Trends in Incidence and Outcomes of Pregnancy-Related Acute Myocardial Infarction (From a Nationwide Inpatient Sample Database)

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Acute myocardial infarction (AMI) during pregnancy is rare but fatal complication. Recent incidence of pregnancy related AMI and trends in the related outcomes are unknown. The Nationwide Inpatient Sample database was utilized from years 2005 to 2014. International Classification of Disease-Ninth Revision were used to identify pregnancy related admissions and AMI. Primary outcome was incidence and trend of AMI related to pregnancy and Secondary outcomes were trends in mortality, resource utilization, and predictors of AMI during pregnancy. Simple logistic regression model was used to calculate predictors of AMI during pregnancy. p Values for trends were generated by Cochrane-Armitage test for categorical variables and simple linear regression for continuous variables. A total of 43,437,621 pregnancy related hospitalization and 3,786 cases of AMI (86% ante-partum and 14% postpartum) were noted during study period. The incidence of AMI during the study period was 8.7 per 100,000 pregnancies with an overall increase in incidence during the study period (relative increase of 18.9%, p <0.001). There was a concomitant decrease in mortality (relative decrease of 40.05%, p <0.001), cost of care (relative decrease of 8.70%, p <0.001), and length of stay (relative decrease of 13.53%, p <0.001). Significant predictors of AMI during pregnancy were higher age of pregnancy, black race, co-morbidities such as hypertension, thrombophilia, diabetes milletus, substance abuse, smoking, hyperlipidemia, heart failure, deep venous thrombosis, transfusion, fluid and electrolyte imbalance, and postpartum complications such as hemorrhage, infection, and depression. In conclusion, the incidence of AMI 2005 to 2014 rose with a concomitant decrease in mortality and resource utilization. High-risk patient characteristics were identified which could be utilized for resource allocation to further improve outcomes. **(Am J Cardiol 2019;123:1220−1227)**

Pregnancy related mortality in the United States has steadily increased from 7.2 deaths per 100,000 live births in 1987 to approximately 17.3 deaths per 100,000 live births in 2013.[1] Cardiovascular diseases have been identified as the leading cause of pregnancy related mortality (15.5%).[2] An incidence rate of 2.8 to 6.2 has been reported for AMI during pregnancy.[3,4] Maternal mortality rate ranging 7% to 11% and fetal mortality rate 5% to 9% has been noted by single centered studies.[5,6] Despite occurring in all ages, risk of AMI with pregnancy increases with advancing maternal age, particularly after 30 years.[3] This is concerning as birth rates have increased for women aged 35 to 44 years[7] in recent years. Despite available information on pregnancy related AMI and its outcomes from small, highly skilled centers, there is a constant need for population-based study which correlate to the United States population in the "real world." Our study is aimed at providing recent trends in pregnancy related AMI and associated outcomes to assess the effectiveness of current practices.

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See page 1226 for disclosure information.

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Methods

We analyzed data from the Nationwide Inpatient Sample (NIS) files from 2005 to 2014.[8] NIS is sponsored by the Agency for Healthcare Research and Quality and is a part of the Healthcare Cost and Utilization Project (HCUP). It is the largest publicly available discharge level data on nearly 8 million inpatient hospitalizations from 1,000 hospitals each year and designed to approximate a 20% sample of the US community hospitals representing more than 95% of the US population.[9] Data in NIS are drawn from all the states participating in HCUP, which comprise approximately 97% of the US population. Each hospitalization is deidentified and maintained in the NIS as a unique entry with 1 primary discharge diagnosis and <24 secondary diagnoses during that hospitalization. Each entry also carries information on patient's demographics, insurance status, comorbidities, primary and secondary procedures, hospital charges, and in-hospital outcomes. The inclusion of discharge weight for each patient allows extrapolation to calculate expected national hospitalization rates. The NIS database results have been shown to correlate well with other hospitalization discharge databases in the United States.[10] It has also been used to explain trends in other acute medical and surgical conditions.[11,12]

