OBSTETRICS

Pregnancy-related cardiovascular deaths in California: beyond peripartum cardiomyopathy

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OBJECTIVE: Maternal mortality rates rose markedly from 2002 to 2006 in California, prompting an in-depth maternal mortality review in a state that comprises one twelfth of the US birth cohort. Cardiovascular disease has emerged as the leading cause of pregnancy-related death in the United States. The primary aim of this analysis was to describe the incidence and type of cardiovascular disease as a cause of pregnancy-related mortality in California. The secondary aims were to describe racial/ethnic and socioeconomic disparities, risk factors, birth outcomes, timing of death and diagnosis, and signs and symptoms of cardiovascular disease and identify contributing factors.

STUDY DESIGN: The California Pregnancy-Associated Mortality Review retrospectively examined a case series of 64 cardiovascular pregnancy-related deaths from 2002 through 2006. Two cardiologists independently reviewed complete inpatient and outpatient medical records including laboratory, radiology, electrocardiogram, chest X-ray, echocardiograms, and autopsy findings for each cardiovascular death and classified cause of death by type of cardiovascular disease. Demographic data, racial disparities, risk factors, signs and symptoms, timing of diagnosis and death, birth outcomes, and contributing factors were analyzed using bivariate comparisons with non-cardiovascular pregnancy-related deaths and population-based data.

RESULTS: Among 2,741,220 California women who gave birth, 864 died while pregnant or within 1 year of pregnancy; 257 of the deaths were deemed pregnancy related, and of these, 64 (25%) were attributed to cardiovascular disease. There were 42 deaths caused by cardiomyopathy, and the pregnancy-related mortality rate from cardiomyopathy was 1.54 per 100,000 births. Dilated cardiomyopathy existed in 29 cases, of which 15 met the definition of peripartum cardiomyopathy. Women with cardiovascular disease were more likely than women who died from noncardiovascular causes to be African-American (39.1% vs 16.1%; $P < .01$) and more likely to use illicit substances (23.7% vs 9.4%; $P < .01$). Thirty-seven percent were obese and 20% had a concomitant diagnosis of hypertension or preeclampsia during pregnancy. Health care decisions in the diagnosis or treatment of cardiovascular disease during and after pregnancy contributed to the fatal outcomes.

CONCLUSIONS: African-American race, substance use, and obesity were risk factors for pregnancy-related cardiovascular disease mortality. Chronic disease prevention and better recognition and response to cardiovascular disease during pregnancy are needed to reduce maternal mortality.

Key words: cardiovascular disease, pregnancy-related mortality

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Cardiovascular disease (CVD) is increasingly recognized as a frequent cause of pregnancy-related morbidity and mortality worldwide[1-3] and is surpassing other medical causes of pregnancy-related mortality in developed countries.[4-6] United Kingdom obstetrical surveillance reported heart disease as a leading cause of maternal deaths from 2010 to 2012 with an incidence of 2.25 deaths per 100,000 live births.[7] United States surveillance data

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TABLE 1
Criteria used for classification of types of cardiomyopathy in pregnancy-related deaths, California, 2002–2006

Terms	Definition
California birth cohort	Women with a live birth or fetal loss within the calendar year
Pregnancy-associated mortality cohort	Women who died while pregnant or within 1 y postpartum from any cause
Pregnancy-related death	Death from causes directly related to the physiological changes in pregnancy or causes aggravated by the pregnancy or its management
Cardiovascular pregnancy-related death	Death in which cardiovascular disease, which is caused or aggravated by pregnancy, is the initiating or critical pathological event leading to death
Type of cardiomyopathy	Hx/S/S, ECHO, and AUT
Dilated cardiomyopathy	Hx/S/S: rales, S3 gallop, pulmonary edema on CXR ECHO: LV ejection fraction less than 40%; LV wall thickness $\leq$1.2 cm; dilated LV AUT: enlarged heart; increased chamber dimensions, wall thickness $<$1.5 cm, no identifiable structural heart disease
Peripartum	Hx/S/S: development of congestive heart failure in the last month of pregnancy or within 5 mo postpartum, absence of preexisting cardiac dysfunction, absence of a determinable cause of cardiomyopathy, and ECHO: documented LV systolic dysfunction
Nonperipartum (secondary to drug and/or alcohol use)	Hx/S/S: documented substance or alcohol use, by positive toxicology screen $\pm$ well-documented history
Nonperipartum (secondary to infection (eg, acute myocarditis)	Hx/S/S: clinical history of recent respiratory or other infection; AUT: inflammatory cells (lymphocytes) on microscopy
Subtype could not be determined	Hx/S/S: outside window for peripartum cardiomyopathy but had no other features to suggest etiology
Hypertrophic heart disease, including cardiomyopathy	Hx/S/S: S4 gallop, systolic murmur; pulmonary edema on CXR ECHO: LV ejection fraction $\geq$40%; LV wall thickness $\geq$1.2 cm AUT: increased heart weight; normal chamber dimensions, wall thickness $\geq$1.5 cm
Primary, potential	Hx/S/S: no documented family history but no cause for secondary hypertrophy
Secondary, hypertension	Hx/S/S: documented blood pressures $\geq$140/90 mm Hg
Secondary, drug use	Hx/S/S: documented history of methamphetamine or cocaine, by positive toxicology screen $\pm$ well-documented history
Secondary, valve disease	ECHO: significant valve abnormality
Etiology could not be determined	Hx/S/S: inadequate documentation for presence of secondary causes and no known family history

AUT, autopsy findings; *CXR*, chest x-ray; *ECHO*, echocardiographic findings; *Hx/S/S*, patient history and clinical signs and symptoms; *LV*, left ventricular.

