Journal of the American Heart Association

ORIGINAL RESEARCH

Changing Incidence and Mechanism of Pregnancy-Associated Myocardial Infarction in the State of California

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BACKGROUND: The objective of this study was to evaluate the temporal trends in pregnancy-associated myocardial infarction (PAMI) in the State of California and explore potential risk factors and mechanisms.

METHODS AND RESULTS: The California State Inpatient Database was analyzed from 2003 to 2011 for patients with *International Classification of Diseases, Ninth Revision* (*ICD-9*) codes for acute myocardial infarction and pregnancy or postpartum admissions; risk factors were analyzed and compared with pregnant patients without myocardial infarction. A total of 341 patients were identified with PAMI from a total of 5 266 380 pregnancies (incidence of 6.5 per 100 000 pregnancies). Inpatient maternal mortality rate was 7%, and infant mortality rate was 3.5% among patients with PAMI. There was a nonsignificant trend toward an increase in PAMI incidence from 2003 to 2011, possibly attributable to higher incidence of spontaneous coronary artery dissection, vasospasm, and Takotsubo syndrome. PAMI, when compared with pregnant patients without myocardial infarction, was significant for older age (aged >30 years in 72% versus 37%, $P<0.0005$), higher preponderance of Black race (12% versus 6%, $P<0.00005$), lower socioeconomic status (median household income in lowest quartile 26% versus 20%, $P=0.04$), higher prevalence of hypertension (26% versus 7%, $P<0.0005$), diabetes (7% versus 1%, $P<0.0005$), anemia (31% versus 7%, $P<0.0001$), amphetamine use (1% versus 0%, $P<0.00005$), cocaine use (2% versus 0.2%, $P<0.0001$), and smoking (6% versus 1%, $P=0.0001$).

CONCLUSIONS: There has been a trend toward an increase in PAMI incidence in California over the past decade, with an increasing trend in spontaneous coronary artery dissection, vasospasm, and Takotsubo syndrome as mechanisms. These findings warrant further investigation.

Key Words: coronary spasm ■ fetal mortality ■ maternal mortality ■ pregnancy ■ pregnancy-associated myocardial infarction ■ spontaneous coronary artery dissection

Deaths related to pregnancy have increased from 7.2 per 100 000 pregnancies in 1987 to 18 per 100 000 pregnancies in 2014 for unclear reasons.[1–3] There has also been a significant increase in the incidence of pregnancy-associated myocardial infarction (PAMI) in a recent nationwide population study.[4] The incidence of PAMI varies from 3 to 10 per 100 000 pregnancies.[4–7] In addition, PAMI has become a common cause of maternal mortality in the United States.[8] Studies have shown significant ethnic variations in the incidence of PAMI and the presence of nontraditional mechanisms.[9,10]

Pregnancy is associated with an increase in blood volume, altered hemodynamics, and a significant increase in circulating progesterone and estrogen levels.[11–13] Hormone replacement therapy is associated with an increase in risk of coronary artery disease and myocardial infarction.[14] Furthermore, maternal age is increasing in the United States and could possibly contribute to an increase in the incidence

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Supplementary Material for this article is available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.121.021056

For Sources of Funding and Disclosures, see page 9.

JAHA is available at: www.ahajournals.org/journal/jaha

CLINICAL PERSPECTIVE

What Is New?

- There has been a trend toward increasing incidence of pregnancy-associated myocardial infarction in the State of California from 2003 to 2011.
- This is potentially attributable to an increasing incidence of spontaneous coronary artery dissection, coronary vasospasm, and Takotsubo syndrome.
- The risk factors for pregnancy-associated myocardial infarction include older age, Black race, hypertension, diabetes, anemia, lower socioeconomic status, smoking, and use of amphetamines and cocaine.

What Are the Clinical Implications?

- Further research is needed to gain insights into the possibly increasing incidence of pregnancy-associated myocardial infarction and its newer mechanisms.
- Potentially modifiable risk factors for PAMI include control of hypertension and diabetes, treating anemia, and avoidance of smoking and recreational drugs.

Nonstandard Abbreviations and Acronyms

PAMI	pregnancy-associated myocardial infarction
SCAD	spontaneous coronary artery dissection
SID	State Inpatient Database

of PAMI. Mortality rate with PAMI is about 8% to 10% in the United States.[15–18] Prior studies have provided some information either in national-level data sets or they are composed of a collection of case series with little information over ethnicities, relation to socioeconomic aspects, trends of PAMI, outcomes based on management strategy selected, and in-depth analysis of change in mechanisms over the years.[4,9,16]

The objective of this study was to identify the trends of PAMI in the State of California, one of the most populated and ethnically diverse states in the United States.[19] In addition, this study aimed to analyze the risk factors, mechanisms, and mortality based on modality of treatment provided. We used the California State Inpatient Database (SID), which captures over 90% of hospitalizations, to address these questions.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Data Source

