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Journal

Lupus Science & Medicine, 10(1)

ISSN

2053-8790

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Publication Date

2023-04-01

DOI

10.1136/lupus-2022-000851

LUPUS SCIENCE & MEDICINE™

Infection-related hospitalisation in young adults with systemic lupus erythematosus: data from the National Inpatient Sample

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To cite: Dhital R, Guma M, Poudel DR, *et al*. Infection-related hospitalisation in young adults with systemic lupus erythematosus: data from the National Inpatient Sample. *Lupus Science & Medicine* 2023;**10**:e000851. doi:10.1136/lupus-2022-000851

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/lupus-2022-000851).

Received 22 October 2022
Accepted 7 January 2023

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ABSTRACT

Introduction Care of young adults with SLE (YA-SLE, 18–24 years) is challenging due to major life transitions co-occurring with chronic healthcare needs. Studies have demonstrated poorer outcomes in the post-transition period. Epidemiological studies focused on serious infection-related hospitalisation (SIH) in YA-SLE are lacking.

Methods We used National Inpatient Sample from 2010 to 2019 to study the epidemiology and outcomes of SIH for five common infections in SLE, namely sepsis, pneumonia, urinary tract infections, skin and soft tissue infections, and opportunistic infections. For time trends, we extended the dataset to cover 2000–2019. The primary outcome was the rate of SIH in YA-SLE compared with adults (25–44 years) with SLE and with young adults without SLE (YA-no SLE).

Results From 2010 to 2019, we identified 1 720 883 hospital admissions with SLE in patients aged ≥18 years. Rates of SIH were similar in young adults and adults with SLE (15.0% vs 14.5%, p=0.12), but considerably higher than in the YA-no SLE group (4.2%, p<0.001). Among SLE with SIH, sepsis followed by pneumonia was the most common diagnosis. Significantly higher proportions of SIH among young adults than adults with SLE were comprised of non-white patients, belonged to the lowest income quartile and had Medicaid. However, only race/ethnicity was associated with SIH among YA-SLE. There was a higher prevalence of comorbid lupus nephritis and pleuritis among young adults compared with adults with SLE and SIH, and both comorbidities were associated with SIH in YA-SLE. Increasing rates of SIH, driven by sepsis, were seen over time.

Discussion YA- SLE had similar rates of SIH to adults with SLE. While hospitalised YA-SLE differed sociodemographically from SLE adults and YA-no SLE, only race/ethnicity was associated with SIH in the YA-SLE group. Lupus nephritis and pleuritis were associated with higher SIH in YA-SLE. Among SLE with SIH, increasing trends of sepsis deserve further study.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Almost half of the patients with SLE hospitalised with infection are <50 years old and of non-white race and have higher infection-related hospitalisation compared with general population controls.

WHAT THIS STUDY ADDS

⇒ Nationally representative epidemiological studies focused on serious infection-related hospitalisation (SIH) in young adults with SLE are scarce. In this study, 'young adults' with SLE had significantly higher SIH rates and poorer outcomes compared with young adults without SLE, but similar to 'adults' with SLE. Many of the studied lupus-related comorbidities, including lupus nephritis, pleuritis, pericarditis and thrombocytopenia, were also significantly higher among young adults compared with adults with SLE, possibly suggesting increased disease severity and associated immunosuppressive therapy, and contributing to comparable rates of SIH among young adults and adults.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Increasing trends of SIH, particularly due to sepsis, deserve further study.

INTRODUCTION

SLE is a complex autoimmune condition with mean age of diagnosis of around 30 years.[1] Paediatric-onset SLE, with diagnosis before 18 years, accounts for 15%–20% of all SLE and similar to SLE in adults, tends to present with more severe disease among non-Caucasian race/ethnicities.[2 3] Infections are the leading causes of hospitalisation and mortality in SLE.[4–6] A sixfold to sevenfold increased risk of infection in SLE compared with the general population has been reported.[7]

Patients with SLE may be inherently more susceptible to infection due to immune dysregulation independent of immunosuppressive medication use. Two possible mechanisms have been suggested. The first proposed mechanism is that acquired immune dysregulation including disruption of mucocutaneous

barriers, immune complex and hypocomplementemia, neutropenia and lymphopenia may lead to an increased susceptibility to infection. The second proposed mechanism is that genetic factors that potentiate SLE are also associated with select primary immunodeficiencies.[5]

Care of young adults with either a new diagnosis of SLE or those transitioning care from paediatric to adult rheumatology is challenging. Young adulthood is a vulnerable period in the life of a patient with chronic disease, due to limited understanding of the disease process and major life transitions that co-occur with chronic healthcare needs, with implications on psychosocial state and treatment adherence.[8] A study reported a mean time of approximately 9 months from last paediatric to first adult provider visit.[9] Poorer outcomes including higher mortality and increased disease activity have been reported in the post-transition period.[9] As the diagnosis of paediatric SLE is typically made during adolescence, the period for acceptance, self-learning and self-management required for transition may not be adequate.[2 10]

A prior study using the US National Inpatient Sample (NIS) noted the average age of patients with SLE with hospitalised infection to be 52.5 years, with almost half of the hospitalised patients being <50 years of age and belonging to non-white race.[11] However, there is a lack of nationally representative epidemiological studies focused on serious infection-related hospitalisation (SIH) in young adults with SLE (YA-SLE). The main objectives of this study were to assess the rates, epidemiology, outcomes (including healthcare utilisation) and time trends of SIH in adults aged 18–24 years ('young adults') with SLE (YA-SLE) compared with adults aged 25–44 years ('adults') with SLE and with young adults without SLE (YA-no SLE).