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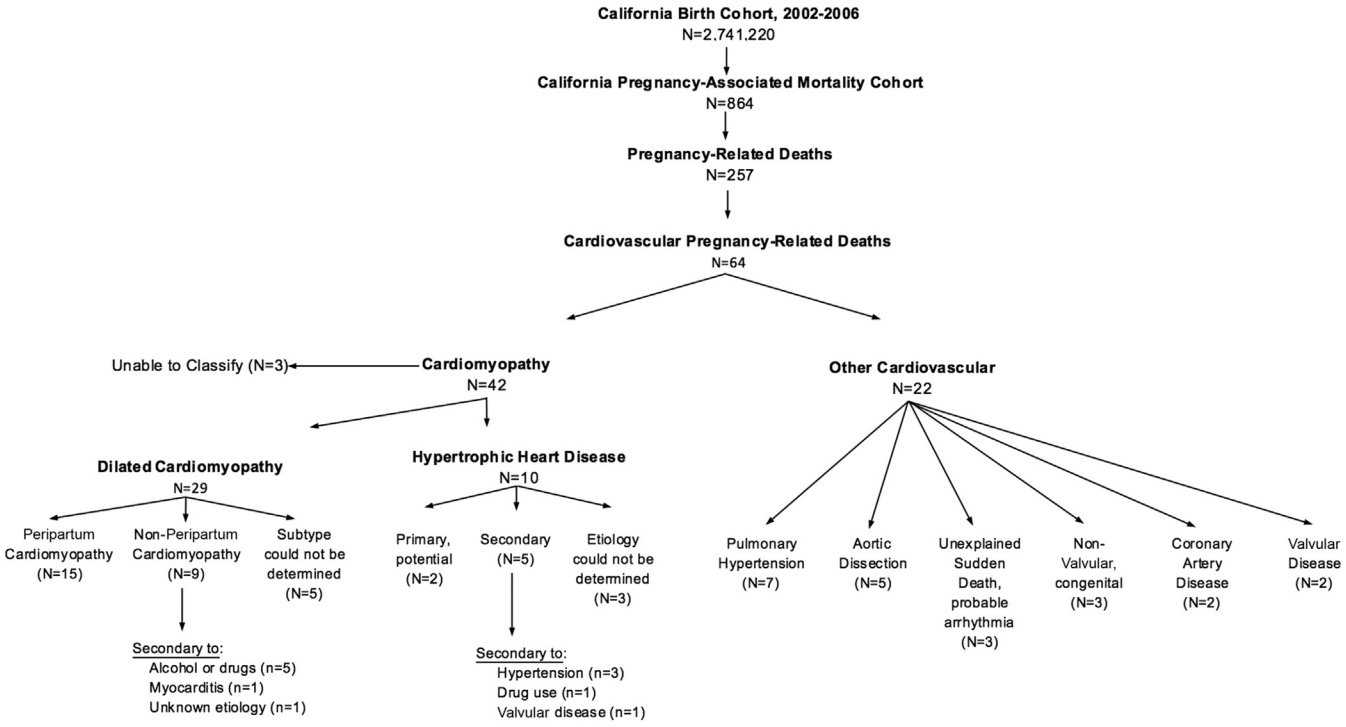
show an increase in cardiovascular pregnancy-related deaths with 3.48 deaths per 100,000 live births from 1998 to 2005[8] to 4.23 cardiovascular deaths during 2006-2010.[9]

Cardiomyopathy contributed to nearly 12% of pregnancy-related deaths for a rate of 0.88 deaths per 100,000 live births during 2006-2009.[10] CVD in pregnancy encompasses a spectrum of cardiac diagnoses with a preponderance of cardiomyopathy. In particular, peripartum cardiomyopathy presents in the last month of pregnancy or within the first 5 months postpartum.[11] Obese African-American women of non-Hispanic origin are particularly at risk for cardiomyopathy.[12] Additionally, more than one third of intensive care unit admissions in pregnancy and postpartum are related to cardiac disease.[13]

The California Pregnancy-Associated Mortality Review (CA-PAMR) was initiated in 2006 in response to rising rates of maternal mortality and retrospectively investigates maternal deaths statewide to inform prevention and quality improvement strategies.[14] The primary objective of this analysis is to describe the incidence and type of CVD as a cause of pregnancy-related mortality. The secondary objectives are as follows: (1) to describe disparities in risk based on race/ethnicity and socioeconomic status; (2) to identify risk factors; (3) to measure birth outcomes; (4) to describe the timing of death and diagnosis; (5) to describe signs and symptoms of CVD identified during

FIGURE 1
Classification of pregnancy-related cardiovascular deaths, California 2002-2006



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pregnancy; and (6) to identify contributing factors.

