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ORIGINAL RESEARCH

Risk Factors and Timing of Acute Myocardial Infarction Associated With Pregnancy: Insights From the National Inpatient Sample

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BACKGROUND: Pregnancy increases the risk of acute myocardial infarction (AMI). The purpose of this study was to examine timing and risk factors for AMI in pregnancy and poor outcome.

METHODS AND RESULTS: National Inpatient Sample (2003–2015) was screened in pregnancy, labor and delivery, and postpartum. There were 11 297 849 records extracted with 913 instances of AMI (0.008%). One hundred eleven (12.2%) women experienced AMI during labor and delivery, 338 (37.0%) during pregnancy and most during the postpartum period (464; 50.8%). The prevalence of AMI in pregnancy has increased (P=0.0005). Most major adverse cardiovascular and cerebrovascular events occurred in the postpartum period (63.5%). Inpatient mortality was 4.5%. Predictors of AMI include known coronary artery disease (odds ratio [OR], 517.4; 95% CI, 420.8–636.2), heart failure (OR, 8.2; 95% CI, 1.9–35.2), prior valve replacement (OR, 6.4; 95% CI, 2.4–17.1), and atrial fibrillation (OR, 2.7; CI, 1.5–4.7; P<0.001). Risk factors of traditional atherosclerosis including hyperlipidemia, obesity, tobacco history, substance abuse, and thrombophilia were identified (P<0.001). Gestational hypertensive disorders (eclampsia OR, 6.0; 95% CI, 3.3–10.8; preeclampsia OR, 3.2; 95% CI, 2.5–4.2) were significant risk factors in predicting AMI. Risk factors associated with major adverse cardiovascular and cerebrovascular events included prior percutaneous coronary intervention (OR, 6.6; 95% CI, 1.4–31.2) and pre-eclampsia (OR, 2.3; 95% CI, 1.3–3.9).

CONCLUSIONS: AMI is associated with modifiable, nonmodifiable, and obstetric risk factors. These risk factors can lead to devastating adverse outcomes and highlight the need for risk factor modification and public health resource initiatives toward the goal of decreasing AMI in the pregnant population.

Key Words: hypertension ■ myocardial infarction ■ preeclampsia ■ pregnancy ■ risk factors

Maternal mortality in the United States continues to rise, partly related to increases in cardiovascular disease.[1] Cardiovascular conditions ranked as the leading cause of pregnancy-related deaths in the United States and accounted for 15.1% of all pregnancy-related deaths from 2011 to 2015.[1] Of the cardiovascular diseases contributing to morbidity and mortality in the pregnant population, acute myocardial infarction (AMI) may have a substantial role.[2] Although its incidence is uncommon relative to other cardiovascular diseases affecting women of childbearing potential, pregnancy can increase the risk of myocardial infarction 3- to 4-fold,[3] and maternal mortality related to AMI in pregnancy has been reported to be as high as 37%.[4–6]

Pregnancy-associated myocardial infarction is on the rise,[6] for reasons that are likely multifactorial. This

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CLINICAL PERSPECTIVE

What Is New?

- There is an increased trend in acute myocardial infarction (AMI) during pregnancy, labor and delivery, and postpartum; gestational hypertensive disorders are associated with and predict AMI as well as major adverse cardiovascular and cerebrovascular events.
- AMI is associated with modifiable and nonmodifiable risk factors such as known coronary artery disease, heart failure, hyperlipidemia, thrombophilia states, substance abuse history, smoking history, obesity, multiple comorbidities, and Black race.
- Most AMI events occurred in the postpartum period, and inpatient mortality was similar in pregnant women compared with other inpatients with AMI, and lower compared with previous studies.

What Are the Clinical Implications?

- Although uncommon, the rates of AMI in the pregnant state are rising in the United States, which warrants further understanding of the cause and risk.
- Hypertensive syndromes led to increased risk of AMI and major adverse events in pregnancy, and therefore warrant closer attention to triggers as well as possible downstream effects on maternal mortality.
- Both modifiable and nonmodifiable risk factors for AMI in the pregnant state have been identified and with appropriate prepregnancy counseling and risk factor modification can facilitate steps towards decreasing the rates of AMI in this population.

Nonstandard Abbreviations and Acronyms

AMI	acute myocardial infarction
CAD	coronary artery disease
MACCE	major adverse cardiovascular and cerebrovascular events
NIS	National Inpatient Sample

rise is perhaps related to increases in detection and increases in traditional cardiovascular risk factors such as diabetes mellitus, hypertension, obesity, hyperlipidemia, and tobacco abuse (or combinations thereof) in women of childbearing potential. Maternal age has increased overall, as well as pregnancies in women of advanced maternal age.

Pregnancy predisposes a woman to changes in vasculature that make her susceptible to unique phenomena. Pregnancy itself subjects women to a hypercoagulable state, in addition to a cardiovascular stress test, with marked hemodynamic alterations in the cardiovascular system such as shifts in fluid balance, increases in cardiac output, increases in blood volume, and increases in heart rate.[7] Other variations in vasculature that are unique to pregnancy include increased uterine arterial resistance and peripheral vasoconstriction, which can give rise to hypertensive disorders of pregnancy such as preeclampsia and eclampsia.[8] Data suggest that hypertensive disorders of pregnancy such as eclampsia are increasing nationally.[9]

Complicating matters further, the cause of AMI in pregnancy been described with diverse variation. Those described have been caused by traditional coronary atherosclerotic plaque burden and stenosis, as well as nontraditional forms of AMI such as coronary thrombosis, coronary dissection, vasospasm, or embolic event. In this study, we sought to identify the timing and risk factors that may be associated with AMI during pregnancy, labor and delivery, and postpartum and major adverse cardiovascular and cerebrovascular events (MACCE) in a contemporary cohort.

METHODS

Data Source

The data that support the findings of this study are available from the corresponding author upon reasonable request. We utilized the National Inpatient Sample (NIS), collected by the Healthcare Cost and Utilization Project. It is the largest, publicly available all-payer inpatient healthcare database in the United States and contains ≈7 million unweighted stays yearly and 35 million weighted inpatient visits. We included discharge records related to pregnancy, labor and delivery, and postpartum periods from 2003 to September 2015 and utilized the *International Classification of Diseases, Ninth Revision* (*ICD-9*) codes to identify discharge records. We did not utilize data beyond September 2015 because hospital administrative data began using *International Classification of Diseases, Tenth Revision, Clinical Modification, Procedure Coding Classification System* (*ICD-10-PCS*). The data within the NIS are deidentified and therefore International Review Board approval was not required for this study.

Patient Characteristics and Variable Definition

Diagnosis and procedure codes were used to identify records of pregnancy, labor and delivery (cesarean

or vaginal), and postpartum (Data S1). Postpartum diagnosis is defined by *ICD-9* code and not by time. AMI was further defined by diagnosis codes. Records with age <18 or >55 years and male or unknown sex were excluded. Patient characteristics were obtained based on status of pregnancy, labor and delivery or, postpartum, only female sex, age categories of 18 to 24, 25 to 29, 30 to 34, 35 to 39, 40 to 44, 40 to 55, race/ethnicity of White, Black, Hispanic, Asian or Pacific Islander, or other/unknown, income quartile of 0 to 25th percentile, 26th to 50th percentile (median), 51st to 75th percentile, 76th to 100th percentile or other, and primary expected payer of Private insurance, Medicaid, Medicare, or Other/unknown. AMI was defined by type, location, and cause. Specific comorbidities were considered and identified by diagnosis codes. Elixhauser Comorbidity Index Scores were utilized through the Healthcare Cost and Utilization Project's Elixhauser Comorbidity Software to assign 2 variables, readmission score and in-hospital mortality, which identify comorbidities.[10,11] Complications in labor and delivery were also identified. Records defined as having eclampsia (severe preeclampsia, mild preeclampsia, and preeclampsia or eclampsia superimposed on pre-existing hypertension and unspecified hypertension complicating pregnancy childbirth or the puerperium were utilized) included those with hypertensive disorders of pregnancy. MACCE (defined as arterial embolism and thrombosis, acute renal failure, arrhythmia, bleeding/transfusion, cardiac arrest, cardiac complications of anesthesia or other sedation in labor and delivery, cardiogenic shock, heart failure, in-hospital death, obstetrical pulmonary embolism, postpartum hemorrhage, respiratory failure or arrest, stroke, atheroembolism, pulmonary embolism, and infarction) and obstetric event rates were obtained.

Statistical Analysis

χ^2 tests or χ^2 tests with exact *P* values based on Monte Carlo simulation when small cell counts (<5) existed in 2-way contingency tables were utilized to examine the marginal association between categorical variables and AMI, as well as between categorical variables and MACCE among patients with AMI. Wilcoxon rank sum tests were used to compare unadjusted marginal differences in continuous variables between patients with and without AMI and between patients with AMI with and without MACCE. The status of records and other factors related to each outcome that were significant ($P<0.05$) based on univariate analysis were further considered in multivariable logistic regression models. The linear trends in the rate of AMI and eclampsia among AMI records over years were examined using the complex survey analysis method with officially provided trend weight for records in years 2003 to 2011 and with discharge weight for records in years 2012 to 2015.[12] The SURVEYFREQ procedure was used to generate yearly frequency of records with AMI and any type of eclampsia among AMI records. Stratum identifier and hospital identifier in NIS data files were used as stratification variable and cluster variable, respectively. In order to correctly account for rate and make accurate inferences about the national populations as suggested by Berglund[13] and West et al,[14] all NIS records from year 2003 to year 2015 remain in the analysis and interested subgroup analysis was carried out using the domain options. *P* value for year was created from the SURVEYLOGISTIC procedure to assess the annual trend over time. Statistical analysis was performed using SAS 9.4 (SAS Institute Inc., Cary, NC) and significance level was set at 0.05.

RESULTS

Patient Characteristics

From 2003 to 2015, a total of 11 297 849 records for pregnancy, labor and delivery, and postpartum were extracted and among these records, 913 instances of AMI were recorded (0.008%). There was a significant increasing in trend for AMI in pregnancy from 2003 to 2015 ($P=0.0005$; Figure 1). Of these 913 records, 111 (12.2%) women experienced AMI during labor and delivery, 338 (37.0%) during pregnancy, and 464 (50.8%) during the postpartum period. Among the women who experienced AMI, 661 (72.4%) were age ≥30 years and this increased with age (Table 1). Most women were White (38.4%), followed by those of Black race (23.4%) as secondarily most frequent. A large proportion of records were described as insured by public insurance (Medicaid or Medicare, 44.9%). Most (55.2%) were described as in <50th median percentile for income quartile. Many patients were described as having coronary artery disease (CAD) as a prior comorbidity (33.6%), with a relative minority noted with prior percutaneous coronary intervention, myocardial infarction, or coronary artery bypass grafting in the AMI group. Prior tobacco use was common (18.9%), as was prior hyperlipidemia (13.0%).