PATIENTS AND METHODS

Data source

The US NIS database for years 2010–2019 was used to identify patients ≥18 years. NIS is the largest publicly available all-payer inpatient database in the USA and is a part of the Healthcare Cost and Utilization Project (HCUP). NIS supplies discharge weights (DISCWT) for the sampled discharges, which when applied to the sample provides a weighted national estimate. Prior to redesign in 2012, the NIS was constructed by retaining 100% of the discharges from 20% of the randomly sampled community hospitals. In 2012, the NIS changed sampling strategy to include 20% discharges from all participating hospitals, in order to provide more precise estimates by reducing sampling error.[12]

Patient selection

SLE was identified using the following International Classification of Disease (ICD) codes: ICD-9 code 710.0 (from January 2010 to September 2015) and ICD-10 M32.xx (from October 2015 to December 2019, without the code M32.0 for drug-induced SLE), due to the change in ICD coding system from ICD-9 to ICD-10 in the USA starting in October 2015. At least one hospitalisation where SLE was in the diagnostic coding was necessary for this study based on past findings demonstrating that this sampling had good positive predictive value (PPV) of 99.4% for SLE.[13]

In this study, the particular group of interest was YA-SLE, as compared with adults with SLE and with YA-no SLE. The age group 18–24 years has been widely accepted in prior literature to define young adulthood. Young adulthood is a vulnerable period in the life of a patient with chronic disease, due to major life transitions that co-occur with chronic healthcare transitions. Although there may be different models for transition of care based on practice patterns, the widely accepted period for transition from child-oriented to adult-oriented healthcare is between the ages of 18 and 21 years. 'Post-transition period' was defined as the first 3 years in adult care in a prior study of childhood SLE;[9] hence, we chose the age group 18–24 years as the representative age group for 'young adults' for the purpose of this study and carried out subanalyses for SIH rates separately for two subcategories for young adults: 18–21 years and 22–24 years. The age group 25–44 years has been used in prior lupus studies as the reference group for 'adults with SLE' and represents the population with peak SLE incidence.[14 15] For this study, hospitalisation was categorised by age groups into young adults (18–24 years) and adults (25–44 years). Adults were chosen as the comparator group to represent an adult population with SLE who might have a better understanding of their disease, and more stable access to care compared with young adults but without the significant comorbidities of older adults (≥45 years), which could contribute to a higher susceptibility to serious infections.

Exploratory variables and outcomes

SIH for five common infections, including septicaemia/bacteraemia (referred to as sepsis), pneumonia, urinary tract infection, skin and soft tissue infection (SSTI) and opportunistic infections (OIs), were identified using select ICD codes for acute infections in the primary diagnosis position (online supplemental table 1). SIH was defined as a sum total of these five infections in the primary diagnosis position. The primary outcome was the rate of SIH in YA-SLE as compared with adults with SLE and with YA-no SLE. Although the methods for defining serious infection differed among studies, the PPVs of discharge diagnoses for administrative codes have been reported around 80% for serious infections for ICD-10 (bacteraemia ~84%, pneumonia ~83%, SSTI ~79%) and about 90% for ICD-9 (pneumonia ~97%, cellulitis 91%, sepsis 83%).[16 17] Other variables included baseline demographic (age, sex, race/ethnicity, income, insurance payer, hospital characteristics) and clinical factors by age group, hospitalisation outcomes and healthcare utilisation (length of stay (LOS), hospitalisation cost, mortality, disposition at discharge), and time trends of SIH in YA-SLE compared with adults with SLE and with YA-no SLE. In HCUP, 'the variable RACE contains a

uniform coding for race and ethnicity. If the data source supplied information on race and ethnicity as separate data elements (RACE_X and HISPANIC_X, respectively), ethnicity takes precedence over race in setting the HCUP uniform values. For example, a patient who is Hispanic and black is assigned to the category of Hispanic (RACE=3 based on information included in HISPANIC_X)'.[18] For income, the HCUP categorical variable ZIPINC_QRTL provides a quartile classification of the estimated median household income derived from zip code-demographic data obtained from Claritas, and indicated by values 1–4, for poorest to wealthiest populations. Because these estimates are updated annually, the value ranges for the ZIPINC_QRTL categories vary by year.[19]