Materials and Methods

Women who died while pregnant or within a year of delivery were identified by linkage of birth, fetal death, and maternal death certificates. When data sources (death certificates and autopsy and toxicology reports) suggested the death may be pregnancy related, defined as deaths directly related to the physiological changes in pregnancy or causes aggravated by the pregnancy or its management, medical records were reviewed by the CA-PAMR Committee.[15]

The committee determined causation of pregnancy-related cardiovascular deaths by ascribing the cause as either cardiomyopathy or other cardiovascular disease, similar to national reporting.[9] Through consensus, the committee also identified contributing factors related to health care providers, health care facilities, or patient circumstances and the degree to which the death might have been prevented.

Health care provider factors included actions involving diagnosis, treatment, and communication processes. Facility factors included systems-level processes involving policies, nursing knowledge, or infrastructure. Patient factors included circumstances, risk factors, or health behaviors contributing to the cause of death.

Preventability was assessed by whether specific and feasible actions, had they been implemented, might have changed the course of the woman's trajectory and led to a nonfatal outcome, as measured on a 4-part continuum: strong, good, some, or no chance. Examples of specific and feasible actions included failure to evaluate the cause of severe shortness of breath and anxiety in a postpartum woman and apparent lack of communication and care coordination among obstetrics and cardiology around a diagnosis of Marfan syndrome.

For this analysis, in 2013, 2 cardiologist members of the CA-PAMR Committee (A.B.H. and E.F.) independently re-reviewed the available series of CVD cases from 2002 to 2006 to confirm CVD causes of death and further classify cardiomyopathy and other CVD subtypes per the criteria listed in Table 1. In cases of discordant coding, the cases were discussed to seek consensus, and if still discordant, a third cardiologist was consulted to adjudicate.

Case data were analyzed using IBM SPSS Statistics version 20.0 (IBM Corp, New York, NY). Demographic variables (age, race, payer source) were derived from the maternal death certificate. Adequacy of prenatal care was calculated using a well-established index, based on 2 independent measures: initiation of care and frequency of visits.[16] Substance use, body mass index, parity, CVD-related clinical variables, and timing of diagnoses were collected from the medical record; heart weight was collected from the autopsy.

The California birth cohort is comprised of women who gave birth or had a fetal death, as reported on California birth and fetal death certificates, and provides a population-based comparison of

TABLE 2
Demographic characteristics of cardiovascular pregnancy-related deaths in California, 2002–2006

Characteristic	All CVD deaths, n (%) (n = 64)	Non-CVD deaths, n (%) (n = 193)	California birth cohort, n (%) (n = 2,741,220)
Age, y			
<20	3 (4.7)	12 (6.2)	257,301 (9.4)
20–34	46 (71.9)	115 (59.6)	2,014,092 (73.5)
≥35	15 (23.4)	66 (34.2)	469,102 (17.1)
Race/ethnicity			
White, non-Hispanic	16 (25.0)	50 (25.9)	793,780 (29.0)
Hispanic	21 (32.8)	91 (47.2)	1,391,656 (50.9)
African-American, non-Hispanic	25 (39.1)	31 (16.1)[a]	146,536 (5.4)[a]
All other/unknown or missing	2 (3.1)	19 (9.8)	401,701 (14.7)
Payer source for delivery			
Medi-Cal/other government	40 (62.5)	106 (54.9)	1,289,446 (47.0)[a]
Private/other	24 (37.5)	87 (45.1)	1,451,774 (52.9)
Adequacy of prenatal care			
Less than adequate care	23 (37.7)	50 (27.0)	663,542 (25.0)[a]
Adequate or better care	38 (62.3)	135 (73.0)	1,993,835 (75.0)
Missing information (excluded from analysis)	3 (4.7)	8 (4.1)	67,589 (2.5)

CVD, cardiovascular disease.

[a] χ^2 analysis compared all CVD deaths with non-CVD deaths and with the California birth cohort ($P < .05$).

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child-bearing women in the same time frame. Comparisons were also made to CA-PAMR pregnancy-related deaths from causes other than CVD for risk factors and clinical characteristics. Statistical significance was determined using the Pearson χ^2 test of independence for categorical variables, and independent *t* tests and nonparametric Mann Whitney tests were conducted for continuous variables. A paired-samples *t* test was conducted for an analysis of average heart weight in CVD cases compared with the average heart weight of nonpregnant women.[17]

All CA-PAMR protocols were approved by the Committee for the Protection of Human Subjects of the State of California and comply with the Health Insurance Portability and Accountability Act. The Stanford University and Public Health Institute Institutional Review Boards exempted analysis of deidentified data on deceased persons.