Cause of AMI

There was no cause of AMI determined for 59.4% of patient records; cause was found in 40.6%. Of these, the cause was coronary atherosclerosis of the native coronary artery (28.3%) or atherosclerosis (0.1%), other specified forms of chronic ischemic heart disease (3.4%), chronic total occlusion of coronary artery (1.3%), dissection of coronary artery (15.0%), primary and secondary thrombophilia hypercoagulable state (2.3%), arterial embolism, and thrombosis (0.7%).

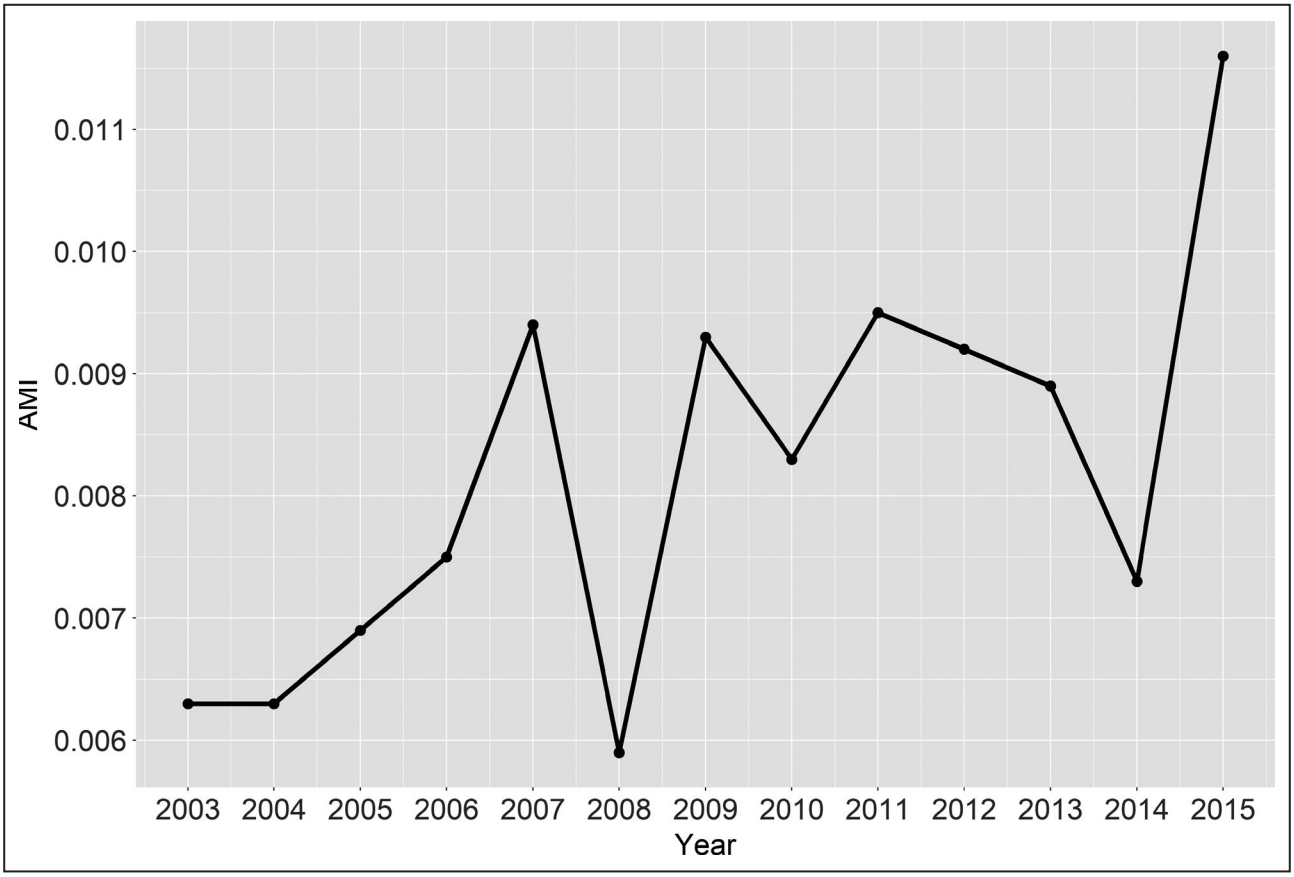

Figure 1. AMI in pregnancy, labor and delivery, and postpartum.
A trend of the prevalence of AMI from 2003 to 2015. AMI (*P*=0.0005, odds ratio, 1.034; 95% CI, 1.015–1.053). AMI indicates acute myocardial infarction.

Location, Timing of AMI, and Revascularization Patterns

Table 2 describes the location and timing of AMI as well as care patterns for revascularization. Notably, 60% of AMI were subendocardial. In addition, only 51.6% received any recorded form of revascularization.

Frequency and Timing of MACCE

Table 3 describes the timing and frequency of MACCE events in AMI records. Most major events occurred postpartum, including death, heart failure, arrhythmia, cardiogenic shock, and cardiac arrest, among others. Events during pregnancy were next most frequent.

Obstetric Complications

Obstetric complications were recorded and analyzed among this population of women who experienced AMI and are represented in Table 4. These complications were found to be more common in the AMI population. Considering specifically hypertensive syndromes, 18.3% of this population experienced any type of eclampsia/preeclampsia. Although there was a significantly increasing in trend for AMI in pregnancy, there was no significant increase in trend noted for eclampsia (*P*=0.1571).

Risk Factors for AMI

Based on univariate analysis for association between AMI and potential factors (patients' age, race/ethnicity, primary expect payer, income quartile, records status, length of stay, Elixhauser Comorbidity Index Scores of readmission, Elixhauser Comorbidity Index Scores of in-hospital mortality, comorbidities, obstetric complications, and complications), significant factors were adjusted in a multivariable logistic regression model (Figure 2 and Table S1). The greatest predictor of AMI during pregnancy was known CAD (odds ratio [OR], 517.4; 95% CI, 420.8–636.2). Other cardiac factors that were strongly associated with AMI were heart failure (OR, 8.2; 95% CI, 1.9, 35.2), prior valve replacement (OR, 6.4; 95% CI, 2.4, 17.0), and atrial fibrillation (OR, 2.7; 95% CI, 1.5–4.7). In terms of known risk factors for traditional atherosclerosis, hyperlipidemia, obesity, and smoking

Table 1. Descriptive Table of Records' Characteristics, and Comorbidities

Variable	AMI (N=913)	No AMI (N=11 328 236)	*P* Value
Patients' characteristics			
Age group, y			
18–24	97 (10.6%)	3 565 596 (31.5%)	<0.0001
25–29	155 (17.0%)	3 232 956 (28.5%)	
30–34	267 (29.2%)	2 805 053 (24.8%)	
35–39	244 (26.7%)	1 390 624 (12.3%)	
40–55	150 (16.4%)	334 007 (2.9%)	
Race			
Asian or Pacific islander	29 (3.2%)	477 406 (4.2%)	<0.0001
Black	214 (23.4%)	1 357 442 (12.0%)	
Hispanic	116 (12.7%)	2 133 452 (18.8%)	
Other/unknown race	203 (22.2%)	2 454 059 (21.7%)	
White	351 (38.4%)	4 905 877 (43.3%)	
Primary expected payer			
Medicaid	382 (41.8%)	4 756 852 (42.0%)	<0.0001
Medicare	28 (3.1%)	79 725 (0.7%)	
Other or unknown	59 (6.5%)	733 353 (6.5%)	
Private insurance	444 (48.6%)	5 758 306 (50.8%)	
Income quartile			
0–25th percentile	280 (30.7%)	3 049 521 (26.9%)	0.0729
26th–50th percentile	224 (24.5%)	2 790 414 (24.6%)	
51st–75th percentile	209 (22.9%)	2 730 030 (24.1%)	
76th–100th percentile	181 (19.8%)	2 550 680 (22.5%)	
Other	19 (2.1%)	207 591 (1.8%)	
Comorbidities and prior cardiovascular history			
Alcohol and substance abuse	19 (2.1%)	59 438 (0.5%)	<0.0001
Atrial fibrillation/flutter	24 (2.6%)	3899 (0.0%)	<0.0001
Cancer	…	13 115 (0.1%)	<0.0001
Coronary artery disease	307 (33.6%)	3249 (0.0%)	<0.0001
Carotid artery disease	…	110 (0.0%)	1.0000
Hyperlipidemia	119 (13.0%)	13 809 (0.1%)	<0.0001
Heart failure		189 (0.0%)	0.0002
Migraine headaches	…	2314 (0.0%)	1.0000
Obesity	96 (10.5%)	401 554 (3.5%)	<0.0001
Substance abuse history	54 (5.9%)	144 162 (1.3%)	<0.0001
Prior CABG	…	249 (0.0%)	<0.0001
Prior implantable cardioverter defibrillator	10 (1.1%)	1461 (0.0%)	<0.0001
Prior myocardial infarction	25 (2.7%)	1692 (0.0%)	<0.0001
Prior PCI	15 (1.6%)	534 (0.0%)	<0.0001
Prior pacemaker placement	…	1769 (0.0%)	0.1315
Prior transient ischemic attack or stroke	13 (1.4%)	5590 (0.0%)	<0.0001
Prior valve replacement	…	1466 (0.0%)	<0.0001
Smoking history	173 (18.9%)	719 274 (6.3%)	<0.0001
Thrombophilia (including history of thrombosis and antiphospholipid syndrome)	51 (5.6%)	49 396 (0.4%)	<0.0001
Records' status			
Pregnancy	338 (37.0%)	652 765 (5.8%)	<0.0001
Labor and delivery	111 (12.2%)	4 359 413 (38.5%)	

(*Continued*)

Table 1. Continued

Variable	AMI (N=913)	No AMI (N=11 328 236)	*P* Value
Postpartum	464 (50.8%)	6 316 058 (55.8%)	
Total deliveries (4 359 542)			
Cesarean delivery	42 (4.6%)	1 974 983 (45.3%)	
Length of stay	4.0±5.0	2.0±1.0	<0.0001

For categorical variables with event <10, amount and proportion were replaced by "…".
AMI indicates acute myocardial infarction; CABG, coronary artery bypass grafting; and PCI, percutaneous coronary intervention.

history, these were all significantly associated with AMI. Other substance abuse and thrombophilia were significant for AMI as well. Hypertensive syndromes of pregnancy such as eclampsia (OR, 6.0; 95% CI, 3.3, 10.8) and preeclampsia (OR, 3.2; 95% CI, 2.5, 4.2) were significant risk factors for AMI. Black race (OR, 1.3; 95% CI, 1.0, 1.5) was notably significant. Obstetric risk factors included postpartum hemorrhage (OR, 2.5; 95% CI, 1.9, 3.2), placental abruption (OR, 1.6; 95% CI, 1.0, 2.3), uterine rupture (OR, 4.2; 95% CI, 1.4, 13.0), postpartum infection (OR, 4.0; 95% CI, 2.7, 5.7) and thrombotic event (OR, 3.8; 95% CI, 2.3, 6.2).