The Deyo-Charlson Comorbidity Index (DCCI) is derived by scores from 17 comorbidities based on ICD codes found in administrative data and can be used to predict long-term mortality.[20] Other clinical factors studied include SLE-related and other comorbidities including lupus nephritis (LN), serositis (pericarditis, pleuritis), seizures, cytopenias, heart failure, cerebral infarction, hypertension, diabetes, obesity and depression. LN was defined as code for SLE plus for any combination of acute or chronic glomerulonephritis, nephritis or nephrotic syndrome, acute or chronic renal failure, or proteinuria (ICD-9 codes 580.00–586.00 and 791.0; ICD-10 codes N17-N19, N00-N06, N08, R80.9). Such an algorithm has a PPV of 80% for identifying LN in a Medicaid population.[21] Additionally, for ICD-10, the codes M32.14 and M32.15 were also used to identify LN (the use of only ICD-10 code M32.14 has a high specificity (99.8%) and PPV (93.9%), with a low sensitivity (32.6%) for identifying LN).[22] In a study using a California population-based hospitalisation database (from 1996 to 2000), Ward *et al* found respiratory failure and sepsis, along with thrombocytopenia, renal disease, heart failure and cerebrovascular accident, to be the most important predictors for in-hospital mortality.[23]

Statistical analysis

The rate of SIH in SLE was calculated by dividing the number of hospital admissions with a primary diagnosis of infection among patients with a secondary diagnosis of SLE divided by the number of hospital admissions with a secondary diagnosis of SLE, using a similar approach as that previously described.[11 24] The baseline demographic features, clinical comorbidities, hospital characteristics and outcomes associated with SIH in YA-SLE were compared with adults with SLE and with YA-no SLE. In addition, a multivariable logistic regression method was used to assess for factors associated with SIH among YA-SLE, adjusted for clustering of hospitalisation by hospital location and teaching status. We checked for multicollinearity in the independent variables using the variance inflation factor (VIF) technique, and all the variables including insurance and income had a VIF <2.5, suggesting no substantial collinearity.[25] Continuous variables were presented as mean (SEM) and categorical variables as counts and percentages. Pearson's X^2 tests were used to compare categorical variables and t-tests to compare continuous variables among groups; a p value of 0.05 was considered to be statistically significant. Statistical software STATA V.13 was used for analysis.[26]

US national estimates from the representative sample discharges were calculated using DISCWT for the observations provided by the NIS. To estimate the national trends, NIS data for 20-year period from 2000 to 2019 were used, and the trend weights (TRENDWT) provided by the NIS were applied.[12 27] Costs for inpatient stays were calculated using the HCUP Cost-to-Charge Ratios for Inpatient Files.[27] The yearly change in the trend of SIH in SLE was analysed as annual per cent change (APC), calculated using the statistical software Joinpoint V.4.5.0.1, which has been used to calculate cancer trends reported by the National Cancer Institute.[28]

RESULTS

Rates of SIH

From the years 2010 to 2019, we identified a weighted national estimate of 307 319 355 hospital admissions for adults ≥18 years of age, of whom 1 832 859 (0.6%) had a discharge diagnosis of SLE in any position and 1 720 883 had a diagnosis of SLE in the secondary diagnosis position. Among them, young adults and adults comprised 72 942 (4.2%) and 482 082 (28.0%) of hospital admissions, respectively. The rate of SIH in the YA-SLE group was similar to the adult group (10 951 of 72 942 (15.0%) vs 69 929 of 482 082 (14.5%), p=0.12) but significantly higher compared with the YA-no SLE group (15.0% vs 4.2%, p<0.001) (figure 1). The rates of SIH were similar among two separate age subcategories of young adults (15.3% for 18–21 years and 14.8% for 22–24 years, p=0.46).

Among young adult and adult patients with SLE with SIH, sepsis followed by pneumonia were the most common primary diagnoses, accounting for 44.9%–49.1% and 20.2%–21.1% of SIH, respectively. In YA-no SLE, sepsis (39.1%), followed by SSTI (25.9%), were the most common primary diagnoses for SIH. Sepsis was more common (17.7% vs 11.2%, p<0.001) and SSTI was less common (44.6% vs 49.1%, p=0.001) in young adults compared with adults with SLE (online supplemental table 2).

Demographic and clinical characteristics and hospitalisation outcomes

Among patients with SLE hospitalised for infections, the race/ethnicity distribution for YA-SLE compared with adults with SLE varied significantly (20% vs 35% white, 43.5% vs 35.4% black and 23.1% vs 18.4% Hispanic patients, respectively, p<0.001). The YA-SLE group compared with the adult group more often belonged to the lowest income quartile (41.1% vs 37.9%, p<0.001) and had Medicaid as their primary payer (43.1% vs 32.1%, p<0.001). Similar demographic differences were