A discharge record was classified as pregnancy related (Pregnancy admission or postpartum admission), if appropriate International Classification of Diseases-Ninth edition, Clinical Modification (ICD-9-CM) was present in any of the diagnostic or procedural fields. A pregnancy admission was defined as any discharge record with a pregnancy-related code (ICD-9 codes 630 to 648) or delivery code (ICD-9 procedural codes 74 for cesarean delivery and 72,73,75,v27, or diagnostic codes 650 to 659 for vaginal delivery). A postpartum admission was defined as any discharge record that included a postpartum diagnosis (ICD-9 codes 670 to 677) and did not also include a delivery code (Supplementary Table 1). This gave us study cohort of 9,115,152 patients with pregnancy related hospital admission. We excluded patients with age <18 years, missing data on age, gender, survival, and/or discharge disposition, type of admission, and length of stay (n = 287,578). This resulted in a cohort of 8,827,574 patients which comprise our study sample. Although NIS represents a 20% stratified random sample of US hospitals, analyses were performed using hospital-level discharge weights provided by the NIS to obtain national estimates of pregnancy related (43,240,000 for pregnancy and n = 197,621 for Postpartum) hospitalizations (Figure 1). Acute myocardial infarction was identified by using ICD-9 CM code 410.xx in both primary and secondary diagnostic field.

The patient level characteristics include demographics (age, race), clinically relevant comorbidities and pregnancy or delivery complications. The ICD-9-CM codes and clinical classification software codes provided by Agency for Healthcare Research and Quality[13] that were used to identify comorbidities are provided in the Supplementary Table 2. The HCUP NIS contains data on total charges for each hospital in the databases, which represents the amount that hospitals billed for services. To calculate estimated cost of hospitalizations, the NIS data were merged with cost to charge ratios available from HCUP.14 Using the merged data elements from the cost to charge ratios files and the total charges reported in the NIS database, we converted the hospital total charge data to cost estimates by simply multiplying total charges with the appropriate cost to charge ratios. These costs are essentially standardized, can be measured across hospitals, and are used for the remainder of this report. Adjusted annual costs were calculated in terms of the 2013 cost, after adjusting for inflation according to the latest consumer price index data released by the US government on February 15, 2017.[14] Similar methods have been used using HCUP databases previously.[15,16]

All the analyses were performed using the designated weight specified in the dataset. Pearson chi square test was utilized for examining the baseline characteristics for categorical variables (expressed in percentages). We used the Cochrane-Armitage test to evaluate the trend of AMI, in hospital mortality and simple linear regression method to calculate trends of Cost of hospitalization. A p value of <0.05 was considered significant. We generated a simple logistic regression model to calculate the odds ratio (OR) with 95% confidence intervals (CIs) for age, race, payment methods, medical conditions, and obstetric complications for predictors of AMI in our study cohort. The statistically and clinically significant risk factors, from the analyses of single independent variables, were included in final multivariable logistic regression model.

The analysis in the present study follows the methodological standards recommended for studies utilizing NIS database. This study was deemed exempt from approval by the Mount Sinai St. Luke's-West hospital Institutional Review board as HCUP is a publicly available database that contains deidentified patient data and no patient consent was required.

Result

During the study period from 2005 to 2014, there were a total of 43,437,621 pregnancy related hospitalizations, which included pregnancy hospitalizations (43,240,000) and postpartum hospitalizations (197,621). Among the pregnancy related hospitalizations, there were 3,786 cases of AMI including 3,252 cases (86%) during pregnancy hospitalization and 534 cases (14%) during postpartum hospitalizations.

The baseline characteristics of patients with and without AMI are shown in Table 1. Compared to those without AMI, the majority of patients with AMI were above 30 years of age (71.4 %) with the highest prevalence among age group 30−34 years (29.1 %), and black population (25.17 %). Most prevalent comorbidities in patients with AMI were hypertension (32.38%), heart failure (24.82%), anemia (21.9%), and hyperlipidemia (13.87%). A significantly higher prevalence of pregnancy related complications was noted in patients with AMI compared to those without it. Most notable pregnancy related complications in descending order were: preeclampsia, eclampsia, and gestational hypertension (28.6% vs 9.71%, p value <0.001), fluid and electrolyte imbalance (22.87% vs 1.23%, p value <0.001), transfusion (14.8% vs 1.2%, p value <0.001),

TABLE 1
Baseline characteristics of patients with and without pregnancy related AMI

