MAYO CLINIC

ORIGINAL ARTICLE

Acute Myocardial Infarction During Pregnancy and the Puerperium in the United States

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Abstract

Objective: To analyze trends in the incidence, in-hospital management, and outcomes of acute myocardial infarction (AMI) complicating pregnancy and the puerperium in the United States.

Patients and Methods: Women 18 years or older hospitalized during pregnancy and the puerperium were identified from the National Inpatient Sample database from January 1, 2002, to December 31, 2014. *International Classification of Diseases, Ninth Revision* diagnosis and procedure codes were used to identify AMI during pregnancy-related admissions.

Results: Overall, 55,402,290 pregnancy-related hospitalizations were identified. A total of 4471 cases of AMI (8.1 [95% CI, 7.5-8.6] cases per 100,000 hospitalizations) occurred, with 922 AMI cases (20.6%) identified in the antepartum period, 1061 (23.7%) during labor and delivery, and 2390 (53.5%) in the postpartum period. ST-segment elevation myocardial infarction occurred in 1895 cases (42.4%), and non-ST-segment elevation myocardial infarction occurred in 2576 cases (57.6%). Among patients with pregnancy-related AMI, 2373 (53.1%) underwent invasive management and 1120 (25.1%) underwent coronary revascularization. In-hospital mortality was significantly higher in patients with AMI than in those without AMI during pregnancy (adjusted odds ratio, 39.9; 95% CI, 23.3-68.4; $P<.001$). The rate of AMI during pregnancy and the puerperium increased over time (adjusted odds ratio, 1.25 [for 2014 vs 2002]; 95% CI, 1.02-1.52).

Conclusion: In patients hospitalized during pregnancy and the puerperium, AMI occurred in 1 of every 12,400 hospitalizations and rates of AMI increased over time. Maternal mortality rates were high. Additional research on the prevention and optimal management of AMI during pregnancy is necessary.

 ■ Mayo Clin Proc. 2018;■■(■):1-11

Acute myocardial infarction (AMI) during pregnancy is an uncommon but potentially devastating complication of the gravid state. Acute myocardial infarction occurs during pregnancy with an incidence of approximately 3 to 10 cases per 100,000 deliveries[1-4] and is associated with 5% to 7% maternal case-fatality rate with grave risks to the developing fetus.[2,3] Hormonal and hemodynamic changes in the cardiovascular system and the hypercoagulable state of pregnancy in part account for the increased risk of AMI during pregnancy, which occurs with a frequency approximately 3- to 4-fold higher than that for nonpregnant women of childbearing age.[5] In addition, previous population-based studies reported that maternal age, tobacco use, hypertension, diabetes mellitus, and thrombophilia are independent risk factors associated with AMI during pregnancy.[2,3] Investigation of AMI during pregnancy or the puerperium has been particularly challenging because of low incidence of events and heterogeneous clinical presentations. Consequently, recent epidemiology and data on the contemporary approaches to the management of AMI during pregnancy are limited. We analyzed hospital admissions from a large national database to evaluate trends in the incidence, in-hospital management, and outcomes of AMI complicating pregnancy and the puerperium in the United States.

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PATIENTS AND METHODS

Data were obtained from the Agency for Healthcare Research and Quality's Healthcare Cost

and Utilization Project National Inpatient Sample (NIS) database from January 1, 2002, to December 31, 2014. The NIS is the largest publicly available all-payer database and contains discharge-level administrative data on inpatient diagnoses and procedures from a 20% stratified sample of US hospitals until 2012 and a 20% stratified sample of discharges from all US hospitals thereafter. Sampling weights were applied to discharge records to generate national estimates for the United States.[6]

Women 18 years or older who were hospitalized during pregnancy and the puerperium were identified using *International Classification of Diseases, Ninth Revision* (*ICD-9*) diagnosis and procedure codes for labor and delivery as well as *ICD-9* diagnosis codes for antepartum and postpartum conditions. The *ICD-9* codes used to identify pregnancy-related admissions are detailed in Supplemental Table 1 (available online at http://www.mayoclinicproceedings.org). Acute myocardial infarction was identified using *ICD-9* diagnosis codes for non—ST-segment elevation myocardial infarction (NSTEMI) (410.71) and ST-segment elevation myocardial infarction (STEMI) (410.01-410.61, 410.81, and 410.91) in any position. In patients with AMI, coronary artery dissection was identified using the *ICD-9* diagnosis code 414.12 and stress (takotsubo) cardiomyopathy was identified using the *ICD-9* diagnosis code 429.83.

In-Hospital Management and Outcomes

Invasive management of AMI was identified using *ICD-9* and Clinical Classifications Software procedure codes for invasive coronary angiography, percutaneous coronary intervention (PCI), or coronary artery bypass grafting (CABG) during inpatient hospitalization. In patients who underwent PCI, procedure codes for bare-metal stent (*ICD-9* procedure code 36.06) and drug-eluting stent (*ICD-9* procedure code 36.07) placement were identified. The procedure code for intravascular ultrasound use was also identified (*ICD-9* procedure code 00.24). Patients who did not have these invasive procedures coded were considered to have been managed conservatively. The primary outcome was in-hospital all-cause mortality.