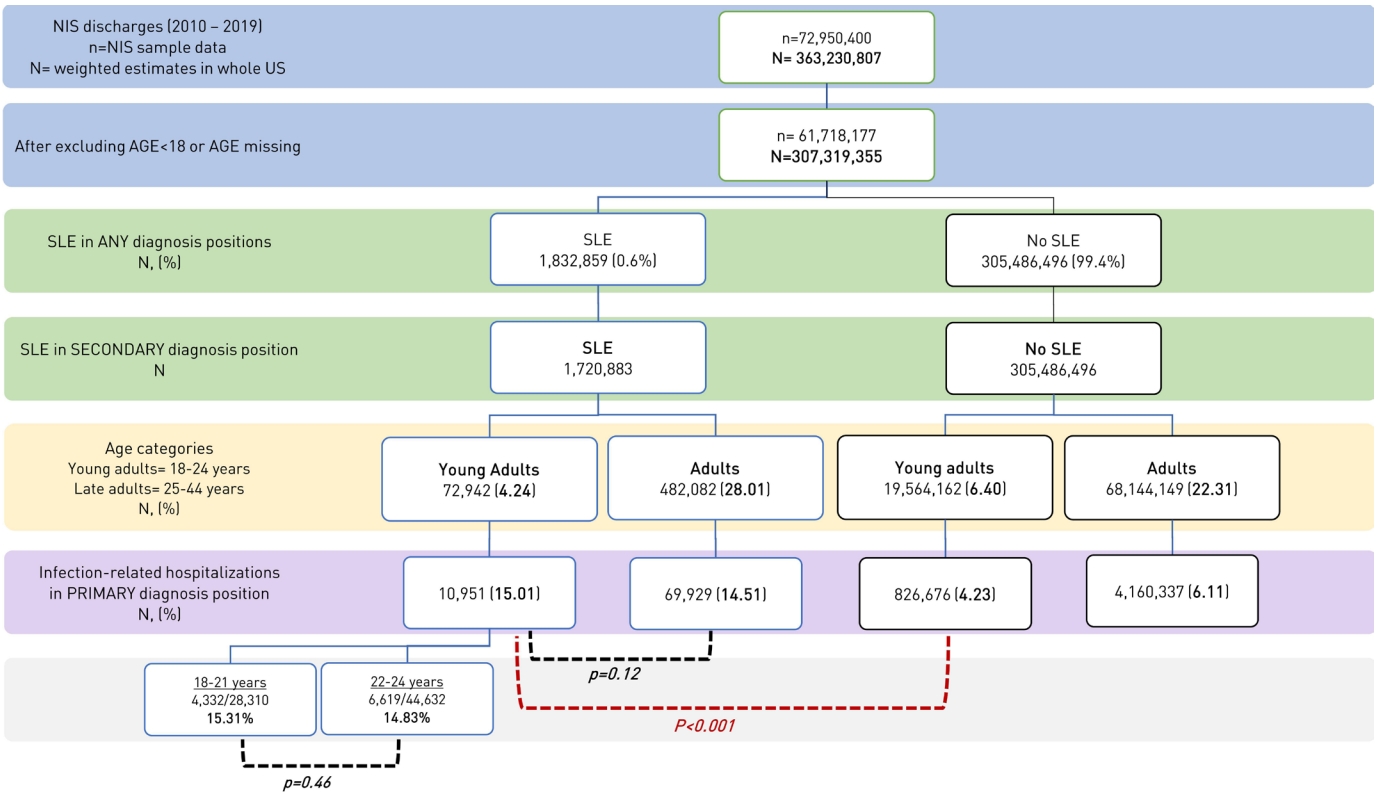


Figure 1 Rates of serious infection-related hospitalisation among young adults with SLE compared with adults with SLE and young adults without SLE; National Inpatient Sample (NIS), 2010–2019.

found when comparing YA-SLE with YA-no SLE (20% vs 54.2% white patients, 41.1% vs 33.5% patients in the lowest income quartile and 43.1% vs 36.2% patients with Medicaid, respectively) (table 1). However, in comparing hospitalised YA-SLE with and without SIH, only race/ethnicity (black, Hispanic and Asian with reference to white race/ethnicity) was associated with increased odds of SIH, whereas Medicaid insurance (reference: private insurance) was not (online supplemental table 3).

DCCI score of ≥2 was considerably higher among YA-SLE compared with YA-no SLE (50.9% vs 9.9%, p<0.001) but lower than adults with SLE (58.7%, p<0.001) (table 1). Young adults compared with adults with SLE hospitalised for infections had higher rates of LN (56.5% vs 44.1%, p<0.001). Many of the other studied lupus-related comorbidities including pericarditis, pleuritis, anaemia and thrombocytopenia were also higher among YA-SLE compared with adults (table 1). Lupus-related comorbidities including nephritis and pleuritis were associated with higher SIH in the YA-SLE group (online supplemental table 3).

Hospital LOS and average cost of hospitalisation in YA-SLE compared with adults were similar (6.2 (SEM 0.2) vs 6.1 (SEM 0.1) days, p=0.55; $15 280 (SEM 577) vs $14 387 (SEM 251), p=0.13) (table 2). The LOS and costs also did not differ for the individual infection categories, except for higher cost for OIs among YA-SLE compared with adults ($25 464 vs $16 633, p=0.04) (online supplemental table 4). Inpatient mortality was higher in adults versus YA-SLE (2.5% vs 1.8%, p=0.03). In contrast, LOS was longer, and average cost of hospitalisation and mortality were higher in YA-SLE compared with YA-no SLE (table 2).

Time trends of SIH

In the 20-year period between 2000 and 2019, we noted increasing trends of SIH in YA-SLE (APC 1.9, p<0.05). Similarly, increasing trends were noted in adults with SLE (APC 2.6, p<0.05) as well as in YA-no SLE from 2.3% in 2000 to 4.8% in 2019 (APC 3.91, p<0.05) (figure 2). When comparing time trends of individual infections between YA-SLE and adults with SLE, the trend for sepsis was noted to be increasing among both groups, whereas other infections followed decreasing trends. Similar trends were observed for YA-no SLE (online supplemental figure 1).