We used the SID, which is a part of the Healthcare Cost and Utilization Project, sponsored by the Agency for Healthcare Research and Quality, for the State of California. The SID is the largest publicly available database and includes all-payer discharge level data with *International Classification of Diseases, Ninth Revision* (*ICD-9*) codes, procedure-related *Common Procedural Technology* (*CPT*) codes, and inpatient mortality data.[20,21] Assignment of patients to a particular income quartile was based on the median income and range at the patient's zip code of residence; data were obtained from Claritas (Cincinnati, OH) PRIZM. To improve comprehensive assessment and inclusion of pregnant patients, we used Clinical Classification Software, which is a clinically meaningful cluster of *ICD-9* diagnoses and *CPT* codes. We analyzed the SID for California from 2003 to 2011, which were the most recent data for which continuous variables were available at the time of our initial analysis. The SID is a publicly available database, with no identifiable patient information; therefore, the study was exempt from review by the institutional review board.

Patient Selection

Pregnancy-related admission was defined using Clinical Classification Software codes (Table S1), which were a cluster of pregnancy-associated codes (*ICD-9* codes 630 to 648) or delivery codes (*ICD-9* codes 74 for cesarean delivery and 72, 73, 75, v27, or 650 to 659 for vaginal delivery). We also included postpartum discharge records up to 6 months after pregnancy (*ICD-9* codes 670 to 677). After we identified pregnant cohort B, we applied Clinical Classification Software code 100, which is a cluster of 39 *ICD-9* codes used for the diagnosis of acute myocardial infarction. That provided us with cohort A, which included all the patients from 2003 to 2011 who were pregnant or postpartum patients with acute myocardial infarction. We further compared patient demographics and baseline clinical characteristics among both cohorts using *ICD-9* diagnosis codes. Next, using *ICD-9* codes, we identified the mechanism of myocardial infarction and prevalence of traditional risk factors over the 9-year period and plotted on the graph to calculate trends over time. The SID also provides ethnicity data.

Study Design

To identify risk factor association and evolution of PAMI over time, we used 2 study designs. First, we analyzed

pregnancies with and without PAMI to identify risk factors. Second, we analyzed the trends over time in incidence PAMI, its mechanisms, and outcomes.

Outcomes

Our primary outcome was to analyze the trends of incidence, mechanisms, and outcomes of PAMI from 2003 to 2011. Our secondary outcome was to identify in-hospital all-cause maternal and fetal mortality with risk-factor association. We further analyzed this outcome based on the treatment or procedures the patient underwent. To identify the treatment options patients received, we used *CPT* codes for coronary angiography, percutaneous intervention, and if the patient underwent surgical revascularization.

Statistical Analysis

A 2-sample *t* test was used to compare means of age and length of stay between pregnant women with and without PAMI. For the rest of the variables, such as clinical characteristics, a Fisher exact test was used to test the association between PAMI and each of these variables. Furthermore, 9-year trends were calculated for mechanisms of acute myocardial infarction, risk factors, and ethnicity involved. A multivariate logistic regression model was performed with all patient demographics and clinical characteristics for pregnant women from 2003 to 2011. A separate logistic regression model was fit for each of the PAMI adverse outcomes including all patient demographics and clinical characteristics for pregnant women with PAMI from 2003 to 2011. The stepwise selection method was used to identify the significant factors to the chance of PAMI and maternal and fetal mortality. A significance (*P* value) level of 0.2 is required to allow a variable into the model, and a significance level of 0.1 is required for a variable to stay in the model. A χ^2 test of independence was performed to test the incidence of PAMI over time. Fisher exact tests were performed to test if the incidence of maternal and fetal mortality were the same over time.

Complete statistical support was provided by the Department of Biostatistics of the University of California, Riverside (K.H.X. and Z.Z.). Data sets were analyzed using SAS 9.4 (SAS Institute).

RESULTS

Demographics and Incidence of PAMI

We analyzed 5 266 039 pregnancy- and puerperium-related discharges in the State of California from 2003 to 2011. We found 341 cases with a diagnosis of PAMI occurring at a rate of 6.5 per 100 000 pregnancies. The highest proportion (32.3%) of PAMI cases were found in the 36 to 40 years age group . The frequency of PAMI was highest for those aged >40 years (39 cases in 140 487 or 28 per 100 000 pregnancies). There was a significantly higher incidence (40 cases in 281 460 or 14.2 per 100 000 pregnancies) among Black patients, followed by White patients (119 in 1 593 995 or 7.4 per 100 000 pregnancies), Asian patients (27 in 498 011 or 5.4 per 100 000 pregnancies), and Hispanic patients (127 in 2 432 003 or 5.2 per 100 000 pregnancies) (Table 1). The highest likelihood of PAMI was among the highest income quartile (66 in 803 231), and the most PAMI cases occurred in the lowest income quartile (34.2%).

