SKIN

RESEARCH LETTER

Analyzing Inpatient Vaccine Reactions Amongst Systemic Lupus Erythematosus Patients in the COVID-19 Era: A National Analysis

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ABSTRACT

Introduction: Systemic lupus erythematosus (SLE) patient hospitalizations were areas of concern during the coronavirus of 2019 (COVID-19) and subsequent vaccine rollout. We aimed to characterize hospitalization trends nationally amongst SLE patients following COVID-19 vaccine rollout.
Methods: The 2016-2020 Nationwide Inpatient Sample (NIS) was queried for SLE hospitalizations using International Classification of Diseases, Tenth Revision (ICD-10) code "M32". SLE hospitalizations with co-morbid vaccine reactions (RX+) were identified using ICD-10 codes "T50.x". Clinical and demographic features and rates of high-risk underlying co-morbidities were compared.
Results: Among total SLE hospitalizations, 1.4% were RX+ between 2016-2020. RX+ patient hospitalizations increased from 2019-2020. RX+ patients exhibited a significantly higher burden of heart disease, chronic kidney disease (CKD), chronic liver or lung disease, HIV, and obesity.
Discussion: Our findings suggest that RX+ SLE patients are slightly older, and have significantly greater proportions of comorbid conditions, namely heart disease, CKD, and diabetes compared to RX- SLE patients. Increased SLE severity may impart an inflammatory burden on patients not explained by immunosuppression alone, making them more susceptible to factors with shared pathogenic risks like vaccine reactions.

INTRODUCTION

During the coronavirus of 2019 (COVID-19) and subsequent vaccine rollout, systemic lupus erythematosus (SLE) patient hospitalizations were areas of concern.[1] Prior studies reported a wide range in frequency of disease flares after COVID-19 vaccine, between 3% and 33%.[2-3] We aimed to characterize hospitalization trends nationally amongst SLE patients following COVID-19 vaccine rollout.

METHODS

The 2016-2020 Nationwide Inpatient Sample (NIS) was queried for SLE hospitalizations using International Classification of Diseases, Tenth Revision (ICD-10) code "M32".[4] NIS is an all-payer inpatient database weighted to represent cases nationwide. SLE hospitalizations with co-morbid vaccine reactions (RX+) were identified using ICD-10 codes "T50.x". Chi-square and t-tests were

used to compare clinical and demographic features and rates of high-risk underlying co-morbidities, as defined by the CDC and coded by ICD-10 coding (**Supplementary Table 1**), between RX+ and RX- SLE inpatients, using a two-sided alpha value of $p<0.05$.

RESULTS

Among 1,082,960 total SLE hospitalizations between 2016-2020, 15,625 (1.4%) were RX+ (**Table 1**). RX+ patient hospitalizations increased from 1.2-1.3% in 2016-2018 to 1.6% in 2019-2020 ($p<0.001$). (**Figure 1**) RX+ patients were on average older (55.0 vs. 52.1 years, $p<0.0001$), with a higher proportion of male (12.4% vs. 11.7%, $p=0.01$) and Black patients (31.6% vs. 30.9%, $p=0.02$). RX+ patients were more likely to be in the highest income quartile (19.7% vs. 17.6%, $p<0.0001$) and use either Medicare (54.0% vs. 49.0%) or self-pay insurance (3.6% vs 3.0%) ($p<0.0001$). RX+ patients had 5% more non-routine discharges, with higher proportions transferred to other facilities (40.5% vs. 35.3%, $p<0.0001$). RX+ patients exhibited a significantly higher burden of heart disease (48.5% vs. 34.1%, $p<0.0001$), chronic kidney disease (CKD) (36.3% vs. 29.7%, $p<0.0001$), chronic liver or lung disease, HIV, and obesity ($p<0.01$) (**Supplemental Table 2).** However, there was no statistically significant difference in vaccine reaction among immunosuppressed patients, defined by ICD-10 codes and including both drug-induced and genetic causes of immunosuppression.

DISCUSSION

Our findings suggest that significant differences exist between RX+ and RX- SLE inpatients, with RX+ patients being slightly older and having significantly greater proportions of comorbid conditions, namely heart disease, CKD, and diabetes. While few studies have investigated the association between lupus severity with comorbidities in SLE patients, a nested case-control study of 240 South African patients in 2019 found that heart disease (odds ratio (OR) 10.39, $p=0.0003$) and CKD (OR 3.08, $p=0.02$) rates were significantly higher in deceased patients with SLE.[5] These findings suggest that increased SLE severity may impart an inflammatory burden on patients not explained by immunosuppression alone, making them more susceptible to factors with shared pathogenic risks like vaccine reactions. Inflammatory conditions likely increased hospitalizations for all SLE patients (**Supplemental Figure 1**), particularly those with greater disease severity, resulting in RX+ patients having a higher proportion of non-routine discharges.

