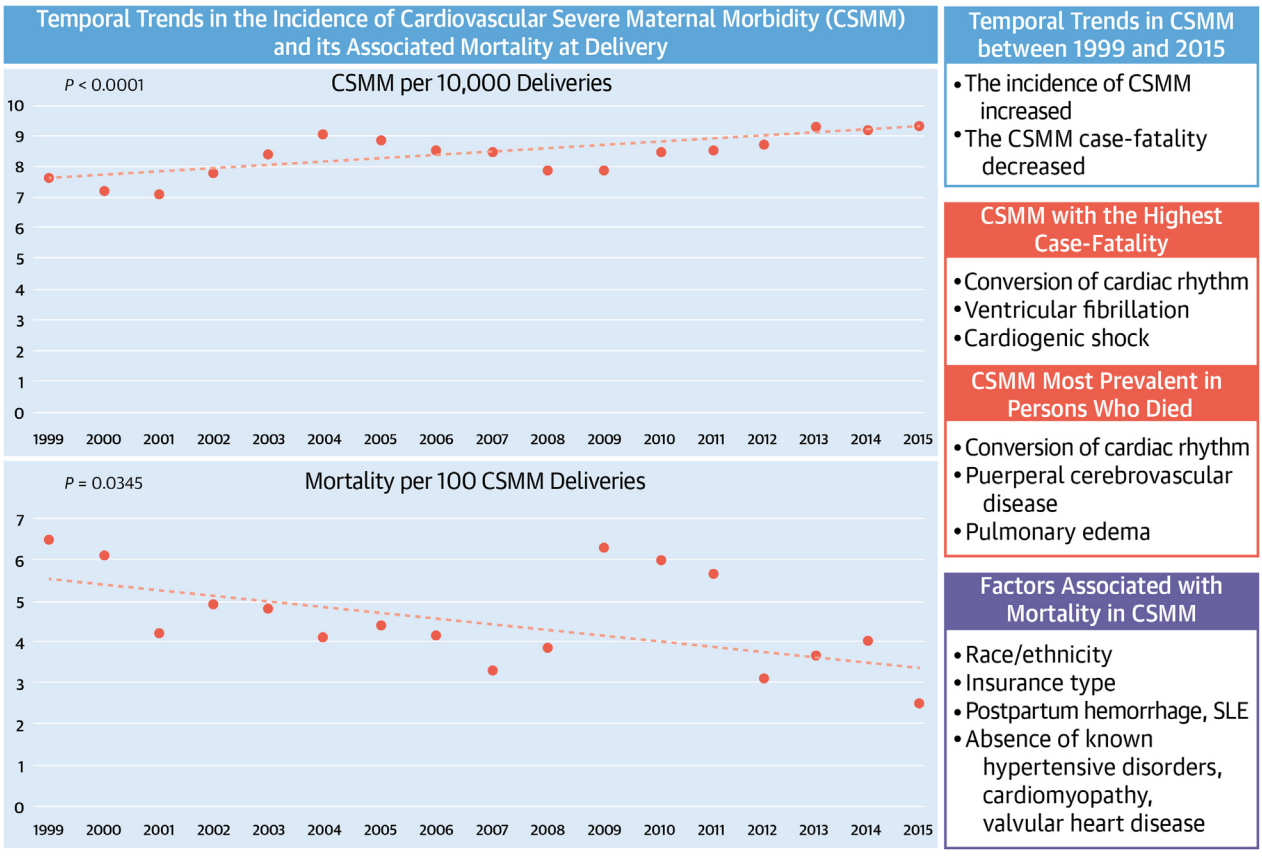
Column chart illustrating the proportion of deaths within each cardiovascular severe maternal morbidity subtype. Not reported if <11 deaths per subtype.

FIGURE 3 Distribution of Cardiovascular Severe Maternal Morbidity Events Among Individuals Who Died



Pie chart illustrating the distribution of CSMM subtypes among individuals who died. Among participants with CSMM who died (n = 495), we measured the number of events for each CSMM subtype/total CSMM events (n = 603*) × 100. *Multiple CSMM subtypes could occur per individual. Acute myocardial infarction and aneurysm subtypes are combined to maintain confidentiality. CSMM = cardiovascular severe maternal morbidity.

CENTRAL ILLUSTRATION **Temporal Trends in Cardiovascular Severe Maternal Morbidity and its Associated Case-Fatality From 1999 to 2015**



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Line graph illustrating **(top)** CSMM per 10,000 delivery hospitalizations from 1999 to 2015 and **(bottom)** mortality per 100 CSMM events from 1999 to 2015. The CSMM subtypes with the highest case-fatality and those most prevalent among persons who died are listed. Factors found to be associated with mortality in CSMM are outlined. CSMM = cardiovascular severe maternal morbidity; SLE = systemic lupus erythematosus.

structural forms of racism will be of paramount importance to reduce pregnancy-related cardiovascular deaths moving forward.[32,33] We identified that participants with CSMM and concomitant postpartum hemorrhage with transfusions or SLE were at higher risk of mortality. This may reflect the challenges in managing CSMM in this complex population, as several clinical risk factors, including hypercoagulability (eg, disseminated intravascular coagulation in postpartum hemorrhage or antiphospholipid syndrome in SLE), unstable hemodynamics (eg, hypotensive shock in postpartum hemorrhage or severe hypertension in SLE), and concurrent medication use (eg, uterotonic agents in postpartum hemorrhage or anticoagulation in SLE), could potentially have worsened cardiovascular outcomes. Thus, multidisciplinary expertise and surveillance in a critical care setting would be warranted for patients with CSMM and either postpartum hemorrhage or SLE.

