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Research paper

Trends in the incidence and in-patient outcomes of acute myocardial infarction in pregnancy: Insights from the national inpatient sample

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ABSTRACT

Study objective: Pregnancy-related morbidity and mortality rates in the United States are rising despite advances in knowledge, technology, and healthcare delivery. Cardiovascular disease is the leading cause of adverse pregnancy outcomes, with acute myocardial infarction (AMI) being a potential contributor to the worse outcomes in pregnancy.
Design/setting: We analyzed data from the national inpatient sample database to examine trends in the incidence and in-hospital outcomes of myocardial infarction in pregnancy from 2016 to 2020.
Participants: Using ICD-10-CM codes, we identified all admissions from a pregnancy-related encounter with a diagnosis of type 1 AMI.
Main outcome: Using the marginal effect of years, we assessed the trends in the incidence of AMI and utilized a multivariate logistic regression model to compare our secondary outcomes.
Results: Of the 19,524,846 patients with an obstetric-related admission, 3605 (0.02 %) had a diagnosis of type 1 AMI. Overall, we observed an approximately 2-fold increase in the trend of AMI from 1.4 to 2.5 per 10,000 obstetric admissions, with the highest incidence trend of 2.5 to 5.2 per 10,000 obstetric admissions seen in Black patients. Among patients diagnosed with AMI, we found significantly higher rates of in-hospital mortality (Adjusted Odds Ratio (AOR): 22.9, 12.2–42.8), cardiogenic shock (AOR:54.3, 33.9–86.6), preeclampsia (AOR: 2.2, 1.65–2.94) and spontaneous abortion (AOR:6.3, 3.71–10.6).
Conclusion: Over the 5-year period, we found increasing trends in the incidence of AMI in pregnancy, especially among Black patients. Incident AMI was also associated with worse pregnancy outcomes.

1. Introduction

Maternal morbidity and mortality rates are rising in the United States (US) despite advancements in healthcare delivery [1]. According to the CDC, pregnancy-related death rates were about 700 per year between 2011 and 2015, rising to >860 maternal-related deaths in 2020 [1,2]. Cardiovascular disease is the leading cause of the high maternal mortality, with approximately 33.3 % of deaths during pregnancy resulting from cardiovascular causes [2]. Similarly, cardiovascular morbidity and mortality from acute myocardial infarction (AMI) during pregnancy, delivery, and postpartum have been on an upward trend [3,4]. AMI during pregnancy has been associated with pregnancy-related changes in cardiovascular physiology, such as hypercoagulability, cardiovascular stress secondary to increased demand, and variations in the peripheral circulation [5]. These alterations also contribute to fatal outcomes of AMI during pregnancy. Previous studies have highlighted the substantial contribution of AMI to cardiovascular-related deaths in pregnancy [3,4]. Our study builds on the results of prior studies and provides updated information on the incidence trends and hospital outcomes associated with AMI in pregnancy. We specifically examined the 5-year incidence trends in AMI between 2016 and 2020 and the racial/ethnic disparities in the incidence trends of AMI. In addition, we evaluated the cardiovascular, obstetric and hospital related outcomes of AMI in pregnancy.

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2. Methods

This study is reported following the strengthening the reporting of observational studies in Epidemiology (STROBE) reporting guidelines [6].

We analyzed hospitalizations between January 1st, 2016, and December 31st, 2020, in the US National Inpatient Sample (NIS). The NIS is the largest publicly available all-payer inpatient database in the US and is maintained by the Agency for Healthcare Research and Quality [7]. The NIS is a 20 % stratified cluster probability sample of non-federal acute care hospitals, stratified according to ownership/control, bed size, teaching status, urban/rural location, and geographic region.

All discharges from these hospitals were weighted to ensure national representativeness. Data from 47 statewide organizations (46 states plus the District of Columbia) encompassing >97 % of the US population were included in the NIS 2016–2020 sampling frame. As many as 30 discharge diagnoses for each hospitalization were recorded using the ICD-10-CM in NIS 2016, and 40 discharge diagnoses and 25 procedures were coded in NIS 2020 database. Principal and secondary diagnoses were also recorded.

Institutional review board approval was waived since all patient data in NIS were de-identified and publicly available.