Potential Risk Factors

Baseline clinical characteristics for patients with and without PAMI are compared in Table 2. Patients with PAMI as compared with patients without PAMI were more likely to have pregnancy-related hypertension (25.5% versus 6.7%), diabetes (6.7% versus 1.1%), anemia (30.8% versus 6.9%), high cholesterol (11.1% versus 0.1%), chronic kidney disease (2.3% versus 0.0%), smoking (5.6% versus 0.6%), amphetamine use (0.9% versus 0.3%), and cocaine use (1.5% versus 0.2%).

In terms of PAMI outcomes, the maternal mortality rate was 7% (24 out of 341 cases), and the fetal mortality rate was 3.5% (12 out of 341 cases). ST-segment–elevation myocardial infarction was present in 43% of the cases and likely the cause of cardiogenic shock in 5.3% and cardiac arrest in 11.1% of patients with PAMI (Table 2). Logistic regression analysis showed a 16-fold increase in the incidence of PAMI for patients aged >35 years, whereas a 3-fold increase for patients with anemia, a 15-fold increase for patients with cardiac and circulatory anomalies, a 4-fold increase with for patients with hypertension, a 7-fold increase for patients with hypercholesterolemia, and a 3-fold increase for patients with systemic lupus erythematosus (Table 3). Lifestyle-related risk factors such as smoking increased risk by 3-fold, cocaine use by 4-fold, and amphetamine use by 6-fold.

Mechanisms and Outcomes of PAMI

We found that the trend of PAMI from 2003 to 2011 was variable throughout the year, ranging from 5 to 8 per 100 000, with a variable maternal mortality rate between 3% and 17% during the study period. There was a total of 24 patients who died out of 341, with a case fatality rate of 7% with PAMI versus 0.0001% with no PAMI. The fetal mortality rate ranged from 1% to 11%, with 12 fetuses overall who died out 341 PAMI cases. It was also noted that there was a trend toward decrease in maternal mortality after 2009, with a slightly increasing trend of PAMI (Figure 1). However, these results were not statistically significant.

Table 1. Comparison of Patient Demographics Between Pregnant Patients With and Without MI

Demographics	Pregnancy with MI, n=341		Pregnancy with no MI, n=5 266 039		*P* value	Standardized mean difference
	No.	%	No.	%		
Mean age, y	27.8		33.6		<0.00001	
Age, y						
<20	7	2.1	685057	13.1	<0.00001	−0.97027
≥21–30	88	25.8	2606618	49.8	<0.00001	−0.96047
≥31–35	97	28.4	1197080	22.9	0.0169	0.315523
≥36–40	110	32.3	603127	11.5	<0.00001	2.03258
>40	39	11.4	140448	2.7	<0.00001	3.349201
Race/ethnicity						
White	119	36.5	1593995	32.3	0.1102	0.190108
Black	40	12.3	281420	5.7	<0.00001	1.218238
Hispanic	127	39.0	2432003	49.3	0.0002	−0.41566
Asian	27	8.3	498011	10.1	0.3120	−0.20066
Native American	0	0.0	5157	0.1	1.0000	−1.00108
Other	13	4.0	117816	2.4	0.0675	0.60928
Patient location, rural percent only	14	5.4	213650	5.4	0.8910	0.004384
Median household income in patient's zip code						
Lowest income quartile	90	34.2	1222901	30.3	0.1796	0.184355
Second quartile	63	24.0	1076532	26.7	0.3299	−0.14008
Third quartile	44	16.7	929949	23.1	0.0155	−0.35681
Highest income quartile	66	25.1	803231	19.9	0.0443	0.324533

MI indicates myocardial infarction.

We found intriguing results in mechanisms of PAMI over 9 years. There was a slight trend of increase in incidence of Takotsubo cardiomyopathy from 0% in 2003 and 9.86% in 2011. Similar trends were noted for coronary vasospasm at 0% in the first 5 years and 5% in 2011 (Figure 2). However, results were not statistically significant. Coronary artery dissection was a cause of PAMI in ≈20% of cases in 2003, which doubled to almost 40% by 2011. However, in 2009 there was reduction in dissection and vasospasm cases as compared with the prior year, followed again by an increase in both in the subsequent year. On the other hand, atherosclerosis as a mechanism of PAMI diminished from almost 80% in 2003 to 45% in 2011 and was lowest in 2010. These trends were associated with year-to-year variation as opposed to a linear increase in their incidences, and vasospasm and dissection were nonexistent until 2007.

Race-based variation in the incidence of PAMI was significant for Black patients, at 14.2 per 100 000 pregnancies; however, because Black patients were a smaller proportion of patients in the State of California they contributed 12.3% to PAMI cases overall. The highest number of PAMI cases were found at ≈40% among Hispanic patients, with an incidence of 5.2 per 100 000 cases. Asian patients remained at ≈5% over 9 years in terms of incidence of PAMI. White patients accounted for 30% of all PAMI cases from 2003 to 2011 (Figure 3). Cocaine use showed 14-fold increase in maternal mortality, and the highest income quartile had significantly reduced maternal mortality. Fetal mortality was mainly affected by anemia, Takotsubo cardiomyopathy, chronic kidney disease, and smoking (Table 4).

