

Heart Failure in Pregnant Women

A Concern Across the Pregnancy Continuum

BACKGROUND: Heart failure (HF) is a leading cause of maternal morbidity and mortality in the United States, but prevalence, correlates, and outcomes of HF-related hospitalization during antepartum, delivery, and postpartum periods remain unknown. The objective was to examine HF prevalence, correlates, and outcomes among pregnancy-related hospitalizations among women 13 to 49 years of age.

METHODS AND RESULTS: We used the 2001 to 2011 Nationwide Inpatient Sample. Rates of HF were calculated by patient and hospital characteristics. Survey logistic regression was used to estimate adjusted odds ratios representing the association between HF and each outcome, stratified by antepartum, delivery, and postpartum periods. Joinpoint regression was used to describe temporal trends in HF and in-hospital mortality. Over 50 million pregnancy-related hospitalizations were analyzed. The overall rate of HF was 112 cases per 100 000 pregnancy-related hospitalizations. Although postpartum encounters represented only 1.5% of pregnancy-related hospitalizations, ~60% of HF cases occurred postpartum, followed by delivery (27.3%) and antepartum (13.2%). Among postpartum hospitalizations, there was a significant 7.1% (95% confidence interval, 4.4–9.8) annual increase in HF from 2001 to 2006, followed by a steady rate through 2011. HF rates among antepartum hospitalizations increased on average 4.9% (95% confidence interval, 3.0–6.8) annually from 2001 to 2011. Women with a diagnosis of HF were more likely to experience adverse maternal outcomes, as reflected by outcome-specific adjusted odds ratios during antepartum (2.7–25), delivery (6–195), and postpartum (1.5–6.6) periods.

CONCLUSIONS: HF is associated with increased risk of maternal mortality and morbidities. During hospitalization, high-risk mothers need to be identified and surveillance programs developed before discharge.

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Key Words: heart failure

■ maternal mortality ■ mothers

■ postpartum period ■ pregnancy

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WHAT IS NEW?

- This study provides national data on national prevalence and outcomes of maternal heart failure stratified by timing (antepartum, delivery, and postpartum) of hospitalizations in the United States.
- About 60% of pregnancy-related heart failure diagnoses occurred during the postpartum period.

WHAT ARE THE CLINICAL IMPLICATIONS?

- Data from the current study may help clinicians to identify those at increased risk of heart failure and associated adverse outcomes.
- Findings of this study lend support to the need for additional surveillance of at risk postpartum women, even before the traditional 6-week follow-up.

In the United States, the rate of pregnancy-related maternal mortality increased from 7.2 deaths per 100 000 live births (1987) to 17.8 deaths per 100 000 live births (2011).¹ The primary reason for the more-than-doubling in pregnancy-related maternal mortality is not understood. Researchers have identified cardiovascular conditions, such as heart failure, (HF) are among the leading nonobstetric causes of maternal mortality.²⁻⁵ The anatomic and hemodynamic changes that occur during pregnancy and the peripartum period impose a physiological stress on the cardiovascular system, which, in some women, may exacerbate existing cardiovascular conditions (eg, hypertension) or lead to development of new cardiovascular conditions, such as cardiomyopathy.⁶ Both can lead to development of HF, which is associated with poor outcomes and high mortality.⁷ After the initial diagnosis of HF, in individuals ≥ 60 years of age, the estimated 1-year survival is 70% to 75% but is reduced to 24% to 54% at 5 years.^{8,9} In adults < 60 years of age with a diagnosis of HF, 1-year mortality rates as high as 25% have been reported.¹⁰

Most studies on HF prevalence have focused on older populations.^{11,12} Therefore, relatively little is known about HF occurrence and HF-related medical encounters among women of reproductive age, particularly throughout the pregnancy continuum (ie, hospitalizations during the antepartum, delivery, and postpartum periods).¹¹ Studies that have included pregnant women have focused on those with existing cardiovascular conditions, such as cardiomyopathy,^{7,13} and have evaluated adverse events only during delivery-related hospitalizations.¹⁴ In the United States, there is dearth of national data on the occurrence of HF during antepartum and postpartum periods, which are collectively relevant to the future health of mothers and children. To fill this void, we used the Nationwide Inpatient Sample (NIS) to examine the prevalence of HF

and its correlates in pregnant women 13 to 49 years of age during inpatient medical encounters across the pregnancy continuum (ie, antepartum, delivery, and postpartum). The analyses explore the associations between HF-associated hospitalization and maternal morbidity and mortality in the United States.

METHODS

Design, Data Source, and Study Population

We conducted a retrospective cross-sectional study using the NIS from the Healthcare Cost and Utilization Project (HCUP) for 2001 to 2011. The analytic methods and study materials will be made available to other researchers for purposes of reproducing the results or replicating the procedure. Researchers can acquire the data used in this study from the HCUP (<https://www.distributor.hcup-us.ahrq.gov>). The NIS is the largest all-payer hospital discharge database, with a 20% sample of all nonfederal community hospitals from participating states (46 states in the year 2011, representing $> 97\%$ of the US population).^{15,16} The NIS is a widely used data set validated against National Hospital Discharge Survey and Medicare Provider Analysis and Review file.¹⁷

Our study population consisted of antepartum, delivery, and postpartum discharges for women 13 to 49 years of age. First, we limited our study population to pregnancy-related hospitalizations using the NEOMAT (Neonatal and/or maternal *ICD-9-CM* diagnosis and/or procedure codes) variable provided by HCUP. We used *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* diagnosis codes to determine whether each woman had a hospitalization during the antepartum, delivery, or postpartum period using a previously published algorithm.^{18,19} Delivery-related discharges were identified using delivery-specific *ICD-9-CM* diagnosis, procedure, and diagnosis-related group codes. Postpartum discharges were identified using V24 code, postpartum diagnosis-related group codes, and presence of the number 4 in the fifth digit of selected *ICD-9-CM* codes. Pregnancy-related discharges that were not indicative of a delivery or postpartum hospitalization were classified as being antepartum related.^{18,19}

Identification of HF Cases and Outcome Measures

Using *ICD-9-CM* diagnosis codes from discharge records, we determined whether each hospitalization had a diagnostic indication of HF (402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, and 428.x). Study outcomes included in-hospital mortality, acute renal failure, pulmonary edema, stroke, puerperal cerebrovascular disease, length of hospital stay, disseminated intravascular coagulation, mechanical ventilation, and cesarean section. All outcomes were also identified using *ICD-9-CM* diagnosis and procedure codes except in-hospital mortality, which was identified using the patient's disposition at discharge. The [Data Supplement](#) provides the complete list of *ICD-9-CM* diagnosis, procedure, and diagnosis-related group codes used in the identification of the study population, HF, and clinically relevant outcomes.