The study population consisted of all inpatient hospitalizations with a primary diagnosis or secondary diagnosis of type 1 AMI during an obstetric related encounter including (pregnancy, delivery, and postpartum) recorded between 2016 and 2020. Patients aged <18 years were excluded. Diagnosis was identified using ICD- 10-CM codes (Obstetric related encounter "O" and Type 1 AMI "I21.0", "I21.1", "I21.2", "I21.3", "I21.4", "I21.9") as recommended by the American College of Obstetricians and Gynecologists and the American College of Cardiology, respectively [8,9].

Demographic variables including age, race, median household income, primary insurance, and co-morbidities (computed from the Charlson Comorbidities Index) were already available in the data set and the ICD-10-CM medical billing codes were identified from review of other nationwide studies on cardiovascular diseases in Pregnancy [3,10,11].

We examined the sociodemographic characteristics of our study population by AMI status as highlighted in Table 1. We analyzed the trends in the incidence of type 1 AMI (primary outcome of interest) and conducted sub-analysis by race/ethnicity. Our secondary outcomes of interest included cardiovascular outcomes (cardiogenic shock, cardiac arrest, use of temporary circulatory support and in-hospital mortality), obstetric related (pre-eclampsia, and spontaneous abortion) and hospital related outcomes (Length of stay and total hospital cost).

Data were analyzed using STATA, version 17 (Stata Corp, Texas, USA). We conducted all analysis using weighted samples for national estimates in accordance with the Healthcare Cost and Utilization Project (HCUP) regulations for NIS databases. Continuous variables were presented as means ± standard deviation (SD) and the differences were tested using a *t*-test. Categorical variables were presented in percentages (%) and compared using the chi-square test. Multiple logistic regression was performed for yearly trends in the incidence of MI using a "year" interaction term as an independent variable and "acute myocardial infarction" as a dependent variable. Incidence rates were obtained using marginal effects following our multiple regression analysis. In addition, we used a multivariate logistic and linear regression analysis to obtain adjusted odds and mean ratios (AOR) for cardiovascular/pregnancy and hospital related outcomes, respectively. Confounders were obtained from a literature review of prior similar studies and included age, race, income status, hyperlipidemia, history of myocardial infarction, chronic kidney disease, diabetes mellitus, hypertension, anemia, and obesity [3–5]. A *p*-value of <0.05 was considered statistically significant and all tests were two-sided with a 95 % confidence interval (CI).

Table 1
Baseline characteristics of the study population by acute myocardial infarction status- National Inpatient Sample: 2016–2020.

Variable	Obstetric Admissions $n = 19{,}524{,}846$		p-Value
	AMI $n = 3605$	No AMI n = 19,521,241	
Patient characteristics	%	%	
Age (years)			<0.001
18–30	31.5	52.8	
31–40	55.2	43.8	
41–50	12.6	3.4	
>50	0.7	0.0	
Race			<0.001
Non-Hispanic White	41.2	52.1	
Non-Hispanic Black	35.6	15.8	
Hispanic	15.2	20.7	
Asian	3.3	6.1	
Native American	0.4	0.8	
Other	4.2	4.6	
Median income (based on zip code)			<0.001
$1–$49,000	41.3	28.3	
$50,000–$64,999	26.4	25.4	
$65,000–$85,999	17.9	24.6	
≥$86,000	14.4	21.7	
Charlson Comorbidity Index Score			<0.001
0	0	92.1	
1	44.5	7.2	
2	36.1	0.5	
≥3	19.4	0.1	
Hospital region			<0.001
Northeast	12.8	16.0	
Midwest	22.5	20.9	
South	44.7	39.4	
West	20.0	23.7	
Comorbidities			
Dyslipidemia	14.0	0.4	<0.001
Stimulant abuse	1.7	0.2	<0.001
Smoking	13.3	6.7	<0.001
Prior MI	4.4	0.0	<0.001
Diabetes Mellitus	4.4	0.1	<0.001
History of Stroke	1.9	0.00	<0.001
Hypertension	6.9	0.2	<0.001
Peripheral Vascular Disease	0.3	0.0	<0.001
Obesity	20.1	9.5	<0.001
Chronic Kidney Disease	4.3	0.2	<0.001
Systemic Lupus Erythematosus	1.5	0.2	<0.001
Anemia	34.8	15.6	<0.001
Thrombophilia	3.1	0.5	<0.001
Venous Thromboembolism	2.9	0.1	<0.001