Risk Factors for MACCE in AMI

Risk factors for MACCE are shown in Figure 3 and Table S2. Factors were significant variables based on univariate analysis between MACCE and potential factors (patients' age, race/ethnicity, primary expected payer, income quartile, records' status, AMI type and location, length of stay, Elixhauser Comorbidity Index Scores of readmission, Elixhauser Comorbidity Index Scores of in-hospital mortality, comorbidities, obstetric complications, and complications). In terms of timing, women in labor and delivery (OR, 3.4; 95% CI, 2.0, 5.7) or in pregnancy (OR, 3.7; 95% CI, 2.5, 5.3) had higher odds of MACCE than those in the postpartum. In terms of location, inferoposterior myocardial infarction was most likely among other locations to have MACCE (OR, 8.2; 95% CI, 1.2, 54.0). Those with preeclampsia or eclampsia superimposed on pre-existing hypertension and unspecified hypertension complicating pregnancy childbirth or the puerperium were at increased risk of MACCE (OR, 2.3; 95% CI, 1.3, 3.9). We also found that that having a prior percutaneous coronary intervention (OR, 6.6; 95% CI, 1.4, 31.2), or fluid and electrolyte imbalance (OR, 2.4; 95% CI, 1.3, 4.2) were risk factors of MACCE in patients with AMI.

Table 2. AMI Location, Type, Distribution, Revascularization Patterns, and Timing in Pregnancy

Location/Variable	Total Number (%) AMI Patients (N=913)	Pregnancy (N=338)	Labor and Delivery (N=111)	Postpartum (N=464)
Anterior	96 (10.5%)	47 (13.9%)	…	42 (9.1%)
Anterolateral	41 (4.5%)	17 (5.0%)	…	18 (3.9%)
Inferolateral	11 (1.2%)	…	…	…
Inferoposterior	12 (1.3%)	…	…	…
Other inferior	55 (6.0%)	30 (8.9%)	…	18 (3.9%)
Other lateral	…	…	…	…
Other specified sites	20 (2.2%)	…	…	14 (3.0%)
True posterior	…	…	…	…
Unspecified site	120 (13.1%)	38 (11.2%)	15 (13.5%)	67 (14.4%)
NSTEMI	551 (60.4%)	185 (54.7%)	71 (64.0%)	295 (63.6%)
STEMI	359 (39.3%)	152 (45.0%)	39 (35.1%)	168 (36.2%)
Other type of AMI	…	…	…	…
Any pattern of revascularization	471 (51.6%)	226 (66.9%)	43 (38.7%)	202 (43.5%)
Coronary angiography	423 (46.3%)	200 (59.2%)	39 (35.1%)	184 (39.7%)
CABG	61 (6.7%)	25 (7.4%)	…	31 (6.7%)
Injection of thrombolytic agent	…	…	…	…
PCI	176 (19.3%)	102 (30.2%)	15 (13.5%)	59 (12.7%)

For levels with event <10, amount and proportion were replaced by "…".
AMI indicates acute myocardial infarction; CABG, coronary artery bypass grafting; NSTEMI, non–ST-segment–elevation myocardial infarction; PCI, percutaneous coronary intervention; and STEMI, ST-segment–elevation myocardial infarction.

Table 3. Frequency and Timing of MACCE in Patients With AMI

MACCE	Total (N, % Among 913 Patients With AMI)	Pregnancy (N=338)	Labor and Delivery (N=111)	Postpartum (N=464)
Total MACCE	556 (60.9%)	149 (26.8%)*	54 (9.7%)*	353 (63.5%)*
In-hospital death	41 (4.5%)	14 (34.1%)	…	24 (58.5%)
Heart failure	229 (25.1%)	57 (24.9%)	16 (7.0%)	156 (68.1%)
Arrhythmia	235 (25.7%)	74 (31.5%)	25 (10.6%)	136 (57.9%)
Cardiogenic shock	58 (6.4%)	19 (32.8%)	…	35 (60.3%)
Cardiac arrest	58 (6.4%)	17 (29.3%)	…	37 (63.8%)
Respiratory failure or arrest	188 (20.6%)	38 (20.2%)	16 (8.5%)	134 (71.3%)
Stroke	25 (2.7%)	…	…	24 (96.0%)
Bleeding/transfusion	139 (15.2%)	33 (23.7%)	12 (8.6%)	94 (67.6%)
Postpartum hemorrhage	85 (9.3%)	…	…	85 (100.0%)
Cardiac complications of anesthesia or other sedation in labor and delivery	…	…	…	…
Arterial embolism and thrombosis	…	…	…	…
Obstetrical pulmonary embolism	30 (3.3%)	…	…	30 (100.0%)
Acute renal failure	92 (10.1%)	24 (26.1%)	…	59 (64.1%)

For levels with event <10, amount and proportion were replaced by "…".
AMI indicates acute myocardial infarction; and MACCE, major adverse cardiovascular and cerebrovascular events.
*All events and percentages to the right of the vertical bar demonstrate the relative percent distribution of patients with events at different time frame in pregnancy, delivery, or postpartum.

DISCUSSION

In this study, we identified the timing and risk factors associated with AMI during pregnancy, labor and delivery, and postpartum as well as MACCE in a contemporary cohort. Women during pregnancy, labor and delivery, and postpartum have a significantly increasing trend in AMI. Risk factors such as gestational hypertensive disorders are associated with and predict AMI as well as MACCE. AMI is associated with modifiable and nonmodifiable risk factors such as known hypertensive syndromes, known CAD, hyperlipidemia, thrombophilia states, substance abuse history, smoking history, obesity, multiple comorbidities, Medicaid insurance status, and Black race (Figure 4). An interplay of modifiable and nonmodifiable risk factors as well as obstetric issues, postpartum timing, and known cardiac disease can lead to adverse outcomes. Most AMI events occurred in the postpartum period, and inpatient mortality was similar in pregnant women compared with inpatients with AMI in the general population. Although uncommon, the rates of AMI in the pregnant state are rising in the United States, which warrants further understanding of the cause. Risk factor modification can facilitate steps towards decreasing the rates of AMI in this population.

Pregnancy-associated myocardial infarction is becoming more common in the United States[15] and internationally,[2] although the incidence may be highest in the United States. Increases in AMI incidence have occurred in lockstep with increases in maternal age, as well as a global rise in obesity and metabolic syndrome.[16] Along with increased maternal age because of delayed maternity, there is an increased likelihood of medical comorbidities such as obesity, hypertension, diabetes mellitus, and dyslipidemia, which lead to increasing traditional cardiovascular risk for AMI. Indeed, we found the presence of multiple comorbidities to be a risk factor for mortality in the AMI pregnant population, as well as modifiable risk factors such as obesity, hyperlipidemia, substance abuse, tobacco abuse, and preeclampsia superimposed on pre-existing hypertension. Pre-existing chronic hypertension is increasingly common in pregnancy, and more than one third of these patients will develop preeclampsia in pregnancy. All these comorbidities have historically been more often associated with worse outcomes among Americans with lower socioeconomic status and from non-White races.[17,18] Although the most frequently affected race in our study was White women, the proportion of Black women with AMI was nearly 2-fold higher than those without AMI. Furthermore, we note that the lowest income quartile made up the largest proportion of patients with AMI in our study and public health insurance (Medicaid+Medicare) was the primary payer for >40% of those patients with AMI. Additionally, prior investigations have noted that pregnant women with lower socioeconomic status often have delays in obtaining care and timely insurance coverage.[19] Known CAD appears to be the strongest risk factor for AMI in pregnancy in our data, which raises the question of

Table 4. Obstetric Complications

Variable	AMI (N=913)	No AMI (N=11 328 236)	*P* Value
Total obstetric complications	424 (46.4%)	2 333 702 (20.6%)	<0.0001
Hypertensive disorder of pregnancy			
Eclampsia (eclampsia complicating pregnancy childbirth or the puerperium)	15 (1.6%)	10 350 (0.1%)	<0.0001
Mild preeclampsia	27 (3.0%)	253 417 (2.2%)	
Preeclampsia or eclampsia superimposed on pre-existing hypertension and Unspecified hypertension complicating pregnancy childbirth or the puerperium	95 (10.4%)	135 032 (1.2%)	
Severe preeclampsia	29 (3.2%)	145 975 (1.3%)	
Transient hypertension of pregnancy	24 (2.6%)	368 744 (3.3%)	0.2862
Antepartum hemorrhage	…	4943 (0.0%)	1.0000
Abruptio placentae and placenta previa	28 (3.1%)	203 876 (1.8%)	0.0040
Fluid and electrolyte imbalance	203 (22.2%)	120 832 (1.1%)	<0.0001
Gestational diabetes mellitus	73 (8.0%)	145 441 (1.3%)	<0.0001
Preterm labor	50 (5.5%)	959 851 (8.5%)	0.0011
Early onset of labor and delivery	48 (5.3%)	724 494 (6.4%)	0.1599
Premature rupture of membranes	…	423 951 (3.7%)	<0.0001
Thrombotic event	27 (3.0%)	7853 (0.1%)	<0.0001
Uterine rupture	…	6169 (0.1%)	0.0019
Laceration	…	258 989 (2.3%)	0.0002
Postpartum infection	41 (4.5%)	64 645 (0.6%)	<0.0001
Postpartum hemorrhage	85 (9.3%)	311 082 (2.8%)	<0.0001

For levels with event <10, amount and proportion were replaced by "…".
AMI indicates acute myocardial infarction.

whether adequate prenatal counseling has occurred in this population, given the likely association with these social determinants of health.

Approximately 60% of women with AMI in pregnancy experienced some form of major adverse cardiovascular and cerebrovascular event, most commonly in the postpartum period. Of the deaths that were recorded, most occurred postpartum. Heart failure and arrhythmias were most common in the postpartum period as well, followed by the pregnancy period. The fewest events overall occurred in the labor and delivery time frame, which may be related to the fact that it is shortest (usually defined by 1–2 days), compared with pregnancy (up to 40 weeks) and postpartum (usually ≈6 weeks). These data are in contrast to a recent meta-analysis by Gibson et al[2] in which the rate of maternal MI was highest antepartum and those reported by Roth and Elkayam[6] to be equal across the periods, but data on types of cardiovascular events were not available.

