Brief Report: Hospitalizations in a Clinical Systemic Lupus Erythematosus Cohort, 1999-2011

Kenjey Chan[1], Alaa Dekis[2], Ann E. Clarke[3,4], Christian A. Pineau[2], Evelyne Vinet[2], Emil Nashi[4] and Sasha Bernatsky[2,3,*]

[1]*Faculty of Medicine, McGill University, Montreal, QC, Canada*

[2]*Division of Rheumatology McGill University Health Centre, Montreal, Quebec, Canada*

[3]*Division of Clinical Epidemiology, McGill University Health Centre, Montreal, Quebec, Canada*

[4]*Division of Allergy and Clinical Immunology, McGill University Health Centre, Montreal, Quebec, Canada*

Abstract: *Introduction*: Health resource use is believed to be significant in systemic lupus erythematosus (SLE). Yet to our knowledge there are no comparisons of hospitalization rates in SLE patients *vs.* the general population. Our objective was to provide recent estimates for hospitalization rates in a large clinical SLE cohort, stratifying by age and sex, and to compare this to the general population.

Methods: We evaluated data from SLE patients on self-reported hospitalizations (in the past year) collected through annual research visits from 1999-2011. We compared hospitalization rates of the SLE patients to the Canadian general population by calculating the standardized incidence ratio (SIR). This represents the ratio of the number of events observed in the SLE cohort to the number of events that would be expected based on Canadian general population hospitalization rates (accounting for age and sex).

Results: Over the interval studied, 433 SLE patients (401 female) provided 2,535 person-years of follow-up. There were 350 reported admissions with an incidence of 13.8 hospitalizations per 100 person-years (13.7 in females, 15.6 in males).

The overall SIR was 1.52; 95% confidence interval (CI) 1.37, 1.69. Stratified by sex, the SIR was 2.18 (95% CI 1.47, 3.11) for males and 1.48 (95% CI 1.32, 1.65) for females. However, stratifying further by age, female SLE patients aged 65 and older tended to have fewer hospitalizations than expected, based on age/sex-specific general population rates.

Conclusions: We documented high rates of hospitalization in SLE, particularly for males. The evidence suggests at least a 50% increase in hospitalization rates in the SLE cohort compared to the general population. The low number of hospitalizations in female SLE patients >65y may be due to chance (since patients aged >65y are a relatively small group), or may be biased by poor self-report or survivorship issues. This demographic thus warrants particular attention in future studies of hospitalization in SLE.

Keywords: Systemic lupus erythematosus, hospitalization, admission.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease of unknown origin that can affect any organ system, including major ones such as the renal and central nervous system. SLE is far more common in women than men, and the peak age of onset is between 15-40y [1, 2]. SLE is estimated to affect approximately 4-5 in 10,000 people in North America [1-5].

Typically, lupus patients experience disease 'flares' which are intermittent and unpredictable. Past studies have shown hospitalization is frequent in lupus patients and is often due to active SLE or infection (which is possibly potentiated by immunosuppressive drugs) [4, 6-9].

*Address correspondence to this author at the Divisions of Rheumatology and Clinical, Epidemiology, McGill University Health Centre, 687 Pine Avenue West, V-Building, V2.09, Montreal, QC, H3A 1A1, Canada;
Tel: 514-934-1934 ext. 44710; Fax: 514-934-8293;
E-mail: Sasha.bernatsky@mcgill.ca

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Hospitalizations are a major component of the total costs for care of patients with SLE [10-12]. Yet there are relatively few data (especially in Canadian patients) [13, 14], and no published comparisons of hospitalization rates in SLE patients *vs.* the general population. Our objective was to provide recent estimates for hospitalization rates in a large clinical SLE cohort and compare these rates to the general population.

MATERIALS AND METHODS

We evaluated data from SLE patients followed within the McGill University Health Centre (MUHC) Lupus Clinic registry. The registry enrolls consecutive unselected patients meeting American College of Rheumatology Criteria, with yearly follow-up visits. Information on self-reported hospitalizations (in the past year) was collected from annual research visits from 1999-2011. From 2006 onward, self-reported information was cross-referenced with computerized records of hospitalizations for our centre.

