Hospitalizations in Patients with Systemic Lupus Erythematosus in an Academic Health Science Center

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ABSTRACT. ***Objective.*** Hospitalization occurs in about 10% of patients with systemic lupus erythematosus (SLE) each year and accounts for most of the direct cost of SLE patient care. We aimed to determine the frequency of admissions of patients with SLE and describe their causes and outcomes.

Methods. We identified all hospitalizations at University Health Network in the periods 2011–2012 and 2013–2015 with an International Classification of Diseases, 10th ed. code of M32 (SLE). A retrospective chart review of these patients categorized them based on SLE care provider and cause of admission. Frequency of emergency room visits and duration of hospitalization were ascertained. Poisson and linear regressions were performed to determine factors associated with frequency and duration of hospitalizations.

Results. There were 247 unique patients with SLE who were hospitalized a total of 491 times: 87.4% were women, average age of 43.9 ± 17.9 years, and disease duration 13.7 ± 12.3 years. Incidental causes were most common (35.6%); 21.4% and 22.4% of admissions were because of active SLE and infection, respectively. The patients with SLE averaged 1.6 hospitalizations lasting 8.5 days. Thirteen percent of hospitalizations resulted in intensive care unit admission, and 2.8% of hospitalizations resulted in death. Patient employment was associated with fewer hospitalizations during 2011–2015. Antimalarial use was associated with fewer hospitalizations as well as shorter length of stay during 2011–2012. The presence of damage correlated with increased hospitalizations. Higher educational level and antimalarial use correlated with shorter length of stay.

Conclusion. Patients with SLE are frequently hospitalized, often because of active SLE or infection, and re-hospitalized within a short period of time. (First Release June 15 2017; J Rheumatol 2017;44:1173–8; doi:10.3899/jrheum.170072)

Key Indexing Terms:
HOSPITALIZATIONS
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Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that predominantly affects women in their childbearing years, with a female-to-male ratio of about 9:1[1]. While the incidence of SLE is believed to be around 1 in 1000, over 300,000 individuals in North America and over 5 million people worldwide are affected by SLE, with the prevalence increasing because of improved survival and better detection of milder cases[2]. SLE is a complex disease that has a variety of manifestations, ranging from clinically quiescent and requiring periodic monitoring to multisystem involvement requiring life-saving intervention. SLE care generally involves reducing disease activity and preventing damage accumulation[1,3].

While the SLE mortality rate has substantially decreased over the past 5 decades, hospitalization of patients with SLE has an estimated occurrence of 10% per year[4]. Hospitalizations contribute to most of the direct cost of care for patients with SLE, which has been shown to be $10,608 per annum in Canada (2010 Canadian dollars) and to range from $13,735 to $20,926 per annum in the United States (2009 US dollars), and exceeds the amount spent on specialist visits, laboratory visits, or medications[5,6]. Among patients with SLE, both the direct medical cost and the costs of hospitalization are obviously substantially greater in individuals with severe SLE compared to those with non-severe SLE[5].

While previous studies have demonstrated a large proportion of SLE hospitalizations to be due to either SLE flare or infections, little work has been done to evaluate the outcomes and longterm prognoses of patients treated by

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dedicated SLE clinics or general rheumatologists and other physicians[7,8,9]. Further, few studies have examined characteristics correlating with frequency and duration of healthcare usage.

We performed a retrospective chart review of all hospitalization of patients with SLE at a large teaching hospital affiliated with the University of Toronto, Toronto, Ontario, Canada. We aimed to quantify the frequency of admissions and assess the causes of, factors associated with, and outcomes of hospitalization. In addition, we aimed to compare outcomes based on SLE care provider. Better understanding of the characteristics and outcomes of hospital admissions will allow for a more targeted approach for the prevention of admission, thus allowing for more efficient use of healthcare resources.

MATERIALS AND METHODS

Patient selection. We searched all hospitalizations occurring during a 2-year period beginning in 2011 and ending in 2012 at the University Health Network (UHN), a network of 3 teaching hospitals affiliated with the University of Toronto. All UHN hospitalizations are coded using International Classification of Diseases, 10th ed. (ICD-10) codes. We used the ICD-10 code for SLE (M32) to identify patient records of hospitalized adults with SLE.