RESULTS

Incidence and type of CVD

From 2002 to 2006, there were 2,741,220 California women who gave birth or had a fetal demise and 864 women who died while pregnant or within 1 year of pregnancy. Initial screening yielded 344 cases for committee review, and 257 were subsequently determined to be pregnancy related by the CA-PAMR Committee. Among the pregnancy-related deaths, nearly a quarter (n = 64) were due to CVD, for an incidence rate of 2.35 CVD deaths per 100,000 live births.

Among the CVD deaths, two-thirds (n = 42) met criteria for cardiomyopathy (1.54 cardiomyopathy deaths per 100,000 live births) and 22 deaths were from other cardiovascular causes (Figure 1). Among the cardiomyopathy deaths, 29 (69%) were from dilated cardiomyopathy (1.06 dilated cardiomyopathy deaths per 100,000 live births) and 10 (24%) were associated with hypertrophic heart disease (HHD) (0.37 HHD deaths per 100,000 live births).

Of the 29 dilated cardiomyopathy cases, 24 deaths had sufficient documentation to determine whether they met the case definition of peripartum cardiomyopathy[18,19] (Table 1), and 15 deaths were attributed to this etiology. Five of the 10 deaths from HHD were determined to be secondary to hypertension, substance use, or valve disease. Two cases were potentially primary hypertrophic cardiomyopathy, and in 3 cases, the etiology could not be determined. The most frequent diagnoses among the other cardiovascular category (n = 22) were pulmonary hypertension (n = 7) and aortic dissection (n = 5).

Racial/ethnic and socioeconomic disparities of all CVD pregnancy-related deaths

Women who died from CVD were more likely than those who died of non-CVD causes to be African-American (39.1% vs 16.1%; $P < .01$) (Table 2). The CVD pregnancy-related mortality rate for African-Americans was more than 8 times higher than that for whites (17.1; 95% confidence interval [CI], 10.4–23.7 vs 2.0; 95% CI, 1.0–3.0 per 100,000 live births, respectively). CVD type did not significantly vary by race/ethnicity. Women who died from CVD were more likely than the California birth cohort to have public insurance (62.5% vs 47%, respectively, $P < .01$) and were significantly less likely than the California birth cohort to have had adequate prenatal care ($P < .05$) (Table 2).

Risk factors for pregnancy-related CVD deaths

Women who died from CVD had a higher frequency of documented substance use than women who died from non-CVD causes (23.7% vs 9.4%; $P < .01$) (Table 3). When self-reported alcohol and tobacco use were included, the proportion of any substance use

TABLE 3
Risk factors for cardiovascular disease pregnancy-related deaths in California, 2002 to 2006

Variable	Cardiovascular pregnancy-related deaths				Noncardiovascular pregnancy-related deaths, n (%) (n = 193)
	All CVD, n (%) (n = 64)	Cardiomyopathy deaths[a] (n = 42)			
		Dilated cardiomyopathy, n (%) (n = 29)	Hypertrophic heart disease, n (%) (n = 10)	Other CVD, n (%) (n = 22)	
Substance use[b]					
Amphetamines or cocaine	7 (10.9)	4 (13.8)	2 (20.0)	1 (4.5)	15 (7.8)
Marijuana, opioids	8 (12.5)	8 (27.6)	—	—	2 (1.0)[c]
Any of the drugs listed previously	14 (27.3)	11 (39.3)	2 (25.0)	1 (5.0)	17 (9.4)[c]
Alcohol	10 (16.9)	7 (24.1)	2 (20.0)	1 (4.5)	7 (3.6)[c]
Tobacco	15 (25.0)	6 (20.7)	4 (40.0)	3 (15.0)	24 (12.4)[c]
Prepregnancy BMI, kg/m^2[d]					
Underweight or normal (<25)	19 (29.7)	8 (27.6)	2 (20.0)	9 (40.9)	76 (41.3)
Overweight (25.0–29.9)	21 (32.8)	7 (24.1)	4 (40.0)	8 (36.4)	61 (33.1)
Obese 1 (30.0–34.9)	11 (17.2)	7 (24.1)	1 (10.0)	3 (13.6)	22 (11.4)
Obese 2 (35.0–39.9)	6 (9.4)	4 (13.8)	—	1 (4.5)	6 (3.3)[a]
Obese 3 (≥40.0)	7 (10.9)	3 (10.3)	3 (30.0)	1 (4.5)	19 (10.3)
Parity[e]					
1	16 (25.0)	6 (20.7)	3 (30.0)	6 (27.3)	60 (31.1)
2–3	33 (51.6)	14 (48.3)	7 (70.0)	11 (50.0)	89 (46.2)
≥4	15 (23.4)	9 (31.0)	—	5 (22.7)	43 (22.6)
Hypertensive disease, including preeclampsia	13 (20.3)	7 (24.1)	4 (40.0)	2 (9.1)	32 (16.6)

BMI, body mass index; *CVD*, cardiovascular disease.

