RMD Open
Rheumatic & Musculoskeletal Diseases

ORIGINAL RESEARCH

Fetal and maternal morbidity in pregnant patients with Lupus: a 10-year US nationwide analysis

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To cite: Mehta B, Jannat-Khah D, Glaser KK, *et al*. Fetal and maternal morbidity in pregnant patients with Lupus: a 10-year US nationwide analysis. *RMD Open* 2023;**9**:e002752. doi:10.1136/rmdopen-2022-002752

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/rmdopen-2022-002752).

Received 26 September 2022
Accepted 12 December 2022

Check for updates

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ABSTRACT

Objective To evaluate and quantify the indicators of fetal and maternal morbidity in deliveries for patients with systemic lupus erythematosus (SLE) compared with deliveries in patients without SLE.

Methods We used retrospective data from the National Inpatient Sample (NIS) to identify all delivery related hospital admissions of patients with and without SLE from 2008 to 2017 using ICD-9/10 codes. Fetal morbidity indicators included pre-term delivery and intrauterine growth restriction (IUGR). 21 indicators of severe maternal morbidity were identified using standard Centers for Disease Control and Prevention (CDC) definitions. Descriptive statistics, including 95% confidence intervals, were calculated using sample weights from the NIS dataset.

Results Among the 40 million delivery-related admissions, 51 161 patients were reported to have SLE. Patients with SLE had a higher risk of fetal morbidity, including IUGR (8.0% vs 2.7%) and pre-term delivery (14.5% vs 7.3%), than patients without SLE. During delivery, mothers with SLE were nearly four times as likely to require a blood transfusion or develop a cerebrovascular disorder, and 15 times as likely to develop acute renal failure than those without SLE.

Conclusion Our study demonstrates that fetal morbidity and severe maternal morbidity occur at a higher rate in patients with SLE compared with those without. This quantitative work can help inform and counsel patients with SLE during pregnancy and planning.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Maternal mortality and fetal mortality in patients with systemic lupus erythematosus (SLE) have been decreasing over the past decade. However, little is known about how the indicators of severe maternal morbidity and fetal morbidity are different between patients with SLE and those without.

WHAT THIS STUDY ADDS

⇒ This study quantifies the fetal and maternal morbidity risk in patients with SLE present compared with patients without SLE.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study serves to inform both patients with SLE and their physicians about maternal and fetal risks in order to promote individual level counselling, and thereby improve outcomes.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder that often affects women in their childbearing years.[1] Maternal and fetal mortality are worse in women with SLE compared with those without SLE.[1] Furthermore, premature birth and intrauterine growth restriction (IUGR) are more frequent in patients with SLE.[2 3] Rates of maternal mortality and severe maternal morbidity are increasing in the USA, likely due to rising rates of obesity, comorbidities, and advanced maternal age.[4] Severe maternal morbidity, defined by the US Centers for Disease Control and Prevention (CDC), includes unexpected outcomes of labour and delivery that result in short- or long-term consequences to a woman's health.[4] Little is known about morbidity in patients with SLE, despite evidence that maternal and fetal mortality have declined in patients with SLE.[5] The primary objective of this analysis is to quantify indicators of fetal and severe maternal morbidity in patients with SLE compared with patients without SLE.

METHODS

Data source

We used data from the National Inpatient Sample (NIS) from 2008 through 2017, which contains data on in-hospital admissions in the USA. The NIS, the largest publicly available inpatient database in the USA, is sponsored by the Agency for Healthcare Research and

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Quality and the Healthcare Cost and Utilization Project (HCUP). Unweighted, it contains data from more than 7 million hospital stays each year. Weighted, it estimates more than 35 million hospitalizations nationally each year. Before 2012, the NIS included all discharge data from more than 1000 hospitals each year, approximating a 20% stratified sample of US community hospitals. Redesigned in 2012, the NIS is now a sample of discharge records from all HCUP-participating hospitals, rather than all discharge records from a sample of hospitals. Inpatient stay records in the NIS include clinical and resource use information available from abstracts derived from state-mandated hospital discharge reports. More than 95% of the US population is represented in the NIS. Because the unit of analysis is the individual hospitalisation no unique patient identifiers are contained in the NIS. This study was deemed exempt by the Hospital for Special Surgery Institutional Research Ethics Review Board (IRB #2018–2272) since NIS is a publicly shared de-identified dataset.