Study design. A retrospective review of hospital charts and electronic health records of all hospitalized patients with SLE between the beginning of 2011 and the end of 2012 (index hospitalization) was undertaken. In addition to demographic data, we recorded the dates and duration of hospitalization; causes and outcomes of admission, surgery, and death; medication usage; ICU admission and duration; and post-discharge medical appointments. Cause of admission was classified based on 1 of 5 categories: active SLE (determined by the admitting physician), SLE damage (musculoskeletal, gastrointestinal, cardiovascular, pulmonary, neuropsychiatric, and renal), other comorbidities (atherosclerotic cardiovascular disease, diabetes, and malignancy); infections, and incidental (adverse drug reactions and complaints of pain). In the event that there was more than 1 cause of admission, we classified the cause of admission based on the primary cause. SLE care provider was classified based on 1 of 3 categories: Lupus Clinic for patients followed at our Lupus Clinic; non-Lupus Clinic, for patients followed by rheumatologists, but not at our Lupus Clinic; and non-rheumatologist, for patients followed by physicians other than rheumatologists.

We followed patients admitted during 2011–2012 for the following outcomes between 2013 and 2015 at the UHN hospitals: longitudinally from the beginning of 2013 to the end of 2015 to assess posthospitalization outcomes. Outcomes assessed included additional hospitalizations, emergency room (ER) visits, surgeries, and death. Study protocols were approved by the research ethics board at UHN (16-5600-BE).

Disease and damage measures. SLE disease activity was measured using the SLE Disease Activity Index 2000 (SLEDAI-2K). SLEDAI-2K is a previously validated modification of the original SLEDAI[10]. Information required to calculate SLEDAI-2K scores was obtained from patient records.

Permanent SLE damage was measured using the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI). The SDI is a previously validated measure of damage caused by either SLE or its treatment or comorbid conditions[11]. SDI scores are calculated from the time of SLE diagnosis and represent permanent damage present. Information required to calculate SDI scores was obtained from patient records and clinical notes.

Statistical analyses. Patients' demographic, socioeconomic, disease characteristics, and treatments were described as mean ± SD or median (interquartile range) for continuous variables and count (percent) for categorical variables. ANOVA tests were performed to make comparisons for normally distributed variables while Kruskal–Wallis tests were done for skewed continuous variables among groups. Posthoc tests were performed to compare within individual groups. Cochran-Armitage trend tests were done to make comparisons for categorical data. Poisson regressions models were created for the number of hospitalizations or ER visits after examining the distribution of outcome variables; linear regressions were performed for length of stay in hospital as the outcome variable. Step-down variable selection method was chosen and Akaike information criterion was used as model-fitting statistics for Poisson, and adjusted R^2 was used as the model-fitting statistic for linear regression; in some models, the main predictors of interest were forced into the multivariable regression. Multivariable regressions were adjusted for patients' demographic, socioeconomic, disease characteristics, and treatments as covariates. Statistical analyses were performed using SAS (SAS Institute). Results were deemed to be statistically significant if the p value was < 0.05.

RESULTS

Frequency of SLE patient admissions. We identified 47,573 unique patients who were hospitalized a total of 68,175 times between 2011 and 2012. From this group, a total of 247 unique patients with SLE were hospitalized a total of 491 times, of which 408 showed a discernible cause for admission. Thus, 0.7% of patients admitted to UHN had SLE, and SLE admissions accounted for 0.6% of global UHN hospitalizations. Because our hospital beds have been restricted, most of our admissions are non-elective and present to emergency departments or are channeled through emergency departments as their route for admission. Our hospital does not have an obstetrical unit, and therefore no pregnancy admissions were included.

Characteristics of hospitalized patients with SLE at first hospitalization. Seventy-one patients (28.7%) were followed at the Lupus Clinic and 159 patients (64.4%) were followed by community rheumatologists (Table 1). A small subset of patients (17, 6.9%) was followed by non-rheumatologists.