DISCUSSION

Infection is the leading cause of hospitalisation and mortality in SLE.[4–6] Singh and Cleveland found that infection-related hospitalisation among adults occurred at a younger age in SLE compared with patients without SLE (median age 52 vs 65), and almost half of the patients with SLE hospitalised with infection were <50 years old and of non-white race.[11] However, there is limited understanding of how the factors associated with SIH and outcomes of SIH may differ among young adults compared with other groups. In this study using a large US national inpatient database, we directly compared the

Table 1 Baseline demographic and clinical characteristics of serious infection-related hospitalisation among young adults with SLE compared with adults with SLE and young adults without SLE, defined as YA: young adults (18–24), adults (25–44); National Inpatient Sample, 2000–2019

Infection-related hospitalisation	YA-SLE	Adults with SLE	YA-no SLE	P value	P value
N (%)	10 951 (15.0)	69 929 (14.51)	826 676 (4.23)	YA-SLE vs adults with SLE	YA-SLE vs YA-no SLE
Baseline demographic characteristics					
Sex (%)					
Male	12.9	10.4	41.7	0.003	<0.011
Female	87.1	89.6	58.3		
Race/ethnicity (%)					
White	20	35.2	54.2	<0.001	<0.001
Black	43.5	35.4	17.3		
Hispanic	23.1	18.4	16.7		
Asian/Pacific Islander	5.1	3	2.1		
Other	4.4	4.3	4.5		
Missing	3.9	3.7	5.2		
Income percentiles (%)					
0th–25th	41.1	37.9	33.5	0.007	<0.001
25th–50th	24.4	23.9	25.3		
50th–75th	19.2	21.3	21.9		
75th–100th	14.1	15.1	17.2		
Missing	1.2	1.8	2.1		
Insurance (%)					
Medicare	13.1	31.3	3.4	<0.001	<0.001
Medicaid	43.1	32.1	36.2		
Private	31.1	27	38.9		
Self	8.7	6.3	15.3		
Other	4	3	5.9		
Missing	—	0.3	0.2		
Hospital location/teaching status (%)					
Rural	5.4	6.8	11	<0.001	<0.001
Urban non-teaching	23.5	27.3	29.6		
Urban teaching	71.1	65.8	59.1		
Missing	—	0.1	0.3		
Baseline clinical characteristics					
Charlson Comorbidity Index					
DCCI ≥2	50.9	58.7	9.9	<0.001	<0.001
Other comorbidities					
Nephritis (including lupus nephritis) and CRF	56.5	44.1	10.2	<0.001	<0.001
Pericarditis	7	3.2	0.5	<0.001	<0.001
Pleuritis	9.5	6.1	3.3	<0.001	<0.001
Seizures	9.5	9.6	5.7	0.87	<0.001
Haemolytic anaemia	1.9	1.2	0.2	0.02	<0.001
Thrombocytopenia	12.3	9.7	4.3	0.001	<0.001
Congestive HF	11.6	12.5	1.7	0.22	<0.001
Cerebral infarction	0.4	0.4	0.2	0.91	0.07

Continued

Table 1 Continued

Infection-related hospitalisation	YA-SLE	Adults with SLE	YA-no SLE	P value	P value
Acute MI	0.5	0.9	0.2	0.01	0.08
Hypertension	43.7	48.5	6.8	0.0004	<0.001
Diabetes mellitus	4.9	13.6	6.9	<0.001	0.0001
Depression	10.8	15.6	7.4	<0.001	<0.001
Obesity	10.3	17.3	9.3	<0.001	0.14

CRF, chronic renal failure; DCCI, Deyo-Charlson Comorbidity Index; HF, heart failure; MI, myocardial infarction.

SIH rates, patient characteristics and outcomes by age categories, focusing on young adults.

SIH was considerably higher in YA-SLE compared with those without SLE and was associated with poorer outcomes. Notably, a higher comorbidity score (DCCI ≥2) was five times more frequent in YA-SLE compared with YA-no SLE, which could account for higher infection rates and worse outcomes. Although YA-SLE comprised a notably lower proportion of hospital admissions compared with adults with SLE, the rates of SIH did not differ between the groups and the outcomes in terms of LOS and cost were similar. While YA-SLE had more demographic risk factors than YA-no SLE and adults with SLE, only race/ethnicity was associated with SIH in the young adult group. Since this study was done prior to the COVID-19 pandemic, it may be of interest to assess how the rates of SIH, particularly related to pneumonia and sepsis, might differ among groups in the years during and after the COVID-19 pandemic as well as the effect of COVID-19 vaccination on SIH rates and outcomes.