[a] There were 3 cardiomyopathy deaths whose subtypes were unable to be determined. As a result, not all values presented in the dilated cardiomyopathy and hypertrophic cardiomyopathy add up to (all) cardiomyopathy deaths (n = 42); [b] Autopsy toxicology reports were data source for amphetamine, cocaine, marijuana, and opioid drug use. Alcohol and tobacco use obtained from self-reported data in medical records. Any substance use includes women with multiple substance use and will not equal the total of individual substances used; [c] χ^2 analysis compared all CVD deaths with non-CVD deaths ($P < .05$); [d] BMI calculated as: weight (pounds)/[height (inches)]^2 × 703. BMI data were missing for 9 of the women who died of non-CVD, and these cases were excluded from analysis. Thus, the total n does not sum to 193 and denominators for the BMI categories varied for non-CVD deaths; [e] Parity of 1 comprises the birth/fetal demise associated with this pregnancy-related death.

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during pregnancy or the postpartum period rose to 32.8% among women with CVD deaths compared with 16.1% among non-CVD pregnancy-related deaths ($P < .01$). The most prevalent underlying conditions among women who died from CVD were obesity (37.5%) based on prepregnancy body mass index (BMI) and hypertension. One fifth of the women who died from CVD (20.3%) had a concomitant diagnosis of hypertension (n = 8) or preeclampsia (n = 4), which was slightly more than the non-CVD deaths (16.6%). No differences in parity were noted (Table 3).

Birth outcomes

Among the 64 women who died from CVD, there were 60 live births and 4 fetal deaths. The average gestational age at the time of delivery was 36.9 weeks (range, 23.3–42.0 weeks; median, 38.4 weeks). The cesarean delivery rate was 53.1% in the CVD group vs 68.6% in the non-CVD group ($P < .05$), with the maternal condition as the most common indication for cesarean delivery within both groups.

Timing of CVD pregnancy-related deaths and diagnosis

Among all CVD pregnancy-related deaths, 1 (1.6%) occurred prior to delivery and 70.3% occurred in the early postpartum period (ie, 42 or fewer days from delivery). Deaths among women with CVD, however, were more likely to occur beyond the 6 week postpartum period compared with women with non-CVD deaths (29.7% vs 7.3%; $P < .001$). Only 5% of other cardiovascular deaths occurred in the late postpartum period compared with 40% of all cardiomyopathy deaths and 55% of dilated cardiomyopathy deaths (Table 4).

Two women (3.1%) had a known history of CVD when they entered prenatal care and 5 (7.8%) were diagnosed during pregnancy. Twenty-six (40.6%)

TABLE 4
Timing of death and diagnosis and postmortem evidence of cardiovascular pregnancy-related deaths in California, 2002 to 2006

Variable	Cardiovascular pregnancy-related deaths				Noncardiovascular pregnancy-related deaths, n (%) (n = 193)
	All CVD, n (%) (n = 64)	Cardiomyopathy deaths (n = 42)[a]		Other CVD, n (%) (n = 22)	
		Dilated cardiomyopathy, n (%) (n = 29)	Hypertrophic heart disease, n (%) (n = 10)		
Time to death from birth or fetal demise					
Mean, d	56	112	12	7	12[b]
Median, d	9.0	67.0	6.5	2	2
Mode, d	0	0	0	0	0
Range (upper, lower)	(0, 340)	(0, 340)	(0, 64)	(0, 53)	(0, 255)
Early (≤42 d postpartum)	45 (70.3)	13 (44.8)	9 (90.0)	21 (95.5)	179 (92.7)[b]
Late (>42 d postpartum)	19 (29.7)	16 (55.2)	1 (10.0)	1 (4.5)	14 (7.3)[b]
Timing of CVD diagnosis					
Preexisting disease	2 (3.1)	—	—	2 (9.1)	N/A
Prenatal period	5 (7.8)	1 (3.4)	1 (10)	3 (13.6)	N/A
At labor and delivery	4 (6.3)	3 (10.3)	—	1 (4.5)	N/A
Postpartum period	22 (34.4)	17 (58.6)	—	5 (22.7)	N/A
Postmortem	31 (48.4)	8 (27.6)	9 (90)	11 (50.0)	N/A
Autopsy performed					
Yes	44 (68.8)	16 (55.2)	9 (90.0)	17 (77.3)	103 (53.4)[b]
Heart weight[a]					
Heart weight data available	40 (62.5)	16 (55.2)	8 (80)	14 (63.6)	Data not available
Heart weight mean, g	443	458	463	424	Data not available
Exceeded normal heart weight, based on body weight[c]	100%	100%	100%	100%	Data not available
Identified as pregnancy related on death certificate[d]					
Yes	33 (51.6)	13 (44.8)	4 (40.0)	15 (68.2)	156 (80.8)[b]
No	31 (48.4)	16 (55.2)	6 (60.0)	7 (31.8)	37 (19.2)

CVD, cardiovascular disease; *N/A*, not applicable.