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Reasons for hospitalizations were examined and categorized into one of the following: SLE-related, infection, childbirth, surgery, trauma, cardiovascular, respiratory, gastrointestinal, neurological, or other. A primary reason was discerned if a hospitalization had multiple causes.

The hospitalization rates of the SLE patients were generated by sex, and age (less than 45y, 45y to 65y, and greater than 65y). The comparator rates (stratified by sex and equivalent age categories) came from the Canadian general population rates (from the years 1999-2011), using hospital discharge rates based on Canadian Institute for Health Information and Statistics Canada [15, 16].

SLE patients were compared to the Canadian general population by calculating the standardized incidence ratio (SIR), which represents the ratio of the number of events (hospitalizations) observed in the SLE cohort, to the number of events that would be expected based on the age and sex-specific Canadian general population hospitalization rates. Confidence intervals were generated by standard methods, assuming a Poisson distribution of the events over person-time [17].

The results are presented both summing all data across 1999-2011, as well as comparing two periods (1999-2005, and 2006-2011) to see if time trends were evident. This research was performed with the approval of the McGill University Health Centre ethics committee, and was conducted in compliance with the Helsinki Declaration.

RESULTS

From 1999-2011, 433 patients were followed at the MUHC Lupus Clinic for a total of 2,535 person-years. At the time of cohort entry, the median age of the SLE cohort was 39 years with a range from 18 to 83 years. The majority of the patients were female (93.6%) and Caucasian (65.6%), while 14.3% of patients were Asian, and 10.9% of patients were African American. A total of 330 hospitalizations were reported by 202 (46.7%) patients, with 126(29%) of these patients reporting more than one hospitalization within the time period. Cross-referencing the self-reported data from 2006-2011 with our institution's electronic hospitalization records revealed only 20 additional hospitalizations that had not been reported, bringing the total number of hospitalizations recorded in our SLE patients to 350.

Information on reasons for hospitalizations was unavailable for 11 of the 350 hospitalizations. The 339 remaining hospitalizations were categorized as follows: 87 (28.6%) SLE-related causes (eg. flare), 51 (15.0%) surgeries, 42 (12.4%) cardiovascular, 38 (11.2%) infections, 30 (8.8%) childbirths, 16 (4.7%) neurological, 14 (4.1%) gastrointestinal, 12 (3.5%) trauma, 10 (2.9%) respiratory (non-infectious), and 39 (11.5%) due to other reasons.

Over the interval studied, there was an incidence of 13.8 hospitalizations per 100 person-years (13.7 in females, 15.6 in males). In the Canadian general population, the average rate during the same time period was 8.7 hospitalizations per 100 person-years (9.9 in females, 7.4 in males). Younger SLE patients had more hospitalizations than older SLE patients (16.3 in patients aged <45y, 11.4 in patients aged 45-65y, and 10.8 in patients > 65y), while the general population had an opposite trend where older patients had a higher hospitalization rate (5.7 in patients <45y, 7.5 in patients 45-65y, and 24.1 in patients > 65y).

The over-all SIR was 1.52 (95% confidence interval, CI 1.37, 1.69). Stratified by sex, the SIR was 2.18 (95% CI 1.47, 3.11) for males and 1.48 (95% CI 1.32, 1.65) for females. However, stratifying further by age, female SLE patients aged >65y actually underwent fewer hospitalizations than expected, based on age/sex-specific general population rates (SIR 0.46; 95% CI 0.29, 0.67). In male SLE patients> 65y, there were 3 hospitalizations observed (compared to 3.44 expected events), and the 95% CI around the SIR was very imprecise in this demographic (0.0, 2.55), due to the relatively low number of older males in our cohort.

From 1999-2005, there was a total of 14.6 hospitalizations in SLE patients per 100 person-years, while this rate was 12.9 from 2006-2011. The over-all SIR from 1999-2005 was 1.58 (95% CI 1.36, 1.82),which was very similar to the SIR from 2006-2011 (SIR 1.48, 95% CI 1.26, 1.73). Stratifying these two calendar periods by age and sex, the same pattern of hospitalization rates were seen in both periods (that is, SLE patients in all age and sex groups had more hospitalizations than the general population, except in the age groups >65, where the estimate in females suggested fewer hospitalizations than expected, and the estimate in males was imprecise).