Covariates

Individual-level sociodemographic and behavioral characteristics were also extracted from the NIS databases. Patient age in years was classified into the following categories: 13 to 19, 20 to 24, 25 to 29, 30 to 34, 35 to 39, 40 to 44, and 45 to 49. We used median household income in quartiles, calculated by HCUP, as a proxy for participants' socioeconomic status. Type of insurance used was grouped into 3 categories: government (Medicare and Medicaid), private (commercial carrier, private health maintenance organization, and preferred provider organization), and other sources (eg, self-pay and charity). In addition, hospital characteristics, such as geographic region (Northeast, Midwest, South, or West), location, and teaching status (rural, urban nonteaching, and urban teaching), were considered. Lastly, we considered the effect of several individual-level behavioral characteristics, including tobacco, alcohol, and drug use. We also used Elixhauser comorbidity software^{20,21} to assess the distribution of comorbidities among study population subgroups and to adjust for the impact of these comorbidities on study outcomes.

Statistical Analyses

The distribution of sociodemographic, behavioral, hospital, insurance, clinical, and pregnancy-related comorbidities by HF status was summarized using descriptive statistics, such as frequencies and rates, across the pregnancy continuum. To provide national estimates, we weighted all estimates using a weighting variable provided by HCUP. Joinpoint regression was used to examine temporal trends of HF during the study period by timing of hospitalization (antepartum, delivery, and postpartum). We also examined trends in inpatient mortality for those with and without a diagnosis of HF. Joinpoint regression analysis is a statistical method that captures changing trends over time and the amount of increase or decrease within each segment. This analysis involves fitting a series of joined straight lines and identifying the best-fitting point or points, called joinpoints, where the rate of increase or decrease is statistically significant. Each joinpoint represents a statistically significant change in trend. The resulting line segment between joinpoints can be expressed as annual percent change.²²

For each exposure–outcome association, a crude model and 2 multivariable models were constructed using survey logistic regression. The first multivariable model adjusted for sociodemographic, behavioral, and hospital characteristics; the second included additional adjustment for a composite indicator of selected pregnancy-related and prepregnancy comorbidities. For brevity, only the second, fully adjusted model is presented. All analyses were conducted using software (SAS 9.4; SAS Institute, Inc, Cary, NC) using a 5% type I error rate and 2-sided hypothesis tests. The study was approved by the institutional review board of the University of Illinois at Chicago.

RESULTS

Prevalence of HF

Among the 50 995 050 pregnancy-related hospitalizations between January 1, 2001, and December 31, 2011, there were 7542 antepartum, 15 620 delivery, and 34 110 postpartum hospitalizations with a diagnostic indication of HF. Across the pregnancy continuum, the overall prevalence of HF among the study population was 112 cases per 100 000 pregnancy-related hospital discharges (95% confidence interval [CI], 107–118). Although the postpartum period represented only 1.5% of pregnancy-related hospitalizations, 60% of all pregnancy-related HFs occurred during the postpartum period, followed by the delivery (27%) and antepartum (13%) periods. The temporal trend in the rate of HF during pregnancy varied by the timing of hospitalization. Among postpartum hospitalizations, HF prevalence showed a statistically significant 7.1% (95% CI, 4.4–9.8) annual increase from 2001 to 2006, followed by no significant temporal changes between 2006 and 2011 (Figure 1). HF prevalence among antepartum hospitalizations significantly increased by an average of 4.9% (95% CI, 3.0–6.8) each year from 2001 to 2011, whereas HF rates during delivery hospitalizations remained unchanged during the study period (Figure 1).

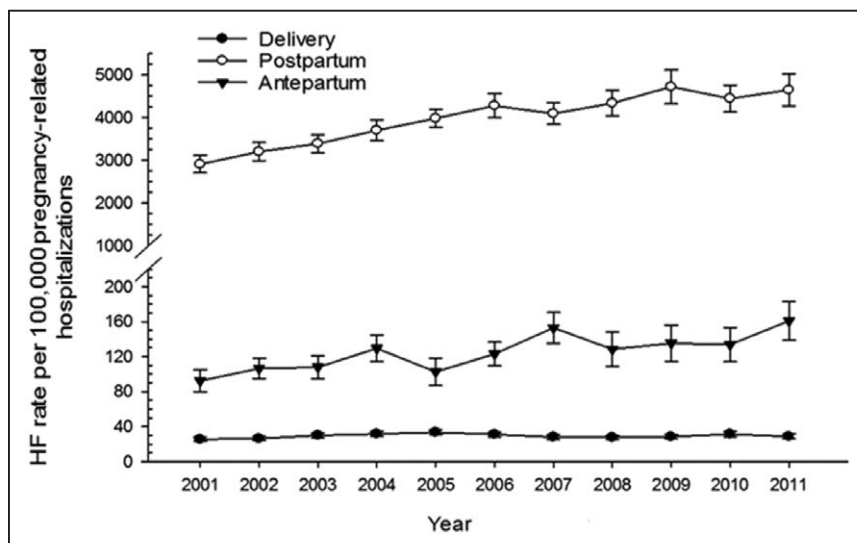


Figure 1. Trends in inpatient diagnosis of heart failure (HF) among antepartum, delivery, and postpartum hospitalizations, United States, Nationwide Inpatient Sample, 2001 to 2011.

Values are rates and SEs of these rates.