Management Trends of PAMI

Figure 4 depicts the detailed trends of various management strategies of PAMI from 2003 to 2011. The conservative approach, which included noninvasive treatment options without a diagnostic coronary angiogram, was received by 183 (54%) out of 341 patients (total patients with PAMI), with a decreasing trend. The total number of patients who underwent at least a coronary angiogram was 158 (46%) out of 341, with an increasing trend by 2011. A similar increasing trend was noted for percutaneous transluminal coronary angioplasty, accounting for 54 (15.8%) out of 341 patients. Coronary artery bypass surgery was performed for 10 patients (2.9%), with no significant change in the trend of this treatment modality. Only one patient received thrombolytic therapy out of 341. There was a 10% mortality rate for coronary artery bypass surgery, percutaneous transluminal coronary angioplasty had a

Table 2. Baseline Clinical Characteristics Compared Between Pregnant Patients With and Without MI

Clinical characteristics	Pregnancy with MI, n=341		Pregnancy with no MI, n=5 266 039		*P* value	Standardized mean difference
Risk factors	**No.**	**%**	**No.**	**%**		
Hypertension without complications	45	13.2	34 854	0.7	<0.00001	18.88104
Hypertension with complication	12	3.5	2654	0.1	<0.00001	60.55164
Pregnancy-related hypertension	87	25.5	352 248	6.7	<0.00001	3.015104
Diabetes	23	6.7	56 909	1.1	<0.00001	5.292841
High cholesterol	38	11.1	5879	0.1	<0.00001	80.53492
Chronic kidney disease	8	2.3	2161	0.0	<0.00001	51.26836
Cardiac and circulatory congenital anomalies	12	3.5	4421	0.1	<0.00001	38.94477
Anemia	105	30.8	364 384	6.9	<0.00001	3.70527
Cancer	6	1.8	12025	0.2	0.0002	6.708521
Heart valve disease	0	0.0	0	0.0	1.0000	NA
Myocarditis	36	10.6	2949	0.1	<0.00001	111.3827
HIV	0	0.0	793	0.0	1.0000	–1.00018
SLE	5	1.5	6873	0.1	<0.00001	10.20779
Coronary atherosclerosis	97	28.4	836	0.0	<0.00001	173.0226
Alcohol abuse	3	0.9	4387	0.1	0.0031	9.535028
Chest pain	3	0.9	5685	0.1	0.0063	7.1422
Stroke/TIA	10	2.9	1361	0.0	<0.00001	84.23669
PAD	1	0.3	327	0.0	0.0210	43.23864
Family history of ischemic heart disease	12	3.5	2995	0.1	<0.00001	54.91405
Smoking	19	5.6	33 471	0.6	<0.00001	7.798743
Cocaine use	5	1.5	808	0.2	0.0002	8.630442
Amphetamine use	3	0.9	2570	0.3	0.007	16.86255
Outcomes of PAMI						
Maternal mortality	24	7	679	0.00015	<0.0001	129.7879
Fetal mortality	12	3.5	429	0.00008	<0.00001	123.3172
STEMI	147	43	NA	NA	NA	
Cardiogenic shock	18	5.3	114	0.0000009	0.00001	131.1477
Cardiac arrest	38	11.1	557	0.000012	0.000001	138.7115

MI indicates myocardial infarction; NA, not applicable; PAD, peripheral artery disease; PAMI, pregnancy-associated myocardial infarction; SLE, systemic lupus erythematosus; STEMI, ST-segment–elevation myocardial infarction; and TIA, transient ischemic attack.

2% mortality rate, and for patients undergoing a diagnostic coronary angiogram there was a 1.5% mortality rate. However, it is not known whether these mortalities are related to the procedure because we included all-cause mortalities. We found that bare-metal stent use was highest in 2003 and decreased over time; on the other hand, drug-eluting stent deployment has significantly increased from 2003 to 2011.

DISCUSSION

The key findings of this study include a possible increase in PAMI incidence over the decade and emergence of Takotsubo syndrome, coronary spasm, and spontaneous coronary artery dissection (SCAD) as mechanisms and delineation of risk factors for PAMI including older age, Black race, hypertension, diabetes, anemia, lower socioeconomic status, smoking, and use of amphetamines and cocaine.

PAMI Incidence

The overall incidence of 6.5 per 100 000 pregnancies is consistent with other reports. However, examination of the data raised a concern for increasing incidence, especially after 2009, though the trend was nonsignificant, most likely because of the small numbers. It would be important to examine the incidence when data become available for subsequent years.