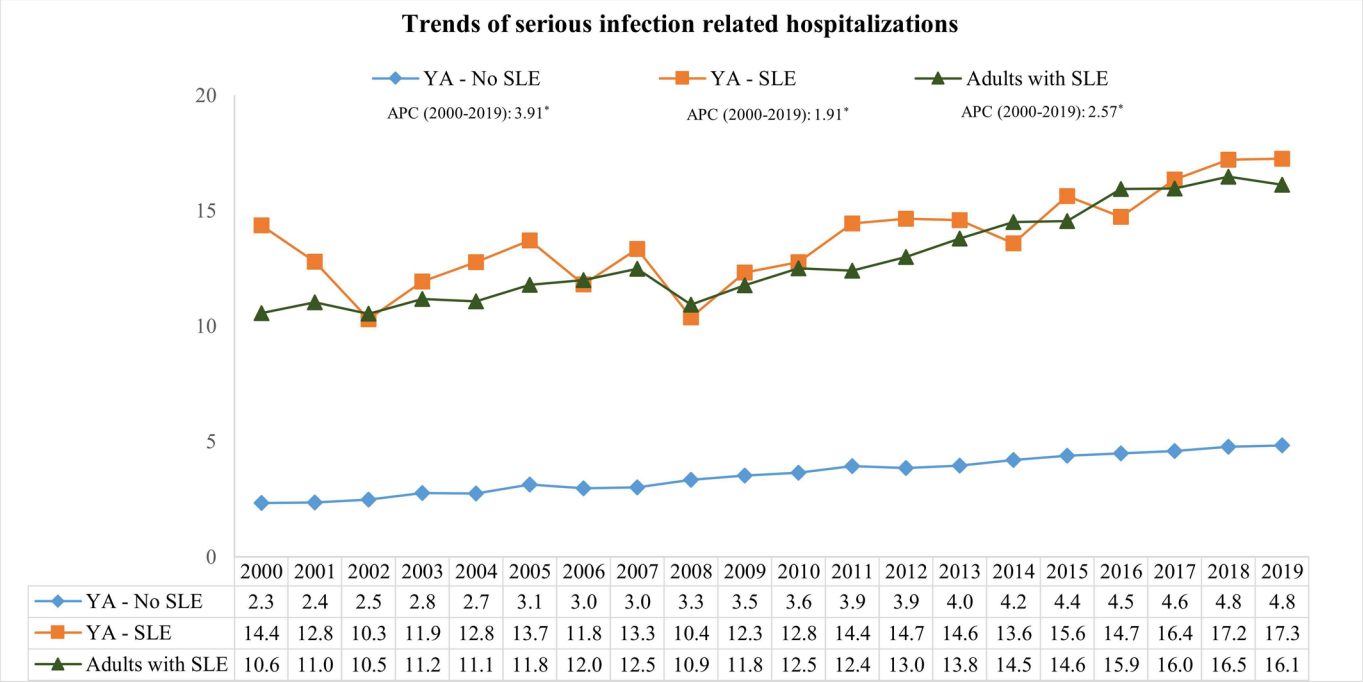
The comorbidity burden was significantly higher in YA-SLE compared with YA-no SLE, as expected. However, most of the studied lupus-related comorbidities, including LN, pleuritis, pericarditis and thrombocytopenia, were also significantly higher among young adults compared with adults with SLE, possibly suggesting increased disease severity and associated immunosuppressive therapy, and contributing to comparable rates of SIH despite YA-SLE comprising only a small portion of overall SLE hospitalisation. Despite this, inpatient mortality was slightly lower in young adults compared with adults (2.5% vs 1.8%), and factors including age, accrual of organ damage over time, cumulative dose of glucocorticoids and other immunosuppressive agents may have contributed, the extent of which would need further exploration using alternate data sources.

Previous studies have reported higher median cost for infection-related hospitalisation in lupus compared with those without lupus;[11] however, it is not clear how the hospitalisation costs may vary across age categories of SLE. In our study of SIH in SLE, we found similar average costs for young adults and adults, and this was true for all individual infections, with the exception of higher average cost for OIs among young adults. Additionally, LOS may itself drive indirect costs due to loss of work days and productivity, which cannot be ascertained from this database. Factors driving the hospitalisation costs for overall SIH and for individual infections may be different in young adults compared with adults, and overall

Table 2 Hospitalisation outcomes of serious infection-related hospitalisation among young adults with SLE compared with adults with SLE and young adults without SLE, defined as YA: young adults (18–24), adults (25–44); National Inpatient Sample, 2000–2019

Infection-related hospitalisation	YA-SLE	Adults with SLE	YA-no SLE	P value	P value
N (%)	10951 (15.0)	69929 (14.51)	826676 (4.23)	YA-SLE vs adults with SLE	YA-SLE vs YA-no SLE
Hospitalisation outcomes					
LOS: mean (SEM); median, days	6.2 (0.2)	6.1 (0.1)	4.5 (0.03)	0.55	<0.001
LOS >3 days (%)	55.7	56.4	38.6	0.54	<0.001
Total cost: $, mean (SEM); median, $	15280 (577)	14387 (251)	10532 (93)	0.13	<0.001
Discharge destination (%)					
Routine (home)	79.5	73.3	82.4	<0.001	0.0001
Non-routine	18.7	24.1	16.6		
Missing	1.8	2.6	1		
Inpatient mortality (%)	1.8	2.5	0.9	0.03	0.003

LOS, length of stay.