Table 1. Distribution of Sociodemographic and Behavioral Characteristics Among Antepartum, Delivery, and Postpartum Hospitalizations by HF Diagnosis in the United States, Nationwide Inpatient Sample, 2001 to 2011

Characteristics	Total n=50 995 050*	Antepartum Hospitalizations (n=4833 438 [9.48%])			Delivery Hospitalizations (n=45 413 844 [89.06%])			Postpartum Hospitalizations (n=747 769 [1.47%])		
		No HF, % (99.84%)	HF, % (0.16%)	OR (95% CI)	No HF, % (99.97%)	HF, % (0.03%)	OR (95% CI)	No HF, % (95.44%)	HF, % (4.56%)	OR (95% CI)
Age, y										
13–19	5 295 181	12.6	5.3	0.5 (0.4–0.6)†	10.1	7.3	0.9 (0.8–1.1)†	11.4	4.0	0.4 (0.3–0.4)†
20–24	12 614 230	27.4	15.4	0.6 (0.5–0.8)†	24.5	16.3	0.9 (0.8–1.0)†	24.9	16.7	0.7 (0.7–0.8)†
25–29	13 873 915	25.7	22.3	Referent†	27.4	20.9	Referent†	25.2	23.2	Referent†
30–34	11 849 175	20.1	27.1	1.6 (1.3–1.8)†	23.6	25.9	1.4 (1.3–1.6)†	21.9	25.0	1.2 (1.1–1.3)†
35–39	5 948 114	10.9	21.4	2.3 (1.9–2.7)†	11.7	21.2	2.4 (2.1–2.6)†	12.6	20.6	1.8 (1.6–2.0)†
40–44	1 327 544	3.0	7.4	2.9 (2.3–3.6)†	2.5	7.8	4.0 (3.5–4.7)†	3.5	8.4	2.6 (2.3–3.0)†
45–49	10 114	0.3	1.2	4.8 (2.9–7.7)†	0.2	0.7	6.1 (3.9–9.4)†	0.4	2.0	4.8 (3.8–6.6)†
Race										
White	20 358 453	36.0	28.9	Referent†	40.4	33.1	Referent†	38.4	31.1	Referent†
Black	5 694 194	18.0	34.7	2.4 (2.1–2.8)†	10.3	23.5	2.8 (2.5–3.1)†	17.0	33.8	2.5 (2.2–2.7)†
Hispanic	9 415 893	17.7	11.8	0.8 (0.7–1.0)	18.6	13.5	0.9 (0.8–1.0)†	15.6	7.0	0.6 (0.5–0.6)†
Other	4 049 416	6.5	5.6	1.1 (0.8–1.4)	8.1	7.9	1.2 (1.0–1.4)	6.7	4.8	0.9 (0.8–1.0)
Missing	11 477 094	21.8	19.1	1.1 (0.9–1.3)	22.6	22.0	1.2 (1.0–1.4)	22.3	23.4	1.3 (1.2–1.5)†
Any tobacco use‡	2 228 631	6.1	10.9	1.9 (1.6–2.3)†	4.2	6.5	1.6 (1.4–1.9)†	6.3	11.6	1.9 (1.8–2.1)†
Any alcohol use‡	86 552	0.7	1.6	2.4 (1.6–3.6)†	0.13	0.6	5.4 (3.4–8.5)†	0.5	0.8	1.5 (1.1–2.0)†
Any drug use‡	720 015	3.5	6.6	1.9 (1.6–2.4)†	1.2	4.6	4.1 (3.4–4.9)†	2.9	3.4	1.2 (1.0–1.4)
Hospital region										
Northeast	8 496 319	18.8	16.6	1.1 (0.8–1.3)	16.4	15.3	1.2 (1.0–1.4)	17.5	12.8	1.0 (0.8–1.2)
Midwest	10 895 777	19.8	20.0	1.2 (1.0–1.5)	21.5	19.7	1.2 (1.0–1.4)	21.9	22.7	1.4 (1.2–1.7)†
South	19 214 383	39.6	45.2	1.4 (1.1–1.7)†	37.4	45.4	1.5 (1.3–1.8)†	39.6	49.3	1.7 (1.5–2.0)†
West	12 388 572	21.8	18.2	Referent†	24.6	19.7	Referent†	21.1	15.3	Referent†
Hospital location										
Rural	6 009 903	11.4	8.2	0.6 (0.4–0.7)†	11.9	6.8	0.5 (0.4–0.6)†	10.2	7.8	0.7 (0.6–0.8)†
Urban nonteaching	21 359 626	37.3	27.3	0.6 (0.5–0.7)†	42.7	34.6	0.6 (0.6–0.7)†	38.1	37.5	0.9 (0.8–1.0)
Urban teaching	23 371 399	51.3	64.5	Referent†	45.4	58.6	Referent†	51.7	54.7	Referent†
Hospital bed count										
Small	5 464 542	9.1	6.4	0.8 (0.6–1.0)	11.0	6.8	0.7 (0.5–0.9)†	9.7	7.6	0.8 (0.7–1.0)
Medium	13 218 304	25.2	23.0	Referent†	26.2	24.3	Referent†	24.7	23.4	Referent†
Large	32 058 082	65.7	70.6	1.2 (1.0–1.4)	62.9	68.9	1.2 (1.0–1.4)	65.6	69.1	1.1 (1.0–1.2)
Household income										
Lowest quartile	13 667 641	32.5	40.4	1.7 (1.4–2.0)†	26.1	34.3	1.7 (1.5–1.9)†	29.4	36.0	1.5 (1.4–1.7)†
Second quartile	12 639 744	24.9	25.0	1.4 (1.1–1.6)†	24.8	24.5	1.3 (1.1–1.4)†	24.9	24.6	1.2 (1.1–1.3)†
Third quartile	12 270 681	22.2	18.2	1.1 (0.9–1.4)	24.3	21.7	1.2 (1.0–1.3)	23.3	21.4	1.1 (1.0–1.2)
Highest quartile	11 484 279	18.3	13.3	Referent†	23.0	17.8	Referent†	20.3	16.5	Referent†
Primary payer										
Medicare/Medicaid	21 472 866	47.4	61.1	1.9 (1.7–2.1)†	41.5	49.7	1.4 (1.3–1.5)†	46.4	51.4	1.2 (1.1–1.3)†
Private	26 133 362	42.5	28.9	Referent†	52.3	44.1	Referent†	45.2	41.8	Referent†
Other	3 388 823	10.1	10.0	1.4 (1.2–1.8)†	6.3	6.2	1.2 (1.0–1.4)	8.4	6.7	0.9 (0.8–1.0)

CI indicates confidence interval; HF, heart failure; and OR, odds ratio.