[a] There were 3 cardiomyopathy deaths whose subtypes could not be determined and were excluded from the cardiomyopathy subtype analysis; [b] Mann-Whitney and χ^2 analysis compared all CVD deaths with non-CVD deaths ($P < .05$); [c] Observed within-person difference between actual and predicted heart weights are not adjusted for age or pregnancy because data are not available; [d] Deaths were assigned an *International Classification of Diseases*, 10th revision, code for obstetric-related deaths (eg, an O code) as the underlying cause of death.

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were diagnosed in the intra- or postpartum periods, and the remaining 31 (48.4%) had a postmortem CVD diagnosis (Table 4). Eight of the postmortem diagnoses occurred among 9 women who experienced sudden cardiac death, 3 of whom satisfied criteria for sudden arrhythmic death because there was no evidence of structural heart disease (Figure 1).[20]

Cardiac tests including electrocardiogram and echocardiogram were performed in 71.9% and 53.1% of the women, respectively (data not shown). Autopsy reports were available in 68.8% (n = 44) of the CVD deaths. Among autopsies with recorded heart weight (n = 40), 100% exceeded the predicted normal heart weight as a function of body weight at the time of delivery. The mean heart weight (443.3 ± 78.0 g) was significantly higher than the predicted mean heart weight among a sample of nonpregnant women (312.4 ± 32.9 g)

TABLE 5
Prenatal and intrapartum signs and symptoms of heart disease, timing of diagnosis among cardiovascular pregnancy-related deaths in California, 2002–2006

Variable	All CVD, n (%) (n = 64)	Cardiomyopathy deaths[a] (n = 42)		Other CVD, n (%) (n = 22)
		Dilated cardiomyopathy, n (%) (n = 29)	Hypertrophic heart disease, n (%) (n = 10)	
Symptoms, at any time				
Shortness of breath/dyspnea	39 (60.9)	19 (65.5)	5 (50.0)	13 (59.1)
Edema (1+, 2+, any lower extremity swelling)	28 (43.8)	14 (48.3)	7 (70.0)	4 (18.2)
Chest pain	22 (34.4)	12 (41.4)	2 (20.0)	7 (31.8)
Fatigue	16 (25.0)	9 (31.0)	1 (10.0)	4 (18.2)
Dizziness	16 (25.0)	10 (34.5)	—	5 (22.7)
Wheezing	12 (18.8)	10 (34.5)	1 (10.0)	1 (4.5)
Palpitations	10 (15.6)	5 (17.2)	—	4 (18.2)
Any of the previously cited symptoms, during following periods				
Prenatal period	24/56 (42.9)	11/24 (45.8)	4 (40.0)	9/20 (45.0)
Labor and delivery	31/61 (50.8)	13/28 (46.4)	6 (60.0)	10/20 (50.0)
Postpartum period	40/50 (80.0)	22/26 (84.6)	5 (50.0)	10/15 (66.6)
Physical examination findings, at any time				
Tachycardia (heart rate >100)	52 (81.3)	26 (89.7)	9 (90)	14 (63.6)
Tachycardia (heart rate >120)	38 (59.4)	21 (75.0)	5 (50.0)	10 (45.5)
Hypertension, mm Hg: ≥140 systolic or ≥90 diastolic	41 (64.1)	22 (75.9)	8 (80.0)	10 (45.5)
Hypoxia (<90% O_2 saturation)	25 (39.1)	17 (58.6)	1 (10.0)	7 (31.8)
Bilateral crackles, S3 gallop rhythm, or heart murmur	28 (43.8)	21 (72.4)	3 (30.0)	6 (27.3)

CVD, cardiovascular disease.

[a] There were 3 cardiomyopathy deaths whose subtypes could not be determined and were excluded from the cardiomyopathy subtypes.

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($P < .01$). CVD deaths were significantly less likely to be identified as pregnancy related by death certificates alone (51.6% concordance with CA-PAMR Committee determinations) compared with non-CVD pregnancy-related deaths (80.8% concordance) ($P < .05$) (Table 4).