Statistical Methodology

Categorical variables were reported as count (percentage) and compared using Rao Scott chi-square tests. Continuous variables were reported as mean ± SE. Comparisons were made using the SAS Software (SAS Institute, Inc.) PROC SURVEYREG procedure for continuous variables and the PROC SURVEYFREQ procedure for categorical variables to incorporate the complex survey design. Testing of trends over time was conducted using the Cochran-Armitage test. Multivariable logistic regression models including patient demographic characteristics, cardiovascular risk factors, and comorbidities as covariates were used to estimate the adjusted odds of AMI. Models included age, race/ethnicity, obesity, obstructive sleep apnea, tobacco use, alcohol abuse, drug abuse, hypertension, dyslipidemia, diabetes mellitus, previous coronary revascularization (with either PCI or CABG), known heart failure, history of atrial fibrillation, rheumatoid arthritis, systemic lupus erythematosus, anemia, and the diagnosis of a malignant neoplasm as covariates for adjustment. Multivariable logistic regression models used to estimate the adjusted odds of invasive management in patients with myocardial infarction also included the diagnosis of STEMI, cardiogenic shock, and hospital characteristics as covariates. Sampling weights were applied to determine national incidence estimates in all analyses according to Healthcare Cost and Utilization Project guidelines guidance.[6] Statistical analyses were performed using SAS version 9.4 (SAS Institute, Inc.). Two-sided *P* values less than .05 were considered to be statistically significant. The NIS is a publicly available, de-identified data set, and the study was exempt from review by the institutional review board.

Patient Involvement

Patients were not involved in developing the research question, study outcome measures, study design, or conduct of the study. No patients provided input into the data analysis or interpretation of the results. There are no plans to disseminate the results of the research to study participants. No patients served as authors or contributors to this work.

RESULTS

Overall, 55,402,290 hospitalizations during pregnancy and the puerperium were identified among women 18 years or older in the United States (an average of 4,261,715 hospitalizations

TABLE 1. Baseline Characteristics of Patients With and Without AMI Complicating Pregnancy and the Puerperium[a,b]

Variable	All hospitalizations during pregnancy and in the puerperium (N=55,402,290)	AMI (n=4471)	No AMI (n=55,397,819)	*P* value
Age (y)	28.00±0.07	33.11±0.20	28.00±0.07	<.001
Race/ethnicity				<.001
Non-Hispanic white	23,588,621 (42.6)	1703 (38.1)	23,586,918 (42.6)	
Non-Hispanic black	6,435,508 (11.6)	992 (22.2)	6,434,516 (11.6)	
Hispanic	10,269,415 (18.5)	564 (12.6)	10,268,851 (18.5)	
Others	4,798,295 (8.7)	364 (8.1)	4,797,931 (8.7)	
Unknown	10,310,450 (18.6)	849 (19)	10,309,602 (18.6)	
Obesity	1,724,958 (3.1)	421 (9.4)	1,724,537 (3.1)	<.001
Obstructive sleep apnea	37,243 (0.1)	62 (1.4)	37,181 (0.1)	<.001
Tobacco use	1,451,408 (2.6)	631 (14.1)	1,450,777 (2.6)	<.001
Alcohol abuse	90,067 (0.2)	53 (1.2)	90,014 (0.2)	<.001
Drug abuse	879,139 (1.6)	314 (7.1)	878,825 (1.6)	<.001
Hypertension	4,626,294 (8.4)	1458 (32.6)	4,624,836 (8.3)	<.001
Gestational hypertension	2,119,699 (3.8)	397 (8.9)	2,119,302 (3.8)	<.001
Preeclampsia/eclampsia	2,261,361 (4.1)	475 (10.6)	2,260,886 (4.1)	<.001
Dyslipidemia	60,420 (0.1)	559 (12.5)	59,861 (0.1)	<.001
Diabetes mellitus	751,824 (1.4)	479 (10.7)	751,345 (1.4)	<.001
Gestational diabetes mellitus	676,874 (1.2)	268 (6.0)	676,606 (1.2)	<0.001
Chronic kidney disease[c]	23,105 (0.1)	69 (2.8)	23,036 (0.1)	<.001
Coronary artery disease	16279 (0.03)	1474 (33)	14805 (0.03)	<.001
Previous coronary revascularization	3723 (0.007)	85 (1.9)	3638 (0.007)	<.001
Percutaneous coronary intervention	2569 (0.005)	68 (1.5)	2501 (0.005)	<.001
Coronary artery bypass grafting	1236 (0.002)	22 (0.5)	1214 (0.002)	<.001
History of TIA/stroke[c]	17793 (0.1)	24 (1)	17,769 (0.1)	<.001
Known heart failure	60,714 (0.1)	853 (19.2)	59,861 (0.1)	<.001
History of atrial fibrillation	16,960 (0.03)	105 (2.3)	16,855 (0.03)	<.001
Anemia	5,364,769 (9.7)	1186 (26.5)	5,363,583 (9.7)	<.001
Rheumatoid arthritis	47,437 (0.1)	15 (0.3)	47,422 (0.1)	<.001
Systemic lupus erythematosus	71,523 (0.1)	25 (0.6)	71,499 (0.1)	<.001
Malignancy	31,155 (0.1)	25 (0.6)	31,130 (0.1)	<.001

[a]AMI = acute myocardial infarction; TIA = transient ischemic attack.
[b]Data are presented as mean ± SE or as No. (percentage).
[c]Comorbidity data available from 2008 to 2014.

per year) from 2002 to 2014. A total of 4,164,077 hospitalizations (7.5%) occurred in the antepartum period, 49,829,753 hospitalizations (89.9%) for labor and delivery, and 1,238,900 hospitalizations (2.2%) in the postpartum period. The timing of the hospitalization with respect to the pregnancy was either unspecified or could not be determined in the remaining 169,560 cases (0.3%).