*Weighted to estimate the national frequency; sum of all groups may not add up to the total because of missing data.

†Statistical significance at $P < 0.05$.

‡Reference group is reflected by the absence of the listed condition/characteristic.

Demographic Characteristics, Lifestyle Factors, and Comorbidities

Across the pregnancy continuum, women with a diagnosis of HF were more likely to be older, black, have documented tobacco, drug, and alcohol use, reside in the Southern region of the United States and in a lower household income area, and be insured by either Medicare or Medicaid (Table 1; Figure 2). Across the pregnancy continuum, women with a diagnosis of HF were substantially more likely to have ≥ 1 comorbidities. Table 2 presents the distribution of 29 Elixhauser comorbidities.^{23,24}

HF and Adverse Maternal Outcomes

The odds of pregnancy-related comorbidities were 2- to 29-fold greater in delivery-related hospitalizations complicated by HF (Table 3). Women with the diagnosis of HF during antepartum, delivery, and postpartum hospitalizations were substantially more likely to experience adverse outcomes (Table 4). For example, compared with hospitalizations without HF, hospitalizations with HF during the delivery, postpartum, and antepartum periods were associated with a 47-fold (adjusted odds ratios [AORs], 46.9; 95% CI, 34.9–63.0), 80% (AOR, 1.8; 95% CI, 1.3–2.5), and 25-fold (AOR, 25.3; 95% CI, 16.4–39.0) increased likelihood of developing pulmonary edema, respectively, even after controlling for demographic, clinical, and pregnancy-related confounders (Table 4).

HF and Maternal Mortality

Over 9% of in-hospital deaths among pregnancy-related hospitalizations nationally were attributable to

HF. Across the pregnancy continuum, compared with women with HF who survived to discharge, those who did not survive were more likely to be older, black, and have multiple comorbidities. Delivery-related hospitalizations with a diagnosis of HF were 32× more likely to result in maternal death before discharge (AOR, 31.9; 95% CI, 19.3–52.8). Mortality risk increased ≈ 16 -fold (AOR, 15.9; 95% CI, 9.5–26.6) and 4-fold (AOR, 4.0; 95% CI, 3.1–5.3) for women with versus without a HF diagnosis during antepartum and postpartum hospitalizations, respectively (Table 4).

The rate of inpatient mortality (deaths per 100 000 pregnancy-related hospitalizations) among hospitalizations for non-HF conditions remained unchanged from 2001 (12.3) to 2011 (11.1). Among women with a diagnosis of HF, there was significant increase in the mortality rate from 548 (2001) to 1318 (2011), reflecting a statistically significant 9.8% annual increase (95% CI, 1.9–18.4; Figure 3).

DISCUSSION

This study provides new information by examining HF prevalence within distinct periods across the pregnancy continuum and by exploring demographic, behavioral, and clinical factors associated with HF diagnoses during pregnancy. First, among a nationally representative sample of women of reproductive age, the prevalence of HF was 112 per 100 000 pregnancy-related hospitalizations. Second, despite comprising <2% of all pregnancy-related admissions, $\approx 60\%$ of pregnancy-related HF diagnoses occurred during the postpartum period. Third, we found that the rate of HF diagnosis among both antepartum and postpartum hospitalizations increased during the study period. Fourth, women

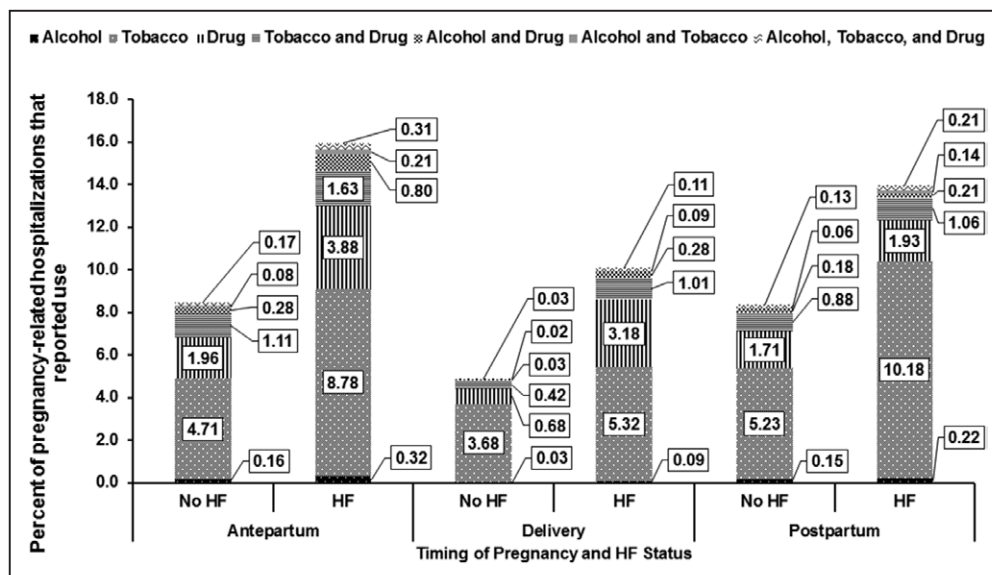


Figure 2. Percentage distribution of lifestyle characteristics among antepartum, delivery, and postpartum hospitalizations by heart failure (HF) status, United States, Nationwide Inpatient Sample, 2001 to 2011.