Insights Into PAMI Risk Factors

Age, hypertension, and diabetes are known risk factors for PAMI. Smilowitz et al showed an increase in PAMI with age using a large national data sample.[4,6,22] It could

Table 3. Logistic Regression Analysis of Significant Risk Factors for Pregnancy-Associated Myocardial Infarction

Effect	Odds ratio estimates			
	Point estimate	95% Wald confidence limits		*P* value
Age, y				
≤20 (referent)	1			
21–30	4.605	1.437	14.761	0.0400
31–35	10.841	3.379	34.778	0.0029
36–40	16.160	5.007	52.160	<0.0001
>40	15.041	4.320	52.371	0.0006
Median household income per zip code				
Lowest income quartile (referent)	1			
Second quartile	0.851	0.585	1.238	0.4254
Third quartile	0.582	0.380	0.889	0.0558
Highest income quartile	0.706	0.475	1.051	0.5320
Hypertension without complications	2.529	1.442	4.436	0.0012
Hypertension with complications	3.933	1.608	9.615	0.0027
Pregnancy-related hypertension	1.644	1.116	2.421	0.0119
High cholesterol	7.298	4.061	13.118	<0.0001
Cardiac and circulatory congenital anomalies	15.296	6.196	37.760	<0.0001
Anemia	3.608	2.583	5.039	<0.0001
SLE	2.990	0.948	9.429	0.0616
Stroke/TIA	9.745	3.504	27.105	<0.0001
Family history of ischemic heart disease	4.434	1.417	13.878	0.0105
Smoking	3.043	1.304	7.101	0.0101
Cocaine use	4.004	1.261	12.710	0.0186
Amphetamine use	6.104	1.271	29.323	0.0239

SLE indicates systemic lupus erythematosus; and TIA, transient ischemic attack.

be explained by the fact that incidence of acute myocardial infarction itself increases with advanced age, resulting in a 15-fold increase in PAMI among women aged >35 years. In addition, physiologic changes during the pregnancy that significantly affect the cardiovascular system include an increase in workload on the heart and blood vessels, which may not be as well tolerated with advanced age, leading to increased risk of PAMI.[15,23] High incidence of PAMI in Black patients is attributable to high prevalence of cardiovascular risk factors at a younger age, which include preeclampsia, hypertension, diabetes, and physical inactivity.[7,24,25] Being in the lower-income quartile was a risk factor for PAMI. These patients have been shown to have a high likelihood of cardiovascular risk factors, poorer pregnancy outcomes, poor access to health care, and the lowest medication compliance rates.[26–28] Potential targets for intervention among groups at highest risk can include smoking cessation; programs for recreational drug avoidance, weight management, treatment of hypertension and diabetes; and programs to improve healthcare access and compliance.

Mechanisms of PAMI

The mechanisms of PAMI seem to be multifactorial. Pregnancy is associated with higher heart rate, blood volume, and cardiac output.[12] Pregnancy is also a hypercoagulable state, and progesterone has a loosening effect on collagen including vascular media. These mechanisms may potentially explain SCAD in susceptible patients.[29,30] We noted an increased trend of SCAD in our population. Tweet et al, in their registry data, have shown that patients with SCAD during pregnancy had a subsequent SCAD event later on in life, emphasizing the structural weakness in the vessels.[31,32] Women in the childbearing age group are considered to have a lower risk of cardiovascular diseases in nonpregnant states. This leads to missed diagnosis, undertreatment, and patients who are less likely to receive intensive management for their disease, more so during the pregnancy.[33,34] Takotsubo cardiomyopathy, presenting as PAMI in almost 20% of our patients in 2011, was nonexistent as a mechanism until 2008. Takotsubo cardiomyopathy usually presents in postmenopausal women associated with sympathetic surge. This could be one of the reasons for the higher incidence in postpartum patients with recent surgical stress, which is reflected in a study by Minatoguchi et al.[35] In addition, an increase in incidence of Takotsubo cardiomyopathy during pregnancy could be related to an overall increase in recognition and improved understanding of the disease processes.[36,37] Similarly, increased use of drug-eluting stents could likely be related to better outcomes as compared with bare-metal stents among the nonpregnant population.[38,39] They also found that most of the cases occurred during administration of catecholamine/vasoconstrictive substances during cesarean section delivery. Unfortunately, we do not have medication administration data available for our analysis. The other reasons for this finding may include the overall increased diagnosis of Takotsubo cardiomyopathy in the United States and increasing maternal age. Minhas et al, in their retrospective analysis, showed a 19-times increase in Takotsubo cardiomyopathy diagnosis between 2006 and 2012 in the United States.[37] Coronary vasospasm was found to be a cause of PAMI in ≈5% of our population. Possible explanations are enhanced vascular reactivity to neurotransmitters such as catecholamine, norepinephrine, and angiotensin II, and endothelial dysfunction can