A total of 4471 cases of AMI (8.1 [95% CI, 7.5-8.6] cases per 100,000 hospitalizations during pregnancy) occurred during the study period. Of these, 922 AMI cases (20.6%; 22.1 cases per 100,000 hospitalizations; 95% CI, 19.0-25.3 cases per 100,000 hospitalizations) were identified in the antepartum period, 1061 AMI cases (23.7%; 2.1 [95% CI, 1.8-2.4] cases per 100,000 hospitalizations) occurred during a hospitalization for labor and delivery, and 2390 AMI cases (53.5%; 192.9 [95% CI, 173.8-212.0] cases per 100,000 hospitalizations) occurred in the postpartum period. The timing of AMI with respect to the pregnancy could not be determined in the remaining 98 AMI cases (2.2%). After multivariable adjustment for demographic characteristics and clinical covariates, the odds of AMI were significantly higher in patients hospitalized during the antepartum (adjusted odds ratio [aOR], 9.25; 95% CI, 7.52-11.38) and postpartum (aOR, 44.40; 95% CI, 36.49-54.03) periods than in

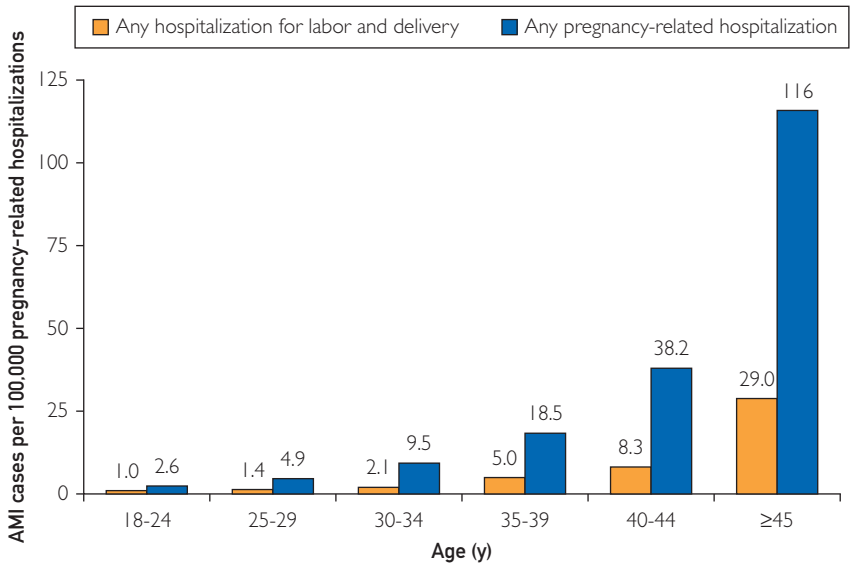

FIGURE 1. Frequency of AMI per 100,000 hospitalizations during pregnancy and for labor and delivery stratified by age group. AMI = acute myocardial infarction.

those hospitalized for labor and delivery. In patients hospitalized for labor and delivery, cesarean sections were associated with a higher frequency of AMI than were vaginal deliveries (4.8 [95% CI, 4.1-5.6] AMI cases per 100,000 hospitalizations for labor and delivery vs 0.86 [95% CI, 0.70-1.0] AMI cases per 100,000 hospitalizations for labor and delivery).

In patients with AMI, STEMI occurred in 1895 cases (42.4%) and NSTEMI occurred in 2576 cases (57.6%). Cardiogenic shock occurred in 290 cases of AMI (6.5%). Coronary dissection was identified in 647 cases of AMI overall (14.5%), occurring in 437 (23.1%) of STEMI cases and 210 (8.2%) NSTEMI cases, as well as in 24.6% of all patients undergoing invasive management. Coronary dissection was diagnosed in 552 (23.1%) AMI cases in the postpartum period, in 29 (2.7%) AMI cases associated with labor and delivery, and in 66 (7.2%) AMI cases in the antepartum period. Takotsubo syndrome was identified in 83 cases of AMI (2.9%) from 2007 to 2014, the years for which the *ICD-9* diagnosis code was available.

The baseline characteristics of patients with and without AMI complicating pregnancy and the puerperium are summarized in Table 1. Women with pregnancy-related AMI were older than those without AMI (mean age, 33.1 years vs 28.0 years; $P<.001$) and were more likely to have cardiovascular comorbidities (Table 1). The incidence of AMI per 100,000 hospitalizations during pregnancy and the puerperium increased significantly with maternal age (Figure 1 and Table 2). In patients with advanced maternal age, defined as age 35 years or more, 23.3 (95% CI, 21.1-25.6) AMI cases occurred per 100,000 hospitalizations during pregnancy. In multivariable analysis, advanced maternal age, black race, tobacco, drug use, hypertension, dyslipidemia, diabetes mellitus, previous coronary revascularization, known heart failure, history of atrial fibrillation, anemia, and a diagnosis of a malignant neoplasm were independently associated with AMI during pregnancy and the puerperium (Table 2).