Limitations include possible error in RX+ coding by recording physician, lack of specific vaccine formulation data, and medication information.

In conclusion, we highlight an increase in vaccine-related SLE hospitalizations during the COVID-19 pandemic, with these patients having similar immunosuppression yet a higher proportion of co-morbidities, most notably heart and kidney disease, compared to other SLE admits.

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Table 1. Baseline demographic and clinical information between RX+ and RX- patients.

	Reaction (n=15625) (1.4%)	No reaction (n=1067335) (98.6%)	p-value
Age	55	52.1	<.0001
Sex			0.0129
Male	1930 (12.36)	124985 (11.71)	
Female	13690 (87.64)	942210 (88.29)	
Race			0.0172
White	7515 (49.29)	513655 (49.27)	
Black	4815 (31.58)	322355 (30.92)	
Hispanic	2030 (13.32)	144620 (13.87)	
Asian or Pacific Islander	335 (2.20)	25785 (2.47)	
Native American	125 (0.82)	7200 (0.69)	
Other	425 (2.79)	29015 (2.78)	
Income Quartile			<.0001
0-25th percentile	5060 (32.88)	365575 (34.75)	
26th to 50th percentile (median)	3905 (25.37)	265755 (25.26)	
51st to 75th percentile	3400 (22.09)	235735 (22.41)	
76th to 100th percentile	3025 (19.66)	184885 (17.58)	
Primary Payer			<.0001
Medicare	8440 (54.02)	522795 (49.04)	
Medicaid	2810 (17.98)	218820 (20.52)	
Private insurance	3560 (22.78)	267300 (25.07)	
Self-pay	560 (3.58)	32025 (3.00)	
No charge	25 (0.16)	2655 (0.25)	
Other	230 (1.47)	22550 (2.12)	
Disposition			<.0001
Routine	9290 (59.46)	690610 (64.73)	
Transfer to short-term hospital	225 (1.44)	24610 (2.31)	
Transfer other: includes Skilled Nursing Facility (SNF), Intermediate Care Facility (ICF), and another type of facility	2570 (16.45)	135210 (12.67)	
Home Health Care (HHC)	2975 (19.04)	172910 (16.21)	
Against medical advice (AMA)	245 (1.57)	22050 (2.07)	
Died in hospital	320 (2.05)	21520 (2.02)	
Discharged alive, destination unknown	0 (0.00)	70.0001 (0.01)	
Severity			<.0001
No class specified	585 (3.74)	79135 (7.41)	

Minor loss of function (includes cases with no comorbidity or complications)	4170 (26.69)	386490 (36.21)	
Moderate loss of function	7920 (50.69)	475790 (44.58)	
Major loss of function	2950 (18.88)	125810 (11.79)	