DISCUSSION

Over-all, as expected, SLE patients had significantly increased rates of hospitalizations, compared to age

and sex matched general population rates. Interestingly, the hospitalization rates in our study are lower than in a US cohort [6]; however, for that study, published in 1992, the SLE cohort likely included a substantial number of inner-city black patients (who often have poor health outcomes, both generally, and specifically for SLE). A more recent Canadian study, published in 2013 estimated hospitalization rates similar to our results [14]. However, that study only estimated hospitalization rates from 2006-2009, in a smaller group of patients (N=96), based on retrospective chart review. Our study provides more updated, prospectively collected data, across a longer interval, in a larger group of patients, allowing us to explore results according to age and sex strata. As well, ours is the first to compare the rates in the SLE sample with general population hospitalization rates.

When comparing the two time periods of 1999-2005 and 2006-2011, there was only a slight downward trend was seen in the later period. Thus, we were unable to demonstrate a definite decrease between the two. This perhaps argues for heightened efforts to maximize SLE care, in order to avoid hospitalizations which are costly and could lead to further complications (e.g. nosocomial infections). However, it bears noting that as a whole, hospitalization patterns in Canada are currently quite stable. Specifically, though the number of total hospitalizations in Canada is presently 31.4% lower than what it was in 1995, most of the decrease occurred prior to 2002. Thus it may not be surprising that we saw no dramatic decrease for hospitalizations within our SLE population, between 1999-2005 and 2006-2011.

The highpoint estimate for the SIR in male lupus patients is consistent with the well-known hypothesis that SLE in males tends to be more severe [1]. The low number of hospitalizations in female SLE patients >65y may be due to chance (since patients aged >65y are a relatively small group), or may be biased by poor self-report or survivorship issues. Regarding the latter, excess mortality risk is highest in the young and in female patients [18-20], so if those patients who were most at risk for hospitalizations (e.g. those with more damage or high co-morbidity) died before 65y, the remaining patients could reflect an SLE population with controlled or mild disease, and potentially with less co-morbidity than in women aged >65y in the general population.

The main causes of hospitalizations described in this cohort were SLE-related (e.g. due to SLE flares), surgical, cardiovascular and infectious. This is similar to what has been described in other studies on SLE hospitalizations [6, 14, 21-23].

Our data are limited in that they came from a single tertiary care centre, which may be biased towards more severe cases of SLE; some of the other published estimates may reflect this same bias. Like other studies we were unable to adjust for race/ethnicity; we note the SLE patients aged >65y did tend to be more likely Caucasian, than younger SLE patients (84.6% *vs*. 64.4%). The difference in ethnicity may account for the lower hospitalizations rates seen in this cohort's older SLE patients, as many studies suggest that non-Caucasian (Black and Asian) patients tend to have increased disease activity compared to Caucasian patients [24-29].

Our study is further limited by the reliance on patient-reported hospitalizations in the year preceding their annual visit. The self-reported information from 2006-2011 was verified in part by checking with computerized records of hospitalizations at our centre, which added only 20 out of the total 350 hospitalizations. Over-all, this suggests a tendency of SLE patients to slightly underreport admissions, so that if anything, our estimates are conservative. Specifically for our efforts to show possible time trends, this magnitude of under-reporting could have produced an estimate for 1999-2005 (when we had no means of cross-referencing with our hospital files) which was a little under-representative, compared to 2006-2011. However, we would not think the rate from 1999-2005 would have changed more than 14%.

Finally, the comparator rates were determined from Statistics Canada although they were not Quebec specific. However, for the majority of Canada, age and sex-standardized hospitalization rates are quite similar, and the Quebec hospitalization rates are well-approximated by the Canadian rates.

CONCLUSION

In conclusion, over-all, as expected, SLE patients had significantly increased rates of hospitalizations, compared to age- and sex-matched general population rates. However, female patients >65y appeared to have fewer hospitalizations than expected, a finding which could be due to chance or bias, and should be confirmed in other samples. Further work on the variables affecting hospitalizations in SLE patients is planned.

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AUTHORS' CONTRIBUTIONS

All authors contributed to the study design and/or data collection and/or data analysis and interpretation and preparation of results, and approval of the manuscript.

COMPETING INTERESTS

None.

ABBREVIATIONS

SLE = systemic lupus erythematosus

SIR = standardized incidence ratio

95% CI = 95% confidence interval

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