	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
YA - No SLE	2.3	2.4	2.5	2.8	2.7	3.1	3.0	3.0	3.3	3.5	3.6	3.9	3.9	4.0	4.2	4.4	4.5	4.6	4.8	4.8
YA - SLE	14.4	12.8	10.3	11.9	12.8	13.7	11.8	13.3	10.4	12.3	12.8	14.4	14.7	14.6	13.6	15.6	14.7	16.4	17.2	17.3
Adults with SLE	10.6	11.0	10.5	11.2	11.1	11.8	12.0	12.5	10.9	11.8	12.5	12.4	13.0	13.8	14.5	14.6	15.9	16.0	16.5	16.1

Figure 2 Trends of serious infection-related hospitalisation among young adults and adults with SLE and young adults without SLE, defined as YA: young adults (18–24), adults (25–44); National Inpatient Sample, 2000–2019. *p<0.05. APC, annual per cent change.

average costs reported here did not account for inflation or regional differences, which needs further exploration.

Between 2000 and 2019, increasing trends of SIH in YA-SLE, adults with SLE and YA-no SLE were noted. A decreasing trend for pneumonia and a significantly increasing trend for sepsis were observed, with sepsis becoming the most common hospitalised infection around 2011. In YA-SLE and adults with SLE, pneumonia-related hospitalisation was about two to three times more frequent in the early study period (2000–2001), whereas the reverse was noted around 2018–2019 with three to five times more frequent sepsis-related hospitalisation. Similar trends have been reported in prior studies of patients with SLE using the NIS database.[11 24] Increased vaccination for, and better outpatient treatment of, pneumonia were suggested by the investigators as possibly contributing to reduced need for hospitalisation. Changes in coding methods for sepsis (with upcoding for sepsis) could also have contributed to an increasing trend over time, and sepsis itself could have been the result of an initial pneumonia or other infections.[24] It is not possible to determine the extent to which this could have happened and the specific causative organisms from the NIS database. Future studies using alternate data sources are needed to specifically explore the specific aetiological factors and initial presenting infection for sepsis.

Based on sampling methodology, NIS is nationally representative and provides 'real-world' healthcare data on a large population. Limitations of our study are reliance on ICD codes used for billing (validity, coding errors, inexact codes), potentially resulting in lack of granularity and accuracy. Additionally, there is a lack of information on the timing of diagnosis, disease activity, organ involvement, medications and test results, restricting clinical interpretation. We used only the primary diagnosis to identify SIH in order to increase specificity, which may have underestimated SIH. It is important to note that the NIS database unit of analysis is hospitalisation and not an individual patient. This may be particularly important when interpreting data prior to redesign in 2012, when the NIS was constructed by retaining 100% discharges from 20% randomly sampled hospitals (instead of 20% sample of discharges from all participating hospitals), increasing the likelihood of recurrent hospitalisation for a single patient to be counted as distinct observations. In 2012, the NIS changed sampling from 100% of discharges from 20% of randomly sampled hospitals to 20% of discharges from all participating hospitals. However, for trend analysis, trend weights (TRENDWT) provided by HCUP were used for trend analysis to make comparable estimates before and after the changes in sampling strategies in 2012 NIS design.[12 27]

In summary, we noted increased rates of SIH in all age groups of adults with SLE, driven by sepsis. Although young adults comprised a lower proportion of overall SLE hospitalisation than adults, they had similar SIH rates and comparable costs, and outcomes compared with adult patients with SLE. Future studies focusing on young adults are needed in order to better understand the aetiologies of infections and factors increasing susceptibility to infection-related hospitalisation in this subpopulation of SLE. Additionally, our finding that hospitalisation due to pneumonia was more common among both young adults and adults with SLE compared with patients without SLE

deserves further study to determine whether patients with SLE are prone to infection from certain organisms and whether targeted vaccines against these causative agents are warranted.

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Contributors RD—conception of the study topic, study design, data analysis, draft preparation and final approval, responsible for overall content (guarantor). MG—critical review, revision and final approval. DRP—literature review, draft preparation and final approval. CC—study design, critical review, revision and final approval. KK—conception of the study topic, critical review, revision and final approval.

Funding RD was funded by a research training grant from NIH/NIAMS (T32AR064194).

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval This study was performed in concordance with the formal HCUP data use agreement and was exempt from requiring institutional review board approval as NIS data are de-identified.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data may be obtained from a third party and are not publicly available. This study was done using the National (Nationwide) Inpatient Sample (NIS) database, which is part of a family of databases developed for the Healthcare Cost and Utilization Project (HCUP). The NIS is a publicly available all-payer inpatient healthcare database (https://www.hcup-us.ahrq.gov/nisoverview.jsp).