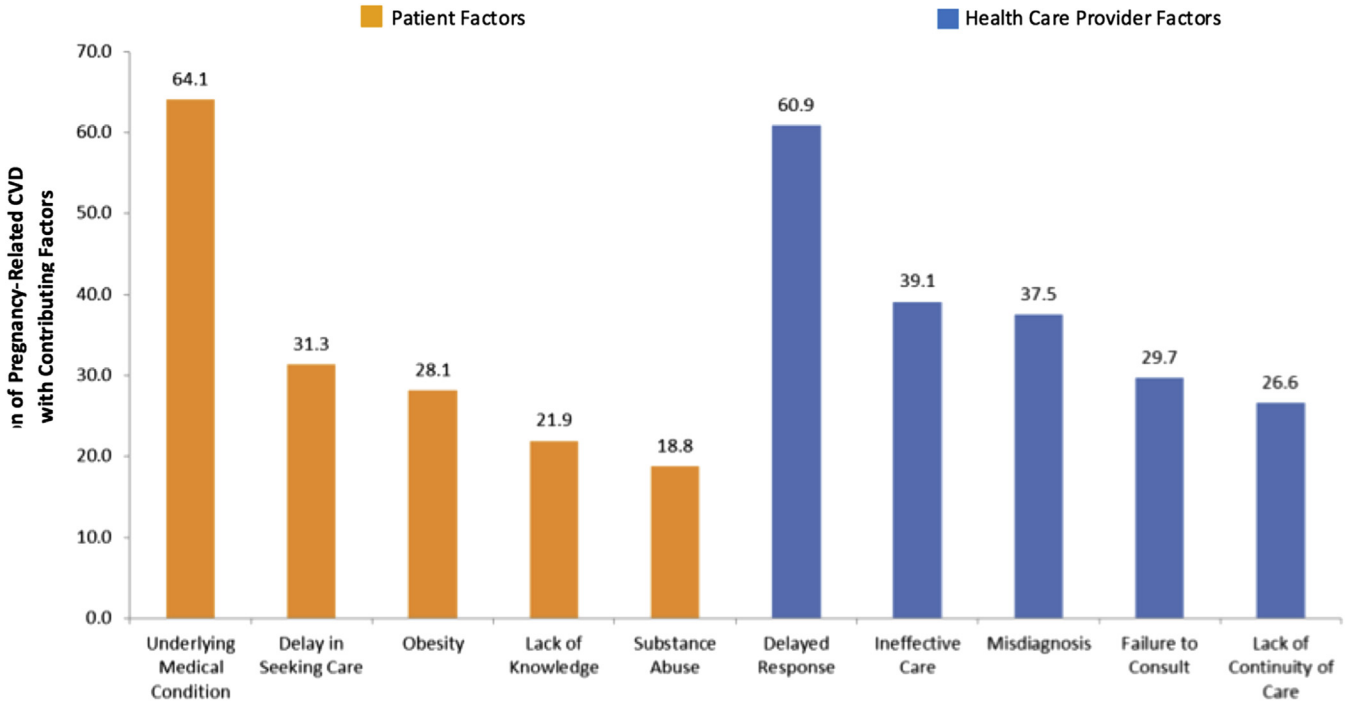
Signs and symptoms of cardiovascular decompensation

CVD symptoms and their timing as well as physical examination findings are shown in Table 5. Eighty-four percent of women who died from CVD presented with symptoms suggestive of cardiopulmonary disease (ie, shortness of breath, palpitations, chest pain, wheezing, or fatigue), which manifested during pregnancy or in the postpartum period. Among the symptomatic women, 61.1% received a referral to a cardiologist for further evaluation; however, only 7% were referred in the prenatal period. The remaining referrals occurred around labor and delivery or postpartum. Only 2 women were diagnosed with CVD prior to delivery, even though 11 women presented with at least 1 symptom consistent with cardiovascular disease during the pregnancy.

Additional findings on cardiomyopathy deaths

Among the 29 dilated cardiomyopathy deaths, risk factors including African-American race, obesity and substance use were even more pronounced. The dilated cardiomyopathy mortality rate was 8.2 (95% CI, 3.6–12.8) deaths per 100,000 live births for African-American women vs 0.88 (95% CI, 0.2–1.5) for white women. Thirty-nine percent of women who died of dilated cardiomyopathy had documented substance use during pregnancy and 48.2% were obese (Table 3).

FIGURE 2
Factors contributing to pregnancy-related cardiovascular deaths, California 2002-2006



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A delay in diagnosis based on failure to respond to clinical warning signs in the history and physical examination was a contributing factor in 45% of the dilated cardiomyopathy deaths. Autopsies among the dilated cardiomyopathy deaths (n = 16) revealed significantly greater heart weights compared with the average heart weights of a sample of nonpregnant women of the same body weight (458 ± 71 g vs 314 ± 34 g, respectively; $P < .001$). Among the women who died with HHD (n = 10) who underwent autopsy (n = 9), the average heart weight was 463 ± 90 g compared with the predicted normal heart weight of 329 ± 33 g based on body weight.

Contributing factors

Overall, the CA-PAMR Committee determined that there was a good to strong chance to alter the outcome in 23.8% of the cardiovascular deaths. Patient and health care provider factors contributed to 70.3% and 68.8% of CVD deaths, respectively (Figure 2). Contributing patient factors included underlying medical conditions (64.1%), delay in seeking care (31.3%), obesity (28.1%), presumed or potential lack of awareness regarding the significance of their condition (21.9%), and substance abuse (18.8%). Health care provider factors included delayed response or management, including diagnosis and treatment (60.9%), ineffective care or treatment (39.1%), misdiagnosis (37.5%), failure to refer or consult (29.7%), and lack of continuity of care (26.6%). Management inadequacies centered on insufficient use of hypertensive medications and misdiagnosis of 8 cases either as new-onset asthma or other respiratory illness.

Comment

This statewide review, the largest and most comprehensive to date, utilized an in-depth investigation of pregnancy-related mortality and identified CVD as the leading cause of pregnancy-related death in California. Detailed review by cardiologists with expertise in high-risk pregnancies provided the means to elucidate the diverse presentations of CVD contributing to pregnancy-related mortality, more so than has been previously described. Almost half of the CVD deaths in this analysis would not have been identified as pregnancy-related based on the death certificate data alone, underscoring the value of an in-depth statewide maternal mortality review.