The majority (87.4%) of hospitalized patients with SLE were women. The average age of our entire cohort was 43.91 ± 17.91 years and the average time since SLE diagnosis was 13.68 ± 12.29 years. The average duration of hospitalization was 8.48 ± 8.91 days. Thirteen percent of the hospital admissions resulted in ICU admission, and 2.8% of hospitalizations resulted in death.

Patients with SLE in our study had an average SDI score of 1.70 ± 1.97. Lupus Clinic patients had significantly greater damage (2.23) when compared with non-Lupus Clinic patients (1.4, $p = 0.0063$). Non-rheumatologist patients also had a high damage index of 2.24.

Cause of admissions and readmissions. Incidental causes, such as adverse drug reactions and complaints of pain, were the most common reason for admission (36.0%; Table 2). The majority of the remaining hospitalizations were attributable to either active SLE (23.9%) or infection (19.0%). Patients hospitalized because of active disease were significantly younger, had shorter disease duration, and had accumulated less damage when compared with patients admitted because

Table 1. Characteristics of hospitalized patients with SLE at first hospitalization. Values are n (%) unless otherwise specified.

Characteristics	Total Cohort, n = 247	Lupus Clinic, n = 71	Non-lupus Clinic, n = 159	Non-rheumatologist, n = 17
Age, yrs, mean ± SD†	43.91 ± 17.91	41.44 ± 16.11	43.90 ± 17.57	54.33 ± 24.59
SLE duration, yrs, mean ± SD†	13.68 ± 12.29	11.67 ± 9.65	12.62 ± 11.09	32.02 ± 17.70
Female	216 (87.4)	61 (85.9)	140 (88.1)	15 (88.2)
Marital status, married vs others	120 (48.6)	34 (47.9)	78 (49.1)	8 (47.1)
Education attained†				
< Grade 8	3 (1.2)	3 (4.2)	0 (0.0)	0 (0.0)
High school	108 (43.7)	21 (29.6)	75 (47.2)	12 (70.6)
College	50 (20.2)	23 (32.4)	25 (15.7)	2 (11.8)
University	86 (34.8)	24 (33.8)	59 (37.1)	3 (17.6)
Employment status, employed vs others†	87 (35.2)	24 (33.8)	60 (37.7)	3 (17.6)
Antimalarial use†	122 (49.4)	46 (64.8)	73 (45.9)	3 (17.6)
Prednisone use†	157 (63.6)	52 (73.2)	99 (62.3)	6 (35.3)
Daily dose, mg, mean ± SD	12.89 ± 11.33	16.67 ± 14.20	11.09 ± 9.24	9.58 ± 6.41
Immunosuppressive use†	93 (37.7)	35 (49.3)	57 (35.8)	1 (5.9)
SDI, mean ± SD/median (interquartile range)†	1.70 ± 1.97/1 (0–3)	2.23 ± 2.19/2 (0–4)	1.40 ± 1.79/1 (0–2)	2.24 ± 2.14/2 (0–4)

† $p < 0.05$ from ANOVA tests for mean difference, Kruskal-Wallis tests for median, and chi-square tests for percentage differences. SLE: systemic lupus erythematosus; SDI: Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index.

Table 2. Causes of admission by the first and second admissions during study period. Values are n (%).

Causes	First Admission, n = 247	Second Admission, n = 141
Active SLE	59 (23.9)	30 (21.3)
Damage	30 (12.2)	15 (10.6)
Other comorbidities	22 (8.9)	12 (8.5)
Infection	47 (19.0)	38 (26.9)
Incidental	89 (36.0)	46 (32.6)

SLE: systemic lupus erythematosus.

of other causes ($p = 0.0004$, $p < 0.0001$, and $p = 0.0005$, respectively; Table 3). Regarding medications, there was no difference in use of antimalarials. Patients with active SLE took significantly higher daily glucocorticosteroids dose, but were less likely to be receiving immunosuppressive therapy at the time of admission than those admitted for damage or infection.