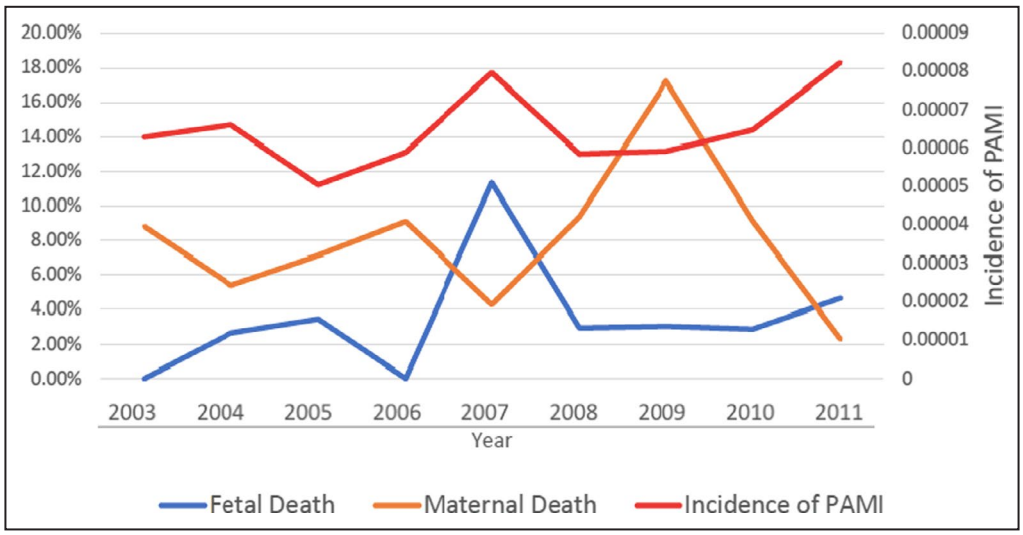

Figure 1. Incidence of pregnancy-associated myocardial infarction (PAMI), fetal mortality, and maternal mortality over time.
P values: fetal mortality=0.4339, maternal mortality=0.6588, incidence of PAMI=0.4710.

lead to vasoconstriction.[40,41] Some of the medications used during pregnancy, such as ergot derivatives, can cause vasospasm as well.[42] Prior studies have shown similar trends of coronary artery dissection and vasospasm.[4,15] We have a similar incidence of 43% ST-segment–elevation myocardial infarction in our patient population as compared with the most recent retrospective study from the national database.

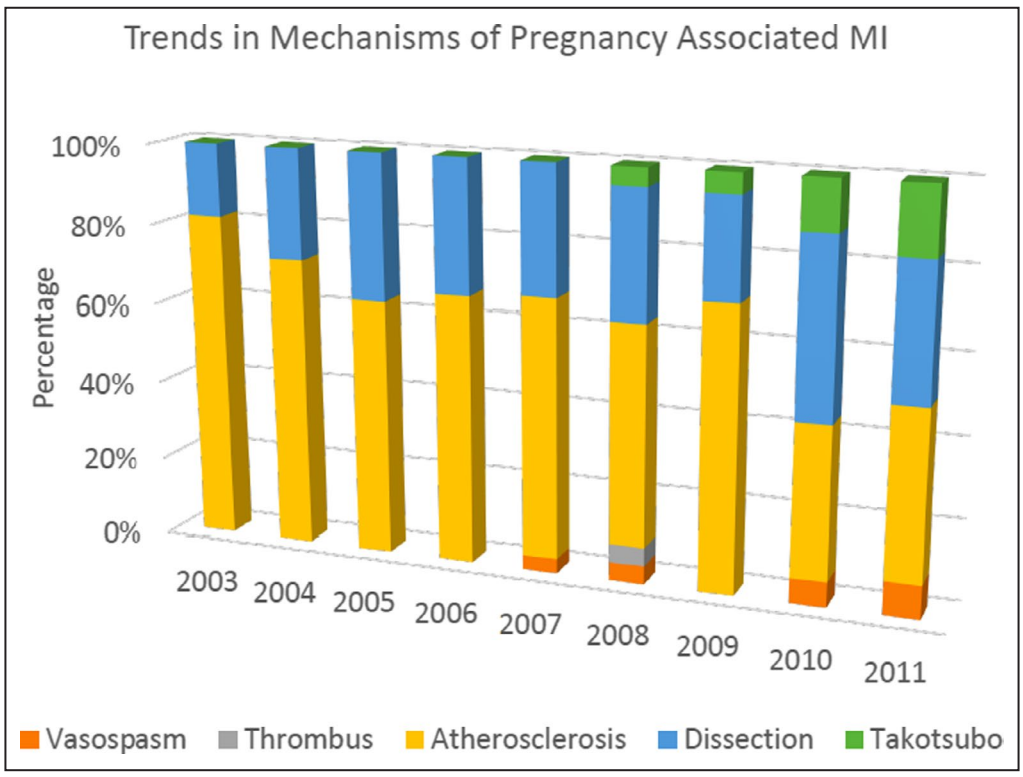

Figure 2. Trends associated with mechanisms of pregnancy-associated myocardial infarction (MI) from 2003 to 2011.
P values: vasospasm=0.7276, thrombus=0.2903, Takotsubo=0.0541, atherosclerosis=0.2584; dissection=0.7277.