Analytic sample

Using *International Classification of Diseases*, ninth revision (ICD-9) codes from 2008 to September 2015 and ICD-10 codes from October 2015 through December 2017, we identified and included all delivery-related hospital admissions of patients with and without SLE. We used the ICD-9 code 710.0 for the years 2008 through September 2015 and ICD-10 code M32* for October 2015 to December 2017. The positive predictive value of the ICD-9 code 710.0 for identifying SLE in inpatient pregnancy populations is 93% or greater.[6] Baseline patient demographics (age, race, and income quartile) and hospital characteristics of region (Northeast, Midwest, South, or West), bed size (small, medium, or large), location (rural or urban), and teaching status were included. We identified comorbid conditions using discharge diagnosis codes and the Elixhauser Comorbidity Index.[7] The Elixhauser Comorbidity Index is a method of categorising comorbidities of patients based on the ICD diagnosis codes found in administrative data, such as hospital abstracts data. We thank the participating HCUP Partners, identified at List of HCUP Data Partners.

Outcome measures

The primary outcomes of interest were fetal morbidity and severe maternal morbidity. Fetal morbidity indicators include pre-term delivery (defined as onset of labour before 37 completed weeks of gestation) and IUGR. The CDC uses a standardised measure containing 21 indicators[4] to define severe maternal morbidity, identified by ICD-9/10 codes (online supplemental table 1). We grouped severe maternal morbidity into six categories[1]: blood transfusion[2]; acute renal failure[3]; puerperal cerebrovascular disorders[4]; eclampsia and disseminated intravascular coagulation[5]; cardiovascular and peripheral vascular disorders including acute myocardial infarction, aneurysm, amniotic fluid embolism, cardiac arrest/ventricular fibrillation, heart failure, pulmonary oedema/acute heart failure, sickle cell disease with crisis, air and thrombotic embolism, and conversion of cardiac rhythm; and[6] general medical issues including hysterectomy, shock, sepsis, adult respiratory distress syndrome, severe anaesthesia complications, temporary tracheostomy, and ventilation.

Statistical analysis

We used descriptive statistics to compare demographic characteristics and outcomes between pregnant patients with and without SLE. Because the NIS database use agreement does not allow presentation of 10 or fewer observations for each cell, we pooled data and collapsed categories so that smaller sample sizes in maternal morbidity would be compliant with NIS-HCUP guidelines. Analyses accounted for the complex survey design, stratification, and clustering of the data per NIS database recommendations, and weights were applied to generate nationwide estimates for each year.[8] To account for the 2012 redesign of the NIS database, our analysis used revised 'trend weights' in place of the original discharge weights for 1998 to 2011, in accordance with HCUP recommendations.[9] Stata software, version 14.0, was used for statistical analysis and an α of 0.05 was used to determine statistical significance

RESULTS

Sample characteristics

From 2008 to 2017, an estimated 51 161 (unweighted 10 297) pregnant patients with SLE were hospitalised in the USA for delivery-related reasons. The total estimated number of non-SLE patients hospitalised for delivery-related reasons was 40 000 000 (unweighted 8 055 025). Compared with non-SLE patients, patients with SLE were older (30.1 years vs 28.2 years), more often African American (24.7% vs 15.0%), and more likely to receive Medicare (5.3% vs 0.7%). A majority of patients with SLE were treated at an urban teaching hospital (70.5% vs 56.2%) and underwent care at a medium- or large-size hospital (90.7% vs 86.3%) compared with pregnant patients without SLE. 45.5% of pregnant patients with SLE had an Elixhauser Comorbidity Index >2 compared with only 3.8% of non-SLE patients (table 1).

Indicators of severe maternal morbidity

Pregnant patients with SLE were about 15 times as likely to have acute renal failure (1.5% vs 0.1%), 11 times as likely to have cardiovascular and peripheral vascular disorders (1.1% vs 0.1%), four times as likely to receive a blood transfusion (4.0% vs 1.1%) or have puerperal cerebrovascular disorders (4.8% vs 1.1%), more than three times as likely to have eclampsia or disseminated intravascular coagulation (DIC) (1.2% vs 0.4%), and more likely to have general medical issues (1.8% vs 0.5%) compared with those without SLE (figure 1).

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Table 1 Characteristics for deliveries of patients with and without SLE