Ninety-nine patients (40.1%) required readmission during the study period (2011–2012). Incidental causes were the leading cause (32.6%) of second admissions. Once again, the majority of the remaining hospitalizations were due to either active SLE (21.3%) or infection (26.9%). The mean time since first admission was 10.3 ± 11.6 months.

Outcomes of patients with SLE. On average, patients with SLE required 1.6 ± 1.1 hospitalizations and 2.2 ± 2.5 ER visits during the study period (2011–2012; Table 4). The mean duration of hospitalization of all patients with SLE was 8.5 ± 8.9 days, and a large proportion (40.1%) of patients with SLE required readmission within the initial 2 years of our study.

During the followup period (2013–2015), 49.0% of the patients returned to the ER at least once and 36.0% required at least 1 additional hospitalization. Of those who used additional healthcare resources, the mean number of ER visits was 1.7 ± 2.9 and the mean number of hospitalizations was 1.0 ± 2.1 (Table 4).

During either the study or followup period, there was

Table 3. Features associated with causes of first admission of patients with SLE. Values are mean ± SD, median (interquartile range), or n (%).

Features	Active SLE, n = 59	SLE Damage, n = 30	Other Comorbidities, n = 22	Infection, n = 47	Incidental, n = 89
Age, yrs†	34.68 ± 12.64	43.90 ± 18.39	55.13 ± 23.02	43.53 ± 15.05	47.61 ± 18.26
SLE duration, yrs†	5.92 ± 6.70	17.23 ± 11.87	16.60 ± 10.53	15.20 ± 12.05	16.23 ± 13.79
SDI†	0 (0–1)	3 (1–4)	2 (0–3)	2 (0–4)	1 (0–3)
Antimalarial-treated	34 (56.7)	13 (43.3)	10 (45.5)	19 (40.4)	46 (52.3)
Prednisone-treated†	34 (56.7)	21 (70.0)	9 (40.9)	39 (83.0)	54 (61.4)
Prednisone dose, mg/day†	18.56 ± 16.45	11.05 ± 8.11	6.67 ± 2.17	12.02 ± 11.09	11.69 ± 8.06
Immunosuppressive-treated†	22 (36.7)	15 (50.0)	3 (13.6)	23 (48.9)	30 (34.1)

† $p < 0.05$ from ANOVA tests for mean difference, Kruskal-Wallis tests for median, and chi-square tests for percentage differences. SLE: systemic lupus erythematosus; SDI: Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index.

Table 4. Outcomes of patients with SLE. Values are mean ± SD/median (interquartile range) unless otherwise specified.

Outcomes	Total Cohort, n = 247	Lupus Clinic, n = 71	Non-lupus Clinic, n = 159	Non-rheumatologist, n = 17
Study period, 2011–2012				
ER visits	2.2 ± 2.5/2 (1–3)	1.9 ± 1.62 /1(1–3)	2.4 ± 2.8/2 (1–3)	2.5 ± 2.3/2 (1–3)
Hospitalization	1.6 ± 1.1/1 (1–2)	1.5 ± 0.7/1 (1–2)	1.7 ± 1.1/1 (1–2)	2.0 ± 1.8/1 (1–2)
Length of stay, days	8.5 ± 8.9/5 (3–8)	8.1 ± 9.3/6 (3–10)	8.5 ± 8.9/7 (4–16)	9.9 ± 7.7/6 (3–10)
ICU admission, n (%)†	32 (13.0)	11 (15.5)	20 (12.6)	1 (5.9)
Death, n (%)†	7 (2.8)	1 (1.4)	4 (2.5)	2 (11.8)
Study period, 2013–2015				
ER visits	1.7 ± 2.9/1 (0–2)	1.8 ± 2.7/0 (0–2)	1.7 ± 3.2/0 (0–1)	0.6 ± 0.9/0 (0–1)
Hospitalization	1.0 ± 2.1/0 (0–1)	1.1 ± 2.80 (0–1)	1.0 ± 1.8/0 (0–1)	0.4 ± 0.7/0 (0–1)
Length of stay, days	10.9 ± 17.5/6 (3–14)	14.5 ± 30.3/7 (3–11)	9.4 ± 9.2/8 (8–16)	0.4 ± 0.7/6 (3–13)
ICU admission, n (%)†	18 (7.3)	5 (7.0)	9 (5.7)	4 (23.5)

† $p < 0.05$ from Kruskal-Wallis tests for median and chi-square tests for percentage differences. SLE: systemic lupus erythematosus; ER: emergency room; ICU: intensive care unit.

insufficient evidence to conclude that there were differences in the frequency and duration of ER visits and hospitalizations based on SLE care provider.