Preeclampsia and pre-existing cardiac disease were more common among women with CSMM than among those without CSMM. Women with hypertensive disorders and pre-existing cardiovascular disease are well-known to be at higher risk of death than the general obstetric population.[31] However, the case-fatality rate among patients with CSMM at the time of delivery was highest among those without a known hypertensive disorder, cardiomyopathy, or valvular heart disease. As such, patients without those conditions were at increased risk of mortality if they developed CSMM during their delivery hospitalization. This finding is consistent with prior studies reporting that most patients who die from cardiac complications in pregnancy are not known for cardiovascular disease

prior to pregnancy.[34-36] As such, any CSMM event requires evaluation by cardiovascular experts, even in the absence of a known cardiovascular disease.

STUDY LIMITATIONS. Our study had several limitations. First, administrative data sets are inherently subjected to misclassification, as they are dependent on the quality of the ICD coding. Diagnostic criteria for preeclampsia evolved in 2013,[37] and the ICD-9 code for peripartum cardiomyopathy was only introduced in 2003.[38] Therefore, these 2 conditions could have been misclassified in our study population. The variable capturing race/ethnicity in administrative data sets lacks nuance, may not reflect individuals' multidimensional racial and ethnic identity, and does not allow for an in-depth examination of its implications.[39,40] The data set did not capture mortality in nonobstetric services and out-of-hospital deaths. As such, postpartum maternal mortality was likely underestimated. In addition, longitudinal follow-up data were not available, including during the postpartum period. As a result, the effect of recurrent pregnancies and postpartum events occurring after delivery hospitalization could not be evaluated. Since an important proportion of CSMM (eg, readmissions for heart failure) and maternal cardiovascular deaths are known to occur in the early and late postpartum periods, future research assessing the relationship between CSMM and mortality beyond delivery hospitalization is required.[31,41-43] Our data set covered the period from 1999 to 2015, and future research highlighting temporal trends in CSMM in more recent years is needed. Finally, granular clinical information such as body mass index of participants or qualitative information regarding the series of events leading to mortality in women with CSMM was not available. Accordingly, confidential enquiries into pregnancy-related deaths and severe maternal morbidity reviews remain essential in understanding the progression from cardiovascular morbidity to mortality.[44]

CONCLUSIONS

The incidence of CSMM at delivery increased from 1999 to 2015. While the case-fatality of CSMM decreased during the study period, it remained elevated. Race/ethnicity, insurance type, postpartum hemorrhage with transfusion, and SLE were factors associated with mortality among women who developed CSMM. Population-based surveillance evaluating cardiovascular morbidity and mortality should continue to be performed on an ongoing basis, as care interventions to reduce adverse cardiovascular outcomes in the obstetric population are being deployed in the US and internationally.[36,45]

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: CSMM during hospitalization for delivery, associated with a 4.44% case fatality, has been on the rise. Thus, it is imperative that all health care providers be familiar with signs and symptoms of cardiovascular decompensation in pregnancy. Pulmonary edema, the most common morbidity event to occur, was present in ~1 in 10 patients with CSMM who died. Accordingly, appropriate investigations, including biomarkers and imaging, to evaluate underlying causes of pulmonary edema should not be delayed. Since patients with CSMM and concomitant postpartum hemorrhage or SLE were at heightened risk of mortality, they should be cared for in a monitored setting. Finally, women who developed CSMM in the absence of known hypertensive disorders, cardiomyopathy, or valvular heart disease were at increased risk of mortality. As such, CSMM events warrant evaluation by cardiovascular experts even in the absence of known predisposing heart conditions.

TRANSLATIONAL OUTLOOK: While overall case-fatality and mortality rates for each CSMM subtypes were described, additional research is needed to examine other short- and long-term sequelae of CSMM, including the effect on mental health and quality of life. In addition to preventing CSMM events, developing interventions focusing on improving pregnancy-specific resuscitative measures once CSMM events are established may contribute to reducing maternal mortality. Using a standardized definition of CSMM may facilitate population-based surveillance to monitor the impact of future initiatives geared toward improving cardiovascular outcomes in pregnancy. Importantly, studies assessing the relationship between CSMM and mortality in the early and late postpartum periods would be required.

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KEY WORDS **maternal mortality, peripartum cardiomyopathy, preeclampsia, pregnancy, severe maternal morbidity**

APPENDIX **For supplemental tables, please see the online version of this paper.**