Variable	Acute myocardial infarction			p value
	No	Yes	Overall	
Total pregnancy related hospitalizations	43433835	3786	43437621	
Age (years)				
<20	6.58%	1.54%	6.58%	<0.001
20-24	24.88%	8.58%	24.88%	<0.001
25-29	28.72%	18.48%	28.72%	<0.001
30-34	24.61%	29.1%	24.61%	<0.001
35-39	12.26%	26.73%	12.26%	<0.001
≥40	2.96%	15.57%	2.96%	<0.001
White	44%	37.72%	44%	<0.001
Black	12.15%	25.17%	12.15%	<0.001
Hispanic	18.86%	12.42%	18.86%	<0.001
Others	9.05%	8.12%	9.05%	<0.001
Missing	15.94%	16.57%	15.94%	<0.001
Hypertension*	8.14%	32.38%	8.14%	<0.001
Thrombophilia (including history of thrombosis and antiphospholipid syndrome)*	0.12%	2.22%	0.12%	<0.001
Anemia§	10.57%	21.9%	10.57%	<0.001
Diabetes mellitus*	1.32%	9.8%	1.32%	<0.001
Obesity‡	3.95%	11.99%	3.95%	<0.001
Migraine headaches*	0.62%	2.24%	0.62%	<0.001
Alcohol and substance abuse*	1.58%	5.82%	1.58%	<0.001
Smoker	1.06%	7.5%	1.06%	<0.001
Hyperlipidemia¶	0.13%	13.87%	0.13%	<0.001
History of myocardial infarction*	0.02%	2.2%	0.02%	<0.001
Hypothyroidism*	2.13%	4.56%	2.13%	<0.001
SLE*	0.14%	0.54%	0.14%	<0.001
Congestive heart failure*	0.13%	24.82%	0.13%	<0.001
DVT*	0.1%	1.3%	0.1%	<0.001
Pregnancy or delivery complication				
Preterm labor*	8.41%	5.48%	8.41%	<0.001
Antepartum hemorrhage*	1.82%	2.49%	1.82%	0.002
Preeclampsia, eclampsia, and gestational hypertension*	9.71%	28.6%	9.71%	<0.001
Postpartum hemorrhage*	3.17%	9.78%	3.17%	<0.001
Transfusion*	1.2%	14.38%	1.2%	<0.001
Postpartum infection*	0.9%	4.87%	0.9%	<0.001
Fluid and electrolyte imbalance*	1.23%	22.87%	1.23%	<0.001
Postpartum depression*	4.99%	10.99%	4.99%	<0.001

DVT = deep venous thrombosis
* ICD 9 CM codes were used to describe these variables and are mentioned in Supplementary Table 2.
‡ Obesity was defined as BMI >30
§ Anemia was defined with Hemoglobin <11
¶ Hyperlipidemia was defined with ICD9 code 272, which represents Pathological conditions resulting from abnormal anabolism or catabolism of lipids in the body.

postpartum depression (10.99% vs 4.99%, p value <0.001), postpartum hemorrhage (9.78% vs 3.17%, p value <0.001), and postpartum infection (4.87% vs 0.9%, p value <0.001).

Overall incidence of AMI was 8.7 per 100,000 pregnancies, with a significant increase in incidence during the study period (relative increase of 18.9%, p <0.001). The magnitude of rise in incidence of pregnancy related AMI was higher during postpartum period compared to pregnancy period (relative increase 43.7% vs 7.5%). Cumulative mortality rate associated with AMI in pregnancy was 4.3%. A significant decline in mortality was noted during study period (relative decrease 40.05%, p <0.001). Average cost of care was 15980 USD and length of stay was 7.3 days. We noted a significant decline in both cost of care and length of stay during study period (relative decrease of 8.70% and 13.53%, respectively) (Figure 2).

The mean hospital stays ranged 4.8 to 9.0 days and varied based on the type and location of AMI. The most common type of AMI was subendocardial infarction (60.9%) with a mean hospital stay of 7.4 days, followed by anterior wall infarction (10.8%) with a mean hospital stay of 6.4 days. Among patients with AMI, heart catheterization, endotracheal intubation, and coronary artery bypass grafting were the most commonly performed procedures (Supplementary Table 3).