While we could not elucidate the cause of MI reliably for all records, possible causes remain the following: traditional atherosclerosis, coronary dissection, thrombus, coronary vasospasm, and embolic events. Conventional thinking is that coronary dissection is quite common in the pregnant population, perhaps partly explaining the relatively low number of women who underwent any form of revascularization (51%). The treatment for spontaneous coronary artery dissection is usually conservative.[20] However, traditional atherosclerosis and plaque rupture may be more common than originally thought because of rises in maternal age and medical comorbidities. Mechanisms may also vary by the timing of the events, with the possibility of atherosclerosis and thrombosis more common in certain time frames, while that of dissection is more common in others. Hemodynamic changes in pregnancy may have a role as well, with marked rises in cardiac output and blood pressure during labor and delivery, while during postpartum, the cardiovascular system has an abrupt increase in preload from the return of blood from the uterus and placenta redirected toward the mother. Moreover, the events may also vary based on relative changes in blood pressure, with abrupt changes noted in preeclampsia accounting for more AMIs, which could translate into either dissections or atherosclerotic plaque rupture. Either way, whether the incidence and cause of AMI associated with pregnancy varies based on timing will require detailed prospective evaluations in

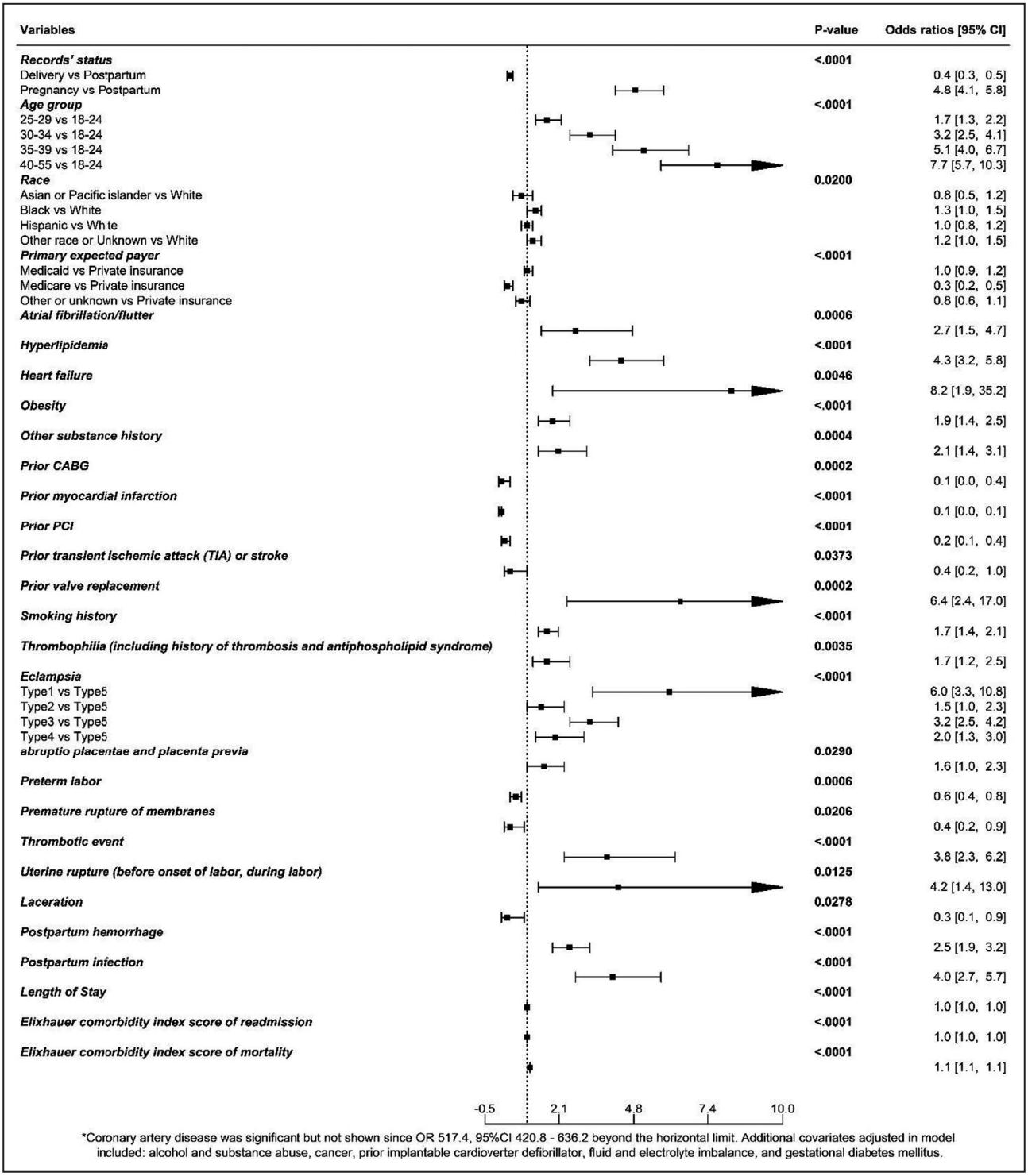

Figure 2. Predictors of AMI in pregnancy.

Forest plot highlighting significant risk factors of AMI in pregnancy. Each type of eclampsia is specified as below:

1. Type 1: Eclampsia (eclampsia complicating pregnancy childbirth or the puerperium).
2. Type 2: Mild preeclampsia.
3. Type 3: Preeclampsia or eclampsia superimposed on pre-existing hypertension and unspecified hypertension complicating pregnancy, childbirth, or the puerperium.
4. Type 4: Severe preeclampsia.
5. Type 5: No.

AMI indicates acute myocardial infarction; CABG, coronary artery bypass grafting; and PCI, percutaneous coronary intervention.

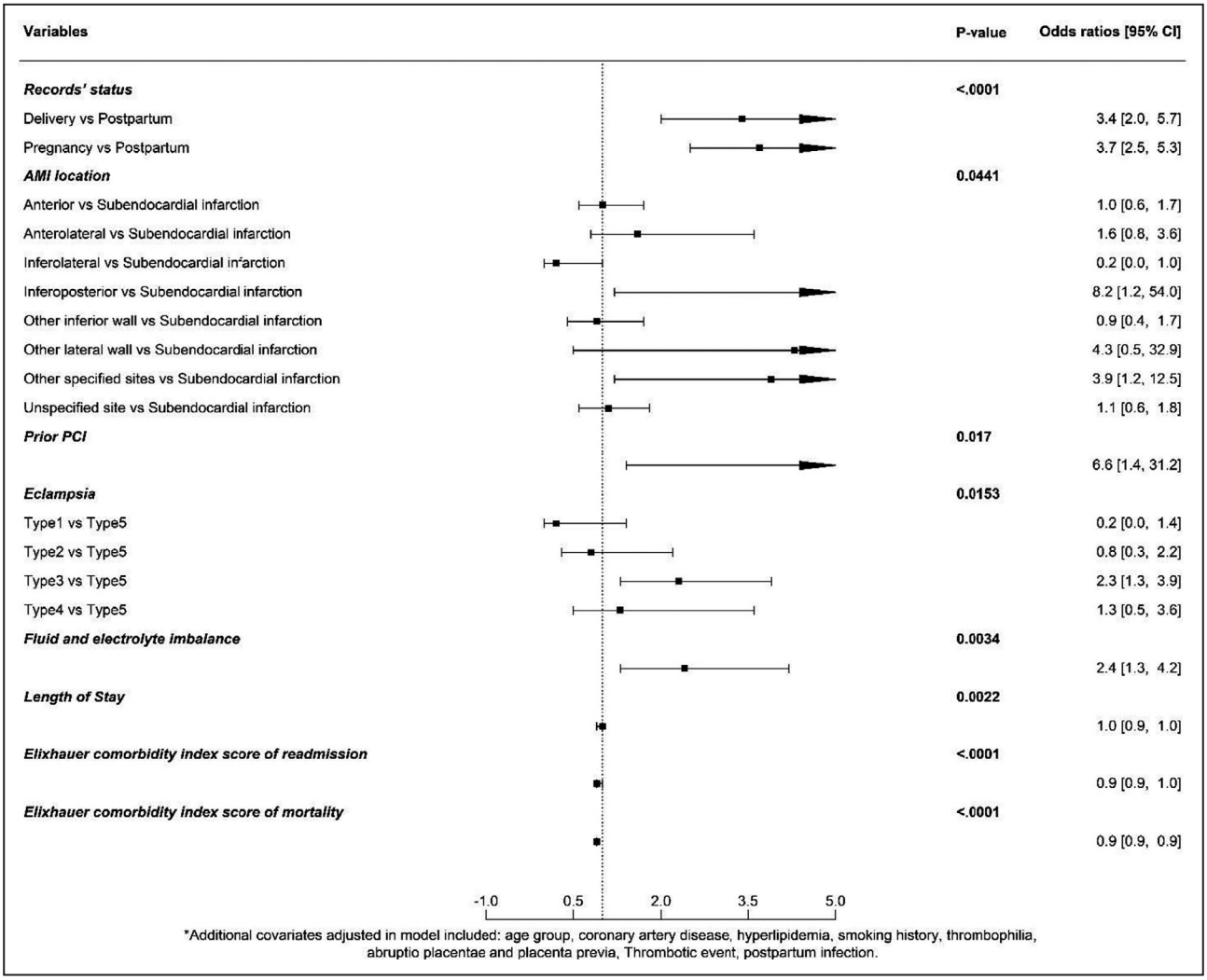

Figure 3. Predictors of MACCE in AMI in pregnancy.
Forest plot highlighting significant risk factors of MACCE in AMI in pregnancy. Each type of eclampsia is specified as below:
1. Type 1: Eclampsia (eclampsia complicating pregnancy, childbirth, or the puerperium).
2. Type 2: Mild preeclampsia.
3. Type 3: Preeclampsia or eclampsia superimposed on pre-existing hypertension and unspecified hypertension complicating pregnancy, childbirth, or the puerperium.
4. Type 4: Severe preeclampsia.
5. Type 5: No.

AMI indicates acute myocardial infarction; MACCE, major adverse cardiovascular and cerebrovascular events; and PCI, percutaneous coronary intervention.

consecutive large-sized studies and application of standard diagnostic criteria. The impact on fetal/neonatal events would need to be explored as well.

Inpatient mortality in pregnant women with AMI was 4.5%, similar to that reported for AMI in the general population.[21] Inpatient mortality is considerably lower than previously reported in the pregnant AMI population,[3,4,6] which is related to multiple issues including the decade in which the data were collected. Diagnosis and treatment of AMI have improved over the past several decades, as well as the use of primary percutaneous coronary intervention in the pregnant population. While a young population with AMI might expected to have a low inpatient mortality rate, multiple issues may be involved such as delays in diagnosis, treatment, hemodynamics of pregnancy, timing of event (whether antepartum, postpartum, or during delivery), among others. Nonpregnant young women with AMI experience inpatient mortality in the 2% to 3.3% range.[22] A limitation of the present and prior studies is the lack of long-term longitudinal data on individual patients. Moreover, patients who died outside the hospital either before or after the hospitalization would not be reported in the NIS and represents a limitation of the