3. Results

A total of 19,524,846 obstetric admissions were identified between 2016 and 2020 in our study population. Of these, 3605 (0.02 %) patients had AMI, with 68.2 % presenting as ST elevated Myocardial infarction (STEMI). In addition, 37.9 % of AMI cases had a secondary diagnosis of Spontaneous Coronary Artery Dissection (SCAD). Patients who had AMI were more likely to be Black patients (35.6 % vs. 15.8 %, $p < 0.001$), and in the lowest median income quartile (41.3 % vs. 28.3 %, $p < 0.001$). They were also more likely to have diabetes mellitus (4.4 % vs. 0.1 %, $p < 0.001$), hypertension (6.9 % vs. 0.2 %, p < 0.001), chronic kidney disease (4.3 % vs. 0.2 %, $p < 0.001$), dyslipidemia (14.0 % vs. 0.4 %, p < 0.001), a history of smoking (13.3 % vs. 6.7 %, p < 0.001) and were more likely to use stimulant medications (1.7 % vs. 0.2 %, p < 0.001) (Table 1).

For our primary outcome of interest, we noted an increase in the incidence trends of AMI from 1.4 to 2.5 per 10,000 (p-trend < 0.001) obstetric admissions within the study duration (2016 to 2020) (Fig. 1).

In our analysis stratified by race/ethnicity, Black patients had the highest incidence of AMI with increasing incidence trends from 2.5 per 10,000 in 2016 to 5.2 per 10,000 (p-trend < 0.001) obstetric admissions

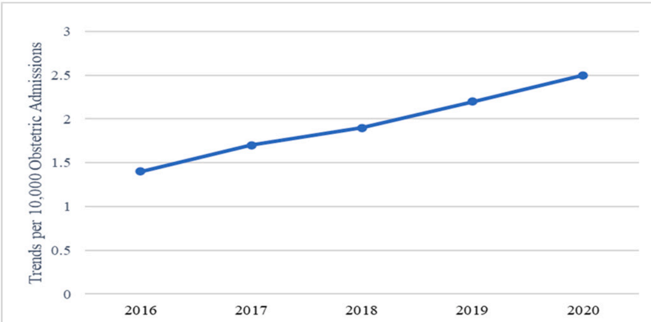

Fig. 1. Trends in the incidence of acute myocardial infarction for all obstetric admissions- National Inpatient Sample: 2016–2020.

in 2020 (Fig. 2). Analysis of the in-hospital outcomes showed that patients with AMI had the highest in-hospital mortality, (adjusted odds ratio (AOR) 22.9, CI: 12.2–42.8, $p < 0.001$), cardiac arrest, (AOR: 51.9, CI: 31.8–84.6, $p < 0.001$), and cardiogenic shock, (AOR: 54.3, CI: 33.9–86.6, p < 0.001) when compared to patients without AMI (Table 2).

For obstetric related outcomes, patients with AMI were more likely to have preeclampsia, (AOR: 2.2, CI: 1.65–2.94, $p < 0.001$), and spontaneous abortion (AOR: 6.3, CI: 3.71–10.6, p < 0.001). We also noted a significantly longer length of hospital stay, (adjusted mean ratio (AMR): 1.48, CI: 1.34–1.63, p < 0.001) and total hospitalization cost (AMR: 2.76, CI: 2.41–3.16 p < 0.001) for patients with AMI.

4. Discussion

Our study examined the trends in the incidence and in-hospital outcomes of AMI in pregnancy. Our key findings were as follows: **(1)** There was an approximately two-fold increase in the total number of AMI admissions associated with obstetric hospitalizations over the 5-year study period. **(2)** The overall incidence of AMI-related obstetric admissions was 0.02 %. **(3)** The proportion of AMI cases was higher in black patients and in patients who earned among the lowest yearly median income. **(4)** Patients with AMI were also more likely to be smokers, stimulants users, and to have obesity and hypertension. **(5)** AMI was associated with higher odds of in-hospital mortality, cardiac arrest, cardiogenic shock, pre-eclampsia, and spontaneous abortion in pregnant women.