On unadjusted logistic regression model, we found age to be significant predictor of AMI. Patients aged 40 or older have highest odds of AMI (OR = 22.3, 95% CI 12.3 to 40.4,

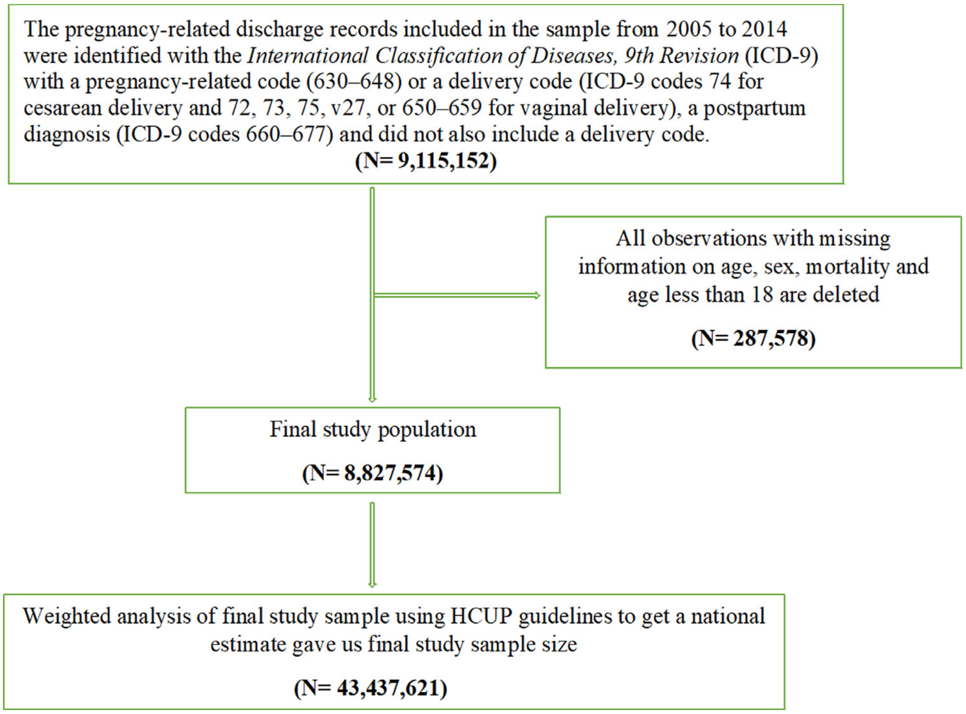

FIGURE 1. Data extraction algorithm.

p <0.001) when compared to patients with age <20 years. Additionally, Black women were more likely to suffer AMI (OR = 2.4, 95% CI 2.0 to 2.9, p <0.001) while Hispanic women had lower odds of AMI during pregnancy (OR = 0.8, 95% CI 0.6 to 0.96, p <0.001) when compared to white women. The socio-economic status of the patient also affected the risk of AMI. Patients with a highest median household income category (76 to 100th percentile) had lower odds of AMI (OR = 0.7, 95% CI 0.6 to 0.9, p = 0.004) when compared to patients with the lowest median household income category (0 to 25th percentile) (Table 2a).

Simple logistic regression of various medical conditions associated with the risk of AMI in pregnancy is shown in Table 2b. Medical conditions associated with significantly higher odds of AMI included congestive heart failure (OR = 265, 95% CI 224.7 to 312.4, p <0.001), hyperlipidemia (OR = 124.1, 95% CI 101.1 to 152.2, p <0.001), thrombophilia including history of thrombosis and antiphospholipid syndrome (OR = 18.5, 95% CI 11.5 to 30, p <0.001), deep vein thrombosis (OR = 13.5, 95% CI 7.2 to 25.2, p <0.001), and diabetes mellitus (OR = 8, 95% CI 6.3 to 10.2, p <0.001). Other medical conditions associated with significantly higher odds of AMI included smoking (OR = 7.5, 95% CI 5.7 to 9.8, p <0.001), hypertension (OR = 5.4, 95% CI 4.7 to 6.3, p <0.001), and alcohol or substance abuse (OR = 3.9, 95% CI 2.9 to 5.3, p <0.001).