Between 2002 and 2006, the incidence of cardiovascular pregnancy-related deaths in California was 2.35 deaths per 100,000 live births, similar to rates reported by the United Kingdom but lower than those reported in a national surveillance.[7-9] Cardiomyopathy was the most common cause of CVD pregnancy-related mortality, with an incidence of 1.54 deaths per 100,000 live births, nearly twice the rate reported by US surveillance data.[10] This study found just one fourth of cardiomyopathy deaths were attributable to peripartum cardiomyopathy, in contrast to previous reports that found this cause to be the most prevalent cardiovascular diagnosis associated with pregnancy.[12,21]

Our methodology demonstrates that detailed review of clinical features, diagnostic testing, and autopsy data permits a more accurate classification of cardiovascular disease, especially for cardiomyopathy. In order of frequency, we identified 3 subpopulations of fatal pregnancy-related CVD: women with multiple risk factors and no prior CVD diagnosis; women with no specific risk factors who developed peripartum cardiomyopathy; and women with preexisting CVD at the time of presentation in pregnancy.

Like previous studies, our study confirmed African-American race, obesity, and hypertensive disorders as risk factors for pregnancy-related CVD deaths.[10,21,22] Although African-American women account for approximately 5.5% of California births, they comprised more than one fifth of all pregnancy-related deaths and nearly 40% of CVD deaths. This suggests that CVD may be contributing to the persistent racial/ethnic disparity in pregnancy-related mortality. The higher incidence of CVD in the African-American population may be partially explained by the increased baseline burden of traditional CVD risk factors,[23,24] but disparities in diagnostic or therapeutic care may also contribute to higher rates of CVD pregnancy-related deaths among African-American women.

Women may present with symptoms and signs suggestive of CVD in the latter half of normal pregnancy because of hemodynamic adaptions, and women with subclinical heart disease typically present during the same time frame.[25] This overlap may explain why the index of suspicion for CVD was not sufficiently high to pursue appropriate diagnosis and initiate treatment, even though the majority of women in our study had signs and symptoms recorded by health care providers in late pregnancy or postpartum. Furthermore, our study found that 30% of women died more than 42 days after delivery, which suggests that women at risk for CVD should have access to health care beyond the customary 6 week postpartum visit.

Of note, in our study only 2 women were noted to have preexisting CVD when they presented for prenatal care. Given a greater prevalence of preexisting CVD diagnoses among the prenatal patient population[26] than observed in this study, we hypothesize that pregnant women with preexisting CVD diagnoses may have been referred to specialists and received appropriate clinical management.

This study is the first to enumerate the extent of pregnancy-related mortality from cardiomyopathy associated with substance use, including methamphetamines and alcohol. This is also the first study to present data on increased cardiac mass. Although there is an expected increase in left ventricular mass during pregnancy of approximately 10%, we demonstrated heart weights far outside the expected range in 100% of those with available autopsy data.

Our study has limitations. The incidence rates may be slightly underestimated because improvements in case selection methodology in the 2005 to 2007 data identified approximately 10 cardiovascular deaths not included in this analysis. The retrospective nature of this review, a small number of missing records, and lack of standardized echocardiographic and autopsy reports precluded accurate classification of all diagnoses. Knowing these limitations, we were careful to assign a CVD classification only to those deaths with sufficient documentation.

Pregnancy-related deaths represent a small number compared with the much higher burden of maternal morbidity attributed to CVD. Based on the estimated 1.4% prevalence of heart disease and 4.84 cases of peripartum cardiomyopathy per 10,000 live births,[12,26] we project an annual number of approximately 7700 cardiovascular cases and 242 new cases of peripartum cardiomyopathy among the nearly 500,000 California women who give birth each year.

Because CVD has been established as the leading cause of maternal mortality during and after pregnancy, heightened clinical suspicion in the presence of CVD signs and symptoms may lead to earlier diagnosis and appropriate care, thus reducing mortality and morbidity. Additional studies are warranted that can help providers distinguish between warning signs of CVD and complaints common to pregnancy. Such studies might assess the predictive value of signs and symptoms of CVD identified by the chart review of the pregnant women in our study with women who have cardiovascular disease and survive the peripartum period and a control group of pregnant women without cardiovascular disease.

Clinical implications

Some clinical implications can be realized from this study. First, pregnancy is a period of frequent interaction with health care and offers an opportunity for providers to detect and treat heart disease, improve pregnancy outcomes, and impact future cardiovascular health. Second, signs and symptoms of normal pregnancy and postpartum may mimic cardiac disease; however, such symptoms should be interpreted with caution when they are severe and occur in the presence of vital sign abnormalities and underlying risk factors. Finally, an increased awareness and index of suspicion for potential CVD diagnosis, preconception counseling, and referral to a higher level of care may help prevent adverse maternal outcomes. ■

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