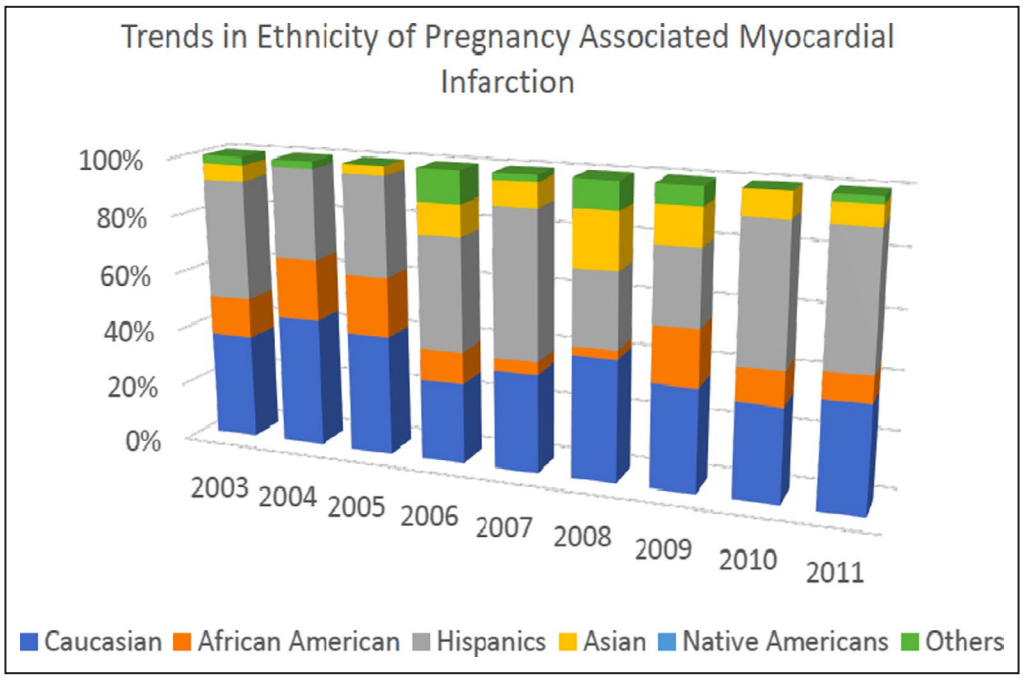

Figure 3. Race and ethnicity variation in the incidence of pregnancy-associated myocardial infarction from 2003 to 2011 in the State of California.
P values: White=0.9084; Black=1607; Hispanic=0.2413, Asian=0.3902, Others=0.1921.

PAMI Management Trends

We found an increasing trend for patients undergoing diagnostic angiography and coronary intervention in the past decade, consistent with a recent study by Smilowitz et al.[4] Roth et al showed an increasing trend toward coronary intervention and reduced mortality in patients with PAMI, further emphasizing the importance of this approach in selected patients.[6] In our analysis, we found ≈50% or more patients were treated conservatively without a diagnostic angiogram, a significantly high proportion when compared with nonpregnant patients with acute myocardial infarction. A possible explanation could be a lack of specific guidelines, increased risk of complications, and radiation risk to the mother and the fetus. We identified increasing trends of more patients receiving drug-eluting stents (>50%) than bare-metal stents, which is still lower than the general population with acute myocardial infarction. It could be caused by the potential

Table 4. Logistic Regression Analysis of Significant Risk Factors for Maternal and Fetal Mortality

Effect	Point estimate	95% Wald confidence limits		*P* value
Odds ratio estimates for maternal mortality				
Median household income per zip code				
Lowest income quartile (referent)	1			
Second quartile	0.322	0.090	1.159	0.4199
Third and fourth quartile	0.028	0.002	0.347	0.0168
Stroke/TIA	9.030	1.014	80.410	0.0486
Cocaine use	14.998	1.499	150.074	0.0212
Odds ratio estimates for fetal mortality				
Chronic kidney disease	12.330	1.682	90.357	0.0134
Anemia	8.251	1.413	48.173	0.0191
Smoking	11.790	0.942	147.519	0.0556
Takotsubo	18.815	1.340	264.136	0.0295

TIA indicates transient ischemic attack.