The proportion of patients with AMI was highest among patients with any preexisting coronary artery disease (CAD) risk factors (tobacco use, hypertension, dyslipidemia, diabetes, or renal disease) in comparison to patients without risk factors (66.1 [95% CI, 59.4-72.7] AMI cases per 100,000 hospitalizations during pregnancy vs 5.2 [95% CI, 4.7-5.7] AMI cases per 100,000 hospitalizations during pregnancy), although 61% of AMI cases were found among patients without established CAD risk factors.

Pregnancy-associated medical comorbidities were also associated with an increased

TABLE 2. Associations Between Clinical Covariates and AMI During Pregnancy and the Puerperium in Multivariable Analyses

Variable	aOR (95% CI) for AMI
Age (y)	
18-24	Reference
25-29	1.96 (1.51-2.54)
30-34	3.66 (2.87-4.67)
35-39	5.81 (4.58-7.37)
40-44	10.30 (7.42-14.29)
≥45	11.49 (6.30-20.95)
Race/ethnicity	
Non-Hispanic white	Reference
Non-Hispanic black	1.46 (1.15-1.85)
Hispanic	0.95 (0.76-1.19)
Others	1.06 (0.783-1.43)
Unknown	1.23 (1.028-1.47)
Obesity	0.96 (0.761-1.20)
Obstructive sleep apnea	0.96 (0.461-2.00)
Tobacco use	3.41 (2.74-4.25)
Alcohol abuse	1.26 (0.59-2.68)
Drug abuse	2.73 (1.99-3.74)
Hypertension	2.46 (2.04-2.97)
Dyslipidemia	13.11 (8.78-19.59)
Diabetes mellitus	1.89 (1.38-2.60)
Previous coronary revascularization	6.38 (2.56-15.90)
Known heart failure	33.65 (24.67-45.90)
History of atrial fibrillation	5.67 (2.75-11.70)
Anemia	2.32 (1.96-2.74)
Rheumatoid arthritis	0.90 (0.17-4.74)
Systemic lupus Erythematosus	1.63 (0.65-4.13)
Malignant neoplasm	4.40 (1.45-13.34)

AMI = acute myocardial infarction; aOR = adjusted odds ratio.

frequency of AMI. Women with gestational diabetes mellitus were more likely to have AMI than women without a diagnosis of gestational diabetes (39.6 [95% CI, 28.4-50.9] AMI cases per 100,000 hospitalizations during pregnancy vs 7.7 [95% CI, 7.1-8.2] AMI cases per 100,000 hospitalizations during pregnancy; $P<.001$). Similarly, AMI was more likely to occur in women with preeclampsia than in those without a diagnosis of preeclampsia (21.0 [95% CI, 16.9-25.2] AMI cases per 100,000 hospitalizations during pregnancy vs 7.5 [95% CI, 7.0-8.1] AMI cases per 100,000 hospitalizations during pregnancy; $P<.001$).

Management of AMI During Pregnancy

Among patients with AMI during a pregnancy-related hospitalization, 2373 (53.1%) underwent invasive management. Patients who underwent invasive management were slightly older, more likely to use tobacco and have dyslipidemia and CAD, and less likely to have kidney disease or anemia (Table 3). Predictors of an invasive approach to AMI during pregnancy after multivariable adjustment are listed in Table 4. Patients were more likely to undergo invasive management of AMI in the postpartum period (69.8%; n=1669) than in the antepartum period (vs 42.7%; n=394; $P<.001$) or during hospitalizations for labor and delivery (vs 24.2%; n=257; $P<.001$). Patients with STEMI were more likely to undergo invasive management than those with NSTEMI (64.6% [1224] vs 44.6% [1149]; $P<.001$). Thrombolysis was performed in 0.8% of cases.

Among patients who underwent invasive management, intravascular ultrasound was performed in 129 cases overall (2.9%), in 4.1% of STEMI cases (n=76) and 2.1% of NSTEMI (n=53) cases, as well as in 9.6% (n=62) of patients with a discharge diagnosis of coronary dissection. Coronary revascularization was performed in 1120 cases of AMI (25.1%) during pregnancy and the puerperium. Percutaneous coronary intervention was performed in 881 cases (78.7%), with stent placement in 753 of these cases (85.5%). Coronary artery bypass grafting was performed in 239 cases (21.3%), and 65 of these patients (27.2%) underwent revascularization with both PCI and CABG. After US Food and Drug Administration (FDA) approval of second-generation drug-eluting stents (2009-2014), drug-eluting stents and bare-metal stents were placed in 53.5% (n=216) and 46.5% (n=188) of patients undergoing PCI with stent placement, respectively. Among patients with coronary artery dissection, coronary revascularization was performed in 443 (68.5%), of whom 42.0% (n=272) underwent PCI, 21.3% (n=138) underwent CABG, and 5.1% (n=33) underwent revascularization with both PCI and CABG.