Simple logistic regression of various obstetric conditions associated with the risk of AMI in pregnancy is shown in Table 2c. Obstetric complications associated with significantly higher odds of AMI included fluid and electrolyte balance (OR = 23.8, 95% CI 20.1 to 28.2, p <0.001), transfusion (OR = 13.7, 95% CI 11.2 to 16.8, p <0.001),

Table 2a
Pregnancy-related acute myocardial infarction by age, race, insurance and median household income

Demographic variable	Frequency (% of AMI cases)	OR (95% CI)	p value
Age (years)			
<20	58 (51.54%)	Referent	
20-24	325 (8.58%)	1.5 (0.8-2.7)	<0.001
25-29	700 (18.48%)	2.7 (1.5-4.9)	<0.001
30-34	1102 (29.1%)	5.0 (2.8-8.9)	0.004
35-39	1012 (26.73%)	9.1 (5.1-16.3)	<0.001
≥40	590 (15.57%)	22.3 (12.3-40.4)	<0.001
White	1428 (37.72%)	Referent	
Black	953 (25.17%)	2.4 (2.0-2.9)	<0.001
Hispanic	470 (12.42%)	0.8 (0.6-0.96)	<0.001
Others	308 (8.12%)	1.0(0.8-1.4)	0.233
Missing	627 (16.57%)		
Median household income category for patient's zip code*			
1. 0-25th percentile	1182 (31.81%)	Referent	
2. 26-50th percentile	974 (26.21%)	0.9 (0.7-1.1)	0.451
3. 51-75th percentile	895 (24.08%)	0.8 (0.7-1.0)	0.841
4. 76-100th percentile	665 (17.9%)	0.7 (0.6-0.9)	0.004
Primary payer			
Medicare / Medicaid	1738 (45.89%)	Referent	
Private including HMO	1797 (47.47%)	0.9 (0.8-1.0)	0.393
Self-pay/no charge/other	252 (6.64%)	1.0 (0.7-1.3)	0.964

CI = confidence interval.
HMO: Health Maintenance Organization
* Represents a quartile classification of the estimated median household income of residents in the patients ZIP Code, derived from ZIP Code-demographic data obtained from Claritas. The quartiles are identified by values of 1 to 4, indicating the poorest to wealthiest populations. Because these estimates are updated annually, the value ranges vary by year. https://www.hcup-us.ahrq.gov/db/vars/zipinc_qrtl/nrdnote.jsp