Table 2. Prevalence Rates and ORs Representing the Association Between Elixhauser Comorbidities and Inpatient Diagnosis of HF, Stratified by Timing of Hospitalization, United States, Nationwide Inpatient Sample, 2001 to 2011

Characteristics*	n=50995050†	Antepartum Hospitalizations (n=4833438 [9.48%])			Delivery Hospitalizations (n=45413844 [89.06%])			Postpartum Hospitalizations (n=747769 [1.47%])		
		No HF, % (99.84%)	HF, % (0.16%)	OR (95% CI)	No HF, % (99.97%)	HF, % (0.03%)	OR (95% CI)	No HF, % (95.44%)	HF, % (4.56%)	OR (95% CI)
Aids	14391	0.1	0.4	4.4 (2.0–10.0)‡	0.02	0.2	8.4 (3.7–19.2)‡	0.06	0.01	0.2 (0.0–1.6)
Alcohol abuse	74001	0.6	1.5	2.3 (1.5–3.7)‡	0.1	0.6	5.4 (3.3–8.8)‡	0.5	0.7	1.5 (1.1–2.0)‡
Deficiency anemia	2831580	6.2	23.0	4.5 (4.0–5.2)‡	6.03	17.8	3.4 (3.0–3.8)‡	10.7	25.4	2.8 (2.7–3.0)‡
Rheumatoid arthritis	100522	0.5	3.0	6.7 (4.5–9.9)‡	0.2	1.4	7.5 (5.4–10.3)‡	0.5	1.2	2.6 (2.0–3.3)‡
Chronic blood loss	3764833	6.9	24.2	4.3 (3.8–5.0)‡	8.2	35.1	6.1 (5.5–6.7)‡	12.9	23.8	2.1 (1.9–2.3)‡
Chronic pulmonary disease	1370522	5.6	17.3	3.5 (3.0–4.1)‡	2.7	9.2	3.7 (3.2–4.3)‡	4.5	11.6	2.8 (2.5–3.1)‡
Coagulopathy	437103	1.1	3.6	3.4 (2.5–4.5)‡	0.9	6.7	7.7 (6.6–9.0)‡	1.5	2.4	1.6 (1.3–1.9)‡
Depression	756044	2.7	5.4	2.0 (1.6–2.6)‡	1.5	2.6	1.8 (1.4–2.3)‡	4.07	6.2	1.6 (1.4–1.8)‡
DM	482057	3.4	12.3	4.0 (3.3–4.9)‡	0.8	5.3	7.1 (5.9–8.5)‡	1.8	6.4	3.7 (3.3–4.2)‡
Complicated DM	60226	0.7	3.8	5.8 (4.4–7.8)‡	0.07	1.5	22.2 (16.5–29.9)‡	0.2	1.2	5.1 (3.8–6.8)‡
Drug abuse	656197	3.5	6.7	2.0 (1.6–2.5)‡	1.2	4.9	4.3 (3.6–5.2)‡	2.9	3.4	1.2 (1.0–1.4)
Hypertension	925577	3.7	37.3	15.6 (13.7–17.7)‡	1.7	24.7	18.8 (17.1–20.6)‡	6.2	35.6	8.4 (7.9–8.9)‡
Hypothyroidism	738690	1.7	4.1	2.5 (1.9–3.3)‡	1.6	3.7	2.4 (1.9–3.0)‡	1.8	3.3	1.8 (1.5–2.2)‡
Liver disorder	56398	0.3	1.0	4.1 (2.0–8.3)‡	0.1	0.7	7.1 (4.7–10.7)‡	0.4	0.8	2.0 (1.4–2.8)‡
Lymphoma	7884	0.04	0.5	13.5 (5.0–36.5)‡	0.01	0.2	14.3 (6.5–31.5)‡	0.05	0.2	4.4 (2.5–7.5)‡
Electrolytes disorder	550030	8.4	21.2	3.0 (2.6–3.4)‡	0.3	15.7	59.9 (53.3–67.3)‡	7.7	21.1	3.2 (3.0–3.4)‡
Metastatic cancer	3408	0.03	0.1	3.8 (1.0–15.0)	0.00	0.04	12.1 (1.7–85.4)‡	0.06	0.02	0.3 (0.04–1.9)
Neuro disorders	256421	1.4	4.0	2.9 (2.2–3.9)‡	0.44	2.1	4.9 (3.7–6.4)‡	1.9	2.2	1.1 (0.9–1.3)
Obesity	1114702	2.5	14.4	6.5 (5.5–7.7)‡	2.36	11.3	5.3 (4.7–6.0)‡	4.4	14.8	3.8 (3.5–4.1)‡
Paralysis	20438	0.1	0.7	5.1 (2.6–9.9)‡	0.03	0.2	5.4 (2.3–12.8)‡	0.3	0.6	1.7 (1.2–2.5)‡
Vascular disorder	5159	0.04	1.1	30.1 (14.4–63.2)‡	0.00	0.3	53.1 (24.1–116.8)‡	0.2	0.3	1.7 (1.0–2.8)
Psychoses	336294	2.3	3.0	1.3 (0.9–1.8)	0.51	1.4	2.8 (2.0–3.8)‡	3.8	2.5	0.7 (0.6–0.8)
Pulmonary diseases§	18150	0.1	7.7	80.9 (65.6–99.6)‡	0.02	7.0	466.8 (403.2–540.4)‡	0.5	7.5	16.6 (14.6–18.7)‡
Renal failure	22387	0.2	7.6	43.6 (34.4–55.4)‡	0.03	1.9	76.1 (57.6–100.4)‡	0.3	3.5	13.2 (10.4–16.6)‡
Tumor, no metastasis	14442	0.1	0.2	2.6 (0.8–8.3)	0.02	0.1	4.9 (1.8–13.3)‡	0.1	0.1	1.0 (0.5–2.3)
Peptic ulcer	1058
Valvular disease	259769	0.6	14.6	29.6 (24.9–35.2)‡	0.53	17.6	39.8 (35.5–44.7)‡	1.0	16.3	18.9 (17.3–20.8)‡
Weight loss	30448	0.4	1.3	3.0 (1.8–5.0)‡	0.02	1.1	64.6 (45.5–91.7)‡	0.5	1.3	2.7 (2.1–3.4)‡
Cardiomyopathy	57272	0.03	39.7	575 (498.3–664.6)‡	1.6	70.8	...‡	0.1	34.5	151.0 (138.9–164.1)‡

Rates of alcohol and drug use, abuse, and dependence that are reported in Table 2 are slightly different from rates reported in Table 1 and Figure 2. Whereas frequencies and rates reported in Table 1 and Figure 2 reflect any documented use of alcohol and drugs, the frequencies and rates reported in Table 2 reflect usage that is defined as a comorbidity according to the Elixhauser comorbidity index; that is, usage only when it is not associated with the primary reason for hospitalization. CI indicates confidence interval; DM, diabetes mellitus; HF, heart failure; and OR, odds ratio.