Outcomes

A total of 203 women (4.5%) died in the hospital after AMI that occurred during pregnancy and the puerperium. In-hospital mortality was significantly higher in patients with AMI than in those without AMI during pregnancy (aOR, 39.9; 95% CI, 23.3-68.4) (Supplemental Table 2, available

TABLE 3. Characteristics of Patients Undergoing Invasive vs Conservative Management of AMI Complicating Pregnancy and the Puerperium[a,b]

Variable	All AMI (n=4471)	Invasive (n=2373)	Conservative (n=2098)	*P* value
Age (y)	33.11±0.20	33.98±0.26	32.13±0.29	<.001
Race/ethnicity				.03
Non-Hispanic white	1703 (38.1)	937 (39.5)	766 (36.5)	
Non-Hispanic black	992 (22.2)	533 (22.5)	459 (21.9)	
Hispanic	564 (12.6)	229 (9.6)	335 (16)	
Others	364 (8.1)	207 (8.7)	157 (7.5)	
Unknown	849 (19)	468 (19.7)	381 (18.2)	
Comorbidities				
Obesity	421 (9.4)	186 (7.8)	236 (11.2)	.07
Obstructive sleep apnea	62 (1.4)	18 (0.8)	44 (2.1)	.08
Tobacco use	631 (14.1)	430 (18.1)	200 (9.5)	<.001
Alcohol abuse	53 (1.2)	29 (1.2)	24 (1.2)	.90
Drug abuse	314 (7.1)	95 (4)	220 (10.6)	<.001
Hypertension	1458 (32.6)	753 (31.7)	705 (33.6)	.50
Gestational hypertension	397 (8.9)	245 (10.3)	152 (7.2)	<.001
Preeclampsia/eclampsia	475 (10.6)	133 (5.6)	342 (16.3)	<.001
Dyslipidemia	559 (12.5)	472 (19.9)	88 (4.2)	<.001
Diabetes mellitus	479 (10.7)	221 (9.3)	258 (12.3)	.14
Gestational diabetes mellitus	268 (6.0)	99 (4.2)	169 (8.1)	<.001
Chronic kidney disease[c]	69 (2.8)	15 (1.1)	54 (5)	.002
Previous coronary revascularization	85 (1.9)	32 (1.3)	53 (2.5)	.16
Percutaneous coronary intervention	68 (1.5)	20 (0.8)	48 (2.3)	.04
Coronary artery bypass grafting	22 (0.5)	12 (0.5)	10 (0.5)	.95
History of TIA/stroke[c]	24 (1)	14 (1)	10 (0.9)	.66
Known heart failure	853 (19.2)	423 (17.9)	430 (20.7)	.29
History of atrial fibrillation	105 (2.3)	39 (1.6)	66 (3.1)	.15
Anemia	1186 (26.5)	517 (21.8)	669 (31.9)	<.001
Rheumatoid arthritis	15 (0.3)	15 (0.3)	15 (0.6)	<.001
Systemic lupus erythematosus	25 (0.6)	11 (0.5)	14 (0.7)	.68
Malignancy	25 (0.6)	15 (0.6)	9 (0.4)	.57
AMI presentation				<.001
STEMI	1895 (42.4)	1225 (51.6)	671 (32.0)	
NSTEMI	2576 (57.6)	1149 (48.4)	1427 (68.0)	
Cardiogenic shock	290 (6.5)	188 (7.9)	102 (4.9)	.03

[a]AMI = acute myocardial infarction; NSTEMI = non–ST-segment elevation myocardial infarction; STEMI = ST-segment elevation myocardial infarction; TIA = transient ischemic attack.
[b]Data are presented as mean ± SE or as No. (percentage).
[c]Comorbidity data available from 2008 to 2014.

online at http://www.mayoclinicproceedings.org). In-hospital mortality was not different among patients with AMI during hospitalizations for labor and delivery in comparison to those in the antepartum (6.6% vs 3.2%; *P*=.10) or postpartum (6.6% vs 4.0%; *P*=.09) periods. Among women with pregnancy-related AMI, in-hospital mortality in patients with STEMI and NSTEMI was similar (5.0% vs 4.2%; *P*=.58). Invasive management of AMI during pregnancy and the puerperium was associated with lower in-hospital mortality than was conservative management in unadjusted analyses (1.8% vs 7.6%; *P*<.001) and after adjustment for demographic and clinical covariates (aOR, 0.17; 95% CI, 0.07-0.42).

Trends in AMI Incidence and Outcomes

Between 2002 and 2013, the rate of AMI that occurred in hospitalizations during pregnancy and the puerperium increased over time (from 7.1 cases per 100,000 hospitalizations in 2002-2003 to 9.5 cases per 100,000 hospitalizations in 2012-2013; *P*<.001 for trend) with

an increase in the frequency of NSTEMI diagnoses ($P<.001$ for trend) and a decrease in the frequency of STEMI diagnoses ($P=.001$ for trend) over time (Figure 2, A). The mean age at hospitalization for labor and delivery also increased during this time (from 27.9±5.9 years in 2002-2003 to 28.3±5.8 years in 2012-2013; $P<.001$). Trends in cardiovascular risk factors in patients hospitalized for labor and delivery are shown in the Supplemental Figure (available online at http://www.mayoclinicproceedings.org). The odds of AMI over time after multivariable adjustment for age and race/ethnicity (aOR, 1.25 [for 2014 vs 2002]; 95% CI, 1.02-1.52) are shown in Figure 2, B. Mortality rates associated with AMI remained stable ($P=.24$ for trend) during the study period (Figure 3).