Cardiovascular disease is one of the leading causes of maternal morbidity and mortality in high-income countries. Pregnancy-related AMI is four times higher in the US compared to Europe and Canada combined [12–14]. Additionally, AMI is three to four times more likely to affect women during pregnancy than similarly aged, non-pregnant women [12–14]. Worldwide, the incidence of pregnancy-related AMI is estimated to be between 0.06 and 10 per 100,000 [15,16]. In our study, the incidence of pregnancy-related AMI was 18 per 100,000 obstetric admissions, which is twice the incidence of a similar nationwide study done between 2002 and 2014 that had 8.1 cases of AMI per 100,000 obstetric hospitalizations [11]. Our study also showed a significant upward trend (2.12 % annually) in the total number of obstetric-related admissions with AMI over the 5-year study period. This is comparable to the outcomes published in a study by *Byomesh Tripathi* et al. [11] which noted a relative increase in the incidence of AMI by 1.89 % per annum over 10 years between 2005 and 2014. While the exact reason for this notable increase in incidence remains unclear, improved testing and the use of high-sensitivity cardiac troponin T may explain some of these findings. Tobias et al. [17], in their study evaluating pregnancy-related acute myocardial infarction, estimate a relative increase of 18 % to 22 % in the incidence of AMI attributed to the use of high-sensitivity cardiac troponin T.

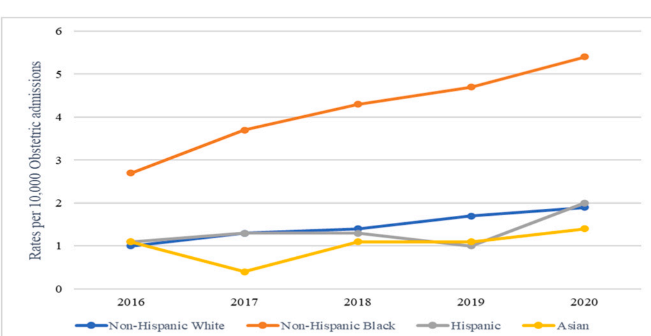

Fig. 2. Trends in the incidence of acute myocardial infarction by race/ ethnicity-National Inpatient Sample: 2016–2020.

Table 2
Acute myocardial infarction outcomes for all obstetric admissions -National Inpatient Sample: 2016–2020.

	Obstetric admissions		Adjusted odds/ mean ratio (Confidence interval)	p-Value
	MI n = 3605	No MI n = 19,521,241		
Cardiac outcomes				
In-hospital mortality	130 (3.6 %)	2305 (0.01 %)	22.9 (12.2–42.8)[a]	<0.001
Cardiac arrest	190 (5.3)	2680 (0.01 %)	51.9 (31.8–84.6)[a]	<0.001
Cardiogenic shock	225 (7.1 %)	1865 (0.01 %)	54.3 (33.9–86.9)[a]	<0.001
Mechanical circulatory support	170 (4.7 %)	680 (0.003 %)	86.1 (46.2–160.4)[a]	<0.001
Pregnancy outcomes				
Preeclampsia	315 (8.7 %)	346,610 (1.8 %)	2.2 (1.65–2.94)[a]	<0.001
Spontaneous abortion	90 (2.5 %)	15,190 (0.1 %)	6.3 (3.71–10.6)[a]	<0.001
Hospital outcomes				
Length of hospital stay (Days)	6.0	2.6	1.48 (1.34–1.63)[b]	<0.001
Total hospital cost ($)	106,317.7	21,545.9	2.76 (2.41–3.16)[b]	<0.001

[a] Adjusted odd ratio.
[b] Mean ratio.