*Reference group is reflected by the absence of the listed condition/characteristic.

†Weighted to estimate the national frequency.

‡Statistical significance at $P < 0.05$.

§Includes conditions represented by the following ICD-9-CM codes: 415.x, 416.x, and 417.9.

with a diagnosis of HF were more likely to have documented alcohol, drug, and tobacco use and to also be diagnosed with ≥ 1 medical or pregnancy-related mor-

bilities. Last, HF is responsible for $\approx 9\%$ of all maternal deaths before discharge and is associated with wide range of adverse outcomes.

Table 3. Prevalence Rates and Adjusted ORs Representing the Associations Between Complications of Labor and Delivery and Inpatient Diagnosis of HF, United States, Nationwide Inpatient Sample, 2001 to 2011

Pregnancy Complications*	Total n=50995050†	Delivery Hospitalizations (n=45413844)		
		No HF, % (99.97%)	HF, % (0.03%)	OR (95% CI)
Preeclampsia	1724850	3.4	28.7	11.4 (10.4–12.4)‡
Eclampsia	52134	0.1	1.7	20.8 (15.7–27.7)‡
Superimposed pre-eclampsia/eclampsia	229887	0.4	10.9	29.0 (26.0–32.4)‡
Eclampsia, all	3499175	6.9	47.1	12.0 (11.1–13.0)‡
Gestational DM	2545816	5.1	8.6	1.8 (1.6–2.0)‡
Placenta previa	257981	0.5	1.2	2.3 (1.7–3.2)‡
Placenta abruptio	544832	1.1	3.9	3.8 (3.1–4.5)‡
Placenta accreta	166530	0.4	0.5	1.5 (1.0–2.5)
Antepartum hemorrhage	398818	0.5	1.7	3.2 (2.4–4.1)‡
Postpartum hemorrhage	1282645	2.7	5.3	2.0 (1.7–2.3)‡

CI indicates confidence interval; DM, diabetes mellitus; HF, heart failure; and OR, odds ratio.

*Reference group is reflected by the absence of the listed condition/characteristic.

†Weighted to estimate the national frequency.

‡Statistical significance at $P < 0.05$.

HF prevalence data related to pregnancy is scarce in the literature. Using data from the National Health and Nutrition Examination Survey, a study reported a HF rate of 0.2% among women 20 to 39 years of age.²⁵ One study that also used 5 years of NIS data (2006–2010) reported a 0.02% HF prevalence (20 per 100000) among women without cardiomyopathy during delivery-related hospitalizations.⁷ None of these studies, although, reported HF prevalence specifically during the pregnancy continuum (antepartum, delivery, and postpartum periods). In the current study, the HF prevalence among antepartum hospitalizations with cardiomyopathy was 0.01% and 0.02% among delivery and postpartum hospitalizations.

About 60% of pregnancy-related HF hospitalizations during the study period occurred during the postpartum period, and ≈5% of all postpartum hospitalizations were associated with HF. These findings highlight the need for close monitoring of high-risk women before discharge after childbirth and through the postpartum period.²⁶ The stable trend in the rate of HF among women hospitalized during the postpartum period from 2006 to 2011, particularly after the increasing HF rate between 2001 and 2006, is encouraging. The leveling off of the HF rate was preceded by several national initiatives led by organizations such as the American Heart Association to increase awareness about cardiovascular health among women

in the general population. However, the increasing HF rates among antepartum hospitalizations, coupled with increasing in-hospital mortality rates observed among women with an HF diagnosis, underscore the need to improve prevention and intervention programs.²⁷

The increasing trend in HF prevalence during the antepartum period may be attributable, at least in part, to the presence of existing cardiovascular risk factors or conditions among women who become pregnant. For example, in our study, women who developed HF were more likely to have comorbidities such as cardiomyopathy, valvular disease, hypertension, and diabetes mellitus (Table 2). Pregnancy-related conditions, including preeclampsia, eclampsia, and gestational diabetes mellitus, were also more common among women with versus without HF during hospitalizations in the delivery or postpartum periods. Women with underlying cardiac disease (eg, cardiomyopathy) may have difficulty adapting to the increased hemodynamic demands of pregnancy, labor, and birth. Those with pronounced heart disease may begin to decompensate before 24 weeks if they are unable to meet the peak cardiac output demands required during midpregnancy.²⁸

Another potential explanation of the increased prevalence of HF during the study period, especially during the antepartum period, could be the improved ability to diagnose HF associated with use of B-type natriuretic peptide test. For example, the Breathing Not Properly Multinational Study demonstrated that using B-type natriuretic peptide improved efficacy in the diagnosis of HF.²⁹ However, in this study, we were unable to assess the degree to which B-type natriuretic peptide was used in the routine evaluation of pregnant patients for HF. The 2005 updated American College of Cardiology (ACC)/American Heart Association (AHA) guidelines recommend use of B-type natriuretic peptide for evaluation of patients presenting in the urgent care setting in whom the clinical diagnosis of HF was uncertain.³⁰ In the 2009 revised American College of Cardiology/AHA guidelines, it was noted that elevated natriuretic peptide levels may lend weight to a suspected diagnosis of HF or trigger consideration of HF when the diagnosis is unknown but should not be used in isolation to confirm or exclude the presence of HF.³¹

Women with preexisting heart disease may develop HF as a result of pregnancy-induced hypervolemia and maximum cardiac output in the third trimester. Most HF develops in the peripartum period when the physiological demands and adjustments of labor, birth, and postpartum place undue burden on compromised cardiac function.²⁸ Consistent with findings of the current study, prior studies that looked at adverse maternal outcomes among women with pregnancy complicated by heart disease also reported increased risk of HF.^{7,32}

In the current study, HF disproportionately impacted women who were of advanced maternal age (>35 years), black, tobacco or alcohol users, insured by