TABLE 4. Multivariable Correlates of Invasive Management of AMI Complicating Pregnancy and the Puerperium From 2008 to 2014

Variable	aOR (95% CI) for the invasive management of AMI
Age (y)	
18-24	Reference
25-29	2.73 (1.19-6.22)
30-34	3.40 (1.66-6.96)
35-39	4.25 (2.01-8.99)
40-44	4.87 (2.22-10.67)
≥45	3.31 (1.24-8.87)
Race/ethnicity	
Non-Hispanic white	Reference
Non-Hispanic black	1.32 (0.83-2.12)
Hispanic	0.61 (0.37-1.00)
Others	1.37 (0.81-2.31)
Unknown	0.54 (0.26-1.11)
Obesity	0.49 (0.27-0.89)
Tobacco use	1.63 (0.96-2.77)
Alcohol abuse	3.10 (0.71-13.66)
Drug abuse	0.22 (0.10-0.48)
Dyslipidemia	6.09 (3.38-10.96)
Chronic kidney disease	0.24 (0.08-0.72)
Previous coronary revascularization	0.42 (0.13-1.35)
Anemia	0.75 (0.50-1.10)
ST-segment elevation myocardial infarction	2.90 (1.90-4.43)
Cardiogenic shock	1.46 (0.80-2.68)
Hospital type	
Rural	Reference
Urban nonteaching	1.31 (0.521-3.31)
Urban teaching	2.00 (0.828-4.84)

AMI = acute myocardial infarction; aOR = adjusted odds ratio.

DISCUSSION

In this analysis of a large national administrative database, AMI occurred in 1 of every 12,400 hospitalizations during pregnancy and the puerperium overall and in 1 of every 46,921 hospitalizations for labor or delivery. Acute myocardial infarction during pregnancy was independently associated with advanced maternal age, tobacco use, hypertension, dyslipidemia, diabetes mellitus, known heart failure, anemia, and malignancy. The frequency of AMI diagnoses during pregnancy and the puerperium increased over time because of an increase in NSTEMI diagnoses. Acute myocardial infarction during pregnancy was strongly associated with increased in-hospital mortality in both unadjusted and multivariable-adjusted analyses. Mortality rates in patients with pregnancy-related AMI remained stable over time at 4.5%.

The increasing incidence of AMI complicating pregnancy is remarkable, as it occurred despite advances in reduction of cardiovascular risk over the past decade. There are a number of plausible explanations for these trends. Greater numbers of patients with advanced maternal age may underlie some of the trends in AMI reported in this analysis, as the mean age at hospitalization for labor and delivery increased over time. In the present study and in previous reports, advanced maternal age is strongly associated with AMI during pregnancy, with up to a 30-fold increased odds in women 40 years or older in comparison to pregnant women younger than 20 years.[3,5] Still, in the present analysis, there was a significant increase in rates of AMI over time after adjustment for age and race ($P<.001$). Increases in AMI diagnoses during pregnancy may also be related to changes in the prevalence of cardiovascular risk factors or the frequency of cardiac biomarker screening during hospitalization for pregnancy and the puerperium. Improved diagnosis of NSTEMI with higher-sensitivity cardiac biomarker assays and increasing provider awareness of AMI in women may also be related to the observed findings.

Mechanisms of AMI during pregnancy are uncertain. In many cases, AMI may be due to conventional acute coronary syndromes. Traditional risk factors, including tobacco use, hypertension, and diabetes, are independently associated with the risk of AMI during pregnancy.[2,3,7] As women of childbearing age are generally perceived to be at low