Factors influencing frequency and duration of hospitalization. The presence of damage correlated with an increased frequency of hospitalizations ($p = 0.024$) and higher education levels correlated with shorter stays in hospital ($p = 0.003$; Table 5). Antimalarial use was associated with both a decreased frequency and duration of hospitalization ($p = 0.012$ and $p = 0.022$, respectively).

Of the 247 patients admitted between 2011 and 2012, 204 were followed in both periods, and 43 (17.4%) were lost to followup after their first admission. During the followup period, patient employment correlated with a decreased frequency of ER visits and hospitalizations ($p = 0.014$ and $p = 0.003$, respectively; Table 6). The presence of damage correlated with an increased number of ER visits and hospitalizations ($p = 0.020$ and $p < 0.001$, respectively) during the followup period. In addition, there was a correlation with the number of ER visits or hospitalizations during the study period and followup period: patients who had visited the ER or were hospitalized during the first 2 years of our study were more likely to visit the ER or be admitted to hospital during the 3 subsequent years ($p = 0.02$ and $p = 0.005$, respectively).

DISCUSSION

Patients with SLE are often hospitalized and re-hospitalized. The mean duration of stay was 8.48 days, with a median stay of 6 days, indicating that the majority of SLE hospitalizations are of short duration. We did not find significant differences in length of stay based on cause of admission. Given that the characteristics of admissions because of active SLE, its

Table 5. Factors affecting frequency and duration of hospitalization during the study period (2011–2012).

Multivariable Poisson Regression on the Outcome of Frequency of Hospitalization	Relative Risk	95% CI	p
Employed vs unemployed	0.850	0.721–1.001	0.051
SDI ≥ 1	1.200	1.024–1.405	0.024†
Antimalarial use	0.821	0.704–0.957	0.012†
Community rheumatologist vs lupus clinic	1.078	0.906–1.283	0.396
Non-rheumatologist vs lupus clinic	1.157	0.856–1.565	0.342
Linear Regression on the Outcome of Days Stay in Hospital (Duration)	**Variable Estimate‡**	**95% CI**	**p**
White vs non-white	–0.142	–0.393 to 0.109	0.269
Married vs single	–0.156	–0.393 to 0.081	0.199
Education levels*	–0.191	–0.317 to –0.065	0.003†
Treated with antimalarial	–0.283	–0.524 to –0.042	0.022†
Treated with immunosuppressive	–0.150	–0.403 to 0.102	0.244
Overall effect of 3 levels of following doctors**	–0.016	–0.238 to 0.206	0.885

* Education levels are coded as 1 = less than grade 8, 2 = grade 8, 3 = high school graduate, 4 = college, 5 = university. ** Following doctors are coded as 1 = lupus clinic, 2 = non-lupus clinic, 3 = non-rheumatologist. ‡ Linear regression was first performed on the nature logarithm transformed outcome variable, then transformed back by exponentiation the parameter estimates. † $p < 0.05$. SDI: Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index.

Table 6. Factors affecting frequencies of ED visits and hospitalizations during the followup period (n = 204 patients who had followup 2013–2015). Other nonsignificant covariates not showing in the table include age, sex, ethnicity, education levels, and followup doctors.