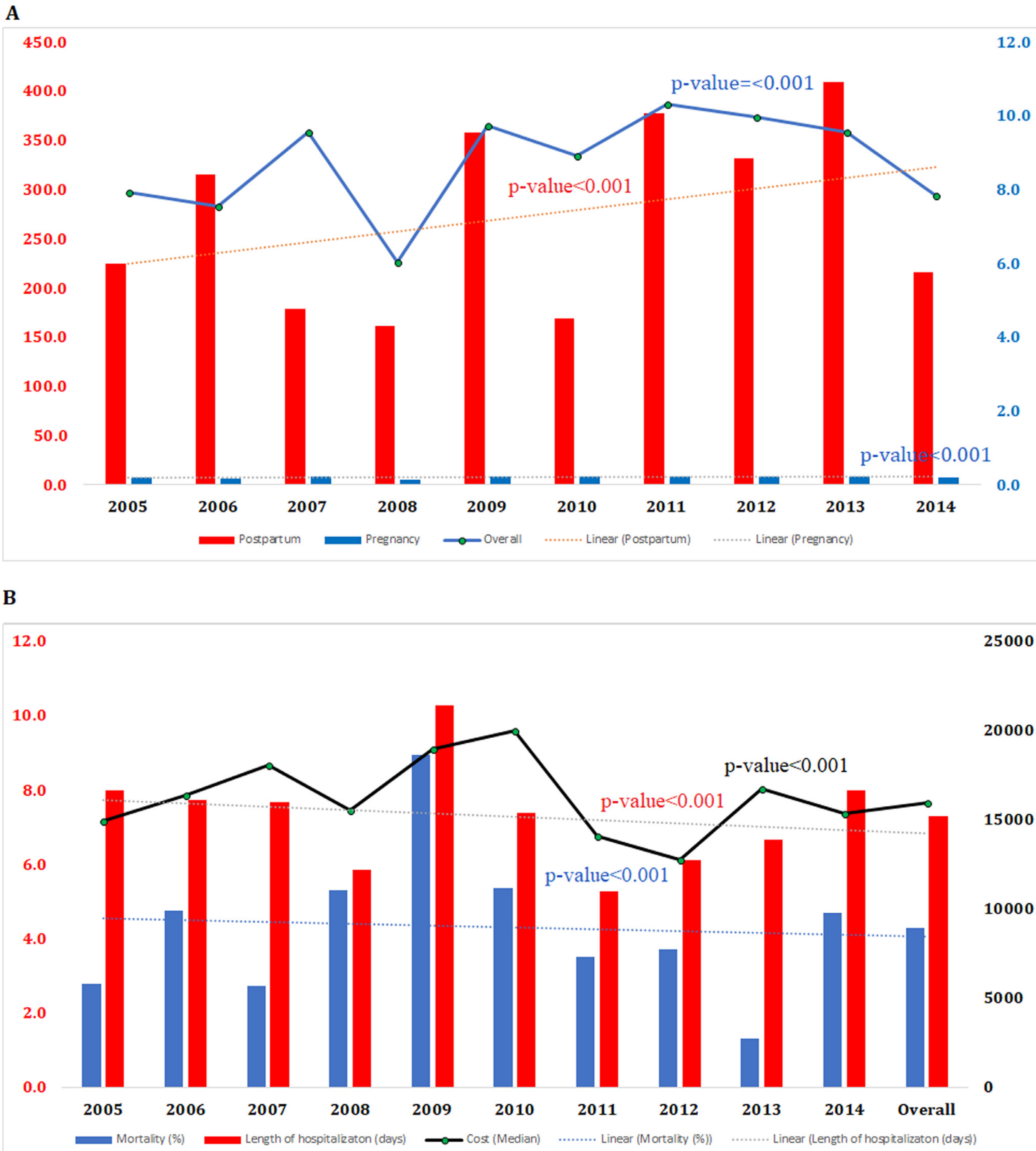

FIGURE 2. Trends in incidence of AMI, mortality, cost of care and length of hospitalization.

postpartum infection (OR = 5.6, 95% CI 4.0 to 7.8, p <0.001), pre-eclampsia, eclampsia, and gestational hypertension (OR = 3.7, 95% CI 3.2 to 4.4, p <0.001), postpartum hemorrhage (OR = 3.3, 95% CI 2.6 to 4.1,p = 0.012), and postpartum depression (OR = 2.3, 95% CI 1.9 to 2.9, p <0.001)(Table 2c).

Multivariable analysis was generated by entering statistically and clinically significant risk factors from simple logistic regression into a multivariable logistic regression model (Table 3). When other risk factors are controlled, age ≥40 years compared to <20 years, black race compared to white, congestive heart failure, hyperlipidemia, thrombophilia including history of thrombosis and

TABLE 2b
Medical conditions and the risk of pregnancy-related acute myocardial Infarction

Medical condition*	Frequency (% of AMI cases)	OR (95% CI)	p value
Hypertension	1226 (32.38%)	5.4 (4.7-6.3)	<0.001
Thrombophilia (including history of thrombosis and antiphospholipid syndrome)	84 (2.22%)	18.5 (11.5-30)	<0.001
Anemia	829 (21.9%)	2.4 (2-2.8)	<0.001
Diabetes mellitus	371 (9.8%)	8 (6.3-10.2)	<0.001
Obesity	454 (11.99%)	3.3 (2.6-4.1)	0.475
Migraine headaches	85 (2.24%)	3.7 (2.3-5.9)	0.043
Alcohol and substance abuse	220 (5.82%)	3.9 (2.9-5.3)	<0.001
Smoking	284 (7.5%)	7.5 (5.7-9.8)	<0.001
Hyperlipidemia	525 (13.87%)	124.1 (101.1-152.2)	<0.001
Hypothyroidism	172 (4.56%)	2.1 (1.5-3.0)	0.057
Congestive heart failure	940 (24.82%)	265 (224.7-312.4)	<0.001
DVT	49 (1.3%)	13.5 (7.2-25.2)	<0.001

AMI = acute myocardial infarction; CI = confidence interval

* Medical conditions defined by ICD 9 CM code mentioned in supplementary Table 2

TABLE 2c
Obstetric complications and the risk of pregnancy-related acute myocardial infarction