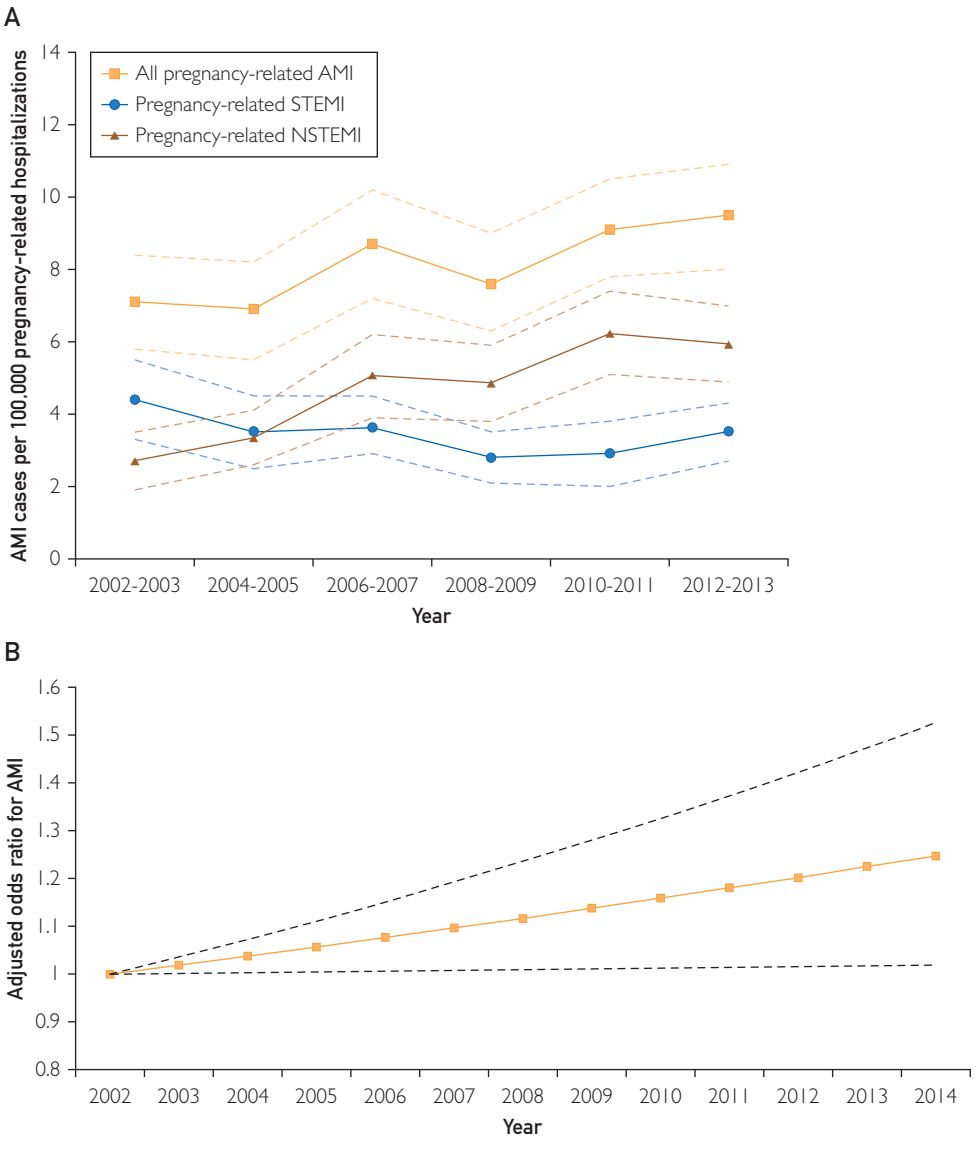

FIGURE 2. A, Trends in the frequency of AMI complicating pregnancy and the puerperium over time. *P*<.001 for trend. B, Odds ratios for AMI associated with pregnancy over time after adjustment for age and race. Adjusted odds ratios are calculated using 2002 as the reference time period. Bars represent 95% CIs. AMI = acute myocardial infarction; NSTEMI = non–ST-segment elevation myocardial infarction; STEMI = ST-segment elevation myocardial infarction.

cardiovascular risk, preexisting ischemic heart disease may be underdiagnosed in this population. Young women with occult CAD may be less likely to receive intensive management of uncontrolled risk factors.[8-11] However, in many cases, AMI may be independent of conventional cardiovascular risk factors. The hypercoagulable state of pregnancy increases the risk of thrombotic coronary syndromes because of increases in fibrinogen and other coagulation factor concentrations coupled with diminished fibrinolysis.[12] Substantial increases in the circulating sex hormones estrogen and progesterone, changes in hemodynamics, hemodilution, and increases in cardiac output during pregnancy can lead to

progressive connective tissue weakening, increased vascular shear stress, and spontaneous coronary artery dissection (SCAD).[13-15] In the present analysis, coronary dissection was documented in 15% of all AMI cases, although previous case series suggest that dissection may occur in up to 40% of AMI cases during pregnancy.[5,7,16] Consequently, SCAD has been frequently cited as a key etiology of AMI during pregnancy and the puerperium.[17] The modest frequency of SCAD in the present analysis may reflect underrecognition or undercoding of this important diagnosis. Therefore, the true incidence and outcomes of SCAD during pregnancy warrant further exploration.

In this cohort, cesarean sections were associated with a higher frequency of AMI than were vaginal deliveries, another important finding that warrants further study. We were not able to assess the potential contributions of hemodilution, anemia, tachycardia, hypertension, surgical stressors, and other mismatches in myocardial oxygen supply and demand during pregnancy in relation to type 2 AMI.[18]

The optimal management of AMI during pregnancy remains uncertain. Based on the European Society of Cardiology guidelines, coronary angiography and PCI are the preferred strategies for patients with STEMI during pregnancy (class I, level of evidence C) and invasive management should also be considered for patients with NSTEMI and high-risk features (class IIa, level of evidence C).[12] An analysis of outcome data from 1992 to 1995 and from 1995 to 2005 time periods revealed a marked increase in the rates of PCI (from 2% to 42%) and a concomitant decrease in the rates of maternal mortality (from 20% to 11%), suggesting an association between invasive management and improved mortality.[5] However, in the present analysis, nearly half of women with AMI complicating pregnancy were managed conservatively. This may be related to concerns about potential complications of coronary angiography and PCI during pregnancy, radiation risks to the mother and fetus, or a perception that atherosclerotic cardiovascular disease is not anticipated in women of childbearing age. Although coronary angiography is necessary to establish a diagnosis of SCAD, PCI in this setting is associated with a high rate of complications and should be reserved for select patients with ischemia refractory to medical therapy.[17] Lower-than-expected invasive management of women with AMI during pregnancy and the puerperium may also relate to uncertainty about the safety of drug-eluting stents or periprocedural anticoagulation and antiplatelet therapy in this setting. Low-dose acetylsalicylic acid is considered relatively safe during pregnancy. Thienopyridines are classified by the US FDA as pregnancy category B, although there is insufficient evidence to establish long-term safety during pregnancy. Furthermore, antiplatelet and anticoagulant therapies are associated with a risk of peripartum hemorrhage. Other guideline-directed medical therapies for cardiovascular risk reduction, including angiotensin-converting enzyme inhibitors (US FDA pregnancy category D) and statins (US FDA pregnancy category X), are contraindicated during pregnancy because of the risk of harm to the fetus.[19]