	SLE deliveries	Non-SLE deliveries
	% (95% CI)	% (95% CI)
N*	51 161 (49 419 to 52 903)	40 000 000 (39 200 000 to 40 700 000)
Age (years)	30.1 (29.9 to 30.2)	28.2 (28.1 to 28.2)
Race		
White	46.2 (44.8 to 47.5)	52.4 (51.7 to 53.1)
African American	24.7 (23.6 to 25.9)	15 (14.6 to 15.4)
Hispanic	18.5 (17.4 to 19.6)	21.5 (20.8 to 22.1)
Other	10.7 (9.9 to 11.5)	11.1 (10.8 to 11.5)
Insurance		
Medicare	5.3 (4.8 to 5.9)	0.7 (0.7 to 0.8)
Medicaid	38.2 (37.0 to 39.4)	43.8 (43.2 to 44.4)
Private insurance	51.8 (50.6 to 53.1)	49.8 (49.2 to 50.5)
Self-pay	1.4 (1.1 to 1.7)	2.7 (2.6 to 2.9)
No charge	†	0.1 (0.1 to 0.2)
Other	3.2 (2.8 to 3.6)	2.8 (2.7 to 3.0)
Income quartile		
0–25	27.7 (26.6 to 28.9)	28 (27.4 to 28.7)
26–50	23 (22.0 to 24.0)	25 (24.6 to 25.4)
51–75	24.8 (23.9 to 25.8)	24.9 (24.5 to 25.2)
76–100	24.5 (23.2 to 25.8)	22.1 (21.4 to 22.8)
Hospital bed size		
Small	9.2 (8.7 to 10.1)	13.7 (13.2 to 14.2)
Medium	24.7 (23.3 to 26.1)	28.8 (28.0 to 29.6)
Large	66.1 (64.5 to 67.7)	57.6 (56.7 to 58.5)
Hospital teaching location		
Rural	5.2 (4.7 to 5.7)	10.4 (10.1 to 10.7)
Urban non-teaching	24.3 (23.0 to 25.6)	33.4 (32.6 to 34.3)
Urban teaching	70.5 (69.1 to 72.0)	56.2 (55.3 to 57.1)
Hospital region		
Northeast	18.9 (17.6 to 20.3)	16 (15.4 to 16.7)
Midwest	18.6 (17.3 to 19.9)	21.1 (20.5 to 21.8)
South	39.1 (37.4 to 40.8)	38.6 (37.7 to 39.5)
West	23.4 (22.0 to 24.8)	24.2 (23.5 to 25.0)
Elixhauser Index		
0	0 (no obs)	80.6 (80.3 to 80.8)
1	54.5 (53.4 to 55.6)	15.6 (15.4 to 15.7)
2–4	43.3 (42.3 to 44.4)	3.8 (3.8 to 3.9)
5+	2.2 (1.9 to 2.5)	0.03 (0.03 to 0.04)
Expenses		
Total hospital charges (US$)	24 978.7 (24 075.7 to 25 881.8)	16 211.1 (16 009.1 to 16 413.1)

% (95% CI) unless otherwise specified. Age and total hospital charges are reported as means.
*Weighted values are listed. Unweighted SLE and non-SLE deliveries were 10 297 and 8 055 025, respectively.
†Per HCUP guidelines, cell sizes ≤10 have been omitted to protect patient confidentiality.
HCUP, Healthcare Cost and Utilization Project; SLE, systemic lupus erythematosus.

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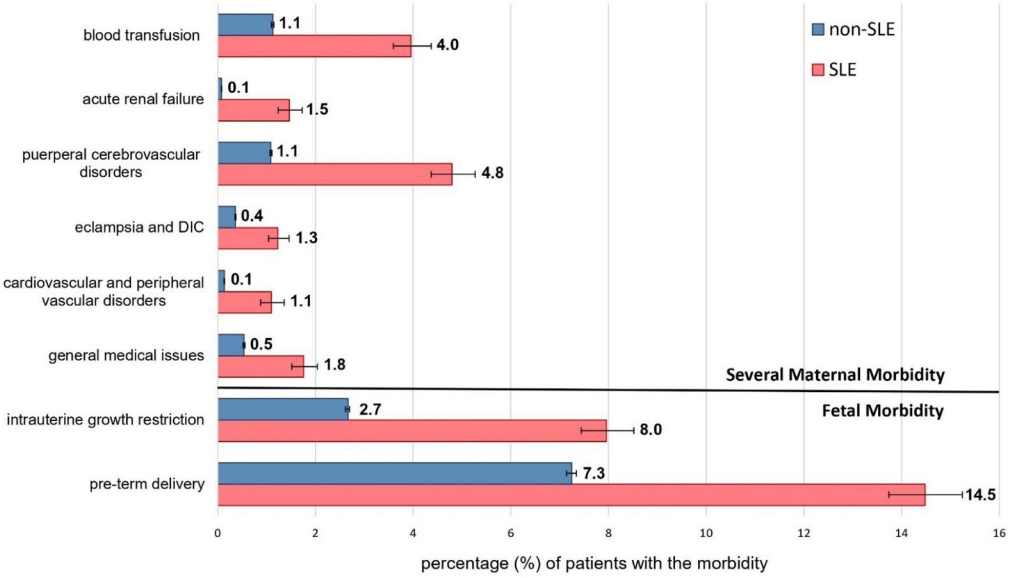

Figure 1 Fetal and severe maternal morbidity outcomes between systemic lupus erythematosus (SLE) and non-SLE patients. Fetal morbidity outcomes were sectioned into two groups: (a) pre-term delivery; and (b) intrauterine growth restriction (IUGR). Several maternal morbidity outcomes were sectioned into six groups: (1) blood transfusion; (2) acute renal failure; (3) puerperal cerebrovascular disorders; (4) eclampsia and disseminated intravascular coagulation; (5) cardiovascular and peripheral vascular disorders which include acute myocardial infarction, aneurysm, amniotic fluid embolism, cardiac arrest/ventricular fibrillation, heart failure, pulmonary oedema/acute heart failure, sickle cell disease with crisis, air and thrombotic embolism, and conversion of cardiac rhythm; and (6) general medical issues which include hysterectomy, shock, sepsis, adult respiratory distress syndrome, and severe anaesthesia complications, temporary tracheostomy, and ventilation. Error bars represent estimates as this is a nationwide weighted analysis. DIC, disseminated intravascular coagulation.