Table 4. Outcome Rates, AORs, and 95% CIs Representing the Association Between HF and Selected Maternal Clinical Outcomes Stratified by Timing of Hospitalization, United States, Nationwide Inpatient Sample, 2001 to 2011

Outcomes	Antepartum			Delivery			Postpartum		
	No HF, %	HF, %	AOR* (95% CI)	No HF, %	HF, %	AOR*† (95% CI)	No HF, %	HF, %	AOR* (95% CI)
Mortality	0.03	1.10	15.9 (9.5–26.6)‡	0.01	0.72	31.9 (19.3–52.8)‡	0.19	1.20	4.0 (3.1–5.3)‡
Pulmonary edema	0.04	1.54	25.3 (16.4–39.0)‡	0.02	2.00	46.9 (34.9–63.0)‡	0.30	0.87	1.8 (1.3–2.5)‡
Prolonged hospital stay§	9.41	30.14	2.6 (2.3–3.0)‡	2.22	58.91	...	10.36	20.67	1.5 (1.4–1.7)‡
Renal failure	0.14	4.25	11.2 (8.6–14.8)‡	0.04	5.24	42.6 (35.0–51.9)‡	0.92	5.42	3.4 (2.9–4.0)‡
Adult RDS	0.31	9.28	17.9 (14.5–22.1)‡	0.05	18.79	195.5 (169.9–225.0)‡	1.20	11.03	6.6 (5.8–7.4)‡
Puerperal CVD	0.20	1.36	4.5 (2.9–7.0)‡	0.03	0.73	12.3 (7.8–19.2)‡
DIC	0.12	1.13	6.2 (3.8–10.2)‡	0.21	3.90	10.2 (8.4–12.4)‡	1.28	1.59	0.9 (0.7–1.1)
Mechanical ventilation	0.21	5.98	14.9 (11.7–19.0)‡	0.04	13.76	145.9 (125.2–169.9)‡	1.03	6.94	4.8 (4.3–5.5)‡
Stroke	0.07	0.64	5.0 (2.6–9.8)‡	0.01	0.13	8.8 (3.2–24.4)‡	0.82	1.17	1.0 (0.8–1.2)
Cesarean section	30.75	71.78	5.8 (5.2–6.4)‡

AOR indicates adjusted odds ratio; CI, confidence interval; CVD, cerebrovascular disease; DIC, disseminated intravascular coagulation; HF, heart failure; OR, odds ratio; and RDS, respiratory distress syndrome.

*Adjustment for age, race/ethnicity, tobacco use, obesity, household income, primary payer, hospital bed count, hospital region, and hospital location/teaching, composite of selected Elixhauser comorbidities (aids, alcohol, anemia, diabetes mellitus, complicated diabetes mellitus, drug use, hypothyroid, liver disease, lymphoma, fluid and electrolyte imbalance, metastasized cancer, renal failure, and tumor).

†Additional adjustment for composite of pregnancy-related comorbidities (placenta abruptio, placenta accreta, placenta previa, gestational diabetes mellitus, antepartum hemorrhage, and postpartum hemorrhage).

‡Statistical significance at $P < 0.05$.

§Additional adjustment for discharge disposition.

Medicare/Medicaid, and who lived in neighborhoods with low median household income. Moreover, the racial disparities in HF prevalence observed in this study are consistent with previous reports on both nonpregnant and pregnant hospitalized women.^{7,33–36} Our findings are similar to prior studies that found associations between HF during pregnancy and alcohol use,³⁷ smoking,³⁸ black race,⁷ and older age.^{39,40} The disproportionate impact of HF highlights the need for continuous targeted surveillance and intervention among pregnant women at higher risk than the general population.

The rate of maternal mortality among women hospitalized with HF increased during the study period,

peaking in 2009 (Figure 3). The spike in HF-related maternal mortality in our study coincides with a similar spike in the overall pregnancy-related maternal mortality in 2009, largely attributed to the 2009 influenza A (H1N1) pandemic.^{41,42} We reported a 1.1%, 0.7%, and 1.2% in-hospital mortality rate among women with HF during antepartum, delivery, and postpartum hospitalizations, respectively. The relatively lower mortality rate among HF patients at delivery could be because of the presence of routine continuous monitoring during intrapartum care. Such monitoring of women in labor and delivery units allows early detection of signs of deterioration, leading to more timely intervention. HF-related in-hospital mortality in our study was relatively

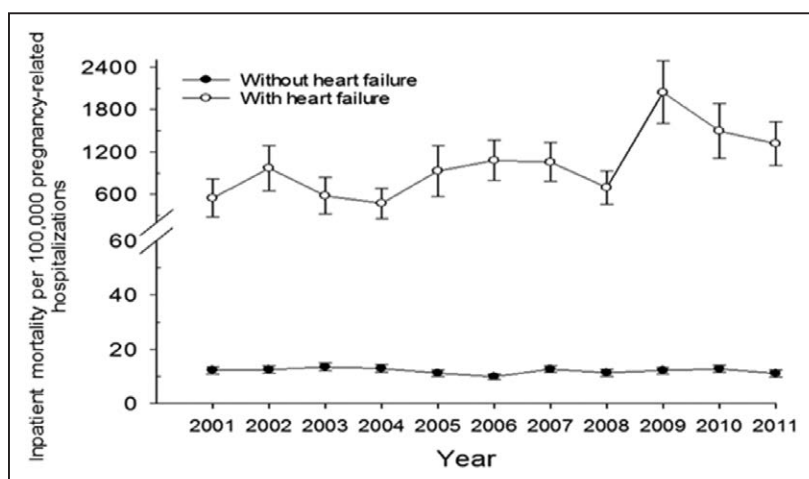


Figure 3. National inpatient maternal mortality trends among women with and without a diagnosis of heart failure, United States, Nationwide Inpatient Sample, 2001 to 2011. Values are rates and SEs of these rates.

similar to previously reported rates of HF among hospitalizations for women <60 years of age.⁴³

In addition to being responsible for >9% of inpatient maternal mortality, HF was also associated with multiple severe maternal morbidities, including pulmonary edema, renal failure, stroke, and puerperal cerebrovascular disease. Women with a diagnosis of HF were also more likely to deliver by cesarean section, be on a mechanical ventilator, and experience a prolonged hospital stay. Therefore, once women are diagnosed with HF, they should be monitored for signs and symptoms, of these adverse conditions.