Obstetric complications*	Frequency (% of AMI cases)	OR (95% CI)	p value
Antepartum hemorrhage	94 (2.49%)	1.4 (0.9-2.2)	0.167
Preeclampsia, eclampsia, and gestational hypertension	1083 (28.6%)	3.7 (3.2-4.4)	<0.001
Postpartum hemorrhage	370 (9.78%)	3.3 (2.6-4.1)	0.012
Transfusion	545 (14.38%)	13.7 (11.2-16.8)	<0.001
Postpartum infection	184 (4.87%)	5.6 (4.0-7.8)	<0.001
Fluid and electrolyte imbalance	866 (22.87%)	23.8 (20.1-28.2)	<0.001
Postpartum depression	416 (10.99%)	2.3 (1.9-2.9)	<0.001

CI = confidence interval

* Obstetric Complications defined by ICD 9 CM code and Procedural codes mentioned in supplementary Table 2,

antiphospholipid syndrome, diabetes mellitus, smoking, deep vein thrombosis, hypertension, alcohol or substance abuse, fluid and electrolyte imbalance, transfusion, postpartum infection, postpartum hemorrhage, and postpartum depression correlated significantly with a higher risk of AMI during pregnancy, whereas Hispanic race, anemia, migraine headaches, preeclampsia, eclampsia, and gestational hypertension lost significance.

Discussion

The following important conclusions can be drawn from our study (1) Incidence rate of 8.7 per 100,000 pregnancies was noted, with a relative increase of 18.9% from 2005 to 2014. A greater rise in incidence of AMI was observed during postpartum period compared to pregnancy period

TABLE 3
Multivariable analysis of significant risk factors

Risk factor	OR (95% CI)	p value
Age		
<20	Referent	
20-24	1.1 (0.6-2.2)	<0.001
25-29	2.4 (1.3-4.4)	0.013
30-34	4.5 (2.5-8.4)	<0.001
35-39	6.5 (3.5-12.1)	<0.001
≥40	10.1 (5.3-19.0)	<0.001
White	**Referent**	
Black	1.6 (1.3-1.9)	<0.001
Hispanic	0.9 (0.7-1.2)	0.072
Others	1.0 (0.7-1.3)	0.199
Medical condition		
Hypertension*	1.9 (1.5-2.5)	<0.001
Thrombophilia (including history of thrombosis and antiphospholipid syndrome)*	4.8 (2.7-8.5)	<0.001
Anemia*	1.2 (1.0-1.5)	0.081
Diabetes mellitus*	1.4 (1.0-1.9)	0.027
Migraine headaches*	1.4 (0.8-2.5)	0.199
Alcohol and substance abuse*	1.7 (1.2-2.6)	0.007
Smoking*	3.3 (2.3-4.6)	<0.001
Hyperlipidemia*	13.2 (9.9-17.6)	<0.001
Congestive heart failure*	26.0 (20.3-33.2)	<0.001
DVT*	2.8 (1.3-6.2)	0.010
Obstetric complications*		
Preeclampsia, eclampsia, and gestational hypertension*	1.3 (1.0-1.7)	0.056
Postpartum hemorrhage*	1.8 (1.3-2.4)	<0.001
Transfusion*	3.2 (2.4-4.2)	<0.001
Postpartum infection*	2.7 (1.9-3.9)	<0.001
Fluid and electrolyte imbalance*	5.2 (4.2-6.6)	<0.001
Postpartum depression*	1.4 (1.1-1.9)	0.013

CI = confidence interval

* Same as tables 2b and 2c

(43.7% vs 17.3%). (2) The overall mortality rate was 4.3%. Mortality and cost of care associated with AMI during pregnancy declined during study period. (3) Higher age, black race, certain comorbidities, and obstetric conditions predicted higher risk of AMI.

We report an incidence rate of 8.7 per 100,000 pregnancies during the years 2005 to 2014. Lower incidence rates have been reported in corporately older studies.[3,4] These differences in incidence rates could certainly be due to temporal, regional, and study design differences but also reflect the shift in mean age of pregnancy,[17] rise in prevalence of obesity,[18] and lesser degree of blood pressure control in American women in recent years,[19] as pointed out in the Multinational Monitoring of trends and determinants in CArdiovascular disease project. Gibson et al[20] reported higher rate of AMI during pregnancy in the United States compared to Canada and European countries. Risk of AMI during postpartum period is likely related to risks of takotsubo cardiomyopathy, coronary thrombosis, and particularly spontaneous coronary artery dissection during this period.[5,6] Elkayam et al[6] reported spontaneous coronary artery dissection as underlying pathology in approximately 67% of cases of AMI during postpartum period. Unfortunately, no effective preventive measures are available for spontaneous coronary artery dissection to date.