Indicators of fetal morbidity

SLE deliveries had a higher rate of IUGR (8.0% vs 2.7%) and pre-term delivery (14.5% vs 7.3%) than non-SLE deliveries (figure 1).

DISCUSSION

In this large 10 year US nationwide sample, we quantify and compare the rates of fetal morbidity and severe maternal morbidity in pregnant SLE and non-SLE patients. Pregnant patients with SLE had a notably increased incidence of acute renal failure, cardiovascular and peripheral vascular disorders, blood transfusion, puerperal cerebrovascular disorders, eclampsia or DIC, and general medical issues. Patients with SLE were more likely to deliver prematurely and experience IUGR. In SLE pregnant patients, the high comorbidity burden likely contributed to the increased risks of fetal and severe maternal morbidity.[10] The majority of SLE deliveries occurred at large and urban teaching hospitals, likely reflecting differences in urban/rural demography, referral patterns, recognition of SLE, and complexities of disease management in these patients. While our prior work showed notable improvement in the recent decade in SLE-related fetal and maternal mortality, morbidity remains exceedingly high.

Our study focuses on maternal and fetal complications in delivery-related hospitalisations of patients with SLE. Among the most relevant studies on the topic of population-based studies in SLE pregnancies is Clowse *et al*'s study, which examined hospitalisations of 13 555 pregnant women with SLE recorded between 2000–2003.[3] Like us, they found that, compared with hospitalised patients without SLE, those who were hospitalised with SLE were more likely to be of older age and identify as African American. To address specifically the detrimental outcomes for pregnant patients with SLE, we narrowed the focus to CDC-defined maternal morbidity and fetal morbidity in pregnant patients with SLE during delivery. Since 2003, new management protocols and new medications have been available.[11] As we reflected on whether these changes improved outcomes, we found that the proportion of patients with SLE suffering pre-term labour decreased (20.8% to 14.5%) but IUGR increased (5.6% to 8.0%), eclampsia increased (0.5% to 1.2%, definitions of eclampsia differed slightly), and transfusion rates increased (2.7% to 4.0%, transfusion rates in non-SLE patients also increased, 0.5% to 1.1%) since 2003. These differences may be due to several factors, such as transfusion thresholds, which may explain the observed increase in transfusion rates, or a higher proportion of patients carrying to term, which may explain the observed increase in IUGR. A higher vigilance or better coding may have contributed to the higher rate of sepsis and stroke in our study.

Among the strengths of this study are the large number of patients (approximately 51 000 SLE deliveries), the description of nationwide data over a decade, and the specific focus on delivery-related events, which improves

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physicians' ability to personalise care. Our study is limited by the fact that NIS uses billing information and discharge diagnosis, which may lead to misclassified diagnoses. This bias was minimised by using validated codes for SLE and CDC indicators of severe maternal morbidity. As NIS does not contain outpatient information, we were unable to capture data for outpatient deliveries, early pregnancy losses, and miscarriages. This defect is likely to be unimportant, since 98.7% of US deliveries occur in hospitals.[12] We are unable to comment on the roles of lupus disease activity, Apgar scores, flares, presence of nephritis, antiphospholipid or anti-Ro/SSA antibodies, or medications[10 13] in our findings since the database lacks such information.

Our study gives population estimates of an increase in fetal and severe maternal morbidity in patients with SLE compared with those without SLE. Despite extensive efforts over the years, there remains substantial risk for both maternal and fetal complications. This information serves to inform both patients and their doctors, promote individual level counselling, and thereby improve outcomes.[11 14]

Contributors BM conceived the presented idea and is the gurantor. DJ-K developed the theoretical formalism, performed the analytic calculations and performed the numerical simulations. BM, KKG, and YL authors contributed to the final version of the manuscript including the writing of the manuscript and the construction of the figures and tables. LRS, DWB, SG, ML, FW, SI and JS provided critical feedback and helped shape the research, analysis, and manuscript.

Funding This study was funded by the Deans Diversity Award at Weill Cornell Medicine. Preliminary results from this study were presented at the European Alliance of Associations for Rheumatology (EULAR) in 2022.

Competing interests None declared.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available in a public, open access repository.

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