Our study also highlights the impact of socio-demography and economic factors on the high incidence of AMI. Black patients and individuals from low-income backgrounds were more likely to present with AMI. Though Black individuals constitute approximately 13 % of the US population, they represent 35.6 % of patients with pregnancy-associated AMI [20,21]. Similar to prior published papers, the high risk of AMI in the Black population may be related to higher rates of pre-existing cardiovascular risk factors such as hypertension, dyslipidemia, smoking, and diabetes mellitus [18,19]. In addition, socioeconomic factors such as low income, lack of education, and poverty may have contributed to this risk [22–26]. In a systematic review and meta-analysis of 11 studies by Aliza Moledina et al. [27] that evaluated the impact of socioeconomic status on outcomes after AMI, low economic status was associated with a 48 % increase in short-term mortality. Another large-scale prospective cohort study of 20 low-income, middle-income, and high-income countries by Annika Rosengren et al. [28], assessed the role of socioeconomic status and cardiovascular disease risk over 7.5 years. They showed that education was the most consistent socioeconomic predictor of cardiovascular outcomes rather than wealth. Low educational status is a surrogate for being under resourced, directly influencing access to information and timely patient care.

With the increasing rates of pregnancy related mortality and mechanisms for this rise being unclear, our study also sought to understand the role of AMI as a contributor to cardiovascular and overall maternal morbidity and mortality rates. AMI was a significant contributor to maternal mortality rates. Pregnant patients who suffered AMI were 22 times more likely to die in the hospital. Our findings are similar to other studies that demonstrated significantly high mortality rates and a case-fatality rate of up to 37 % with the potential to lose both mother and baby [12,29–31].Patients with pregnancy-related AMI also experienced a higher rate of pregnancy-related complications, such as pre-eclampsia, and spontaneous abortion. In a study by Balgobin et al. [4], it was noted that 18.3 % of gestating women with AMI experienced either eclampsia or preeclampsia. Notably, in our study, patients with AMI were more likely to have hypertension, diabetes mellitus, a higher rate of smoking and illicit drug use, all of which have been strongly linked to the presence of ischemic heart disease as a result of systemic endothelial disfunction and enhanced vascular activity [32–36]. Futhermore, studies have shown that surges in estrogen and progesterone during pregnancy may lead to weakening of the tunica media leading to the formation of dissection planes in coronary vessels [37]. Vascular compromise to the uterine circulation in the setting of hypertensive diseases and AMI leads to decreased uterine perfusion and therefore high rates of spontaneous abortion. In addition to worse clinical outcomes, AMI in pregnancy results in an economic strain on the patients, their support system, and the healthcare system. Patients with AMI are more likely to stay longer in the hospital, leading to increased utilization of resources and higher hospital costs as demonstrated in our study.

Our study demonstrates the need for future strategies that focus on primary and secondary prevention of AMI in pregnant women. We advocate that guidelines for the management of AMI in pregnant women should incorporate social determinants of health. Finally, increasing national awareness about AMI risk factors, the role of SCAD and the adverse cardiovascular and mortality outcomes in pregnancy through national public health campaign initiatives can be beneficial.

The limitations of this study include the potential for bias from unadjusted and unmeasured confounders from the retrospective design, even though we performed a detailed multivariate analysis. The lack of long-term longitudinal data on individual patients and limited data on the symptoms on presentation, severity and trimester at hospital presentation are additional study limitations. Furthermore, information on the timing of intervention could not be assessed using our database. Using an inpatient sample limits the generalizability of our results to outpatient settings in the post-discharge period. Although the ICD-10 codes used in this study have been validated with good accuracy, there is still a small possibility of under-coding or miscoding. However, the effect of coding errors is likely to be insignificant due to our large sample size.

This study demonstrates an increasing trend in the incidence of AMI in pregnancy with an interplay of low socioeconomic status and racial/ethnic disparities resulting in the high rates of AMI in pregnancy. We also highlight the poor prognosis carried by pregnancy related MI to both the mother and child. A low threshold for evaluation of AMI should be made in patients with high risk features presenting with chest pain, and prompt treatment should be instituted to reduce the high case fatality rate. Future directions should include development of tools that incorporate risk assessment in addition to addressing adverse social determinants of health in the management of these pregnant patients.

CRediT authorship contribution statement

Favour Markson: Conceptualization, Methodology, Software. **Rimaskep Garba Shamaki**: Writing original draft preparation. **Akanimo Antia**: Data curation, Result compilation. **Anita Osabutey**: Conceptualization, Writing- Reviewing and Editing. **Modele Ogunniyi:** Supervision, Reviewing and Editing.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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