We noted an overall mortality rate of 4.3% among pregnant patients with AMI. Previously published studies have reported higher case fatality rates related to AMI in pregnancy.[3,4,21] We also noted a favorable trend in mortality due to pregnancy related AMI with a >40% decline over study period. Improved mortality in our study compared to older studies is likely driven by better implementation of multidisciplinary approaches, relatively better understanding of nonatherosclerotic AMI as well as increased institutional and operator awareness in recent years. We noted a declining cost of care during the study period which may reflect the salutary effect of early interventions due to improved diagnostic capabilities.

Our study sought to explore high-risk characteristics that predict AMI during pregnancy. Not surprisingly, we noted higher age to be strongly associated with risk of AMI during pregnancy with age ≥40 years had highest odds with more than a 10-fold increase in risk with age ≥40 years. Association of rising age with AMI in pregnancy has been noted before[3,4] but a more than 10-fold risk in age group ≥40 years hasn't been reported. This is an important finding as a rise in mean age of pregnancy[17] and birth rates among the age group 40 to 44 years[22] is expected to bring increased healthcare cost burden in United States. Additionally, we found hypertension, diabetes milletus, smoking, and hyperlipidemia as predictors of AMI during pregnancy, which is not surprising as these are well-established conventional risk factors for coronary artery disease.[3,23] Contrary to James et al,[3] black race remained independently associated with a higher risk of AMI during pregnancy, even after adjusting for conventional risk factors for coronary artery disease (CAD) in multivariate model. High risk of AMI during pregnancy in black population appears to be related to socioeconomic factors (i.e. limited access to high quality care, poor insurance coverage, and insufficient care access and prenatal counseling) in addition to high prevalence of comorbidities. This assumption is supported by the fact reported in our study that those with highest mean household incomes had decreased risk of AMI during pregnancy.

In line with previously published studies,[3,24] we found DVT, thrombophilia, heart failure, and drug abuse to be independent predictors of AMI during pregnancy. Pregnancy itself is a hypercoagulable state and coexisting DVT and thrombophilia predispose patients to coronary thrombosis which is a well-recognized nonatherosclerotic phenomenon of AMI in pregnant women. Similarly, drug abuse causes coronary spasm. Unable to meet high demand due to hemodynamic stress during pregnancy, heart failure patients are expected to be at high risk of type II AMI.

Certain pregnancy related conditions were found to be predictors of AMI. Preeclampsia predicted AMI in single variable unadjusted model but lost significance when adjusted for other risk factors, such as early age, black race, hypertension, diabetes, and thrombophilia, possibly reflecting the fact that preeclampsia itself is more prevalent in these subgroups.[25,26] Hemorrhage, infection, and depression were associated with a higher risk of AMI in pregnancy. These findings are in accordance with observations made by James et al.[3] Hemorrhage itself can lead to type II AMI but high utilization of vasospastic drugs such as methylergonovine to treat uterine atony could be an additional contributing factor. Similarly, infections and postpartum depression are now well-recognized risk factors for AMI.[27,28] Smeeth et al[27] reported increased risk of vascular events, including AMI and stroke, after acute infections, possibly due to systemic inflammation. However, the role of increased hemodynamic stress due to infections cannot be disregarded.

Like any other large database study our study also has few limitations. NIS, being an administrative database, is prone to errors related to coding inaccuracies. Long-term outcomes of pregnancy induced AMI were not reported in our study due to database limitation. We couldn't estimate AMI related fetal mortality rate due to similar reasons. However, our study is one of the largest available on pregnancy related AMI from data across the nation thus providing "real world" representation. In conclusion, we noted an increasing incidence of AMI during pregnancy in recent years but with concomitant improvement in mortality and resource utilization. Overall, these findings point toward improvement in diagnostic and treatment approaches.

Disclosures

None of the authors has any disclosures relevant to the content of the manuscript.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2019.01.030.

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