Multivariable Poisson Regression	Relative Risk	95% CI of Relative Risk	p
No. ED visits 2013–2015			
Employed vs unemployed, 2011–2012	0.586	0.382–0.899	0.014
SDI ≥ 1, 2011–2012	1.576	1.073–2.315	0.020
No. ED visits, 2011–2012			
No. hospitalizations, 2013–2015			
Employed vs unemployed, 2011–2012	0.449	0.263–0.764	0.003
SDI ≥ 1, 2011–2012	3.091	1.843–5.182	< 0.001
Prednisone dose, mg/day, 2011–2012	1.034	1.018–1.049	< 0.001
No. hospitalizations, 2011–2012	1.205	1.059–1.371	0.005

ED: emergency department; SDI: Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index.

comorbidities, or other causes are substantially different, we question the extent to which some patients were sufficiently treated, especially given that over 40% of patients with SLE required readmission during our study. Yazdany, *et al* demonstrated that 16% of patients hospitalized for SLE required readmission within a 30-day period[12], compared with 40% of our population over 2 years. Their study examined hospital admissions in 810 hospitals in 5 states in the United States. They looked at overall cause of admission and found that younger age at admission, African American race/ethnicity, having insurance, and having more severe SLE manifestations were associated with readmission within 30 days[12].

Antimalarial use correlates with decreased frequency and duration of hospitalization. Antimalarial use correlated with about 18% decreased frequency of hospitalization and about 25% decreased duration of hospitalization. These findings further support the importance of use of antimalarial drugs in the treatment of SLE; previous work has shown antimalarial drugs to both reduce SLE activity and prevent flares and improve survival[13,14].

SLE patient characteristics differ based on SLE care provider. Patients with SLE in our study who were hospitalized had SLE for over a decade, during which time they accumulated substantial SLE damage. Our Lupus Clinic patients had higher SDI scores than non-Lupus Clinic patients, and we assumed this to be because our Lupus Clinic is a referral center for many complicated SLE cases in the Greater Toronto Area and the province of Ontario, Canada. This difference in SDI score may explain why we were unable to observe differences in healthcare outcomes of patients with SLE followed by our Lupus Clinic and those followed elsewhere.

The small cohort of patients followed by non-rheumatologists was significantly older than the remainder of the cohort and had SLE for a longer duration than the other patients. Of note, however, the SDI scores of patients followed by non-rheumatologists were comparable to those of Lupus Clinic patients. This may be due to the less vigorous management of the comorbidities in these patients.

Patients with SLE are often hospitalized because of active disease or infection. Incidental causes, such as adverse drug reactions and complaints of pain, were the most common reason for admission. Besides incidental causes, the majority of admissions were because of either infections or SLE activity. The high proportion of infections throughout the course of the disease has been previously shown[15]. This can be attributed to active disease and immunosuppressive therapies, both making these patients more susceptible to infections.

The distribution of causes of readmissions was very similar to the distribution of causes of initial admissions. This repeating pattern suggests incomplete resolution of the main problem in the first admission.

Patients tend to be admitted for active SLE early on in the course of disease. When compared with the rest of the cohort, patients admitted because of active SLE tended to be younger (mean age = 34.68 ± 12.64 yrs) and to have SLE for a shorter duration (mean duration = 5.92 ± 6.70 yrs). These patients also had lower SDI scores (mean SDI = 0.82 ± 1.47), most likely because they had SLE for a shorter duration. This may suggest more aggressive disease earlier in the course, requiring more intensive therapeutic intervention.

Limitations of our study include the possibility that ICD-10 codes may have underestimated SLE admissions in our institution. In addition, we do not have followup information on 43 (17.4%) of the patients admitted during 2011–2012. Some of these patients may have been admitted to other hospitals during this period. However, these patients were not included in the regression analysis regarding the outcomes. Another possible limitation is that we did not distinguish between patients with single admissions and readmissions in the first study period.

The strength of our study is that it represents admissions to a large academic complex of 3 teaching hospitals where patients are seen by the same rheumatology team.

Patients with SLE are frequently hospitalized, often because of active SLE or infection, and re-hospitalized within a short period of time. Early on in the course of disease, admitted patients have less accumulated damage and tend to be admitted because of active disease. As the duration of disease increases, SLE damage accumulates, and patients are more likely to be hospitalized because of treatment side effects or damage accumulation. Hospitalizations of patients with SLE continue to place an enormous burden on both patients with SLE and their families and the healthcare system.

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