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REFERENCES

1 Hochberg MC, Boyd RE, Ahearn JM, *et al*. Systemic lupus erythematosus: a review of clinico-laboratory features and immunogenetic markers in 150 patients with emphasis on demographic subsets. *Medicine (Baltimore)* 1985;64:285–95.
2 Sadun RE, Schanberg LE. Transition and transfer of the patient with paediatric-onset lupus: a practical approach for paediatric and adult rheumatology practices. *Lupus Sci Med* 2018;5:e000282.
3 Levy DM, Peschken CA, Tucker LB, *et al*. Influence of ethnicity on childhood-onset systemic lupus erythematosus: results from a multiethnic multicenter Canadian cohort. *Arthritis Care Res (Hoboken)* 2013;65:152–60.
4 Manadan AM, Kambhatla S, Gauto-Mariotti E, *et al*. Reasons for hospitalization and in-hospital mortality in adult systemic lupus erythematosus. *ACR Open Rheumatol* 2020;2:683–9.
5 Barber MRW, Clarke AE. Systemic lupus erythematosus and risk of infection. *Expert Rev Clin Immunol* 2020;16:527–38.
6 Dhital R, Pandey RK, Poudel DR, *et al*. All-cause hospitalizations and mortality in systemic lupus erythematosus in the US: results from a national inpatient database. *Rheumatol Int* 2020;40:393–7.
7 Herrinton LJ, Liu L, Goldfien R, *et al*. Risk of serious infection for patients with systemic lupus erythematosus starting glucocorticoids with or without antimalarials. *J Rheumatol* 2016;43:1503–9.
8 Allen T, Reda S, Martin S, *et al*. The needs of adolescents and young adults with chronic illness: results of a quality improvement survey. *Children (Basel)* 2022;9:500.
9 Son MB, Sergeyenko Y, Guan H, *et al*. Disease activity and transition outcomes in a childhood-onset systemic lupus erythematosus cohort. *Lupus* 2016;25:1431–9.
10 Pratsidou-Gertsi P. Transition of the patient with childhood-onset SLE. *MJR* 2016;27:94–7.
11 Singh JA, Cleveland JD. Hospitalized infections in lupus: a nationwide study of types of infections, time trends, health care utilization, and in-hospital mortality. *Arthritis Rheumatol* 2021;73:617–30.
12 NIS trend weights. Available: https://www.hcup-us.ahrq.gov/db/nation/nis/trendwghts.jsp [Accessed 13 Oct 2022].
13 Hanly JG, Thompson K, Skedgel C. Identification of patients with systemic lupus erythematosus in administrative healthcare databases. *Lupus* 2014;23:1377–82.
14 Chang JC, Xiao R, Knight AM, *et al*. A population-based study of risk factors for heart failure in pediatric and adult-onset systemic lupus erythematosus. *Semin Arthritis Rheum* 2020;50:527–33.
15 Nasonov E, Soloviev S, Davidson JE, *et al*. The prevalence and incidence of systemic lupus erythematosus (SLE) in selected cities from three Commonwealth of independent states countries (the Russian Federation, Ukraine and kazakhstan). *Lupus* 2014;23:213–9.
16 Wiese AD, Griffin MR, Stein CM, *et al*. Validation of discharge diagnosis codes to identify serious infections among middle age and older adults. *BMJ Open* 2018;8:e020857.
17 Lo Re V 3rd, Carbonari DM, Jacob J, *et al*. Validity of ICD-10-CM diagnoses to identify hospitalizations for serious infections among patients treated with biologic therapies. *Pharmacoepidemiol Drug Saf* 2021;30:899–909.
18 Available: https://www.hcup-us.ahrq.gov/db/vars/race/nisnote.jsp [Accessed 13 Dec 2022].
19 Healthcare cost and utilization project (HCUP) NIS notes. Available: https://www.hcup-us.ahrq.gov/db/vars/zipinc_qrtl/nisnote.jsp [Accessed 13 Dec 2022].
20 Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol* 1992;45:613–9.
21 Chibnik LB, Massarotti EM, Costenbader KH. Identification and validation of lupus nephritis cases using administrative data. *Lupus* 2010;19:741–3.
22 Li T, Lee I, Jayakumar D, *et al*. Development and validation of lupus nephritis case definitions using United States Veterans Affairs electronic health records. *Lupus* 2021;30:518–26.
23 Ward MM, Pajevic S, Dreyfuss J, *et al*. Short-term prediction of mortality in patients with systemic lupus erythematosus: classification of outcomes using random forests. *Arthritis Rheum* 2006;55:74–80.
24 Jinno S, Lu N, Jafarzadeh SR, *et al*. Trends in hospitalizations for serious infections in patients with rheumatoid arthritis in the US between 1993 and 2013. *Arthritis Care Res (Hoboken)* 2018;70:652–8.
25 Corporate Finance Institute. Variance inflation factor (VIF). Available: https://corporatefinanceinstitute.com/resources/data-science/variance-inflation-factor-vif/ [Accessed 24 Dec 2022].
26 StataCorp. *Stata statistical software: release 13*. College Station, TX: StataCorp LP, 2013.
27 Healthcare Cost and Utilization Project (HCUP). HCUP databases. Rockville, MD Agency for Healthcare Research and Quality; Available: www.hcup-us.ahrq.gov/nisoverview.jsp [Accessed 31 Dec 2017].
28 Joinpoint regression program - surveillance research program. Available: https://surveillance.cancer.gov/joinpoint/ [Accessed 05 May 2019].