In-hospital mortality of 4.5% in the present analysis is similar to mortality in previously published reports.[3] The maternal case-fatality rate after AMI was highest during the peripartum period and lower in the antepartum and postpartum periods.[2,5] This finding may be related to bleeding risks associated

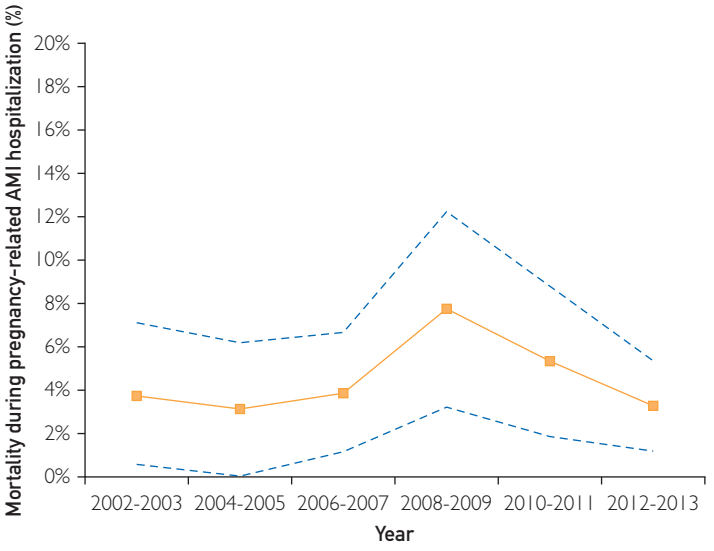

FIGURE 3. Trends in the mortality of AMI complicating pregnancy and the puerperium over time. *P*=.24 for trend. AMI = acute myocardial infarction.

with labor and delivery that may preclude the use of preferred medical and percutaneous therapies for AMI.

There are several limitations to the present analysis. First, trimester of pregnancy could not be determined from this large administrative data set, nor could the sequence of AMI and delivery when both events occurred during the same hospital admission. Similarly, the duration of the postpartum period is not specified by *ICD-9* codes and could not be definitively established for this analysis, although it is conventionally defined as the 6-week period after delivery. However, thrombotic risks may persist beyond this 6-week time period.[20] Second, because of the limitations of *ICD-9* coding data from a national hospital data set, detailed findings from coronary angiography were not available for patients who underwent invasive management. As such, the frequency of atherosclerotic plaque rupture, intraluminal thrombus formation, coronary artery dissection, and coronary artery spasm could not be determined from these data. Similarly, the incidence of specific comorbidities associated with coronary artery dissection, such as fibromuscular dysplasia, was also not available. Rates of coronary dissection in this cohort were lower than those reported in a small series of AMI during pregnancy.[7] Because many women did not undergo coronary angiography for AMI in the present study, underascertainment of coronary dissection is possible. Third, in-hospital medical management was not recorded in this administrative data set and was not available for the present analysis. Fourth, there is potential for undercoding and miscoding from administrative data sets, especially for cardiovascular risk factors and comorbidities in patients with and without AMI during pregnancy. Changes in *ICD-9* coding over time may have also affected the study findings and represent an unavoidable limitation of an analysis of a large administrative database. Fifth, treatment patterns may have evolved substantially over the 13-year time period used for the present analysis. Specifically, increasing recognition of the ischemic risks during pregnancy, greater sensitivity of cardiac biomarkers, and improvements in PCI may have affected the present findings. As a consequence, definitive statements regarding the benefit of invasive therapy in this small cohort identified over a long time period may be unreliable. Sixth, although maternal in-hospital mortality was reported in the present study, fetal and newborn outcomes were not available. Finally, the study findings were derived from the US population and may not be generalizable to other cohorts.

CONCLUSION

In a large national database from the United States, AMI occurred in 8.1 cases per 100,000 hospitalizations during pregnancy and the puerperium. Overall, 53% of patients with AMI during pregnancy underwent invasive management and 25% underwent coronary revascularization. Invasive management was independently associated with lower mortality. Despite contemporary management strategies, maternal mortality rates remained high.

SUPPLEMENTAL ONLINE MATERIAL

Supplemental material can be found online at: http://www.mayoclinicproceedings.org. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.

Abbreviations and Acronyms: **AMI** = acute myocardial infarction; **aOR** = adjusted odds ratio; **CABG** = coronary artery bypass grafting; **CAD** = coronary artery disease; **FDA** = Food and Drug Administration; ***ICD-9*** = *International Classification of Diseases, Ninth Revision*; **NIS** = National Inpatient Sample; **NSTEMI** = non–ST-segment elevation myocardial infarction; **PCI** = percutaneous coronary intervention; **SCAD** = spontaneous coronary artery dissection; **STEMI** = ST-segment elevation myocardial infarction

Grant Support: The work was supported by award 5T32HL098129 (N.R.S.) from the National Heart, Lung, and Blood Institute of the National Institutes of Health.

Potential Competing Interests: The authors report no competing interests.

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