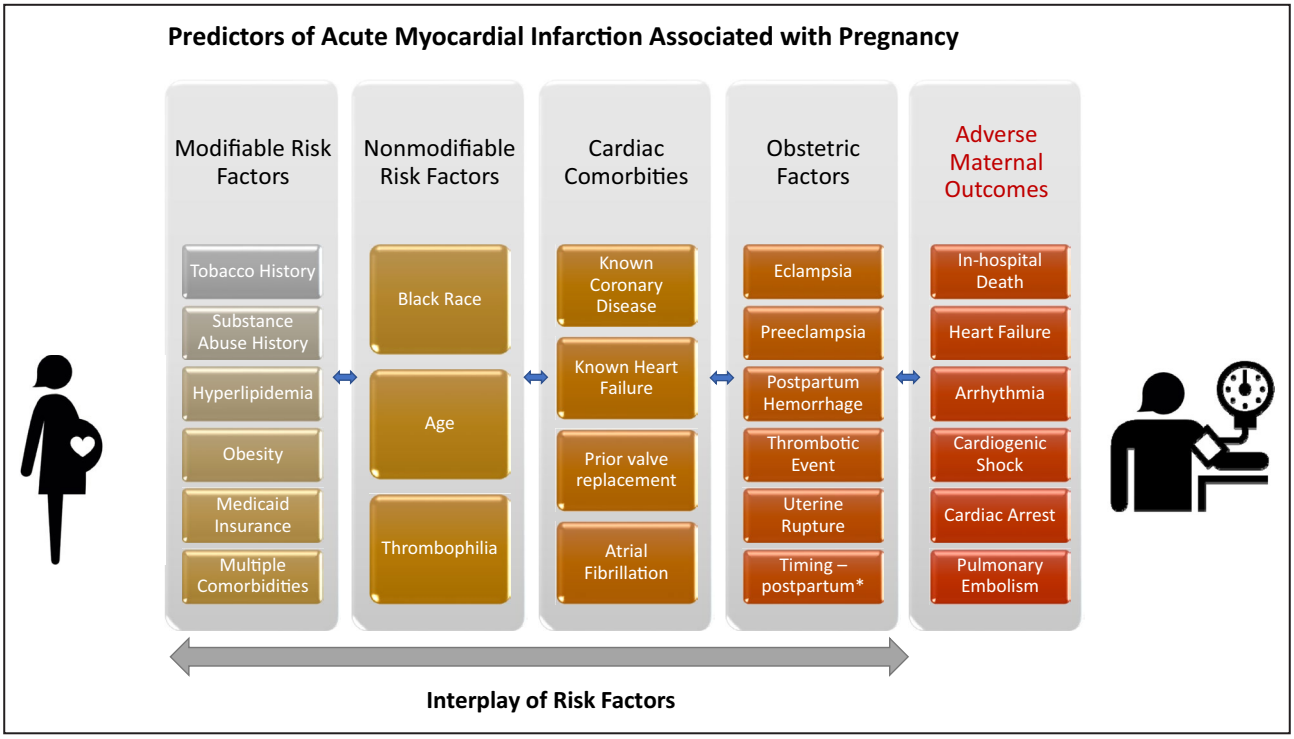

Figure 4. AMI in pregnancy.
An interplay of risk factors including modifiable, nonmodifiable, cardiac, and obstetrical factors lead to adverse outcomes in this population. *Postpartum period may be a period of elevated risk. AMI indicates acute myocardial infarction.

data. The reviews by Roth and Elkayam[6] as well as that by Hankins et al,[4] both with higher mortality rates, may reflect the reporting of more severe cases in the literature, as well as those from earlier decades in which the management practices of AMI were different.

Overall, the strength of the present analysis is the documentation of the timing of MACCE in AMI associated with pregnancy as well as the risk factors for AMI associated with pregnancy, and also the risk factors associated with MACCE in this population. Obstetric complications were higher in patients with AMI compared with those without, suggesting an interplay of obstetric, cardiac, and patient-specific modifiable and nonmodifiable risk factors leading to a perfect storm of AMI associated with pregnancy. Additional variables include the risk of postpartum timing, hypertensive disorders of pregnancy, as well as known cardiac disease that can lead to adverse outcomes. Although uncommon, the rates of AMI in the pregnant state are rising in the United States, which warrants further understanding of the cause. Prepregnancy counseling and risk factor modification are considered critical in the evaluation of women before pregnancy. Risk factor modification can facilitate steps towards decreasing the rates of AMI in this population.

Study Limitations

Our study has several important limitations. The NIS was especially valuable in studying AMI, which has a low incidence in pregnancy, because it allowed for a large, contemporary, representative US sample of records. This data set has been utilized in the past to study hospitalization trends and its predictors in patients with pregnancy and other forms of heart disease, such as preexisting cardiomyopathy, congenital heart disease, and myocardial disorders.[23,24] However, the data are restricted to inpatient, labor- and delivery-related hospitalizations, and maternal data on disease verification among others were not available. Deaths, events, or hospitalizations after the index labor and delivery hospitalization would not be included. Late maternal mortality is a real and devastating issue. Although *ICD-9* codes have imperfect sensitivity and specificity, prior data do show a high level of accuracy (>90%) in ascertaining cardiovascular disease diagnoses.[25] Undercoding or miscoding are possibilities, although this would be unlikely to bias the results, because even a small number of misclassifications would not have a sizable effect on summary estimates of the large number of records included herein. Investigating the role of increased body mass index as a risk factor for AMI in this population was limited because of body mass index of the pregnant population being confounded by gestational weight gain. Our inability to distinguish whether increased body mass index was caused by obesity at the start of pregnancy or caused by the gestational weight gain led to the use of the diagnosis code of obesity rather

than numerical body mass index value. Limitations on the cause of AMI were apparent and warrant further study in prospective registries. Moreover, the NIS does not distinguish whether a condition is present on admission; therefore, verification of preexisting diagnoses can be difficult; furthermore, certain aspects of patient history, imaging data, laboratory values, medications, and long-term follow-up were not available for analysis. Despite these limitations, it is validating that our data substantiated existing paradigms about AMI, including cardiac and obstetric complications.

CONCLUSIONS

The timing and risk factors associated with AMI during pregnancy, labor and delivery, and postpartum as well as MACCE in a contemporary cohort were identified. Women during pregnancy, labor and delivery, and postpartum have had a significantly increased trend in AMI. Novel risk factors such as hypertensive syndromes of pregnancy are associated with and predict AMI as well as MACCE. AMI is associated with modifiable and nonmodifiable risk factors such as known hypertensive syndromes, known CAD, hyperlipidemia, thrombophilia states, substance abuse history, smoking history, obesity, and Black race. Though not directly examined, we suspect that elements of socioeconomic status and other social determinants of health are likely associated with delays and barriers to appropriate health care in this population. An interplay of modifiable and nonmodifiable risk factors as well as obstetric issues and known cardiac disease can lead to adverse outcomes. Risk factor modification as well as increased implementation in public health resources for pregnant patients may facilitate steps towards decreasing the rates of AMI in this population.

ARTICLE INFORMATION

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Puja B. Parikh, MD, MPH reports honoraria; Self; Medtronic, Inc., AstraZeneca Pharmaceuticals, LP. The remaining authors have no disclosures to report.

Supplementary Materials

Data S1
Tables S1–S2

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SUPPLEMENTAL MATERIAL

Data S1.

A1 Pregnancy, Delivery and Postpartum:

Pregnancy diagnosis codes	630, 6310, 6318, 632, 63300, 63301, 63310, 63311, 63320, 63321, 63380, 63381, 63390, 63391, 63400, 63401, 63402, 63410, 63411, 63412, 63420, 63421, 63422, 63430, 63431, 63432, 63440, 63441, 63442, 63450, 63451, 63452, 63460, 63461, 63462, 63470, 63471, 63472, 63480, 63481, 63482, 63490, 63491, 63492, 63500, 63501, 63502, 63510, 63511, 63512, 63520, 63521, 63522, 63530, 63531, 63532, 63540, 63541, 63542, 63550, 63551, 63552, 63560, 63561, 63562, 63570, 63571, 63572, 63580, 63581, 63582, 63590, 63591, 63592, 63600, 63601, 63602, 63610, 63611, 63612, 63620, 63621, 63622, 63630, 63631, 63632, 63640, 63641, 63642, 63650, 63651, 63652, 63660, 63661, 63662, 63670, 63671, 63672, 63680, 63681, 63682, 63690, 63691, 63692, 63700, 63701, 63702, 63710, 63711, 63712, 63720, 63721, 63722, 63730, 63731, 63732, 63740, 63741, 63742, 63750, 63751, 63752, 63760, 63761, 63762, 63770, 63771, 63772, 63780, 63781, 63782, 63790, 63791, 63792, 6380, 6381, 6382, 6383, 6384, 6385, 6386, 6387, 6388, 6389, 6390, 6391, 6392, 6393, 6394, 6395, 6396, 6398, 6399, 64000, 64001, 64003, 64080, 64081, 64083, 64090, 64091, 64093, 64100, 64101, 64103, 64110, 64111, 64113, 64120, 64121, 64123, 64130, 64131, 64133, 64180, 64181, 64183, 64190, 64191, 64193, 64200, 64201, 64202, 64203, 64204, 64210, 64211, 64212, 64213, 64214, 64220, 64221, 64222, 64223, 64224, 64230, 64231, 64232, 64233, 64234, 64240, 64241, 64242, 64243, 64244, 64250, 64251, 64252, 64253, 64254, 64260, 64261, 64262, 64263, 64264, 64270, 64271, 64272, 64273, 64274, 64290, 64291, 64292, 64293, 64294, 64300, 64301, 64303, 64310, 64311, 64313, 64320, 64321, 64323, 64380, 64381, 64383, 64390, 64391, 64393, 64400, 64403, 64410, 64413, 64420, 64421, 64510, 64511, 64513, 64520, 64521, 64523, 64600, 64601, 64603, 64610, 64611, 64612, 64613, 64614, 64620, 64621, 64622, 64623, 64624, 64630, 64631, 64633, 64640, 64641, 64642, 64643, 64644, 64650, 64651, 64652, 64653, 64654, 64660, 64661, 64662, 64663, 64664, 64670, 64671, 64673, 64680, 64681, 64682, 64683, 64684, 64690, 64691, 64693, 64700, 64701, 64702, 64703, 64704, 64710, 64711, 64712, 64713, 64714, 64720, 64721, 64722, 64723, 64724, 64730, 64731, 64732, 64733, 64734, 64740, 64741, 64742, 64743, 64744, 64750, 64751, 64752, 64753, 64754, 64760, 64761, 64762, 64763, 64764, 64780, 64781, 64782, 64783, 64784, 64790, 64791, 64792, 64793, 64794, 64800, 64801, 64802, 64803, 64804, 64810, 64811, 64812, 64813, 64814, 64820, 64821, 64822, 64823, 64824, 64830, 64831, 64832, 64833, 64834, 64840, 64841, 64842, 64843, 64844, 64850, 64851, 64852, 64853, 64854, 64860, 64861, 64862, 64863, 64864, 64870, 64871, 64872, 64873, 64874, 64880, 64881, 64882, 64883, 64884, 64890, 64891, 64892, 64893, 64894	
Delivery	Cesarean procedure codes	740, 741, 742, 743, 744, 7491, 7499
	Vaginal diagnosis codes	V270, V271, V272, V273, V274, V275, V276, V277, V279, 650, 65100, 65101, 65103, 65110, 65111, 65113, 65120, 65121, 65123, 65130, 65131, 65133, 65140, 65141, 65143, 65150,