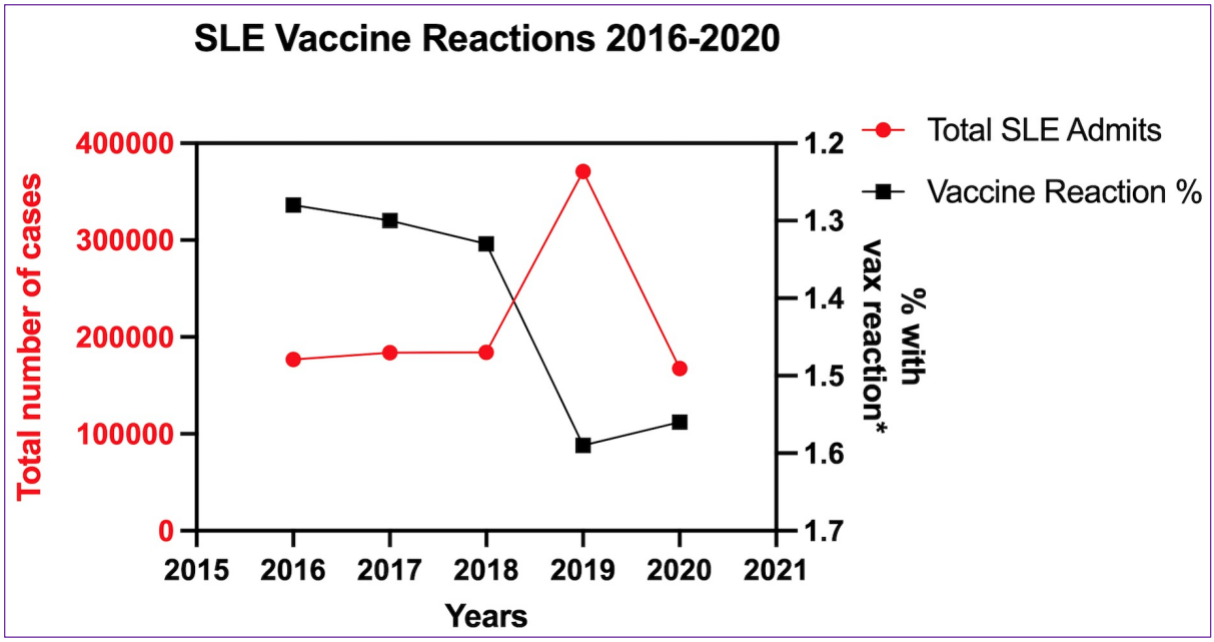

Figure 1. SLE vaccine cases over time. The red line (left y-axis) indicates total SLE hospitalizations, and the black line (right y-axis) indicates the relative proportion of cases due to vaccine reactions. *Note: the right y-axis is in descending order from top to bottom (i.e. greater numbers are lower on the graph).

References:

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Supplemental

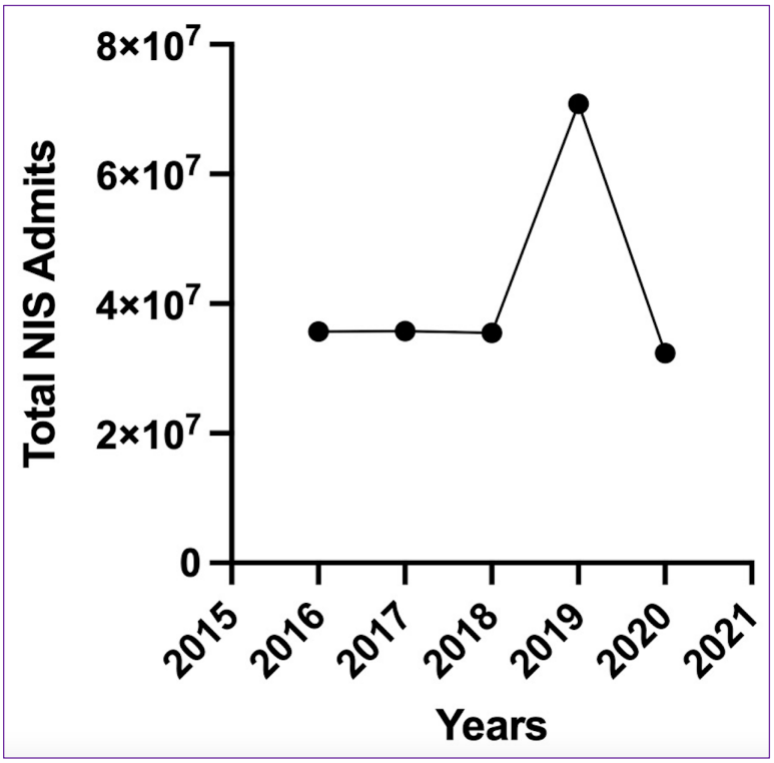
Supplemental Table 1. ICD-10 codes of included variables.

Co-Morbidities	ICD-10 coding
Elderly	R54, age variable in NIS
Chronic Liver Disease	K70-K77
Chronic Lung Disease	J40-J4A
Dementia	F01-F09
Disability	F7X
Heart Disease	I3X-I5X
Immunocompromise	D8X
Pregnancy	Z3X
HIV	B20
Sickle Cell Disease	D57
Tobacco Use	Z72
Diabetes Mellitus	E08-E13
CKD	N18
Obesity	E66

Supplemental Table 2. Co-morbidities of included patients.

Co-Morbidities	Reaction (n=15625) (1.4%)	No reaction (n=1067335) (98.6%)	p-value
Elderly (> 65 years old)	5285	287010	<.0001
	(33.82)	(26.89)	
Chronic Liver Disease	1320	69590	<.0001
	(8.45)	(6.52)	
Chronic Lung Disease	4605	299820	0.0001
	(29.47)	(28.09)	
Dementia	695	36055	<.0001
	(4.45)	(3.38)	
Disability	20	2355	0.014
	(0.13)	(0.22)	
Heart Disease	7580	363950	<.0001
	(48.51)	(34.1)	
Immunocompromise	420	28295	0.775
	(2.69)	(2.65)	
Pregnancy	60	38090	<.0001

	(0.38)	(3.57)	
HIV	60	2435	<.0001
	(0.38)	(0.23)	
Sickle Cell Disease	95	11680	<.0001
	(0.61)	(1.09)	
Tobacco Use	165	11745	0.5973
	(1.06)	(1.1)	
Diabetes	3695	221900	<.0001
	(23.65)	(20.79)	
CKD	5675	317030	<.0001
	(36.32)	(29.7)	
Obesity	3710	201470	<.0001
	(23.74)	(18.88)	



Supplemental Figure 1. Total admits in the NIS database over time.