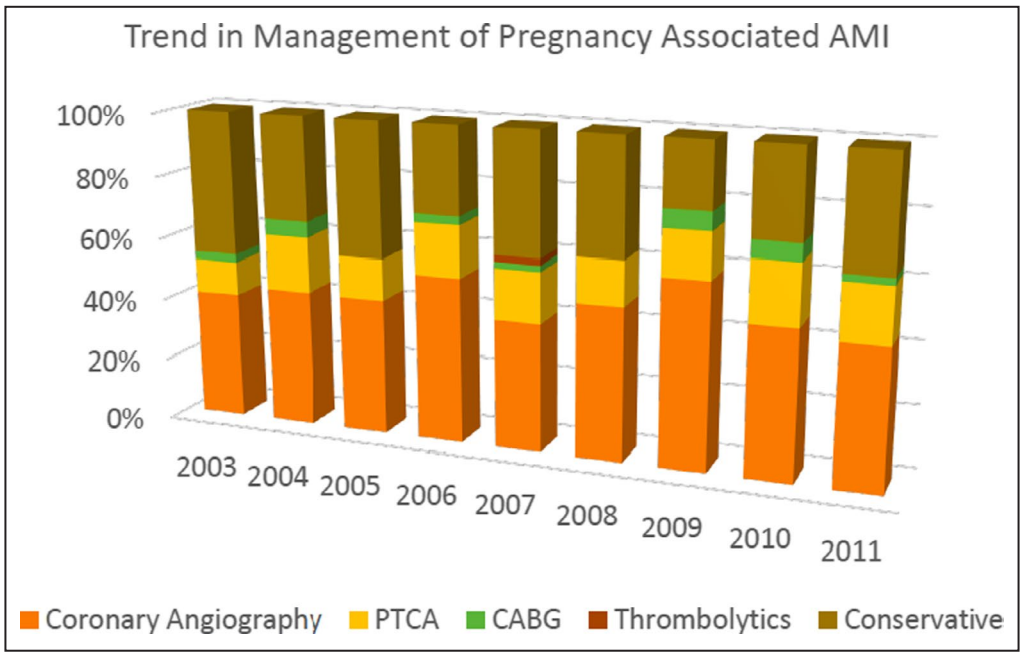

Figure 4. Comparison of treatment modalities for patients with pregnancy-associated acute myocardial infarction (AMI) from 2003 to 2011.
CABG indicates coronary artery bypass graft; and PTCA, percutaneous transluminal coronary angioplasty.

increase in peripartum bleeding and lack of safety data for Plavix and newer antiplatelet agents to use in this population.

Study Limitations

Some of the limitations of our study include lack of details of obstetric history, medication information, and precise gestational age of the patient. The severity of comorbidities and risk factors for cardiovascular diseases are not available, which could be useful to further risk stratify the patients. In addition, detailed information on coronary angiography is not available, which can provide more precise information on the number of vessels involved, type of lesion, location of the disease, and its severity. Almost 50% of the patients did not undergo any diagnostic procedure to identify whether they had SCAD, Takotsubo syndrome, or atherosclerotic coronary artery disease. Also, this is a database used for administrative purposes, and coding is manually entered. Codes may have changed over the study period, which has the potential for coding-related error. Over the 9-year period of this study, there have been significant changes in the diagnosis of myocardial infarction, its management, and increased awareness of PAMI. We had data sets only until 2011 at the time of the initial analysis, though more recent data sets are now available. Lastly, this study includes populations from the State of California only up to 2011, which differs from other states in many respects, and the findings could not be generalizable to other cohorts.

CONCLUSIONS

There has been a trend toward increasing PAMI incidence in the State of California over the past decade, with a higher incidence among the Black population and lower socioeconomic groups. There are several lifestyle-related and nontraditional risk factors for PAMI, which could possibly contribute to the development of prevention strategies for this catastrophic entity. Potential targets for intervention include smoking cessation, programs for recreational drug avoidance, weight management, treatment of hypertension and diabetes, and programs to improve healthcare access and compliance. Coronary vasospasm, SCAD, and Takotsubo syndrome have emerged as new mechanisms for PAMI. These findings warrant further investigation.

ARTICLE INFORMATION

Received May 21, 2021; accepted August 25, 2021.

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Acknowledgments

The abstract of this article was selected for Young Investigator Award finalist at the American College of Cardiology 2019 Annual Meeting.

Sources of Funding

None.

Disclosures

Dr Bairey-Merz reports personal fees from iRhythm and personal fees from Med Intelligence during the conduct of the study and personal fees from Bayer Advisory Board outside the submitted work. Dr Bairey Merz serves on the Board of Directors for iRhythm and receives fees paid through Cedars Sinai Medical Center from Abbott Diagnostics and Sanofi. Dr Elkayam reports support from Astra Zeneca, Zoll, and Merck outside the submitted work. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the article. The remaining authors have no disclosures to report.

Supplementary Material

Table S1

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SUPPLEMENTAL MATERIAL

Table S1. Inclusion Criteria for pregnant patient based on Clinical Classification Software (CCS).

CCS Code	CCS Diagnosis Categories
177	Spontaneous abortion
178	Induced abortion
179	Post abortion complications
180	Ectopic pregnancy
181	Other complications of pregnancy
182	Hemorrhage during pregnancy; abruptio placenta; placenta previa
183	Hypertension complicating pregnancy; childbirth and the puerperium
184	Early or threatened labor
185	Prolonged pregnancy
186	Diabetes or abnormal glucose tolerance complicating pregnancy; childbirth; or the puerperium
187	Malposition; malpresentation
188	Fetopelvic disproportion; obstruction
189	Previous C-section
190	Fetal distress and abnormal forces of labor
191	Polyhydramnios and other problems of amniotic cavity
192	Umbilical cord complication
193	OB-related trauma to perineum and vulva
194	Forceps delivery
195	Other complications of birth; puerperium affecting management of mother
196	Other pregnancy and delivery including normal