		65151, 65153, 65160, 65161, 65163, 65170, 65171, 65173, 65180, 65181, 65183, 65190, 65191, 65193, 65200, 65201, 65203, 65210, 65211, 65213, 65220, 65221, 65223, 65230, 65231, 65233, 65240, 65241, 65243, 65250, 65251, 65253, 65260, 65261, 65263, 65270, 65271, 65273, 65280, 65281, 65283, 65290, 65291, 65293, 65300, 65301, 65303, 65310, 65311, 65313, 65320, 65321, 65323, 65330, 65331, 65333, 65340, 65341, 65343, 65350, 65351, 65353, 65360, 65361, 65363, 65370, 65371, 65373, 65380, 65381, 65383, 65390, 65391, 65393, 65400, 65401, 65402, 65403, 65404, 65410, 65411, 65412, 65413, 65414, 65420, 65421, 65423, 65430, 65431, 65432, 65433, 65434, 65440, 65441, 65442, 65443, 65444, 65450, 65451, 65452, 65453, 65454, 65460, 65461, 65462, 65463, 65464, 65470, 65471, 65472, 65473, 65474, 65480, 65481, 65482, 65483, 65484, 65490, 65491, 65492, 65493, 65494, 65500, 65501, 65503, 65510, 65511, 65513, 65520, 65521, 65523, 65530, 65531, 65533, 65540, 65541, 65543, 65550, 65551, 65553, 65560, 65561, 65563, 65570, 65571, 65573, 65580, 65581, 65583, 65590, 65591, 65593, 65600, 65601, 65603, 65610, 65611, 65613, 65620, 65621, 65623, 65630, 65631, 65633, 65640, 65641, 65643, 65650, 65651, 65653, 65660, 65661, 65663, 65670, 65671, 65673, 65680, 65681, 65683, 65690, 65691, 65693, 65700, 65701, 65703, 65800, 65801, 65803, 65810, 65811, 65813, 65820, 65821, 65823, 65830, 65831, 65833, 65840, 65841, 65843, 65880, 65881, 65883, 65890, 65891, 65893, 65900, 65901, 65903, 65910, 65911, 65913, 65920, 65921, 65923, 65930, 65931, 65933, 65940, 65941, 65943, 65950, 65951, 65953, 65960, 65961, 65963, 65970, 65971, 65973, 65980, 65981, 65983, 65990, 65991, 65993
	Vaginal procedure codes	720, 721, 7221, 7229, 7231, 7239, 724, 7251, 7252, 7253, 7254, 726, 7271, 7279, 728, 729, 7301, 7309, 731, 7321, 7322, 733, 734, 7351, 7359, 736, 738, 7391, 7392, 7393, 7394, 7399, 750, 751, 752, 7531, 7532, 7533, 7534, 7535, 7536, 7537, 7538, 754, 7550, 7551, 7552, 7561, 7562, 7569, 757, 758, 7591, 7592, 7593, 7594, 7599
Postpartum diagnosis codes	66000, 66001, 66003, 66010, 66011, 66013, 66020, 66021, 66023, 66030, 66031, 66033, 66040, 66041, 66043, 66050, 66051, 66053, 66060, 66061, 66063, 66070, 66071, 66073, 66080, 66081, 66083, 66090, 66091, 66093, 66100, 66101, 66103, 66110, 66111, 66113, 66120, 66121, 66123, 66130, 66131, 66133, 66140, 66141, 66143, 66190, 66191, 66193, 66200, 66201, 66203, 66210, 66211, 66213, 66220, 66221, 66223, 66230, 66231, 66233, 66300, 66301, 66303, 66310, 66311, 66313, 66320, 66321, 66323, 66330, 66331, 66333, 66340, 66341, 66343, 66350, 66351, 66353, 66360, 66361, 66363, 66380, 66381, 66383, 66390, 66391, 66393, 66400, 66401, 66404, 66410, 66411, 66414, 66420, 66421, 66424, 66430, 66431, 66434, 66440, 66441, 66444, 66450, 66451, 66454, 66460, 66461, 66464, 66480, 66481, 66484, 66490, 66491, 66494, 66500, 66501, 66503, 66510, 66511, 66520, 66522, 66524, 66530, 66531, 66534, 66540, 66541, 66544, 66550, 66551, 66554, 66560, 66561, 66564, 66570, 66571, 66572, 66574, 66580, 66581, 66582, 66583, 66584, 66590, 66591, 66592, 66593, 66594, 66600, 66602,	

	66604, 66610, 66612, 66614, 66620, 66622, 66624, 66630, 66632, 66634, 66700, 66702, 66704, 66710, 66712, 66714, 66800, 66801, 66802, 66803, 66804, 66810, 66811, 66812, 66813, 66814, 66820, 66821, 66822, 66823, 66824, 66880, 66881, 66882, 66883, 66884, 66890, 66891, 66892, 66893, 66894, 66900, 66901, 66902, 66903, 66904, 66910, 66911, 66912, 66913, 66914, 66920, 66921, 66922, 66923, 66924, 66930, 66932, 66934, 66940, 66941, 66942, 66943, 66944, 66950, 66951, 66960, 66961, 66970, 66971, 66980, 66981, 66982, 66983, 66984, 66990, 66991, 66992, 66993, 66994, 67000, 67002, 67004, 67010, 67012, 67014, 67020, 67022, 67024, 67030, 67032, 67034, 67080, 67082, 67084, 67100, 67101, 67102, 67103, 67104, 67110, 67111, 67112, 67113, 67114, 67120, 67121, 67122, 67123, 67124, 67130, 67131, 67133, 67140, 67142, 67144, 67150, 67151, 67152, 67153, 67154, 67180, 67181, 67182, 67183, 67184, 67190, 67191, 67192, 67193, 67194, 67200, 67202, 67204, 67300, 67301, 67302, 67303, 67304, 67310, 67311, 67312, 67313, 67314, 67320, 67321, 67322, 67323, 67324, 67330, 67331, 67332, 67333, 67334, 67380, 67381, 67382, 67383, 67384, 67400, 67401, 67402, 67403, 67404, 67410, 67412, 67414, 67420, 67422, 67424, 67430, 67432, 67434, 67440, 67442, 67444, 67450, 67451, 67452, 67453, 67454, 67480, 67482, 67484, 67490, 67492, 67494, 67500, 67501, 67502, 67503, 67504, 67510, 67511, 67512, 67513, 67514, 67520, 67521, 67522, 67523, 67524, 67580, 67581, 67582, 67583, 67584, 67590, 67591, 67592, 67593, 67594, 67600, 67601, 67602, 67603, 67604, 67610, 67611, 67612, 67613, 67614, 67620, 67621, 67622, 67623, 67624, 67630, 67631, 67632, 67633, 67634, 67640, 67641, 67642, 67643, 67644, 67650, 67651, 67652, 67653, 67654, 67660, 67661, 67662, 67663, 67664, 67680, 67681, 67682, 67683, 67684, 67690, 67691, 67692, 67693, 67694, 677

A2 AMI:

Inclusion	41000, 41001, 41010, 41011, 41020, 41021, 41030, 41031, 41040, 41041, 41050, 41051, 41060, 41061, 41070, 41071, 41080, 41081, 41090, 41091
Exclusion	41002, 41012, 41022, 41032, 41042, 41052, 41062, 41072, 41082, 41092

A3 BMI:

BMI	< 19	V850
	19 – 24	V851
	25 – 30	V8521, V8522, V8523, V8524, V8525
	> 30	V8530, V8531, V8532, V8533, V8534, V8535, V8536, V8537, V8538, V8539, V8541, V8542, V8543, V8544, V8545

A4 AMI characteristics:

Type	NSTEMI	41071
	STEMI	41001, 41011, 41021, 41031, 41041, 41051, 41061, 41081, 41091

	Not further characterized (Other)	41000, 41002, 41010, 41012, 41020, 41022, 41030, 41032, 41040, 41042, 41050, 41052, 41060, 41062, 41070, 41072, 41080, 41082, 41090, 41092
Location	Anterolateral	41000, 41001, 41002
	Anterior	41010, 41011, 41012
	Inferolateral	41020, 41021, 41022
	Inferoposterior	41030, 41031, 41032
	Other inferior wall	41040, 41041, 41042
	Other lateral wall	41050, 41051, 41052
	True posterior wall	41060, 41061, 41062
	Subendocardial infarction	41070, 41071, 41072
	Other specified sites	41080, 41081, 41082
	Unspecified site	41090, 41091, 41092
Etiology	Coronary atherosclerosis of native coronary artery	41401
	Atherosclerosis	4400, 4401, 44020, 44021, 44022, 44023, 44024, 44029, 44030, 44031, 44032, 4404, 4408, 4409
	Dissection of coronary artery	41412
	Arterial embolism and thrombosis	44401, 44409, 4441, 44421, 44422, 44481, 44489, 4449
	Thombophilia-primary hypercoaguable state	28981
	Thombophilia-secondary hypercoaguable state	28982
	Coronary artherosclerosis	41400, 41401, 41402, 41403, 41404, 41405, 41406, 41407
	Aneurysm and dissection of heart	41410, 41411, 41412, 41419
	Chronic total occlusion of coronary artery	4142
	Coronary atherosclerosis due to lipid rich plaque	4143
	Coronary atherosclerosis due to calcified coronary lesion	4144
	Other specified forms of chronic ischemic heart disease	4148
	Chronic ischemic heart disease, unspecified	4149

A5 Comorbidities:

Atrial fibrillation/flutter	42731, 42732
Hyperlipidemia	53*

Coronary artery disease	101*
Prior myocardial infarction	412
Prior PCI	V4582
Prior CABG	V4581
Carotid artery disease	43310
Prior transient ischemic attack (TIA) or stroke	V1254, 4380, 43810, 43811, 43812, 43813, 43814, 43819, 43820, 43821, 43822, 43830, 43831, 43832, 43840, 43841, 43842, 43850, 43851, 43852, 43853, 4386, 4387, 43881, 43882, 43883, 43884, 43885, 43889, 4389
Prior pacemaker placement	V4501
Prior implantable cardioverter defibrillator	V4502
Prior valve replacement	V433
Heart failure	39891, 4280, 4281, 42820, 42821, 42822, 42823, 42830, 42831, 428.32, 42833, 42840, 42841, 42842, 42843, 4289, 40201, 40211, 40291, 40401, 40403, 40411, 40413, 40491, 40493, 4250, 4251, 42511, 42518, 4252, 4253, 4254, 4255, 4257, 4258, 4259
Thrombophilia (including history of thrombosis and antiphospholipid syndrome)	2738, 2869, V1251, 28652, 28653, 28659, 28981, 28982, 28983, 28984, 28989, 2899, 79579
Migraine headaches	34600, 34601, 34602, 34603, 34610, 34611, 34612, 34613
Alcohol and substance abuse	64830, 64831, 64832, 64833, 64834, 30500, 30501, 30502, 30503
Smoking history	3051, 64900, 64901, 64902, 64903, 64904, 98984, V1582
Other substance history	30520, 30521, 30522, 30523, 30530, 30531, 30532, 30533, 30540, 30541, 30542, 30543, 30550, 30551, 30552, 30553, 30560, 30561, 30562, 30563, 30570, 30571, 30572, 30573, 30580, 30581, 30582, 30583, 30590, 30591, 30592, 30593
Cancer	1400, 1401, 1403, 1404, 1405, 1406, 1408, 1409, 1410, 1411, 1412, 1413, 1414, 1415, 1416, 1418, 1419, 1420, 1421, 1422, 1428, 1429, 1430, 1431, 1438, 1439, 1440, 1441, 1448, 1449, 1450, 1451, 1452, 1453, 1454, 1455, 1456, 1458, 1459, 1460, 1461, 1462, 1463, 1464, 1465, 1466, 1467, 1468, 1469, 1470, 1471, 1472, 1473, 1478, 1479, 1480, 1481, 1482, 1483, 1488, 1489, 1490, 1491, 1498, 1499, 1500, 1501, 1502, 1503, 1504, 1505, 1508, 1509, 1510, 1511, 1512, 1513, 1514, 1515, 1516, 1518, 1519, 1520, 1521, 1522, 1523, 1528, 1529, 1530, 1531, 1532, 1533, 1534, 1535, 1536, 1537, 1538, 1539, 1540, 1541, 1542, 1543, 1548, 1550, 1551, 1552, 1560, 1561, 1562, 1568, 1569, 1570, 1571, 1572, 1573, 1574, 1578, 1579, 1580, 1588, 1589, 1590, 1591, 1598, 1599, 1600, 1601, 1602, 1603, 1604, 1605, 1608, 1609, 1610, 1611, 1612, 1613, 1618, 1619, 1620, 1622, 1623, 1624, 1625, 1628, 1629, 1630, 1631, 1638, 1639, 1640, 1641, 1642, 1643, 1648, 1649, 1650, 1658, 1659, 1700, 1701, 1702, 1703, 1704, 1705, 1706, 1707, 1708, 1709, 1710, 1712, 1713, 1714, 1715, 1716, 1717, 1718, 1719, 1720, 1721, 1722, 1723, 1724, 1725, 1726, 1727, 1728, 1729, 17300, 17301, 17302, 17309, 17310, 17311, 17312, 17319, 17320, 17321, 17322, 17329, 17330, 17331, 17332, 17339, 17340,