Strengths of this study include the use of a nationally representative sample of hospital discharges in the United States. The NIS contains hospital discharge data from ≈1000 US community hospitals with ≈8 million discharge records annually.^{44,45} The database contains a wide range of demographic, behavioral, hospital, and clinical variables, allowing for control for potential confounders. Nevertheless, our study has limitations common with the use of retrospective, administrative data. First, the NIS is a discharge-level database without the ability to link records for the same person; therefore, we cannot determine whether 2 discharge records are for the same woman or 2 different women, and this increases the chance of double-counting. A second limitation is that the databases lack data on treatment received by patients, which prevents our analyses from assessing effectiveness of various treatment approaches in managing HF among these patients. Third, identification of cases, behaviors, and clinical diagnoses using *ICD-9-CM* codes is subject to errors in coding. Finally, summaries reported in this study are descriptive and exploratory, and the use of extremely large, national datasets, such as the NIS, may have increased the likelihood of finding statistical significance.

CONCLUSIONS

Early identification of women at increased risk of developing HF would likely allow clinicians to initiate monitoring and early intervention. Women are usually discharged from the hospital within 2 to 3 days after delivery and not evaluated by their healthcare providers again until 6 weeks postpartum. At-risk mothers require surveillance during this period, ideally from a multidisciplinary team that includes HF specialists. Multidisciplinary management of HF has been linked to better outcomes and fewer readmission rates.^{46,47} In addition, women's knowledge and expectations about their risk status during delivery-related hospitalization can have an impact on their ability to seek timely medical attention and mobilize awareness and support among their social network during the postpartum period.⁴⁸ In light of the disproportionate HF-related maternal morbidity and mortality burden experienced by the poor, those

of advanced maternal age, and black women, there is a need for increased awareness and public health measures to address risk factors and promote prevention strategies among these historically disadvantaged population subgroups.

ACKNOWLEDGMENTS

We thank Kevin Grandfield, Publication Manager for the University of Illinois at Chicago Department of Biobehavioral Health Science, for editorial assistance.

SOURCES OF FUNDING

This project is partly supported by internal funding from University of Illinois at Chicago, College of Nursing.

DISCLOSURES

None.

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FOOTNOTES

Received February 28, 2017; accepted November 30, 2017.

The Data Supplement is available at <http://circheartfailure.ahajournals.org/lookup/suppl/doi:10.1161/CIRCHEARTFAILURE.117.004005/-/DC1>.

Circ Heart Fail is available at <http://circheartfailure.ahajournals.org>.

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Heart Failure in Pregnant Women: A Concern Across the Pregnancy Continuum
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Circ Heart Fail. 2018;11:

doi: 10.1161/CIRCHEARTFAILURE.117.004005

Circulation: Heart Failure is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX
75231

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Print ISSN: 1941-3289. Online ISSN: 1941-3297

The online version of this article, along with updated information and services, is located on the
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Supplemental Material

Supplement 1: List of International Classification of Diseases, Ninth Edition, Clinical Modification Codes Used to Identify Selected Clinical and Behavioral Conditions.

Condition	^{a,b} International Classification of Diseases, 9 th Edition, Diagnosis/Procedure Code
Exposure	
Heart Failure	402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, and 428.x
Study groups	
Delivery hospitalization	650.x, V27.x, (72.x, 73.x, 74.x) ^b
Postpartum hospitalization	664.04, 664.14, 664.24, 664.34, 664.44, 664.54, 664.64, 664.74, 664.84, 664.94, 665.24, 665.34, 665.44, 665.54, 665.64, 665.74, 665.84, 665.94, 666.04, 666.14, 666.24, 666.34, 667.04, 667.14, 668.04, 668.04, 668.14, 668.24, 668.84, 668.94, 669.04, 669.14, 669.24, 669.34, 669.44, 669.84, 669.94, 670.04, 670.14, 670.24, 670.34, 670.84, 671.04, 671.14, 671.24, 671.44, 671.54, 671.84, 671.94, 672.04, 673.04, 673.14, 673.24, 673.34, 673.84, 674.04, 674.14, 674.24, 674.34, 674.44, 674.54, 674.84, 674.94, 675.04, 675.14, 675.24, 675.84, 675.94, 676.04, 676.14, 676.24, 676.34, 676.44, 676.54, 676.64, 676.84, 676.94, 677, V24.x,
Antepartum hospitalization	Within NEOMAT but not delivery or postpartum hospitalization
Comorbidities	
Elixhauser comorbidities	List of comorbidities and associated ICD-9-CM code can be found (Quan 2005 et al.) at: http://czresearch.com/dropbox/Quan_MedCare_2005v43p1130.pdf .
Gestational diabetes	648.8x
Gestational hypertension	642.3x
Pre-eclampsia	642.4x, 642.5x
Eclampsia	642.6x
Placenta previa	641.0x, 641.10, 641.11
Placenta abruption	641.2x
Placenta accreta	667.0x
Antepartum Hemorrhage	641.1x, 641.3x, 641.8x, 641.9x,
Postpartum Hemorrhage	666.0x, 666.1x, 666.2x
Behavioral history	
Tobacco use	305.1, 649.0x, 989.84
Maternal outcomes	
Pulmonary Edema	518.4
Acute renal failure	584x, 669.3x
Adult RDS	518.5x, 518.81, 518.82, 518.84, 799.1x
Puerperal CVD	430.x, 431.x, 432.x, 433.x, 434.x, 437.x, 671.5x, 674.0x, 997.2x, 999.2x
DIC	286.6x, 286.9x, 666.63x
Mechanical ventilation	967.x
Stroke	431, 433.01, 433.11, 433.21, 433.31, 433.81, 433.91, 434.01, 434.11, 434.91
Cesarean section	(74x) ^b

^aThe code suffix “x” represents all possible codes that follow the stated code prefix. ^bprocedure codes, not diagnostic codes were used to define Cesarean section