	17341, 17342, 17349, 17350, 17351, 17352, 17359, 17360, 17361, 17362, 17369, 17370, 17371, 17372, 17379, 17380, 17381, 17382, 17389, 17390, 17391, 17392, 17399, 1740, 1741, 1742, 1743, 1744, 1745, 1746, 1748, 1749, 1750, 1759, 1760, 1761, 1762, 1763, 1764, 1765, 1768, 1769, 179, 1800, 1801, 1808, 1809, 181, 1820, 1821, 1828, 1830, 1832, 1833, 1834, 1835, 1838, 1839, 1840, 1841, 1842, 1843, 1844, 1848, 1849, 185, 1860, 1869, 1871, 1872, 1873, 1874, 1875, 1876, 1877, 1878, 1879, 1880, 1881, 1882, 1883, 1884, 1885, 1886, 1887, 1888, 1889, 1890, 1891, 1892, 1893, 1894, 1898, 1899, 1900, 1901, 1902, 1903, 1904, 1905, 1906, 1907, 1908, 1909, 1910, 1911, 1912, 1913, 1914, 1915, 1916, 1917, 1918, 1919, 1920, 1921, 1922, 1923, 1928, 1929, 193, 1940, 1941, 1943, 1944, 1945, 1946, 1948, 1949, 1950, 1951, 1952, 1953, 1954, 1955, 1958, 1960, 1961, 1962, 1963, 1965, 1966, 1968, 1969, 1970, 1971, 1972, 1973, 1974, 1975, 1976, 1977, 1978, 1980, 1981, 1982, 1983, 1984, 1985, 1986, 1987, 19881, 19882, 19889, 1990, 1991, 1992, 20000, 20001, 20002, 20003, 20004, 20005, 20006, 20007, 20008, 20010, 20011, 20012, 20013, 20014, 20015, 20016, 20017, 20018, 20020, 20021, 20022, 20023, 20024, 20025, 20026, 20027, 20028, 20030, 20031, 20032, 20033, 20034, 20035, 20036, 20037, 20038, 20040, 20041, 20042, 20043, 20044, 20045, 20046, 20047, 20048, 20050, 20051, 20052, 20053, 20054, 20055, 20056, 20057, 20058, 20060, 20061, 20062, 20063, 20064, 20065, 20066, 20067, 20068, 20070, 20071, 20072, 20073, 20074, 20075, 20076, 20077, 20078, 20080, 20081, 20082, 20083, 20084, 20085, 20086, 20087, 20088, 20100, 20101, 20102, 20103, 20104, 20105, 20106, 20107, 20108, 20110, 20111, 20112, 20113, 20114, 20115, 20116, 20117, 20118, 20120, 20121, 20122, 20123, 20124, 20125, 20126, 20127, 20128, 20140, 20141, 20142, 20143, 20144, 20145, 20146, 20147, 20148, 20150, 20151, 20152, 20153, 20154, 20155, 20156, 20157, 20158, 20160, 20161, 20162, 20163, 20164, 20165, 20166, 20167, 20168, 20170, 20171, 20172, 20173, 20174, 20175, 20176, 20177, 20178, 20190, 20191, 20192, 20193, 20194, 20195, 20196, 20197, 20198, 20200, 20201, 20202, 20203, 20204, 20205, 20206, 20207, 20208, 20210, 20211, 20212, 20213, 20214, 20215, 20216, 20217, 20218, 20220, 20221, 20222, 20223, 20224, 20225, 20226, 20227, 20228, 20230, 20231, 20232, 20233, 20234, 20235, 20236, 20237, 20238, 20240, 20241, 20242, 20243, 20244, 20245, 20246, 20247, 20248, 20250, 20251, 20252, 20253, 20254, 20255, 20256, 20257, 20258, 20260, 20261, 20262, 20263, 20264, 20265, 20266, 20267, 20268, 20270, 20271, 20272, 20273, 20274, 20275, 20276, 20277, 20278, 20280, 20281, 20282, 20283, 20284, 20285, 20286, 20287, 20288, 20290, 20291, 20292, 20293, 20294, 20295, 20296, 20297, 20298, 20300, 20301, 20302, 20310, 20311, 20312, 20380, 20381, 20382, 20400, 20401, 20402, 20410, 20411, 20412, 20420, 20421, 20422, 20480, 20481, 20482, 20490, 20491, 20492, 20500,

	20501, 20502, 20510, 20511, 20512, 20520, 20521, 20522, 20530, 20531, 20532, 20580, 20581, 20582, 20590, 20591, 20592, 20600, 20601, 20602, 20610, 20611, 20612, 20620, 20621, 20622, 20680, 20681, 20682, 20690, 20691, 20692, 20700, 20701, 20702, 20710, 20711, 20712, 20720, 20721, 20722, 20780, 20781, 20782, 20800, 20801, 20802, 20810, 20811, 20812, 20820, 20821, 20822, 20880, 20881, 20882, 20890, 20891, 20892, 20900, 20901, 20902, 20903, 20910, 20911, 20912, 20913, 20914, 20915, 20916, 20917, 20920, 20921, 20922, 20923, 20924, 20925, 20926, 20927, 20929, 20930, 20931, 20932, 20933, 20934, 20935, 20936, 20940, 20941, 20942, 20943, 20950, 20951, 20952, 20953, 20954, 20955, 20956, 20957, 20960, 20961, 20962, 20963, 20964, 20965, 20966, 20967, 20969, 20970, 20971, 20972, 20973, 20974, 20975, 20979, 2300, 2301, 2302, 2303, 2304, 2305, 2306, 2307, 2308, 2309, 2310, 2311, 2312, 2318, 2319, 2320, 2321, 2322, 2323, 2324, 2325, 2326, 2327, 2328, 2329, 2330, 2331, 2332, 23330, 23331, 23332, 23339, 2334, 2335, 2336, 2337, 2339, 2340, 2348, 2349, 2350, 2351, 2352, 2353, 2354, 2355, 2356, 2357, 2358, 2359, 2360, 2361, 2362, 2363, 2364, 2365, 2366, 2367, 23690, 23691, 23699, 2370, 2371, 2372, 2373, 2374, 2375, 2376, 23770, 23771, 23772, 23773, 23779, 2379, 2380, 2381, 2382, 2383, 2384, 2385, 2386, 23871, 23872, 23873, 23874, 23875, 23876, 23877, 23879, 2388, 2389, 2390, 2391, 2392, 2393, 2394, 2395, 2396, 2397, 23981, 23989, 2399
Obesity	27800, 27801, 27802, 27803, 2781

*: Variable was defined by CCS diagnosis code and all the 15 CCS diagnosis code columns were searched.

Elixhauser Comorbidity Index Scores:
HCUP official website offers Elixhauser Comorbidity Software to assign two variables that identify comorbidities in hospital discharge records: *readmission score* and *in-hospital mortality score*. “These two comorbidity index scores can be used in analyses in place of the 29 HCUP comorbidities variables, which include Acquired immune deficiency syndrome, Alcohol abuse, Chronic blood loss anemia, Chronic pulmonary disease, Coagulopathy, Congestive heart failure, Deficiency Anemias, Depression, Diabetes w/ chronic complications, Diabetes w/o chronic complications, Drug abuse, Fluid and electrolyte disorders, Hypertension, Hypothyroidism, Liver disease, Lymphoma, Metastatic cancer, Obesity, Other neurological disorders, Paralysis, Peptic ulcer Disease x bleeding, Peripheral vascular disease, Psychoses, Pulmonary circulation disease, Renal failure, Rheumatoid arthritis/collagen vas, Solid tumor w/out metastasis, Valvular disease, Weight loss. The comorbidity index scores for each observation are calculated as a weighted sum of each of the binary comorbidity variables on the record. ” (More detailed information about Elixhauser Comorbidity Software can be referred at https://www.hcup-us.ahrq.gov/toolssoftware/comorbidity/comorbidity.jsp)

A6 Complications occurred mainly in course of labor and delivery:

Postpartum hemorrhage	66600, 66602, 66604, 66610, 66612, 66614, 66620, 66622, 66624, 66630, 66632, 66634
Postpartum infection	67000, 67002, 67004, 67010, 67012, 67014, 67020, 67022, 67024, 67030, 67032, 67034, 67080, 67082, 67084
Laceration (third/fourth degree/unspecified/vulvar and perineal hematoma during delivery/anal sphincter tear complicating delivery, not associated with third degree perineal laceration)	66420, 66421, 66424, 66430, 66431, 66434, 66440, 66441, 66444, 66450, 66451, 66454, 66460, 66461, 66464

A7 Obstetric complications and other obstetric variables:

Preterm labor	64400, 64403, 64410, 64413, 64420, 64421	
Transient hypertension of pregnancy	64230, 64231, 64232, 64233, 64234	
Any type of Eclampsia*	Eclampsia (Eclampsia complicating pregnancy childbirth or the puerperium)	64260, 64261, 64262, 64263, 64264
	Severe preeclampsia	64250, 64251, 64252, 64253, 64254
	Mild preeclampsia	64240, 64241, 64242, 64243, 64244
	Pre-eclampsia or eclampsia superimposed on pre-existing hypertension and unspecified hypertension complicating pregnancy childbirth or the puerperium	64270, 64271, 64272, 64273, 64274, 64290, 64291, 64292, 64293, 64294
Gestational diabetes mellitus	64800, 64801, 64802, 64803, 64804, 25000	
Antepartum hemorrhage	64090, 64091, 64093	
Abruptio placentae and placenta previa	64110, 64111, 64112, 64113, 64120, 64121, 64122, 64123, 64130, 64131, 64132, 64133, 64180, 64181, 64182, 64183, 64190, 64191, 64192, 64193	
Fluid and electrolyte imbalance	2760, 2761, 2762, 2763, 2764, 27650, 27651, 27652, 27661, 27669, 2767, 2768, 2769	
Tranfusion	9900, 9902, 9904, 9907	
Intrauterine growth restriction	76490, 76491, 76492, 76493, 76494, 76495, 76496, 76497, 76498, 76499	
Premature rupture of membranes	65810, 65811, 65813	
Early onset of delivery	64420, 64421	
Uterine rupture (before onset of labor, during labor)	66500, 66501, 66503, 66510, 66511	

A8 Major adverse cardiovascular and cerebrovascular events (MACCE) in AMI patients:

In-hospital death (variable Y/N)	NIS data variable "DIED"
Cardiac arrest	4275
Cardiogenic shock	78551
Postpartum hemorrhage	66600, 66602, 66604, 66610, 66612, 66614, 66620, 66622, 66624, 66630, 66632, 66634
Bleeding / Transfusion	9900, 9901, 9902, 9903, 9904, 9905, 9906, 9907, 9908, 9909, 2851, 36243, 36281, 36361, 36362, 36372, 36441, 37632, 37742, 37923, 4230, 430, 431, 4320, 4321, 4329, 4560, 45620, 5307, 53082, 53100, 53101, 53120, 53121, 53140, 53141, 53160, 53161, 53200, 53201, 53220, 53221, 53240, 53241, 53260, 53261, 53300, 53301, 53320, 53321, 53340, 53341, 53360, 53361, 53400, 53401, 53420, 53421, 53440, 53441, 5346, 53461, 5693, 5780, 5781, 5789, 56881, 59970, 59971, 71910, 71911, 71912, 71913, 71914, 71915, 71916, 71917, 71918, 71919, 7847, 7848, 78630, 78631, 78639, 4590, 92300, 92301, 92302, 92303, 92309, 92400, 92401, 92410, 92411, 92420, 92421, 9243, 9244, 9245, 9248, 9249, 9222, 92231, 92232, 92233, 9228, 9229, 99811, 99812
Heart failure	4280, 4281, 42820, 42821, 42822, 42823, 42830, 42831, 42832, 42833, 42840, 42841, 42842, 42843, 4289, 40291
Arrhythmia	4260, 42610, 42611, 42612, 42613, 4262, 4263, 4264, 42650, 42651, 42652, 42653, 42654, 4266, 4267, 42681, 42682, 42689, 4269, 4270, 4271, 4272, 42731, 42732, 42741, 42742, 4275, 42760, 42761, 42769, 42781, 42789, 4279
Stroke	431, 43300, 43301, 43310, 43311, 43320, 43321, 43330, 43331, 43380, 43381, 43390, 43391, 43400, 43401, 43410, 43411, 43490, 43491, 4350, 4351, 4352, 4353, 4358, 4359, 436
Cardiac complications of anesthesia or other sedation in labor and delivery	66810, 66811, 66812, 66813, 66814
Pulmonary embolism and infarction	515
Arterial embolism and thrombosis	44401, 44409, 4441, 44421, 44422, 44481, 44489, 4449
Artheroembolism	44501, 44502, 44581, 44589
Obstetrical pulmonary embolism	67300, 67301, 67302, 67303, 67304, 67310, 67311, 67312, 67313, 67314, 67320, 67321, 67322, 67323, 67324, 67330, 67331, 67332, 67333, 67334, 67380, 67381, 67382, 67383, 67384
Respiratory failure or arrest	5173, 5185, 51851, 51852, 51853, 51881, 51882, 51883, 51884, 7991
Acute renal failure	5845, 5846, 5847, 5848, 5849, 586

Table S1. Multivariate Predictors of AMI in Pregnancy.

Variable	Odds ratio with 95% C.I.	P-value*
Records' status		
Labor and delivery vs Postpartum	0.4 (0.3, 0.5)	<.0001
Pregnancy vs Postpartum	4.8(4.1, 5.8)	
Length of Stay	1.0 (1.0, 1.0)	<.0001
Elixhauer comorbidity index score of readmission	1.0 (1.0, 1.0)	<.0001
Elixhauer comorbidity index score of mortality	1.1 (1.1, 1.1)	<.0001
Age group		<.0001
25-29 vs 18-24	1.7 (1.3, 2.2)	
30-34 vs 18-24	3.2 (2.5, 4.1)	
35-39 vs 18-24	5.1 (4.0, 6.7)	
40-55 vs 18-24	7.7 (5.7, 10.3)	
Race/ethnicity		0.0200
Asian or Pacific islander vs White	0.8 (0.5, 1.2)	
Black vs White	1.3 (1.0, 1.5)	
Hispanic vs White	1.0 (0.8, 1.2)	
Other race or Unknown vs White	1.2 (1.0, 1.5)	
Primary expected payer		<.0001
Medicaid vs Private insurance	1.0 (0.9, 1.2)	
Medicare vs Private insurance	0.3 (0.2, 0.5)	
Other or unknown vs Private insurance	0.8 (0.6, 1.1)	
Alcohol and substance abuse	1.1 (0.7, 2.0)	0.6620
Atrial fibrillation/flutter	2.7 (1.5, 4.7)	0.0006
Cancer	0.5 (0.2, 1.3)	0.1763
Coronary artery disease	517.4 (420.8, 636.2)	<.0001
Hyperlipidemia	4.3 (3.2, 5.8)	<.0001
Heart failure	8.2 (1.9, 35.2)	0.0047
Obesity	1.9 (1.4, 2.5)	<.0001
Other substance history	2.1 (1.4, 3.1)	0.0004

Variable	Odds ratio with 95% C.I.	P-value*
Prior CABG	0.1 (0.0, 0.4)	0.0002
Prior implantable cardioverter defibrillator	0.6 (0.3, 1.4)	0.2291
Prior myocardial infarction	0.1 (0.0, 0.1)	<.0001
Prior PCI	0.2 (0.1, 0.4)	<.0001
Prior transient ischemic attack or stroke	0.4 (0.2, 1.0)	0.0373
Prior valve replacement	6.4 (2.4, 17.0)	0.0002
Smoking history	1.7 (1.4, 2.1)	<.0001
Thrombophilia (including history of thrombosis and antiphospholipid syndrome)	1.7 (1.2, 2.5)	0.0035
Any type of Eclampsia		<.0001
Eclampsia (Eclampsia complicating pregnancy childbirth or the puerperium) vs No	6.0 (3.3, 10.8)	
Mild preeclampsia vs No	1.5 (1.0, 2.3)	
Preeclampsia or eclampsia superimposed on pre-existing hypertension and Unspecified hypertension complicating pregnancy childbirth or the puerperium vs No	3.2 (2.5, 4.2)	
Severe preeclampsia vs No	2.0 (1.3, 3.0)	
Abruptio placentae and placenta previa	1.6 (1.0, 2.3)	0.0290
Fluid and electrolyte imbalance	1.1 (0.8, 1.4)	0.5183
Gestational diabetes mellitus	0.8 (0.6, 1.1)	0.1741
Preterm labor	0.6 (0.4, 0.8)	0.0006
Premature rupture of membranes	0.4 (0.2, 0.9)	0.0206
Thrombotic event	3.8 (2.3, 6.2)	<.0001
Uterine rupture (before onset of labor, during labor)	4.2 (1.4, 13.0)	0.0127
Laceration	0.3 (0.1, 0.9)	0.0278
Postpartum hemorrhage	2.5 (1.9, 3.2)	<.0001
Postpartum infection	4.0 (2.7, 5.7)	<.0001

AMI: Acute Myocardial Infarction; CABG: Coronary Artery Bypass Grafting; PCI: Percutaneous Coronary Intervention

Table S2. Multivariate Predictors of MACCE in AMI in Pregnancy.

Variable	Odds Ratio, 95% C.I.	P-value*
Records' status		<.0001
Labor and delivery vs Postpartum	3.4 (2.0, 5.7)	
Pregnancy vs Postpartum	3.7 (2.5, 5.3)	
Length of Stay	1.0 (0.9, 1.0)	0.0022
Elixhauer comorbidity index score of readmission	0.9 (0.9, 1.0)	<.0001
Elixhauer comorbidity index score of mortality	0.9 (0.9, 0.9)	<.0001
Age group		0.2814
18-24 vs 30-34	0.7 (0.4, 1.4)	
25-29 vs 30-34	1.3 (0.8, 2.1)	
35-39 vs 30-34	0.8 (0.5, 1.2)	
40-55 vs 30-34	1.0 (0.6, 1.7)	
AMI location		0.0441
Anterior vs Subendocardial infarction	1.0 (0.6, 1.7)	
Anterolateral vs Subendocardial infarction	1.6 (0.8, 3.6)	
Inferolateral vs Subendocardial infarction	0.2 (0.0, 1.0)	
Inferoposterior vs Subendocardial infarction	8.2 (1.2, 54.0)	
Other inferior wall vs Subendocardial infarction	0.9 (0.4, 1.7)	
Other lateral wall vs Subendocardial infarction	4.3 (0.5, 32.9)	
Other specified sites vs Subendocardial infarction	3.9 (1.2, 12.5)	
True posterior wall vs Subendocardial infarction	0.0 (0.0, I)	
Coronary artery disease	0.9 (0.6, 1.3)	0.5744
Hyperlipidemia	1.4 (0.9, 2.4)	0.1542
Prior PCI	6.6 (1.4, 31.2)	0.0170
Smoking history	0.9 (0.6, 1.3)	0.5488
Thrombophilia (including history of thrombosis and antiphospholipid syndrome)	1.0 (0.4, 2.4)	0.9539
Eclampsia		0.0153

Variable	Odds Ratio, 95% C.I.	P-value*
Eclampsia (Eclampsia complicating pregnancy childbirth or the puerperium) vs No	0.2 (0.0, 1.4)	
Mild preeclampsia vs No	0.8 (0.3, 2.2)	
Preeclampsia or eclampsia superimposed on pre-existing hypertension and Unspecified hypertension complicating pregnancy childbirth or the puerperium vs No	2.3 (1.3, 3.9)	
Severe preeclampsia vs No	1.3 (0.5, 3.6)	
Abruptio placentae and placenta previa	0.3 (0.1, 1.0)	0.0555
Fluid and electrolyte imbalance	2.4 (1.3, 4.2)	0.0034
Thrombotic event	0.6 (0.1, 2.8)	0.5632
Postpartum infection	0.3 (0.1, 1.3)	0.1055

MACCE: Major adverse cardiovascular and cerebrovascular events; AMI: Acute Myocardial Infarction; CABG: Coronary Artery Bypass Grafting; PCI: Percutaneous Coronary Intervention